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Knee & Shoulder Arthroscopy And Arthroplasty ISKSAA

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ISKSAA International Society for Knowledge for Surgeons on Arthroscopy and Arthroplasty

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Aims and Scope

Journal of Arthroscopy and Joint Surgery (JAJS) is committed to bring forth scientific manuscripts in the form of original research articles, current concept reviews, meta-analyses, case reports and letters to the editor. The focus of the Journal is to present wide-ranging, multi-disciplinary perspectives on the problems of the joints that are amenable with Arthroscopy and Arthroplasty. Though Arthroscopy and Arthroplasty entail surgical procedures, the Journal shall not restrict itself to these purely surgical procedures and will also encompass pharmacological, rehabilitative and physical measures that can prevent or postpone the execution of a surgical procedure. The Journal will also publish scientific research related to tissues other than joints that would ultimately have an effect on the joint function.

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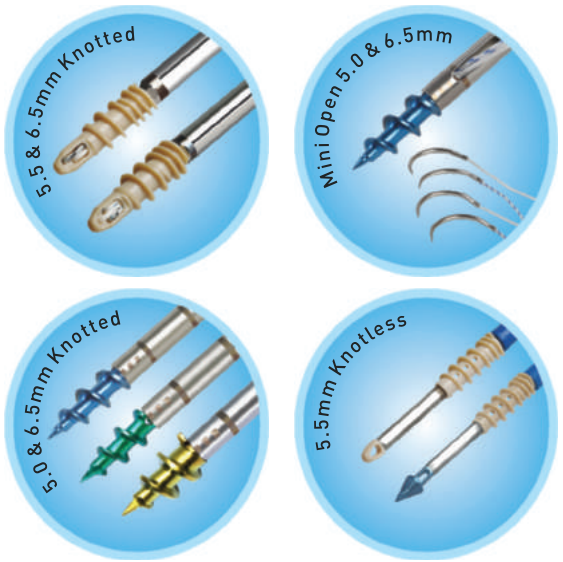

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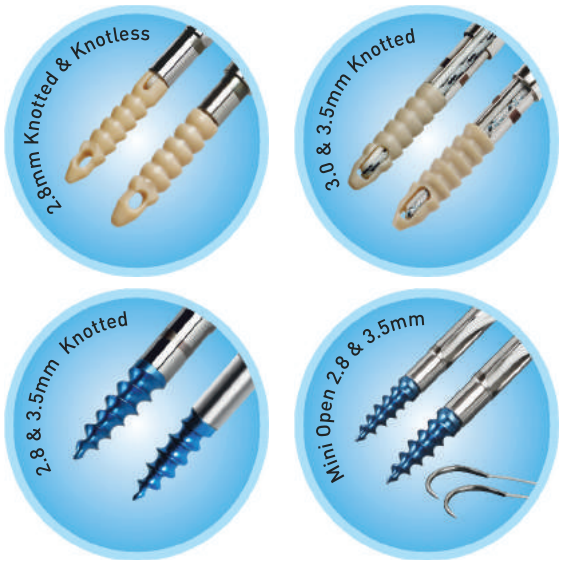

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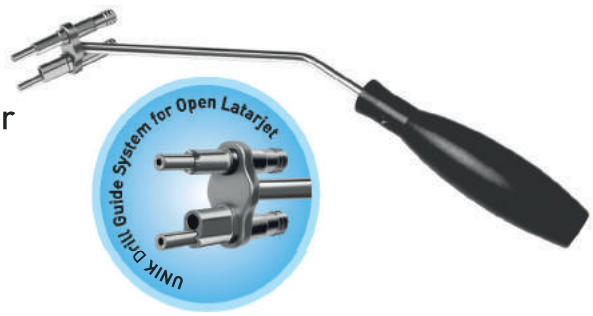

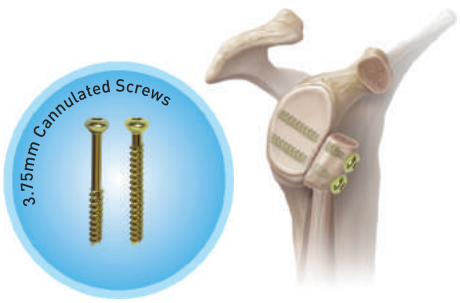

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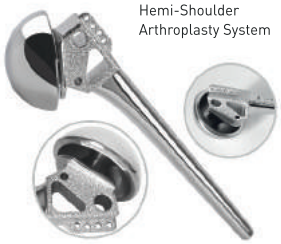

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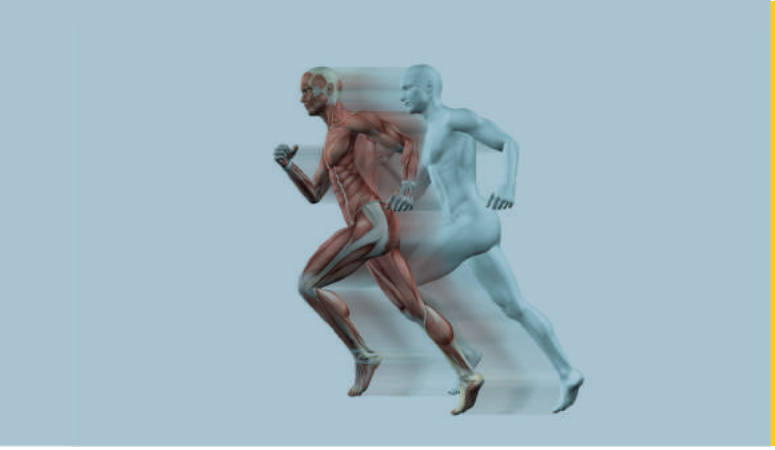

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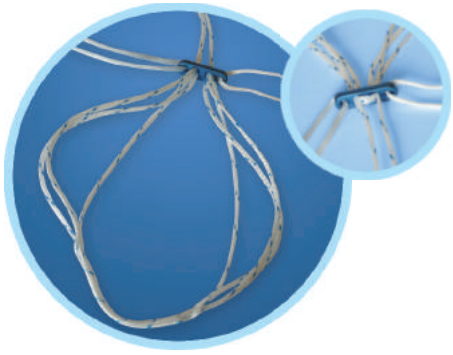

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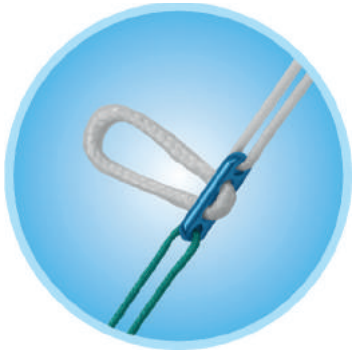

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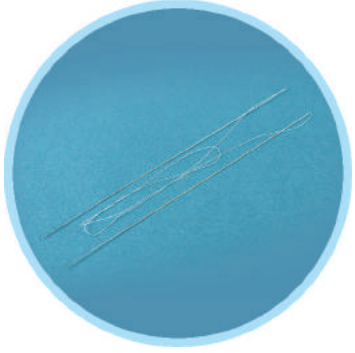

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Editorial

Doctors as soldiers in times of pandemic

Keywords:
Pandemic
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Doctors as soldiers

The medical profession has been considered a 'noble' profession and usually enjoys a high level of trust from the general public.[1] Despite this position of trust, doctors as the face of an often inadequate healthcare system, occasionally bear the brunt of attacks by patients and their families who are frustrated by the failures of the healthcare system.

With the advent of Covid-19, doctors are finding themselves in an unusual situation of being hailed as soldiers and heroes in the 'war' against the virus. With the accolades, there has been a demand and an expectation that doctors should live up to this tag. This can create an awkward position for doctors. Are they happy being the focus of this adulation, which is very likely to be temporary, whilst trying to live up to the public demands? Use of such militaristic language to describe the medical profession can be a double-edged sword. Public opinion can easily turn against its heroes. There have already been accusations that some doctors have not been turning up for work and demands have been made to force any doctors to return to work, using the 'soldier' analogy against them.[2]

Being a 'hero' involves (a) going beyond the expected duties; (b) at a personal risk to oneself; (c) with a desire to help others and (d) with no expectations of any advantage in return.[3] This is not entirely the role of a doctor even in the course of a pandemic. Doctors do have a 'duty of care' to patients but this duty is not limitless. We can be expected to take care of the patients but cannot be expected to put our own lives at risk in the care of the patients. Nobody would expect a surgeon to donate his or her kidney to save the life of a patient; similarly, without adequate personal protective equipment (PPE), we cannot expect doctors to treat highly infectious patients. Yet healthcare workers are still expected to go to work, whilst the rest of the population is asked to protect themselves by limiting any external contact.

The duty of care of a healthcare professional can best be described as a 'social contract' between the profession and society at large. By this contract, healthcare workers get a certain privilege in society and in return, they have a 'duty to treat' patients, even at a degree of risk to their personal wellbeing. The privileges bestowed by this social contract are accompanied by certain responsibilities. One of them being that doctors are held to a greater accountability and higher threshold of conduct compared to the other professions. Inherent in this social contract model, however, is a reciprocity from the society. In return for the doctor's duty to treat, society is expected to treat them with respect and to do their own part, including adherence to social distancing guidelines.[3] The use of militaristic language, portraying doctors as soldiers or heroes, takes emphasis away from the reciprocal nature of this social contract. This risk leaving healthcare workers embittered and disillusioned, as they may feel that they are alone in fulfilling their side of the mutual obligation.

Even before this pandemic, doctors have been battling systemic issues in the health economy, issues that foster unhealthy work environments, with expectations of a 24/7 availability leading to a life-work imbalance.[4] The COVID-19 pandemic has increased the demand on physicians' time, along with an increased intensity of work. Physicians must deal with concerns relating to their own and their families' wellbeing, whilst dealing with ever changing roles and expectations.

Doctors have often put others health and wellbeing over their own but now have to make a decision between protecting their family's health over treating a highly infectious patient. As more knowledge about the disease is gained, physicians have had to adapt to everchanging guidelines and to incorporate it into their practice at short notice. Many had to adapt to different work roles, with which they often found themselves uncomfortable. Alongside this, many physicians had to deal with the mental trauma of illness affecting their colleagues or family, as well as being witness to a tragedy affecting their patients by a disease where patients often are denied the support blanket of their families for reasons of infection transmission, leading to health professionals often being the sole provider of emotional comfort, whilst also managing their medical needs. Even doctors who are not on the forefront of this 'war' are still affected, for example, financially, by an almost complete absence of fee-paying patients requiring elective surgery. This is likely to lead to long-term psychological and personal effects on the medical professionals. Being called a 'hero' and applauded in public is not going to put a salve on this wound. Doctors are humans too. They are entitled to their own fears and anxieties. If public and authorities don't support them, they would not be able to carry out their important role in serving people.

Amnesty International in its July, 2020 document 'Exposed, Silenced, Attacked: Failures to protect health and essential workers during the pandemic', report that over 3000 health care workers (HCWs) have lost their lives due to COVID-19 during the current pandemic.[5] Besides physical harm, HCWs treating patients during a pandemic are at increased risk of psychological distress and post-traumatic stress, as shown a recent metaanalysis.[6] Risk factors for psychological distress included being younger, being more junior,

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being the parents of dependent children, or having an infected family member. Longer quarantine, lack of practical support, and stigma also contributed. Clear communication, access to adequate personal protection, adequate rest, and both practical and psychological support were associated with reduced morbidity.[6] Surveys of HCWs from different nations have reported high levels of anxiety, depression and insomnia during this pandemic.[7] There is an added risk of 'moral injury' where doctors have to take decision on the allocation of scarce resources to a large number of severely unwell patients. This ethical conflict adds to the psychological distress.[8]

Health care workers speaking about the working conditions have faced restrictions or reprisals. There have been reports in at least ten countries of health workers being evicted from where they live, there being attempts to evict them, them finding it hard to find a place to live or facing stigma where they reside. Amnesty International recorded instances in at least eleven countries, where health and essential workers have even been attacked or subjected to violence on the way to work, in their workplaces, as well as by their community or neighbours, and in their homes. Further, in May 2020, 13 medical and humanitarian organisations representing 30 million healthcare professionals issued a declaration condemning "over 200 incidents of COVID-19 related attacks [against health workers] – a trend that endangers these vital frontline responders and the communities they serve".[5,9] Recently, in a first case of its kind, a healthcare professional in United kingdom has been reported for a 'fitness to practice' investigation for allegedly delayed attendance to patient because of inadequate personal protective equipment.[10]

This Covid crisis has shone a light on inadequacies in health care systems in every country. Whilst doctors appreciate the clapping, it would be even better to have clarity on testing, isolation and proper availability of PPE. In the long term, it would be best to be able to work in healthcare systems which are adequately funded and where the staff is valued, both by the people and by the government. Doctors don't want short term plaudits to suit the current media narrative. They want a society where they feel confident to be able to provide best possible care for their patients, irrespective of the health care system or patients' financial situation. This is a job of the governments and for the societies which vote for these governments. Doctors and their patients deserve better !

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Review article

Diabetes and rotator cuff repair: A narrative review

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ABSTRACT

Diabetes has been postulated to be a risk factor for both rotator cuff (RC) tears and poorer functional outcomes after rotator cuff repair (RCR) surgery. The purpose of this review is to explore and better understand the role of diabetes on functional outcomes and retear rates after RCR surgery. Population based studies have shown that diabetes acts as an independent risk factor for RC tears and RCR surgery. The two prevailing hypothesis on this subject, the local and systemic hypothesis, propose that diabetes, through a variety of pathways, acts to reduce tendon quality and disrupts tendon architecture. This leads to a lower load to failure of the cuff tendons and a poorer healing response to the tear itself. Animal and lab-based studies have supported these theories. Clinical studies of RCR in diabetics have found a trend towards higher complication rate, but similar functional outcomes, when compared to non-diabetics. These trends need to be validated by studies with higher levels of evidence.

1. Introduction

Diabetes affects almost all organ systems of the human body. Studies of the musculoskeletal system have showed a decrease in skeletal mass, altered bone mineral density and impaired fracture healing in the individuals with uncontrolled diabetes.[1] Bone-to-bone healing is compromised in diabetics and the effect of sustained hyperglycaemia in bone-to-tendon healing, as in rotator cuff repairs, is becoming better understood.

The shoulder in diabetics continues to generate immense interest in both the orthopaedic and physician fraternities. Diabetes has been associated with shoulder stiffness and adhesive capsulitis,[1,2] however there is little data on its role in rotator cuff (RC) tears or outcomes after rotator cuff repair (RCR). Despite the paucity of data, surgeons continue to regard diabetics as poor healers and those with high complication rates after RCR surgery and patients are often explained the same in pre-operative counselling sessions.

The purpose of this review is to summarize the available literature on outcomes of rotator cuff surgery in individuals with diabetes, and to better understand the underlying mechanisms for diabetic rotator cuff tendons.

2. General population-based data on diabetes and RC tears

Diabetes has been postulated to be a risk factor for RC tears. Several recent population-based studies{Citation} have shown that diabetes is an independent risk factor for RC tear (Table 1). Three of these studies focus on Taiwanese Health Insurance Database and two studies focus on the Finnish Health survey population database, which introduces population bias. It is important for similar cohort studies to be conducted in all countries so that cross-country and cross-study comparisons can be made.

To better understand these population based trends, two recent systematic review and meta-analysis have found that there is low-moderate quality evidence for an association between rotator cuff related shoulder pain and type 2 DM[3] and that diabetes itself is associated with a higher risk of all tendinopathies,[4] including rotator cuff tendinopathies.

A handful of sonographic studies attempted to validate these findings. Abate et al. (2010) found that tendon thickness and degenerative features were more common in diabetics when adjusted for age. Further, they found an age independent higher rate of asymptomatic RC tears in diabetics compared to controls,

Abbreviations: AGE, Advanced glycosylation end product; ASES, American shoulder and elbow society; DM, Diabetes mellitus; MMP, matrix metalloproteinases; MRI, magnetic resonance imaging; RC, rotator cuff; RCR, rotator cuff repair; ROM, range of motion; UCLA, University of California Los Angeles; VEGF, vascular endothelial growth factor.

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Table 1
Population based studies of diabetes and rotator cuff tear epidemiology. DM = Diabetes mellitus; RC = rotator cuff; RCR = rotator cuff repair.

Authors	Year of Publication	Population studied	Key Study Findings
Rechardtetl al[3]	2010	Finnish Health Survey	Type 2 DM was associated with shoulder pain in men; and Type 1 DM was associated with chronic RC tendinopathy in men
Miranda et al[4]	2005	Finnish Health Survey	Type 2 DM associated chronic RC tendinopathy
Lin et al.[5]	2015	Taiwanese Health Insurance Database	Diabetes is an independent risk factor for development of RC disease (RC tears and tendinopathy)
Hsu and Sheu[1]	2016	Taiwanese Health Insurance Database	Patients with diabetes, regardless of insulin use, have higher risk of developing RC tears and tendinopathy
Huang et al[6]	2016	Taiwanese Health Insurance Database	Diabetes is an independent risk factor for RCR surgery (incidence of RCR surgery in diabetics vs non-diabetic cohorts: 41/100000 vs 26/100000)
Zakaria et al.[7]	2013	Western Australian postcode population	Type 2 DM higher risk of RC tears

along with more effusions in synovial bursa and more biceps tenosynovitis.[5] This suggests that diabetics have a higher prevalence of asymptomatic tears compared to controls, and that the overall condition of the cuff and associated structures is inherently worse in diabetics when compared to non-diabetic controls. However, in another sonographic study of patients being referred for sonographic examination for the diagnosis of shoulder pain aetiology, Kang et al. (2010) found no difference in the odds ratio for RC tears in diabetic versus non-diabetic patients presenting with shoulder pain.[6]

3. How diabetes impacts the rotator cuff tendon

There are two general hypotheses for how diabetes impacts tendons – the local hypothesis and the systemic hypothesis.

3.1. Local hypothesis

According to the local hypothesis, joint tissue damage in diabetes is caused by an excess of advanced glycosylation end products (AGEs) that form at a slow and constant rate accumulating over time in the normal body.[7] However, in diabetes, their formation is markedly accelerated due to the increased availability of glucose. These AGEs form covalent cross-links within collagen fibers, altering their structure and functionality.[8] This cross linking is thought to cause deterioration of the biologic and mechanical function of tendons and ligaments.[9] Further, once formed, AGEs can only be degraded if the protein they are linked to is degraded, hence the highest accumulation of AGEs is observed in tissues with net lower turnover rates such as a cartilage, bone and tendon[8] – such as the rotator cuff.

In addition to their role in accumulation and altering tissue architecture and function, AGEs act via other pathways to negatively alter tendon structure. They have been shown to upregulate proinflammatory mediators and dysfunctional cell phenotypes,[10,11] and to impair growth factor signalling and increase apoptosis.[12,13] Taken together, the AGEs deposit in the rotator cuff of individuals with diabetes at a very high rate, alter the tendon quality and structure, are resistant to degradation, and upregulate pro-inflammatory mediators to induce an apoptotic state. This would have a net effect of weakening the tendon, decreasing the load to failure, and simultaneously setting of an inflammatory cascade.

Independently, hyperglycaemia also has been shown to increase intracellular water, cellular edema and decrease the synthesis or sulfation of glycosaminoglycans.[14] The microvascular disease state induced by hyperglycaemia may contribute to tendon damage, leading to tissue hypoxia, overproduction of oxygen free radicals and a permissive apoptotic environment.[15] There is reduced neovascularization found within degenerative tendons of diabetic patients consistent with decreased levels of VEGF.[16] Thus, new blood vessel production is reduced, and existing blood vessels become diseased, with a net effect of reduced blood supply to the tendons leading to secondary hypoxia and apoptosis, weakens the tendon.

Much interest has been placed on VEGF, a glycoprotein that plays an important role in neovascularization and increased vascular permeability. VEGF levels are decreased in diabetic tendons as mentioned above, however they are increased in the subacromial bursa of patients with rotator cuff tears, a phenomenon documented by Handa et al. (2006), who studied expression in 67 patients undergoing RCR surgery.[17] This upregulation of VEGF in the subacromial bursa of patients is thought to induce synovial proliferation and subsequent motion pain. The authors concluded a correlation between VEGF expression and the clinically lower ROMs in their diabetic cohort immediately before surgery, suggesting that VEGF expression plays a role in development of shoulder stiffness in diabetics. Further work is needed to better understand the role of VEGF in both the subacromial bursa and the tendon itself in patients with RC tears.

Recently there has been interest in the role played by peroxisome proliferator-activated receptor gamma (PPAR-y) in diabetic tendinopathy, another cytokine involved in neovascularization pathway. Downregulation of PPAR-y in diabetic individuals can limit vessel and nerve ingrowth, and affect neurogenesis, which reduces pain perception.[18] Consequently, diabetic patients, with supressed pain signals, can excessively load their rotator cuff tendons, without concomitant increased pain levels, leading to tears secondary to overuse.[8]

Overall, according to the local hypothesis, local changes in cuff architecture, resulting from AGE deposition and decreased microvasculature, would ultimately lead to a weaker tendon and an increased propensity to failure. Once the failure event sets in, the lack of neoangiogenesis and the upregulation of the inflammatory cascade would have a deleterious effect on tendon healing.

3.2. Systemic hypothesis

As an alternative to the above local hypothesis, a systemic hypothesis has been proposed in the literature. This is built around the theory that diabetic patients experience increased adiposity and this adipose tissue is a powerful endocrine and signalling organ. White adipose tissue has been found to generate more than 50 adipokines, including adiponectin, chemerin and leptin19. These adipokines exert their action on tissues via endocrine, paracrine, autocrine or juxtracrine crosstalk in a wide variety of ways. White adipose tissue in obese individuals, secondary to diabetes, has 4–5

Table 2
Clinical studies on diabetes and rotator cuff repair surgery. RCR = rotator cuff repair; ASES = American shoulder and elbow society; MRI = magnetic resonance imaging; ROM = range of motion; UCLA = University of California Los Angeles.

Author and Year	Study Population and Type	Follow-up period and measures	Key Findings
Chen et al (2003)[49]	Open RCR repair; 30 diabetic patients vs 30 matched non-diabetics; case-control	Mean follow-up period = 34 months; American Shoulder and Elbow Society (ASES) score	Similar functional outcomes in diabetics vs non-diabetics; 6 times higher complication rate and more infection in diabetics
Kim et al (2018)[50]	180 patient retrospective cohort study; medium and large tears only; Arthroscopic RCR	2 year follow-up; MRI	Rate of retear higher in diabetics, confirmed on multi-variate analysis model
Dhar et al (2013)[51]	Retrospective review 56 diabetics vs 67 non-diabetics, Arthroscopic RCR	1 year follow-up, ROM, ASES and Penn Shoulder Score (PSS)	Patients with diabetes had reduced forward elevation, abduction and external rotation; no difference in retear or complication rate between both groups
Clement et al (2010)[52]	Retrospective case-control study; 32 diabetics vs 32 matched non-diabetics; Arthroscopic RCR	1 year follow-up; ROM and Constant score	No significant differences in constant scores between both groups; diabetics had less forward elevation and external rotation
Berglund et al (2018)[53]	Prospective cohort study; 627 patients (diabetics and non-diabetics); Arthroscopic RCR	1 year follow-up; ASES score and pain score	Diabetics had worse pain and functional outcomes at 6 months and 1 year post-surgery; earlier recovery plateau observed in diabetics around 6 months post-surgery
Blonna et al (2017)[54]	Prospective cohort study; 65 patients; Arthroscopic RCR	6 month follow-up; ROM	Diabetes associated with moderate stiffness post surgery; reduced ROMs in diabetics
Cho et al (2015)[55]	Retrospective cohort study; 335 shoulders (271 non-diabetics vs 64 diabetics); Arthroscopic RCR	6 months follow-up; MRI, ROM, Constant score and University of California at Los Angeles (UCLA) score	2.5 times higher retear in diabetics; no difference in functional outcomes, pain or ROM
Le et al (2014)[56]	Retrospective cohort study; 1000 patients; Arthroscopic RCR	6 months follow-up; ultrasound	No difference in retear rates between diabetics and non-diabetics
Huberty et al (2009)[57]	Retrospective cohort study; 489 patients; Arthroscopic RCR	8 months mean follow-up; ROM	No difference in post-operative stiffness between diabetics and non-diabetics
Borton et al (2020)[58]	Retrospective review; 462 patients; Arthroscopic RCR	Mean follow-up 5.6 years; complication rate profiling	Diabetic patients have 2 times higher risk of complications compared to non-diabetics; 2 times higher risk of infection and 4 times higher risk of post-operative stiffness

fold higher macrophage concentration than in lean individuals.[20] The inflammatory mediators such as IL-6 and TNF-a produced by adipocytes recruit more macrophages which in turn release more inflammatory mediators, setting off a vicious cycle of a pro-inflammatory cascade and establishing a systemic state of chronic, sub-clinical, low grade inflammation which may act as a prolonged disruptor of tendon haemostasis.[21,22] Further, the migration of immune cells into adipose tissue decreases the circulating levels of such cells and, as a result, the release of probiotic factors, such as tissue growth factor-B, is reduced, which may have a detrimental effect on tendon healing.[23]

Recent work has focused on the role of adipokines in tendon disorders. These adipokines can modulate cytokines and prostanoids, as well as production of MMPs,[24] which lead to local tissue damage. Most of the studies of adipokines in the field of orthopaedic surgery have focused on their role in cartilage destruction and knee arthritis, with a severe lack of studies on tendon disorders. Most of our knowledge of their possible effects on tendons are inferential from these cartilage-based studies.

Leptin has been found to be a powerful pro-inflammatory cytokines, upregulated in patients with osteoarthritis, and though to exert its cartilage destructive capabilities through the upregulation of matrix metalloproteinases (MMPs).[25,26] Adiponectin is a powerful stimulator of the immune system and stimulates chondrocytes to release IL6 and various MMPs.[27,28] Resistin and visfatin, pro-inflammatory cytokines, have been linked to inflammatory degradation of joint cartilage.[29] However, through the activation of TGF-B, they may also exert an anti-inflammatory effect on tissues.[30] A newer generation of adipokines in the form of chemerin, lipocalcin 2 and serum amyloid A3 are also been shown to influence chondrocyte pathophysiologyand are now being actively studied for their role in skeletal disorders[31] A recent study looking at the role of adipokines in upper extremity soft tissue disorders such as rotator cuff tendinitis, found that higher levels of resistin and visfatin were associated with better recovery whereas higher levels of leptin inhibited recovery from these disorders.[32]

Overall, according to the systemic hypothesis, the high adiposity state induced by diabetes acts as a powerful endocrine organ to stimulate both recruitment of macrophages and release of adipokines, in effect setting up a chronic pro-inflammatory state in the body. This pro-inflammatory state, when combined with the systemic actions of adipokines, leads to a vicious cycle with local tissue damage and weakening of tendon architecture.

4. Animal and lab studies of diabetic tendons

Histological studies have showed that diabetic tendons suffer from a loss of tissue viscoelasticity,[33] less fibrocartilage and organized collagen network and an increased AGE deposition at the bone-tendon interface.[34] Diabetic collagen fibres are poorly organized and larger than normal and show higher degrees of polymerization because of increased intra- and inter-molecular interactions.[35,36] Additionally, diseased tendons in patients with diabetes have less amount of fibroblast proliferation and lymphocyte infiltration.[35]

Biomechanically, these changes both thicken and weaken the tendon[37] and reduce the Young's modulus of elasticity,[38] leading to a decreased load to failure.[39,40]

5. Diabetes and rotator cuff repair (RCR) surgery

5.1. Animal and lab studies

Although many studies have examined the role of diabetes on animal tendons in general, only a handful of studies exist that have studied the rotator cuff specifically. Bedi et al. (2010) studied

tendon healing characteristics after RCR surgery in diabetic rats compared with non-diabetic rats. In the diabetic group, there was less fibrocartilage and organized collagen, and increased AGE deposition at the tendon-bone interface. Further, the healing junction had reduced ultimate load to failure compared to non-diabetic controls.[41] Thus the structure of the cuff tendon is weakened with a less anatomic healing response leading to a higher risk for rupture.

Additionally, the pro-inflammatory state of diabetic rotator cuff tendons may further weaken the tendon through the expression of lysing proteases which distort tissue architecture. An over expression of MMP-9 and IL-6 in diabetic rotator cuff, when compared to non-diabetic tendons, was demonstrated in diabetic cuff tendons undergoing RCR surgery.[42] Hyperglycaemic rat shoulder tendons have been shown to exhibit significantly increased IL-1B and AGE staining localized to the insertion and mid-substance of the tendon, and TNF-a levels increased in the superior capsule but not tendon proper.[43] In their study of IL 1B levels in the subacromial fluid of diabetic patients versus controls, Siu et al. (2013) found that diabetic patients with RC tears had higher IL-1B levels in the subacromial fluid compared to controls, and that these higher levels were correlated with poorer functional and pain scores in this cohort.[44]

These changes reflect a pro-inflammatory state of the tendon in diabetes which ultimately affects both tendon architecture and tendon healing properties, leading to higher failure rates and poorer outcomes. The role of inflammatory mediators in influencing functional outcomes after RCR is of great importance, considering the volume of data supporting the role of inflammatory mediators and their impact on tendon architecture (as mentioned above). However, there is a paucity of data on their role in rotator cuff tears specifically. This avenue of research needs to be better understood and may provide a pathway for immunomodulators given to diabetic RCR patients for promoting better functional outcomes.

5.2. Clinical studies

It has been postulated that diabetic patients do poorly after RCR surgery, either due to shoulder stiffness or tendon retear. A few studies have endeavoured to better understand this dictum (Table 2).

There is a general trend towards higher complication rates, especially retear rates and infections, and reduced post-operative range of motion parameters in diabetics. Despite this, functional outcomes appear to be similar between diabetics and non-diabetics after RCR surgery. Further prospective studies and randomized controlled trials are needed to be better understand and validate these trends.

When post-operative stiffness does occur in diabetics, it appears that arthroscopic capsular release is the procedure of choice with excellent functional outcomes post-release for shoulder stiffness.[45] Park et al. (2014) found that in diabetic patients with shoulder stiffness post RCR, capsular release combined with manipulation had better clinical and functional outcomes compared to manipulation alone.[46]

There is a renewed interest in the role of adequate glycaemic control during the peri-operative period and its effect on functional outcomes after RCR surgery in diabetics. Cho et al. found that when adjusted for glycaemic control according to HbA1c levels; those with poor glycaemic control (HbA1c > 7%) have a 2.5 times higher retear rate than those with good glycaemic control.[47] In their study of 264 patients, Miyatake et al. (2018) found that in diabetic patients with good peri-operative glycaemic control have no difference in functional and structural outcomes, including retear rates, after ARCR.[48] The role of adequate glycaemic control during the peri-operative period in reducing retear rates and improving functional outcomes needs to be further explored to provide an avenue for safe surgical management of diabetic RCR patients.

6. Conclusion

Diabetes acts as an independent risk factor for both rotator cuff tears and rotator cuff repair surgery. The current prevailing hypotheses on this topic postulate that diabetes weakens the cuff architecture, reducing the load to failure, and decreases the tendon healing ability. These findings have been supported by animal and lab-based studies, however there is a paucity of such studies for rotator cuff tendons specifically. Clinical studies of diabetics undergoing rotator cuff repair have found higher complication rates, including retear rates, but similar functional outcomes to non-diabetics. These trends need to be validated by studies with higher evidence levels. Further research needs to focus on the role of adipokines and growth factors in rotator cuff repair healing and a better understanding of the influence of good peri-operative glycaemic control on functional outcomes and complication rates.

Declaration of competing interest

The authors have no conflict of interest or potential conflict of interest with regards to this study.

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Research paper

Mortality and other complications after revision joint arthroplasty: Investigating the modifiable independent predictors

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ABSTRACT

Objective: The aim of this study was to determine the mortality rate and other complications after revision total joint arthroplasites (TJAs) during the first year of follow-up and to identify the patient-related risk factors predicting mortality, major and minor complications and prolonged hospital stay.
Methods: The hospital's database program was used to identify patients who had undergone revision hip arthroplasty (114 patients) or revision knee arthroplasty (87 patients) between the years 2013 and 2018. Patients' demographics and perioperative data were collected.Relationships between the perioperative factors and the outcomes were tested using univariable analysis. Significant variables were analyzed using a multivariate logistic regression model.
Results: The mortality rates during the first year of follow-up of RHA and RKA patients were 7% and 3.3%, respectively ($p = 0.356$). The rates of major complications in RHA and RKA patients were 13.2% and 6.9% ($p = 0.150$) and the rates of minor complications were 14.9% and 11.5%, respectively ($p = 0.481$). The mean length of hospital stay was 9.8 ± 11.8 days for RHA patients and 8.3 ± 10 days for RKA patients ($p = 0.002$). Being over the age of 80, having undergone septic revisions and having an ASA score greater than 2 were independent risk factors for mortality and major complications during the first year of follow-up. Blood transfusion, a BMI greater than 30 and re-revision surgery were independent predictors for minor complications and prolonged length of stay at the hospital.
Conclusion: Being over the age of 80, having undergone septic revisions and having an ASA score greater than 2 were independent risk factors for mortality and major complications during the first year of follow-up. Blood replacement, a BMI greater than 30 and re-revision surgery were independent predictors for minor complications and prolonged length of stay at the hospital. Blood transfusion is the important modifiable independent predictor for complications and prolonged hospital stay after revision TJAs.

1. Introduction

The rapid increase in the number of primary joint arthroplasty in the last decade causes the number of revision joint arthroplasty to increase gradually. In a future projection study conducted in the United States, it is predicted that between 2005 and 2030, primary total hip arthroplastics will increase by 174% and primary total knee arthroplasties by 673%. In the same study, it was shown that the number of revision hip arthroplasty will increase by 137% and revision knee arthroplasty by 601%.[1,2]

Revision arthroplasties have a relatively high rate of mortality and major complications. In a regional United States study, analyzed 4953 primary total hip arthoplasty(THA), 10,163 primary total knee arthroplasty(TKA), 496 revision hip arthoplasty (RHA) and 606 revision knee arthoplasty (RKA), show that one year mortality rates are 1,1% for THA, 0,9% for TKA, 2,2% for RHA, 4,3 for RKA %.[3]

Choi et al.[4] reported that mortality rates after revision hip arthroplasty were 33% in the septic group and 22% in the aseptic group during their 5–6 years of follow-up. In another study Choi and Bedair,[5] the authors reported that mortality rates after revision

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knee arthroplasty were 18% in the septic group and 3% in the aseptic group after four years of follow-up. Badarudeen et al.[6] showed that mortality rates after RHA was 2,2% in 3555 patients during their 1 year of follow-up. Yao et al.[7] reported that 10 years mortality rates after RKA were 47% in the septic group, 46% in the fracture group, 34% in the aseptic loosening group.

Considering that revision arthroplasty numbers are increasing rapidly and mortality and complications are common, approved metrics are needed for risk classification in this patient population to potentially alleviate these events.[8] Determination of predictors on mortality, complications and length of hospital stay after revision TJAs can provide medical optimization by making better preoperative preparation. It may also provide patients to be better informed on the basis of evidence and reduce the cost.[9]

The aim of this study was to determine the mortality rate and other complications after revision total joint arthroplasites (TJAs) during the first year of follow-up and to identify the patient-related risk factors predicting mortality, complications and prolonged hospital stay.

2. Materials and methods

2.1. Data collection

An analysis of the hospital software program database between 2013 and 2019 was performed. Social Security Institution Healthcare Practice Communique codes were used to identify all patients who had revision hip or knee arthroplasties for all causes. Analysis results identified 201 patients. All patients were included in the study because the data of all patients were available.

A variety of demographics and preoperative characteristics including age, sex, the American Society of Anesthesiologists (ASA) score, septic or aseptic revision, body mass index (BMI), anesthesia technique (general or regional), diabetes, hypertension, smoking, chronic obstructive pulmonary disease (COPD), congestive heart failure, chronic renal disease, neurologic disease, ejection fraction (EF), preoperative hemoglobin level, perioperative variables such as blood replacement, duration of surgery, vasoactive drug use, stay at intensive care, complications and length of hospital stay were collected. The Central Population Administration System (CPAS) was used to identify all patients who died within the first postoperative year.

Patients having at least one of the following major or minor complications were divided into two groups.[10,11] Major, life-threatening complications included pulmonary embolism, cardiac arrest, myocardial infarction, unplanned intubation, sepsis, acute renal failure, cerebrovascular accident and death. Minor, not acutely life-threatening complications included urinary tract infection, deep vein thrombosis, pneumonia, peripheral nerve injury, wound infection.

Age, ASA score, BMI, EF and preoperative hemoglobin values were grouped under two sections; 80>/<80, 1–2/3-4, >30/<30, <60/>60, >10/<10, respectively. Preoperative anemia was defined as a hematocrit level less than 35%, based on the definitions from the World Health Organization.[12]

2.2. Statistical analysis

Continuous variables were reported as mean ± standard deviation (SD) while categorical variables were reported in percentages. Differences between the groups were evaluated using the *t*-test for continuous data and Fisher's exact test for categorical variables.

A bivariate analysis was first performed to identify the potential predictors and confounders. Variables with $p < 0.2$ were taken as multivariate analysis candidate variables. The variables that were taken as candidate variables were tested with the backward elimination (Wald) method and the final logistic regression model was used. The value of the log likelihood was minimized, the Hosmer-Lemeshow test value for goodness of fit was $p > 0.05$ and the correct classification ratio was the highest.

The independent effect of each predictor was reported using odds ratios (ORs) and 95% confidence intervals (CIs). P values less than 0.05 were considered statistically significant. All statistical analyses were performed using the SPSS v.24.0 Trial Version (IBM Inc., Armonk, NY, USA).

3. Results

A total of 201 patients were included in the study. Those who had undergone RHA accounted for 56.7% (114) of the patients (septic:20.2% (23); aseptic: 79.8% (91)), while the remaining 43.3% (87) had undergone RKA (septic: 33.3%(29), aseptic: 66.7% (58)) (Table 1). The mortality rate during the first year of follow up was 3.3% (3/91) in the aseptic hip group, 21.7% (5/23) in the septic hip group, 1.7% (1/58) in the aseptic knee group and 6.9% (2/29) in the septic knee group (Table 1).

Preoperative demographics and characteristics of patients were statistically analyzed (Table 2). There was no statistically significant difference other than BMI and neurological disease. While BMI was higher in the knee group, neurological diseases were higher in the hip group.

. Bivariate analysis (Table 3) showed that age >80, anesthesia technique (general), ASA score >2, septic revisions, smoking, COPD, congestive heart failure, ejection fraction <60%, blood replacement, vasoactive drug use, postoperative intensive care and hospital stay were predictors for mortality during the first year of follow-up. Age >80, an ASA score >2, re-revision surgery, hypertension, septic revisions, smoking, COPD, congestive heart failure, ejection fraction <60%, blood replacement, vasoactive drug use, postoperative intensive care and hospital stay were predictors for major complications. An ASA score >2, a BMI >30, septic revisions, re-revision surgeries, COPD, congestive heart failure, blood replacement and postoperative hospital stay were predictors for minor complications. An ASA score >2, re-revision surgeries, BMI >30, COPD, congestive heart failure, a preoperative hemoglobin level <10 g/dL, ejection fraction <60%, blood replacement and major and minor complications were predictors for prolonged length of stay hospital.

Multivariate analysis (Table 4) showed that age >80, septic revisions and an ASA score >2 were independent predictors for mortality of revision TJAs during the first year of follow-up. Age >80, an ASA score >2 and septic revisions were independent predictors for major complications, blood transfusion, a BMI >30 and re-revision surgeries were independent predictors for minor complications after revision TJAs. Blood transfusion, re-revision surgeries, a BMI >30 and an ASA score >2 were independent predictors for prolonged hospital stay after revision TJAs. Multivariable analysis showed that blood transfusion is the important modifiable independent predictor for minor complications and prolonged hospital stay after revision TJAs.

4. Discussion

The data from the US National Hospital Discharge Survey shows that the total number of revision procedures almost doubled for revision hip arthroplasties and tripled for revision knee arthroplasties from 1990 to 2002.[1] Patients who underwent revision arthroplasty are more prone to complications, of which periprosthetic joint infection and mortality are the most devastating.[13,14] Compared with other surgical procedures the in-hospital

Table 1
Distribution of arthroplasty surgeries based on cause and location, mortality rates during the first year follow-up.

