UNIVERSIDAD DE GRANADA

Programa De Doctorado En Medicina Clínica Y Salud Pública

Diferencias Funcionales Y Clínicas Entre El Autoinjerto De Tendón Después De La Reconstrucción Del Ligamento Cruzado Anterior

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ABSTRACT

Anterior cruciate ligament (ACL) injury is a common knee injury with an incidence of between 32 and 80 cases per 100,000 inhabitants every year worldwide. Reconstruction of the ACL is the standard surgical method that aims to repair knee stability, improve both clinical and functional outcomes, achieve a rapid return to sport (RTS) and reduce the potential risk of knee osteoarthritis. Quadriceps tendon autografts (QTA) have become more popular in the last 20 years because of their advantages over knee stability and muscle strength recovery . Patellar tendon autografts (PTA) and hamstring tendon autografts (HTA) are the most commonly used autografts. Therefore, choosing ACL reconstruction autografts remains controversial because of their advantages and disadvantages.

Consequently, a series of objective were proposed , divided into four objectives: The first phase of this doctoral thesis mainly aimed 1) To review the literature and compare isokinetic strength tests, functional outcomes, and knee anteroposterior laxity between QTA and HTA or PTA after ACL reconstruction. And the second phase aimed, 2)To analyse the sociodemographic and clinical characteristics of patients with injured ACLs before reconstruction surgeries. 3) To compare the difference of PROM, CROM and FROM between patients following ACL reconstruction with BQTB, QTA, or HTA at three evaluation periods (Pre – 3 months, Pre – 6 months, and Pre – 12 months) after rehabilitation protocol. 4) To compare the difference of CROM and FROM between the injured side and non-injured side of all ACL reconstruction patients at 12 months of follow up. To achieve the objectives of the both phases, two methodology were caried: A systematic review and meta-analysis for the first phase and Randomized Control Trail for the second phase of the doctoral thesis.

The results of this doctoral thesis were;

1) The first phase of the thesis adds further quantitative data analysis to previously published systematic reviews. The QTA showed better and significant results in knee flexion strength compared with HTA and similar results to PTA at 3-, 6-, and 12- months. HTA showed better and significant results in knee extension strength at 6 months and similar results at 12 months compared to QTA. 2) The BQTA showed the major disadvantage in terms of surgery failure due to intraoperative patella fracture and therefore the delay of rehabilitation process and return to sport. 3)All of the three groups (BQTA, QTA, and HTA) showed a similar result in terms of PROM during all of the evaluation times. However, all patients showed massive improvement between pre-surgery and the final follow-up. 4)All of the three groups (BQTA, QTA, and HTA) showed a similar result in terms of knee anteroposterior laxity, sonographic measurements, PPT, and VAS. However, the HTA group showed better improvement of thigh girth measurement during the 3 - and 6-months follow-up test. Moreover, all patients showed huge improvement between 3 - and 12-months follow-up. 5)The HTA group showed better improvement of knee extension muscle strength during the first 6 months. The three groups showed similar knee extensions muscle strength results at 12 months follow-up. A similar result was found for all groups in terms of knee flexion muscle strength and SLHT. The RTS criteria was in favour of HTA at 6 months and similar between all groups at 12 months. Furthermore, both sides showed an improvement regarding the FROM. 6)The side-to-side comparison showed similar results regarding knee anteroposterior laxity, sonographic measurements, PPT, and VAS. However, the non-injured side had better results in terms of thigh girths measurements and knee flexion and extension isokinetic test.

LIST OF ABBREVIATIONS

ACL reconstruction	Anterior Cruciate Ligament reconstruction
ATT	Anterior Tibialis Tendon
ANOVA	Analysis Of Variance
BMI	Body Mass Index
BQTA	Bone Quadriceps Tendon Autograft
CKRS	Cincinnati Knee Rating System
cm	Centimetre
CROM	Clinical Reported Outcomes Measurement
FROM	Functional Reported Outcomes Measurement
CI	Confidence Interval
H/Q	Hamstring/Quadriceps
HTA	Hamstring Tendon Autograft
IKDC	International Knee Documentation Committee
kg	Kilograms
kg/m2	Kilograms / Metres Square
KOOS	Osteoarthritis Outcome Score
kPa	Kilopascal
LKS	Lysholm Knee Score
LSI	Limb Symmetry Index
m	Metre
mm	Millimetre
MNAR	Missing Not At Random
MRI	Magnetic Resonance Imaging
Nm	Newton-Metre
PROM	Patient Reported Outcomes Measurement

PTA	Patellar Tendon Autograft
QTA	Quadriceps Tendon Autograft
RoB 2	Cochrane Risk-Of-Bias Tool For Randomised Trials
ROBINS-I	Risk Of Bias In Non-Randomized Studies - Of Interventions
ROM	Range Of Motion
RTS	Return To Sport
SLHT	Single Leg Hop Test
VAS	Visual Analog Scale

INTRODUCTION

ACL Injury

Anatomy And Biomechanics Of ACL.

The anterior cruciate ligament (ACL) is a thick bundle-like shape of collagen fibres covered by dense connective tissue and contains 50.3 % non-uniform diameter fibre, 43.7% uniform diameter fibre, and 6 % elastic fibre[1]. The ACL is attached to the lateral femoral condyle, the posterior part of the inner surface, and runs anteriorly and distally to the tibial plateau between intercondylar eminences anteriorly[2] . Throughout the literature, relevant authors separate the ACL into two bundles: the anteromedial bundle (AMB) and the posterolateral bundle (PLB) . Meanwhile, other research has divided the ACL into three bundles (AMB, intermediate band, and PLB)[1]. However, it is generally accepted that the ACL is divided into two bundles[1]. The ACL bundles have been named according to their specific attachment to the tibia[3,4].

The anatomical studies showed ACL morphological characteristics with a length range from 31 to 38 millimetres (mm) and its width range from 10 to 12 mm. Specifically, the AMB width ranges from 6 to 7 mm and the posteromedial bundle ranges from 5 to 6 mm[2]. Regarding the ACL cross-section area, it increases distally and started proximally with 34 mm^2 and ended with 42 mm^2 distally[2]. The shape of the ACL is irregular and changes with different knee flexion degrees[3]. Therefore, these anatomical characteristics provided good biomechanical characteristics for the ACL studied. The ultimate load and failure to stiffness for young people between 22–35 years of age were 2,160 N and 242 N/mm, respectively[5].

These biomechanical characteristics provided the main function of the ACL, which is knee stability by preventing the anterior transition of the tibia bone relative to the femoral bone and by preventing knee hyperextension[1]. However, the provided resistance from the ACL is varied depending on joint angle[5]. The strongest resistances provided by the ACL are at 30° of knee flexion with an average resistance of 82-89% and a slightly lower resistance at 90° of knee flexion with an average of 74-85%[5]. The second function of the ACL is to limit knee internal rotation especially when the knee is closed to full flexion[3,4]. The third and most minor function is to resist valgus and varus knee movement, especially under weight-bearing positions[3,4]. In addition, knee stability is assisted by stabiliser muscles that apply force to the knee joint[4].

ACL injury and classification

All ligament ruptures are classified depending on the location of the tear into five types by Van-Der J. et al.[6] as the following: type 1 tear (within the proximal part and located 10 % proximally of the ligament), type 2 tear (located between 10% and 25 % proximally of the ligament), type 3 tear (located between 25% and 75% proximally of the ligament), type 4 tear (located between 75% and 90 % proximally of the ligament), and type 5 tear (located between 90% and 25% until the distal end of the tear)[6]. Aside from the general ligament classification, an ACL tear is classified into complete rupture or partial rupture[7].

Epidemiology of ACL injury

ACL tear is one of the most common knee injuries, which affects mainly young people who are engaged in high-level physical activity and participate in individual and collective sports[8]. Its incidence is estimated to be between 32 and 80 cases per 100,000 inhabitants every year worldwide and more than 25,000 injuries per year in the World wide[8–13].

The injury of the ACL is more related to collective sports, like football or rugby, with high incidence, while basketball, handball, and skiing has lower injury frequency[14]. Moreover, the injury rate was affected by years of experience such as in football. A new study by Lepley L. et al.[15] reported that 80% of players with

ACL injuries had less than three years of experience. Moreover, 55% of them were injured during the pre-season[15]. In addition, the mentioned study reported 63% of the patients were injured during the game and 37% were injured during practising and conditioning[13,16]. Regarding the injury rate, the overall ACL injury rate was 0.35 injuries per 1000 hours of exposure in the first division of Spanish football players[16].

Patient age was not reported as the determining factor for ACL injury[17]. However, patient gender is considered a determining factor[17]. The National Collegiate Athletic Association (NCAA) mentioned a three-time higher incidence among females compared to males[18]. The female patient has a higher incidence due to her anatomical and biomechanical factors—such as quadriceps dominant deceleration, decreased intercondylar notch width, hormonal effects, and increased valgus knee angulation companies with cutting or landing—in addition to skeletal anatomy differences[17].

Aetiology of ACL

Depending on the mechanism injury, patients could suffer from an isolated ACL injury or ACL concomitant with other knee injuries[18,19]. A study by Sayampanathan A. [19]and his colleagues in Singapore reported 56.2% of the total patients (N = 256) had comminated injuries[19]. The high rate of concomitant injuries was the medial meniscus at 62.7%, the lateral meniscus at 31.9%, and the posterior cruciate ligament at 5.42% of the total patients[19].

ACL injury could be comminated or not depending on the mechanism of the injury, which is classified into contact and non-contact injury[17]. A recent study from Della-Villa et al.[17] on football players showed 44% of ACL injuries were non-contact, 44% were indirect contact, and only 12% were direct contact [14]. The mechanism of contact injuries was direct trauma on the knee during landing or direct trauma to the knee leading to hyperextension[17]. Similarly, the most common mechanisms of non-contact injury were: first, during the deceleration task with the knee joint in extension and valgus rotation while the foot is fixed with the playing surface and the bodyweight moved over the injured side[20]; second, during cutting manoeuvres or directional change with speed deceleration[20]; third, landing after a jump on near full extension and fixed foot with the playing surface[20]. All of these situations involved knee varus, valgus, or rotation combined with anterior knee transition especially when the knee flexion is between 20° and 30° where the ACL is almost isolated[20].

ACL injury has been correlated to different risk factors that have been described as intrinsic, extrinsic, and others [20–22]. The intrinsic risk included physiological (e.g., female gender, BMI higher than >19.9), anatomical (e.g., knee joint laxity and narrow intercondylar notch, an increase in ACL length, a decrease of ACL width, increase in lateral or posterior tibial plateau slope), biomechanical (e.g., high knee valgus, high knee valgus and leg length discrepancy, a deficit in hip abductor, hip external rotator or hamstring muscle or imbalance between quadriceps and hamstring muscle group), and neuromuscular factors (e.g., muscle weakness of knee abductor and knee flexor hip external rotator) [20–22]. Besides all, ACL injury was related to extrinsic risk factors such as playing surface, sport level, or high participation in sport. Finally, patients' previous contralateral ACL injury showed more than 30% of recurrent injury[20–22].

Diagnosis of ACL

The diagnosis of ACL injury starts from the first moment of injury where the mechanism of injury, signs, symptoms, and clinical history could be the first indicators of the clinical picture of ACL injury[23,24]. Further, a diagnostic test (i.e., the Lachman test or anterior drawer test) is necessary to clarify the knee status and address the stability issue[25,26]. Finally, medical imaging is used to confirm the exact diagnosis and to differentiate from similar diagnoses such as an epiphyseal fracture or sleeve fracture of the patella [23,26].

