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Chemoprophylaxis in lower limb immobilization : A systematic review and meta-analysis

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The aim of this systematic review and meta-analysis is to review the effectiveness of low molecular weight heparin (LMWH) and novel oral anticoagulants (NOACs) for thromboprophylaxis in trauma patients treated with lower limb immobilisation.

All randomized controlled trials (RCTs) comparing thromboprophylaxis to no prophylaxis or standard for prevention of VTE in patients with lower limb trauma treated with immobilisation were included.

Eight studies totaling 3190 patients were included. The overall incidence of thromboembolic events in the control group ranged from 2.3% to 40% (137/871) and from 0% to 37% (77/884) in the LMWH group (RR 0.57; 95% CI = 0.45 to 0.73), P < 0.00001. One cohort study demonstrated equivalence of NOACs in VTE rate to LMWH with another demonstrating a significant reduction in VTE rates.

Our results demonstrate that LWMH is an effective agent in reducing DVT in these patients with an acceptable safety profile.

Keywords : Trauma ; Lower extremity ; Anticoagulants ; Thromboembolism

INTRODUCTION

Deep vein thrombosis (DVT) is a common complication following lower limb immobilization occurring in between 5% and 39% of cases *(18)*. Immobility is a well-known risk factor for DVT in surgical patients. A recent meta-analysis estimated an overall incidence of venous thromboembolism (VTE) of appropriately 20% in patients with ankle fractures *(25)*. Considering that the meta-analysis excluded high risk patients e.g. patients with malignancy, this rate is likely to underestimate the true value. Furthermore, the incidence of VTE in surgically-managed lower limb trauma is significantly higher in patients not administered thromboprophylaxis *(5)*, up to 58%.

Given the reported incidence of venous thromboembolism in lower limb trauma patients, adequate and appropriate interventions are needed to prevent such complications. Despite this, there is controversy as to whether chemical thromboprophylaxis is beneficial in patients managed with lower limb immobilisation. The American College of Chest Physicians do not recommend thromboprophylaxis in patients with

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isolated lower extremity injuries below the knee requiring immobilization without a history of VTE *(4)*. Comparatively, the Royal College of Emergency Medicine supports the use of thromboprophylaxis in ambulatory patients with isolated limb injury who are immobilised in a below knee plaster cast (20). Meanwhile, the British College of Standards in Haematology recommends prophylaxis for high-risk patients only *(2)*. A Cochrane meta-analysis in 2014 of 1490 patients found that low-molecular weight heparin (LMWH) significantly reduces the incidence of DVT in patients who have their lower limb immobilised by any modality whether operated or not *(25)*. Given the discrepancies in guidelines it is unsurprising there are variations in the way thromboprophylaxis is employed. A survey among Dutch surgeons found that in 12% of hospitals thromboprophylaxis was not used in these patients, while in 44% thromboprophylaxis was administered only to those with a high thrombotic risk *(26)*. In a survey in Italy, great heterogeneity was found in the timing and use of thromboprophylaxis in these patients. Similarly, a survey in the UK demonstrated that in 62% of departments thromboprophylaxis is not routinely provided to lower-limb trauma patients patients *(3)*.

These variations can be attributed to several factors. Lower-limb trauma patients treated conservatively are often managed on an outpatient basis or treated in the emergency department. As a result, conducting studies on this group of patients can be more difficult. Due to the variation in guidelines and the paucity of studies investigating VTE in lower-limb immobilization compared to

History

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#50	Add	Search (#40 OR #48)	303641	06:23:32
#49	Add	Search (#3 OR #5 OR #12 OR #14 OR #15)	217710	06:22:58
#48	Add	Search ((("Antithrombins"[Mesh]) OR "Platelet Aggregation Inhibitors"[Mesh]) OR "Anticoagulants"[Mesh])	89100	06:21:48
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#5	Add	Search "Pulmonary Embolism"[Mesh]	33354	06:01:09
#3	Add	Search "Venous Thrombosis"[Mesh]	47530	05:59:56