	Hip		Knee		Total	
	Number of cases	Mortality	Number of cases	Mortality	Number of cases	Mortality
Aseptic	91	3 (3.3%)	58	1 (1.7%)	149	4 (2.7%)
Septic	23	5 (21.7%)	29	2 (6.9%)	52	7 (13.5%)
Total	114	8 (7%)	87	3 (3.4%)	201	11 (5.5%)

Table 2
Demographics and preoperative characteristics of the patients.

	Hip (n = 114)	Knee (n = 87)	p*
Age (age range)	66 (26–87)	67 (27–85)	0.393
Gender (female/male)	75/39	65/22	0.173
ASA score			
1–2	98	82	0.057
> 2	16	5	
Ejection fraction <60	5	2	0.701
Hemoglobin level <10	10	2	0.128
Hematocrit level <%35	8	2	0.192
BMI >30	24	38	**0.001**
Diabetes	29	24	0.732
Hypertension	66	61	0.075
Smoking	12	8	0.755
Chronic obstructive pulmonary disease	5	5	0.749
Congestive heart failure	6	2	0.470
Chronic renal disease	7	3	0.519
Neurologic disease	13	3	**0.039**
Anesthesia technique			
Regional	73	70	**0.011**
General	41	17	
Duration of surgery (hours)	3.5^{2-7}	3^{2-6}	0.059
Blood replacement (units)	3 (0–14)	2 (0–8)	< **0.001**

*Significant p values are written in bold.

Table 3
Bivariate analyses.

	Mortality at 1 year	Major complication	Minor complication	Length of hospital stay
Age (years)	**0.02**	**0.002**	0.495	0.333
Gender	0.314	0.188	0.417	0.424
Knee/Hip	0.356	0.150	0.481	**0.002**
Septic/Aseptic	**0.008**	**0.016**	< **0.001**	**0.001**
Re-revision	0.115	**0.019**	**0.001**	< **0.001**
BMI (>30/<30)	1.00	0.216	**0.003**	**0.037**
Anesthesia technique (Regional/General)	**0.036**	0.119	0.414	0.37
ASA score (1–2/>2)	< **0.001**	< **0.001**	**0.002**	< **0.001**
Diabetes	0.485	0.444	0.377	**0.054**
Hypertension	0.058	**0.024**	0.207	0.063
Smoking	**0.002**	**0.009**	0.319	0.574
Chronic obstructive pulmonary disease	< **0.001**	< **0.001**	**0.031**	**0.02**
Congestive heart failure	< **0.001**	**0.039**	**0.013**	< **0.001**
Chronic renal disease (cr > 1.6 mg/dL)	0.096	0.281	1.000	0.166
Neurologic disease	0.214	0.225	0.456	0.194
Ejection fraction (>60/<60)	**0.001**	**0.026**	0.239	**0.03**
Preoperative hemoglobin level (>10/<10)	0.530	0.631	0.390	**0.015**
Preoperative hematocrit level (>30/<30)	0.438	1.00	0.627	**0.019**
Blood replacement	**0.004**	**0.002**	< **0.001**	< **0.001**
Duration of surgery	0.257	0.987	0.439	**0.071**
Vasoactive drug use	**0.001**	**0.001**	0.105	**0.016**
Postoperative intensive care	< **0.001**	< **0.001**	**0.026**	< **0.001**
Major complications	< **0.001**	-	< **0.001**	**0.03**
Minor complications	**0.008**	< **0.001**	-	< **0.001**
Postoperative hospital stay	**0.002**	**0.03**	< **0.001**	-

*Significant p values are written in bold.

mortality rate of septic revision THA was higher than for interventional coronary procedure, cholecystectomy, kidney transplant and carotid surgery.[15] The primary purpose of this study was to evaluate mortality and major complications after revision TJAs and identify the independent risk factors. The secondary objective in this study was to identify the independent risk factors contributing to minor complications and prolonged hospital stay after TJAs. A patient's comorbidity is a renowned risk factor which is associated

Table 4
Multivariate analysis for 1- year mortality, major complications, minor complications and length stay hospital.

	Independent predictors OR (95% CI)			
Mortality at 1-year	Age (>80)	ASA score (>2)	Septic	–
	7,009 (1,07–45,73)	3,948 (0,91–18,56)	5,798 (1,06–31,64)	
Major complication	Age (>80)	ASA score (>2)	Septic	–
	4,592 (1,30–16,12)	10,16 (3,31-31,17)	2,66 (0,92–7,73)	
Minor complication	Blood replacement	BMI (>30)	Re-revision	–
	1,36 (1,14–1,62)	3,39 (1,36–8,44)	1,94 (1,10–3,41)	
Length of stay hospital	Blood replacement	BMI (>30)	Re-revision	ASA score (>2)
	1,30 (0,72–1,89)	2,41 (0,43–5,25)	2,31 (0,31–4,31)	11,21 (6,69–15,73)

with an increased complication and mortality rate after revision arthroplasties and thus may be used as a predictor for mortality.[9] In our study, we used the ASA score; an ASA score of 3–4 was a predictor of mortality after revision surgery for septic and aseptic reasons.

In our study the mortality rate during the first year of follow up was %3.3 in the aseptic hip group, 21.7% in the septic hip group, 1.7% in the aseptic knee group and 6.9% in the septic knee group. Age >80, septic revisions and an ASA score >2 were independent predictors for mortality of revision TJAs during the first year of follow-up. Blood transfusion is the important modifiable independent predictor for minor complications and prolonged hospital stay after revision TJAs.

Choi et al.[5] reported that mortality rates after revision hip arthroplasty were 33% in the septic group and 22% in the aseptic group during their 5–6 years of follow-up. In another study Choi and Bedair,[6] the authors reported that mortality rates after revision knee arthroplasty were 18% in the septic group and 3% in the aseptic group after 4 years of follow-up. The mortality rates in our study are lower than those studies, but the follow-up periods of these studies are 4–6 years. Long follow-up periods explain high mortality rates. Choi et al.[4,5] reported a higher mortality rate in the septic group compared to the aseptic group. This finding is agreement with our results. In our study, septic revision was identified an independent factor for mortality after revision arthroplasty.

Liodakis et al.[16] analyzed 2643 aseptic RHA and 2445 aseptic RKA cases between 2011 and 2012 using the US national database. 30-day mortality rates were reported 1% for aseptic revision THAs and 0,1% for aseptic revision TKA. The mortality rates in our study were higher than this study. The long follow-up period and the small number of patients may have caused this difference. Liodakis et al. also reported that low preoperative hematocrit was modifiable independent predictor for all complications and prolonged hospital stay. This finding is in agreement with our result. In our study blood transfusion was determined as the important modifiable independent predictor for minor complications and prolonged hospital stay.

In another study by Lindberg-Larsen et al.,[17] 1490 aseptic hip revision patients were analyzed and 90-day mortality rate was determined as 1.4%. In our study 1 -year mortality rate for aseptic hip group is 3,3%. These results are also compatible. In the study of Badarudeen et al.,[18] 3555 patients who underwent revision THAs were analyzed and a 1-year mortality rate was determined as 2.11%. The mortality rates in our study were higher than this study. In our study, 20.2% of the revision THAs constitute septic group. In the study of Badarudeen et al., 11,3% of revision THAs constitue septic group. The fact that our septic revision THA rate is high increases our mortality rate.

Parvizi et al.[19] reported that octogenarians had a mortality rate of 58.8% after a mean of 5.3 years following revision hip arthroplasty. Increasing age was identified as a risk factor of long term mortality for revision arthroplasty in our study. Parvizi et al. also reported that the mortality rate for the patients with an ASA score of 3 or 4 was higher than that for patients with lower scores. In our study, ASA score 3 or 4 also was identified as a predictive factor of mortality.

A. Shahi et al.[15] analyzed 173,591 patients who undergoing revision TJA in their study. They showed that the in-hospital mortality rate for septic TJA was higher than aseptic revision TJA. They also showed that increasing age was risk factor for in-hospital mortality. Gundtoft et al.[20] reported that the adjusted relative mortality risk was 1,87 for septic revision compared with aseptic revision. Zmistowski et al.[21] showed that mortality was significantly greater in patients with septic revision compared with those undergoing aseptic revision. These findings are in agreement with our results.

In present times, tranexamic acid is widely used in arthroplasty cases to reduce bleeding and the need for replacement. In our clinic, we routinely use intravenous tranexmaic acid in primary and revision arthroplasty cases in the absence of contraindications. Intravenous tranexamic acid was used in all patients in our study. In our study, 14 units of erythrocyte transfusion were performed for one patient. We have seen that this is caused by postoperative gastrointestinal bleeding. Blood transfusion was not performed in a total of four patients. When we examined the records of these patients, we found that all of the patients' preoperative hemoglobin values were over 13 g/dL and all of them were aseptic revision.

This study had two strengths. First, all our patients were treated by same surgeon and same center. Thus, it was possible to access the right and detailed clinical data. Second, we succeeded in identifying distinct risk factors that may in complications and mortality following revision arthroplasty. ASA score, septic background and increasing age are important factors predictive of outcome. These findings are in agreement with previous studies. The bivariate analysis also showed smoking, COPD, congestive heart failure, ejection fraction <60%, blood transfusion, vasoactive drug use, postoperative intensive care and hospital stay were predictors for mortality during the first year of follow-up.

This study had certain limitations. It was retrospective and number of patients were limited. Another limitation was that the revision surgery was not separated. We didn't separate revision surgeries; partial, total, debridement, Girdlestone, first or second stage surgery. We just did not accept debridements as a revision. Despite the above-mentioned limitations, the findings of this study are useful for medical optimization before revision arthroplasty.

5. Conclusion

Revision arthroplasties have a relatively high rate of mortality and major complications. If we had the ability to predict which patients would have postoperative complications, we could decrease the mortality and complication rates. In addition, we could inform the patients about the evidence-based risks of revision TJAs. For this reason, preoperative examination and

preparation should be performed carefully and revision surgeries should be performed in centers experienced in critical care.[22] Preoperative anemia and blood replacement are the important modifiable independent predictors for both complications and prolonged hospital stay following revision TJAs. A multidisciplinary approach is important in decreasing the mortality and complication rate. Further studies are required to analyze the effects of predictive factors on the patient outcome.

Credit author statement

Mustafa Kavak : InvestigatioN , Methodology, Writing - Original Draft, Kerem Başarır: Conceptualization, Methodology, Sancar Alp Ovalı: Investigation, Formal analysis, Anar Keremov: Writing-Reviewing and Editing.

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Research paper

The effect of bio psychosocial model of rehabilitation on pain and quality of life after total knee replacement: A randomized controlled trial

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ABSTRACT

Background: Osteoarthritis (OA) is one of the most prevalent joint disorder and its prevalence in people aged over 65 years is 33.6%. After total knee replacement, 10%–34% of patients report persistent long term pain because of central and peripheral sensitization. A recent systematic review provided moderate-level evidence that for chronic post-surgical pain in case of TKR, pain catastrophizing can be used as an independent predictor. There is paucity of literature on bio psychosocial model based rehabilitation on TKR.

Methods: Subjects were randomized into two groups, experimental group received biopsychosocial model based rehabilitation (pain coping skill training). Control group received standard protocol post-TKR for the facilities in research setting. Primary outcome measure used was pain catastrophizing scale (PCS) and secondary outcome measures were SF-36 and Timed up and go test (TUG). Subjects were assessed for outcomes before the surgery and after 4 weeks of intervention.

Results: Total 30 subjects were enrolled out of which 12 subjects in the experimental group and 11 subjects in the control group were analysed. Between group analysis showed statistical significance in PCS total ($p = 0.0001$). SF- 36 PCS component showed statistical significance ($p = 0.0001$). SF-36 MCS component and TUG did not show statistical significance between the groups.

Conclusion: Bio psychosocial model based rehabilitation involving pain coping skill training reduces pain catastrophizing after total knee replacement surgery. Biopsychosocial model based rehabilitation was found to be effective in improving pain, quality of life and function post TKR.

1. Introduction

Osteoarthritis (OA) is one of the most prevalent joint disorder with characteristic structural changes of progressive loss of articular cartilage, development of subchondral bone cysts and formation of osteophytes.[1] OA affects 240 million people globally. The prevalence of OA increases with age and for those aged 65 years and over the prevalence was 33.6%.[2] The conservative management of knee OA includes various pharmacological and non-pharmacological interventions. Recent Cochrane review suggest that amongst various physical therapy intervention like strengthening, low-impact aerobic exercises, neuromuscular education; there is highly reliable evidence which suggests that land based therapeutic exercises are beneficial in reducing knee pain and improving physical function.[3] When conservative treatment fails to relieve symptoms, total knee replacement (TKR) is a surgical procedure most commonly performed to alleviate pain and improve function in individuals with end-stage OA.[4] The average and median rate of primary and revision total knee replacement was 175 and 149 procedures/100,000 population globally.[5]

Following TKR 10%–34% of patients after total knee replacement report long term pain after 12 months of surgery.[7] Moderate pain is experienced by subjects after total knee replacement.[8] A study on patients' expectation after total knee replacement revealed that

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relief from pain was ranked the highest among all expectations followed by psychological well-being and then participation in social activities.[11] While analysing the sample of patients' from U.S, it is found that a large number of patients who had strong emotional health, shown notable improvement in post-surgical functional capacity in case of total knee replacement, almost 33% of patients who had poor preoperative emotional health shown less improvement in functional capacity.[12] Study has revealed that psychological factors play a significant role in recovery from surgery and functional outcome and it may be considered for TKR patients.[13]

There is central and peripheral sensitization to pain that leads to increased rate of persistent pain after TKR.[6] A recent systematic review provided moderate-level evidence that pain catastrophizing can independently be used to predict the chronic pain post-TKR.[9] Study on pre-operative mental well-being and the outcome of knee replacement revealed that pre-operative mental component score on SF12 has a significant effect on the outcome of the surgery.[10]

The traditional biomedical model of disease explains patient's illness is the result of physiological or anatomical cause. The emphasis of biomedical model is on the patient's body. The limitation of this model is that the factors such as environmental, social, behavioural and psychological aspects of patient's ailments are not considered.[14] Also its dualistic viewpoint conceived that body and mind are functioning independently and separately. The biopsychosocial model focuses on disease and illness, with illness considered as complex interaction of social, biological and psychological factors.[15] This model takes into account social, biological and psychological factors & their dynamic interaction throughout the course of disease.[16] Biopsychosocial approaches include behavioural treatment, cognitive behaviour therapy, group education, coping skill training.[17] A systematic review on multidisciplinary biopsychosocial rehabilitation for sub-acute low back pain documented that there is moderate evidence of positive effectiveness of this approach.[18]

Coping skill training on patients with osteoarthritis and musculoskeletal disorders has been proven effective but there is lack of literature on its implication on patients with total knee replacement.[19] Psychological factors needs to be addressed during postsurgical rehabilitation in case of total knee replacement.[16] A study on pain coping skill training for patients with elevated pain catastrophizing who are scheduled for knee arthroplasty has shown preliminary evidence suggesting that the training may be highly efficient for reducing pain, catastrophizing and disability.[20] A review showed that biology, psychology, culture and environment (complex interface of biopsychosocial cultural factors) contribute to ethnic group differences in pain responses.[21]

Postoperative outcomes may be improved by means of Interventions which specifically target pain associated with psychological risk factors.[22] Biomedical, psychosocial factors, beliefs and perception of condition in a social context influence postsurgical adjustment to chronic pain in case of TKR. Biopsychosocial framework may be utilized to improve patient care.[23] Bio psychosocial model of rehabilitation with standard care could possibly benefit the overall outcome after the total knee replacement instead of isolated psychological or standard rehabilitation. There is paucity of literature on biopsychosocial model based rehabilitation on TKR. Hence, this study aims to integrate biopsychosocial model based rehabilitation along with standard TKR protocol and to compare the effect of biopsychosocial model rehabilitation on subjects who have undergone total knee replacement with standard rehabilitation protocol.

2. Methodolgy

The study was approved by Institutional Research Committee of Manipal College of Health Professions, Manipal. A total of 86 subjects undergoing total knee replacement were screened in orthopaedic in-patient department of physiotherapy, Manipal Hospital, Bangalore, India. The inclusion criteria were age: 50–85 years, subjects diagnosed with knee osteoarthritis according to (criteria for OA diagnosis- Altman) posted for elective TKR, subjects were excluded if posted for staged TKR, revision or bilateral TKR. Subjects who scored 16 or more out 52 on pain catastrophizing scale. Patients who scored less than 16 were excluded as they did not fall into pain catastrophize category. History was taken for all the patients regarding pre-existing psychiatric problem and medication. Participants were excluded if diagnosed other than knee osteoarthritis like rheumatoid arthritis, any neurological impairment which affects lower extremity function, a major medical, cardiac or vascular event in the past year which affects the functional performance of the lower extremity and any total hip replacement or other surgeries in either leg in the past year. Severe psychiatric disorder and exacerbation of COPD participants were also excluded.

2.1. Sample size calculation

Sample size estimation was calculated before the initiation of the trial with 5% level of significance, 80% power, anticipating a minimally clinically important difference of 8 in the primary outcome measure of pain catastrophizing scale. With a dropout rate of 20% the analysis shown a required sample of 15 subjects in each group.

After obtaining the written informed consent from the eligible participant's baseline data for the outcome measures of PCS, SF36, TUG was collected. The subjects were randomized into experimental and control group using block randomization.

The control group received the standard TKR rehabilitation protocol that focused on range of motion and strength training for the operated knee.[24,25] The standard rehabilitation protocol for TKR is given in the (Appendix-I). Exercises commenced on post-operative day POD-0 according to the standard rehabilitation protocol. By POD 1, knee range of motion exercises and full weight bearing walking with long leg brace and walker support was started. The subjects were treated by a qualified physiotherapist until discharge from the hospital (twice daily) with each sessions lasting about 40–60 min. By the time of discharge all participants should achieve 80–90° flexion, display independence and be able to independently transfer and ambulate with knee brace and walker support. All exercises were started with 10 s hold, 10 repetitions and 1 set, twice daily. Following discharge the subjects were continued with the supervised exercise programme of 4–5 session per week for 4 weeks.

The experimental group was given biopsychosocial model based rehabilitation which included pain coping skill training (PCST) along with standard rehabilitation for four weeks. The pain coping skill training (Appendix –2) included 8 sessions starting with progressive muscle relaxation (PMR).[20] Pain coping skill training lasted for 40–60 min along with standard TKR rehabilitation exercise. The subjects were taught progressive muscle relaxation on POD-0 and were advised to practise it when they experienced increased pain for example after ambulation and after knee flexion exercise. On POD-1 subjects were instructed to use activity/rest cycling during the day. The participants were taught to identify automatic negative thoughts and replace it with positive coping thoughts during the exercise and throughout the day. Subjects were asked to imagine a pleasant image of their choice (beach,

Mountain View) and try to relax.

The subjects were encouraged to do pleasant activity which they like for example reading a book. The coping skills were practised during each session and the subjects were encouraged to use the learned coping skills in their daily life during functional activities.[26] To incorporate the social component of the biopsychosocial model following was included in the rehabilitation protocol; education of family members about motivating the patient, the procedure of TKR and what functional activities should be expected from the patient.[16] To incorporate the psychological component of the biopsychosocial model following was included in the rehabilitation protocol; patients were educated about TKR, functional outcome expected post operatively, surgical pain after the surgery and about exercise protocol. Components of pain controlling skill training included progressive muscle relaxation, mini practise, activity/rest cycling, negative automatic thoughts/coping thoughts, pleasant activity scheduling, pleasant Imagery, problem solving and monitoring maintenance.[20]

Participants were asked to perform home exercises as described in the study protocol (appendix I and II) on non-supervised days. All the participants received the intervention by one therapist to standardize the implementation. The participants were asked to keep a log book for exercise adherence and during the follow up they were asked to clarify the same. All the participants underwent a cruciate retaining total knee replacement and sub vastus approach under spinal anaesthesia by the same orthopaedic team. No adverse events or major complications were recorded during the post-operative care. Also, the study participants did not underwent any bone graft or constrained implants.

2.2. Primary outcome measure

2.2.1. Pain catastrophizing scale

Pain catastrophizing scale (PCS) was used to check the pain catastrophizing scores in all subjects. Subjects filled PCS at baseline and at 4 weeks. Computation of the PCS total score included summing responses to all 13 items. PCS total scores ranges from 0 to 52. The PCS subscales are computed by summing the responses to the following items: Rumination: Sum of items 8, 9, 10, 11 Magnification: Sum of items 6, 7, 13 Helplessness: Sum of items 1, 2, 3, 4, 5, 12.[34]

2.3. Secondary outcome measure

2.3.1. SF-36

The SF 36 health survey is a 36 item survey of health status and health related quality of life. The SF-36 is comprised of 8 subscales. Subjects filled out SF36 at baseline and at 4 weeks after TKR. Permission was taken for using SF 36 from quality metric. MCID of physical domains of SF-36 is 11.56 (physical function), 16.86 (bodily pain). MDC ranged from 19.50 (physical function) to 41.23 (social functioning).[35]

2.3.2. Timed up and go

Timed up and go is used to assess function. In this test individuals were instructed to rise from a standard arm chair, walk to a tape mark 3 m away at a comfortable pace, then return to a sitting position with the back against the chair. Recording of the time to perform the task, use of armrests and walking aids were done. In older adults, this test has excellent interrater and intrarater reliability and is responsive to postoperative changes with regards to TKR. The intra class co-relation coefficient is 0.80(95% CI: 0.560).

3. Data analysis

The data was analysed using descriptive statistics to determine the means and standard deviation. “SPSS 16.00 for windows” software was used for the analysis. SF-36v2 was analysed using “Health outcomes scoring software 4.5 for windows 7.” Independent *t*-test was applied for between the group analysis and paired *t*-test was applied for within the group analysis.

4. Results

Thirty subjects were enrolled in the study according to eligibility criteria. Baseline outcome measures and demographic data were taken preoperatively (Table 1). All subjects were randomly allocated to experimental (n = 15) and control group (n = 15). Total of 12 in the experimental group and 11 in the control group could complete the study. The results are projected as mean and standard deviation. The mean age of the subjects in the experimental group is 66.17 and control group is 66.91. There were 3 drop outs in the experimental group and 4 in the control group as subjects experienced issues with distance and commuting and postoperative complication (exacerbation of COPD)(Fig. 1)

At the end of 4 weeks analysis was done for a total of 12 subjects in the experimental group and 11 subjects in the control group (Table-2).Between the groups analysis shown a statistically significant change for PCS total and SF-36 PCS component with a mean difference of 11.8 (7.4–16.1) and 25.9 (19.1–32.7) respectively. Pain catastrophizing scale within group analysis of for experimental group showed statistical significance in PCS total score (Fig. 2) as well as all 3 components of PCS helplessness (Fig. 3), rumination (Fig. 4) and magnification(Fig. 5).However SF- 36 MCS component and TUG did not shown a statistical significance between the groups at the end of 4 weeks of intervention (Table-3).

5. Discussion

The aim of the study was to investigate the effect of biopsychosocial model based rehabilitation on subjects undergoing total knee replacement who have elevated levels of pain catastrophizing. The primary outcome measure was pain catastrophizing scale, secondary outcome measures were SF-36 and timed up

Table 1
Demographics and baseline outcome variables.

Variables	Experimental (n = 12) Mean ± SD	Control (n = 11) Mean ± SD	p value
Age	66.17 ± 7.08	66.91 ± 9.02	0.828
Gender Female:Male	12:0	7:4	0.021
Height	162.33 ± 8.38	165 ± 8.14	0.449
Weight	69.30 ± 8.09	73.90 ± 5.80	0.135
BMI	26.29 ± 2.27	27.22 ± 1.84	0.306
Baseline TUG	31.82 ± 17.60	25.73 ± 11.59	0.343
Baseline PCS Total	24.83 ± 5.96	24.73 ± 5.19	0.964
Pre Helplessness	11.67 ± 2.93	11.64 ± 3.13	0.981
Pre Rumination	9.67 ± 2.22	9.27 ± 1.42	0.622
Pre Magnification	3.50 ± 1.97	3.82 ± 1.72	0.686
SF36 physical function	26.66 ± 21.24	33.18 ± 16.01	0.419
SF36 role physical	40.10 ± 17.96	34.09 ± 23.77	0.499
SF36 bodily pain	31.66 ± 19.14	34.45 ± 20.16	0.737
SF36 general health	65.41 ± 14.77	67.27 ± 16.96	0.782
SF36 vitality	45.83 ± 19.27	61.36 ± 15.00	0.033
SF36 social functioning	46.87 ± 15.19	60.22 ± 28.40	0.101
SF36 role emotional	48.61 ± 21.85	52.27 ± 28.64	0.962
SF36 mental health	65.33 ± 18.44	65.45 ± 21.50	0.958

SD- Standard deviation, BMI- Body mass index, TUG-Timed up and go test, PCS- Pain catastrophizing scale, SF36- Short form 36.

Table 2
Within group analysis.

Outcome Variable		Baseline (Mean ± SD)	Post 4 weeks intervention (Mean ± SD)	Mean difference (95% CI)	p value
PCS Total	Experimental group	24.83 ± 5.96	4.83 ± 2.20	−20.0 (−23.8 to −16.1)	0.0001*
	Control group	24.73 ± 5.19	16.64 ± 6.90	−8.0 (−13.5 to −2.6)	0.0055*
SF- 36 PCS component	Experimental group	35.27 ± 7.32	9.21 ± 7.90	−26.0 (−32.5 to −19.6)	0.0001*
	Control group	37.32 ± 6.91	35.13 ± 7.8	−2.1 (−8.7 to 4.3)	0.4938
SF- 36 MCS component	Experimental group	47.85 ± 9.16	12.17 ± 7.82	−35.6 (−42.8 to −28.4)	0.0001*
	Control group	44.11 ± 11.56	10.02 ± 7.56	−34.0 (−42.7 to −25.4)	0.0001*
TUG	Experimental group	31.82 ± 17.60	23.25 ± 6.67	−8.5 (−19.8 to 2.6)	0.129
	Control group	25.73 ± 11.59	24.00 ± 7.91	−1.7 (−10.5 to 7.0)	0.687

*p value < 0.05.
TUG-Timed up and go test, PCS- Pain catastrophizing scale, SF36- Short form 36.

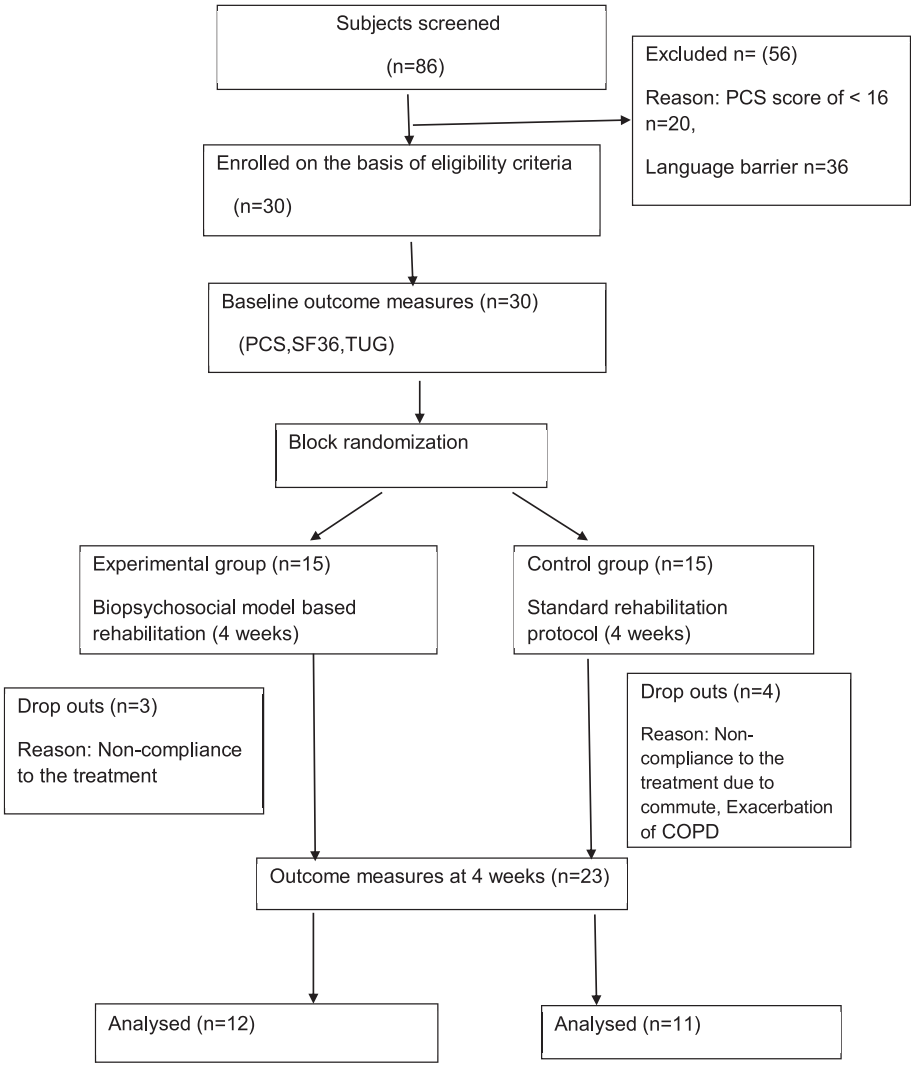

Fig. 1. Study flow chart.

and go test. Patients were excluded due to language barrier in this study as the protocol of pain coping skill training requires understanding of the language. This study only recruited participants who had scored 16 or more out of 52 (pain catastrophizing) on PCS scale. Score lower than 16 on PCS scale does not indicate pain catastrophizing and thus patients scoring less than 16 were not included in the study. After 4 weeks post-operative rehabilitation programme, participants of experimental group showed an improvement in all three components of pain catastrophizing scale and SF-36 physical component score.

PCS total mean score was 24.83 at baseline and 4.83 for the experimental group after 4 weeks. The difference of 20 points was found, it exceeded the mean score of 10 which was observed at 3 months follow up in study by Forsythe et al.[27]In a quasi-experimental study by Riddle et al., subjects in pain coping skill training group showed PCS mean change score of 10.3 points higher than the usual care group at 2 months follow up.[20] The reason for improvement can be due to the effect of biopsychosocial model

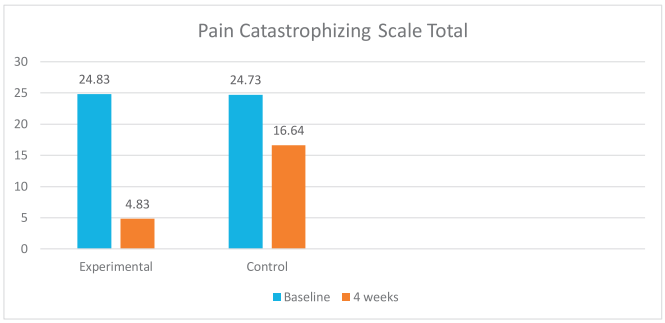

Fig. 2. PCS total at baseline and 4 weeks in experimental and control group.

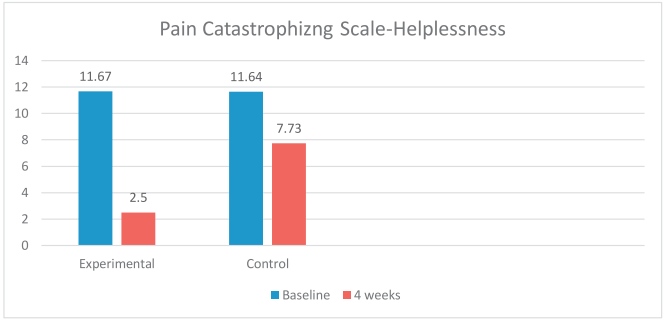

Fig. 3. PCS-Helplessness at baseline and 4 weeks in experimental and control group.

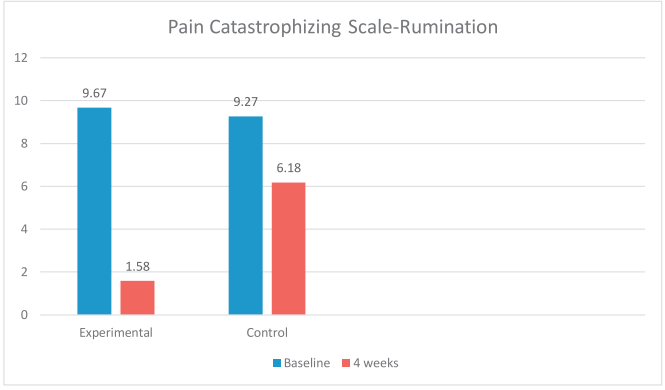

Fig. 4. PCS Rumination at baseline and 4 weeks in experimental and control group.

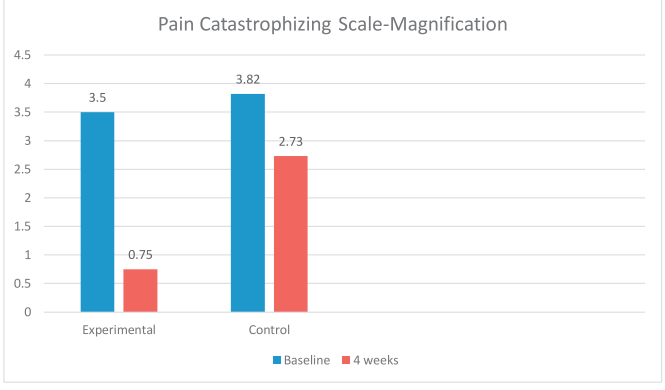

Fig. 5. PCS-Magnification at baseline and 4 weeks in experimental and control group.

Table 3
Between group analysis.

Outcome measures	Baseline to 4 weeks Mean (95% CI)	p value
PCS Total Post	11.8 (7.4–16.1)	0.0001*
SF- 36 PCS component	25.9 (19.1–32.7)	0.0001*
SF- 36 MCS component	−2.1 (−8.8 to 4.5)	0.510
TUG Post	0.7 (−5.5 to 7.0)	0.807

*p value < 0.05.
TUG-Timed up and go test, PCS- Pain catastrophizing scale, SF36- Short form 36.

based rehabilitation. The components of pleasant imagery, progressive muscle relaxation, use of coping thoughts, activity/rest cycle, pleasant activity scheduling could have reduced the catastrophic thinking thereby reducing the pain. The analysis of the control group also showed improvement in PCS total, rumination and magnification but it was less than observed in the experimental group.

Multiple systematic reviews provided strong evidence that different forms of cognitive behaviour therapy and training for pain coping skills are effective in treating patients with various forms of chronic pain.[28–30] The findings of present study also similar with the findings of study by Pellino TA et al. which showed that coping method of diverting attention was related to lower postoperative pain scores and ignoring the pain was associated with higher pain after total hip and knee arthroplasty.[31] Pleasant imagery was included in the pain coping skill training for the experimental group and showed similar results with the finding of a study by Thomas et al. which showed that guided imagery resulted in lower levels of anxiety and pain at all the time points.[32]

The functional performance was evaluated using timed up and go test. This measure did not achieve statistical significance between the groups. The findings of this study were similar with the previous study by Bade et al. which states that there is significant deficit in functional measures at 1 month post total knee replacement surgery.[33]

Experimental group demonstrated statistical significance in the physical component summary of SF-36; physical function, bodily pain, social functioning within the group. The mean score for the component of SF-36 PCS at baseline for the experimental group was 35.27 ± 7.3 which decreased to 9.21 ± 7.9 at 4 weeks and was statistically significant. The difference in mean score was 26 points this exceeded the MCID and showed clinically significant.

The changes in the SF-36 components in the experimental group can be attributed to the intervention of present study. Reason for improvement in PCS could be that the intervention of the present study addresses pain management through coping skills and pleasant imagery technique that directly influences network of brain regions which are associated with catastrophic thinking. Neuroimaging research has shown relation between catastrophic thinking and pain experience.[34] The reduction in pain could have led to improvement in the experimental group on the subscales of physical function and social functioning.

In the present study we did not observe a statistical difference in mental component summary of SF-36. This study had a follow up period only till 4 weeks; this short duration can be the reason for no significant improvement in SF- 36 MCS. Same was also observed in a study by Fitzgerald et al. in which physical function deteriorated at 1 month post TKR while bodily pain improved.[35] In another study it was observed that SF-36 scores were significantly improved at 6 months and 12 months after the surgery.[36] A pilot study by McKay et al. assessed the rehabilitation exercise on quadriceps strength and health related quality of life using SF 36. Their study findings at 6 weeks revealed that here was a significant time effect on the PCS of the SF-36, but there was no time treatment

interaction. The MCS, however, showed no time effect, but there was a significant time group interaction.[37]

The current study findings revealed MCS component did not show statistical significance in this study. This could be possibly due to the MCS subscale may require a long duration to observe a significant changes. The knee osteoarthritis subjects typically have a gradually worsening of arthritis symptoms. Patients' expectation immediately following the knee replacement surgery may be another determinant which will have an influence on the result of MCS subscale. The patient's expectation like full relief of pain and enhanced function seems to be a major cause of unsatisfactory outcomes and satisfaction following TKR.

The observations from this study suggest that biopsychosocial model based rehabilitation may be started post-operatively without any adverse effects. It is evident that central sensitization plays a major role in chronic pain experienced by OA patients. OA patients with high levels of centrally mediated symptoms experienced severe pain and showed increased analgesic requirement after TKR in early postoperative period. As far as postoperative pain relief is concerned, these patients are at greater risk of persistent pain and low patient satisfaction.[38] The most significant predictor of dissatisfaction is painful total knee replacement.[39] Early postoperative assessment should be considered to identify those patients at risk of dissatisfaction.[40]

Recent systematic review has concluded that there is moderate level evidence suggesting for chronic post-surgical pain following TKA; pain catastrophizing is an independent predictor.[9] The experimental group in this study was found to show greater and more clinically meaningful improvements than the control group in all three components of PCS scale, SF-36 physical function, bodily pain and social functioning subscales. Therefore biopsychosocial rehabilitation can be considered following TKR along with standard rehabilitation protocol.

6. Future recommendation and limitations

Future research should be undertaken on long term effect of biopsychosocial model based rehabilitation on subjects who have underwent total knee replacement. Patients were excluded due to language barrier in this study. Further studies can also investigate the effect of this intervention on patients who score <16 out of 52 on PCS scale. Research may also be done to check role of this intervention on both genders as in this study experimental group had female subjects in spite of randomization. Future studies can be done to find specific results of the pain coping skill training on different stages of OA.

7. Conclusion

Biopsychosocial model based rehabilitation involving pain coping skill training reduces pain catastrophizing at 1 month post intervention following total knee replacement surgery. Biopsychosocial model based rehabilitation was found to be effective in improving pain, quality of life and function post TKR. Biopsychosocial model based rehabilitation can be used for patients with elevated pain catastrophizing who are undergoing TKR. This method of rehabilitation can yield better post-surgical outcomes.

Credit author statement

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Declaration of competing interest

The author reports no conflict of interest.

Appendix 1 and 2. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jajs.2020.09.005.

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Review article

Metal hypersensitivity in total knee arthroplasty

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ABSTRACT

Metals used in total knee arthroplasty cause hypersensitivity reactions in some patients. These reactions are known to be immune-mediated and are more likely to affect individuals with pre-existing metal sensitivity, but their mechanism is not fully known. It is difficult to predict pre-operatively whether a patient will be affected and there is no reliable investigation to guide implant choice. There appears to be little value in screening all patients for metal sensitivity before implantation as various studies have shown no significant difference in outcomes or failure rates post TKA in patients with history of metal sensitivity. However, the existing assessment tools are not specific enough to identify subtle problems with potential metal sensitivity association.

Symptoms of hypersensitivity reactions following total knee arthroplasty are often non-specific and difficult to differentiate from other acute presentations following total knee arthroplasty, for example infection. Metal hypersensitivity reactions are often a diagnosis of exclusion, and for this reason they are most likely under-diagnosed and under-reported. Management is controversial but periprosthetic hypersensitivity reactions will often ultimately require revision if no other cause is found. Metal debris are a concern in total hip arthroplasty and could represent another cause of metal-related pathology in total knee arthroplasty. Non-metallic materials are currently in development which may represent a preventative solution for metal hypersensitivity reactions in total knee arthroplasty, potentially also addressing additional concerns around the use of metallic implants such as the high density and thermal conductivity of the material in comparison with the replaced tissue.