During an acute ACL injury, patients experience intense pain in the knee joint area and swelling around the knee joint with red skin colour. Moreover, some patients could recognize their ACL injury especially within the first 48 hours after injury[26]. On the other hand, chronic ACL injury demonstrates instability instead of pain and swelling[26].

As mentioned before, the second diagnostic phase is the clinical diagnostic test and the first introduced test was the Lachman test in 1976 by Joseph T. et al.[25] The test showed a high level of sensitivity = 0.81 and specificity = 0.81[23]. Further, an anterior drawer test with sensitivity = 38 and specificity = 81 and a pivot shift test with sensitivity = 28 and specificity=81 were widely used for clinical evaluation[23]. However, the last introduced test was the lever sign test with sensitivity = 0.38. The mentioned tests were the subjective reported tests. However, KT-1000 and KT-2000 arthrometers were included to report objective numerical data; in the last decade, this was reported frequently through the published literature[23,27,28].

Medical imaging considers the third and the confirmation phase of ACL injury including both magnetic resonance imaging (MRI) and diagnostic arthroscopy[24,26]. Of these, MRI was more used during the diagnosis because it is not an invasive method[29]. In addition to confirming ACL injury, MRI helps to add more information about meniscal tear, other ligament tears, and osteochondral injuries[24,26]. The study of Crawford R et al.[30] mentioned more than 80% of patient diagnoses were made depending on MRI compared to the "gold standard diagnostic methods", like arthroscopy [30]. This great use of MRI returns to the 87% highly sensitive and the 93% specificity[31]. However, 15% of ACL patients might be wrongly diagnosed using MRI; therefore, the final confirmation during the surgery with the arthroscopic techniques is more accurate[30,31].

ACL Injury Treatment

History of ACL treatment

ACL treatment began during the 19th century with ACL repair. It was documented in the first decade of the 20th-century[32]. Robert Adams was the first recorded surgeon to repair the ACL and, unfortunately, the surgery was not successful[32]. However, at Leeds University, in 1903 Robson and his colleagues performed the first successful ACL repair[32,33]. At the same time, Martin Kirschner (1910), and John Davis (1913), described their techniques in ACL repair[2 32–34]. During the 20th century, the selection of treatment types was controversial. Between the conservative approach and surgical approach, several studies utilised conservative treatment over surgical treatment if the menisci and the cartilage were healthy[34]. The surgical approach gained more popularity after evaluation of all the possible surgical techniques[32–34].

The surgical approach included both ACL repair and reconstruction[35]. The discovery and the popularity of surgical repair started before reconstruction[33,36]. ACL repair was conducted by applying a direct suture to the ACL ligament, inserting internal bracing to ensure the healing process of the ligament, or inserting a dynamic-spring screw into the tibia and the ACL[33,35]. This showed a positive result in proprioception, faster recovery time, and less surgical morbidity issues of the ACL[37] . On the other hand, this surgery shows a high rate of ACL re-injury. A recent systematic review and meta-analysis shows only 30 % of injured patients were treated with repair techniques and 70 % were treated with ACL reconstruction. Lately, Mall et al explained that the future of ACL repair might involve the use of biological agents[38].

In 1929, the first ACL reconstruction by Mitchell Langworthy happened[35]. The definition of ACL reconstruction according to Van Eck et al[35] was "the functional restoration of the ACL to its native dimensions, collagen orientation and insertion sites" [39]. Reconstruction started with the iliotibial band. The first use of patellar tendon autograft was in 1936 from Willis Campbell through femoral and tibial tunnels [34]. A few years later in 1939, the semitendinosus tendon autograft was used[34]. During the second half of the 20th century, all reconstruction techniques were developed with the use of the different surgical tunnels, fixation systems, and different grafts (free bone patellar tendon, bone-patellar tendon-bone, semimembranosus, semitendinosus, biceps femoris, quadriceps tendon, free bone-quadriceps tendon, and bone-quadriceps tendon)[32]. The reconstruction surgery was done either with allograft or autograft. Autografts showed better function and clinical results and lower reinjury time, while allografts showed some advantages such as faster return to sport RTS and no graft site morbidity[32,34].

Since the first arthroscopic ACL reconstruction occurred in 1980, the arthroscopic approach gained more popularity over the open surgical technique due to its advantages including recovery time and lower anterior knee pain [32,34,40]. Therefore, most of the surgeons performed intra-articular techniques, which allowed a huge replication of ACL reconstruction[32,41–48]. Moreover, the huge replication of the arthroscopic approach led to novel debates regarding tendon autografts. The Patellar tendon and hamstring tendon are considered the most used autografts since 1980[33,43,44,49–51].

Autografts

Patellar tendon Autograft (PTA)

Since the 1980s, PTA autograft has been considered the gold standard to reconstruct the ACL. The first use of the PTA was in 1936 by the English surgeon Willis Campbell[32]. A study by Bowman E. et al.[52] showed the preference of 518 orthopaedic surgeons in the US; 52% of the surgeons preferred PTA with young age patients [52]. PTA demonstrates advantages compared to other autografts, such as low graft failure rate and high knee stability[51–53]. Regardless, PTA has some disadvantages which are anterior knee pain, quadriceps deficit, and donor site morbidity[51,53]. Further, in clinical and functional characteristics, PTA showed good mechanical characteristics in terms of ultimate load (1810 N), cyclic stiffness (151 N/mm), and ultimate stiffness (324 N/mm) [54].

Hamstring tendon Autograft (HTA)

The hamstring tendon is considered to be the second preferred autograft with 48% approval in a US surgical survey[52]. This commonly comprises 2,4 or 6 fascicules from semitendinosus and gracilis tendons[54,55]. The surgeon's interest in using the HTA for grafting started during the 1990s due to less anterior knee pain and better result in quadriceps when compared to PTA and QTA[43,53,56]. However, HTA autograft was associated with hamstring strength deficit, abnormal knee biomechanics such as increase valgus motion, and a slightly higher rate of graft failure [51,53,57,58]. Further then, in clinical and functional characteristics, four bundles of HTA showed comparable mechanical characteristics in comparison with other autografts in terms of ultimate load (1750 N), cyclic stiffness (273 N/mm), and ultimate stiffness (433 N/mm)[54].

Quadriceps tendon Autograft(QTA)

After the most used autografts PT and HTA, the QTA autograft has gained more popularity in the last decade[52]. Xerogeanes J. et al. [29]consider it the "graft of the future" due to its special anatomical properties: "a graft of consistent length (7 to 8 cm), depth (6 to 7 mm), and width (9 to 10 mm) can be harvested with careful surgical technique without violation of the suprapatellar pouch" [29,51,59,60]. The published research showed anterior knee pain and donor site morbidity with PTA and a high deficit of hamstring muscle strength with HTA. Therefore, many surgeons started to preferentially select QTA autograft[61,62], especially for the young and athletic population, but even still, QTA has not been studied widely as of yet[51,53,63,64].

A recent study by Ajrawat P. et al[53] showed similar quadriceps strength data in comparison with HTA while anterior. At the same time, anterior knee pain and donor site morbidity were less in QTA when compared to PTA[51,53]. On the other hand, QTA shows some disadvantages related to quadriceps deficit compared to HTA [51,53]. Scientific research has compared QTA to PTA and HTA [51,53,65]. However, the use of BQTA or QTA without patellar bone is considered a new controversial point. Bone-QT (BQTA) has been compared less in term of strength, functional, isokinetic, either graft failure[54,66,67].

QTA has been investigated within many studies (strength, functional ss, isokinetic, KT, graft failure)[51,53]. A biomechanical comparison was done between BQTA and QTA. BQTA is characterised by ultimate load (1450N), cyclic stiffness (157 N/mm), and ultimate stiffness (370N/mm)[53] . While QTA without bone achieved slightly lower results in terms of ultimate load (1260N), cyclic stiffness (172 N/mm), and ultimate stiffness (257N/mm)[53].

Reconstruction Autograft Comparison

The comparison between different autografts include various measurements which classify into three categories: Patient Reported Outcomes Measurements (PROM) which includes general subjective questionnaires , Clinical Reported Outcomes Measurements (CROM) which includes clinical measurement such as knee laxity, knee morphology and donor site morbidity, and Functional Reported Outcomes Measurements (FROM) which cover muscle strength evolutions hop tests.

Autograft comparison regarding PROMS

The subjective patient-reported outcome is a specific scale to evaluate patient status before and after surgery[51,53,68–71] .The most mentioned patient-reported outcome in the literature was the International Knee Documentation Committee (IKDC), Lysholm questionnaire, the Knee Injury and Osteoarthritis Outcome Score (KOOS), and Tegner questionnaire. Also, sport-specific scales such as the Cincinnati scale were present[44,51,53,68,69,71]. All patient-reported outcomes addressed patient abilities (such as jumping, running, squatting) or patient complaints (such as stability, pain, limping) [51,53,68,71]. A recent systematic review and meta-analysis of 19,196 patients compared IKDC scores between reconstruction autografts and demonstrated no significant result between PTA, HTA, and QTA [51].

Autograft comparison regarding CROMS

Knee anteroposterior laxity.

The clinical result of ACL injury is stability loss [72]. Therefore, the main aim of ACL reconstruction surgery is to restore knee stability[72]. Different variables affect knee stability after surgery, such as tunnel position or type of autograft[73]. Furthermore, regaining knee stability was associated with an improvement of the athletic functional questionnaire, knee muscle strength, and rapid return to sporting activity[74].

Moreover, there are different ways to evaluate knee stability, as it was mentioned before with manual subjective tests (such as the Lachman test, pivot shift test, anterior drawer test, lever sign test) and with objective arthrometers such as KT-1000 and KT-2000[23,75]. All of the knee tests were used to diagnose knee anteroposterior laxity [23,75].

Through the published studies regarding knee anteroposterior laxity. and type of autograft, a systematic review and meta-analysis compared the stability of different autografts with KT-2000[76]. It showed that reconstructed ACLs with PTA group had better stability than those with HTA[72.] Accordingly, patients with QTA showed better stability than patients with PTA and HTA[76]. On the other hand, a study from Hurley et al.[77] showed similar stability results among patients with QTA and HTA[53,77].

Knee morphology

Knee morphological measurement such as muscle thinness, harvested tendon diameter or cartilage measurements were measured recently before and after the reconstruction surgery[78,79]. The recent attention of some correlation found between knee morphology and patient recovery such as quadriceps enlargement during the rehabilitation. Besides that, the contribution of knee morphology to ACL injury risk[78]. The previous studies used MRI and diagnostic ultrasound to evaluate the patients. But only a few studies measured knee morphology before and after the ACL reconstruction surgery[78,79].

Donor site morbidity.

The most characteristic donor site morbidity is anterior knee pain, which reflects the chief complaint of the reconstructed patient after the surgery [53]. Regarding the differences between patients' autografts, patients reconstructed with QTA showed lower donor site morbidity compared to patients reconstructed with PT and HT[53,78]. Similarly, Ajrawat P et al.[53] showed lower anterior knee pain with QTA group compared to PT group[53]. However, no significant differences were found between the HTA and QTA groups[53]. On the other hand, the study of Marin-Alguacil et al.[78] showed no statistical differences between HTA and QTA patients in different five-point pain pressure threshold tests [78]. Patient pain level was always measured with the Visual Analogue Scale (VAS)[51]. In addition, recent studies measured the pain pressure threshold of different points around the knee such as the patellar tendon and quadriceps tendon[78].