Appendix 1: Search Strategy: ("Antithrombins"[Mesh]) OR "Platelet Aggregation Inhibitors"[Mesh]) OR "Anticoagulants"[Mesh]) OR ("Anticoagulants" [Pharmacological Action]) OR "Platelet Aggregation Inhibitors" [Pharmacological Action]) OR "Factor Xa Inhibitors" [Pharmacological Action]) OR "Antithrombins" [Pharmacological Action]) OR abciximab OR clopidogrel OR enoxaparin OR fondaparinux OR heparin OR lamifiban OR reviparin OR warfarin OR apixaban OR argatroban OR bivalirudin OR dabigatran OR darexaban OR edoxaban OR eisenstasin OR inogatran OR lefaxin OR lepirudin OR melagatran OR otamixaban OR rivaroxaban OR ximelagatran) AND ("Immobilization"[Mesh]) OR "Casts, Surgical"[Mesh]) OR "Braces"[Mesh]) OR "Splints"[Mesh]) OR "Lower Extremity/injuries"[Mesh]) OR (lower-leg fracture* OR ankle fracture* OR lower limb fracture*)) AND ((DVT OR PE OR VTE OR thromboprophylaxis OR thrombopreventive* OR chemoprophylaxis OR chemopreventive*) OR ("Thrombosis"[Mesh:noexp]) OR "Thromboembolism"[Mesh:NoExp]) OR "Venous Thromboembolism"[Mesh:NoExp] OR "Pulmonary Embolism"[Mesh]) OR "Venous Thrombosis"[Mesh])).

patients undergoing hip and knee surgery, there is an inconsistent use of thromboprophylaxis in these patients. However, considering the risk and burden of VTE, it is necessary to review the evidence behind the preventative strategies.

The majority of current literature regarding thromboprophylaxis in lower-limb immobilisation refers to the use of LWMH as a thromboprophylactic agent. Novel oral anticoagulants (NOACs) are increasingly being used for VTE prevention in patients undergoing elective orthopaedic surgery procedures, such as hip and knee replacements. As well as being safe and convenient, many studies have demonstrated clinical efficacy of NOACs in reducing the incidence of VTE after hip and knee replacement surgery *(17)*. As such, rivaroxaban has been recommended as a thromboprophylactic agent for patients undergoing hip or knee replacements *(1)*. Considering the rates of VTE in elective patients are comparable to those of lower-limb trauma patients, the role of NOACs as a thromboprophylactic agent in these patients must be considered.

As such, the aim of this systematic review and meta-analysis was to review the effectiveness and safety profile of low molecular weight heparin and novel oral anticoagulants for thromboprophylaxis in lower-limb trauma patients.

MATERIALS AND METHODOLOGY

A protocol for this meta-analysis and systematic review was established by the authors prior to commencing the study. The search criteria and algorithm can be found in Appendix 1.

All relevant published and unpublished randomized controlled trials comparing thrombo-prophylaxis (either LMWH or an oral anticoagulant) to no prophylaxis (either placebo or no treatment) or standard of care (SOC) in the hospital or outpatient setting for prevention of VTE in patients with immobilised lower limb fractures or soft tissue injuries were included in the data analysis. Cohort studies and controlled trials were included as part of the qualitative review.

The literature search was performed using the following MEDLINE (Medical Literature Analysis and Retrieval Online, Bethesda, MD), EMBASE (Exerpta Medica Database, Amsterdam, Netherlands) and Cochrane Central Trials Register (CENTRAL) for papers published up to and including 1st January 2016. Google Scholar was also searched. Search terms and the search algorithm used are shown in Appendix 1

The studies and search strategy was independently evaluated by two of the authors (M.K. and S.O.). Any disagreements were resolved by discussion and review by a third author (A.D). Among the potentially eligible studies, studies including polytraumatized patients or patients with a femoral fracture were excluded from the meta-analysis. Non-randomised controlled trials were excluded from the meta-analysis. Studies comparing one different types of chemoprophylaxis were included in the qualitative review. Where identified, duplicate studies were excluded. Only full articles were considered in the analysis. A Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram is shown in Figure 1.

Chemoprophylactic agents investigated included LMWH, aspirin and oral anticoagulants. Each type of intervention was analysed separately.