1. Introduction

Total knee arthroplasty (TKA) is a widely utilised treatment for end-stage knee arthritis. Over 1 million TKA have been recorded in the England and Wales National Joint Registry (NJR) from 2003 and over 110,000 were recorded in the UK alone in 2017.[1] Rates of TKA are increasing, with an estimated increase of up to 600% in the USA over a 25 year period. The TKA is a financially efficient and generally clinically effective procedure. However, 10–25% patients are dissatisfied with their outcome, and less than 10% report no problems following TKA.[2]

With more patients requiring TKA because of expanding indications and increasing life expectancy, TKA revision surgery burden is expected to increase. Aseptic loosening is the most common cause of failure requiring revision. A less common but increasingly recognised cause of implant failure is that of metal-related pathology, estimated to account for 1.6% of all TKA revisions.[3]

The England and Wales NJR reports 18% of patients were revised for unexplained pain, a significant proportion.[1] It is likely that many of this subgroup suffer from metal-related pathology and that the 1.6% officially recorded is likely a gross underestimate. A number of different material combinations are available for TKA implants including metal alloys, ceramic, polyethylene, and polyetheretherketone (PEEK). The implant material in primary surgery

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Abbreviations

ACD	allergic contact dermatitis
ARMD	adverse reactions to metal debris
ALVAL:	aseptic lymphocyte-dominated vasculitis-associated lesions
PEEK	polyether ether ketone
MoM	metal-on-metal
MoP	metal-on-polyethylene

and in revision following unexplained pain was not recorded in the NJR report. The majority of TKA consist of a femoral component of cobalt-chromium alloy, which articulates with a polyethylene tibial component which usually has a metal backing.

Metal particles are released from metallic components by mechanical wear or corrosion. In some patients, metal sensitivity may cause implant-related hypersensitivity reactions, typically presenting as allergic contact dermatitis (ACD) and/or implant failure. Diagnosis is challenging and presentations often mimic chronic infection, with persistent painful synovitis, reduced range of motion and effusion.[4] Screening for metal hypersensitivity preoperatively and the relevance of a history of ACD in response to metal both remain controversial. Management of patients following TKA who present with sequelae of metal hypersensitivity has limited evidence basis, but may culminate in revision.[4]

Adverse reaction to metal debris (ARMD) is an umbrella term first described by Langton et al., in 2010. Its mechanism is not fully elucidated but is known to have an immune-mediated component dominated by lymphocytic activity, and to lead to characteristic histological changes which differ from those seen in osteolysis induced by polyethylene debris. Metal ions are released, and evidence suggests a component of systemic hypersensitivity. ARMD is particularly prevalent in patients with metal-on-metal implants.

This paper will focus mainly on the mechanism, management and screening for metal sensitivity. There will also be a discussion on the role of metal debris in TKA failure, and of possible strategies to avoid the impact of metal-related pathologies in TKA.

2. Hypersensitivity

2.1. Basic science

The classical definition of allergy is type 1 hypersensitivity. This is IgE-mediated, occurs over seconds to minutes and may result in anaphylaxis. Type I, II and III reactions do not usually occur with metal. Although termed "allergic contact dermatitis", cutaneous reactions to metal seen in the general population are generally believed to be caused by type IV, delayed-type hypersensitivity reactions. These are mediated by T-cell lymphocytes.[5]

In cutaneous sensitisation, chemical allergens (haptens) access the stratum corneum and combine with proteins which bind to dendritic cells.[4] These cells drain from the skin via afferent lymphatics and present the hapten-protein complex to lymphocytes, initiating clonal expansion and sensitisation. Metallic allergens may sensitise via a different mechanism; metals in contact with biological systems corrode and produce ions.[5] As they differ from chemical allergens, these metal ions must form specific coordination complexes with proteins to allow immune recognition. The end result remains the same however, and an adaptive immune response sensitises to further exposures to the relevant metal.

In implant-related hypersensitivity reactions ions can be released chemically by corrosion, or by mechanical processes such as wear. Once the ion has combined with a protein it is not known which cell responsible for presenting the metal-protein complex. In addition to dendritic cells, other possible candidates for which cell is responsible for presenting the metal-protein complex include epithelial cells, macrophages, lymphocytes and parenchymal tissue cells.[5] Hypersensitivity reactions appear to be delayed cell-mediated responses, although debate remains about its precise mechanism.[4,5]

2.2. Incidence

The prevalence of metal sensitivity in the general population, as defined by positive results on test dermal patching, is 10–15%.[4] Patients with total joint arthroplasties (TJA) have a higher prevalence of metal sensitivity than the general population; a literature review found a prevalence of 25% in patients with well-functioning TJA implants and 60% in failed or poorly functioning implants.[5] Similar results have been found in TKA specifically. Granchi et al. studied 94 patients. They used dermal testing with haptens representative of cobalt and titanium-based alloys.[6] 15% of candidates for TKA without implants, 44% of those with stable implants and 57% with loose implant tested positive for sensitivity to one or more metal hapten. Positive patch testing was not significantly predictive of implant failure, and it is not known whether patients with metal sensitivity are more likely to have implant failure, or if implant failure sensitises patients. The authors suggested patients with previous symptoms of metal allergy were more likely to have TKA loosening, but their reported hazard ratio of 4 did not reach statistical significance.[6] While the specific revision burden caused by metal hypersensitivity is not known, the Australian Orthopaedic Association National Joint Registration recorded that 1.6% of all TKA revisions were caused by metal-related pathology. The implant materials and models of this subset were not individually reported.[3]

2.3. Clinical presentation & symptoms

Most of the ACD cases described in the literature following orthopaedic and other metallic implants were eczematous, while some were urticarial, bullous, or vasculitic. The majority resolved with removal of the implant and had positive patch tests.[7] As TKAs are implanted deep within the tissues away from the skin, metal hypersensitivity reactions may present differently. Dermatitis has also been reported in TKA.[8] Verma et al. studied 30 patients with localised dermatitis over the implant following TKA, the majority of which were eczematous in presentation. Interestingly only 7 of the 15 patients tested had positive patch testing results for metal.[8] The eruption was located on the lateral aspect of knee in all cases and so in those with negative patch tests neuropathy dermatitis secondary to intra-operative saphenous nerve lesion could be considered. Systemic dermatitis has also been known to occur following TKA, typically localising to body flexures.[7]

In addition to a full history and examination, blood tests including C-reactive protein, erythrocyte sedimentation rate and blood cultures must be performed. The presentation will often mimic chronic infection, however serum inflammatory markers are generally only mildly raised. Other more common causes of an acutely painful knee must also be considered, including aseptic loosening, hemarthrosis, dislocation and fracture.[4]

Metal hypersensitivity is a diagnosis of exclusion. Metal ion levels are raised in patients with well-fixed and well-functioning TKA, and so are little use in diagnosing metal hypersensitivity.[4,9] When investigations suggest metal hypersensitivity, allergy testing should be performed. Patch testing is generally first line. It is low cost and allows testing for a number of different metals.[10]

However, patch testing can be insufficiently sensitive or specific, and Granchi et al. found it was unable to differentiate between a stable and a failed implant.[11] It may reflect a purely cutaneous reaction, rather than an immunological response at the implant site.[12] Where available lymphocyte transformation testing (LTT) is often utilised to detect more systemic reactions. In LTT, patient lymphocytes and monocytes are challenged with metal salts, and their proliferation in response to these antigens quantified. LTT results correlate with poorly functioning implants and suspected metal hypersensitivity, but it is not possible to derive causality from a positive test result.[13] A recent study of 27 TKAs without evidence of infection or loosening revised for pain and suspected metal allergy found that "LTT results were insufficient for diagnosis of TKA failure due to an immune reaction".[14] Other authors suggest the combined use of patch testing and LTT to better inform management decisions, but again warn that neither are reliably sensitive or specific.[12,13]

Thyssen et al. propose diagnostic criteria for implant-related allergic contact dermatitis, including a time scale of weeks to months following implantation, positive patch testing for implant metal, localised eruption and recovery following revision.[10] For periprosthetic presentation, they suggest considering histology consistent with delay-type hypersensitivity, positive patch testing, positive *in vitro* testing, and recovery following revision. Suspicion of metal hypersensitivity as compared with aseptic loosening secondary to polyethylene wear is increased in patents with earlier symptoms following implantation (weeks to months vs years), previous history of metal allergy and presence of severe dermatitis or painful persistent synovitis.

In patients with painful TKA where no obvious cause is found, it is possible that their symptoms are related to metal sensitivity. No reliable test currently exists which is able to identify metal hypersensitivity reaction in such cases. Patients will typically present recurrent knee effusions and undergo a plethora of investigations without any meaningful outcome.

2.4. Dealing with hypersensitivity

For patients with persistent dermatitis with no evidence of periprosthetic disease, first line management should be topical steroids, and good results have been noted.[4,8] There have been limited reports of TKA revision for severe dermatitis refractory to steroid treatment, with complete post-operative resolution. For example a patient with widespread dermatitis following TKA (Depuy, PFC, CoCrMo lot 290,105/Ti6Al4V lot 1,016,010, Warsaw, Indiana, USA) had a highly positive patch test result with chromium only. All symptoms resolved following revision with a zirconium-niobium alloy prosthesis (Smith&Nephew, Oxinium, Zr-2.5Nb, Memphis, Tennessee, USA).[15]

For patients with TKA and hypersensitivity reaction affecting the implant, most patients will require revision surgery. Extensive synovectomy is required to reduce metal ion burden, and augmentation of bone stock may be necessary to ensure stability.[16] Suitable materials for revision implants include ceramics, oxidised zirconium, titanium or zirconium alloy, and cobalt chromium coated with zirconium nitride or titanium nitride.

Revision surgery must remain a last resort, and only when there is adequate confidence in the diagnosis. It must be emphasised that metal hypersensitivity as the cause of implant symptoms remains a diagnosis of exclusion. Other causes must be ruled out first, especially infection. Patient counselling for revision surgery for metal hypersensitivity in TKA must be appropriately guarded. They should be aware that there are no recognised guidelines, and evidence for revision surgery is limited.[4]

2.5. Predicting (screening) for hypersensitivity

Implant-related metal hypersensitivity may necessitate revision surgery, a costly undertaking with associated morbidity. Metal sensitivity prevalence increases following TKA and more patients have positive patch tests in failing implants.[17] This may reflect sensitisation following implant failure, rather than pre-existing sensitivity increasing probability of implant failure.

Most authors recommend against screening all patients prior to TKA, citing prohibitive costs and unnecessary use of more expensive implants for little benefit. They generally suggest patch-testing only in patients with a known history of previous significant metal hypersensitivity or prior implant failure due to metal hypersensitivity.[10,18] While the majority of failed implants have positive patch test results, it is likely that only a small subset of patients with positive patch test results will react to a TKA implant of that metal. In addition, Thyssen et al. found no difference in THA revision rates in a national registry for patients who had positive patch test results with implant metals as compared with those who did not.[19] The material and manufacturer of the implants used in the subset of patients who underwent revision surgery was not recorded. This still is an evolving field and our understanding will improve with time.

3. Pathology related to metallic wear particles

Adverse reaction to metal debris (ARMD) is used as a general term to encompass all adverse effects on periprosthetic tissues caused by TJA metal debris. The term was introduced to highlight local adverse reactions to metal-on-metal hips.

Aseptic loosening is the most common cause of TKA revision, representing 23% of early failures (less than two years post-operative), and 51% of late revisions (over two years post-operative),[20] This was previously believed to be caused by cement. However, despite improvements in cementing technique, aseptic loosening continued.[21] Polyethylene wear debris were suggested as an alternative cause by Amstutz et al. It was shown that wear particles activated periprosthetic macrophages, which in turn release osteoclast activating factor, oxide radials and hydrogen peroxide, and causes fibrosis, vascular proliferation and cell necrosis.[21] Polyethylene debris is now established as the main cause of aseptic loosening.

Metal-on-metal (MoM) hip bearings were developed due to improved wear characteristics and became very popular, but in the early 2000s it became apparent that metal debris was a serious issue.[22] and MoM hips have a ten year revision rate of 14–27%.[1] Willert et al. first described aseptic lymphocyte-dominated vasculitis-associated lesions (ALVAL) in 19 MoM THA revisions. The majority of these revisions had demonstrated osteolysis or radiolucencies, recurrence of pain and the development of a large effusion. Periprosthetic histological findings were of a predominance of lymphocytes, macrophages, a large volume of fibrin exudate and necrosis.[23] Revision with MoM THA resulted in recurrence, while revision with metal-on-polyethylene (MoP) did not. The primary prostheses were cemented in two hips, of hybrid fixation in one and cementless in 16. Two of the cemented stems were made of iron-based alloy S30, the other of Ti6Al–7Nb alloy. All uncemented stems were made of Ti-6Albased alloys. 14 of the 16 cementless stems were revised without cemented, while all cemented stems were revised with cement. The implant type used in revision was not recorded. The longevity of MoP revisions likely reflects the reduction in source of metal debris in MoP hips compared with MoM hips. The Oxford group also published a case series on MoM hip resurfacing implants which present with pain at the groin, lateral hip or buttock.[24] They noted findings of locally destructive

non-infective masses which they termed "pseudotumours". These were characterised by extensive necrosis and dense connective tissue. Some also contained cystic degeneration, and almost all contained metal wear particles. Histological findings were similar to those seen in ALVAL. The majority required revision surgery.

Most MoM wear particles are less than 100 nm. These are smaller than active polyethylene debris (100–1000 nm). The mechanism of immune activation is controversial, but as with polyethylene debris, local macrophages appear to phagocytose metal particles. However, in contrast to polyethylene debris the macrophages then present the resulting metal-protein complexes to circulating lymphocytes and initiate a cell-mediated hypersensitivity reaction dominated by lymphocyte activity in a process which seems to resemble type IV hypersensitivity. Positive patch testing is also more prevalent in failed MoM THAs compared with controls.[25]

Most published literature on ARMD focuses on MoM THA and the main concern with respect to metal debris in TKA tends to focus on metal debris produced intraoperatively. MoM hips generate metal particles at the junction between the femoral head and socket, that between the head and stem of the femoral component, and at junctions between modular components. Higher revision rates for ARMD in MoM hips reflect this. Revision to MoP articulation reduces but does not entirely eliminate sources of metal debris. Wear simulation studies demonstrated that 12% of wear debris by mass for a metal-on-polyethylene TKA were metal, suggesting metal debris could also contribute to metal-related adverse events in TKA.[26] Modular connections in contemporary TKAs may be a source of metal ions.

4. Alternative materials for TKA

One of the biggest challenges in orthopaedics is the development of wear resistant materials which reduce the generation of particles, while continuing to perform to a high standard. To this end, moderately cross-linked polyethylene tibial components and oxidised zirconium femoral components have demonstrated significant improvements.[27,28] Ceramic bearings also have excellent wear properties, are chemically inert and corrosion resistant. Mid- and long-term survival rates are comparable to commonly used alloy components; its brittleness and therefore potential for implant fractures limited its application previously but more recent generations have eliminated this.

Polyetherketone (PEEK) is a thermoplastic polymer. It is relatively biologically inert, strong and stiff. PEEK is also lightweight compared with metal alloys. Hallab et al. studied the effect of PEEK particles on macrophages. They demonstrated a reduced cytokine release response *in vitro* compared with ultra-high molecular weight polyethylene, suggesting PEEK is more biocompatible.[29] Anecdotally, patients with TKA complain of difficulty with extremes of temperature and are more aware of their knee in particularly hot or cold environments. It could be related to the thermal conductivity of metal used in implants, and a material with low thermal conductivity such as PEEK may prevent this. PEEK could represent an alternative material for use in TKA, but clinical data for its application in TKA is still relatively limited.

5. Conclusion

Implant-related hypersensitivity reactions are a cause of revision which is likely greatly underreported and could represent an unexploited opportunity to reduce revision rates for TKA. It is possible that these reactions may be a causative factor in the persistent dissatisfaction seen in some patients following TKA. In MoM hips, the local effect of a high load of metal debris is the cause of a greater failure rate. In MoP TKA, patient-dependent systemic hypersensitivity is the mechanism of failure. The diagnosis of hypersensitivity reactions is challenging and often not possible. Following routine investigations to rule out more common causes of implant failure, patch testing and LTT are the two most commonly utilised methods. Independently they have poor sensitivity and specificity in the identification of metal hypersensitivity as the cause of implant failure.[11–14] Together their accuracy is improved, but they remain a guide to the surgeon rather than explicit diagnostic tests.[4,12] They must be treated in the context of the clinical presentation. Screening for metal sensitivity preoperatively is neither practical nor reliable. The management of metal hypersensitivity reaction associated with TKA is controversial and there is little evidence available. Surgeons therefore have little guidance in deciding if revision surgery, with its associated morbidity, is the correct choice. Prevention is most likely the best approach to the problem. Prostheses without metal are one possibility, providing they are biomechanically strong, biologically inert and cost-effective. Current metal-based prostheses have significant inertia due to economy and the availability of longitudinal outcome data. While research into alternative materials continues it is unlikely to result in large scale adoption in the near future.

Author contributors

SWK performed the literature search and the wrote the manuscript draft. All other co-authors have contributed equally to editing and have seen the final manuscript and approved it.

Declaration of competing interest

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Research paper

Does D-Dimer really help in the diagnosis of chronic periprosthetic joint infections (PJI)? A case-control study

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ABSTRACT

Introduction: The differential diagnosis between aseptic and septic total joint arthroplasty (TJA) revision is fundamental in order to be successful in the surgical treatment. Several serum biomarkers have been proposed as gold standards in the diagnosis of Periprosthetic Joint Infections (PJI). The aim of the current study was (1) to evaluate serum levels of D-dimer in a retrospective series of PJIs diagnosed by traditional methods and (2) to compare the D-dimer performance as a diagnostic test with other well established PJI biomarkers in a case-control study.

Materials and methods: A total of 159 TJA revisions were included in the study database: 55 implants in 55 patients met the inclusion criteria. The final study group included 33 aseptic and 22 septic (with micro-organism isolation) TJA revisions; these two groups were not statistically different in terms of demographics. All patients were preoperatively tested with the following serologic tests: erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), fibrinogen, D-dimer and white blood cell (WBC) count. A standard univariate logistic analysis was performed in order to investigate the association between chronic PJI and the serologic tests.

Results: A gram-positive microorganism was isolated in 15 patients whereas a gram-negative microorganism was isolated in 7 patients. Univariate analysis showed that high D-dimer, ESR or fibrinogen were not associated with a PJI occurrence, whereas high CRP and WBC count >10.000 cells/mm^3 were significantly elevated in chronic PJI patients. A multivariate analysis confirmed that leukocytosis was a significant predictor of PJI.

Conclusions: This study showed that D-dimer had a low sensitivity and specificity in diagnosing chronic PJI, especially when evaluated as a single diagnostic biomarker.

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1. Introduction

Periprosthetic joint infection (PJI) is one of the worst complications in arthroplasty surgery with an incidence between 1 and 4% after primary total knee arthroplasty (TKA) and between 1 and 2% after primary total hip arthroplasty (THA).[1–3] PJI can lead to a devastating clinical outcome if not properly and timely diagnosed. Unfortunately, early diagnosis can be very challenging because PJIs are not routinely detected by a single test. Multiple criteria have been proposed to help the orthopaedic surgeon to identify a PJI.[4–6] In 2013, delegates from the Musculoskeletal Infection Society (MIS) and European Bone and Joint Infection Society (EBJIS) met in a joint conference and defined diagnostic criteria for PJI, distinguishing major and minor criteria,[6] which were further updated in 2018 with the introduction of a specific scoring system for their interpretation.[7]

According to the American Academy of Orthopaedic Surgeons (AAOS) Guidelines on PJI diagnosis,[8] serum biomarkers currently represent the first line-screening tools for PJI. This approach was endorsed even during the International consensus meeting (ICM) on PJI.[7] Multiple serum biomarkers have been proposed for the

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early identification of a PJI,[9,10] including erythrocyte sedimentation rate (ESR) and C-Reactive Protein (CRP).[6]

A close connection between the coagulation cascade and infection/inflammation mechanisms is well known.[11,12] In this scenario, D-dimer, a fibrin degradation fragment primarily used to rule out acute pulmonary embolism or deep vein thrombosis (DVT), appeared to be a promising and cost-saving PJI diagnostic tool, showing high sensitivity (89%) and specificity (93%).[13] Both Parvizi et al. and the ICM group included D-Dimer in the scoring system used to diagnose the presence of a PJI,[7,14] and the threshold of 860 ng/mL was proposed as the optimal cut-off value for diagnosis.[7,14] However, recent findings questioned the reliability of D-dimer as a marker for PJI in this field.[15–17]

The aims of the current study were to evaluate serum levels of D-dimer in a retrospective series of PJIs diagnosed by traditional methods, and to compare the D-Dimer performance as a diagnostic test with other well established PJI biomarkers (i.e. ESR, CRP) in a case-control study. The authors hypothesized that D-Dimer would have low sensitivity and specificity in diagnosing PJI.

2. Materials and Methods

We reviewed our Institutional Hospitalization Database (HD) and Operating Room Registry (ORR) to retrospectively identify and enroll patients who had surgery between January 1st, 2011 and June 30th, 2019. Inclusion criteria were: age greater than 18 years, primary prosthetic joint revision (defined by ICD-9 diagnosis codes 996.60 [Infection and inflammatory reaction due to unspecified device, implant, and graft], 996.41 [Mechanical loosening of prosthetic joint] and 996.43 [Prosthetic joint implant failure/breakage]). Exclusion criteria included: concurrent chronic inflammatory diseases, heavy smoking (≥25 cigarettes a day), presence of malignancies, renal or hepatic failure, re-revision arthroplasty, concomitant infections other than PJI, and acute PJIs as defined by the ICM on PJI in 2018.[7]

Patients were classified into two groups: "infected" (PJI positive) and "non-infected" (PJI Negative). Chronic PJI diagnosis was originally made according to the criteria defined by the MIS and the 2013 International Consensus Conference.[4,6] The major chronic PJI inclusive criterion was a double positive culture from synovial fluid and/or intra-articular specimens.

All patients gave consent for data collection for scientific purposes at the time of surgery. Due to the retrospective nature of the study, a specific informed consent form was not required. All data were processed according to current privacy regulations and the standards of good clinical practice.

Patients' medical records were reviewed by two observers not involved in the original surgery (GT, AB). Patient data were extracted and placed in a specific evaluation grid. The following data were collected at baseline: age, gender, American Society of Anesthesiologists (ASA) score, type of the original surgical procedure (primary THA or TKA), species of the isolated pathogen, serum ESR value, serum CRP value, serum fibrinogen value, serum D-dimer value, serum white blood cell (WBC) count. All blood samples were collected at the time of first surgery, namely before the prosthesis removal for cases and before revision arthroplasty for the controls.

With regard to statistical analysis, frequencies and percentages were used for descriptive statistics. The chi-squared test, or Fisher's exact test when applicable, were used for categorical variables, while the *t-test* was used for comparisons between parametric quantitative variables. Quantitative variables are reported using the mean and standard deviation (SD) in the case of Gaussian distribution and median and interquartile range (IQR) in the case of non-Gaussian distribution. In order to investigate the association between chronic PJIs and a variety of potential predictors (including ESR ≥ 30 mm/h, CRP ≥ 10 mg/L, fibrinogen ≥ and 519 mg/dl, d-dimer ≥ 860 mg/dl[7,18] and WBC ≥ 10,000 cells/mm^3,[19] see Table 1), we performed a univariate logistic analysis. All results were expressed as hazard ratios (HR) with 95% confidence intervals (CI). To evaluate the individual contribution of each independent factor, variables that showed a significant association in the univariate analysis were included in a multivariate regression model. Significance was set at $p < 0.05$. Statistical analyses were performed using the software package SPSS 18.0: PASW Statistic, Inc, Chicago, IL.

3. Results

A total of 159 revision arthroplasties were identified after registry review. Among these, after reviewing patient medical records, 45 were excluded because of incomplete data, 83 because they presented one of the comorbidities included among the exclusion criteria, 23 because they underwent re-revision arthroplasty and 8 because they resulted in acute PJIs (see Fig. 1). Therefore, 55 patients were included in the present study. According to the diagnostic criteria of chronic PJIs[4,6] 33 cases were classified as "non-infected" and 22 as "infected".

Patient demographics are shown in Table 2. The infected and non-infected groups did not differ in age, sex, or joint affected by the prosthesis loosening. The ASA score distribution was similar in both groups.

Regarding the culture isolates, in 15/22 of the "infected" patients a Gram-positive bacterium was detected (most commonly *Staphylococcus aureus* [8/15 patients]), while in 7 cases Gram-negative rods were isolated (Table 3).

Based on the univariate analysis, infection occurrence was not associated with the level of D-dimer, ESR, or fibrinogen (Table 4) (HR 2.217 [CI: 0.545–9.01], $p = 0.266$, HR 2.244 [CI: 0.704–8.48], $p = 0.159$, and HR 0.321 [CI: 0.71–1.45], $p = 0.14$, respectively).

However, high CRP values and leukocytosis were significantly more common in patients with chronic PJIs according to the univariate analysis (HR 6.0 [CI: 1.106–32.537], $p = 0.038$ and HR 16.150 [CI: 3.718–70.142], $p < 0.001$, respectively) (Table 4). Based on the multivariate analysis, leukocytosis was confirmed as a significant predictor of PJI (HR 14.642 [CI: 3.20–66.82], $p = 0.001$) (Table 4).

4. Discussion

This study confirmed the authors hypothesis that D-dimer has a low sensitivity and specificity in diagnosing PJI, especially when evaluated as a single diagnostic biomarker.

Septic loosening has been shown to be responsible of 14.8% of all TKR and 9.8% of all THR worldwide.[20] The treatment of this severe complication is based on several techniques including debridement, antibiotics and implant retention (DAIR); debridement, antibiotic pearls, and retention of the implant (DAPRI); and one stage or two stage revision.[21–25] PJI can lead to devastating outcomes if not properly diagnosed. In the absence of a single diagnostic test with absolute accuracy, a combination of clinical, laboratory and imaging findings is necessary to define a PJI.

Table 1
Cut-off values investigated in the present study.

Biomarker	Cut off
ESR	30 mm/h[7]
CRP	10 mg/L[7]
D-dimer	860 μg/l[7]
Fibrinogen	519 mg/dl[18]
WBC	10,000 cells/mm3[19]

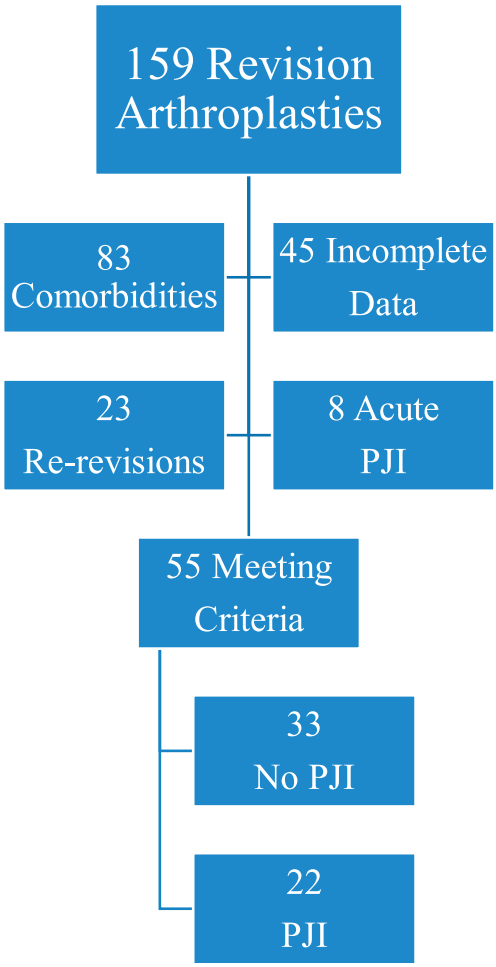

Fig. 1. Flow-chart of population selection.

Table 2
Patients demographics.

	Infected (n = 22)	Non infected (n = 33)	P-value
Age (mean)	69	71	0.56
Sex (F)	15	16	1
ASA score (mode)	3	3	n.a.
TKA n. (%)	11 (50%)	13 (56%)	0.76
THA n. (%)	11 (50%)	10 (44%)	

Table 3
Culture isolation.

Bacteria	Species	n.
Gram positive (n = 15)	*Staphylococcus aureus*	8
	S. epidermidis	5
	Enterococcus faecalis	1
	S. warnerii	1
Gram negative (n = 7)	*Pseudomonas aeruginosa*	2
	Acinetobacter baumannii	2
	Acinetobacter spp.	1
	Proteus spp.	1
	E. coli	1

In order to reduce the need for clinician discretion in diagnosing PJI, the MIS in 2011 produced some specific criteria.[4] According to these criteria, a PJI should be diagnosed when at least one of the 2 main criteria, or 4 out 6 of the secondary criteria, were observed (Table 5). Afterwards, IDSA defined PJI through several statements[5] (Table 5). In 2013, MIS and EBJIS, during a Consensus Conference in Philadelphia, produced a series of diagnostic criteria to define a PJI.[6] These definitions, based on major and minor criteria, improved diagnostic safety and facilitated treatment (Table 5). Recently, Parvizi et al. introduced a scoring model to diagnose PJI through minor criteria[14] that was lately adopted by the ICM on PJI.[7]

Historically, the first step for PJI diagnosis has been the evaluation of serum biomarkers.[8,26] Several serum biomarkers were proposed to identify a PJI, with controversial data in terms of specificity and sensitivity.[10,27] Recently, Shahi et al. identified D-dimer as a promising biomarker for both chronic and acute infections.[13] In their study the authors demonstrated a high specificity and sensibility for D-dimer values $\geq$ 860 ng/ml.[13]

A close connection between the coagulation cascade and infection/inflammation mechanisms has been shown by several authors.[11,12] Fibrin deposition is promoted by bacteria and proinflammatory cytokines through three main pathways: tissue factor-mediated thrombin generation, dysfunctional physiological anticoagulant mechanisms, and impaired fibrin removal due to alteration of the fibrinolytic system.[12] Fibrinogen is the precursor of fibrin and was demonstrated to be a valuable test to identify PJI.[18]

D-dimer is a fibrin degradation product released into the blood following the fibrin clot breakdown by plasmin and was originally used in screening DVT or PE.[12,21–23]

Lee et al. observed that D-dimer levels sharply increased after both THA and TKA and peaked at postoperative day 1 (peak level 4.5 μ g/dl).[28] In their study, D-dimer levels decreased to nearly baseline levels at postoperative day 2 and then slowly elevated again and reached a second peak at postoperative week 2[28]; because of this kinetic, D-dimer was proposed as a valuable serum biomarker for early identification of PJI. In fact, in the same study, serum CRP and ESR levels remained elevated until postoperative day 5 and day 3, respectively, thus reducing their usefulness as diagnostic tools in the early post-operative period.[28]

Interestingly, several authors recently questioned the reliability of D-Dimer as a biomarker of PJI.[15–17] The current study showed that D-Dimer, fibrinogen, and ERS were not associated with developing a PJI; our findings were in accordance with the observations by Huang et al. that, in a case-control study on 101 patients, demonstrated that D-Dimer was not able to distinguish between septic and aseptic loosening.[15] Moreover, Pannu et al. retrospectively reviewed 172 revision arthroplasties (62 non-infected, 49 infected) and observed a low specificity (32.3%) of the D-Dimer cut-off proposed by the 2018 ICM on PJI.[17] According to those authors, the reliability of this biomarker increased when a higher cut-off was considered (D-Dimer> 2300 ng/mL).[17]

Lu et al.,[29] in 2020, published a systematic review and meta-analysis study on the diagnostic accuracy of D-dimer for PJI which included 34 studies and 1587 patients: the pooled diagnostic D-dimer sensitivity and specificity were 0.82 (95% CI, 0.70–0.89) and 0.70 (95% CI, 0.55–0.82) respectively; the results of their subgroup analysis showed that serum D-dimer might have a higher diagnostic accuracy than plasma D-dimer for PJI and D-dimer had better accuracy in subgroups with Caucasian and African American races that in subgroups with East Asian races. Those authors concluded that D-dimer has limited performance for the diagnosis of PJI and has a poorer diagnostic value than that of CPR and ESR.

This discrepancy in the literature regarding D-Dimer validity as a PJI diagnostic test might be explained by the patient selection criteria and the non-specificity of the coagulative cascade. In fact, this cascade is easily activated by several conditions (i.e. Systemic Lupus Erythematosus, polymyalgia rheumatica, myelodysplastic syndrome, and multiple myeloma) that could lead to a high

Table 4
Results of the univariate and multivariate analysis for infection.

Univariate logistic regression			
Variable	HR	95% C·I.	p value
Sex	0.938	0.265–3.313	0.92
Age >65 yrs	1.306	0.377–4.524	0.674
ESR >30 mm/h	2.244	0.704–8.48	0.159
CRP >10 mg/L	6.000	1.106–32.537	0.038
D-dimer > 860 μg/l	2.217	0.545–9.01	0.266
Fibrinogen >519 mg/dl	0.321	0.71–1.45	0.14
Leukocytosis >10,000	16.150	3.718–70.142	<0.001
Multivariate logistic regression			
Variable	HR	95% C·I.	p value
CRP >10 mg/L	4.728	0.647–34.54	0.126
Leukocytosis >10,000	14.642	3.20–66.82	0.001

Table 5
Diagnostic criteria for PJI.

Year	Association	Criteria
2011	Musculoskeletal Infection Society[4]	Definite PJI: Sinus tract communicating with joint OR growth of same organism in 2 or more periprosthetic tissue cultures Possible PJI: three or more of the following minor criteria: • Erythrocyte sedimentation rate (ESR) > 30 mm/h AND C-reactive protein (CRP) > 10 mg/L • Synovial fluid white blood count >3000 cells/μl or ++ change on leukocyte-esterase test strip • Synovial fluid PMN >80% • >5 PMN/HPF on histologic analysis of periprosthetic frozen section • A single positive culture
2013	Infectious Diseases Society of America[5]	Definite PJI: sinus tract communicating with joint OR growth of same organism in 2 or more periprosthetic tissue cultures OR the presence of purulence surrounding the prosthesis without an alternative cause Possible PJI: any of the following: • Growth of a virulent organism from a single tissue biopsy or synovial-fluid sample • Presence of acute inflammation on histopathologic examination of periprosthetic tissue at time of surgical debridement of prosthesis removal
2013	International Consensus Meeting on PJI (between Musculoskeletal infection society and European Bone and Joint Infection Society)[6]	Two positive periprosthetic cultures with phenotypically identical organisms, or * A sinus tract communicating with the joint, or * Having three of the following minor criteria: Elevated serum C-reactive protein (CRP) AND erythrocyte sedimentation rate (ESR) - Elevated synovial fluid white blood cell (WBC) count OR ++change on leukocyte esterase test strip - Elevated synovial fluid polymorphonuclear neutrophil percentage (PMN%) - Positive histological analysis of periprosthetic tissue - A single positive culture

expression of D-Dimer.[15,30] In the current study, we applied strict inclusion criteria, which could have been responsible for the disagreement between our report and the report by Shahi et al.[13] Therefore, considering the observation made by Xiong et al. on the lower specificity and sensitivity of the D-Dimer test when compared to ESR and CRP,[16] it might be hypothesized that the D-Dimer should be interpreted only in association with the former well-known outperforming biomarkers.[28]

An interesting finding of our study was that Leukocytosis (>10,000), a known diagnostic factor for septic arthritis,[31] was the biomarker with the strongest association with chronic PJI among all those biomarkers we investigated. This observation was quite surprising, considering that previous reports clearly found that serum WBC had low sensitivity and specificity in PJI diagnosis[32]; because of this, blood WBC count has not been included in any of the available guidelines for PJI detection, in contrast to synovial WBC count.[3] Historically, synovial WBC has been considered a reliable PJI diagnostic test, especially in the acute setting,[32] and a correlation between serum and synovial WBC was previously observed, although considered weak.[33] The relevance of leukocytosis observed in our population might be partly explained by the exclusion criteria originally established in the study design: in fact, we included only chronic PJI and leukocytosis might be observed in both chronic infection and chronic non-specific inflammation.[34] This hypothesis was supported by the study conducted by Claassen et al. that reported an extremely high sensitivity (98%) for leukocytosis >10,000 as a diagnostic test in a cohort of 46 patients with chronic PJI.[35]

Our study has multiple limitations. First, the small sample size might have underpowered the statistical analysis; however, the authors decided to use strict inclusion criteria to rule out comorbidities that might alter the serum biomarkers levels that were investigated. Another limitation was the use of three different ICD-9 codes as PJI screening tools and, thus, a few patients might not be included; however, those criteria were considered the gold standard for the diagnosis of PJI at the time of the start of the study.

5. Conclusions

This study demonstrated that serologic biomarkers still represent the first line of investigations in PJI diagnosis. D-Dimer is one of the promising serum biomarkers for PJI diagnosis; however, its relevance is questionable and should not be used as a single, diagnostic PJI test. In our population, a solitary increase in D-dimer and fibrinogen was not associated with the diagnosis of PJI. Therefore, we believe that none of them should be evaluated for PJI diagnosis without also investigating the other outperforming biomarkers, for example, ESR and CRP. CRP combined with serum

leukocytosis were the only relevant factors associated with PJI in the present study. Although leukocytosis was not included in recent diagnostic guidelines,[6,14] it might still play a role in the identification of chronic PJI.

The future research in PJI diagnostic should address molecular techniques that can identify DNA in a synovial fluid sample[36]: among those, next-generation sequencing (NGS), which has the ability to sequence bacterial DNA, represents a modern and innovative diagnostic methodology which could be associated to standard serologic biomarkers to promptly and efficiently identify the PJI infecting organism. A modern PJI diagnostic protocol should aggregate clinical findings, serologic biomarkers and synovial fluid testing (including genetic).

Author statement

Giuseppe Toro, conceived of the presented idea, wrote the manuscript with input from all authors, performed data collection and analysis. Adriano Braile, conceived of the presented idea, performed data collection and analysis, wrote the manuscript with input from all authors. Emanuela Zappulo, performed data collection and analysis. Alfredo Schiavone Panni, were in charge of overall direction and planning. Pier Francesco Indelli, conceived of the presented idea, were in charge of overall direction and planning.

Declaration of competing interest

All author declare that they have no conflict of interest.

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Research paper

Validation of Harris hip score in the indian population

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ABSTRACT

Purpose: The purpose of this study is to validate the Harris hip score (HHS) in the Indian population.
Methods: In a prospective study, 310 patients (432 hips) were evaluated by two observers using HHS as the joint-specific outcome measure and Medical Outcomes Study 12-Item Short-Form Health Survey (SF-12v1) as a generic health measure. The HHS was tested against SF-12v1 for construct validity, criterion validity, test-retest reliability, inter-observer reliability, and internal consistency reliability.
Results: Multiple domains of HHS such as total score, pain, function, gait, activities of daily living and deformity showed ceiling effects. The SF-12v1 and HHS showed an acceptable level (0.04 at $P < 0.010$) of construct validity and criterion validity for total scores and function domain. The test-retest reliability and interobserver reliability were excellent with Goodman-Kruskal Gamma value of one. The internal consistency of the questionnaires was excellent with Cronbach's alfa coefficient of 0.743.
Conclusion: The HHS is reliable and responsive with acceptable construct and criterion validity, but it has high ceiling effects.

Credit author statement

This study was conducted in the Department of Orthopedics, Postgraduate Institute of Medical Education and Research, Chandigarh, India as a part of a dissertation submitted by Dr. Vanyambadi Jagadeesh for his M.S. degree in Orthopedics under guidance of Dr RK Sen and Dr S Aggarwal. The initial concept was prepared by RKS, SA, SKT and SKS. The data were collected by VJ, SKT and PS. The data were analyzed and statistical analysis was performed by SKS. The final draft was prepared by SKT, VJ and RKS. All the authors read the final manuscript and approved for publication.

1. Introduction

In the era of evidence-based medicine, the use of clinically relevant patient outcome measures in clinical research is paramount.[1,2] The Harris Hip Score (HHS) is one such measure which has frequently been used by health care providers to evaluate the functional outcome of the hip joint after a disease or following an intervention.[3,4] Sir William Harris in 1969 developed this score to evaluate the outcome of Smith-Peterson mould arthroplasty of the hip in young men who had been treated with this procedure for their long-standing secondary hip osteoarthritis.[5] Since then, the HHS has been validated (only construct validity and in arthroplasty patients-not with all psychometric criteria) in few western

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countries.[5,6] However, validation of this score in the Indian population is still lacking. The Indians are different from western patients with respect to their hip functional demands. The activities like squatting, cross-legged sitting and sitting on the floor are invariable and essential for Indians/Asians for cultural and social reasons.[7–12] These activities are not advisable after hip arthroplasty, and if we consider HHS as a specific outcome measure of arthroplasty, it seems an appropriate tool for hip function. However, HHS is now widely used for hip function outcome for all hip joint pathology and as an outcome measure of all types of hip intervention (arthroscopy, trauma, etc.).[3,4] Hence HHS needs validation in Indians/Asians with all types of hip joint pathology and interventions.