Autograft comparison regarding FROMs

Muscle strength.

Pre-post-rehabilitation programs aim primarily to improve muscle strength in patients with reconstructed ACLs[75,80,81]. Patients with high muscle strength were associated with high functional and biomechanical results and less possibility of osteoarthritis[15,82–85]. In addition, recent studies showed that patients with better muscle strength have a lower ACL reconstruction failure rate[75,86]. Thus, all of the mentioned cons of muscle-strengthening lead to the importance of choosing appropriate measurement methods[75,86].

Muscle strength was measured with different methods including manual muscle testing, isometric strength testing, and isokinetic strength testing[87–89]. Among them, the isokinetic strength test with dynamometry is considered the gold standard test to quantify muscle strength reported data, which allows the examiner to choose between different angular velocities and repetitions of the movement duration between each test[90–94]. The final result of isokinetic tests was reported as peak torque or hamstring to quadriceps (i.e., the H/Q Ratio)[65]. Both results were shown as strength value for the injured side or as limb symmetry index (Injured /None-injured limb* %)[95]. Finally, the main aim of all rehabilitation programs for ACL reconstruction with muscle strength was to achieve more than 90% of an H/Q ratio or LSI[95].

The literature demonstrates that choosing tendon autografts was associated with quadriceps and hamstring muscle deficit depending on the used autograft[75]. Through the comparison of the three most used autografts (PTA, HTA, and QTA), reconstructed ACLs with PTA group showed quadriceps deficit in normal results after one year compared to reconstructed ACLs with HTA[5]. Similarly, patients reconstructed with grafted HTs showed hamstring muscle deficit during the first three months after surgery compared to PTA or QTA ACL patients' groups[5,68]. Moreover, the QTA groups showed a higher quadriceps deficit compared to those with HTA[65].

Hop tests.

Static knee stability has consistently been measured after ACL reconstruction since 1976[25]. More recently, many surgeons emphasised the importance of measuring dynamic knee stability and balance with hop tests or other balance tests[74]. Hop tests are performance-based measures used to assess the combination of muscle strength, neuromuscular control, confidence in the limb, and the ability to tolerate loads related to sports-specific activities[74]. The main hop tests mentioned in the literature are one leg hop tests, triple hop tests, and cross over hop tests. Of these, one leg hop tests are considered the most used for ACL reconstruction patients[74,96,97].

Through the literature, the results of hop tests were reported as a distance of the hop or side-to-side comparison as the limb symmetry index, or LSI (injured /non-injured *100%)[68]. When comparing ACL autografts, a recent systematic review and meta-analysis showed no significant result between patients with HTA and PT[53]. However, patients with QTA showed more significant results compared to patients with HTA in one leg hop test and cross over test[53].

Rehabilitation Of ACL Reconstruction Surgery

The rehabilitation process has experienced significant changes between traditional and new protocols[44,75,98–100]. In terms of the duration of the protocols, the traditional protocols include 12 months of rehabilitation and the new protocols include around 6 months. The new protocol allows faster progression due to higher intensity rehabilitation protocols [44,75,99,101]. The differences between traditional and accelerated rehabilitation protocols were not only in their respective durations. But, in the allowed activities in each phase such as full knee full extension, it was allowed at the third month in the traditional rehabilitation protocols and at the first week in the accelerated rehabilitation protocols [44,75,98–100].

Over the last decade, accelerated rehabilitation programs included in general three to four phases. Pre-surgery protocols consist of one phase and aim to achieve 90% of quadriceps limb symmetry index[50,75]. Post-surgery protocol consists of four to five phases during six months [44,75,98]. Both phases would form the standard rehabilitation protocol [44,75,98]. During the application of the post-surgical rehabilitation program, it is considered important that each patient meet specific criteria to start the next phase in rehabilitation protocols[44]. The first phase in rehabilitation aims to achieve quadriceps control, improve knee extension, and control inflammation[44,75]. The second stage seeks to improve knee flexion, achieve full knee extension, and progress from isometric to isokinetic knee exercise. In addition, improving gait pattern is included[44,98].The objective of the third phase is to improve balance and to introduce sport-specific exercises [44,75,98]. The fourth phase aims to introduce plyometric exercise, running, cutting manoeuvers, and agility training [44,75,98]. The final stage transits patients from rehabilitation centres to fitness facilities, where patients continue their rehabilitation protocol [44,98,100,102].

Patients return to their sport activities after ACL reconstruction is related to different variables. First, RTS after surgery is considered differently between each sport type such as non-contact sports from the 4th month and contact from the 6th month. Second, the isokinetic strength test by comparing the injured side to the no-injured side implies the patient might achieve more than 90% for their LSI. Third, functional outcomes such as Cincinnati or Lysholm IKDE where the patient must achieve more than 90% of the total score are significant. Fourth, functional outcome “hop test” by comparing injured side to no-injured side suggests the patient might achieve more than 90% for their LSI[24,75].

However, there is evidence that the type of graft used in reconstruction may delay the starting time of the mentioned rehabilitation phases [24,57,75]. In addition, special consideration might be necessary for each graft. Reconstructed patients with PT need special attention during quadriceps strengthening on the patellar tendon due to donor site morbidity[24,26,75,103]. This is in addition to dealing with the anterior knee pain [39]. On the other hand, reconstructed patients with HTA delayed their resisted hamstring exercise to 12 weeks after the surgery to allow for full recovery [29,75]. A few studies report the consideration of rehabilitation programs with patients reconstructed with QTA[29]. Of these, Freddie H. F. et al.[104] reported refracture of patella bone during rehabilitation program which might indicate the possibility of delaying high-intensity exercise with BQTA reconstructed patients[58]. Therefore, it seems necessary to study the impact of each type of graft on rehabilitation protocols[26,75]

Thesis Justification

The current literature has revealed many studies comparing HTA with PTA[24,105], a good number of studies comparing QTA with HTA or PTA, and a fewer number of studies comparing BQTA with HTA or PTA[29,44,49,51,76,103,106]. The majority of the mentioned studies compared PROMS or CROMS or only FROMs between the same patients[47,107,108]. And just a small number of studies compared PROMS and FROMs[77,107]. On the same side, to our knowledge there were no articles comparing BQTA with QTA and HTA in terms of PROMS, CROMS and FROMs. Therefore, the mentioned publications indicate the first major gap of knowledge is the lack of information comparing QTA or BQTA with the other autografts mainly in FROMs beside PROMS and CROMS. On the same point, the second gap of knowledge is the lack of information comparing BQTA with QTA and HTA in terms of PROMS , CROMS, and FROM.

OBJECTIVES

1. The first phase of this doctoral thesis mainly aimed to review the literature and compare isokinetic strength tests, functional outcomes, and knee anteroposterior laxity between QTA and HTA or PTA after ACL reconstruction.
2. To analyse the sociodemographic and clinical characteristics of patients with injured ACLs before reconstruction surgeries.
3. To compare the difference of PROM (LKS and CKRS) between patients following ACL reconstruction with BQTA, QTA, or HTA at three evaluation periods (Pre – 3 months, Pre – 6 months, and Pre – 12 months) after rehabilitation protocol.
4. To compare the difference of CROM (knee anteroposterior laxity, architecture measurements, muscle girth, VAS, and PPT) between patients following ACL reconstruction with BQTA, QTA, or HTA at three evaluation periods (Pre – 3 months, Pre – 6 months and Pre – 12 months) after rehabilitation protocol.
5. To compare the difference of FROM (muscle strength and single leg hop tests) between patients following ACL reconstruction with BQTA, QTA, or HTA at three evaluation periods (Pre – 3 months, Pre – 6 months, and Pre – 12 months) after rehabilitation protocols.
6. To compare the difference of CROM and FROM between the injured side and non-injured side of all ACL reconstruction patients at 12 months of follow up.

METHODOLOGY

Methodology Of The First Part.

Protocol and registration

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [109]. A detailed protocol for the systematic review was registered in the International Prospective Registry of Systematic Reviews (PROSPERO). It can be accessed with the code CRD42020191849. According to the PRISMA guidelines, the specific question posed for this review was, "which tendon autograft for anterior cruciate ligament reconstruction is better for strength recovery in athletes?".

Study eligibility

Studies were selected for inclusion based on the following criteria: (1) comparative studies; (2) participants aged between 16 and 45 years who had undergone ACL reconstruction surgery with a tendon autograft; (3) strength assessment using the isokinetic strength test; (4) accessible online full text (in any case, consideration was given to contacting the authors if access to the full text online was not available); and (5) studies published in English or Spanish. Studies such as reviews, case reports, monographs, guidelines, surveys, commentaries, conference papers and/or unpublished data were excluded, as well as studies performed on animals or in vitro.

Literature search

The comprehensive search occurred between January and March 2021 in the Medline (via PubMed search engine), Scopus, Web of Science and Cochrane Library databases using the following search terms ((ACL reconstruction OR ACLR) AND (Quadriceps autograft OR quadriceps tendon OR QT) AND (isokinetic dynamometer OR isokinetic test)). To select information, the descriptors used were obtained from the Medical Subjects Heading (MeSH) database. The information was filtered using terms and keywords related to ACL reconstruction and rehabilitation procedures, combined with Boolean operators and search techniques adapted to each database. Additionally, the reference lists of retrieved reports were manually searched for additional references. The search equation was developed and replicated by two independent researchers (F.H. and C.F.-L.) autonomously and independently to ensure the reliability of the results.

Study selection and data abstraction

This systematic review was developed independently by two authors (F.H. and C.F.-L.), who screened by title and abstract first and then by full text. Studies were evaluated in both phases according to the eligibility criteria mentioned above. If disagreement occurred between the reviewers, a third external reviewer (M.L.-L.) participated to decide whether to include or exclude the article. When completing both screenings, the search strategy was re-executed if additional studies were added to the literature and were retrieved for inclusion (latest search released on 1 March 2021).

The data abstraction process was performed by two researchers (F.H. and C.F.-L.). One first selected the data, and then the other verified this selection for accuracy. If any disagreement occurred, a third researcher (M.L.-L.) was asked to make a final decision. The collected data items were as follows: (1) first author; (2) year of publication; (3) study design; (4) clinical entity responsible for the study; (5) sample size; (6) type of intervention(s); (7) if applicable, details of control or comparison groups; and (8) main findings.

Risk of Bias Assessment

The risk of bias of the included studies in this systematic review was determined by two independent reviewers (F.H. and M.L.-L.) and was evaluated using specific scales depending on the type of study, following the instructions given by the Cochrane Handbook for Systematic Reviews of Intervention[110] and the National Institutes of Health (NIH)[111].

Randomized controlled trials (RCTs) were evaluated using the Revised Cochrane risk- of-bias tool for randomized trials (RoB 2)[112]. This common tool is used for randomized trials and has been updated in the last year. It assesses bias in five distinct domains (e.g., randomization process, intended interventions, missing data, measurements, and results). Observational studies were evaluated using the Cochrane's tool Risk Of Bias In Non-Randomized Studies—of Interventions (ROBINS-I) with five level judgment criteria (low, moderate, serious, critical, and no information) for each domain. ROBINS-I tool assessed seven distinct domains (confounding, selection of participants, classification of interventions, deviations from intended, missing data, measurement of outcomes and selection of the reported results)[112,113].