In each selected study, data were independently assessed by two authors (M.K. and S.O.) assessing

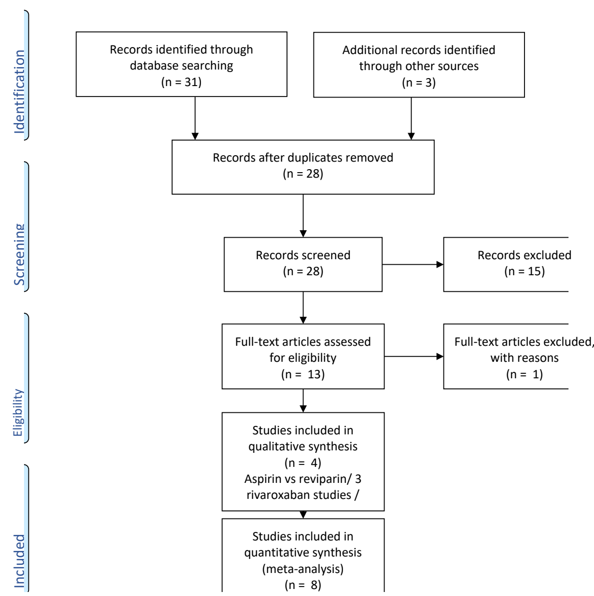

Figure 1. — PRISMA Diagram.

for study quality, study design and endpoints. The quality of studies in the meta-analysis were consensually assessed employing the Jadad score. All studies with a score of 3 or less were excluded.

The primary outcome of the meta-analysis was the incidence of VTE. This included a) overall VTE, b) subjects with clinically significant VTE (i.e. asymptomatic proximal deep-vein throm-

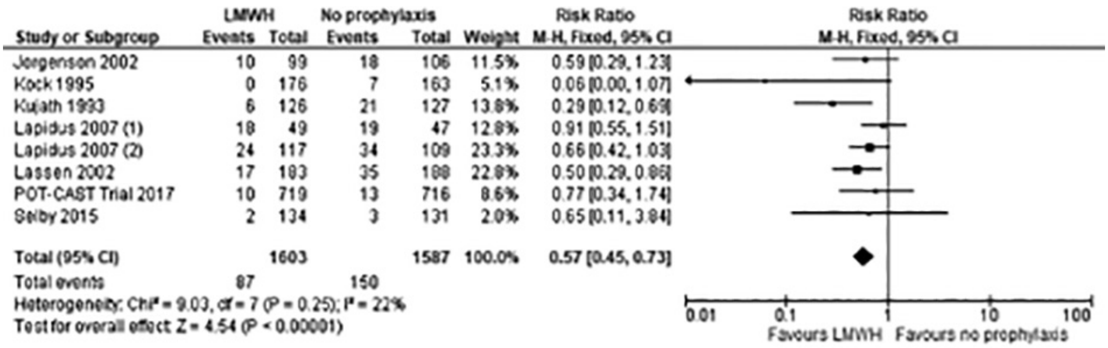

Figure 2. — Forrest plot comparing LMWH with placebo or no prophylaxis with overall VTE as outcome.

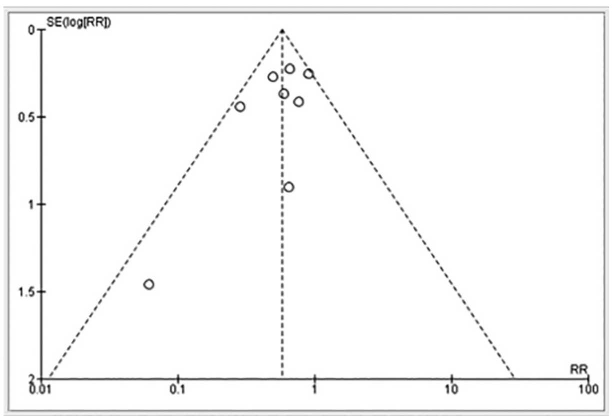

Figure 3. — Funnel plot comparing LMWH with placebo or no prophylaxis with overall VTE as outcome.