This study was designed to assess whether the HHS is a valid and reproducible measure for functional outcome evaluation of the hip joint in the Indian population or not. The self-administered generic questionnaire, the Medical Outcomes Study 12-item Short-Form Health Survey (SF12v1-abbreviated version of SF-36[13–17]), one of the most frequently used health status measures nowadays, was taken as the 'standard' measure for criterion validity in this study.

2. Materials and methods

2.1. Patient recruitment

A prospective, observational study was designed to evaluate the reliability, validity and responsiveness of the HHS. The inclusion criteria included the patients between 18 and 80 years with unilateral/bilateral hip pathologies who were on medical treatment or already had been operated. Any patient with systemic illness, neuromuscular disorder, spine disease or other lower limb pathology or history of previous surgery on other joints of the lower limb was excluded. The clinical hip evaluation was performed using HHS, and the health status of the patients was evaluated using SF12v1[18,19]. An orthopedic surgeon (who was not a part of the operating team), and a physiotherapist, independently evaluated the patients on separate occasions. The institutional ethics committee permission was obtained, and the patients were recruited after the informed consent.

2.2. Patient evaluation

Three hundred and ten patients with 432 hip pathologies were enrolled in this study. All 432 hips (cohort 1) were evaluated for HHS and SF-12v1 in the outdoor clinic. For test-retest reliability, 79 patients (108 hips) were re-evaluated within two weeks by both the surgeon and the physiotherapist using both the assessment tools. Ninety hips (cohort 2) were reassessed after 3 months (second clinical examination), 61 hips (cohort 3) were reassessed after six months (third clinical examination), and 51 hips (cohort 4) were reassessed after 12 months (fourth clinical examination). These follow up evaluations were performed to look for responsiveness and validity testing.

The mean age was 35.50 ± 10.872 years (range 20–75 years). The peak age group was between 20 and 35 years. There were 265 males (375 hips) and 45 females (57 hips). The right hip was involved in 103 patients; left hip in 85 patients, and both sides were involved in the remaining 122 patients. The distribution of the hip pathology as per the etiologies included 120 post-traumatic hips, 265 osteonecrotic-hips and 47 secondary arthritic hips. Of the 120 post-traumatic hips, 27 hips had received nonoperative treatment for femoral-head fracture-dislocation/acetabulum fractures, 86 hips had undergone open reduction and internal fixation of femur head/femur neck/acetabular fractures, and 7 hips had been treated with arthroplasty. In the osteonecrosis group, 162 hips were on medical treatment, 86 hips were operated with core decompression surgery, and 17 hips were treated with arthroplasty. Similarly, in patients with secondary arthritis, 31 hips were assessed preoperatively, 11 hips were assessed after total hip arthroplasty, and the other five patients were evaluated after miscellaneous surgical procedure. The postoperative hips were evaluated at least one year after the surgical intervention. The validity, reliability and consistency of HHS were tested against SF12v1 using Statistical Product and Service solutions version16.0 for Windows (SPSS Inc, Chicago, IL).

2.3. Validity

The floor and ceiling effects describe the frequency of extreme scores. The outcome instrument designed for severe disease or functional limitation may show ceiling effects if used for patients who are more functionally capable. Contrary to it, there may be floor effect if the outcome, designed to evaluate patients with less severe disease, are used for evaluation of more severe problem.[20–23] The ceiling effect is considered as acceptable if <15% of patients achieve the maximum score.[23]

Construct validity inspects the level to which the results from the questionnaire support the predefined hypotheses. The hypothesis in the current study was that patients who had high comorbidities, perceived poorer overall health status, or patients who had changed activities were considered as a poor outcome. This was evaluated by correlating the questionnaire scores with the characteristics of the patients (comorbidities, perceived overall health status, and changes in activities) as represented by changes in generic health questionnaires SF12v1. It was evaluated by Pearson's or Spearman's correlation between the total score of HHS with the domain of interest in SF-12v1. It was considered significant at the 0.1% level ($p < 0.001$). Construct validity was also tested for divergent validity and convergent validity in the domains and individual items using Pearson's and Spearman's correlation coefficients. The same domains in the outcome measuring tools should have a higher correlation (for example, pain in the HHS and the Bodily pain of Physical Component Summary) than with other domains, such as function. Regarding convergent and divergent validity for individual items (for example, two items gait and ADL of 'function' domain), the questionnaires should not correlate or have minimal correlation with each other (gait and ADL) reflecting that the questionnaires should evaluate the same area of interest but not interrelated.[20–23]

Criterion validity is present when the scores correlate with an accepted standard measure of the condition being evaluated. The Spearman rho for the criterion validity was acceptable if it was more than 0.40 and $p < 0.001$. The SF-12v1 is one of the best validated and commonly used general scoring system. Thus, SF-12v1 was used as the standard in the current study.

2.4. Reliability

Reliability is defined as the degree to which the measurement is free from measurement error. The total score, domains, and items were correlated with Pearson's and Spearman's correlation coefficient. Inter-observer reliability between the surgeon and the physiotherapist was also tested using Goodman-Kruskal's gamma, Pearson's and Spearman's correlations for items, domains, and total score of the HHS.

Internal consistency reliability was tested for the questionnaires and within the different domains of HHS and SF-12v1 using Cronbach's alpha coefficient. Cronbach alpha coefficient of >0.7 was taken as satisfactory.[24] Pearson's correlation coefficient was

used to compare the domains in HHS. The correlation was considered as poor if correlation coefficient (r) was <0.3, moderate if r was 0.3–0.6, good if r was 0.6–0.8, and excellent if r was >0.8.

2.5. Responsiveness

Responsiveness is the capability of a questionnaire to distinguish clinically important changes over time in groups[21-.4] The patients in this study were divided into groups based on age (<and ≥70 years), sex (male and female), total HHS score (<70 and ≥ 70) and hip disability based on Charnley classification (A or B; C excluded). Differences among these groups were evaluated using the Mann-Whitney *U* test.

3. Results

3.1. Validity

Floor and ceiling effects (Figs. 1 and 2)

There were few floor values, but several domains of HHS showed ceiling effects. The total score, pain, function, gait, ADL, and deformity showed ceiling effects (Figs. 1 and 2). The pain domain in HHS had a mean value of 38.61 (range 10–44; SD. 6.088) points with the 65th percentile showing the ceiling value of 44 points. The mean value of the function domain was 38.53 (range 4–52; SD. 10.284) with the 95th percentile showing the maximum 52 points. The 'ADL domain' (an important parameter) showed high ceiling effects with a mean value of 10.94 (SD 3.053) (Fig. 2). The mean score for deformity was maximum (3.77, nearly 100%) showing peak ceiling values.

Construct validity (Table 1)

The total HHS showed moderate correlation with SF-12v1, Physical Component Summary (PCS) and Mental Component Summary (MCS) ((Pearson's correlation coefficient r > 0.3 but < 0.6, SPEARMAN'S rho > 0.4, P < 0.001). The pain of HHS had moderate correlation with PCS-12 (Spearman's correlation coefficient r = 0.395, P < 0.001) and MCS-12 (r = 0.327,P < 0.001). Function domain also had moderate correlation with a Spearman's rho value of 0.493 and 0.418 with PCS and MCS respectively (P-value < 0.001).

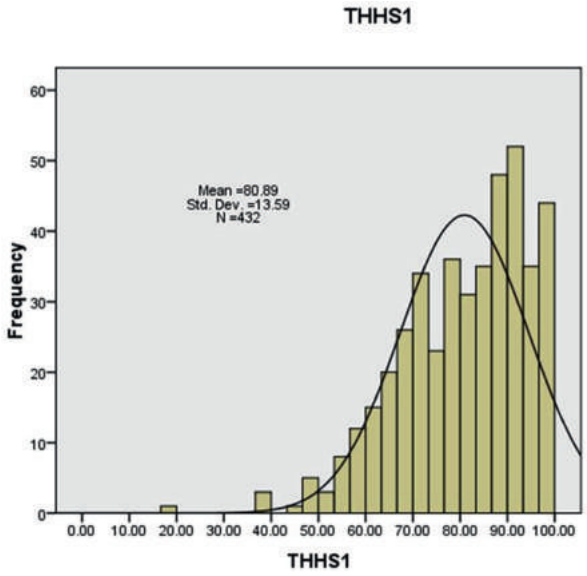

Fig. 1. Histogram for the total score of HHS showing high ceiling effect in 432 observations from the parent sample with a mean value of 80.89 and standard deviation of 13 reflecting that majority of the patients in the sample were scoring high (above 70).

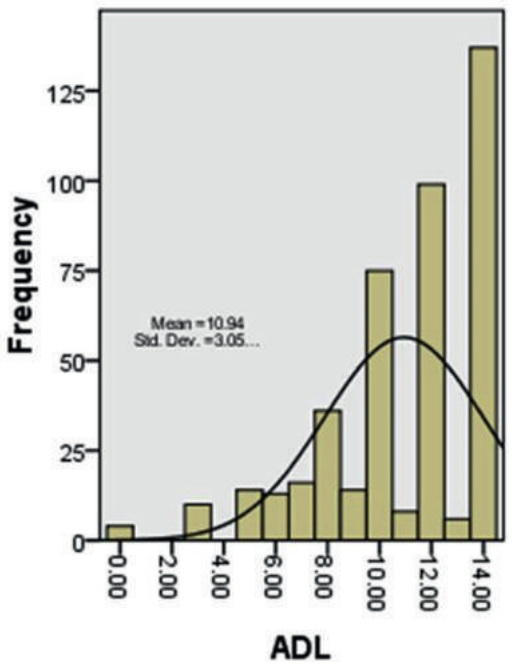

Fig. 2. Histogram showing high ceiling effects in activities of daily (ADL) living item, the maximum possible score was 14 with a mean value of 10.94 and standard deviation of 3.053 reflecting that majority of the patients in the sample scored nearly full points in activities of daily living.

The internal construct validity was tested for questionnaires in individual items of the function domain. The individual components of gait such as limp, support and distance walked had moderate correlations among themselves as shown by Spearman's correlation coefficient rho values of 0.422, 0.437, 0.464, respectively (P-value < 0.001, Table 2). The individual questionnaires for ADL such as stair climbing, tying socks and shoes, sitting on a chair and public transport had moderate correlations among themselves with a Spearman's rho values of 0.296, 0.315, 0.320, 0.346, 0.468, 0.470 at P-value < 0.001, indicating good divergent validity (Table 2).

3.2. Criterion validity

In the current study, the SF12v1 was taken as the standard measure. The data in the cumulative sample was negatively skewed, so Spearman's correlation was taken to test for content validity. The accepted level of correlation with the standard was Spearman's rho >0.40 and p < 0.001. In the present study, the total score and function domain of HHS had accepted level of correlation with SF-12v1 (Spearman's rho 0.564 for total scores and 0.500 for function domain at P-value < 0.001). Pain domain had rho values of 0.394, 0.335 and 0.327 with SF12v1, PCS-12, and MCS-12, respectively, which was below an acceptable level of criterion validity (P < 0.001).

3.3. Responsiveness

There was a gross difference between groups (P < 0.001) scoring < 70 and ≥ 70 in both HHS and SF12v1. There was no statistical difference (p > 0.05) between patients groups, divided as per age (<50 and ≥ 50 years) and gender (male and female), in the distribution of total score in both instruments. There was no statistical difference (p > 0.05) between the native and artificial hip group in the distribution of total score in both instruments. It

Table 1
Correlations between items, domains and total scores of HHS and SF12v1 measured with Spearman's Rho.

Spearman's Correlations										
		HHS	Pain	FUNCTION	GAIT	ADL	MOTION	Deformity	PCS	MCS	SF12V1
HHS	rho value	1.000									
	Sig. (2-tailed)	.									
Pain	rho value	.626**	1.000								
	Sig. (2-tailed)	.000	.								
FUNCTION	rho value	.896**	.277**	1.000							
	Sig. (2-tailed)	.000	.000	.							
GAIT	rho value	.857**	.251**	.967**	1.000						
	Sig. (2-tailed)	.000	.000	.000	.						
ADL	rho value	.771**	.265**	.831**	.673**	1.000					
	Sig. (2-tailed)	.000	.000	.000	.000	.					
MOTION	rho value	.548**	.357**	.433**	.377**	.461**	1.000				
	Sig. (2-tailed)	.000	.000	.000	.000	.000	.				
Deformity	rho value	.164**	.054	.070	.073	.059	.174**	1.000			
	Sig. (2-tailed)	.001	.258	.146	.131	.219	.000	.			
PCS	rho value	.520**	.335**	.486**	.444**	.462**	.276**	-.013	1.000		
	Sig. (2-tailed)	.000	.000	.000	.000	.000	.000	.793	.		
MCS	rho value	.453**	.327**	.395**	.335**	.429**	.206**	.067	.343**	1.000	
	Sig. (2-tailed)	.000	.000	.000	.000	.000	.000	.167	.000	.	
SF12V1	rho value	.564**	.394**	.500**	.439**	.512**	.263**	.048	.666**	.921**	1.000
	Sig. (2-tailed)	.000	.000	.000	.000	.000	.000	.319	.000	.000	.

**. Correlation is significant at the 0.01 level (2-tailed).
The total score of HHS had moderate correlation with the total score of SF12v1 (Gold Standard) with a Spearman's rho value 0.564, an acceptable level of criterion validity at P value < 0.001. The same level of correlation was found with individual PCS and MCS components with a Spearman's rho value 0.520 and 0.453. Function domain had Spearman's rho value 0.500, 0.486, 0.395 with SF12v1, PCS, and MCS respectively supporting an acceptable level of criterion validity. Pain domain had rho value 0.394, 0.335, 0.327 with SF12V1, PCS, and MCS respectively below an acceptable level of criterion validity at P value < 0.001. Motion and Deformity domain had poor or no correlation with any of PCS or MCS or SF12v1. PCS-Physical Component Summary, MCS- Mental Component Summary.

Table 2
Correlations between the individual components of items of HHS measured with Spearman's Rho for evaluating internal construct validity.

Spearman's Correlations								
		Limp	Support	Distance walked	Stairs	Socks & Shoes	Chair sitting	Public transport
Limp	rho value	1.000						
	Sig. (2-tailed)	.						
Support	rho value	.437**	1.000					
	Sig. (2-tailed)	.000	.					
Distance walked	rho value	.464**	.422**	1.000				
	Sig. (2-tailed)	.000	.000	.				
Stairs	rho value	.526**	.510**	.584**	1.000			
	Sig. (2-tailed)	.000	.000	.000	.			
Socks & Shoes	rho value	.472**	.326**	.345**	.470**	1.000		
	Sig. (2-tailed)	.000	.000	.000	.000	.		
Chair sitting	rho value	.187**	.207**	.300**	.296**	.346**	1.000	
	Sig. (2-tailed)	.000	.000	.000	.000	.000	.	
Public transport	rho value	.355**	.523**	.395**	.468**	.320**	.315**	1.000
	Sig. (2-tailed)	.000	.000	.000	.000	.000	.000	.

**. Correlation is significant at the 0.01 level (2-tailed).
The individual components of the Gait-limp, support, and distance walked had moderate correlations as shown by Spearman's correlation coefficient rho values 0.422, 0.437, 0.464, at P value < 0.001. The individual questionnaires for the activities of daily living-the stair climbing, tying socks and shoes, sitting on a chair and public transport had moderate correlations with a Spearman's rho values 0.296, 0.315, 0.320, 0.346, 0.468, 0.470 at P value < 0.001.

reflects that HHS shows the clinical results without the influence of an artificial hip similar to generic instruments like SF12v1. There was no statistical difference (P = 0.872) between Charnley groups A and B in the distribution of total score in HHS. However, in SF12v1, there was a statistically significant difference in total scores between patients with unilateral hip disease versus patients with bilateral hip diseases. It indicated that patients with the bilateral hip diseases had general health quality different from unilateral hip disease as reflected by a statistically significant difference in SF12v1 scores in these patients (P = 0.001).

3.4. Reliability

The test-retest reliability and inter-observer reliability were excellent for the total score of HHS (r = 0.877 to 0.999), pain domain (r = 0.862 to 0.996) and function domain (r = 0.911 to 1). In individual component of motions for test and retest reliability in two observations, there was only moderate to good correlations (for flexion r = 0.687, 0.661, for abduction r = 0.580, 0.545, for adduction r = 0.533, 0.410, for external rotation r = 0.650, 0.622, for internal rotation r = 0.474, 0.545) with p-value < 0.01. For inter-observer reliability as evaluated by the orthopedic surgeon and the physiotherapist in two observations, only flexion and external rotation had excellent correlation (r = 0.897, 0.946 for flexion, r = 0.824, 0.858 for external rotation); the rest of motions had only moderate to good correlation. The test and retest reliability for the total score was good for SF12v1 (r = 0.779).

Goodman-Kruskal Gamma of nearly 1 (total score = 1, pain = 1,

function = 0.997 to 0.998, combined ROM = 0.994 to 0.998) indicated high inter-observer reliability in total score, pain, function, and combined range of motion. For individual motions, only flexion and abduction motions had good inter-observer reliability (gamma = 0.890, 0.960 for flexion, gamma = 0.643, 0.930 for abduction).

The internal consistency among the individual components of HHS was acceptable (Cronbach's alpha of 0.743).

4. Discussion

Well-designed self-reported, patient-centred questionnaires are very useful for determining health traits. The rationale behind the present validation study was based on the concept that the outcome instrument was meant for a population for which it was originally designed.[20–23,25–28] For the outcome instrument to be used in a new population, it must be revalidated rigorously using all the psychometric criteria.[20–23,25–29] We observed, the HHS as a reliable and responsive outcome score for hip pathology with acceptable construct and criterion validity in the Indian population, but it has a high ceiling effect.

In the present study, we applied validity and reliability tests of HHS against SF-12v1. HHS is a joint-specific outcome instrument, whereas SF-12 is a measure of health-related quality of life (HRQOL).[30,31] The question arises, 'how come one can compare a joint-specific outcome measure with HRQOL measure?'. The HRQOL is a type of patient-reported outcome, which is today considered an important outcome of medical treatment and research. It is defined as the quantitative evaluation of the impact on subjective health and daily life function, caused by own health status, diseases, and symptoms.[18,19,26,27] Inclusion of isolated hip pathology in this prospective study indicated that the HRQOL of patients evaluated in this study was solely because of the hip problem and thus, genuinely assessed the impact of the disease on general health quality.

Another question that may arise is that 'why selectively SF-12 was chosen as the standard measure?' A study from Hong Kong found that SF-12 clarified a larger proportion of the variances of SF-36 scores among Chinese population.[30] Other studies have also revealed that the SF-12 summary measures well replicate the SF-36 summary measures, and demonstrate similar responsiveness to change.[31–35] SF-12 has been validated in a variety of population and also, in different ethnic and cultural groups.[13,14,19,30–40] SF-12 is short, easy to use with better patient compliance and responsiveness[18.] In this context, SF-12 fulfils all the requirements and hence, suitable for a standard measure.

We found several domains of HHS (total score, pain, function, gait, ADL, and deformity) that showed ceiling effects. The ability of a functional outcome measure to differentiate the relevant clinical improvements after any surgical intervention is important.[41] Ceiling effects may hide these differences as the patients have already scored the maximum possible score and cannot improve further on that score. This problem of HHS has already been highlighted in a systematic review by Wamper et al. They advocated that initially when HHS was proposed, it was meant to detect the outcome of Smith-Person mould arthroplasty in severe osteoarthritis of the hip secondary to acetabular fracture healing. Now, the improvement in implant designs and techniques have improved the outcome, and the indications of joint replacement are also broadened. They concluded that HHS needs modification with the improvement in implant design to counteract the ceiling effect. However, only a small fraction of patients in our study belong to the arthroplasty group, and we cannot agree fully (though it may be partially true) with the explanation of Wamper et al.[4] The use of HHS has widened, and it is now considered a universal tool for hip outcome evaluation for all types of pathology and intervention (trauma, injection, arthroscopy, etc.).[41] The perception of pain and functional demands for Indian population are different (as reflected in this study with ceiling effects observed in these domains).[42,43] As the pain tolerance capacity (based on the subjective component of pain) of Indians/Asians are good, they score high in this domain, and hence any intervention or treatment is unlikely to indicate the improvement in pain as per the points allocated to pain in HHS. Similarly, the ceiling effects, as observed in function and ADL in this study, were not surprising. The functional demands of Indian patients are high, and for daily activities like squatting, cross-legged sitting or sitting on the floor, it needs deep flexion and adequate abduction and external rotation of the hip. So, the less demanding hip functions (like tying shocks and shoe, sitting on the chair or public transport that do not need extreme of flexion, abduction or external rotation) included in function and ADL of HHS are of minor importance and can be performed even with diseased hip by an Indian. Therefore, they give maximum score preoperatively or before treatment and hence, any change in score after treatment or intervention is unlikely to be revealed in HHS.

Regarding construct validity, the total HHS, pain and function domains showed moderate correlation with SF-12v1, PCS and MCS. However, the deformity remained constant. The SF-12v1 and HHS showed an acceptable level (Spearman rho >0.04 at $P < 0.010$) of construct and criterion validity (for total scores and function domain, Cronbach alfa >0.7). The test and retest reliability and interobserver reliability were excellent (Goodman-Kruskal Gamma nearly one). The internal consistency was also acceptable with Cronbach's alfa coefficient of 0.743.

The original perspective of Harris[5] was that HHS is equally applicable to different hip problems and also to different methods of treatment. Till date, there is no validation study to support this original perspective of Harris. In the current validation study, the sample of observations included evaluation of varieties of traumatic and non-traumatic hip pathologies preoperatively and postoperatively in an attempt to support the versatility and comprehensive nature of HHS as a functional hip evaluation system for any hip problem, and as an outcome tool to evaluate different modalities of management (conservative, operative intervention, or arthroplasty). In this study, the responsiveness of joint-specific instrument HHS and generic health measure SF-12 was found almost equivalent when the patients were grouped as per their age, sex and total score. The hypothesis that a generic questionnaire would be more sensitive to changes in general health was supported by analyzing Charnley classification (unilateral hip patients differ in general health quality when compared to bilateral hip patients but on HHS there was no difference). The hypothesis that a generic questionnaire would show changes in general health based on gender was not supported in the present study, probably because of the small female cohort.

There are a few limitations in this study. SF-12, taken as a standard measure in this study has not yet been validated in Indians. We assume that the priorities of ADL are almost constant across Asia (China, Japan, Malaysia and India). The SF-12 has been validated in many Asian countries and is being used as a standard measure of HRQOL.[2,29,30,37–40] Thus, its use in the study as a reference measure is justified. Evaluation of the patients by multiple observers (more than 2) would have increased the reliability of HHS.

To conclude, The HHS is reliable and responsive with acceptable construct and criterion validity for evaluation of hip function among Indians, but it has high ceiling effects.

Role of authors

This study was conducted in the Department of Orthopaedics, Postgraduate Institute of Medical Education and Research, Chandigarh, INDIA as a part of dissertation submitted by Dr. Vanyambadi Jagadeesh for his M.S. degree in Orthopedics under guidance of Dr RK Sen and Dr S Aggarwal. The initial concept was prepared by RKS, SA, SKT and SKS. The data were collected by VJ, SKT and PS. The data were analyzed and statistical analysis was performed by SKS. The final draft was prepared by SKT, VJ and RKS. All the authors have read the final manuscript and approved for publication.

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Declaration of competing interest

Nothing to disclose.

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Correlation of measurements of hamstring graft used in ACL reconstruction with preoperative anthropometric measures among Indian males- A prospective study

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ABSTRACT

Background: Preoperative estimation of the Length and Diameter of the Semitendinosus (ST) and Gracilis (G) graft or hamstring graft can succor surgeons to choose appropriate grafts and plan the surgery. Our aim of the study is to test the hypothesis that anthropometric correlations do influence the thickness and length of the hamstring graft in Indian males.

Methods: Age, sex, height, weight, BMI, thigh-length, length, and thickness STG graft from 128 consecutive patients who underwent ACL reconstruction using STG graft was collected. Bivariate correlation analysis using Pearson's correlation coefficient (r) was used to test the strength and direction of relationships between the interval levels of variables.

Results: Thigh-length, the height of the patient had a positive correlation with the final length and diameter of the graft, the thickness of doubled, tripled, and quadrupled ST, doubled-G which was statistically significant ($p < 0.01$). BMI demonstrated a significant positive correlation with the total length of the hamstring graft ($r = 0.29$; $p = 0.001$) and also with the diameter of the doubled and tripled ST graft ($p < 0.01$). Lifestyle of patient had a positive correlation with final diameter of the graft ($F = 4.588$; $p = 0.012$), Length of the G graft ($F = 6.874$; $p = 0.001$), diameter of the doubled ST ($F = 6.182$; $p = 0.003$), triple ST ($F = 3.769$; $p = 0.0126$), quadrupled ST ($F = 8.029$; $p = 0.001$). While the Age and Weight did not correlate with graft thickness or length.

Conclusion: This study demonstrated that thigh-length, height, BMI, lifestyle had a positive correlation with the hamstring graft length and diameter whereas age and weight had no co-relation. Hence, we conclude the use of anthropometric measurements in the preoperative planning plays a role of in predicted length and thickness of STG graft and aid in preoperative planning and predict the possible need for alternate grafts in ACL reconstruction surgery.

1. Introduction

Rupture of the Anterior Cruciate Ligament (ACL) is amongst the most common ligamentous injuries of the knee.[1] Different surgical techniques using allograft, autograft like Semitendinosus–Gracilis (STG), bone-patellar tendon, quadriceps, etc are used for the reconstruction of a ruptured anterior cruciate ligament with excellent clinical results, but graft selection is still a controversial issue.[2–5] Semitendinosus–gracilis (STG) autograft are being used with an increasing frequency because of good clinical results, low donor site morbidity, and improved fixation methods.[6–9] However, Diameters and Lengths of autogenous STG show clinically significant anatomic variation.[10–12]

Pre-operative knowledge of the hamstring graft length and diameter is considered, not only of clinical importance but also of great value in assisting surgeons in making appropriate and

Abbreviations: ST, Semitendinosus; G, Gracilis; ACL, Anterior Cruciate Ligament; BMI, Body mass index.

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informed decisions regarding the graft choices. There are numerous occasions where surgeons are caught up intra-operatively with insufficient graft length or diameter required for appropriate reconstruction procedures. It is important to not only be prepared for obtaining alternate grafts on such occasions but also to counsel and obtain consent from the patient preoperatively. Therefore, pre-operative anticipation of the size of STG autograft can be beneficial for better preparedness of surgery. Preoperative anthropometric parameters of patients like height, weight, body mass index, and thigh-length are known to influence the size of hamstring graft but how each parameter influence is controversial.[13–16] Moreover, the influence of the lifestyle of patients based on his activity levels is not studied in the literature. Hence, the purpose of this study was to test the hypothesis that lifestyle and anthropometric variables like age, weight, Body Mass Index (BMI), Thigh-length of Indian males have a positive co-relation with thickness and length of STG graft.

2. Methods

A total number of 128 male patients with ACL tear visiting the Orthopaedics Department in our institution, from July 2018 to May 2020 were evaluated after taking institutional ethical committee approval. All skeletally mature male patients with isolated ACL tear proven clinically and radiologically with appropriate clinical tests and MRI were included in the study with prior consent. Female patients, children with open physis, the patient's undergone ACL reconstruction previously, patients with multiple ligamentous injuries, patients treated using grafts other than STG, and patients with neuromuscular diseases were excluded from this study.

Preoperatively, anthropometric measurements like Age, Height, BMI (Bone Mass Index), Thigh-length, etc were recorded for all patients included. Thigh-length was measured from the anterior superior iliac spine (ASIS) to the Superolateral border of the patella. Furthermore, we divided the lifestyle of patients into a sedentary, moderate, and active lifestyle based upon the overall daily physical activity that the person is involved in the workplace as well as in recreational sports. An office worker with no recreational sports or other physical activity was considered to have a sedentary lifestyle, whereas, a construction worker or sportsperson involved in rigorous physical activity most of the day was considered to have an active lifestyle. The patient was prepared for ACL Reconstruction using Semitendinosus and Gracilis graft.

The surgical technique for obtaining the grafts during the ACL reconstruction surgery consisted of a 2–3 cm vertical anteromedial incision on the proximal tibia, at the level of the insertion of Semitendinosus and gracilis muscles. Following this, the tendon of the STG muscle was dissected individually and was then de-inserted against the bone along with periosteum and removed using a graft stripper. After the removal of the attached muscle and fat, the length (cm) of the graft was measured using an autoclaved metal ruler. Ends of the tendon are whip-stitched using Non-absorbable 2-0 Ethibond suture. The diameters of the Semitendinosus and Gracilis grafts were measured using graft sizer available from ConMed/Stryker, which measured from range 3 mm–12 mm with 0.5 mm increments and the minimum diameter that allowed smooth passage of the entire graft completely was taken as the graft diameter [Fig. 1]. Doubled, Tripled and Quadrupled diameter of Semitendinosus tendon, and Doubled diameter of gracilis tendon was measured using graft sizer. Lastly, the final length and diameter of the two tendons were combined and measured. The final graft was prepared from a combination of doubled gracilis with either doubled or tripled ST graft (double-double or triple-double configuration). ACL reconstruction was done using a standard technique in which the femoral tunnel was drilled via accessory Antero-medial portal; the tibial tunnel was drilled using appropriate Tibial-Zig for anatomic single-bundle ACL reconstruction. The graft was fixed on the femur side using Endo-button and tibial side using an Interference screw (Titanium or Bio-absorbable).

All characteristics were summarized descriptively. For

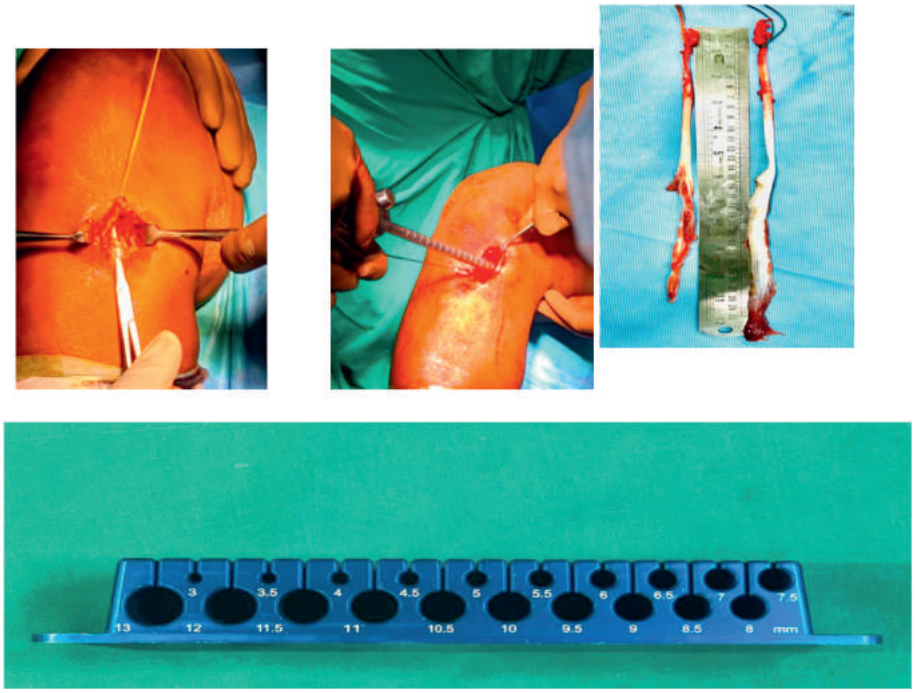

Fig. 1. Harvesting and measurement of the graft a) identification of STG b) harvesting ST with stripper c) measuring length of the graft using metal scale d) measuring diameter using graft sizer.

continuous variables, the summary statistics of mean ± standard deviation (SD) were used. For categorical data, the number and percentage were used in the data summaries and diagrammatic presentation. The difference between the means of analysis variables between two independent groups was tested by unpaired *t*-test. Bivariate correlation analysis using Pearson's correlation coefficient (r) was used to test the strength and direction of relationships between the interval levels of variables.

If the p-value was <0.05, then the results were considered to be statistically significant otherwise it was considered as not statistically significant. Data were analyzed using SPSS software v.23.0 and Microsoft office 2007.

3. Results

This study included 128 Indian males with a mean age of 30.86 ± 10.09 (range 17–52 years). The mean and SD of various preoperative anthropometric measurements were as follows: Weight 66.51 ± 7.93 (range 48–84 kg), Height 167.40 ± 6.33 (range 144–179 cm), BMI (23.74 ± 2.63 (range 17.7–32.4) and Thigh-length 50.01 ± 2.42 (range 41–58 cm) [Table 1].

After graft preparation, the mean length of Semitendinosus and Gracilis were 28.19 cm (±2.79 SD) and 22.43 cm (±1.24 SD) respectively. The mean diameter of the Semitendinosus graft after it was doubled, tripled, and quadrupled are 4.53 cm (±1.61 SD), 5.99 cm (±1.53 SD), and 7.06 cm (±0.86 SD) respectively. The mean graft diameter of gracilis when doubled was 3.85 cm (±0.84 SD). Triple-double configuration i.e tripled ST and doubled G was used in about 78% of the patients, double-double configuration was used in 18% and quadrupled-double configuration was used in 4% of patients. The mean length and diameter of the final graft prepared from STG were 8.14 (±0.56) and 8.04 (±0.67). 73.8% of patients had a final STG diameter of 8 mm or more, 26.2% of patients had a final STG diameter of less than 8 mm in which 14.3% of patients had a final diameter of 7 mm [Table 2].

Bivariate correlation analysis used to test the strength and direction of relationships between the variables showed that patient's height demonstrated a significant positive correlation with final length of the STG graft ($r = 0.26$; $p = 0.004$), length of the ST ($r = 0.49$; $p = <0.001$), the final diameter of the STG graft ($r = 0.21$; $p = 0.02$), and the diameter of the Semitendinosus when graft was doubled ($r = 0.23$; $p = 0.009$), tripled ($r = 0.22$; $p = 0.013$) and quadrupled ST ($r = 0.18$; $p = 0.05$) and diameter of doubled Gracilis graft (r = 0.22; p = 0.014). Thigh-length also showed a significant positive correlation with final STG graft length (r = 0.26, P = 0.003) and ST graft length (r = 0.47, P = <0.001), final diameter of STG graft (r = 0.22, P = 0.045), diameter of tripled ST graft (r = 0.22; p = 0.014)[Table 3]. Furthermore, BMI of patients demonstrated a significant positive correlation with ST length graft ($r = 0.21$; $p = 0.018$), G length ($r = 0.26$; $p = 0.003$) and the total length of the hamstring graft ($r = 0.29$; $p = 0.001$) and also with the diameter of the doubled Semitendinosus graft ($r = 0.18$; $p = 0.041$) and tripled Semitendinosus ($r = 0.24$; $p = 0.007$)[Table 3][Fig. 2]. There was also positive correlation between the lifestyle of patient with final diameter of the STG graft ($F = 2.866$; $p = 0.012$), diameter of the doubled Semitendinosus ($F = 6.182$; $p = 0.003$), tripled Semitendinosus graft ($F = 3.769$; $p = 0.0126$) and quadrupled Semitendinosus graft ($F = 8.029$; $p = 0.001$)[Table 4]. However, no statistically significant correlation between age and weight with hamstring graft length or diameter.

Table 1
Shows the mean values of the anthropometric parameters.

Descriptive Statistics	Range	Mean	SD
AGE (yrs)	17–73	30.86	10.09
WEIGHT (kg)	48–84	66.51	7.93
HEIGHT (cm)	144–179	167.40	6.33
BMI (kg/m2)	17.7–32.4	23.74	2.63
THIGH LENGTH (cm)	41–58	50.01	2.42
SD LENGTH	22–33	28.19	2.79
SD DOUBLED	0–5	4.53	1.61
SD TRIPLED	4–6.5	5.99	1.53
GR LENGTH	20–25	22.43	1.24
GD DOUBLED	3–5	3.85	0.84
FINAL DIAMETER	7–10	8.04	0.67
FINAL LENGTH	7–9	8.14	0.56

Table 2
Distribution of the final graft diameter.

Final Diameter (mm)	Number	Percent (%)
7	18	14.3
7.5	15	11.9
8	60	47.6
8.5	16	12.7
9	10	7.9
9.5	4	3.2
10	3	2.4

4. Discussion

The STG autograft is one of most preferred graft amongst the surgeons for ACL reconstruction. An ideal graft size to achieve successful outcome is controversial and not well defined in literature. Snaebjornsson et al.,[17] in a study of 2240 patients, with every increment of 0.5 mm in the STG graft diameter between 7 mm and 10 mm, the likelihood of a patient requiring revision surgery after primary ACLR was 0.86 times lower. Spragg et al.,[18] concluded that within the range of 7.0–9.0 mm, there was a 0.82 times lower likelihood of being a revision case with every 0.5-mm incremental increase in graft diameter. Conte et al.,[19] in their systematic review

Table 3
Correlation coefficient between study variable and demographic parameters among total cases.

Parameters	Age (yrs)		Weight (kg)		Height (cm)		BMI (kg/m2)		Thigh Length (cm)	
	r value	p value	r value	p value	r value	p value	r value	p value	r value	p value
ST LENGTH	0.07	0.431	0.11	0.228	0.49	<0.001*	−0.21	0.018*	0.47	<0.001*
DST DOUBLED	−0.12	0.175	−0.04	0.686	0.23	0.009*	−0.18	0.041*	0.16	0.069
DST TRIPLED	−0.11	0.232	−0.08	0.387	0.22	0.013*	−0.24	0.007*	0.22	0.014*
DST QUADRAPLED	−0.05	0.587	0.00	0.967	0.18	0.05*	−0.12	0.189	0.14	0.115
GR LENGTH	−0.05	0.545	−0.13	0.149	0.17	0.052	−0.26	0.003*	0.14	0.114
DGR DOUBLED	−0.10	0.268	−0.03	0.767	0.22	0.014*	−0.17	0.061	0.17	0.062
FINAL DIAMETER	−0.09	0.313	0.02	0.826	0.21	0.02*	−0.10	0.274	0.17	0.045*
FINAL LENGTH	0.01	0.947	−0.11	0.229	0.26	0.004*	−0.29	0.001*	0.26	0.003*

Note: * significant at 5% level of significance (p < 0.05), DST, DGR stand for the diameter of Semitendinosus and gracilis respectively.