Data Analysis

To pool the results quantitatively and develop the proposed meta-analysis, as well as to generate corresponding forest plot graphs, STATA software was used (StataCorp. 2019; Stata Statistical Software: Release 16; StataCorp LLC, College Station, TX, USA). Only studies comparing the use of HTA vs. QTA or PTA vs. QTA and reporting valid isokinetic strength data obtained using an isokinetic dynamometer were included in this quantitative combination. Thus, a total of five studies were included in the meta- analysis[42,68,114,115]. The data were obtained from the tables or text of the articles, extracting the means and standard deviations (SD) of the follow-up values at 6 months, 12 months or 24 months. Where these data were not reported, the mean and SD were calculated from the available data based on the protocol previously published by Wan et al. [116]. The included studies were combined according to the follow-up, speed used (60◦/s or 180◦/s) and movement employed (knee flexion or knee extension). A random effects model of the DerSimonian and Laird method, which considers variations within and between studies, was used. Forest plots were developed to visualize individual study summaries and pooled estimates. Cochran's Q statistic and the I^2 value were used to study heterogeneity between studies. Cohen's D was calculated for each of the original studies and an overall estimator, and a two-sided (P value < .05) was considered statistically significant. Because of the low number of studies (<10), a more in-depth study of publication bias was not possible.

Methodology Of The Second Part.

Participants

The study sample consisted of 78 completely injured ACL patients who were divided in three experimental groups depending on the type of tendon autograft: (1) BQTA with 26 reconstructed knees, (2) QTA with 26 reconstructed knees, and (3) HTA with 26 reconstructed knees. All of the patients had a complete ACL tear and were diagnosed by clinical examination and MRI. Moreover, all tears were confirmed during the surgery with the diagnostic arthroscopic technique. The participants were recruited from the Department of "Cirugía Ortopédica, Mutualidad Andaluza de Futbolistas" and through advertisements in local sports clubs.

Ethical approval for the study was granted by the Biomedical Investigation Ethics Committee, Granada, Spain (CEi-GRANADA Ref: LCA-V2) and conducted in accordance with the Declaration of Helsinki[117]. All measurements were conducted between February 2020 to April 2022 at the Faculty of Health Sciences, at the University of Granada. All participants gave signed informed consent before being formally enrolled. And parents have signed for patients under 18 years before the inclusion in the study if the patient passed the following criteria.

Inclusion and exclusion criteria.

The inclusion criteria of the study were:

1. Less than six months between the diagnosis and the surgery.
2. Quadriceps (QTA or BQTA) or hamstring tendon autograft surgery.
3. Footballer for more than 3 years.
4. Between 16 and 40 years old.

The exclusion criteria were;

1. Surgery applied with autografts with a patellar tendon.
2. Joint injury or previous surgery on the affected knee.
3. Any musculoskeletal injury (4 weeks before the surgery) or an untreated chronic injury.
4. Period between surgery and injury is more than 6 months.
5. Failure to sign the informed consent form.
6. If the surgeon removed more than 50% of either the lateral or medial meniscus.
7. If the patient had articular cartilage lesion greater than grades II on Outerbridge scale.

Sample size calculation

To carry out an approximation to the necessary sample size, a previous study by our colleagues on the recovery of strength after ACL reconstruction was used (Martin-Alguacil J. L. et al., 2018[68]), assuming an alpha error of 5% and an estimated statistical power of 95% based on knee extension isokinetic test had defined a minimum sample of 22 participants in each group. G * Power 3.1 software was used. The study started with 78 patients: 26 in each group (BQTA, QTA, HTA) after assuming 20% as possible dropouts in the study.

Variables

The variables of this doctoral thesis were arranged intro the three groups are PROMS, CROMS and FROMs, and were taken respectively.

Variables of PROMS

Lysholm Knee Scale LKS

The Lysholm scale is used to measure the participants' subjective satisfaction in terms of functional capacity after surgical intervention[118,119]. The Lysholm knee score consists of eight sub-criteria that provide global calculation of all items which are: limp, support, blockages, instability, pain, swelling, stair climbing, and crouch down[119]. A total score is considered a normal function of 95-100 points, a score between 84-94 is considered good, a score between 66-83 is considered regular, and any score below 65 is considered poor[119]. Moreover, 50% of the total score is based on symptoms of pain and instability[119]. The LKS showed high reliability (ICC = .97)[119], and a recent Spanish validation of the test showed Test-retest reliability level was high (ICC = .92)[118].

Cincinnati Knee Rating System CKRS

The Cincinnati Knee Rating System scale is used to determine the clinical outcome of different knee operations, which consist of eight sub-criteria: pain, inflammation, knee stability, general level of activity, stairs claiming, walking, running, and jumping or turning around. The total score of the test was 100 points [120].

The global rating score was reported in a 0-to-100-point score. The overall points rating was distributed as 20 points for knee symptoms, 15 points for daily function and sport activity, 20 points for knee joint stability, 10 points for morphological finding, and 10 points for functional testing. Finally, the global score was reported by summing the points[120].

The score results in 6 levels. Level 6 was awarded when the patient achieved the same athletic level before the surgery. Level 4 was awarded when the activity of daily living (ADL) was possible with rare symptoms. Level 2 ADL caused moderate symptoms and frequent limitations, and level 0 was when ADL caused severe, persistent symptoms[121]. The Cincinnati Knee Rating System shows a high-reliability score with (ICC = .70)[121] .

Variables of CROMS

Knee laxity

Anterior-posterior laxity was defined as "the A-P translation of the tibia relative to the femur that occurred between the posterior and anterior shear load limits"[122]. KT-2000 Arthrometer (MEDmetric, San Diego, CA, USA) was used to measure anterior-posterior laxity. The patient was in a supine position with 25º knee flexion and a pillow was placed below the knee. The arthrometer was stabilised vertically with the tibia and the patients were asked to relax their muscles. The KT-2000 arthrometer (ICC = .81) [122,123].

Sonographic measurements

To evaluate knee muscles, architecture, and cartilage thickness, an ultrasound device (MyLab 25, Esaote Medical Systems, Genova, Italy) was used with a 12 MHz linear probe with 6-point depth penetration. The participant was asked to lay down in a supine position with the knee flexed to 45º and a wedge was placed below the knee to support it. The probe was placed on the quadriceps tendon, 3 cm from the patella to measure tendon depth from two horizontal and sagittal directions, and tendon width was measured from the sagittal direction. While the knee cartilage was measured from a supine position with knee full flexion and the probe was placed above the patella bone perpendicular to the patient thigh.

All of the ultrasound measurements were done by the same physiotherapist on the non-injured side and injured side, respectively. The ultrasound device showed high reliability with quadriceps muscle (ICC =.95) and for cartilage thickness (ICC = .71)[57,124].

Muscle girth measurement

Thigh muscle girth is defined as the circumference of the thigh which is measured when the participant stands with separated legs and the body weight is distributed equally to both sides[125,126]. The patients were asked to lay down and relax with legs slightly separated, and the examiner measured the circumference 15 cm above the patella bone for both legs. The measurement was done with 1.5-m non-elastic fibreglass cloth tape measure (TT-SR26, China Eastern Tape Measure Manufacturer Co., Ltd., Ningbo City, Zhejiang, China). The tape measure was found to be highly reliable with (ICC = .92)[126] .

Donor site morbidity

The visual analogue scale (VAS) is a horizontal line scale with 10 cm length which evaluates the subjective sense of pain. The right extreme limit represents the best value (zero) and at the extreme left, the limit represents the worst value (ten). The patient had to choose their level of pain at that moment for the injured knee. This instrument has been widely used as it showed high reliability with intraclass correlation coefficient (ICC= .97)[127].

Pressure Pain Threshold (PPT) is defined as the minimum quantity of pressure that must be applied to change the sensation for the first time from pressure to pain[128]. To measure PPT, an electronic algometer (Somedic AB, Farsta, Sweden) was used, which applied constant pressure of 30 Kpa/s with a probe of 1 cm^2 for the following points: 1) vastus lateralis, 2) vastus medialis, 3) patellar tendon, 4) quadriceps tendon, and 5) hamstring tendon. Each point was performed three times with a half-minute period of rest. The average of the three trials was calculated. The patients were trained to push the button when the sensation changed from pressure to pain. The algometer showed high reliability with ICC = .91[129].

Variables of FROMs

Muscle strength

Muscle strength was measured with isokinetic dynamometry which is defined as "a means of exercising and testing extremities using maximal torque production at a specified velocity of limb movement, and the system matches the subject's effort and maintains a set velocity"[130]. The Genu 3 dynamometer (Easytech, Firenze, Italy) was used to determine hamstring and quadriceps muscle strength.

The participants started with ten minutes of stationary bicycle warm-up. And after warm-up, they were instructed to sit with 90° of hip flexion and 85° of knee flexion and stabilised with a thigh and chest strap. The test started with the uninjured leg and performed 3 repetitions at an angular velocity of 60°/s, 5 repetitions at an angular velocity of 180°/s, and 15 repetitions at an angular velocity of 300°/s with a one-minute break between each test. Then, the same procedure was applied to the injured leg.

The results of the tests included mid torque and peak torque for knee flexor extensor, hamstring/quadriceps ratio (H/Q ratio), knee extensor peak torque/body weight, and knee flexion peak torque/body weight, all of the strength outcome were reported for the three angular velocities 60°/s ,180°/s and 300°/s. The data were shown for each body side. Then Limb Symmetry Index LSI (calculated as limb symmetry index = (injured side/non-injured side) * 100%) was calculated for use as peak torque. The isokinetic dynamometry is a highly reliability instrument (ICC = .88)[131].

Single leg hop test

One leg hop test considers a knee dynamic stability test, which aims for patients to jump with a single leg as far as possible and land firmly without losing balance. The test distance is the distance between the start line and the heel of the landing foot after the jump[96]. All participants started with a 10-minute warm-up with a stationary bicycle; then, the participant was instructed to hop as far as possible in the forward direction and to land firmly on the same leg. The test was not reported if the participant lost balance, made additional hops after the touchdown or if the other leg touched down early. Before the test, the full description was provided to the patients and a few trials of the test were permitted until the patient gained confidence. The test was repeated three times and the highest score was recorded. All participants were asked to start with the uninjured leg. The results of the test are shown for each side. Then limb symmetry index was calculated as (limb symmetry index = (injured side/non-injured side) * 100%). Moreover, the reliability score was(ICC = .94)[96].

Process.

Patient inclusion, randomization.

The participants randomly allocated to either to BQTA, QTA or HTA(ratio 1:1:1) using block randomization with numbers generated by a computer running EPIDAT 4.2 software (Xunta de Galicia, Spain). The randomization sequence was prepared by external researcher with no involvement in the study and blinded from the hypothesis was the only researcher who has the access of the patient group. After the randomization, the surgeon was allowed to know each patient group, and the patient was informed about the graft type that was used in the surgery and all of the patient was blinded form the hypothesis. All assessors and data analysers at all time points will be blind to the participant group.

Patient evaluation.