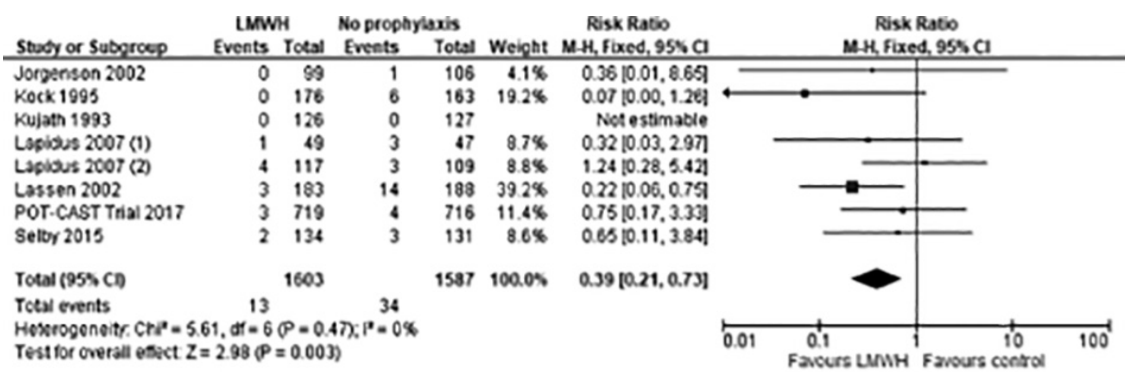

Figure 4. — Forrest plot comparing LMWH with placebo or no prophylaxis with clinically significant VTE as outcome.

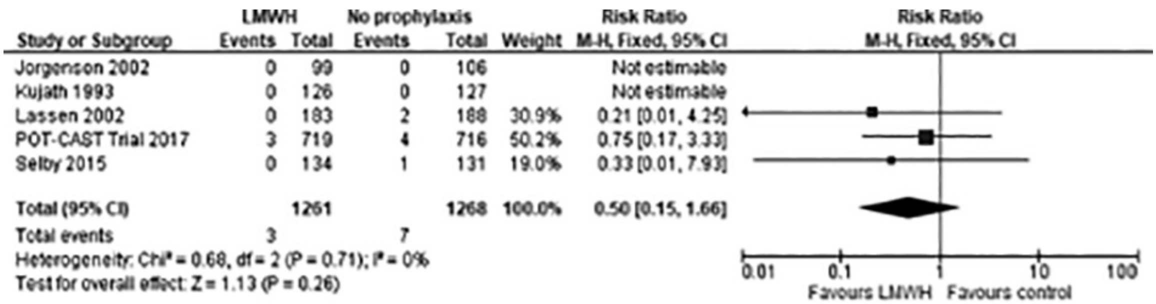

Figure 5. — Forrest plot comparing LMWH with placebo or no prophylaxis with PE as outcome.

Table 1 — Characteristic of included trials in meta-analysis

Author	Year	Blinding	Leg Injury	Treatment	LMWH	Control	Assessment	No. of subjects
POT-CAST Trial	2017	Open	Fracture or soft tissue injury	Conservative or Sugery	Dalteparin 2500IU or nadroparin 2850IU during immobilisation	No treatment	US	1435
Selby R	2015	Double	Fracture	Surgery	Dalteparin 5000IU for 14 days	Placebo	US	265
Lapidus LJ (1)	2007	Double	Ankle fracture	Surgery	Dalteparin 5000IU for 5 weeks	Placebo	Venography	272
Lapidus LJ (2)	2007	Double	Achilles tendon rupture	Surgery	Dalteparin 5000IU for 6 weeks	Placebo	Venography	105
Lassen MR	2002	Double	Achilles tendon rupture or fracture	Conservative or surgery	Reviparin 1750IU during immobilisation	Placebo	Venography	440
Jorgensen PS	2002	Single	Fracture or soft tissue injury	Conservative	Tinzaparin 3500IU during immobilization	No treatment	Venography	300
Kock HJ	1995	Open	Fracture or soft tissue injury	Conservative	Certoparin 3000IU during immobilization	No treatment	US + venography if US positive	339
Kujath	1993	Open	Fracture or soft tissue injury	Conservative	Nadroparin 1850IU during immobilisation	No treatment	US + venography if US positive	253

bosis and any symptomatic confirmed venous thromboembolic events including PE) and c) Pulmonary embolism (PE). Secondary outcome was safety of thromboprophlaxis categorised as a) major bleeding and b) minor bleeding.

Relative risks and 95% confidence intervals were calculated to determine the effect of the thromboprophylactic agent compared with no prophylaxis in each study. Heterogeneity was quantified calculated Cohran's Q test. Where significant heterogeneity ($P \leq 0.1$) was detected, a random effects model for calculating relative risk (RR) was used. Otherwise, a fixed-effects model was used. A forrest plot was created demonstrating

RR and corresponding 95% confidence intervals with a RR of >1 indicating no prophylaxis is superior, <1 indicating chemoprophylaxis is superior and equal to 1 indicating no difference between intervention and no intervention. A funnel plot was also created to detect publication bias. All statistics were performed using SPSS. P ≤0.05 indicates significant results.