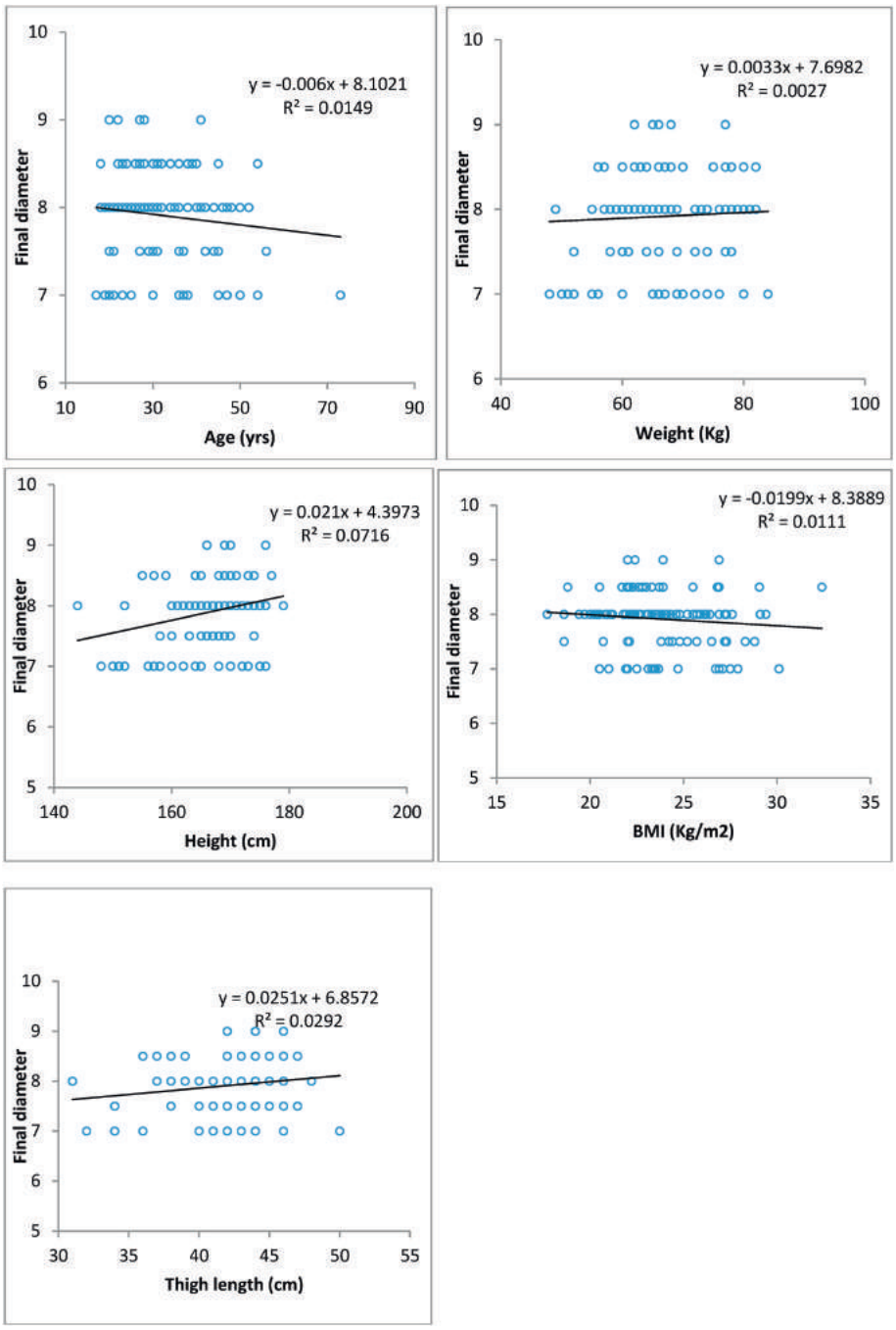

Fig. 2. Dot diagram shows the correlation of the final STG graft diameter with age, weight, height, BMI, and thigh-length respectively.

concluded that there was 6.8 times greater relative risk of failure for STG grafts ⩽ 8 mm in diameter. Magnussen et al.[20] in a study of 256 hamstring autograft used for ACL reconstructions, subdivided the number of revisions depending on graft size, they found that in grafts >8 mm the rate of revision ACL surgery was 1.7% (1 in 58 patients). On the other hand, when the graft size was 7.5 mm–8 mm, 9 of 139 patients (6.5%) required a revision ACL surgery, respectively, compared with 8 of 59 patients (13.6%) with grafts of ⩽ 7 mm in diameter. Various animal studies assessing graft strength have demonstrated that thicker graft (10 mm) failures are due to screw pull out, while smaller graft (8 mm) failures are associated with tendon rupture.[21] The grafts of smaller diameter may not be able to compensate when put under stress after ACL reconstruction.[22] So, if we are able to predict inadequate size of graft pre-operatively, it will not only help the surgeons to decrease the rate of revisions, also helps in preparing for alternate options of graft and better counselling of patients regarding the same. In our study, the final graft diameter varied between 7 mm and 10 mm, we aimed to get graft diameter of preferably more than 8 mm by varying configuration of STG graft, we found that 14% of patients were having diameter of less than 7 mm if quadrupled (doubled ST and doubled G) STG was used. We achieved graft diameter of 7 mm or above by having configuration of tripled ST with doubled G in these patients. So most commonly used configuration in our study was tripled ST with doubled gracilis which accounted for 78% of the patients. In our study, we tried to correlate, analyze and further add

Table 4
Comparison of Mean length by Activity.

Parameters (Mean ± SD)	LIFESTYLE BASED ON DAILY ACTIVITY			F value	p value
	SEDENTRY	MODERATE	ACTIVE		
ST LENGTH	28.03 ± 1.83	27.7 ± 1.83	28.33 ± 1.77	0.749	0.475
DST DOUBLED	22.11 ± 1.19	21.5 ± 0.71	22.69 ± 1.24	6.182	0.003*
DST TRIPLED	3.64 ± 0.35	3.75 ± 0.49	3.96 ± 0.69	3.769	0.026*
DST QUADRAPLED	5.19 ± 0.45	5.35 ± 0.58	5.6 ± 0.53	8.029	0.001*
GR LENGTH	6.25 ± 0.53	6.5 ± 0.82	6.69 ± 0.6	6.874	0.001*
DGR DOUBLED	3.83 ± 0.36	3.75 ± 0.35	3.86 ± 0.31	0.561	0.572
DGR TRIPLED	4.53 ± 0.21	4.55 ± 0.16	4.53 ± 0.31	0.037	0.963
FINAL DIAMETER	7.79 ± 0.63	7.85 ± 1.08	8.17 ± 0.6	4.558	0.012*
FINAL LENGTH	8.03 ± 0.45	8.1 ± 0.47	8.26 ± 0.59	2.866	0.061

to the knowledge in the available literature with respect to finding a correlation of length and thickness of hamstring graft used, with preoperative Anthropometric measures. We assent to the hypothesis that anthropometric variables do have a predictive influence on the thickness and the length of the hamstring graft obtained. However, influence of each variable may vary.

Ma et al.,[12] stated height was significant factor to determine graft diameter, although they found that height correlated with graft diameter only in men population. *Boisvert* et al.[23] also concluded height remains the most significant measurement for the prediction of quadrupled hamstring diameter. *Tuman* et al.[16] showed that height is the best predictor among Anthropometric data in hamstring graft size. In our study, mean height was 167.40 ± 6.33 cm, and range [144–179 cm] which was lesser, compare to various studies of western population and it was statistically significant predictor not only with the final diameter and length of the hamstring graft but also diameter of Doubled Tripled and Quadrapled ST. Mean length of ST was 25.19 ± 1.64 cm which gave us final length of at least 7–8 cm length when tripled which was adequate for fixing the graft. By multiple regression analysis equations, height of less than 150 cm which constituted about 8% of our patients had significant risk of having graft diameter of less than 7 mm.

We found no correlation of patient's age with hamstring graft length or diameter. In this study patients evaluated were from age group of 17–56 years, with a mean age of 30.86 ± 10.09 years, which was found in accordance with others studies conducted by *Pichler* et al.,[11] *Ma* et al.,[12] *Schwartzberg* et al.,[14] *Treme et* al[15], *Boisvert* et al.,[23] and consistently found that age is not related to graft size.

Correlation of the final graft length and diameter with Body Mass Index (BMI) is controversial. In a study of 50 patients, who underwent ACL reconstruction, by *Treme* et al.[12] suggested that the best predictor of graft diameter appears to be patient weight, followed by BMI. The patients with graft diameter less than 7 mm had BMI of less than 18 kg/m^2; However, BMI of less than 18 kg/m^2 did not predict who had graft diameters of less than 7 mm. They suggested that patients with a higher BMI and larger thigh circumference could be expected to have grafts of large diameter. *Tuman* et al.[8] concluded that BMI does not appear to accurately predict hamstring diameter and should not be relied upon before harvesting. They suggested that lean body mass may be a better predictor of hamstring tendon graft diameter that is, heavier persons with greater lean body mass and greater muscle strength would likely have larger diameter tendons than a heavier person with less lean body mass and weaker muscles. The findings in our study is similar to *Tuman* et al.,[8] though BMI had positive correlation with diameter doubled and tripled ST, it had no correlation with final diameter.

There are limited studies in literature correlating lifestyle of the patient with graft dimensions. *Treme* et al.[8] suggested that activity level of the patient had no correlation with graft dimensions, suggesting athleticism does not effect hamstring tendon size. In our study, the mean diameter of the graft in sedentary, moderately active and active lifestyle were 7.79 ± 0.63, 7.85 ± 1.08 and 8.17 ± 0.6 respectively. We found that lifestyle had a significant correlation with the final diameter of the graft (F value = 4.558, and p value = 0.012) i.e patients with active lifestyle tend to have larger sized graft when compared to the one with sedentary lifestyle.

Thigh length measurements also help in evaluation of graft length and diameter. *Goyal* et al.[24] found Thigh length significantly correlating with graft length ($r = 0.44$, $p < 0.001$), and quadruple diameter ($r = 0.35$, $p = 0.002$). They concluded thigh-length can be used as a sensitive tool for the prediction of graft length and diameter. *Treme* et al.[12] found strong correlations for graft lengths with thigh length measurement. Shorter persons with shorter leg, thigh, and shank lengths tended to have shorter gracilis and Semitendinosus grafts. Similarly, *Schwartzberg* et al.[11] also found a strong correlation between thigh length and hamstring length ($r = 0.73$, $P < 0.001$), however, thigh length ($r = 0.42$, $P < 0.001$) had only moderate correlations with graft diameter. In our study, we too found that thigh length had a strong co-relation with graft length and diameter. By multiple regression analysis equations, thigh length of less than 42 cm had significant risk of having graft diameter of less than 7 mm.

Limitations of this study are exclusion of females. This is because female patients undergoing ACL reconstruction in our institution were very few and thus gender based correlation could not evaluated. The percentage of body fat and lean body mass was not taken into consideration which would have better indicator than BMI measurement of the graft was done using the increment of sizer 0.5 mm and better callipers could have been used for more accurate measurement. Even though all grafts were taken by fellowship trained experienced surgeons, there could be minor variation in graft harvesting technique and defining ends of graft.

On the basis of above discussion, it has been observed, that anthropometric data in Indian males do influence the hamstring graft length and diameter but different parameter influence it in different manner. Thigh length, height, lifestyle had a positive correlation with the hamstring graft length and diameter whereas age, BMI and weight had no co-relation. In simple words a tall patient with active lifestyle tends have larger diameter and short obese/malnourished male with sedentary lifestyle tends to have smaller graft. By multiple regression analysis equations, Height less than 150 cm, thigh length of less than 42 cm had significant risk of having graft diameter of less than 7 mm. Hence, we conclude the use of anthropometric measurements in the preoperative planning plays a role of in predicting length and thickness of STG graft and aid in pre operative planning and predict possible need for alternate grafts in ACL reconstruction surgery.

Credit author statement

Nuthan Jagadeesh: Conceptualization, Methodology, Validation, Formal analysis, Investigation,Resources, Data curation, Writing - original draft, Writing -review & editing, Visualization, Supervision, Project administration. **Vishwanath M Shivalingappa**: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Data curation, Writing -review & editing, Supervision. **Tushar Dhawan**: Methodology, Validation, Data curation, Investigation, Writing - original draft, Writing - review & editing. **Arjun Mandri:** Investigation, Data curation, Writing - review & editing.

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Research paper

A CT based evaluation of femoral and tibial tunnel widening after double bundle ACL reconstruction

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ABSTRACT

Introduction: Among the postoperative phenomenon of ACL reconstruction, tunnel enlargement has been reported consistently, regardless of the technique used. It could be clinically relevant in post operative follow up and revision surgery. This study evaluated the magnitude of tibial and femoral bone tunnels enlargement after arthroscopic double-bundle anterior cruciate ligament (ACL) reconstruction by the Computed Tomography Scan.

Methods: Forty patients undergoing arthroscopic double-bundle ACL reconstruction using multistranded hamstring graft, were included in the study. CT scan was performed on second postoperative day and at follow-up of 6 month. Tunnels were evaluated by digitally measuring the widths, perpendicular to the long axis of the anteromedial (AM) and posterolateral (PL) tunnels, on an oblique coronal, saggital and axial plane at 3 levels: aperture, midway, and suspension point. Bony bridge thickness at aperture and minimum distance between two tunnels to anticipate communication was also computed.

Results: Femoral tunnel measurement showed statistically significant enlargement at aperture and midway. At the aperture, enlargement of AM and PL tunnel was 21.95% and 26.16% whereas at midway, enlargement was 20.05% and 24.5%. At the suspension point, enlargement was 3.97% and 7.1%. On tibial side, order of significant enlargement was midway of AM = 21.16% and PL = 31.78% followed by aperture of AM = 18.9% and PL = 28.84% and finally suspension point of AM = 17.84% and PL = 25.21%. Average bony bridge thickness at femoral and tibial aperture was 0.291 ± 0.059 and 0.231 ± 0.105 cm respectively with 10% of the patients showed merging of tunnels at aperture.

Conclusion: CT scan is an effective way to determine the tunnel position and enlargement after ACL reconstruction. There is a significant widening of femoral and tibial tunnels at 6 months follow-up of arthroscopic double bundle anterior cruciate ligament reconstruction. Tunnel widening could be a serious problem after double-bundle ACL reconstruction.

1. Introduction

Bone tunnel widening is a well-known phenomenon after reconstruction of the Anterior Cruciate Ligament with autologous tendon grafts.[1,2] It was first observed in the early 1990s with bone-patellar tendon-bone grafts[3] and until now, the exact mechanism of tunnel expansion and the long term outcome of this phenomena has not been fully understood. Previous literature suggests that the phenomena of tunnel widening could be due to biological and biomechanical factors.[4–7] Biologically, tunnel enlargement could be seen due to bone resorption caused by raised level of osteolytic cytokines (IL-1β, IL-6, IL-8, TNF-α, bone morphogenetic proteins and nitric oxide) in the synovial fluid,[1,5,8–11] foreign body immune response and heat necrosis as a drilling response.[12] Biomechanically, tunnel enlargement could be due to repeated longitudinal movement of graft in bone tunnel while mobilizing the knee joint (bungee-cord effect),[5,7,13] redirecting forces at the tunnel aperture,[14] graft fixation in relation to the joint line,[15] stress deprivation of bone within the tunnel wall, improper graft tunnel placement and aggressive rehabilitation.[7,16–19] The synovial bathing effect could also be associated to tunnel enlargement, as, the synovial

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fluid might swim into the space between the autologous graft and tunnel wall and thus alter the graft's biological fixation.[20]

Tunnel widening might be clinically relevant in revision surgery because the enlarged tunnels may complicate graft placement and fixation[1,2] and in double bundle ACL reconstruction as there are chances of tunnels getting merged. There are more concerns regarding a revision ACL reconstruction following the double-bundle reconstruction because of the potential need for a staged reconstruction in which the tunnels are bone grafted first, followed by the actual revision surgery performed after the bone graft has been incorporated.[21] Tunnel communication in double-bundle ACL reconstruction could also occur while drilling the tunnels, if the tunnels are placed too close to each other.[22,23] For evaluation, Digital radiography has been considered a reliable method for measurement of bone tunnel widening since long, but Computed tomography scan enables more accurate measurement of tunnels in multiple planes. The purpose of this study was to assess the magnitude of enlargement of tunnels and minimum distance between the two anatomically placed anteromedial and posterolateral tunnels on the femur and tibia with help of CT-Scan in arthroscopic double-bundle ACL reconstruction surgery using multi-stranded autogenous hamstring grafts.

2. Material and methods

2.1. Patients

A total of forty patients with ACL tear who met the inclusion criteria were included in this prospective study and underwent double bundle anterior cruciate ligament reconstruction. 34 patients were male and 6 were female. The age of the patients ranged from 20 to 42 years. Patients less than 18 or more than 50 years of age were excluded from the study. Also, patients with multi ligament injuries and those who had previous knee surgeries were excluded. The surgeries were done by an experienced surgeon. Autologous multistranded hamstring graft was used in all the cases as ACL substitute. The fixation method on the femoral side was titanium endobutton (Endobutton CL, S&N) and on the tibial side bioabsorbable interference screws were used.

Post operatively, all the knees were placed in knee immobiliser with full extension. On the first post operative day, patients were allowed progressive weight bearing and isometric exercises for muscular strength were initiated. At two weeks, 90° ROM was achieved. At 4 weeks post surgery, knee immobiliser and crutches were removed and full ROM was advised. After 2 months, brisk walking followed by jogging was allowed. At 6 months, running was allowed with return to sports activities.

2.2. CT-scan assessment

CT-Scan of the knee was performed on helical (spiral) multidetector scanner (Somatom definition AS, 128 slice) with 0.625 mm-thick slices and 0.6 mm incrementation using bone and standard algorithm by placing the patient in the supine position without the administration of intravenous contrast.

Two-dimensional multiplaner images were created on the workstation by use of bone (Osteo) algorithm on oblique coronal, oblique saggital and oblique axial planes. Bone tunnels diameter were measured perpendicular to the axis of tunnel in the oblique coronal, oblique saggital and oblique axial planes. Diameter were assessed at three level in all three planes, the aperture (AM3 and PL3 in femur and AM1and PL1 in tibia), the furthest point (proximal suspension point AM1 and PL1 in femur and distal point AM3 and PL3 in tibia) and midway between aperture and furthest point (AM2 and PL2 in both femur and tibia). All CT measurement were done at workstation. Bony bridge thickness was evaluated at aperture of femoral and tibial tunnels. Minimum distance between two tunnels at any level was also measured (Fig. 1A–F).

The reference tunnel diameter measurements were taken as follows:

FAM = Average Femoral anteromedial tunnel diameter (oblique saggital, coronal and axial), FPL = Average Femoral posterolateral tunnel diameter (oblique saggital, coronal and axial), 1 = suspension point, 2 = midway and 3 = aperture in femoral tunnels, TAM = Average Tibial anteromedial tunnel diameter (oblique saggital, coronal and axial), TPL = Average Tibial posterolateral tunnel diameter (oblique saggital, coronal and axial), 1 = aperture, 2 = midway and 3 = suspension point in tibial tunnels.

3. Statistical analysis

The Wilcoxon test was used to compare the amount of tunnel enlargement with the CT findings at 2nd post operative day. Significance was reported at the 95% confidence level ($P < 0.05$). For Difference with means, *t*-test was used for normally distributed data. Data analysis was done with SPSS version 20 software. Qualitative data was expressed in percentages. Quantitative data expressed in means, median, and standard deviation.

4. Result

In our study, forty patients underwent double bundle ACL reconstruction with average age of 26.4 years (youngest was 20 years and oldest was 42 years). Majority (70%) of patient were below 30 years of age. During ACL reconstruction, average intra-operative drill size used for AM and PL femoral and tibial tunnels were 7.1 mm and 5.6 mm respectively. There was high Inter-observer and Intra-observer reliability on CT measurements. On evaluation, CT-Scan at 2nd postoperative day showed almost uniformly cylindrical tunnels. The average diameter (oblique saggital, oblique coronal and oblique axial) of tunnels at different level (aperture, midway, suspension point) on both femoral and tibial side were measured (Table 1). CT scan at 6 months showed femoral tunnels to be funnel shaped and tibial tunnels being barrel shaped. On comparison between CT scan on second post operative day and CT scans measurements at 6 months, the femoral and Tibial tunnel diameters showed a progressive increase in size at all levels. Femoral tunnel measurement showed statistically significant enlargement at aperture and midway. At aperture, enlargement of AM tunnel was 21.95% ($p = 0.001$) and that of PL tunnel 26.16% ($p = 0.001$). At midway, enlargement was of 20.05% ($p = 0.002$) of AM and 24.5% ($p = 0.003$) of PL tunnel. At suspension point, enlargement of AM tunnel was 3.97% ($p = 0.344$) and that of PL 7.1% ($p = 0.200$) which not significant statistically. Tibial tunnel measurement showed statistically significant enlargement in both AM and PL tunnel diameter at all three levels. Maximum enlargement was seen midway with AM enlargement of 21.16% ($p < 0.001$) and PL of 31.78% ($p < 0.001$) tunnels. At aperture, enlargement of AM tunnel was 18.9% ($p < 0.001$) and that of PL tunnel was 28.84% ($p = 0.001$). Suspension point showed least dilatation with AM tunnel dilatation of 17.84% ($p = 0.002$) and PL tunnel of 25.21% ($p = 0.003$). (Table) Average bony bridge thickness at femoral and tibial aperture was 0.291 ± 0.059 cm and 0.231 ± 0.105 cm respectively. 10% of the patients showed merging of tunnels at apertures.

4.1. Short term clinical follow up

There were no significant post operative complications. There

were no gross laxity, instability, flexion contracture or need of support for ambulation post surgery. The mean pre-operative Lysholm's score was 61.4/100. At the end of one year, the mean Lysholm's score was 91.07. The IKDC 2000 subjective knee score improved by a mean of 36.4 at the end of one year. Clinical result was not co related with tunnel widening because of less number of patients and short duration of follow up.

5. Discussion

The principal findings of this study were as follows: (1) The percentage widening of the femoral AM tunnel at aperture, midway and suspension point was 21.95, 20.05 and 3.97% and that of femoral PL tunnel was 26.16, 24.5 and 7.1%. Tibial AM tunnel showed 18.9, 21.16 and 17.84% and the PL tunnel showed 28.84, 31.78 and 25.21% widening at aperture, midway and suspension point. (2) The tibial PL tunnel showed significantly more widening as compared to the other tunnels. (3) Femoral tunnel showed maximum widening at the aperture level while the tibial tunnels showed maximum widening at middle. (4) Minimum widening, among all the tunnels, was at suspension point of femoral AM tunnel.

Bone tunnel widening is a well recognized complexity after ACL reconstruction.[20] A large common AM-PL bone tunnel at the joint line with bone loss might result in primary stability problems, as well as fixation problems with revision surgery.[23] Different authors have proposed different theories and used different type of adaptation in their technique of ACL reconstruction to prevent the widening phenomena. In a review of literature, Hoher et al. had discussed about aetiology as well as possible adaptive measures for preventing bone tunnel widening and concluded that prevention of bone tunnel enlargement could be achieved by a more anatomical initial graft fixation that results in lesser longitudinal motion of the ACL graft in the bone tunnel under cyclic loading conditions (bungee-effect) compared to graft fixation away from the normal anatomic attachment sites (suspensory fixation).[24]

Siebold et al.[23] analysed the tunnel widening in double bundle ACL reconstruction done via low accessory AM portal. They found tunnel widening of femoral AM and PL tunnel to be 34 and 46%. Tibial tunnel widening of AM and PL tunnel was 20 and 38%. Their results showed more tunnel enlargement than our study except in tibial AM tunnel where the result were similar. They also found PL

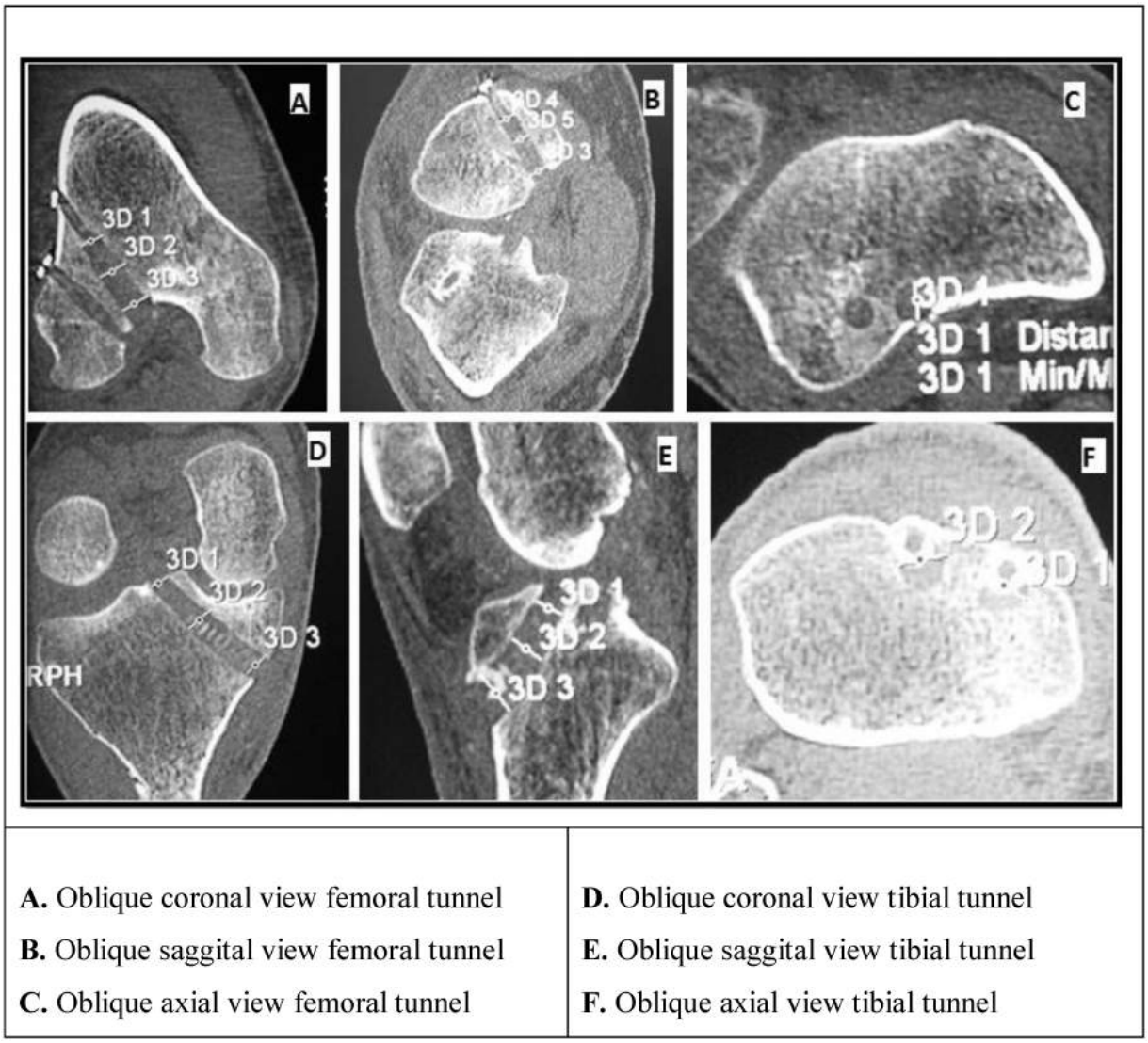

Fig. 1. A. Oblique coronal view femoral tunnel, B. Oblique saggital view femoral tunnel, C. Oblique axial view femoral tunnel, D. Oblique coronal view tibial tunnel, E. Oblique saggital view tibial tunnel, F. Oblique axial view tibial tunnel.

Table 1
Femoral and Tibial tunnel Diameters.

Tunnel	Intra-Operative Drill Size (cm) (Mean ± S.D)	Tunnel Diameter At Post-Op Day 2 (cm) (Mean ± S.D)	Tunnel Diameter At 6 Month (cm) (Mean ± S.D)	p-value	Percentage Enlargement
FAM1	0.71 ± 0.073	0.729 ± 0.076	0.758 ± 0.101	0.344	3.97%
FAM2		0.728 ± 0.074	0.874 ± 0.045	0.002	20.05%
FAM3		0.729 ± 0.073	0.889 ± 0.103	0.001	21.95%
FPL1	0.56 ± 0.084	0.577 ± 0.086	0.618 ± 0.079	0.200	7.1%
FPL2		0.575 ± 0.085	0.716 ± 0.089	0.003	24.5%
FPL3		0.577 ± 0.084	0.728 ± 0.084	0.001	26.16%
TAM1	0.71 ± 0.073	0.741 ± 0.075	0.881 ± 0.066	<0.001	18.9%
TAM2		0.742 ± 0.073	0.899 ± 0.087	<0.001	21.16%
TAM3		0.740 ± 0.072	0.872 ± 0.093	0.002	17.84%
TPL1	0.56 ± 0.084	0.579 ± 0.071	0.746 ± 0.081	0.001	28.84%
TPL2		0.579 ± 0.071	0.764 ± 0.123	<0.001	31.78%
TPL3		0.579 ± 0.071	0.725 ± 0.117	0.003	25.21%

tunnels widening to be more when compared to AM tunnels. In this study communication of the bone tunnels occurred in 41% of patients. Beyaz et al.[33] compared tunnel widening between single and double bundle ACL reconstruction. Comparing the AM tunnel, they found more widening in double bundle as compared to single bundle ACL reconstruction. Achtnich A et al. performed a comparative study between double bundle and single bundle ACL reconstruction with hybrid fixation technique and evaluation done on MRI at 6–8 month. Similar to our study, there was significant ($P < 0.001$) average tunnel widening (38%–42%) in all bone tunnels in both groups, but percentage of enlargement slightly higher than our study. 2 cases in that study showed tibial tunnel communication at follow-up.[30]

Sabat et al.[3] compared the tunnel widening in ACL reconstruction using transfix versus endobutton for femoral fixation of the graft. They found femoral tunnel widening was significantly less in the Transfix group when compared with the EndoButton group in ACL reconstruction. They also found a decrease in tunnel widening at level of tibial tunnel aperture, when bio-screw tip–to–joint line distance was 10–15 mm, and suggested that probably aperture fixation increases synovial fluid tracking into tibial tunnel and lead to widening. Comparison between use of hamstring and patellar tendon autograft in ACL reconstruction for tunnel widening was done by Webster et al. They proposed that the bone chunk of patellar tendon autografts acts as a bone graft and releases osteoinductive protein into the bone tunnel and thus reduces the tunnel widening.[25] Clatworthy et al. observed no enlargement in the patellar tendon group and marked enlargement in the hamstring group when femoral side fixed with suspensory fixation method and concluded that graft fixation has a subtle effect on tunnel enlargement.[26,27]

In co-relation between tunnel widening and rehabilitation, Murty et al. suggested that immobilisation, for initial postoperative 2 weeks, showed correlation with increased tunnel widening.[28] Iorio R et al. noted, less aggressive rehabilitation protocol resulted in an acceptable rate of tunnel enlargement.[20] Yu and Paessler,[19] Clatworthy[26,27] and L'Insalata et al.[29] suggested that following a non-aggressive rehabilitation protocol resulted in marked reduction of micro motion of the graft in the tibial tunnel, thus reducing the synovial tracking and osteolytic cytokines level in synovial fluid and hence lesser tunnel widening.

In our study, intraoperative drill size were closely matched with 2nd day post-operative CT measurement, similar results were seen by Iorio R et al.,[20] whereas, Achtnich A et al. showed slight increase in the diameter.[30]

Average bony bridge thickness at femoral and tibial aperture was 0.291 ± 0.059 cm and 0.231 ± 0.105 cm respectively in our study. Our results of femoral tunnels are similar to the bony bridge thickness of 0.29 ± 0.11 cm as found by Basdekis G et al.[31] The bone bridge thickness varies according to the respective tunnel diameter and placement of PL tunnel. Thus the standard deviation shows some variability in tunnels position. Around 10% of our patients showed merging at femoral and tibial aperture.

Studies demonstrate that measuring bone tunnels by X-ray can result in underestimating the real diameter of tunnel enlargement and CT scanning has been recommended for evaluating the dimension of the bone tunnels.[4,20,25,32] CT scan has been shown to be an effective and reliable technique to analyse tunnel position and dimensions after ACL reconstruction.[32] We measured the tunnel dimensions in three planes i.e oblique coronal, saggital and axial and then calculated the mean value. It provided us the tunnel data in entirety and not just based on information from one cut view. Different regions of the tunnel were assessed separately for widening and all aspects of the tunnel were observed. This is the strength of this study.

However, our study has limitations too. Firstly, the small number of sample size. Secondly, the surgeries were performed by a single surgeon. A particular technique of drilling tunnels can affect the position and hence widening of the tunnel in future. Finally, we did not get the CT scans of the patients done at 1 year of follow up to limit the radiation exposure. It might have shed more light on final status of the tunnel and whether tunnel dilatation occurs up to 1 year after surgery or not.

6. Conclusion

To conclude, there was significant widening of femoral and tibial tunnels at 6 month postoperatively, after arthroscopic double bundle anterior cruciate ligament reconstruction using autologous hamstring graft and fixation done with endobutton at femoral side. Margin of errors were present in our technique in tunnel placement showed by merging of femoral and tibial tunnels at some level. CT scan evaluation for tunnel widening post anterior cruciate ligament reconstruction provides a much better description of the when compared to radiographs. It is a reliable and reproducible method to ascertain tunnel position and dimension. We recommend CT imaging as a tool for post operative tunnel analysis after ACL reconstruction.

Credit author statement

Saurabh Dutt – writing-original draft preparation, visualisation. Shekhar Tank – Data curation, project administration. Rakesh Sehrawat – Formal analysis. Dhananjaya Sabat – writing –review and editing. Vinod Kumar – Conceptualization, methodology, investigation.

Declaration of competing interest

The authors report no conflict of interest. Authors have no financial aid to declare.

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Research paper

Combination of chondroitin sulfate and hyaluronic acid increases amount of fibroblast, collagen and decreases adhesion of achilles tendon after repair

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ABSTRACT

Background: This study was designed to evaluate the effects of chondroitin sulfate (CS) combined with hyaluronic acid (HA) on rat's post surgically repaired achilles tendon rupture at 21 day post injury.
Methods: Achilles tendon of 28 male rats *(Rattus Novergicus var wistar)* were cut and repaired by modified Kessler technique and circular cast were applied after repair. Samples were allocated into four test group: group 1 as control had a simple tendon repair, group 2 which had hyaluronic acid administered at repair site, group 3 which had chondroitin sulfate per orally and group 4 which had combination of chondroitin sulfate per orally and hyaluronic acid administration at repair site. The rats were sacrificed at 21 days post-op and tendons were evaluated histopathologically to count the amount of fibroblast, peritendon adhesion (using microscopic Tang scoring system) and quantitative amount of collagen using colorimetric analysis.
Results: Treatment groups (groups 2, 3, and 4) had a significantly increased amount of fibroblast ($p < 0.05$) and group 4 had significantly increased tendon healing time proved by abundant fibroblast transformed to tenocyte compared to other groups. In group 4, peritendinous adhesion significantly reduced ($p < 0.05$) and there were significantly increased amount of collagen in treatment groups compared to control group ($p < 0.05$) analyzed by colorimetric.
Conclusions: These findings suggest that a combined treatment of chondroitin sulfate and hyaluronic acid could be an effective therapeutic regime in restoring the morphological properties of achilles tendon in rats model, and might provide useful knowledge for future clinical trial studies in tendon ruptures.

1. Introduction

Achilles tendon rupture is one of the most feared injuries causing a significant disability for athletes. Epidemiologic study in America on 2013 reported 406 cases of achilles tendon rupture on general population in America; 275 cases (68%) were caused by sports injury. Basketball caused most of these cases of all sports injuries, followed by tennis and soccer.[1] Another study showed from 1988 to 2011, from 18 NBA players (National Basketball Association) whom suffered from Achilles tendon rupture and had the tendons repaired, 7 players were retired from NBA, 1 player played for 1 season only and the rest only played for 2 seasons. This fact indicates that Achilles tendon rupture caused a significant decrease in athletes performances and can jeopardize the athletes professional career.[2] The management of Achilles tendon rupture on athletes requires a period of time, including rehabilitation time between 6 months until 1 year.[2] Passive and active exercise during rehabilitation process following tendon repair must be performed in a sequence and a specific time to prevent rupture of a previously repaired tendon. If the healing process was good, rehabilitation can be performed immediately, therefore, increasing the recovery time for athletes.[3] The tendon healing process begins at inflammation phase, followed by proliferative phase and the last is remodeling

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phase. Proliferative phase (days until several weeks) is characterized by an increase in growth factor, new fibroblasts, and new vascularization. These fibroblasts synthesize collagen precursor in their endoplasmic reticulum.[4] Normally, the formation of fibroblast is influenced by several factors including glycosaminoglican (GAG). Chondroitin sulfate is a type of GAG which was found abundantly among other GAG in the body.[5–7] Chondroitin sulfate could increase the amount of FGF-2 (*Fibroblast Growth Factor-2*).[8–13] FGF-2 is a growth factor that could increase the proliferation of fibroblast.[14–16] Recent study proved that the administration of chondroitin sulfate on rat had increased the number of fibroblast and the density of collagen.[17] Another component of GAG that can influence the tendon healing process is hyaluronic acid.[5–7] One experimental study proved that hyaluronic acid could decrease the adhesion of tendon and increase the architectural organization of the tendon,[3] through the inhibition of NF-kB[18]**.** Based on this data, the author wants to study the effect of chondroitin sulfate and hyaluronic acid given together in combination that act on a different pathway for a better enhancement of Achilles tendon rupture healing process compared to each single treatment.

2. Material and methods

2.1. Experimental animals

28 adult male white rats *(Rattus Novergicus var wistar)* aged 2–3 months weighing 150–200 g were used and divided into 4 groups. First group had tenotomy, repaired and used as control; second group got tenotomy, repaired and injected with hyaluronic acid at the repaired site; third group had tenotomy, repaired and was given chondroitin sulfate orally; last group got tenotomy, repaired and administered with combination of chondroitin sulfate orally and injected with hyaluronic acid at the repaired site.

2.2. Preparation of tendon

All of the rats were given prophylactic antibiotic with cefotaxime injection 15 mg/kg[19] and anesthetized with ketamine (40 mg/kg)[20] via intraperitoneal injection. Both legs were cleaned and shaved with savlon, 70% alcohol and povidone iodine. Skin at achilles tendon area was incised at the both leg and achilles tendon was tenotomised at 0.5 cm length from its insertion. The remaining tendon repaired with modified Kessler technique and was treated according to its group. We put padding and circular cast on the leg for all group.

2.3. Administration

Chondroitin sulfate with a dose of 7mg/200 gr (2 ml) was given through a tube for 21 days orally to rats in group 3 and 4. Hyaluronic acid with a dose of 0.8 mg/ml was injected at the repaired tendon site of rats on group 2 and 4 once only before the application of padding and long leg cast. 21 days after administration, the rat was sacrificed and the achilles tendon was obtained. One tendon was used for histological evaluation and the other was used for quantitative evaluation.

2.4. Sample collection procedure

Sample was taken after 21 days. The rat's cervical vertebra was dislocated to collect the sample. The skin was incised and tendon was obtained for 1 cm starting from 0.5 cm of its insertion to the proximal. Left Achilles tendon was kept in formaldehyde 10% for histological evaluation and the right tendon undergo colorimetric test to calculate the number of collagen.

2.5. Histological evaluation

The obtained tendon was fixed by immersion in 10% neutral-buffered formalin. Subsequently, specimens were dehydrated and embedded in paraffin wax. Sections were stained with Haematoxylin & Eosin and evaluated under a light microscope. Fibroblasts and adhesion degree were evaluated. Fibroblasts were counted per 10 fields with a 400× magnification and adhesion degree was evaluated according to Tang score.[21]

2.6. Collagen measurement

Total collagen assay is based on the detection of hydroxyproline. Hydroxyproline was formed post translation from specific proline residues by action of the enzyme prolylhydroxylase. The measurement of collagen is started by complete hydrolysis of tissue samples in 12 M HCl at 95 °C for 20 h. It is best to use a minimum of 50 μL of sample and 50 μL of HCl 12 M. After incubated, the tube was left in a room until it reached a room temperature. The tube was centrifuged in 13000 rpm speed for 10 min. The supernatant was obtained and diluted minimum for 2x. HCl 4 M was used for dilution. 35 μL of hydrolyzed sample was obtained for analysis. Prepare a standard collagen solution for comparison of collagen measurement. 125 μL of standard collagen solution with 1200 μg.mL concentration in acetate acid 0.02 M mixed with 125 μL of HCl 12 M in a screw-capped tube until it reach a concentration of 600 μg/mL in HCl 6 M. Tube was closed tightly and incubated for 20 h in 95 °C temperature. After incubated, left it in room until it reached room temperature and next centrifuged it in 13000 rpm speed for 10 min. The supernatant obtained was used as a standard solution. The assay (we used Biocolor Sircol Soluble Collagen Assay) measured the total amount of collagen present in the sample. Colorimetric was analyzed at 570 nm.

2.7. Statistical analysis

Statistical analysis were carried out using 20.0 edition of SPSS. Test for homogeneity of variation by Levene's test and examining residual plot, while test for normality by One-Sample Kolmogorov-Smirnov test. Normality and/or homogeneity of variance assumptions for other variables were not satisfied and prior to statistical analysis these variables were logarithmically transformed to fulfill model assumptions. Statistical analysis of data was assessed using one-way analysis of variance (ANOVA) and continued with Tukey test. Data was presented as mean ± standard deviation. The level of significance was set at $p < 0.05$. Comparison of histological and collagen scores across groups was performed with Tukey Post- Hoc Test, and the alpha level is set at 0.05. The relationship between chondroitin sulfate and hyaluronic acid to collagen production were tested with Regression Analysis. For adhesion level measurement, Kruskal Wallis test was used and continued with Mann Whitney test. The alpha level is set at 0.05.

3. Results

The fibroblasts evaluation and collagen measurement results of

Table 1
Results of fibroblasts and collagen measurement.

Group	n	Mean Collagen (μg/ml)	Mean Fibroblast (cells)
Normal	7	0.358 ± 0.030	208.143 ± 24.627
HA	7	0.578 ± 0.023	497.286 ± 21.975
CS	7	1.029 ± 0.067	920.286 ± 49.152
HA + CS	7	0.651 ± 0.068	688.429 ± 35.911

study are presented in Table 1; adhesion degree is presented in Table 2.