All of the included patients had their pre-surgical, 3,6 and 12 months post-surgical. The four evaluation times were done with a blind physical therapist. Regarding the pre-evaluation, it was performed one week before the surgery. The evaluations are arranged in the following order: patient sociodemographic data, PROMS (LKS and CKRS), CROM (anterior-posterior laxity, sonographic measurements, muscle girth, VAS and PPT) Then, ten minutes of warm-up by stationary bicycle was followed by FROM (knee isokinetic strength and SLHT). All of the evolutions started the non-injured and injured sides was conducted.

Surgical process

The surgery started with preoperative assessments to confirm the ACL injury and to determine if there was an associated injury such as meniscal injury by the use of diagnostic arthroscopic techniques. The diagnosis was done from the anteromedial view; meanwhile, the accessory of the medical portal was established above the joint line and two centimetres away from the medial edge of the patellar tendon. A third portal was inserted to get a visualisation of the femoral footprint, which was inserted into the intermedial portal above the second portal.

Preparation of the tunnels and graft fixation

The graft size determined the diameter of the tibial tunnel which was established with the use of a drill tibial guide (pinn ACL guide, CONMED, Largo, FL, USA) placed medially to the anterior horn of the lateral meniscus in the centre of the anatomical ACL footprint. Then the surgeon established the femoral tunnel with the placement of (K wire) in the centre of the anatomical femoral footprint in the bifurcated ridge below the lateral intercondylar ridge. It was drilled while the knee maintained 20º flexion. Subsequently, with the use of the drill bit the tunnel was drilled and the graft insertion was passed 20 mm inside the femoral tunnel. A bioabsorbable screw, two millimetres smaller than the tunnel diameter, was used in BQTA and QTA while a suspensory extracortical fixation button (RIGIDLOOP, DePuy Synthes, Raynham, MA, USA) was used in the hamstring group. The final step was fixing the tibial side at 20º of knee flexion with the use of a bioabsorbable interference screw matching the size of the drill bit.

Bone-Quadriceps Tendon Autograft BQTA

The surgeon harvested quadriceps tendon dimensions of 70 to 80 mm long, 7 mm depth, and 10 mm width, with 20- to 25-mm-long, 7-mm-thick trapezoidal bone block was obtained from the patellar base[42]. And the grafting was directed 5 cm proximally through the centre of the quadriceps tendon. The harvest was done with the use of a scalpel and both ends of the tendon were sutured with 2 absorbable sutures.

Quadriceps Tendon Autograft QTA

The surgeon harvested quadriceps tendon dimensions of 70 to 80 mm long, 7 mm depth, and 10 mm width, starting from the proximal edge of the patella directed 4 cm proximally through the centre of the quadriceps tendon. The harvest was done with the use of a scalpel and both ends of the tendon were sutured with two absorbable sutures.

Hamstring Tendon Autograft HTA

The surgeon harvested 4 cm of the hamstring tendon starting above the tibial tubercle and directed it proximally and centrally. Both tendons were harvested with tendon strippers. Both tendons were doubled and formed four fascicles of the hamstring tendon used.

Rehabilitation process

All of the included patients in the three groups had the same rehabilitation programs with the same physical therapist and were situated in the same rehabilitation centre. The therapist was blind to the patient's group and the investigation details.

The rehabilitation program included six phases, which were: Presurgical Rehabilitation, Intermediate Postoperative Phase, Early Postoperative Phase, Late Postoperative Phase, Transitional Phase, and Follow Up Phase. The patient had to achieve special criteria to pass to the next rehabilitation phase. All of the phases and their criteria are described in Table N. However, there was special consideration for some groups of participants who were delayed with the progression from one phase to the next. Of those, patients with HTA had resistive hamstring exercise within the first 12 weeks to limit donor site irritation. The patient who had meniscal repair had slower progression during the first 8 weeks, especially with knee flexion; the knee was not allowed to pass more than 45 degrees under loading.

Data analysis

Descriptive statistics were measured for all of the variables. The mean ± standard deviation for continues data and as percentage (%) for categorical data. The normality was checked with Shapiro–Wilk test and Levern test to examine the homogeneity of variances. Chi-square test was used to measure the difference between groups for baseline variables. A repeated measure analysis of variance (ANOVA) was conducted with outcome variables (LKS, CKRS, Anterior-posterior laxity, Sonographic measurements, Muscle girth measurements , VAS, PPT, Muscle strength and Single leg hop test) as dependent variables, groups (BQTA, QTA and HTA groups) as between-subjects variables, time (pre - 3, pre - 6, and pre - 12 months of follow-up) as within-subjects variable. And the post-hoc (Bonferroni adjustment) was used for or pair-wise comparisons. Supporting analyses were conducted using multiple imputation in which missing measures and exam scores were imputed to create five databases that were analysed in parallel in the missed data was No Missed At Random (MCAR)[132]. Statistically, differences were considered significant for P-values such that ($p < .05$), and all statistical analysis was used with the IBM Statistical Package for the Social Sciences (SPSS) version 25.

Table 1. The rehabilitation program.

Phases	Weeks	Objective	Treatment	Millstones
Presurgical Rehabilitation	4 weeks	Full knee extension ROM. Minimal knee effusion. Full-extension during straight leg raise.	Knee flexor strength exercise. Knee extensor strength exercise.	Patients with full knee extension range of motion (ROM), absent or minimal effusion, and no knee extension lag during a straight leg raise preoperatively have better postsurgical outcomes, such as returning to previous levels of activity and demonstration of normal knee function
Intermediate Postoperative Phase	week 1	Full knee extension. 90° of knee flexion. Patellar mobilisation.	Neuromuscular electrical stimulation Knee patellar mobilisation. Gait training.	Active and passive ROM up to 90 knee flexion Quadriceps contraction with patellar extension

		To control pain and inflammation.	Stationary bike exercise. Home training program: supine wall slides, self-patellar mobilizations 30 to 50 times per day, quadriceps exercise and straight leg raise 3 time a day (3X10).	
Early Postoperative Phase	Week 2	To achieve full ROM To activate knee muscles. To control knee effusion. To obtain a normal gait mechanism.	ROM exercise through the pain-free range. Incision mobilisation after skin healed . Wall squats. Functional brace if swelling allows. Prone hangs . Knee Patellar mobilisation.	Active knee flexion up to 110. Walking with a full extended knee and free of crutches. Stair reciprocal claiming . SLR without knee extension. The patient-reported outcome of more than 65 % in the overall evaluation.

Intermediate Postoperative Phase	Week 3-5.	Muscle endurance To achieve full ROM To improve muscle strength. To control knee effusion. To obtain a normal gait mechanism.	Tibiofemoral mobilizations if joint mobility is limited. Achieve more than 10 minutes per day of bike. Strat with balance and proprioceptive tasks.	Achieve knee flexion with only 10 differences with the uninvolved side. Achieve more than 60% of LSI-quadriceps muscle strength.
Late Postoperative Phase	Week 6-8.	To progress the athlete to full unilateral weight-bearing activities through improving strength training and work capacity	Progress all exercises in intensity and duration. Start running progression. Move to a fitness facility when all milestones are achieved.	Achieve more than 80% of LSI-quadriceps muscle strength. Achieve normal gait. Achieve full ROM and similar to the non-injured side. Knee effusion of trace or less

Transitional Phase	Week 9 - 12.	To improve high athletic abilities in multi-direction running and sport-specific tasks based on sport type.	Sports-specific “football” tasks. Agility training	The patient reported an outcome of more than 70 %. Achieve more than 85% of Single leg Hop tests. Achieve more than 85% of LSI-quadriceps muscle strength.
Follow-up Functional And Function Testing	From 4-12 months.	To improve high athletic abilities in multi-direction running and other specific tasks based on sport type	Increase the progression of transition phase exercise. Emphasise single-leg exercise and progress in the plyometric exercise	The patient reported an outcome of more than 70 %. Achieve more than 85% of SLHT Achieve more than 85% of LSI-quadriceps muscle strength.

LSI Limb Symmetry Index ROM Range Of Motion SLHT Single Leg Hop Test

RESULTS

To answer the first objective.

"The first phase of this doctoral thesis mainly aimed to review the literature and compare isokinetic strength tests, functional outcomes, and knee anteroposterior laxity between QTA and HTA or PTA after ACL reconstruction".

General overview

A total of 150 records were initially identified through database searching. **Figure 1** shows the flow details of the selected trials in the different phases. The main reason for excluded articles was not comparing different autografts or not performing the isokinetic strength test. Finally, this systematic review included ten studies published between 2004 and 2020. Seven studies compared QTA vs. HTA[58,68,114,115,133–135], and three studies compared QTA vs. PTA[42,47,136]. Overall, the systematic review agglutinated 754 participants, of whom 376 had a QTA (271 male and 105 female; 27.01 ± 5.3 years), 267 had an HTA (187 male and 80 female; 22.46 ± 4.9 years), and 111 had a PTA (94 male and 17 female; 27.59 ± 7.5 years). Patient BMI was reported in seven studies involving 440 patients, of whom 219 had a QTA with 23.68 ± 1.1 kg/m2, 206 had an HTA with 24.11 ± .41 kg/m2 and 15 had a PTA with 23.6 ± 0 kg/m2[42,47,58,68,114,134,135].

Seven studies reported the meniscal tear percentage from the total sample (QTA = 50.03%, HTA = 43.27% and PTA = 60.54%)[42,114,115,133–136] .The time between diagnosis and surgery was reported in seven articles (QTA = 12.72 ± 7.01 months; HTA = 10.78 ± 6.29 months; PTA = 16.48 ± 10.96 months)[42,47,58,114,133,135,136]. The athletic status was only mentioned in four articles[68,114,133,136], three trials included only athletic patients[68,114,136], and Guney-Deniz H. et al.[133] did not include athletes. Regarding the study design, three were randomised control trials[68,134,136], one was a comparative study[42], five were cohort studies[47,58,68,114,134,135], and one was a cross-sectional study[133]. (**Table 1**) displays the characteristics of the different intervention.