RESULTS

At final follow up, no patients were found to have gross malalignment or gait abnormalities as assessed clinically and no complications were reported. All patients reported being satisfied and reported excellent results. The ROM was full in all cases. No complaints of hardware irritation were noted.

Side-to-side MCL integrity showed a firm end point on valgus stress test with no gross side-to-side differences at full extension in all the cases. Two cases demonstrated 1+ valgus instability at 30° of knee flexion. Both were treated for combined MCL and PCL tear.

Average IKDC-subjective scores demonstrated statistically significant improvements from 63 ± 2 to 93 ± 4 (P value<0.05).Lysholm scores demonstrated statistically significant improvements from 67 ± 4 to 92 ± 3 (P value<0.05) after surgery.

DISCUSSION

The superficial MCL is the largest structure of the medial part of the knee and originates from 3.2 mm proximal and 4.8 mm posterior to the medial epicondyle at the center of knee motion on the medial femoral epicondyle of the femur *(20,21,23)*. According to LaPrade et al. and Brantigan et al., the superficial MCL has 2 attachments on the tibia *(15,5,6)*. The proximal attachment of the superficial MCL inserts directly over the anterior arm of the semimembranosus approximately 1 cm below the knee *(15,5,6)*, and the distal attachment inserts on the proximal tibia just anterior to the posteromedial crest of the tibia and posterior to the pes anserine insertion, five to seven centimeters (cm) below the joint line, with an average length of 11 cm (10-12 cm) and an average width of 1.5 cm *(20,21,6,25)*. The superficial MCL consists of anterior and posterior portions which play different rolls anatomically *(21,3)*.The deep MCL is the thick part of the middle third of the medial capsule, also known as the middle capsular ligament which originates inferior to the medial epicondyle of the femur and inserts on the tibia 1 cm below the joint line *(20,21)*. MCL also provides a resistance to external rotational forces to the lower extremity *(3)*.

Ligament injuries account for up to 40 percent of all knee injuries, and of these, medial collateral ligament (MCL) injuries appear to be the most common *(21,3,19)*. I Bollen et al. demonstrated that the incidence of combined ACL and MCL tear is approximately 30% of incidence of ACL tears alone *(26)*. A portion of these patients need surgical reconstruction of the MCL. Also some MCL injuries may not respond well to conservative treatment and require surgical treatment *(16,22)*.

There have been several techniques described for MCL reconstruction. However, these procedures are not without possible concurrent morbidity and issues, including extensive surgical exposure, donor site morbidity, loss of motion, non-anatomic graft placement, and technical complexity with double-bundle constructs *(20,3,1,16,8,26).*

Marx et al introduced a new technique for MCL reconstruction that involved using an Achilles allograft. They reconstructed the MCL at the same time as ACL reconstruction *(20)*. The authors reported advantages such as no donor site morbidity, secure fixation with bone-to-bone healing on the femur, small skin incisions, and isometric reconstruction *(20)*.

Although we found this technique to have good results, we observed some issues and aimed to resolve them by introducing a modification to Marx's technique.

In this technique, we utilized an Achilles allograft without any bony attachment. We reconstruct the MCL in the first stage and other ligamentous injuries in the second stage when adequate knee ROM was achieved through rehabilitation. We feel there are several benefits to this modified technique. Knee range of motion may be improved by utilizing a two stage technique with a physical therapy protocol initiated between stages. Additionally, the use of allograft tendon eliminates potential donor site morbidity, and fixing the graft with anchor sutures may eliminate fixation site irritation and avoid the need for removal of hardware. Also, fixing the allograft in 2 places, the anatomical proximal and distal footprints of the superficial MCL, kept the allograft in contact with the bone along the entire surface of the tibia. This may enhance tendon-bone healing and may allow for more physiologic function due to achieving a more anatomic footprint.

Marx, et al. emphasized using tendoachilles allograft with a calcaneal bone block to promote bone-bone healing. He used a screw and a washer for fixing the bony part of the allograft into the tibia *(20)*. However, the medial proximal side of the leg has little subcutaneous coverage, and using screws and washer may cause hardware irritation necessitating future removal. In order to address this problem, we used anchor sutures to fix the allograft to the tibia. This technique minimizes potential irritation of metallic devices under the skin.