From the histological evaluation, we found tenocyte in group 4 (showed in Figs. 1 and 2), which was not found in the other group (showed in Figs. 3–8). So we make the comparison table for the tenocyte count on each group which presented in Table 3. Fibroblast was differentiated morphologically from tenocyte from its spindle shaped cell with a dark heterochromatic nucleus. Tenocyte was identified microscopically through its filament shaped in fibrocollagen stroma with Haematoxylin & Eosin stain viewed in 100× magnification. The results confirmed by an expert pathologist.

Histological analysis shows that collagen level is as many as 2.224 with significant level as many as 0.111, and fibroblast level 2.125 with its significant level 0.123. Based on *Mann-Whitney* test, control group had significant differences with group 2 (HA) and with group 4 (HA + CS) with p-value < 0.05. Group 3 (CS) had significant differences with group 4, while group 3 didn't have significant differences with control group.

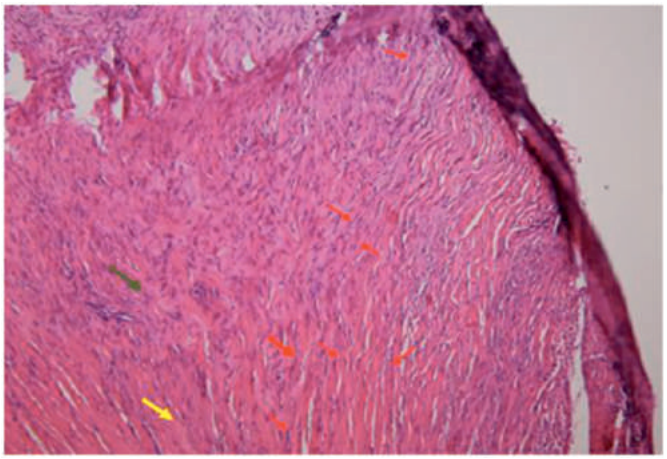

Fig. 1. Histological image of group 1 (control group) with 100× magnification. The red arrow showed the filament, the gray arrow showed the fibroblast and the yellow arrow showed the collagen.

4. Discussion

To find out the administration effect of chondroitin sulfate and hyaluronic acid on repaired Achilles tendon, fibroblast level, collagen level, and adhesion degree were calculated microscopically. Research was conducted using 4 groups. First group was control group which was injected with normal saline 0.2 ml percutaneously on sample's Achilles tendon, Second group was injected with 0.8 mg/ml hyaluronic acid percutaneously on sample's Achilles tendon, third group was fed orally with chondroitin sulfate through tubes with dose of 7 mg/200 gr/day, and fourth group was injected with 0.8 mg/ml hyaluronic acid percutaneously on sample's Achilles tendon and combined with administration of chondroitin sulfate with a dose of 7 mg/200 gr/day orally through tubes.

In the second group, the injection of hyaluronic acid was given based on a literature which said it was proved to reduce tendon adhesion and enhance tendon's architectural organization,[3] through inflammation signal inhibition mechanism (NF-kß).[18] The result from this study is that hyaluronic acid can enhance fibroblast and collagen level, and reduce adhesion during healing process on repaired Achilles tendon and it was synchronized with the previous study. The third group was administered orally with chondroitin sulfate. Based on a recent research, chondroitin sulfate has an effect on increasing fibroblast level and collagen density[17] through stimulation of FGF-2 (Fibroblast Growth Factor-2)[8–13]. FGF-2 is a growth factor that can increase the proliferation of fibroblast.[14–16] From this study it was proved that chondroitin sulfate could only increase the level of collagen and fibroblast without repair of tendon adhesion.

The fourth group was injected with hyaluronic acid combined with administration of chondroitin sulfate orally. There was an increase of fibroblast level 3x and collagen level 2x compared to control group. Histological data also showed a different result in growth level of fibroblast between each group. Exact kind of fibroblast was seen on control group, second group, and third

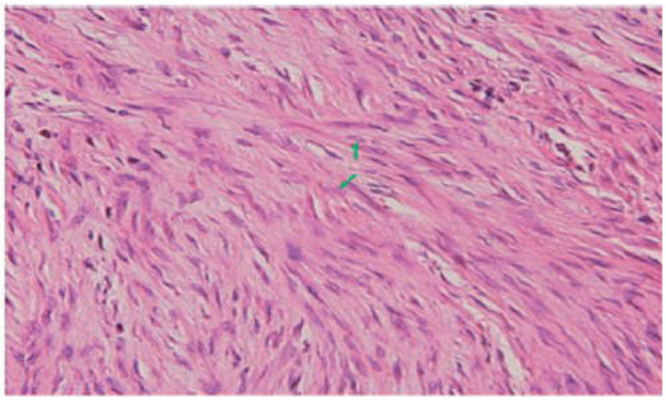

Fig. 2. Histological image of group 1 (control group) with 400× magnification. The blue arrow showed the fibroblast.

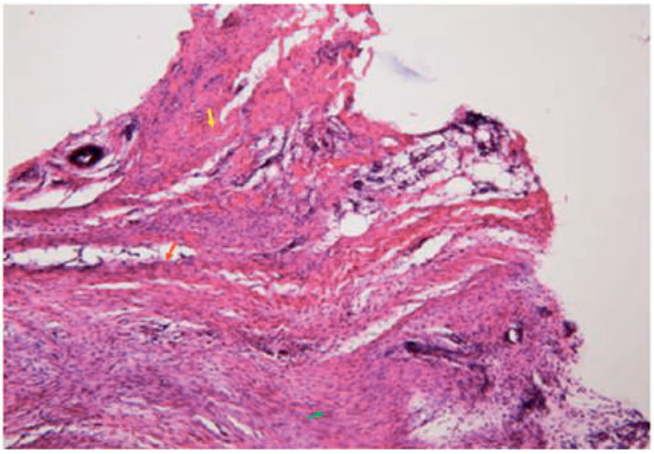

Fig. 3. Histological image of group 2 (hyaluronic acid group) with 100× magnification. The red arrow showed the filament, the yellow arrow showed the collagen and the green arrow showed the fibroblast.

Table 2
Results of Adhesion degree based on Tang method (in Tang score).

Repetition	Control	HA	CS	HA + CS
1	5	3	4	0
2	5	3	4	2
3	5	4	5	0
4	4	3	5	2
5	5	2	4	2
6	4	4	4	0
7	5	3	4	0

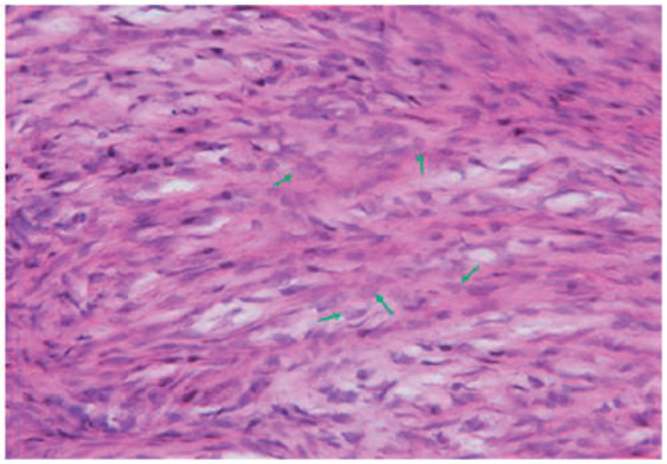

Fig. 4. Histological image of group 2 (hyaluronic acid group) with 400× magnification. The green arrow showed the fibroblast.

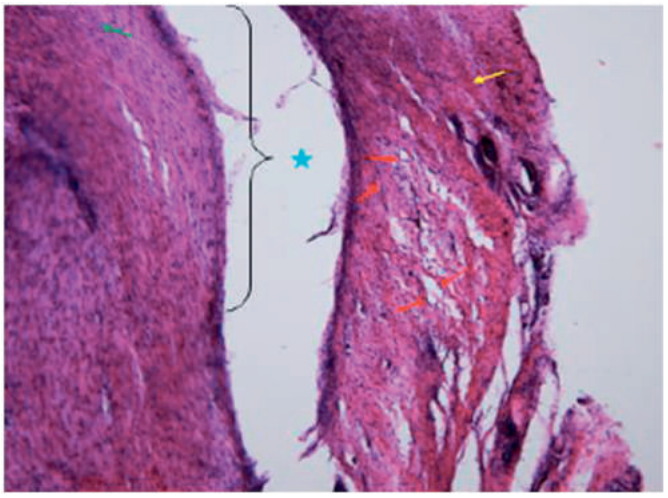

Fig. 5. Histological image of group 3 (chondroitin sulfate group) with 100× magnification. The red arrow showed the filament, the yellow arrow showed the collagen, the green arrow showed the fibroblast and the blue star showed the area of where the tendon has been joined.

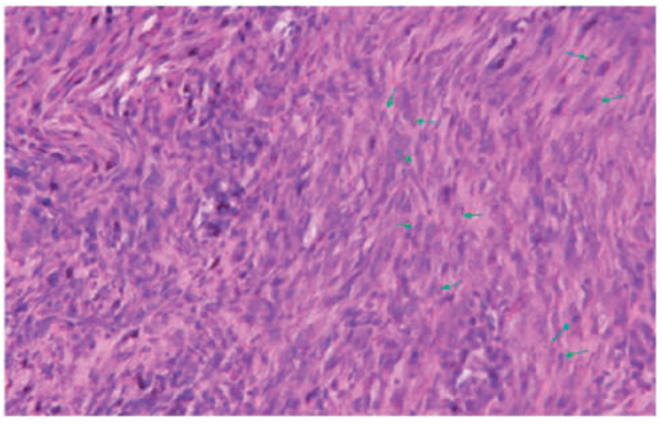

Fig. 6. Histological image of group 3 (chondroitin sulfate group) with 400× magnification. The green arrow showed the fibroblast.

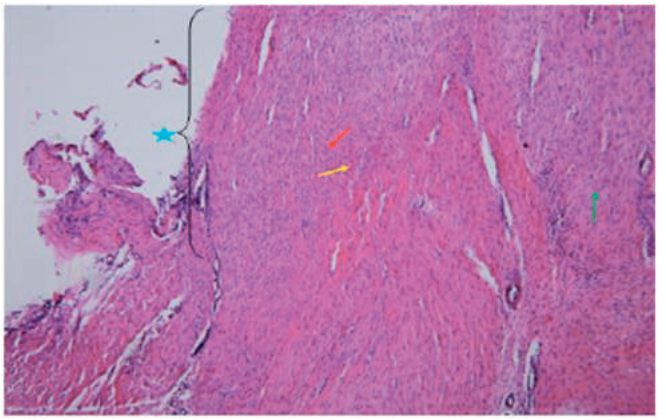

Fig. 7. Histological image of group 4 (hyaluronic acid and chondroitin sulfate group) with 100× magnification. The red arrow showed the filament, the green arrow showed the fibroblast, the yellow arrow showed the collagen and the blue star showed the area where the tendon has been joined.

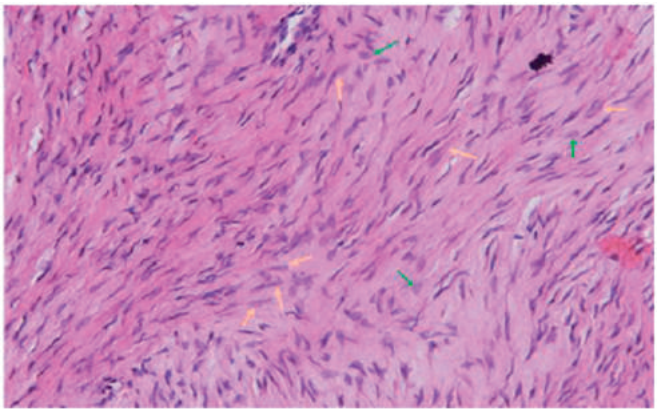

Fig. 8. Histological image of group 4 (hyaluronic acid and chondroitin sulfate group) with 400× magnification. The yellow arrow showed the tenocyte and the green arrow showed the fibroblast.

Table 3
Tenocyte count.

Kelompok	Kontrol	HA	CS	HA + CS
Fibroblast (cells)	208	497	920	265
Tenocytes (cells)	0	0	0	423

group, with a difference in the level of its amount. As for the fourth group, there was a difference in the amount of fibroblast. There was also differentiation of fibroblast to fibrocyte or tenocyte (fibroblasts found in tendon). From this observation, it seems that the healing process was significantly different between the fourth group and the other groups. The fourth group surpassed the healing process of the other.

5. Conclusions

As for conclusion of this study, the administration of chondroitin sulfate and hyaluronic acid increased fibroblast and collagen level, and decreased tendon adhesion on the healing process of a repaired Achilles tendon in rat. The administration of chondroitin sulfate orally combined with the injection of hyaluronic acid percutaneously can enhance the differentiation process of a fibroblast to

tenocyte on the healing process of a repaired Achilles tendon in rat.

Conflict of interest statement

This study is not under consideration for other publication. This study is not in relevant financial, activities outside the submitted work. This study did not have any patents, whether planned, pending or issued, broadly relevant to the work. This study had no other relationship/conditions/circumstances that present a potential conflict of interest.

Funding/support statement

This study is not under any funding/financial support by any organization.

Declaration of competing interest

None.

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Research paper

A 10 Year clinical, laboratory and arthroscopic data analysis of bacterial septic arthritis of adult native knee: A hospital-based study

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ABSTRACT

Objective: A hospital-based study was conducted to analyze the clinical, laboratory and arthroscopic data of bacterial septic arthritis of the native knee in adults treated over ten years.
Method: Between 2010 and 2019, the clinical, laboratory and arthroscopic data of all adult patients who underwent Arthroscopic debridement for diagnosed or suspected septic arthritis of the knee were reviewed from the medical records. Statistical analysis was performed to compare these characteristics between positive and negative cultures and between patients with or without co-morbidities. Further, these characteristics were also compared between patients who had *Staphylococcus aureus* infection versus non-Staphylococcal infection.
Results: The data from 106 cases comprising of 86 males and 20 females were analyzed. The mean age of the study population was 51.04±15.38 years. Positive cultures were observed in only 38 cases (35.84%). Between positive and negative cultures, statistically significant differences were found for haemoglobin levels, CRP, total protein in the synovial fluid, duration of antibiotic course and length of hospital stay. Between patients with or without co-morbidities, statistically, significant differences were found for patients 'age, haemoglobin levels, RBS, HbA1c, Serum Urea, Creatinine, ESR, CRP, the total duration of antibiotic course and length of hospital stay. No major differences were observed between patients with *Staphylococcus aureus* related and non-Staphylococcus aureus related infections.
Conclusion: In most of the cases no organisms were isolated from the synovial fluid or the tissues. Among the positive cultures, *Staphylococcus aureus* was the most common organism isolated, with nearly half of them (42.8%) being MRSA. Patients with positive cultures and associated medical co-morbidities were treated with a longer duration of the antibiotic course and had a longer hospital stay. Awareness among the clinicians and microbiologists about the new emerging infections in the native knee is vitally important.

Authors contribution

Sandesh Madi, Concept, Design, Data collection, Manuscript preparation, Final approval, Srikant Natarajan, Design, Data analysis, Manuscript preparation, Final approval, Sujayendra Murali, Concept, Data collection, Manuscript preparation, Final approval, Vivek Pandey, Design, Data analysis, revising manuscript critically for important intellectual content, Final approval, Kiran Acharya, Concept, Data analysis, revising manuscript critically for important intellectual content, Final approval.

1. Introduction

Septic arthritis of a joint is an Orthopaedic emergency that demands immediate intervention. It has been defined as pathogenic inoculation of the joint by direct or indirect (hematogenous) routes.[1] A delayed presentation or intervention would lead to irreversible joint destruction causing significant disability, which occurs in about 25–50% of affected cases.[2] Fortunately, the overall

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incidence of septic arthritis is rare with an estimate of 4–10 cases per 100,000 people per year.[2] In the adult population, Knee is the most frequently affected joint. Despite the prompt intervention, the septic arthritis of knee has been associated with a 7% mortality within 90 days and about 1% of patients having knee arthroplasty within 1 year and 9% within 15 years.[3] Such is the potential adverse complications of septic arthritis with serious short term as well as long term consequences.

An accurate clinical diagnosis of septic arthritis can be quite challenging. Depending upon the duration of the condition, a typical clinical presentation may include joint pain, swelling (effusion), limited or painful range of movements, a local rise of temperature and fever. However, many non-infectious conditions such as inflammatory arthritis, crystal arthropathy and an acute flare-up of osteoarthritis, also mimic similar clinical picture leading to confusion and delay in the management. Nevertheless, a high index of suspicion is usually warranted and 'a hot swollen joint' is to be considered potentially septic unless proved otherwise. Furthermore, the presence of an associated medical illness such as Diabetes Mellitus, Rheumatoid Arthritis, Malignancy, and renal failure pose significant risk factors for the development of Septic Arthritis. Patients on immunosuppressive or immunomodulating medications are also vulnerable to joint infections.

The diagnosis of septic arthritis is predominantly based on detailed medical history and clinical examination. Radiological investigations such as x-rays, Ultrasonography and Magnetic Resonance Imaging have a limited role in the evaluation as they can neither provide a definitive diagnosis nor help in differentiating from other similar joint conditions. Arthrocentesis (joint aspiration) and synovial fluid analysis are extremely valuable in determining the presence of an infection within the joint. Common laboratory parameters routinely used as supportive evidence of infection include complete blood cell count, complete metabolic panel, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP).[4] Surgical intervention is usually in the form of Arthrotomy or more popularly Arthroscopic debridement. *Staphylococcus aureus* (S.aureus) is the most common organism isolated from infected joint.[4] Thus, an empirical broad-spectrum antibiotic is usually started to cover the gram-positive infection and shifted to a suitable antibiotic regimen based on the culture reports.

The present study aimed to conduct an epidemiological analysis on the clinical, laboratory and intra-operative findings of adult patients with septic knee arthritis who underwent Arthroscopic debridement in our department between 2010 and 2019. We also aimed to identify the potential differences in the profile of the patients between positive and negative cultures, patients with or without co-morbidities and patients with S. aureus related infections versus non- S. aureus-related infections.

2. Methods

This was a single-centre, retrospective, Hospital-based study of all adult patients who underwent arthroscopic debridement for septic arthritis of native knee between 2010 and 2019. The diagnosis of septic arthritis was based on the clinical findings and/or aspiration of purulent fluid from the joint, and/or identification of any micro-organism by Gram staining and culture of joint fluid or synovium. Medical records of these cases were retrieved after the approval of the Institutional Ethics Committee. Clinical data included patients' age, sex, side involved, symptoms such as fever, joint pain and knee swelling, duration of symptoms, most likely route of infection (classified as Hematogenous – when no other infection source was identified, contiguity – infection present around the joint, and direct inoculation – following intra-articular injections/trauma), any medical co-morbidities, and Charlson's Co-morbidity Index (CCI) score.[5] Laboratory data consisted of Complete Blood Count – Hemoglobin (Hb), White Blood Cell (WBC), Poly Morpho-Nuclear cells (PMN) count, ESR (Erythrocyte Sedimentation Rate), CRP (C-Reactive Protein), Platelet count, Random Blood Sugars (RBS), Glycated haemoglobin (HbA1c), Renal Function Test -Serum Urea and Creatinine, Synovial Fluid Analysis, Gram staining, Histopathology, and Blood cultures. All these investigations were performed as per the standard protocol followed in our NABL (National Accreditation Board for Testing and Calibration Laboratories) accredited labs.

Co-morbidities identified in the study were defined as Diabetes Mellitus (HbA1c >6.5%),[6] Anemia (Hb < 11.2 g/dL),[7] Hypertension (>140 mmHg Systolic Blood pressure or >90 mm Hg of Diastolic Blood Pressure),[8] Heart disease (Ischemic Heart disease/Cardiomyopathy/Infective Endocarditis), Chronic Kidney Disease (kidney damage with an estimated glomerular filtration rate <60 ml/min/1.73m^2, persisting for >3 months),[9] Chronic Liver disease (Cirrhosis/Hepatitis B or C infection), Rheumatoid Arthritis (2010 ACR/EULAR criteria),[10] Primary Hypothyroidism (TSH concentrations >4·0 mIU/L),[11] Chronic Lung Disease (Chronic Obstructive Pulmonary Disease), Malignancy (Breast carcinoma, Non-Hodgkin's Lymphoma) and Retro-positive (HIV infection).

Gaechter classification system was used to classify the stage of joint infection based on the Arthroscopic findings.[12] Any incomplete data, septic arthritis of a joint other than the knee, Tubercular or fungal septic knee arthritis, presence of crystals in the joint fluid confirmed on polarized microscopy and open knee debridement were excluded from the study. Further, data was also collected regarding the duration of both intravenous and oral antibiotics and the total duration of hospital stay.

Statistical analysis was performed using IBM SPSS Software version 25. The parameters were compared for patients between positive and negative cultures, patients with or without co-morbidities and patients with S. aureus related infections versus non-S. aureus-related infections and any potential differences were identified. A two-tailed independent *t*-test was used for parametric testing of dependable variables. The categorical variables were analyzed using the χ^2 test. P-value of <0.05 was considered statistically significant. The mean and standard deviation were used for descriptive statistics.

3. Results

A total of 113 adult patients had undergone arthroscopic debridement for diagnosed or suspected septic arthritis of the native knee at our Hospital between 2010 and 2019.106 cases met the inclusion criteria and the data was analyzed. There were 86 males (81.13%) and 20 females (18.86%). The mean age of the study population was 51.04±15.38 years (range 21–80 years). In 49 cases right knee was involved, 47 cases left knee was involved and 5 cases had bilateral involvement. Out of these 106 cases, 89 had been operated by senior Arthroscopy Surgeons (KA & VP) and the remaining 17 cases had been performed by Fellowship-trained Junior Consultant (SM). 72 cases had been performed in the elective list and the remaining 34 cases were taken up in the emergency list (After Office Hours). Hematogenous route of infection was seen in 82 cases (77.35%), contiguity spread was observed in 17 cases (16.03%) and direct inoculation was seen in 7 cases (6.6%). 21 patients (19.8%) had undergone previous surgery to the ipsilateral limb in the last one year. Joint pain and swelling were present in all cases at the time of presentation; however, fever (>37.5 °C) was present in only 57 cases (53.77%). The mean duration of symptoms at the time of presentation was 11.45±7.31 days (range 2–28 days). The mean time lapse between presentation and surgical intervention was 2.6 days (range 0–15 days). 23 patients (21.6%) had taken

at least a single dose of intravenous antibiotics prior to sample collection and intervention.

The medical co-morbidities were present in 63 cases (59.43%). The most common co-morbidity was Diabetes Mellitus, seen in 35 cases (55.56%) followed by Anemia, seen in 26 cases (41.26%). The prevalence of other co-morbidities is shown in Table 1. The mean number of comorbidities per patient was 1.08±1.21 (ranging from 0 to 5). The mean CCI score was 2.04±2.13.

The mean total leukocyte count was 11,272± 5625 per mm^3 and the Neutrophil count was 69.8±10.7%. Leukocytosis (WBC count > 11.000 per mm^3) was seen in 39/106 cases (36.79%). The mean ESR was 74.8 ± 32.8 mm/h and the mean CRP was 119.34± 99.05 mg/dL. In the synovial fluid analysis, the mean WBC count was 51656± 17027 cells/mm^3 (20,700–1,20,000 cells/mm^3) and the mean differential count (% Poly-Morpho Nuclear cells) was 90.6 ± 9.4%. In the chemistry studies of the synovial fluid, the mean total protein was 4.18 ± 1.16 g/L, the mean glucose was 74.75 ± 35.83 mg/dL and the mean LDH was 3406.7±1949.9 IU/L.

All the patients had undergone Arthroscopic debridement of the knee and the intra-operative findings were recorded in the Arthroscopy proforma. According to the Gaechter classification, 48 cases could be classified as stage II, 43 cases as stage III, 15 cases as stage IV and none as stage I. 98 cases had undergone single arthroscopic procedure whereas 8 cases required more than one debridement. The joint fluid and the synovial tissues were sent for Gram staining, culture, and Histopathology. The Gram staining could identify the organism as Gram-positive or Gram-negative (Cocci or Bacilli) in only 17 cases (16.03%). Positive cultures were noted in 38 cases (35.84%). S. aureus was the most common organism isolated, present in 21 cases (55.26%), including 9 cases (42.85%) of Methicillin-Resistant *Staphylococcus aureus* (MRSA). Other organisms isolated are shown in Table 2.

In two cases, two organisms were concurrently isolated from the infected joint. One patient with Diabetes Mellitus and renal failure had *Morganella morganii & Klebsiella pneumoniae* infection. The second patient had an open injury to the knee 4 months back and had Acinetobacter baumannii & *Klebsiella pneumoniae* infection. Blood cultures were positive in 12 cases (11.32%). In all cases, the histopathological features were suggestive of either acute or chronic synovitis. The mean total duration of intravenous antibiotics was 9.83±4.78 days (range 5–28 days) and oral antibiotics were 18±8.85 days (range 5–42 days). The mean total duration of hospital stay was 11.00±7.49 days (range 5–60 days). A repeat Arthroscopic 'wash-out' procedure had been performed in eight cases. Out of these, five cases were performed within ten days, two cases within three weeks and in one case, two months after the primary procedure.

When the parameters were compared for patients between positive and negative cultures, statistically significant differences were found for Hb, CRP, total protein in the synovial fluid, duration of the antibiotic course (oral and intravenous) and length of hospital stay. (Table 3).

When the parameters were compared for patients with or without co-morbidities statistically significant differences were found for patients 'age, Hb, RBS, HbA1c, ESR, CRP, blood urea, creatinine, the total duration of antibiotics and length of hospital stay (Table 4).

When the parameters were compared for patients with S. aureus related infections versus non- S. aureus -related infections statistically significant differences were found for only HbA1c (Table 5).

Further, a statistically significant association was found between positive cultures and patients with associated co-morbidities (P-value 0.026). Advanced Gaechter's stages (III/IV) were also noted among patients with co-morbidities, although not statistically significant (Table 6). There were no statistically significant differences for any of these parameters between patients with S. aureus and non- S. aureus -related infections.

4. Discussion

There have been several interesting observations in the study. First, is the relatively low percentage of positive cultures despite strong clinical suspicion. Second, Anemia being second largest co-morbidity risk factor associated with septic arthritis. Third, is the alarmingly high percentage of MRSA infections isolated from the positive cultures. Lastly, previously unreported, emerging nosocomial infections affecting the native knee have been identified in this series.

4.1. Clinical presentation

Clinical features of septic arthritis of the native knee joint are often variable. At the time of presentation, fever (>37.5 °C) was present in only half of the cases (53.77%), whereas joint pain and swelling were universally present. Similarly, Helito et al. found that

Table 1
Co-morbidities identified in the study.

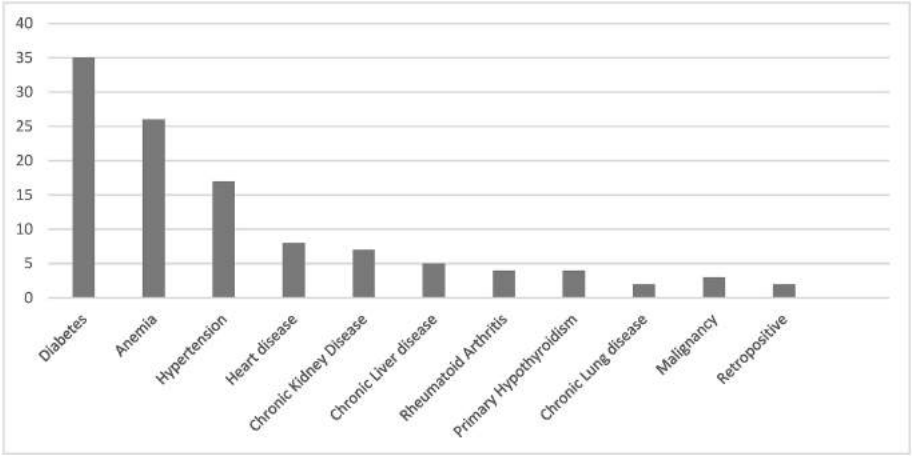

Table 2
Micro-organisms identified in the study MSSA - Methicillin Sensitive Staphylococcus Aureus.

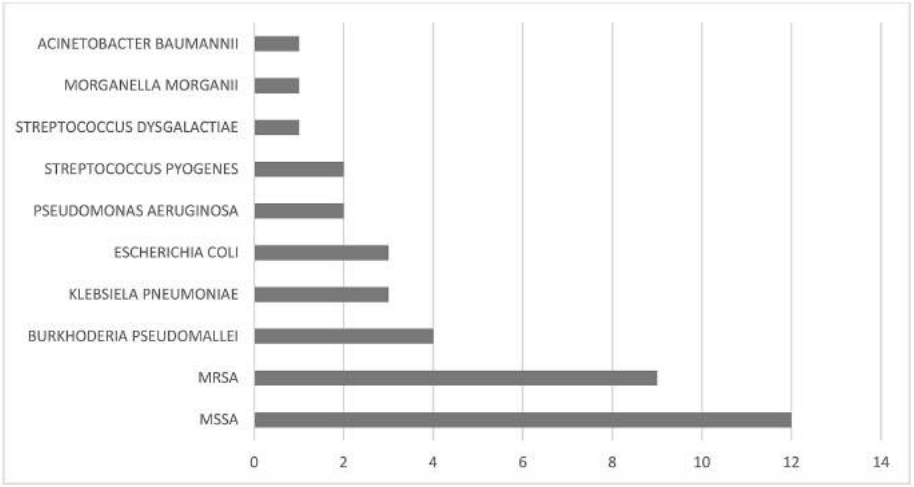

Table 3
Comparison of parameters between patients with positive and negative cultures.

Parameters	Negative (n = 68) (Mean ± SD)	Positive (n = 38) (Mean ± SD)	P Value
Age	49.54 ± 15.85	53.74 ± 14.32	0.18
Hb (G/dl)	11.76 ± 1.74	10.46 ± 2.1	**0.001**
RBS (mg/dl)	136.76 ± 68	156.68 ± 92.74	0.208
HbA1c (%)	6.06 ± 1.77	6.64 ± 2.2	0.144
WBC (per mm^3)	10955.88 ± 5640.69	11839.47 ± 5629.63	0.441
PMN (%)	68.76 ± 11.3	71.68 ± 9.51	0.181
ESR (mm/hr)	70.68 ± 31.56	82.18 ± 34.15	0.083
CRP (mg/dl)	94.7 ± 75.17	163.46 ± 120.4	**0.002**
Blood Urea (mg/dl)	32.09 ± 26.2	42.92 ± 37.88	0.123
Serum Creatinine (mg/dl)	1.25 ± 1.39	1.75 ± 2.15	0.208
Platelet count X 10^9/L	356.84 ± 141.14	319.97 ± 144.14	0.203
WBC (Synovial fluid) cells/μL	51728.3 ± 15143.5	51528.4 ± 20186.9	0.95
PMNs (%) (Synovial fluid) (%)	90.43 ± 10.39	91.13 ± 7.53	0.714
Total Protein (Synovial fluid) (G/dl)	4.37 ± 1.07	3.85 ± 1.26	**0.027**
Glucose (Synovial fluid) (mg/dl)	74.83 ± 33.72	75.05 ± 39.28	0.97
Lactate Dehydrogenase (LDH) (IU/I)	3251.61 ± 1711.39	3684.34 ± 2395.14	0.275
Intravenous antibiotics (days)	8.32 ± 3.56	12.53 ± 5.5	<**0.001**
Oral antibiotics (days)	15.54 ± 6.64	22.61 ± 10.49	<**0.001**
Total Antibiotics duration (days)	23.79 ± 9.03	35.13 ± 14.1	<**0.001**
Hospital stay (days)	9.5 ± 5.31	13.71 ± 9.82	**0.005**

fever at the time of admission was seen in only 33% cases.[13] Thus, the presence or absence of fever at the time of presentation may not be accurate or reliable, and the mere local signs of a red-hot swollen joint should raise the suspicion of potential infection.

Even though septic arthritis is considered as an Orthopaedic emergency, there appears to be a delay in the clinical presentation and diagnosis. In the index series, the mean duration between the onset of symptoms and presentation to the hospital was 11.45±7.31 days (range 2–28 days). Other inflammatory and degenerative knee disorders also mimic similar clinic picture and could lead to delay in the accurate diagnosis. Elsissy et al. rightly noted that the presentation is often 'subacute' in nature and the diagnosis should strongly rely on clinical suspicion.[4] Furthermore, for suspicious cases, timely referral of these patients to higher centres should also be strongly emphasized to prevent potential complications from a delayed presentation.

4.2. Associated risk factors

Age >60 years and co-morbidities such as Diabetes Mellitus, Rheumatoid Arthritis (RA), renal failure, cirrhosis and injury or surgical procedures to the joint are considered as associated risk factors.[4] The mean age of this study population was 51.04±15.38 years, which is comparable with other previous similar series.[14,15] Diabetes Mellitus (55.56%) was the most common co-morbidity followed by Anemia (41.26%) and 19.8% of patients had undergone previous surgery to the ipsilateral limb in the last one year. Diabetes Mellitus is a growing epidemic worldwide and is the single largest risk factor in several studies.[13,15,16] Whereas, Ruksasakul et al. had noted hypertension (47.6%) as the most common morbidity in their series followed by Diabetes Mellitus (30.7%).[2] In addition to Diabetes Mellitus, Dias et al. had observed the pharmacological immunosuppression as the main risk factor.[17]

It has been noted that there is a 4–15 times greater risk of developing septic arthritis in patients with RA than the general

Table 4
Comparison of parameters between patients with and without co-morbidities.

Parameters	Absent (n = 43) (Mean ± SD)	Present (n = 63) (Mean ± SD)	P Value
Age	44.35 ± 15.42	55.62 ± 13.68	**<0.001**
Hb (G/dl)	12.55 ± 1.15	10.44 ± 1.96	**<0.001**
RBS (mg/dl)	110.65 ± 28.54	166.6 ± 91.88	**<0.001**
HbA1c (%)	5.09 ± 0.75	7.07 ± 2.1	**<0.001**
WBC (per mm^3)	10562.79 ± 5214.91	11757.14 ± 5881.59	0.285
PMN (%)	68.07 ± 10.91	70.98 ± 10.54	0.172
ESR (mm/hr)	62.3 ± 28.65	83.33 ± 32.96	**0.001**
CRP (mg/dl)	83.91 ± 69.32	143.54 ± 109.07	**0.001**
Blood Urea (mg/dl)	25.47 ± 10.15	43.14 ± 38.02	**0.001**
Serum Creatinine (mg/dl)	0.89 ± 0.28	1.79 ± 2.13	**0.002**
Platelet count X 10^9/L	351.47 ± 135.36	338.27 ± 148.24	0.642
WBC (Synovial fluid) cells/μL	48860.7 ± 16549.91	53565.08 ± 17215.15	0.16
PMNs (%) (Synovial fluid) (%)	90.26 ± 12.59	90.97 ± 6.56	0.704
Total Protein (Synovial fluid) (G/dl)	4.44 ± 1.15	4.01 ± 1.15	0.058
Glucose (Synovial fluid) (mg/dl)	80.3 ± 31.96	70.96 ± 38.03	0.18
Lactate Dehydrogenase (LDH) (IU/I)	3356.11 ± 1949.95	3441.3 ± 1964.89	0.82
Intravenous antibiotics (days)	9 ± 3.33	10.39 ± 5.51	0.14
Oral antibiotics (days)	14.93 ± 5.14	20.22 ± 10.16	**0.002**
Total Antibiotics duration (days)	23.88 ± 7.17	30.57 ± 14.28	**0.005**
Hospital stay (days)	8.86 ± 2.79	12.47 ± 9.18	**0.01**

Table 5
Comparison of parameters between patients with Staph. Aureus infection and non-staph aureus infection.

Parameters	S. aureus (n = 21) (Mean ± SD)	Non-S. aureus (n = 17) (Mean ± SD)	P Value
Age	52.43 ± 12.27	55.35 ± 16.77	0.553
Hb (G/dl)	10.65 ± 2.3	10.23 ± 1.86	0.543
RBS (mg/dl)	158.29 ± 96.05	154.71 ± 91.37	0.908
HbA1c (%)	5.83 ± 1.73	7.63 ± 2.36	**0.01**
WBC (per mm^3)	11780.95 ± 4710.8	11911.76 ± 6748.32	0.944
PMN (%)	70.4 ± 10.2	73.25 ± 8.61	0.367
ESR (mm/hr)	87.29 ± 32.67	75.88 ± 35.87	0.313
CRP (mg/dl)	142.02 ± 125.5	189.93 ± 111.76	0.227
Blood Urea (mg/dl)	34.43 ± 20.23	53.41 ± 50.95	0.163
Serum Creatinine (mg/dl)	1.67 ± 2.38	1.84 ± 1.89	0.81
Platelet count X 10^9/L	349.86 ± 145.61	283.06 ± 137.55	0.158
WBC (Synovial fluid) cells/μL	49391.9 ± 18265.2	55124.7 ± 22066.6	0.38
PMNs (%) (Synovial fluid) (%)	89.19 ± 8.41	93.53 ± 5.64	0.077
Total Protein (Synovial fluid) (G/dl)	4.07 ± 1.25	3.58 ± 1.25	0.243
Glucose (Synovial fluid) (mg/dl)	64.19 ± 31.86	85 ± 45.2	0.1
Lactate Dehydrogenase (LDH) (IU/I)	3765.7 ± 2411.6	3980.4 ± 2463.9	0.78
Intravenous antibiotics (days)	11.23 ± 4.25	14.11 ± 6.51	0.1
Oral antibiotics (days)	20.67 ± 6.52	24.58 ± 13.79	0.25
Total Antibiotics duration (days)	31.9 ± 9.19	38.7 ± 17.99	0.14
Hospital stay (days)	11.76 ± 5.59	16.17 ± 13.14	0.17

population.[4] Despite the comparable prevalence of RA between India (0.75%) and the western world,[18] RA was found in only 4/63 cases (6.3%) in this series. This contrasts with a higher prevalence of RA noted by Helito et al. (18.34%),[13] Khan et al. (8.9%)[15] and Al Arfaj et al. (16.7%)[19] and a lower prevalence noted by Ruksasakul et al. (2.2%).[2] Nutritional Anemia being a significant health problem in the developing countries, it is not surprising to see Anemia as the second-highest risk factor in the series. Furthermore, patients with positive cultures had a lower Hb (mean 10.46 ± 2.1 G/dl), which was statistically significant (P-value <0.001).

The intra-articular steroid or Hyaluronic acid injection for the management of Osteoarthritis is a common practice. Contrary to other studies,[2,13,20] none of the cases in this series had developed septic knee following intra-articular injection. Further, in contrast to the western population,[21] none of the cases had any history of intravenous drug abuse.

4.3. Laboratory profile: blood & synovial fluid

All cases had presented with an elevated ESR (>20 mm/h) and CRP(>0.5 mg/dL) levels. Apart from supporting the diagnosis of infection, both CRP & ESR are extremely valuable in monitoring response to the given treatment (medical/surgical). CRP values return to normal range within 1–2 weeks of starting treatment whereas ESR remains elevated for a few weeks even after the resolution of infection.[4]

In septic arthritis, the previous conventional characterization of synovial fluid was WBC >50,000 cells/mm,[3] total protein levels >3 g/dl, a glucose levels of 20–100 mg/dL less than serum levels and an elevated LDH levels.[22] However, Li et al. noted that the WBC counts widely vary and it was <50,000 cells/mm^3 in more than 1/3rd of adult patients with septic arthritis.[23] Further, Baran et al. noted that in both general and immunocompromised population, the percentage of PMNs in the synovial fluid was a more sensitive predictor of joint infection than the absolute WBC count.[24] The chemistry studies (such as total protein, glucose, albumin, lactate, amylase, LDH) of the synovial fluid has not been useful in differentiating between septic and other forms of arthritis due to wide variations in their values. Recently, several novel diagnostic synovial fluid markers such as Procalcitonin, IL-6, lactate levels and

Table 6
The analysis of categorical variables using the $\chi 2$ test.