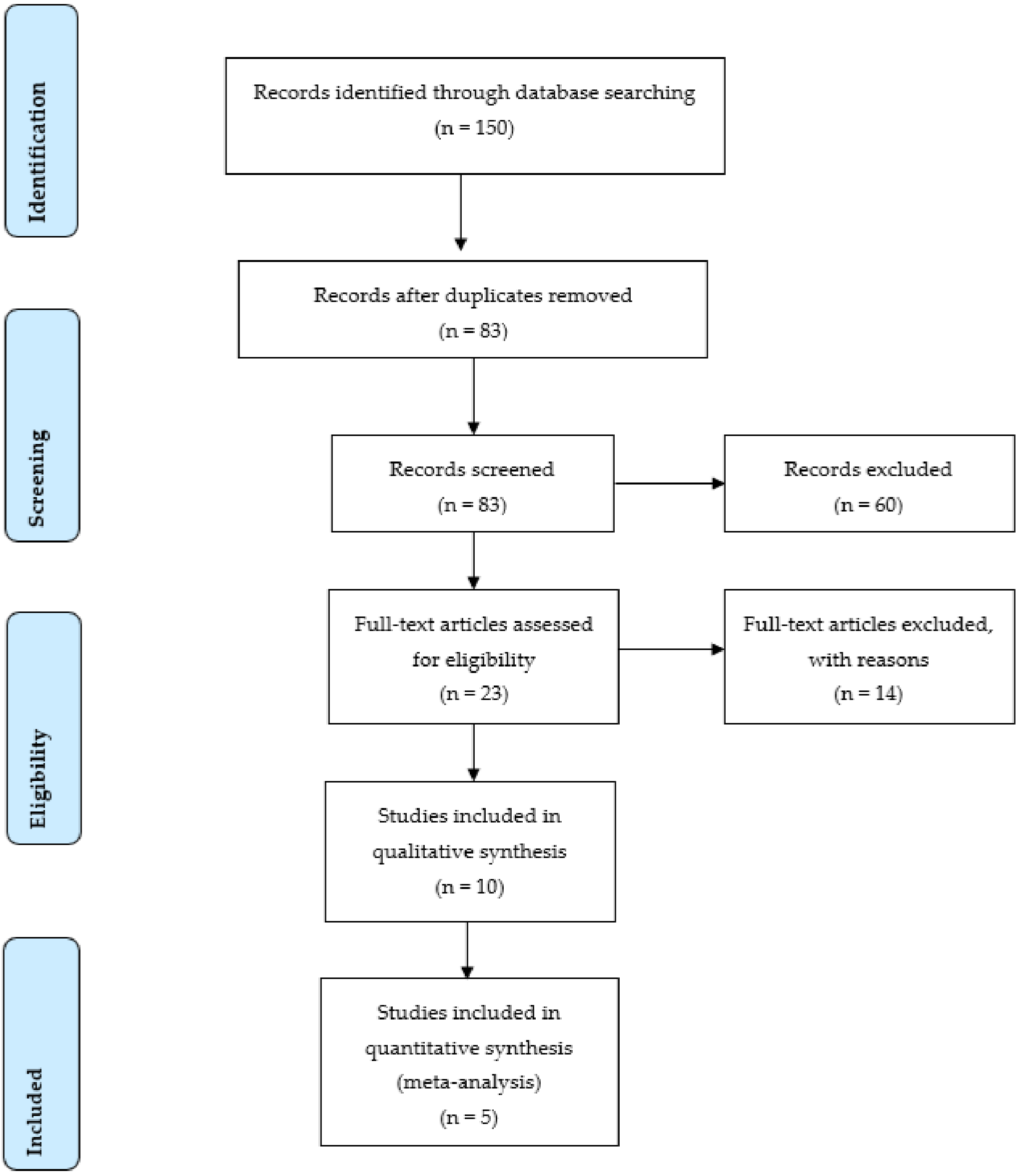

Identification
Screening
Eligibility
Included
Records identified through database searching
(n = 150)
Records after duplicates removed
(n = 83)
Records screened
(n = 83)
Records excluded
(n = 60)
Full-text articles assessed
for eligibility
(n = 23)
Full-text articles excluded,
with reasons
(n = 14)
Studies included in
qualitative synthesis
(n = 10)
Studies included in
quantitative synthesis
(meta-analysis)
(n = 5)

Figure 1. **PRISMA flow chart of search and study selection.**

Risk of bias

Two independent authors evaluated the risk of bias using the Cochrane risk-of-bias tool for randomised trials (RoB 2) for three randomised control trials [13] and Risk Of Bias In Non-Randomized Studies - of Interventions (ROBINS-I) for seven non-randomised studies [14]. Two of three studies showed a high risk of bias, and the highest risk was in the "deviation from intended intervention" domain (**Figure 2**). However, most of the non-randomised studies had a serious risk of bias, and the highest risk of bias was found in the "bias due to confounding" domain (**Table 2**).

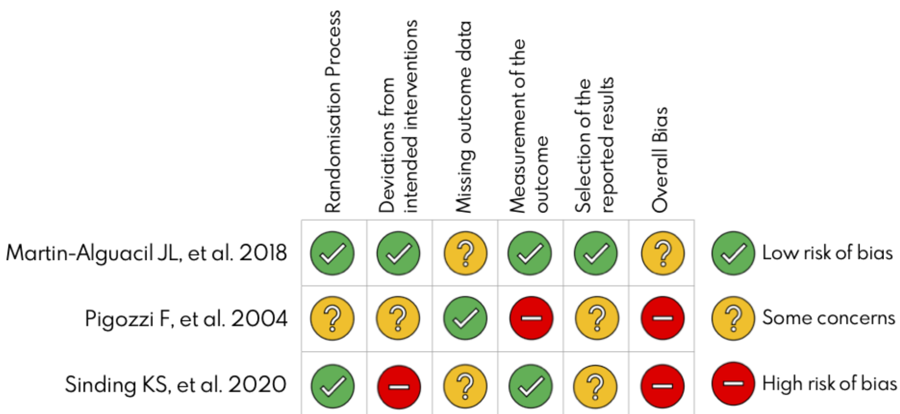


Figure 2. Cochrane collaboration risk of bias summary.

Table 2. ROBINS-I scale for the risk of bias assessment of non-randomised studies.

	D1	D2	D3	D4	D5	D6	D7	Overall judgement
Cavaignac E., et al 2017	Serious	Low	Low	Low	Serious	Low	Low	Serious
Csapo R., et al 2018	Moderate	Moderate	Low	Low	Low	Low	Serious	Serious
Fischer F., et al 2017	Moderate	Low	Low	Low	Low	Low	Low	Moderate
Han X. S., et al 2008	Serious	Low	Low	Low	Critical	Low	Moderate	Critical
Guney-Deniz X., et al 2020	Serious	Low	Low	Low	Low	Low	Low	Serious
Hunnicutt J. L., et al 2019	Serious	Low	Low	Low	Low	Low	Moderate	Serious
Lee J. K., et al 2016	Serious	Moderate	Low	Low	Low	Low	Moderate	Serious

D1, Bias due to confounding; D2, Bias in the selection of participants into the study; D3, Bias in the classification of interventions; D4, Bias due to deviations from intended; D5, Bias due to missing data; D6, Bias in the measurement of outcomes; D7, Bias in selection of the reported results.

Combined Outcomes

All the included investigations reported patient post-surgery outcomes with similar follow-up time points (one trial post 3 months[3], 5 studies post 6 months[42,58,68,115,136], 2 studies post 8 months[47,115], 4 studies post one year [42,68,134,135], and 3 studies post 2 years[42,47,134]).

Three months

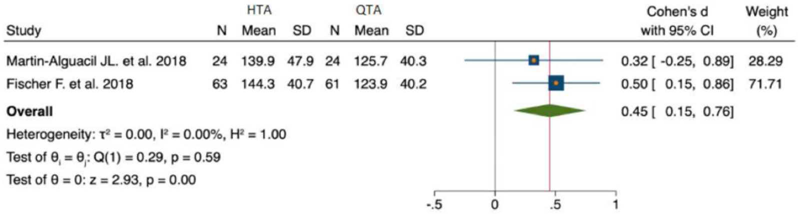
Martin-Alguacil J.L. et al.[68] compared QTA vs. HTA 3 months after surgery and showed a significant increase in knee extension strength test in favour of the QTA group. No significant differences were reported between the groups in knee flexion strength test, functional outcome, or anteroposterior laxity.

Six months

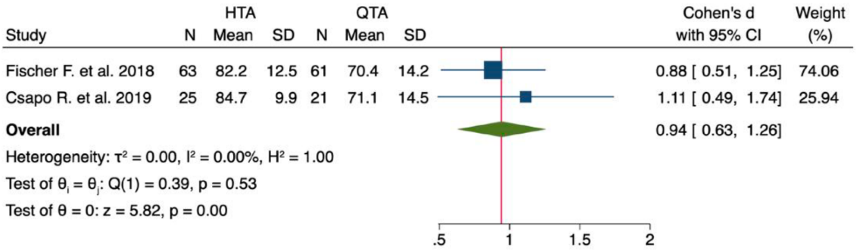
Four studies compared QTA vs. HTA[58,68,114]; three mentioned better and significant results for the QTA group in the knee extension strength test[68,114,115]. The pooled results were as follows: extension peak torque at 60°/s (.45; 95% Confidence Interval (CI), .15 to .76; P = .00; I^2 = 0%; Figure. 3.a); extension limb symmetry index (LSI) at 60°/s (.94; 95% CI, .62 to 1.26; P = .00; I^2 = 0%; Figure. 3.b)[114,115]. Similarly, the QTA group demonstrated better and more significant results in the knee flexion strength test[7]. The pooled results were as follows: flexion peak torque at 60°/s (.25; 95% CI, .05 to .55; P = .10; I^2 = 0%; Figure. 3.c)[68,115]; flexion-LSI at 60°/s (.44; 95% CI, -.75 to -.14; P = .00; I^2 = 0%; Figure. 3.d)[114,115]. At the same evaluation point, two studies compared QTA vs. PTA[42,136]. Pigozzi et al.[136] reported better and significant results for QTA in the knee extension strength and knee flexion strength tests. However, Han X et al.[42] demonstrated no significant differences between the groups in the knee extension strength test or knee flexion strength test.

Regarding functional outcomes, 2 studies compared QTA vs. HTA. Martin-Alguacil et al.[68] showed no significant differences between the QTA and HTA groups. By contrast, Cavaignac et al.[58] showed significant differences between the QTA and HTA groups. No study has compared QTA vs. PTA regarding functional outcomes. Concerning knee anteroposterior laxity, two studies compared QTA vs. HTA[58,68]. Cavaignac et al.[58] reported better and significant results within the QTA group. However, Martin-Alguacil et al.[68] reported no differences between the groups. Additionally, only the study of Pigozzi et al.[136] reported knee anteroposterior laxity between QTA and HTA and showed no significant differences between the autografts.

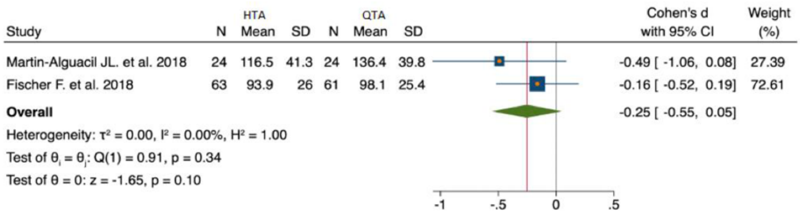
3.a: Comparison of knee extension QTA vs. HTA after 6 months.
Outcome: Peak torque at 60°/s



3.b: Comparison of knee extension QTA vs. HTA after 6 months.
Outcome: Limb Symmetry Index at 60°/s



3.c: Comparison of knee flexion QTA vs. HTA after 6 months.
Outcome: Peak torque at 60°/s



3.d: Comparison of knee flexion QTA vs. HTA after 6 months.
Outcome: Limb Symmetry Index at 60°/s

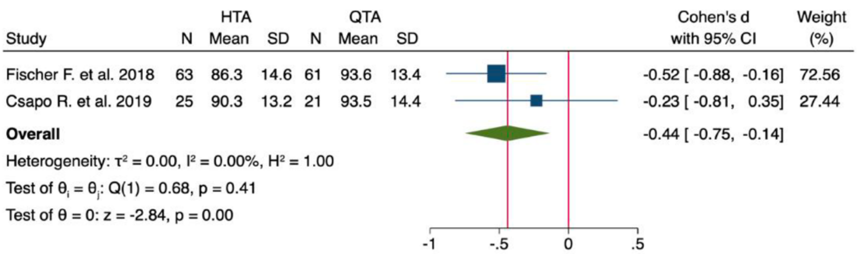


Figure 3. Forest plots for knee isokinetic strength test at 60°/s and 180°/s at 6 months[68,114,115].