Marx, et al. looked for the most isometric point for attaching the allograft on tibia during surgery. Feeley, et al. performed a cadaveric study to determine the femoral and tibial fixation sites that would result in the most isometric MCL reconstruction technique *(10)*. They concluded that MCL reconstruction performed with the femoral attachment of the MCL within the femoral footprint and the tibial attachment within the footprint of the MCL would result in the least graft excursion when the knee was cycled between 0° and 90° *(10)*. In our technique, we used the anatomical footprint of the MCL for attachment rather than checking for the isometric site according to Feeley et al *(10)*.

In another study Bin et al. repaired or reconstructed medial or lateral ligament complexes in the first surgical stage within 2 weeks of injury. In the second stage, when full range of motion was obtained 3 to 6 months later, they reconstructed the ACL and/or the PCL. They evaluated their final outcomes based on stress radiographs, range of motion assessment, Lysholm score, Tegner activity stage, and International Knee Documentation Committee rating. All patients recovered full ROM, the mean Lysholm score was 87.6 points (range, 65 to 100 points), the mean Tegner stage was 3.9 (range 3 to 5) and the final overall IKDC rating was normal in 3 knees, nearly normal in 8, and abnormal in 4.They concluded that the 2-stage surgical approach resulted in good outcomes in terms of range of motion and stability *(26)*. In our series, we reconstructed the MCL in the first stage and the ACL and/or the PCL in the second stage. We didn't experience any loss of ROM in our patients. Marx reported 2 cases of losses of 15° of flexion. Although this difference may not be statistically significant, two stage reconstruction may lead to better range of motion.

The most important limitation of our study was the low number of cases without a comparison group. Although the candidates for this type of reconstruction are few and other studies have reported similar numbers, a larger cohort is needed to conclusively demonstrate the benefits of this modification. Additionally, longer term follow-up is required to assess the long term efficacy of this technique.

In our patients with multi ligament-injured knees, valgus laxity and ROM were effectively restored through a 2-step surgical reconstruction. Patient-reported functional results were significantly improved postoperatively at the last follow-up. We feel that our modification of Marx's techniques may benefit patients by reducing metallic hardware irritation, and potentially restoring full return of knee ROM and stability.

List of abbreviations : ACL : Anterior Cruciate Ligament ; PCL : Posterior Cruciate Ligament ; MCL : Medial Collateral Ligament ; IKDC : International Knee Documentation Committee ; ROM : Range of Motion.

REFERENCES

1. **Azar FM.** Evaluation and treatment of chronic medial collateral ligament injuries of the knee. *Sports Med Arthroscopy Review.* 2006 ; 14 : 84-90.
2. **Bin SI, Nam TS.** Surgical outcome of 2-stage management of multiple knee ligament injuries after knee dislocation. *Arthroscopy.* 2007 ; 23 : 1066-72.
3. **Borden PS, Kantaras AT, Caborn DN.** Medial collateral ligament reconstruction with allograft using a double-bundle technique. *Arthroscopy* 2002 ; 18 : 1-6.