Parameters	Values	N	Co-morbidities				Chi square	P value
			Absent		Present			
			Count	Column N %	Count	Column N %		
Age	<30	13	10	23.30%	3	4.80%	21.77	**0.001**
	31–40	13	9	20.90%	4	6.30%		
	41–50	29	7	16.30%	22	34.90%		
	51–60	18	10	23.30%	8	12.70%		
	61–70	21	5	11.60%	16	25.40%		
	>70	12	2	4.70%	10	15.90%		
Sex	F	20	7	16.30%	13	20.60%	0.317	0.574
	M	86	36	83.70%	50	79.40%		
Side	L	47	15	34.90%	32	50.80%	2.899	0.407
	L (B/L)	5	2	4.70%	3	4.80%		
	R	49	24	55.80%	25	39.70%		
	R (B/L)	5	2	4.70%	3	4.80%		
Charlson's Co-morbidity Index score	0	29	25	58.10%	4	6.30%	44.11	**<0.001**
	1	24	11	25.60%	13	20.60%		
	2	19	4	9.30%	15	23.80%		
	3	14	3	7.00%	11	17.50%		
	4	7	0	0.00%	7	11.10%		
	5	4	0	0.00%	4	6.30%		
	6	3	0	0.00%	3	4.80%		
	7	4	0	0.00%	4	6.30%		
	9	1	0	0.00%	1	1.60%		
	10	1	0	0.00%	1	1.60%		
Culture	**Negative**	68	33	76.70%	35	55.60%	4.989	**0.026**
	Positive	38	10	23.30%	28	44.40%		
Gaechter classification	II	48	23	53.50%	25	39.70%	3.726	0.155
	III	43	17	39.50%	26	41.30%		
	IV	15	3	7.00%	12	19.00%		

lactate to glucose ratio have been explored to establish the diagnosis of septic arthritis. However, these observations need further validation.

4.4. Tissue & fluid cultures

The incidence of negative cultures reported varies from one series to another. Helito et al. had reported 22.8% (24/105 cases),[13] Eberst-Ledoux et al. reported 19% (74/398 cases),[25] and in a prospective multicentric study by Gupta et al. reported 43%.[26] In contrast, in 64.15% of cases suspected to be septic arthritis in this series, no organisms were isolated from the synovial fluid or the tissues. Initiation of antibiotics before the patient is taken up for the debridement and biopsy could be one of the reasons for negative culture results. Other possible causes include quality of the laboratory investigations, inclusion criteria of the reporting series and local habits.[25]

Recently, Pool et al. noted that 84% (42/52) tissue cultures obtained at surgery were equal to joint needle aspiration and suggested that starting antibiotic therapy before surgery can be considered.[27] However, in this series, only in 16.03% Gram staining was positive and in rest of the cases mostly pus cells were identified with no added diagnostic value. We believe that the patients must be taken up for the debridement at the earliest opportunity and synovial fluid aspiration and biopsy should be performed before the initiation of any antibiotics. Failure to identify any organism on cultures despite the presence of pus within the joint creates a clinical dilemma in further management. In the event of a negative culture report, the decision regarding the appropriate choice, dosage, and duration of the antibiotics can be challenging. Nevertheless, Gupta et al. had concluded that in both culture-proven as well as clinically suspicious cases, the morbidity and mortality on follow up were similar.[28] Thus, all suspicious cases should also be treated like confirmed cases despite microorganisms being conspicuously absent.

When the parameters were compared for patients between positive and negative cultures, statistically significant differences were found for Hb levels, CRP, total protein in the synovial fluid, duration of the antibiotic course (oral and intravenous) and length of hospital stay. In comparison, Dias et al. observed that patients with or without an isolate exhibited similar characteristics for clinical, laboratory and radiological features.[17] However, they noted that patients with positive cultures had a statistically significant higher number of patients with associated risk factors and required a longer duration of antibiotic treatment and hospital stay. Similarly, Helito et al. found no significant differences between positive and negative culture groups except for a longer duration of hospital stay.[13] In the index series, Blood cultures were positive in 12 cases (11.32%) where Dias et al. noted positive blood cultures in 9.4%.[17]

4.5. Microbiological profile

S.aureus was the most common organism isolated from the cultures and this concurs with the findings of most of the series on septic arthritis.[13,16,19,25,26,28–30] In contrast to these studies, Ruksasakul et al. noted Group B Streptococcus (37.7%) more commonly than S. aureus (23.4%) in their series.[2] Further, we observed that nearly half of S. aureus infections were MRSA positive, and thus warranted a prolonged antibiotic course and a longer duration of hospital stay. Despite the infection control measures in place, the increasing nosocomial MRSA infections is an alarming trend. However, Dubost et al. noted no significant changing trends in the proportion of MRSA cases in the last three decades in their centre and accounted for only 13%.[16] Environmental and host factors determine the prevalence of the type of microorganism in a centre and it can vary widely. Thus, the appropriate choice of empirical antibiotics should be based on the local antibiogram.

Four cases of Melioidosis septic knee were noted in the series,

out of which three cases were diabetic. The clinical presentation is often confused with tubercular infections leading to delay in the accurate diagnosis, especially where tuberculosis is endemic. Further, Melioidosis warrants a long-term multidrug therapy, longer hospital stays and a close follow-up to look for any relapse. Burkholderia pseudomallei has been an emerging infection in this part of the world and awareness among Clinicians and Microbiologist would lead to prompt diagnosis and management.[31]

We found two cases with uncommon infections: Acinetobacter baumannii and *Morganella morganii*. Both are emerging nosocomial infections, especially in an ICU setting. These rare infections have not been previously reported in any septic arthritis series and are worrisome. Limited treatment options endanger critically ill patients potentially increasing the morbidity as well as mortality. Lastly. Unlike in Australia,[30] we found no cases of gonococcal arthritis in the series, which could be attributed to the cultural and environmental factors.

Arthroscopic profile: Arthroscopic debridement and biopsy is becoming widely popular in the management of knee septic arthritis. Improved visualization of the structures of within the joint, allows joint lavage, synovectomy, and drainage, less scarring and early return to rehabilitation are some of the claimed advantages of Arthroscopy over conventional Arthrotomy.[32] Recently, several comparative studies have found both short-term and long-term benefits of Arthroscopy over open surgical debridement.[33,34]

In the index series, eight cases had required more than one debridement because of recurrent joint effusion. Recently, Stake et al. had identified a concurrent infection and a higher synovium WBC count as risk factors for a 'repeat washout' procedure.[35] Although not statistically significant, advanced Gaechter's stages (III/IV) were noted among patients with co-morbidities. Currently, there is no consensus regarding the choice of intervention (arthroscopy vs arthrotomy) for the given stage of infection. From the available literature, Elsissy et al. had noted that stages I/II/even III can be managed effectively by arthroscopy and stage IV warrants open arthrotomy.[4] In our series, 15 cases with stage IV had undergone arthroscopic debridement. Since we did not follow-up with these cases, we cannot comment further on the outcomes of the intervention.

Limitations: This was a retrospective, observational, single-centre study. We did not follow up the cases for the assessment of any short or long-term functional outcomes or complications. However, the main objective of this study was to characterize the clinical, laboratory and arthroscopic profile of the patients with a septic native knee. A prospective evaluation of long-term morbidity and mortality and the impact of the intervention is strongly recommended. Second, we clubbed all the common co-morbidities and compared the parameters with patients with no identified co-morbidity. We did not evaluate the impact of each co-morbidity in the development of septic knee and its sequelae. Further, in 21.6% cases, intravenous antibiotics in varying dose, duration and types had been started before sample collection and evaluation. This would have a significant bearing in terms of observed clinical presentation, laboratory values and isolation of organisms from the aspirate/biopsy. However, it is not uncommon to see suspected cases treated with empirical antibiotics and then referred to higher centres for further management. Thus, a detailed treatment history at the time of presentation is strongly advocated. Lastly, the microbiological profile described in this series would differ from other centres. Thus, a population-based study would be more relevant, especially in understanding the prevalence of certain infections and formulating community-based preventive measures.

5. Conclusion

The diagnosis and management of septic arthritis remain challenging to date. Local clinical signs should raise the suspicion of potential joint infection. In most cases, no organism is isolated. In positive cultures, S. aureus dominates the chart, with nearly half of them being MRSA. Patients with positive cultures and associated co-morbidities may require a longer course of antibiotics and a longer duration of hospital stay.

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Declaration of competing interest

None.

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Research paper

Five-years outcome of medial patellofemoral ligament reconstruction in isolated post-traumatic tear: A retrospective study

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ABSTRACT

Introduction: Medial patellofemoral ligament (MPFL) reconstruction is the procedure of choice for lateral patellar dislocation. However, studies depicting the long terms results of this procedure is lacking. The present study was conducted to evaluate the functional outcomes after MPFL reconstruction at a minimum of five years follow-up.

Methods: This study was retrospective evaluations of patients who underwent MPFL reconstruction by basket weave method. A total of 35 patients (37 knees) with isolated MPFL tear who met the inclusion criteria were included in this study. These patients were assessed for functional outcome scores including Kujala score, International Knee Documentation Committee (IKDC) score, Lysholm score and Tegner activity score at a minimum follow-up of 5 years.

Results: The mean follow-up was 81.57 ± 16.07 months and mean age of patients was 19.56 ± 8.02 years. There was no re-dislocation in any of the patients but 4 patients had apprehension test positive (10.81%). The mean Kujala score, IKDC score and Lysholm score preoperatively and postoperatively after MPFL reconstruction were 62.20 ± 16.86 and 90.32 ± 16.42 respectively ($p < 0.0001$); 58.62 ± 14.34 and 85.15 ± 7.65 respectively ($p < 0.0001$); 68.21 ± 10.72 and 95.30 ± 8.02 respectively ($p < 0.0001$) at the five-year follow-up. Mean Tegner score pre-injury and post-surgery was 6.23 ± 2.10 and 5.82 ± 1.90 respectively ($p = 0.38$) at a mean follow-up of five years.

Conclusions: MPFL reconstruction surgery for isolated MPFL tears without any associated bony deformity, or soft tissue alterations has a good long-term functional outcome.

1. Introduction

Medial patellofemoral ligament (MPFL) is a primary restraint to lateral patellar dislocation and keeps patella centred within the trochlear groove from 0 to 30° of knee flexion.[1,2] With an inherent six degrees valgus angle at the knee, there exists a tendency of the patella to move out of trochlea with the contraction of the quadriceps, which is prevented by MPFL.[3] Acute patellar dislocations as a result of some traumatic injury accounts for 94–100% MPFL injuries in first time dislocations.[4] An incidence of 43 per 100,000 athletic population is reported for acute lateral patella dislocations.[5]

Several criteria's have been proposed to guide the surgical management and preferences vary greatly among the different surgeons.[6] Procedures including MPFL reconstruction and patellar realignments have been described for lateral patellar dislocations.[4,7,8] Re-dislocation after MPFL reconstructions is uncommon and patient's satisfaction is high.[9] A prospective analysis of MPFL reconstruction patient's data reported that 84.1% of athletes returned to their previous level of sports participation, with only 1.2% reporting recurrent patellar instability.[10] Further, Lind et al. in their review, reported good outcomes after MPFL reconstructions, as re-dislocation rates were lower than 7%.[11]

Currently, there is a lack of agreement or available objective criteria by which physicians evaluate patients' knee function after MPFL reconstruction to dictate when the patient can safely return to the sporting activity.[12] Conventionally, patients' range of motion, flexibility, anatomic alignment, strength, and other subjective

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criteria were analysed before clearance was given to a sportsperson to return to sports.[13] A recent systematic review found that for most studies, the rehabilitation guidelines for athletes undergoing MPFL reconstruction include weight and range of motion restrictions, while only 18.9% of studies included objective or patient-centric criteria in determining return to sports.[14] In addition, there remains a more than normal risk of adolescent athletic population after MPFL reconstruction over a period of a few years, which necessitates the need for long-term follow-up studies to better define the functional outcomes.[15]

MPFL reconstruction for patellar reconstruction reported to be an excellent procedure for patellar instability. However, there is lack of data regarding the long term efficacy of this procedure. The present study was conducted with aim to study the long-term functional outcomes using various scores in patients who underwent MPFL reconstruction for patellar instability.

2. Materials and methods

2.1. Patient selection and data

This is a retrospective study. The data of patients who got operated for MPFL reconstruction from 2012 to 2015 was taken from registry maintained in the operation theatre, which was further scrutinised from admission files kept in the medical records department to see for isolated MPFL tear without any associated soft tissue or bony abnormalities like trochlear dysplasia, patella alta, etc. These selected patients were than included in the study and the follow-up data was taken from the electronic supplementary material, maintained in the department of the orthopaedics.

All the surgeries have been performed by a single surgeon (RG) using Basket weave method of MPFL reconstruction.[16] In this study, functional outcome was assessed using Kujala score,[17] International Knee Documentation Committee (IKDC) score,[18] Lysholm score[19] and Tegner score[20] and clinical outcome using patellar apprehension test.[21] The Kujala score is a self-administered, knee-specific scale with 13 items assessing the following: limp, mobility aid dependency, walking, stair climbing, squatting, running, jumping, prolonged sitting with the knee flexed, pain, swelling, instability, thigh atrophy, and flexion deficiency. The scale is scored from 0 to 100, with lower scores representing greater disability. Lysholm's system is an evaluation system that includes three functional criteria and five subjective criteria. The maximum score is 100 points, in which: 91 to 100 points is considered excellent; 84 to 90, good; 65 to 83, fair; and 64 or less, unsatisfactory. All told, 50% of the total score is based on the symptoms of pain and instability. The IKDC is a 10-item knee-specific measurement tool assessing symptoms, sport activity, and function; it is scored by summing the individual items and then transforming the score to a scale from 0 to 100. A score of 100 represents no limitations with activities of daily living or sport activities and the absence of symptoms. The Tegner activity scale is a one-item score that graded activity based on work and sports activities on a scale of 0–10. Zero represents disability because of knee problems and 10 represent national or international level soccer. Inclusion criteria's for this study were: 1) Patients operated for isolated MPFL tear in the last 10 years 2) Age: 11–40 years 3) suffered a lateral patella dislocation following trauma including road side accident, pivoting, cutting or jumping activities 4) complaints of recurrent patella dislocation 5) completed post-surgical rehabilitation protocol. Exclusion Criteria's were: 1) All patients with multi-ligamentous tears 2) associated conditions like trochlear dysplasia, patella alta, etc. The preoperative diagnoses were made using a combination of clinical and radiological examination including X-rays and Magnetic Resonance Imaging. X rays were used to rule out patella, patella baja and any bony avulsions. MRI was used to confirm diagnosis of MPFL tear and to rule out any trochlear dysplasia [Tibial Tuberosity- Trochlear Groove (TT-TG) distance].[22](Fig. 1). (See Fig. 2)

2.2. *Surgical Technique*[16]

Hamstring graft was harvested and pre-tensioned. The medial retinaculum was identified and a plane was achieved between the first and this second layer of the retinaculum. A 1 cm skin incision was made in the region overlying the medial epicondyle and adductor tubercle. A broad, strong sleeve of ligamento-periosteal tissue was elevated from this saddle groove between these two bony prominences. The two limbs of the graft were then shuttled through the plane between the first and second layer of the retinaculum to be delivered through the medial para-patellar incision. The graft was sutured to this sleeve to achieve the femoral fixation at Schottle's point.[23] The retinaculum incision at the site was sutured back over it. This proximal limb was then fixed to the extensor retinaculum at the level of proximal extent of the native MPFL. The distal limb was fixed at the level of lower extent of the original MPFL. To achieve a robust soft tissue fixation on the patella, the graft was passed alternately below and above the extensor retinaculum sleeves on the anterior aspect of the patella and sutured using pretzel stitches technique in 30° knee flexion, making sure patella is fixed on to the femur in trochlea.

2.3. Rehabilitation protocol

The knee was immobilized in 30° flexion in a rigid long knee brace for two weeks and patient was kept toe touch weight bearing. Active range of motion and quadriceps strengthening exercises

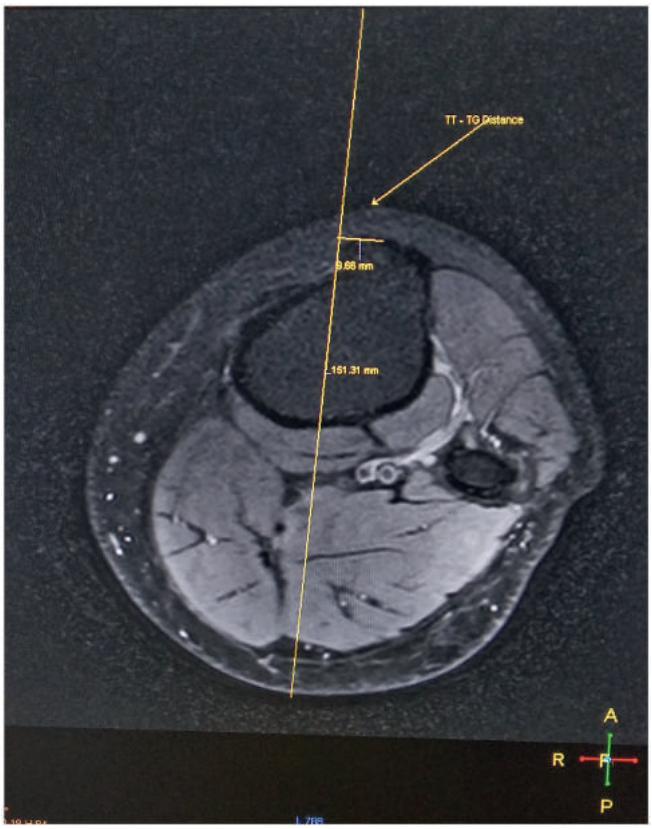

Fig. 1. Image depicting the method of calculation of TT-TG distance on MRI.

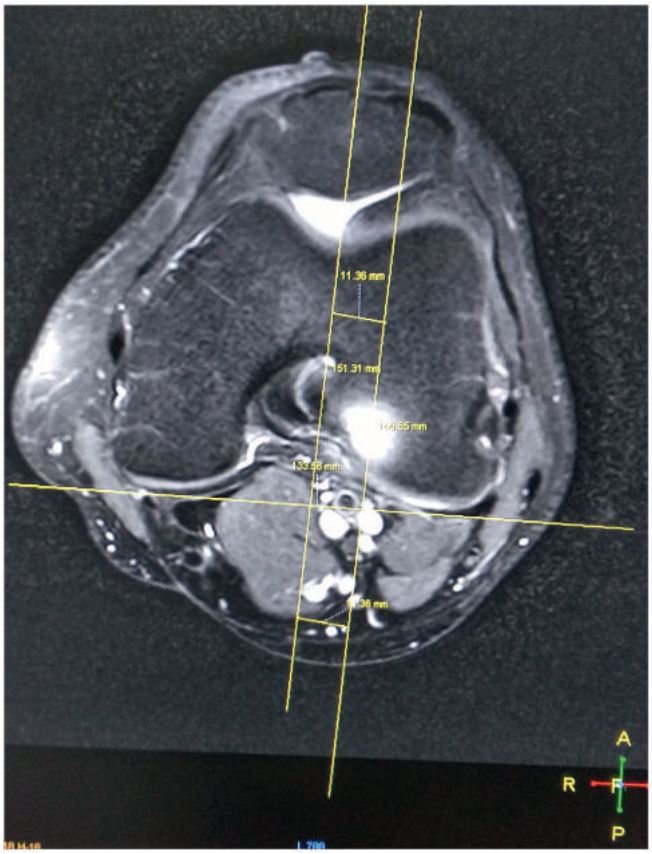

Fig. 2. Image depicting the method of calculation of TT-TG distance on MRI.

were started following suture removal. The brace was discontinued after six weeks. Following this foot, ankle, hip and core stabilization exercises were initiated. Balance and proprioception training was followed by resumption of sports at four months.

2.4. Statistical analysis

The group comparison was made by means of confirmatory analysis. For the statistical analysis the parameter-free rank analysis of variance with repeated measurements according to Brunner (SAS) followed by non-parametric tests as post hoc test with two linked samples (Wilcoxon test) and two independent samples (Mann-Whitney test) was used. The Pearson chi-square test was used to analyse nominally scaled data. All the statistical tests were two-sided and performed at a significance level of $\alpha = 0.05$. The analysis was conducted using IBM SPSS STATISTICS (version 22.0).

3. Results

A total of 37 knees of 35 patients (29 males, 6 females) fulfilled the inclusion criteria (Table 1). The mean follow-up was 81.57 ± 16.07 months and mean age at operation was 19.56 ± 8.02 years (Table 1). The mean time from injury to surgery was 3.20 ± 2.64 months (Table 1). Left knee was involved in 17 patients and right knee was involved in 20 patients (Table 1). Average number of episodes of dislocation before surgery were 3.96 [range 3–6] Table 1). There was no re-dislocation in any of the patients but 4 patients had apprehension test positive (10.81%). The mean TT-TG distance was 10.12 ± 0.59 mm (Table 1). The mean Kujala score, IKDC score and Lysholm score preoperatively and postoperatively after MPFL reconstruction were 62.20 ± 16.86 and 90.32 ± 16.42 respectively ($p < 0.0001$); 58.62 ± 14.34 and 85.15 ± 7.65 respectively ($p < 0.0001$); 68.21 ± 10.72 and 95.30 ± 8.02 respectively ($p < 0.0001$) at the five-year follow-up (Table 2). Mean Tegner score pre-injury and post MPFL reconstruction was 6.23 ± 2.10 and 5.82 ± 1.90 respectively ($p = 0.38$) at a mean follow-up of five years (Table 2).

Table 1
Demographic details and preoperative variables of patients who underwent isolated MPFL reconstruction.

Mean Age (years)	19.56 ± 8.02
Males: Females	29:6
Number of episodes of patella dislocation (Pre-operative)	3.96 (2–6)
Side Involves (Left: Right)	17:20
Duration from Injury to surgery (months)	3.20 ± 2.64
TT-TG distance on MRI (mm)	10.12 ± 0.59

4. Discussion

In this study, significant improvement was observed post MPFL reconstruction surgery in functional outcome scores including Kujala score, IKDC score and Lysholm score at a minimum follow-up of five years. Further, mean Tegner activity score was comparable before MPFL injury and post MPFL reconstruction surgery. There was no incidence of re-dislocation after surgery.

Deie et al. and Camp et al. in their case series reported good functional outcomes using Kujala score at a mean follow-up of 3.2 years.[24,25] Similarly, Christiansen et al., Schottle et al., Steiner et al., Tomkins et al. and Oliva et al. in their respective studies reported Kujala scores of 84, 83, 85.7, 73.4 and 90.7 respectively, which is within 75th percentile of the reported mean value of the Kujala score of the present study.[26–30] However, in all these studies either the author's combined some bony or soft tissue procedure with MPFL reconstruction or left the associated bone dysplasia and soft tissue problems as it is and proceeded with an isolated MPFL reconstruction, which might affect the long-term outcomes.

Tomkins et al. in their study on MPFL repair and MPFL reconstruction reported IKDC scores of 75.6 ± 8 and 62.3 ± 18.5 respectively at a mean follow-up of 2 years and thus lower IKDC score in MPFL reconstruction group, but that is not always possible due to the chronicity of the injury.[29] Shams et al. in their case control study on functional outcomes in athletes and healthy controls reported IKDC scores of 89.2 ± 7.6 and 98.1 ± 2.0, respectively at a mean follow-up of 385 days and thus lower score in the MPFL reconstruction group.[31] Contrary to these two studies, Akhtar et al. in their case series of 3.2 years follow-up reported significant improvement in mean IKDC scores.[32] Similarly Suganuma et al. in their retrospective study of 2 years reported significant improvement in mean IKDC score at a minimum follow-up of 2 years post MPFL reconstruction surgery.[26] The contrasting results in the literature add to the existing dilemma and emphasis on the need of more long term follow-up studies. The present study reports significant improvement in IKDC scores post MPFL reconstruction.

Table 2
Results of Kujala score, IKDCscore, Lysholm score and Tegner activity score at a mean follow-up of 5 years.

N = 37	Preoperatively	Postoperatively at 5 year follow-up	P value
Kujala score	62.20 ± 16.86	90.32 ± 16.42	<0.0001
IKDC score	58.62 ± 14.34	85.15 ± 7.65	<0.0001
Lysholm score	68.21 ± 10.72	95.30 ± 8.02	<0.0001
Tegner score	6.23 ± 2.1	5.82 ± 1.9	0.38

In the present study significant improvement was observed in Lysholm score at a minimum follow-up of 5 years post MPFL reconstruction surgery. We were not able to identify any other study evaluating Lysholm score following MPFL reconstruction though Albuquerque et al. and Briggs et al. in their article reported that Lysholm score is a useful tool to measure outcomes subjective in nature and evaluate performance and activity restrictions both before and after knee surgery, judging the effectiveness of surgical treatment.[33]

Csintalan et al. in their case series reported that the mean Tegner activity score pre-injury and post MPFL surgery were found to be comparable and reported good functional results after MPFL reconstruction surgery.[34] Similarly Camp et al. and Tomkins et al. in their respective studies found no change in pre-injury and post MPFL reconstruction Tegner activity score corresponding to the present study.[25,29] But these studies had some limitations. These studies had a small sample size with a heterogeneous cohort of patients. Associated bony and soft tissue variations were present along with, which were not addressed in all the patients. Further, the heterogeneity of the surgical techniques and rehabilitation protocols is another variable of these studies that may have affected the outcomes. Scheinder et al., Fisher et al. and Matic GT et al. in their systematic reviews reported mean Tegner activity score of 5.7, 5.4 and 5.8 respectively post MPFL reconstruction, which is quite similar to the mean post MPFL reconstruction Tegner value of the current study of 5.82.[10,12,19,21,33,35]

The literature for MPFL reconstruction in recurrent patellar instability demonstrates lower re-dislocation rates, anywhere from 0 to 11% in four recent studies, which comprehends the results of the present study.[36,37] Further, we had 4 patients with the positive apprehension test post MPFL reconstruction.[36,37] Some other authors have reported similar results[38–40] whereas others showed no patients with a positive postoperative apprehension test.[41,42] Christiansen et al. reported a postoperative positive apprehension sign in 41% (18/44) of patients.[43] Deie et al. reported on one patient with a retained apprehension sign which had medial instability postoperatively.[24] The average passive lateral glide was 1.5 quadrants postoperatively. Comparable results were seen in other studies with average recorded translations of 1.6, 1.8, and 1.25 after MPFL reconstructions respectively.[24,34] Hence, the results of the current study are in conformity with the previous literature though we agree with the other author's that patellofemoral pathology being extremely complex, only few of its aspects can be solved by MPFL reconstruction.[24,34,41–43]

Patellofemoral joint instability when associated with bony changes like trochlear dysplasia, patella alta, etc., presents a significantly higher failure rate and below-average functional improvements when isolated MPFL reconstruction is carried out.[4,44] Further, several authors have reported long-term influence on the patellofemoral cartilage when some realignment procedure or bony procedure was performed along with MPFL reconstruction and this led to poor functional outcome.[45–47] Many criteria's have been proposed to guide the surgical management but the indications remain somewhat arbitrary, and there is relatively little evidence to support any specific measures.[4] Further, there exists little documentation related to isolated MPFL tears in literature without any associated bony or soft tissue anatomical abnormality, which enlightens the need of long-term functional outcomes for enhanced evaluation of MPFL reconstructions, which remains elusive in literature.[4]

In the present study, all the bony deformities and soft tissue problems were excluded beforehand by clinically examination and radiographic imaging including MRI. To best of our knowledge, most of the mentioned reports in literature have either included some additional procedure along with MPFL reconstruction or have left them as it is without adding any simultaneous bony or soft tissue procedure, which does not reflect the correct way of measuring the functional outcome for isolated MPFL reconstruction surgery. Redler et al. and Hopper et al. in their studies have emphasized the importance of doing simultaneous bony procedure for trochlear dysplasia along with MPFL reconstruction in order to provide better long-term functional outcomes.[48,49] Fabricant et al. in their studies have reported poor functional outcomes with isolated MPFL reconstruction in patients with associated variations in patella height and have highlighted the need of doing some soft tissue procedure along with the MPFL reconstruction surgery for recurrent lateral patellar dislocation.[50] Damasena et al. in their report have reported better patient satisfaction, when they were treated with simultaneous bony correction procedure and MPFL reconstruction surgery for recurrent patellar dislocation along with trochlear dysplasia.[51] Further, some studies have reported poor outcomes when MPFL reconstruction was done with some metal screws or endobutton.[16,29] In the present study, the basket weave technique was used for MPFL reconstruction, where no metal implant was used for fixation and hence would have caused less damage to patellofemoral cartilage, though we couldn't examine that radiologically with MRI after MPFL reconstruction surgery.[16] Further, this surgery can be performed in adolescent age groups who are at high risk for recurrent dislocation and where physis are open without causing any damage to the growth plate.[16] In addition, parallel recording of the Kujala score, IKDC score, Lysholm score and Tegner activity score provides a better measure reflecting the complex situation of the patients by combining objective and subjective parameters.

This study had a number of limitations. This was a single centre study with a small sample size; however, a homogenous group of patients were enrolled for the study operated by a single surgeon. Further, other recent studies, evaluating outcomes in MPFL repair or reconstruction demonstrate that these are not high volume surgeries and therefore large numbers of study patients are difficult to obtain. As far as other concomitant procedures, there were limited cartilage or meniscus procedures which would have potentially affected the data, though they were not evaluated in the present study.

5. Conclusion

MPFL reconstruction surgery for isolated MPFL tears without any associated bony deformity, or soft tissue alterations has a good long-term functional outcome.

Credit author statement

Ravi Gupta, Conceptualization, Methodology. Akash Singhal, Data curation. Anil Kapoor, Wrote the manuscript. Gladson David, Editing of the manuscript. Atul Rai Sharma, Review of Literature.

Declaration of competing interest

The authors had no conflict of interest related to research and authorship is granted to only those individual who have contributed substantially to the manuscript.

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Case report

Role of proximal tibio-fibular joint stability in anterior cruciate ligament reconstruction- A case report and review of literature

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ABSTRACT

Among the many factors that have been described as a cause of ACL graft failure, mechanical factors such as secondary restraint laxity mostly untreated posterolateral rotatory instability have been suggested by many authors as the main cause of graft failure. Surgical reconstruction of the postero-lateral complex (PLC) and lateral collateral ligament (LCL) in combination with ACL reconstruction is recommended, since solitary reconstruction of the cruciate ligament may result in high in-situ force in the graft and early failure of ACL reconstruction. Proximal fibula being an attachment site to various structures that provides lateral and posterolateral rotatory stability to the knee, makes proximal tibio-fibular joint (PTFJ) an integral part of lateral and posterolateral ligamentous complex. Injury to PTFJ has been described in association with multi-ligament knee injuries and fractures of tibial plateau and tibial shaft. Isolated injury to this joint has been associated with various sports like wrestling, skiing, parachute jumping, soccer etc. In case of isolated injury to ACL, injury to PTFJ is often missed. We describe a case of ACL injury along with PTFJ injury, suffered during motorcycle accident. We also describe the importance of PTFJ stability in ACL reconstruction.

1. Introduction

Surgical reconstruction of the postero-lateral complex (PLC) and lateral collateral ligament (LCL) in combination with anterior cruciate ligament(ACL) reconstruction is recommended by LaPrade et al., since solitary reconstruction of ACL may result in high in situ force in the graft and early failure of ACL reconstruction.[1] Proximal fibula being an attachment site to various structures that provides lateral and posterolateral rotatory stability to the knee, makes proximal tibio-fibular joint (PTFJ) an integral part of lateral and posterolateral ligamentous complex. Thus, its integrity is important for the success of ACL reconstruction.

In case of ligamentous injuries of the knee joint, injury to PTFJ is often missed. Although injury to PTFJ is one of the rare injuries of knee joint, these injuries are much more common than previously thought. Injury to PTFJ has been described in association with multi-ligament knee injuries and with fractures of tibial plateau and tibial shaft.[2,3] Intensity of the force leading to multi-ligament knee injury and lower extremity fractures can disrupt the stability of proximal tibio-fibular joint if the injury occurs in a flexed knee, when proximal tibiofibular joint is most vulnerable. Isolated injury to PTFJ is seen in sports like wrestling, skiing, parachute jumping, soccer etc. In such cases anterolateral dislocation of the PTFJ is most common and it results from a fall on a hyperflexed knee with the foot inverted and plantar flexed, such as landing with a flexed knee caught under the body.

Combined injury of ACL with PTFJ and importance of PTFJ in ACL reconstruction has not been described in English literature. We describe a case of ACL injury along with PTFJ injury, suffered during motorcycle accident. We also describe the importance of PTFJ stability in ACL reconstruction.

2. Case description

38 years male, came to our outpatient clinic in April 2018, with complaints of instability of right knee joint for two months. There was a history of motorcycle accident after which patient had developed knee swelling, which subsided over one week. After this

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patient started having difficulty in going downstairs, and in pivoting activities. The patient's occupation is office-based desk job but he occasionally plays outdoor sports. On examination anterior drawer test, Lachman test and pivot shift test were all positive and were grade 3. A clinical diagnosis of complete ACL tear was made. On MRI (Fig. 1(a) and (b)), radiologist reported a complete tear of the ACL, and there were no other ligament or meniscal injuries. Patient underwent arthroscopic ACL reconstruction using adjustable loop endobutton on femoral side and bio-interference screw fixation on tibial side (Fig. 1(c) and (d)). In 2nd post-operative month patient complained of lateral knee pain, more during climbing upstairs and downstairs. On examination of knee, PTFJ ballotment test was positive. There are no clinical symptoms and signs of common peroneal nerve injury. Preoperative MRI (Fig. 2(a) and (b)) were again evaluated by us and opinion of a separate senior radiologist was also taken, which revealed

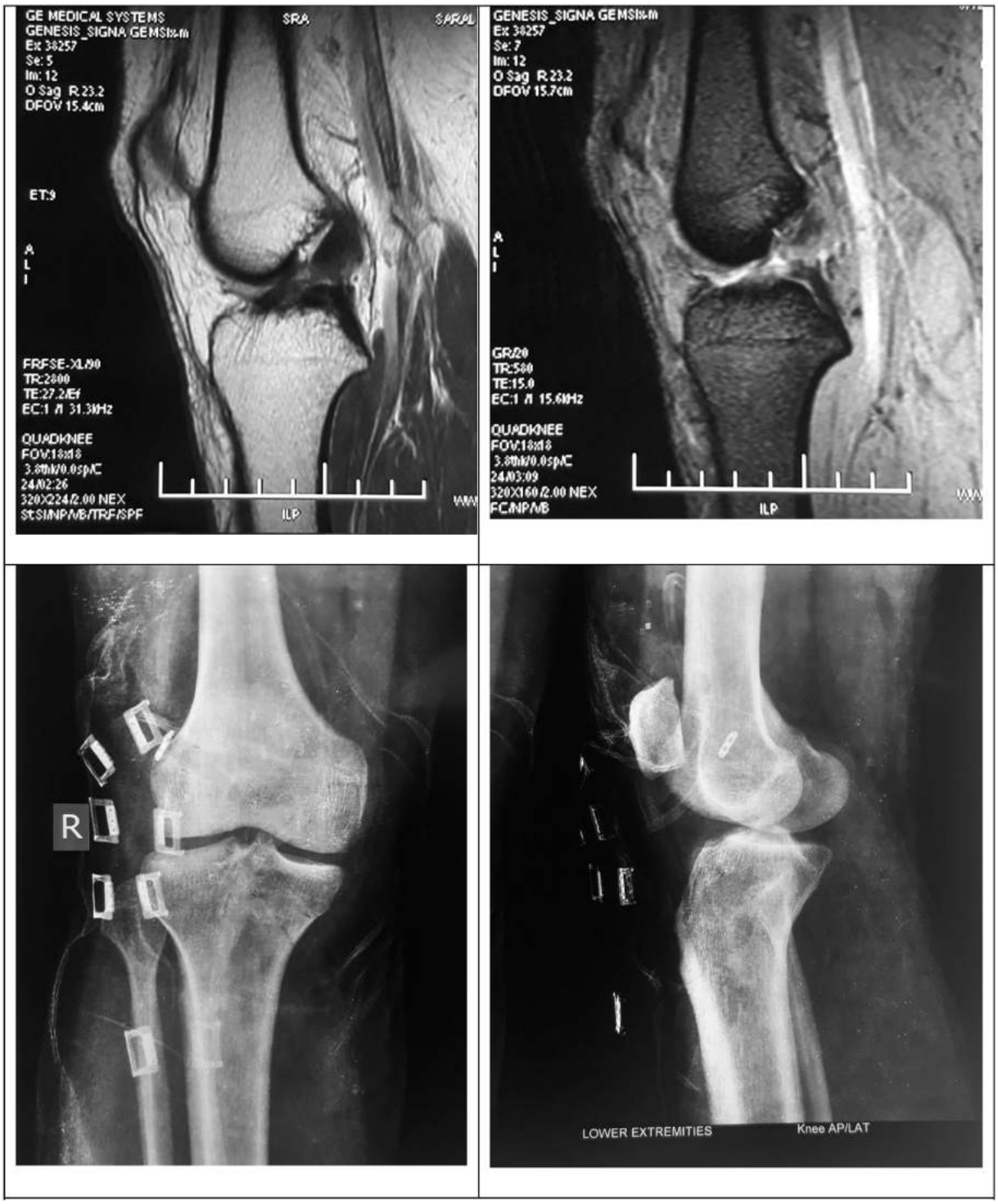

Fig. 1. a) Preoperative MRI: T1 fat sat image showing complete ACL tear. b) Preoperative MRI: T2 image showing complete ACL tear, c) Postoperative Xray of right knee AP view after ACL reconstruction, d) Postoperative Xray of right knee lateral view after ACL reconstruction.

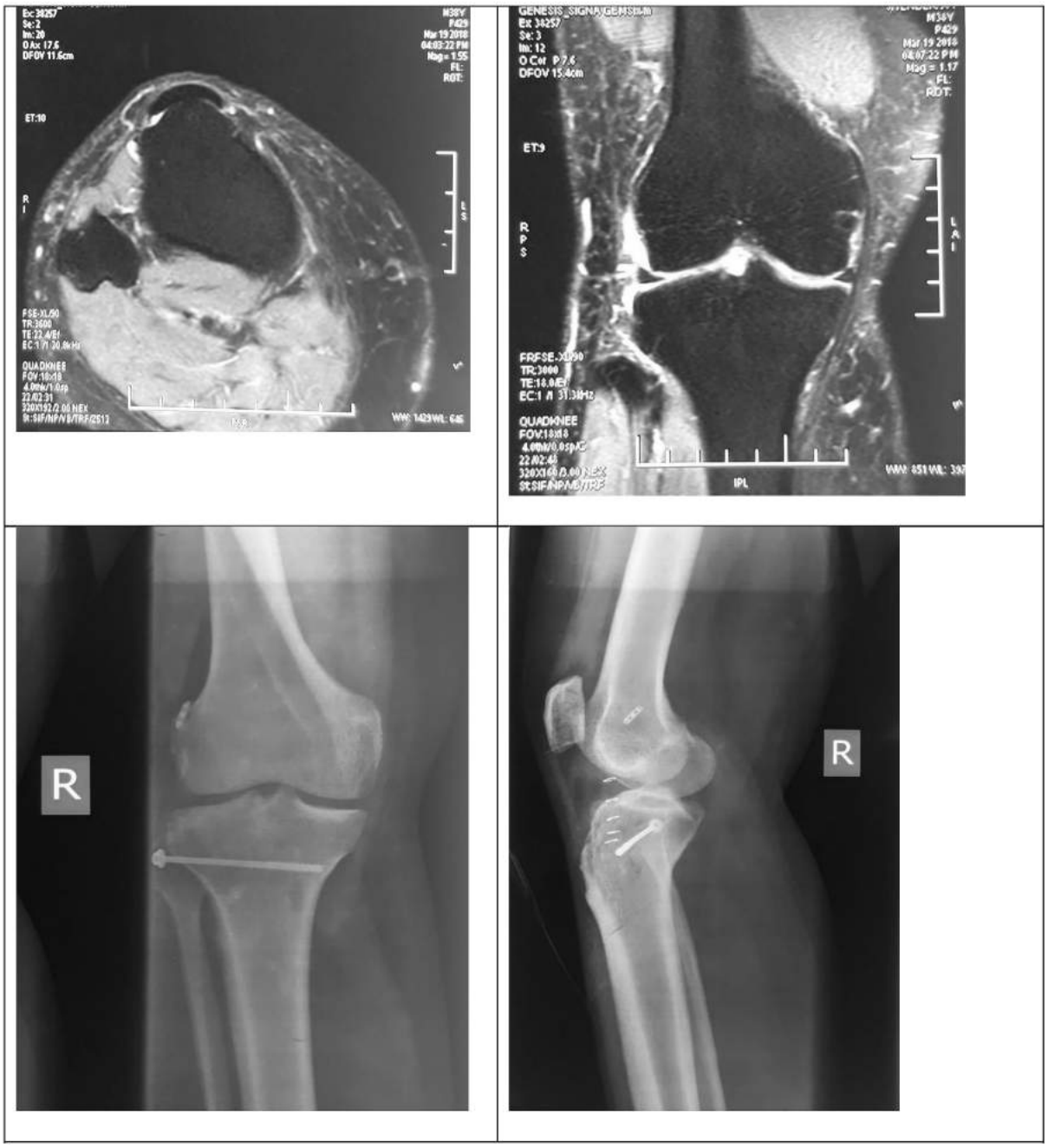

Fig. 2. a) Preoperative MRI T2 axial image showing proximal tibiofibular joint(PTFJ) dislocation, b) Preoperative MRI T2 coronal image showing hyperintensity in PTFJ, suggestive of PTFJ injury, c) Postoperative Day 1 Xray of right Knee AP view after second surgery for PTFJ fixation with 4.0 mm CCS, d) Postoperative Day 1 Xray of right knee lateral view after PTFJ fixation.

dislocation of PTFJ, which was earlier missed. In June 2018, patient underwent second surgery and open reduction and fixation of PTFJ was done using 4.0 mm cannulated cancellous screw (Fig. 2(c) and (d)). After fixation of PTFJ patients lateral knee pain subsided completely and patient had no difficulty in climbing stairs up and down. Also there are no symptoms and signs of common peroneal nerve injury postoperatively. At 6 months of follow up patient had no complaints of lateral knee pain (Fig. 3(a) and (b)). At 1 year of follow up patient complained of slight prominence of screw on medial proximal leg, but there were no complaints of lateral knee pain. Xray of right leg AP and lateral view revealed possible fibrous union at PTFJ and protruding of screw from medial proximal tibia (Fig. 3(c) and (d)). The 4.0 mm CCS was subsequently removed and patient was relieved of impingement and there were no complaints of lateral knee pain or difficulty in climbing stairs.