Twelve months

The third evaluation point was approximately 12 months after surgery (12 months:[58,68,134,135]; 13.5 months:[133]). Four studies compared QTA vs. HTA[68,133–135], of which two reported no significant differences in the knee extension strength test[78,134]. Two studies reported better and more significant results with the HTA group in the knee extension strength test[133,135]. The pooled results were as follows: knee extension LSI at 60°/s (39; 95% CI, - .32 to 1.11; P = .28; I^2 = 70.14%; Figure. 4.a)[133,134]; knee extension LSI at 180°/s (.56; 95% CI, -.23 to 1.35; P = .16; I^2 = 78.66%; Figure. 4.b)[133,134]. Only one study showed significant results in the knee flexion strength test for the QTA group[134], and the knee flexion strength test showed no significant results in three studies[68,133,135]. The pooled results were as follows: knee flexion-LSI at 60°/s (.46; 95% CI, -.79 to -.12; P = .01; I^2 = 0%; Figure. 4.c)[133,134]; knee flexion-LSI at 180°/s (.66; 95% CI, -1.00 to -.32; P = .00; I^2 = 0%; Figure. 4.d). Additionally, only Han et al.[42] compared QTA vs. PTA at 12 months and reported no significant differences between the groups. Finally, no significant differences were found between QTA and HTA regarding functional outcomes[68,133–135] or knee anteroposterior laxity[68,134,135]. No study has compared QTA vs. PTA concerning functional outcomes or knee anteroposterior laxity.

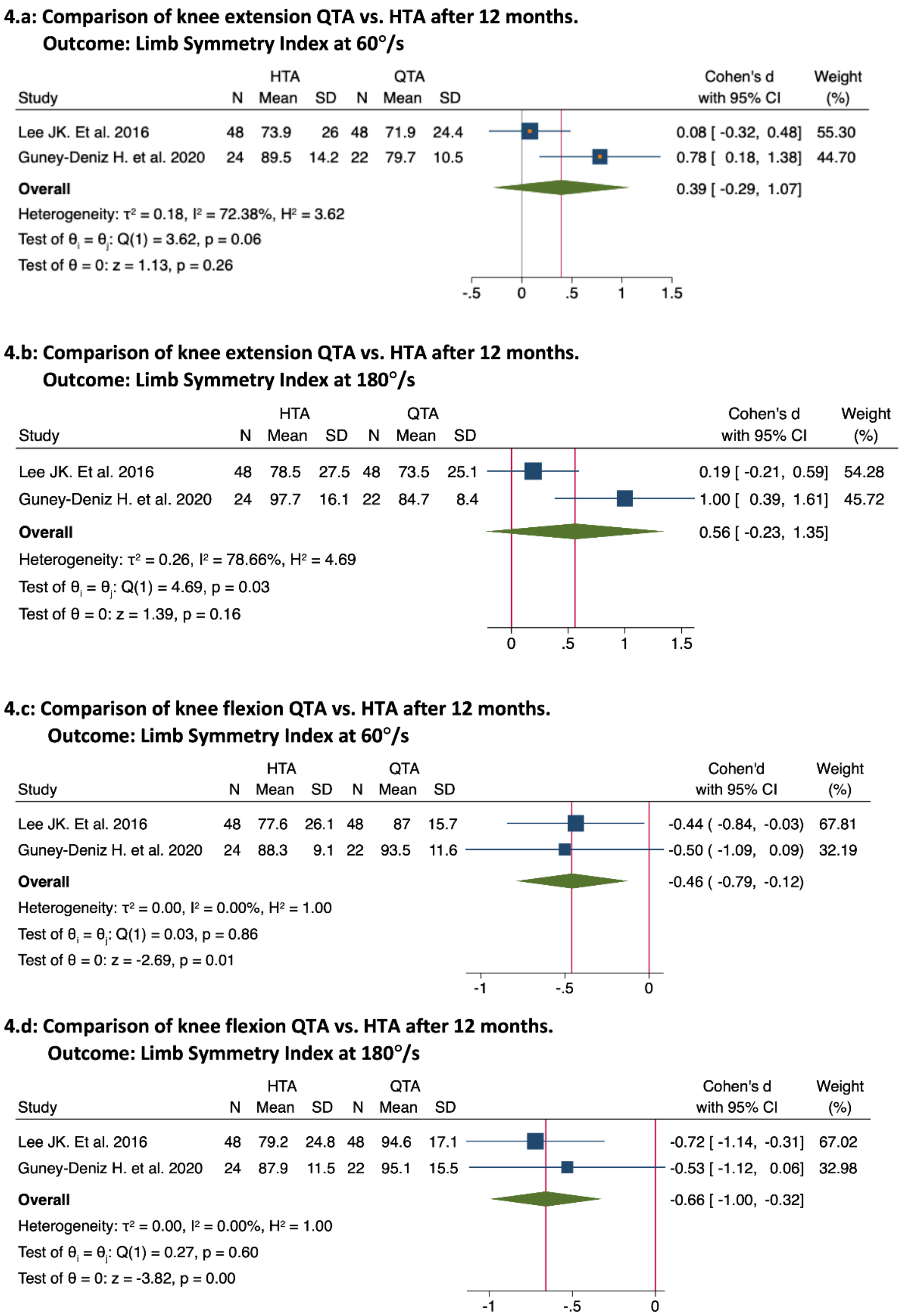


Figure 4. Forest plots for knee isokinetic strength test at 60°/s and 180°/s at 12 months[133,134].

Twenty-four months

The fourth evaluation point was approximately 24 months after surgery[5,10]. Only Lee et al. [134] compared QTA vs. HTA and reported no significant differences in the knee extension strength test and significant differences in the knee flexion strength test for the QTA group. Similarly, Han et al.[42] compared QTA vs. PTA and mentioned no significant differences in the knee extension strength test. Finally, no significant differences were found in functional outcomes or knee anteroposterior laxity between QTA and HTA[68,134] or between QTA and PTA[42].

Return to sport and rehabilitation protocols

Return to sport evaluation was different in the reviewed articles. Seven of ten studies described their rehabilitation protocol and return to sport criteria[42,68,115,133–136]. Post rehabilitation timing was mentioned in four studies[68,134,136]. Three studies had a 6-month accelerated rehabilitation program[68,134,136], and one project had a 12-month non-accelerated rehabilitation program[135]. However, an 80% to 90% level of quadriceps strength recovery is considered a criterion for patients to fully recover their activity and return to sport[42,135,136].

Post rehabilitation protocols were mentioned in seven studies with variations in their progression and phases [42,68,115,133–136].. Four rehabilitation programs started with pain and inflammation control in the first week [68,133,135,136], and full Range Of Motion (ROM) was achieved between three and six weeks [42,68,115,133,134,136]. Although muscle strengthening started with static knee exercise in the first and second weeks[42,68,115,133,134,136], dynamic knee exercises were introduced between the second and fourth weeks[68,115,133,135]. Additionally, four protocols included closed kinetic chain exercises [68,115,133,135]. Martin-Alguacil et al.[68] and Lee et al.[134] included open kinetic chain exercises. After that, four rehabilitation programs included running between 3 and 4 months. By contrast, three studies did not mention running in their protocols.

After the last phase of the rehabilitation protocols, RTS criteria were applied in six studies [42,68,115,133,134,136]. Time after surgery was mentioned in all criteria [42,68,133,134,136]. Guney-Deniz et al. [133] allowed RTS after 3 months. Five studies permitted RTS after 6 months[42,68,134,136]. By contrast, Sinding et al.[135] allowed RTS after one year. The second criterion was an isokinetic strength test of the injured limbs of more than 80% to 90% of the non-injured limbs[133,134,136]. The last criterion was a single-leg hop test of more than 80% to 90% of injured limbs [133,134,136]. Additionally, Hande et al.[133]was the only study to consider functional outcomes as RTS criteria.

To answer the second objective.

"To analyse the sociodemographic and clinical characteristics of patients with injured ACLs before reconstruction surgeries".

Sociodemographic and clinical characteristics

In the clinical part of the thesis, 78 patients with injured ACLs participated and were randomly allocated into three experimental groups: BQTA, QTA, and HTA. Each of the three groups had 26 participants. However, patients 5, 6, and 11 from the BQTA group were dropped at 3-, 6-, and 12- months, respectively. Three of them were released due to patellar-bone fracturing during the surgery and the others were removed due to Covid-19 restrictions. Two patients from the QTA group were released at 6 and 12 months of follow-up procedures. One patient was removed because they moved from the city where they lived, and the other one was removed because of Covid-19 restrictions. For the HTA group, one was released at 3 and 6 months, and four patients were released at 12 months. One patient was too busy to participate in the follow-up evaluations, and the other three patients were removed due to Covid-19 restrictions (**Figure 5**). The study sample does not show statistically significant differences between experimental groups in the sociodemographic or clinical characteristics, except for the education level (P = .08) and BMI (P = .044). All of the sociodemographic data (age, sex, civil status, education level, smoking, alcohol consumption, weight, height, Body Mass Index (BMI), fat percentage, muscle percentage, competition level, and dominant side) and clinical data (injured side, crutches (3^{rd} day), bike (3^{rd} week), running (4^{th} month), return to normal activity (6^{th} month), and return to pre-injury level (6^{th}month)) are demonstrated in (**Table 3)**.

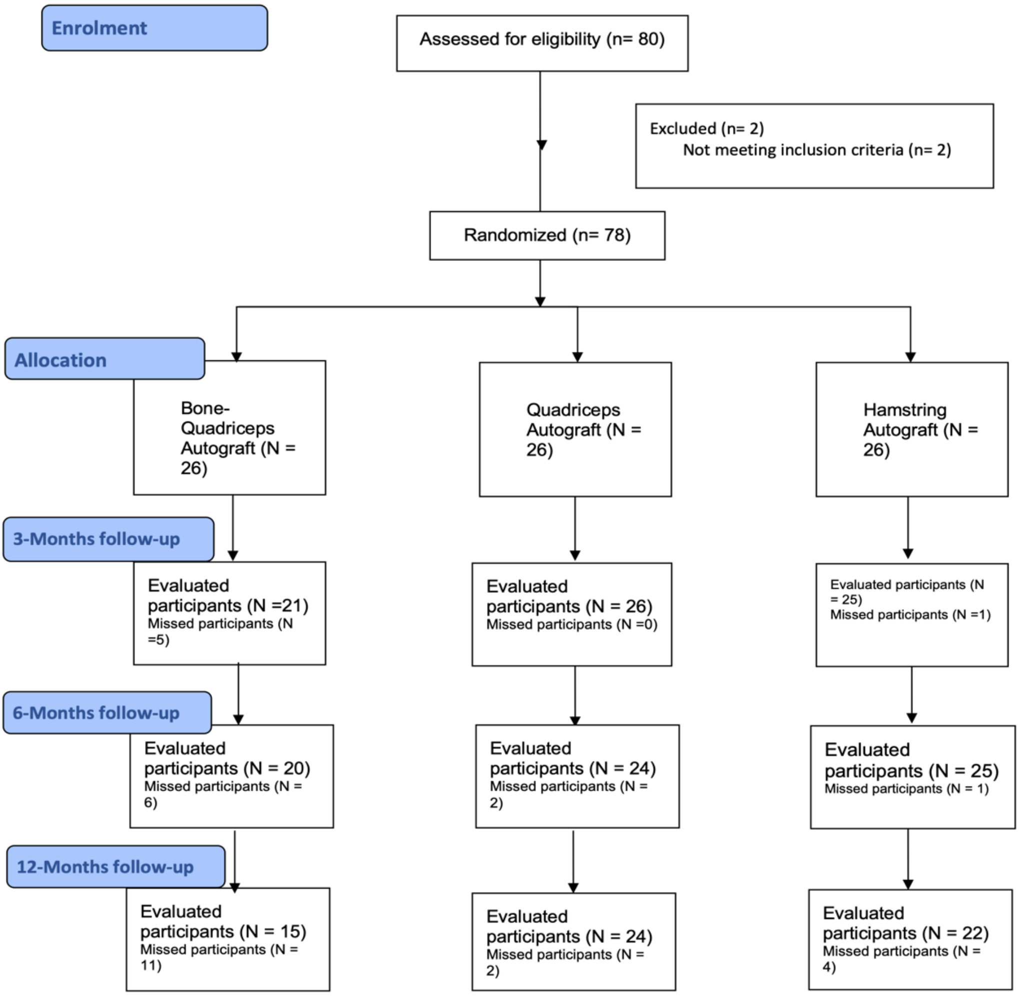


Figure 5. Flowchart of the study participants.