4. **Bosworth MD.** Transplantation of the semitendinosus for repair of laceration of medial collateral ligament of the knee. *J Bone Joint Surg Am.* 1952 ; 34 : 196-202.
5. **Brantigan OC, Voshell AF.** The mechanics of the ligaments and menisci of the knee joint. *J Bone Joint Surg Am.* 1941 ; 23 : 44-66.
6. **Brantigan OC, Voshell AF.** The tibial collateral ligament: its function, its bursae, and its relation to the medial meniscus. *J Bone Joint Surg Am.* 1943 ; 25 : 121-31.
7. **Edson CJ.** Conservative and postoperative rehabilitation of isolated and combined injuries of the medial collateral ligament. *Sports medicine and arthroscopy review.* 2006 ; 14 : 105-10.
8. **Fanelli GC, Tomaszewski DJ.** Allograft use in the treatment of the multiple ligament injured knee. *Sports medicine and arthroscopy review.* 2007 ; 15 : 139-48.
9. **Feeley BT, Muller MS, Allen AA, Granchi CC, Pearle AD.** Biomechanical comparison of medial collateral ligament reconstructions using computer-assisted navigation. *The American journal of sports medicine.* 2009 ; 37 : 1123-30.
10. **Feeley BT, Muller MS, Allen AA, Granchi CC, Pearle AD.** Isometry of medial collateral ligament reconstruction. *Knee Surgery, Sports Traumatology, Arthroscopy.* 2009 ; 17 : 1078-82.
11. **Grood ES, Noyes FR, Butler DL, Suntay WJ.** Ligamentous and capsular restraints preventing straight medial and. *J. Bone Joint Surg. Am.* 1981 ; 63 : 1257-69.
12. **Indelicato PA.** Non-operative treatment of complete tears of the medial collateral ligament of the knee. *J Bone Joint Surg Am.* 1983 ; 65 : 323-9.
13. **Kim SJ, Lee DH, Kim TE, Choi NH.** Concomitant reconstruction of the medial collateral and posterior oblique ligaments for medial instability of the knee. *J Bone Joint Surg,* Br Vol 2008 ; 90 : 1323-7.
14. **Kovachevich R, Shah JP, Arens AM, Stuart MJ, Dahm DL, Levy BA.** Operative management of the medial collateral ligament in the multi-ligament injured knee: an evidence-based systematic review. *Knee surgery, sports traumatology, arthroscopy.* 2009 ; 17 : 823-9.
15. **LaPrade RF, Engebretsen AH, Ly TV, Johansen S, Wentorf FA, Engebretsen L.** The anatomy of the medial part of the knee. *J Bone Joint Surg Am.* 2007 ; 89 : 2000-10.
16. **Larson RL.** Combined instabilities of the knee. *Clin Orthop Rel Res* 1980 ; 147 : 68-75.
17. **Lind M, Jakobsen BW, Lund B, Hansen MS, Abdallah O, Christiansen SE.** Anatomical reconstruction of the medial collateral ligament and posteromedial corner of the knee in patients with chronic medial collateral ligament instability. *Am J Sports Med.* 2009 ; 37 : 1116-22.
18. **Loredo R, Hodler J, Pedowitz R, Yeh LR, Trudell D, Resnick D.** Posteromedial corner of the knee: MR imaging with gross anatomic correlation. *Skeletal Radiol.* 1999 ; 28 : 305-11.
19. **Majewski M, Susanne H, Klaus S.** Epidemiology of athletic knee injuries: A 10-year study. *Knee.* 2006 ; 13 : 184-8.
20. **Marx RG, Hetsroni I.** Surgical technique: medial collateral ligament reconstruction using Achilles allograft for combined knee ligament injury. *Clin Orthop Rel Res*. 2012 ; 470 : 798-805.
21. **Phisitkul P, James SL, Wolf BR, Amendola A.** MCL injuries of the knee: current concepts review. *Iowa Orthop J.* 2006 ; 26 : 77.
22. **Robins AJ, Newman AP, Burks RT.** Postoperative return of motion in anterior cruciate ligament and medial collateral ligament injuires The effect of medial collateral ligament rupture location. *Am J Sports Med* 1993 ; 21 : 20-5.
23. **Robinson JR, Sanchez-Ballester J, Bull AM, de WM Thomas R, Amis AA.** The posteromedial corner revisited An anatomical description of the passive restraining structures of the medial aspect of the human knee. *J Bone Joint Surg,* Br Vol. 2004 ; 86 : 674-81.
24. **Torkaman A, Yazdi H, Hosseini MG.** The Results of Single Bundle Versus Double Bundle ACL Reconstruction Surgery, a Retrospective *Study and Review of Literature. Medical Archives.* 2016 ; 70 : 351.
25. **Warren LF, Marshall JL.** The supporting structures and layers on the medial side of the knee: an anatomical analysis. *J Bone Joint Surg Am.* 1979 ; 61 : 56-62.
26. **Wijdicks CA, Griffith CJ, Johansen S, Engebretsen L, LaPrade RF.** Injuries to the medial collateral ligament and associated medial structures of the knee. *J Bone Joint Surg Am.* 2010 ; 92 : 1266-80.
27. **Yazdi H, Torkaman A, Ghahramani M, Moradi A, Nazarian A, Ghorbanhoseini M.** Short term results of anterior cruciate ligament augmentation in professional and amateur athletes. *J Orthop Trauma.* 2017 ; 18 : 171-6.