3. Review of literature and discussion

Proximal fibula gives attachment to various structures like LCL, biceps femoris, popliteo-fibular ligament (PFL), arcuate ligament and fabello-fibular ligament providing lateral and posterolateral rotatory stability to the knee. Injury to PTFJ results in disruption in continuity between attachment site of these structures and the knee joint. Thus, PTFJ injury cause dissipation of stabilising forces

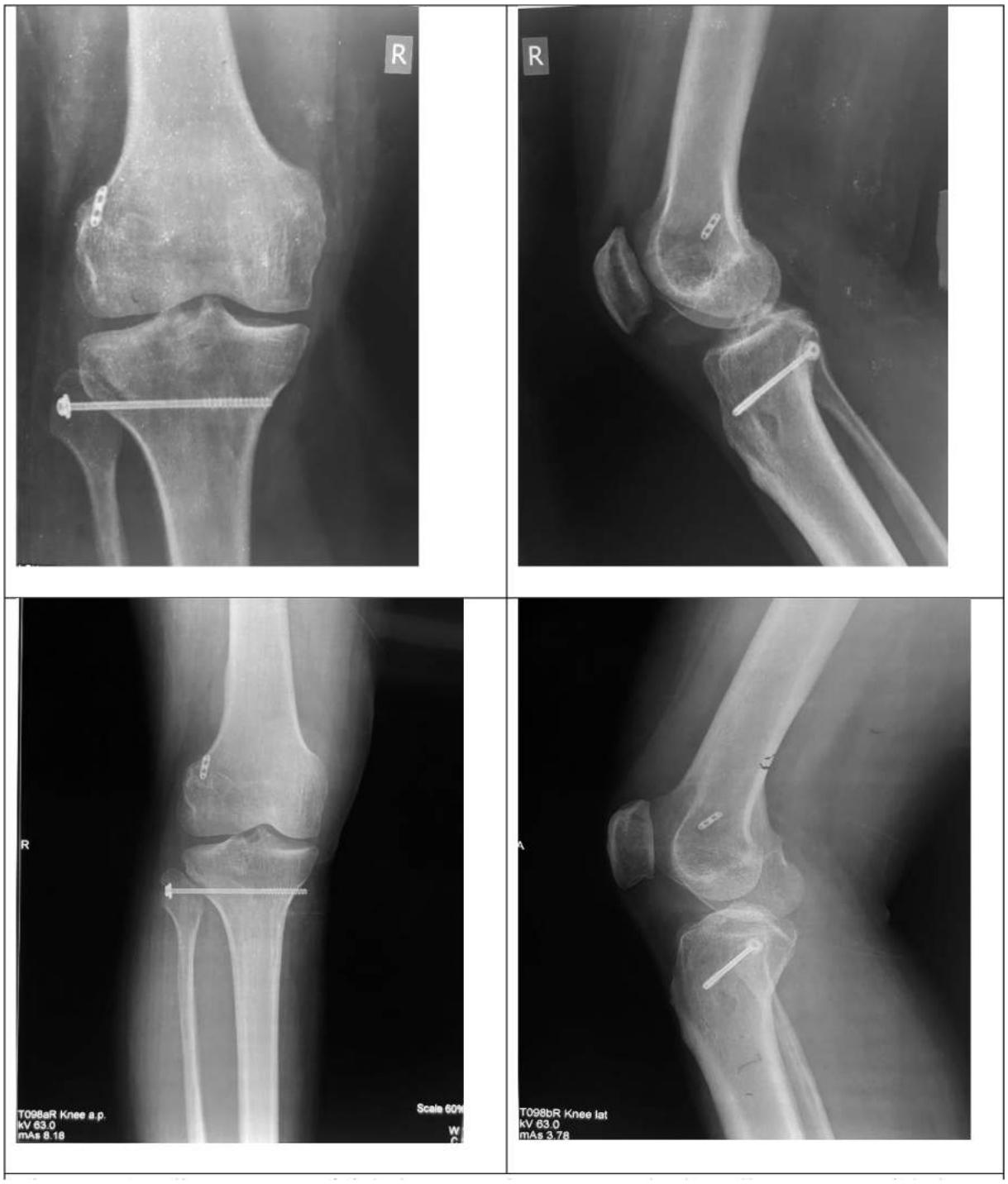

Fig. 3. a) Follow up Xray of right knee AP view at 6 months, b) Follow up Xray right knee lateral view at 6 months, c) Follow up Xray right knee AP view at 1 year showing possible fibrous union at PTFJ and screw protruding from medial proximal tibia, d) Follow up Xray right knee lateral view at 1 year.

that these structures exert on the knee joint. This leads to failure of these structures to provide lateral and posterolateral rotatory stability to the knee joint in cases of PTFJ injury. Thus, PTFJ injury can be considered as equivalent to LCL and PLC injury.

Ménétrey et al., described various factors as the cause of ACL graft failure like patient factors; biological factors; surgical technique such as graft placement and tensioning; graft material allograft versus autograft and post-operative rehabilitation program.[4] In a recent review by Dean and LaPrade, they had found that when the static structures of the PLC remain deficient after ACL reconstruction, one can expect increased tension on the ACL reconstruction graft and thus an increased risk for both acute and chronic graft failure.[5] Kim et al. measured anterior laxity using KT2000 arthrometer and concluded that combined ACL and PLC reconstruction allows less anterior tibial translation than isolated ACL reconstruction, hence lesser forces on ACL graft.[6]

Cadaveric biomechanical studies by a few authors have better explained the role of PLC in knee stability and its interaction with

cruciate ligaments.[1,7,8] These studies assessed either the force on ACL graft or laxity parameters with intact PLC and after sequential cutting of PLC structures. LaPrade et al. has shown that there is significant increase in force on ACL graft with varus loading at both 0° and 30° of knee flexion after fibular collateral ligament transection andthe force on ACL graft is further increased at higher angle of knee flexion and also if varus loading is coupled with internal-external rotation movements. With additional sequential cutting of popliteofibular ligament and popliteus tendon there is a further increase in ACL graft force.[1] Without intact PLC structures, reconstructed ACL fails to control static AP laxity beyond 30° of knee flexion and even a partial lesion of PLC will cause ACL reconstruction to fail to prevent knee laxity if internal-external rotations are taken into consideration.[7] According to the cadaveric study of Plaweski et al., varus laxity is increased in extension only after the sectioning of the lateral collateral ligament, and external rotation in varus and translation of the lateral tibial plateau increased with increasing flexion from 30 to 90° after isolated popliteofibular ligament sectioning. After reconstruction, there is restoration of external varus rotation in extension, translation of the lateral tibial plateau at 90° of knee flexion and kinematics of knee similar to the normal knee.[8]

A retrospective clinical outcome study by Lee et al. found significant improvement in knee scores viz. OAK (Orthopadishe Arbeitsgruppe Knie) and IKDC (International Knee Documentation Committee) after reconstructions of both the ACL and PLC in 44 knees with combined ACL and PLC injuries. The measures of anterior instability viz. anterior stress radiography and mean side-to-side displacement difference dropped significantly and in 91%, rotational stability was same or better as compared to the normal side.[9] Dhillon et al., evaluated outcomes of conservatively managed Type A and Type B PLC injuries in ACL reconstruction patients and found that follow up IKDC scores of concomitant Type A PLC injury patients were similar to the group with isolated ACL reconstruction and IKDC scores of group with concomitant Type B PLC injuries were significantly poorer. They concluded that conservative management of a concomitant Type B PLC injury adversely affects the outcomes of ACL reconstruction, whereas Type A PLC injuries on the other hand do well without surgery and can be left as such even when associated with ACL tear.[1010]

These studies reinforce the clinical observation that in presence of rotatory knee instability due to PLC injury, ACL reconstruction may fail, by adverse effect of higher insitu forces stressing the graft. Thus, additional surgical procedure for reconstruction of PLC is recommended even in case of partial combined PLC lesion. As PTFJ forms an integral part of the PLC, its integrity is utmost for the success of reconstruction or repair procedure for PLC or structures on the lateral aspect of the knee and also, its stability is essential for a successful outcome of ACL reconstruction.

PTFJ can be stabilised using any of the techniques described in the literature such as direct repair, reconstruction of supporting ligament with split bicep femoris tendon or autograft (like semitendinosus tendon) and various screw/pin constructs. In our case we had used 4.0mm cancellous cannulated screw inserted across all the four cortices. Although, this technique is simple but one must take care of the ACL tunnel while inserting screw for PTFJ stabilisation.

4. Conclusion

Clinical assessment of PTFJ has never been a part of routine examination of ligamentous injuries of knee joint. Attention should be given to the stability of proximal tibiofibular joint while assessing and operating ACL injury patients. To prove our hypothesis further biomechanical studies are required to assess and quantify the role of PTFJ stability in anterior cruciate ligament reconstruction.

Declaration of competing interest

None.

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Case report

A case report of neglected patellar dislocation with postoperative complication of thyroid storm mimicking infection - A double whammy

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ABSTRACT

We report a case of 22year old male admitted with the history of 4-year-old post traumatic neglected patellar dislocation initially treated with native treatment, presented to us with painful and restricted knee ROM and extensor lag. After complete pre operative work up, diagnostic knee arthroscopy with open reduction, combined proximal and distal realignment procedure (medial retinacular, VMO repair and tibial tuberosity transfer) was done. Postoperatively patient developed high-grade fever, tachycardia, hypertension and investigations were not correlating with infection. Further clinical manifestations made us to think of some other hyper metabolic state and thyroid function test was done which revealed thyrotoxicosis. A diagnosis of thyroid storm was made in our case according to Burch-Wartofsky score and Japanese thyroid association criteria. Patient was treated with antithyroid drugs, beta-blockers and steroids and responded well. Timely recognition and aggressive management helped to prevent high mortality and morbidity in this case. He was subjected to aggressive rehabilitation after 6 weeks and on regular follow up tibial tubercle transfer healed well with excellent outcome on Kujala Anterior Knee Pain Scoring at latest follow up of 2 years in spite of an unexpected dreadful complication. A complex case of neglected patellar dislocation well planned and executed surgery an unexpected, unusual complication of thyroid storm with very high mortality was timely diagnosed and managed well hence this double whammy experience is worth sharing.

1. Introduction

It is estimated that 2%–3% of the knee joint injuries will involves patella, with 29/100000 per capita risk of a first-time patellar dislocation in adolescents following sports injury.[1] Neglected patellar dislocation is a rare condition can be either congenital or acquired, the patella here lies laterally and is irreducible. Managing this condition can be challenging combined soft-tissue and bony procedure will be needed, rarely corrective osteotomies[2] or arthroplasty may be useful.

Thyroid storm an extremely rare postoperative complication with mortality of 10–30% can present as fever, tachycardia, sweating, tremor, agitation, weight loss, arrhythmia, heart failure caused by an excess of beta adrenergic activity and can even lead to death, usually precipitated by poor drug compliance, infection, surgery or anaesthesia.[3] We report double whammy of neglected patella dislocation with postoperative thyroid storm successfully saving life and patella.

1.1. Case report

22 years male admitted with history of trauma 4-years back had neglected patellar dislocation undiagnosed and natively treated. Presented to us with painful knee ROM affecting his ADL. On examination a puckered scar over the anterior aspect of knee, patella dislocated laterally with a jog of movement, empty trochlear groove, quadriceps wasting present, no Warmth, swelling, crepitus or malalignment of limb; ROM- 20° - 120° flexion possible, extensor lag was present. Examination of other joints was clinically normal.

Standard X-rays AP, lateral and skyline views were taken showing laterally displaced patella, [Fig. 1]. Dejour grade D

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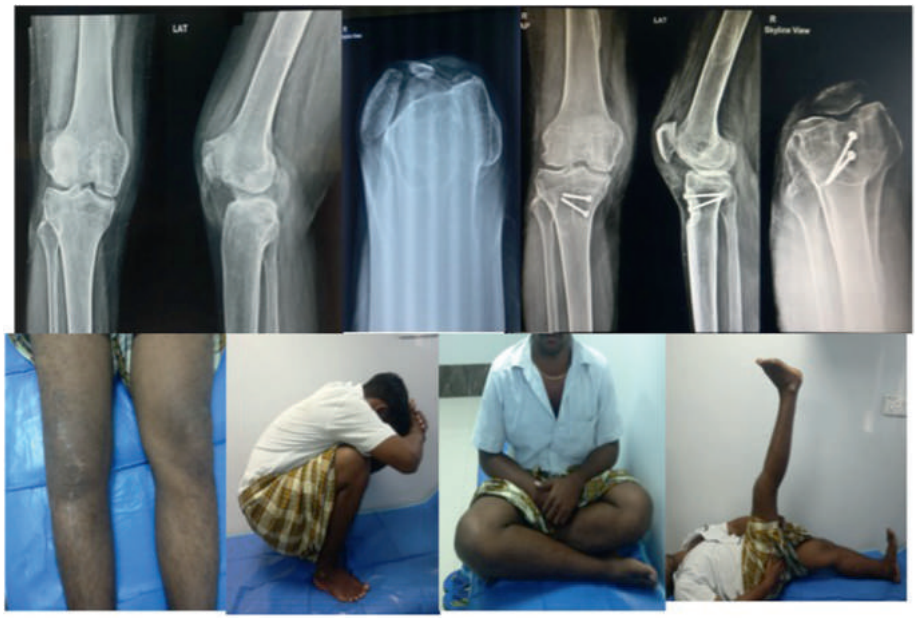

Fig. 1. Collage of Preop X-ray showing laterally dislocated patella with flat trocheal and loose body and Post operative outcome at latest follow up with x-ray showing healed osteotomy with well-reduced patella.

trochealar dysplasia, Crossing sign, Supratrochlear spur and double contour were present. MRI and CT scan was done for further evaluation of TT-TG distance and Insall Salvatti ratio (1.80) [Fig. 2]. There was no limb malalignment.

Preoperative investigations and preanaesthetic evaluation were normal except for a squint eye, which was evaluated at 4 years of age and treated conservatively.

He was taken up for surgery under epispinal anaesthesia; diagnostic knee arthroscopy was done followed by open reduction of patella combined proximal and distal realignment procedure (medial retinacular and VMO repair with tibial tuberosity transfer)

Standard Midline incision puckered scar along with loose body removed, medial parapatellar retinaculum was stretched and thinned out, femoral and patellar surface cartilage was found to be worned out. Patella was struck laterally adhered, arthrolysis, adhesiolysis, proximal release and tibial tubercle osteotomy was done to mobilise the patella. Medial crater was created at appropriate level for tibial tuberosity transfer, placing patella on the trocheal and fixed with 2 cannulated cancellous screws. Knee ROM was done to confirm the mobility and stability of patella. Medial retinaculum and vastus medialis obliqus (VMO) was repaired in mild flexion fixation confirmed under C-arm [Fig. 3]. Thorough wound wash was given tourniquet was deflated and hemostasis was achieved wound closure done in layers and compressive dressing applied with long knee immobilizer, there was no distal neurovascular deficit.

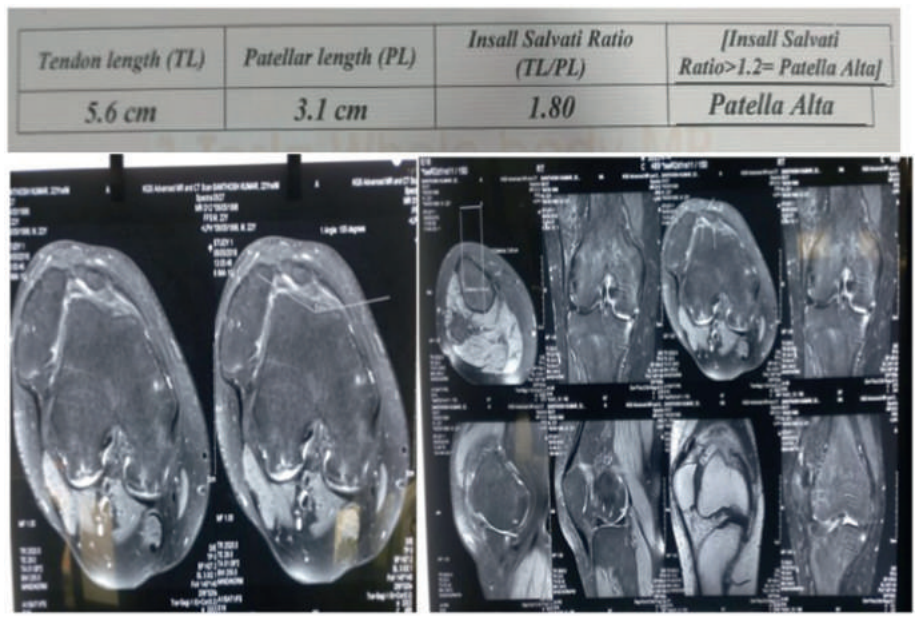

Fig. 2. MRI findings depicting the pathoanatomy with altered indices.

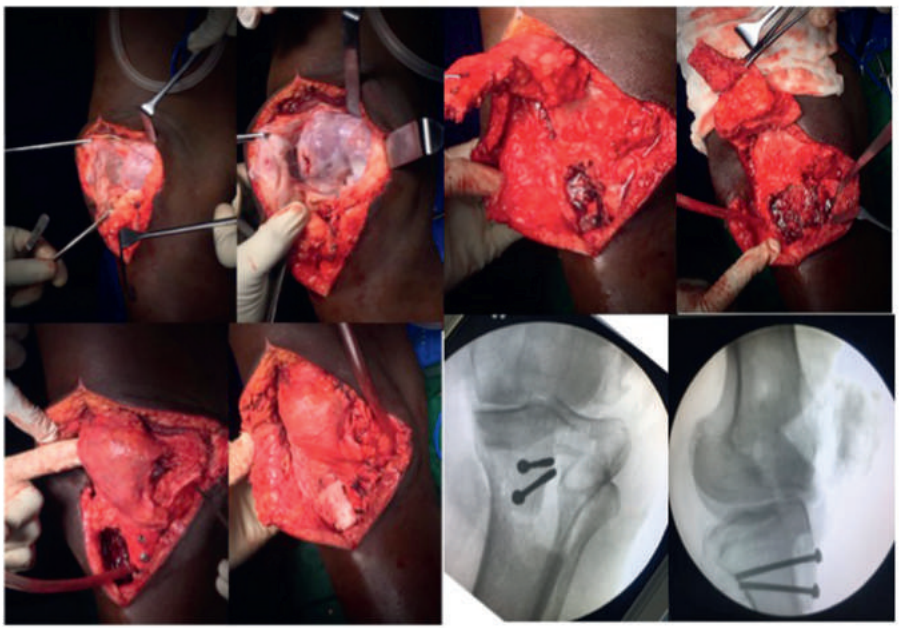

Fig. 3. Intraoperative findings step-by-step procedure of proximal and distal realignment procedure with final C-arm pictures.

Intraoperative period was uneventful. 4–6 hours after surgery patient developed high grade fever (103° F), tachycardia (130/min), hypertension (180/100 mm hg) along with severe pain over surgical site for which he was treated with titrated intravenous opioids and NSAIDS, antipyretics and other cooling measures. Symptoms continued on first POD. Epidural analgesia was initiated and pain reduced significantly but tachycardia (140/min) and fever spikes (103^0 F) persisted wound inspection was uneventful. Inflammatory markers with blood and wound cultures were done. Intensivist and anaesthetist took over further management.

On 2nd POD patient had nausea, vomiting, altered sensorium (restlessness, disorientation), but no clinical signs of meningism and CT brain was normal. A blood sample for thyroid function test was sent which revealed severe hyperthyroidism(FT_3 - 17.05 pg/dl, FT_4 - 80.71 ng/dl and TSH 0.08mu/l). A diagnosis of thyroid storm was made according to Burch-Wartofsky score[4] and Japanese thyroid association criteria.[5]

Endocrinologist opinion obtained, patient was started on tablet carbimazole 20 mg BID, tablet propranolol 40mg TID and I V dexamethasone 4 mg BID with adequate hydration. Patient showed drastic improvement, repeat thyroid function test revealed decrease in T3 and T4 levels, and was discharged on 10th POD with antithyroid medications. He had delayed wound healing but was uneventful and was followed up at regular intervals protected rehab was done till 6weeks with only isometric exercises and ROM as permissible.

After 6 weeks x-rays were good and he was advised aggressive rehab. Tibial tubercle transfer healed well by 16 weeks gained reasonably good movements. Excellent outcome was seen with a score of 88 on Kujala Anterior Knee Pain Scoring (AKPS)[6] system at latest follow up of 2 years [Fig. 1]

2. Discussion

The patella is the largest sesamoid bone, post traumatic or acquired persistent dislocation of patella is a rare condition.[7] Early diagnosis is important, thereby allowing surgical correction and avoiding late sequalae, including early degenerative changes in the knee.

MPFL is an important patellar stabilizer, with the trochlear groove providing further patellar stability with deeper knee flexion. Variants in trochlear morphology can predispose to maltracking or even gross subluxation/dislocation.[1]

The main anatomical factors responsible for patellar instability are trochlear dysplasia, an excessive distance between the tibial tubercle and the trochlear groove (TT-TG), excessive patellar tilt, and a high-riding patella (patella alta). Secondary factors affecting the stability of the patella are excessive femoral anteversion, external rotation deformity of the tibia, genu recurvatum, and genu valgum.[8]

A standard 3-view radiographic series includes a standing flexion posteroanterior, lateral, and 45° flexed axial Merchant view of the knee. While there are numerous measurements available like Insall-Salvatti index, Caton-Deschamps index (CDI), Blackburn-Peal ratio to quantify the patellar height.[1]

Surgical procedures may be divided into those that address the soft tissues (Lateral release, Vastus medialis advancement, Repair or reconstruction of the medial patellofemoral ligament), and bony changes (Tibial tubercle transfers, Trochleoplasty). In order to remedy patellar instability, the surgeon may need to combine soft-tissue and bony procedures. In our case as there was increased Insall Salvatti ratio and TT-TG angle more than 20, we planned for open knee arthrolysis, combined proximal and distal realignment procedure (tibial tuberosity transfer, medial retinacular and VMO repair).

Postoperative thyroid storm is a rare life threatening manifestation of hyperthyroidism with 0.22% incidence.[9] The diagnosis of thyroid storm needs high index of suspicion based on signs and symptoms. Burch-Wartofsky score and Japanese thyroid association criteria gives reliable criteria to diagnose thyroid storm though not definitive. Our patient had Burch- Wartofsky score of 80 that indicates very high likelihood of thyroid storm, and also by Japanese thyroid association criteria. In a survey of Japanese patients with thyroid storm, the leading cause of death includes multiorgan failure and congestive heart failure [15].

Pharmacological therapy involves antithyroid drugs, beta-

blockers and corticosteroids. Timely diagnosis and treatment of thyroid storm can have gratifying outcome though mortality and morbidity is as high as 10–30%.

3. Conclusion

Posttraumatic neglected patellar dislocation is a rare complex condition needs proper evaluation; planning and careful surgical intervention. Thyroid storm as postoperative complication is very rare with high mortality may mimic infection, precipitated by poor drug compliance, infection, surgery or anaesthesia. Timely diagnosis and treatment can be life saving. Certain questions here remains lingering, should we routinely do thyroid function test in all patients or high-risk patients only, could this situation have been avoided if we would have preoperatively done thyroid function test.

Declaration of competing interest

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Case report

Arthroscopic removal of intrarticular acetabular exostosis and follow up at 5 years: A case report

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ABSTRACT

Osteochondromas represent the most common benign bone tumors in children; they usually have isolated involvement but may also present in multiplicity as multiple hereditary exostoses (MHEs) disease, an autosomal dominant disorder with a prevalence of 1 in 50000 in the general population.

In MHEs the growing physis (distal femur, proximal tibia, forearm, proximal humerus) are commonly affected and intraarticular lesions are rare; even if osteochondromas often appear to be painless, slow growing tumors, functional impairment is a possible complication because of bone growth reduction, joint deformation and restricted motion, neurovascular compression. Therefore, surgical excision may be required: in literature only few cases of intraarticular hip exostoses are described, and their treatment is heterogeneous; moreover, long follow up are lacking regarding arthroscopic removal.

Hereby we present the case of a 9-year old patient affected by MHE with involvement of left acetabulum, its treatment by arthroscopy and the satisfactory result at 5 years of follow up.

1. Introduction

Osteochondromas are the most common benign bone tumors, occurring in 3% of general population. In 15% of osteochondromas multiple hereditary lesions are present (multiple hereditary exostoses): the disorder is genetically determined with an autosomal dominant transmission.[1] Children are commonly involved in MHE and the typical sites of growing are represented by the metaphyseal regions of long bones (femur, humerus, tibia, forearm); despite osteochondromas are often asymptomatic, they can cause significant deformities, restriction of range of motion and growth disturbance.

Intraarticular, symptomatic lesions of the hip may also occur, but they are rarely described in literature[1–5]: a surgical treatment is usually indicated but there is not a current agreement about the optimal approach. Open surgery through anterior or anterolateral approach to the hip and surgical dislocation[1–3] and arthroscopic removal are the main options. Only two similar cases of arthroscopic treatment have been published[4,5] but both are incomplete.

We report a case of successful arthroscopic removal of acetabular exostosis in a young patient affected by MHE disease, with a 5-year follow up.

2. Methods

A 9-year old girl affected by multiple hereditary exostoses came to the clinic complaining about progressive left hip pain and limping. She used a crutch as walking aid; no previous trauma was reported. The clinical examination showed a complete hip range of motion, with pain in internal/external rotation and on weightbearing.

Radiographs of the pelvis revealed multiple lesions at the right femur (already known), the presence of an acetabular fossa exostosis with femoral head subluxation and a coxa valga on the left side (Fig. 1A and B). In addition, CT scan and 3D reconstructions were performed to evaluate exostosis features better (Fig. 1C and D). Because of the clinical symptoms and the possible growing of the lesion with femoral head displacement we decided to arthroscopically excise the osteochondroma. The patient was placed in lateral decubitus and standard anterolateral portal was created under fluoroscopy in order to avoid any damage to the labrum and to the femoral head cartilage. The 70° arthroscope is then inserted

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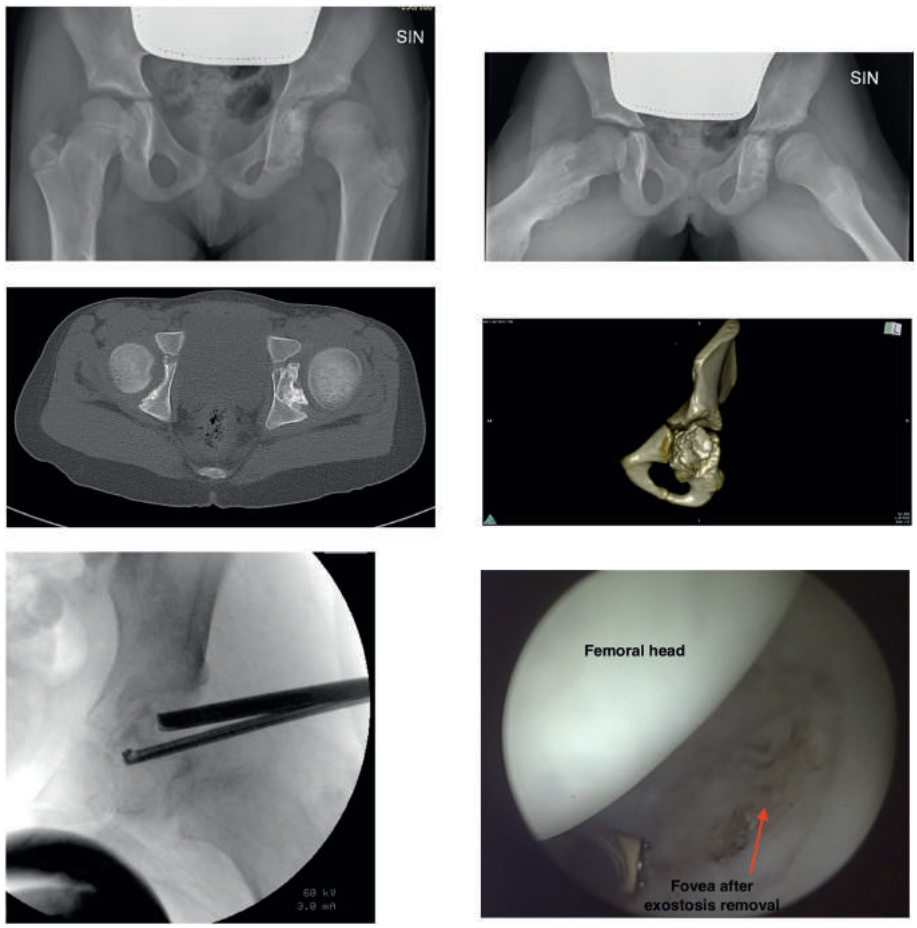

Fig. 1. A-B-C-D-E: Preoperative anteroposterior (A) and lateral (B) view showing the intracetabular lesion. Axial view (C) and 3D CT reconstruction (D). Intraoperative image intensifier view (E) and arthroscopic (F) view of the fovea after exostosis removal.

into the hip. The capsular triangle between the labrum and femoral head is visualized and a second (anterior) portal is created perforating this triangle. Arthroscopically the lesion was observed clearly, located in the acetabular fossa and extended to the medial wall (Fig. 1E). No sign of cartilage lesion were recorded. With motorized instrumentation (high speed burr) we performed the exostosis excision paying attention not to damage the cartilage surfaces of the femoral head and the remaining part of the acetabulum. Only an exiguous cartilage removal was necessary for assuring complete exostosis excision, and removed cartilage was in the non-weight bearing area of the joint. Nevertheless, the young age appears to be a positive predictive factor for cartilage regeneration (Fig. 1F). Finally, the osseous material removed was sent to the histologic analysis: the biopsy result confirmed the diagnosis of benign lesion. After surgery we recommended the patient to use two crutches for 30 days and touch weight-bearing was prescribed for the same period.

3. Results

The patient has been followed for 5 years: in this period of time she has denied hip pain on weightbearing or limping recurrence; she has been able to perform sports (soccer) and her daily activities. At three months of follow up, radiographs showed a better congruence of the femoral head and the acetabulum, with an intact fossa and a developed medial wall without signs of tumor recurrence. At five years of follow up, the patient is asymptomatic; at pelvis radiographs the femoral head is relocated in the centre of the joint and a progressive correction of the coxa valga is evident. A slight acetabular dysplasia persists, but its clinical value appears to be unremarkable: in fact, range of motion at 5 years is complete and internal/external rotations are painfulness. (Fig. 2A–D).

4. Discussion

As already mentioned, only two reports in literature[4,5] discuss about arthroscopic removal of hip intra-articular exostoses: the pathology itself is quite rare and the procedure is technically demanding, requiring experience and extensive training. Three papers suggested to perform open surgery[1–3] and surgical dislocation through anterior or lateral approach in order to preserve posterior vessels to the femoral head. In comparison, arthroscopy is a less invasive option and decreases the risk of iatrogenic damages; moreover, it allows immediate weight bearing post operatively in contrast to a non-weight bearing period of minimum 6 weeks after surgical dislocation. The previous reports published about arthroscopic exostoses removal took their patients under surveillance for 6 months[4] and 3 years[5]; unfortunately only Bonnomet[4] showed a single post-operative CT-scan image. To our knowledge, there is no published report describing acetabular adaptation on the long run in those cases. It is worthwhile underlining the importance of treating intra-articular exostoses early, when the acetabulum still has a remodelling potential; in our case the relocation of the femoral head appears to be progressive, and a slight acetabular

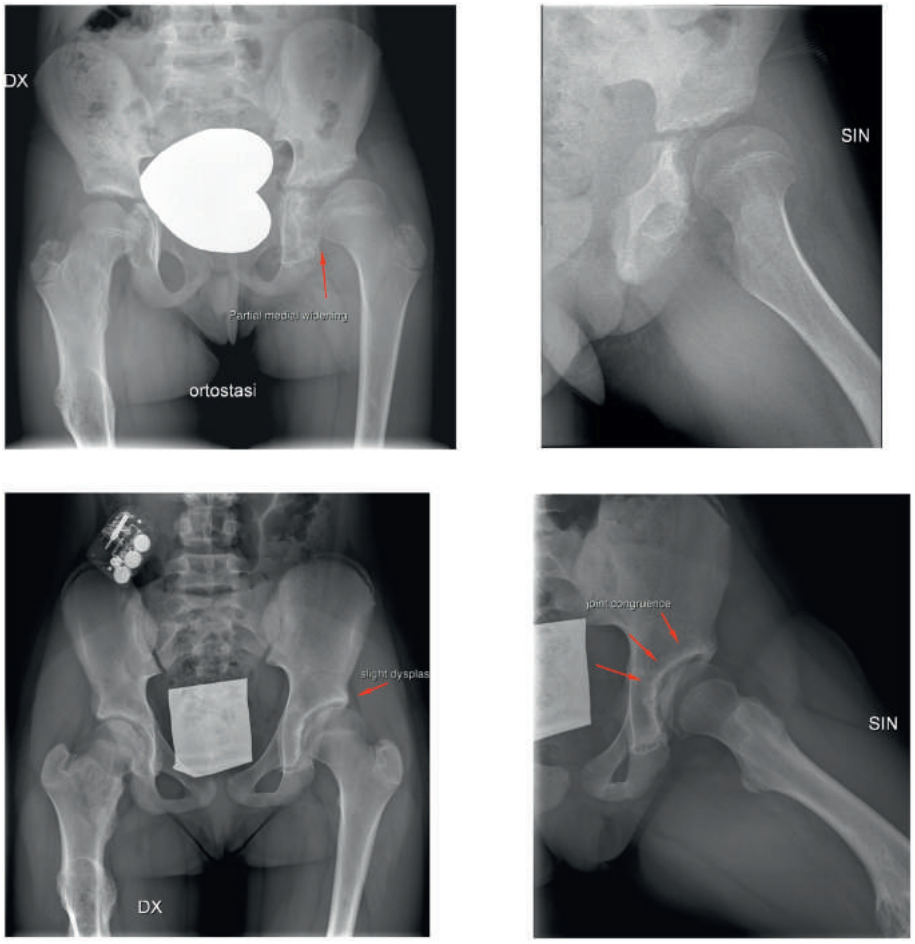

Fig. 2. A-B-C-D: Postoperative (3 months) anteroposterior (A) and lateral (B) view showing complete removal of the intracetabular lesion without relocation of the femoral head. Postoperative (5 years) anteroposterior (C) and lateral (D) view showing the relocation of the femoral head.

dysplasia, even if asymptomatic, persists at 5 years after surgery.

In conclusion, arthroscopy is a reliable option to treat intra-articular exostoses especially in children and adolescents: it reduces the risk of vascular damages to the femoral head, avoids visible scars, allows lesion removal with minor cartilage impairment and it does not seem to affect the bone remodelling potential. In expert hands the arthroscopic visualization of the exostosis can be clear and safe, and the removal may be complete without recurrences.

Declaration of competing interest

None.

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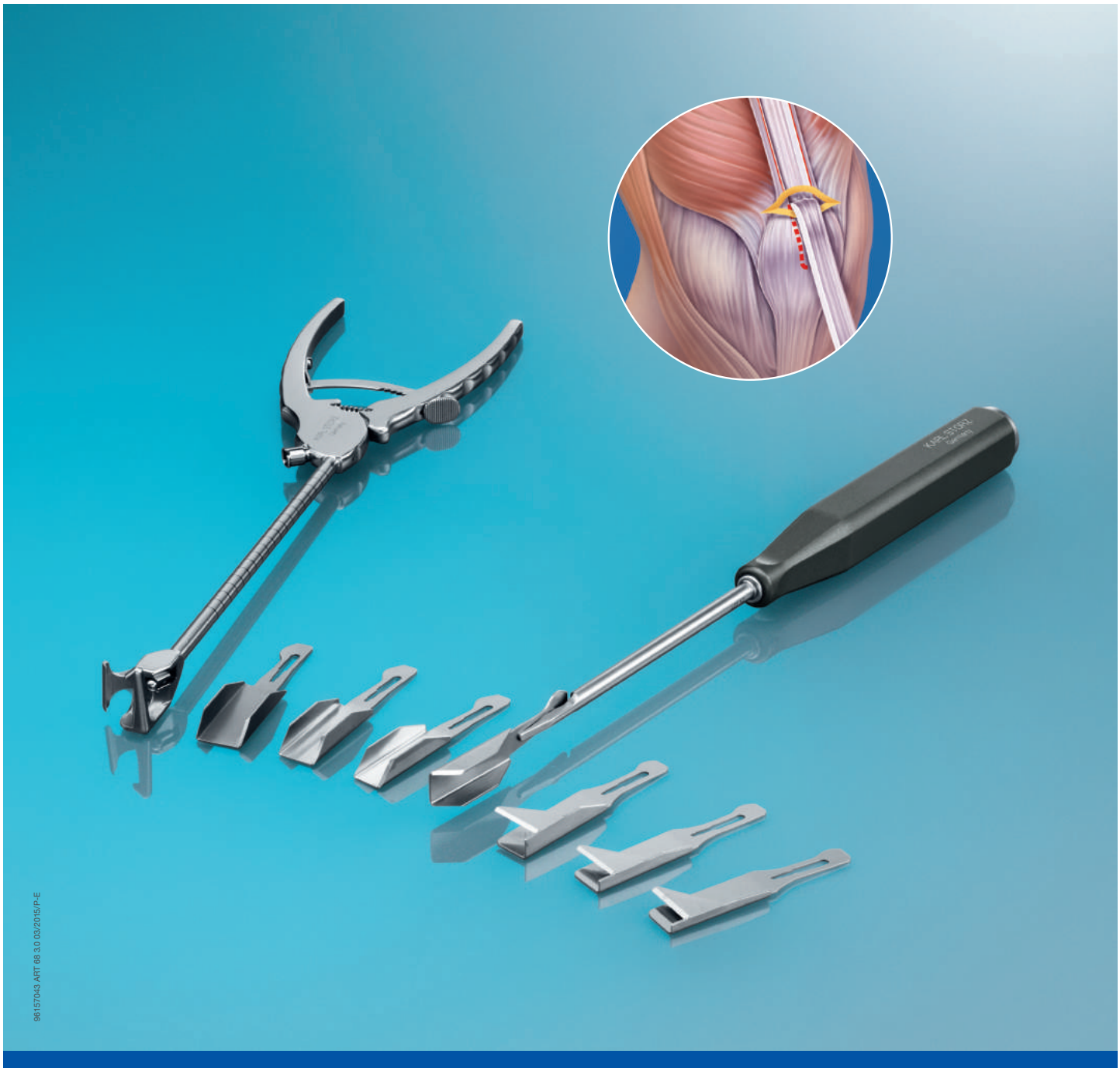

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