Table 3. Sociodemographic and clinical characteristics of the participants.

	BQTA	QTA	HTA	Total	P value
Age	22.5±5.6	18.7±3.4	19.5±4.0	20.3±4.7	.14
Sex					
Male	23(88.5)	23(88.5)	20(76.9)	66(84.6)	.41
Female	3(11.5)	3(11.5)	6(23.1)	12(15.4)	
Civil status					
Single	25(96.2)	26(100)	26(100)	77(98.7)	.36
Married	1(3.8)	0(0)	0(0)	1(1.3)	
Education level					
Basic	10(38.5)	8(30.8)	8(30.8)	26(33.33)	**.08**
Medal	5(19.2)	14(45.2)	12(38.7)	31(39.7)	
High	11(42.3)	4(15.4)	6(23.1)	21(26.9)	
Smoking					
Not smoker	21(80.8)	26(100)	24(92.3)	71(91.0)	.51
Smoker	5(19.2)	0(0)	2(7.7)	7(9.0)	
Alcohol consumption					
No alcohol	12(46.2)	13(50)	16(61.5)	41(52.6)	.75
Monthly	12(46.2)	11(42.3)	7(26.9)	30(38.5)	
Weekly	1(3.8)	2(7.7)	2(40.0)	5(6.4)	
Daily	1(3.8)	0(0)	1(3.8)	2(2.6)	
Weight (kg)	75.5±13.1	69.0±9.2	70.6±13.8	71.8±12.3	.14
Height (m)	172.4±8.5	171.9±6.1	165.3±27.2	169.9±16.9	.25
BMI (kg/m²)	25.1±3.5	22.8±2.3	24.1±3.6	24±3.3	**.044**
Fat percentage	19.2±5.1	18.6±7.2	19.6 ±8.4	19.1±7.1	.89
Muscle percentage	34.8±4.5	32.7±4.1	32.3±6.5	33.2±5.2	.22

Injured side					
Left	13(50)	14(53.8)	11(42.1)	38(48.7)	.96
Right	13(50)	12(46.2)	15(57.7)	40(51.3)	
Dominant side					
Left	9(34.6)	4(15.4)	6(23.1)	19(24.4)	.26
Right	17(65.4)	22(84.6)	20(76.9)	59(75.6)	
Competition level					
Professional	6(23.1)	3(11.5)	0(0)	9(11.5)	.10
Federal	20(76.9)	22(84.6)	25(96.2)	67(85.9)	
Other	0(0)	1(3.8)	1(3.8)	2(2.6)	
Meniscus injury					
No	12(46.2)	5(19.2)	11(42.3)	28(35.9)	.91
Yes	14(53.8)	21(80.8)	15(57.7)	50(64.1)	
Crutches (III Day)					
No	11(50.0	7(26.9	5(19.2)	23(31.1)	.61
Yes	11(50.0	19(73.1)	2180.8)	51(68.9)	
Bike (III Week)					
No	12(42.5)	10(38.5)	10(38.5)	32(43.2)	.44
Yes	10(45.5)	16(61.5)	16(61.5)	42(56.8)	
Running (III Month)					
No	10(45.5)	4(15.4)	9(34.6)	23(31.1)	.72
Yes	12(54.5)	22(82.6)	17(65.4)	51(68.9)	
Return to normal activity					
No	0(0)	2(9.1)	1(4.8)	3(5.5)	.82
Yes	12(100)	20(90.9)	20(95.2)	52(94.5)	
Return to pre injury level					
No	6(50)	10(45.5)	9(42.9)	25(45.5)	.92
Yes	6(50)	12(54.5)	12(57.1)	30(54.5)	

Data are shown as Mean ± SD or Mean(frequency) BQTA Bone Quadriceps Tendon Autograft HTA Hamstring Tendon Autograft Kg Kilograms Kg/m^2 Kilograms / Metres Square kPa Kilopascal QTA Quadriceps Tendon Autograft

To answer the third objective.

"To compare the difference of PROM (LKS and CKRS) between patients following ACL reconstruction with BQTA, QTA, or HTA at three evaluation periods (Pre – 3 months, Pre – 6 months, and Pre – 12 months) after rehabilitation protocol".

Lysholm Knee Score (LKS)

The repeated ANOVA of the LKS over time x autograft type did not show any significant differences for LKS (F = 1.54, P = .168) between experimental groups at 3-, 6-, and 12- months of follow up (**Table 4**).

Cincinnati Knee Rating System (CKRS)

The analysis of CKRS over time x autograft type did not show any significant differences (F = .44, P = .8) between the three autograft groups at 3-, 6-, and 12-months of follow up (**Table 4**).

Table 4. Patient reported outcome measures at 3-, 6-, and 12-months follow-up.

Autograft type	Pre - 3 Months Evaluation	Pre - 6 Months Evaluation	Pre - 12 Months Evaluation
LKS			
BQTA	-.28 ± 24.17 (-10.73 - 10.17)	14.46 ± 17.2 (7.2 - 21.72)	16.56 ± 14.67 (10.21 - 22.9)
QTA	6.36 ± 15.2 (.22 - 12.49)	12.08 ± 15.6 (5.77 - 18.38)	11.14 ± 11.96 (6.31 - 15.97)
HTA	9.72 ± 21.65 (.97 - 18.46)	13.04 ± 20.32 (4.83 - 21.24)	9.21 ± 10.09 (5.14 - 13.29)

CKRS			
BQTA	3.31 ± 16.23 (-3.25 - 3.18)	16.27 ± 16.68 (9.22 - 23.31)	24.02 ± 16.96 (16.69 - 31.35)
QTA	7.06 ± 21.57 (-1.65 - 4.23)	13.21 ± 19.49 (5.33 - 21.08)	21.91 ± 16.21 (15.36 - 28.45)
HTA	3.36 ± 19.12 (-4.9 - 3.99)	15.38 ± 17.9 (8.16 - 22.61)	25.29 ± 18.13 (17.97 - 32.62)

Data are shown as Mean ± SD (95% CI) BQTA Bone Quadriceps Tendon Autograft HTA Hamstring Tendon Autograft QTA Quadriceps Tendon Autograft.
*a-b Significant between BQTA and QTAA groups–interaction time (repeated ANCOVA test, $p < .05$), *a-c Significant between BQTA and HTA groups–interaction time (repeated ANCOVA test, $p < .05$), *b-c Significant between QTA and HTA groups–interaction time (repeated ANCOVA test, $p < .05$).

To answer the fourth objective.

"To compare the difference of CROM (knee anteroposterior laxity, architecture measurements, muscle girth, VAS, and PPT) between patients following ACL reconstruction with BQTA, QTA, or HTA at three evaluation periods (Pre – 3 months, Pre – 6 months and Pre – 12 months) after rehabilitation protocol".

Knee anteroposterior laxity.

Regarding the knee anteroposterior laxity, the analysis of interaction time x autograft type did not display any significant results between participant groups (F = 1.31, P = .24) for the injured knee (**Figure 6**).

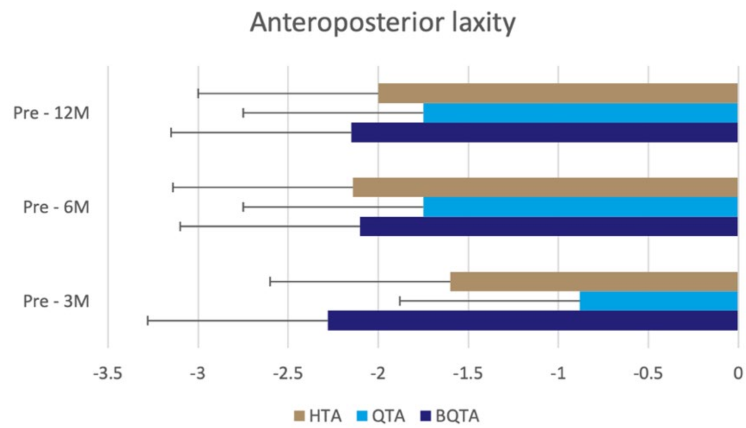


Figure 6. Knee anteroposterior laxity at 3-, 6-, and 12-month follow-up.

Sonographic measurements

The repeated ANOVA of the sonographic measurements over time x autograft type did not show any significant differences for quadriceps tendon depth "sagittal view" (F = 1.48, P = .18), quadriceps tendon depth "transversal view" (F = .58, P = .73), or for knee cartilage thickness (F = .90, P = .49). However, the analysis showed significant differences for quadriceps tendon width (F = 2.37, P = .032) at 3-, 6-, and 12- months of follow up (**Table 5**) and the post hoc analysis did not show any significant differences between autograft groups (**Table 5**).

Muscle girth

The analysis of thigh girth of injured leg over time x autograft type displayed significant differences (F = 2.20, P = .046) at 3-, 6-, and 12- months of follow up **(Table 3)**. The post hoc analysis showed significant differences between the BQTA group and HTA group (**Table 5**).

Table 5. Sonographic measurements and muscle girth at 3-, 6-, and 12- months.

Autograft type	Pre - 3 Months Evaluation	Pre - 6 Months Evaluation	Pre - 12 Months Evaluation
Quadriceps tendon depth injured side “sagittal view" (mm)			
BQTA	.06 ± .16 (-.02 - .13)	.11 ± .27 (-.12 - .11)	.25 ± .37 (.09 - .41)
QTA	-.03 ± .23 (-.12 - .06)	-.02 ± .23 (-.12 - .07)	.11 ± .29 (-.01 - .23)
HTA	.03 ± .15 (-.03 - .09)	-.02 ± .23 (-.11 - .07)	.16 ± .24 (.06 - .26)
Quadriceps tendon width injured side (mm)			
BQTA	.14 ± .46 (-.06 - .34)	.08 ± .47 (-.12 - .29)	.19 ± .67 (-.1 - .47)
QTA	-.14 ± .47 (-.32 - .05)	-.14 ± .45 (-.32 - .04)	.43 ± .65 (.16 - .69)

HTA	-.08 ± .61 (-.32 - .17)	.08 ± .45 (-.1 - .26)	.21 ± .43 (.04 - .39)
Quadriceps tendon depth injured side (mm)			
BQTA	.02 ± .09 (-.02 - .06)	.04 ± .12 (-.01 - .09)	.19 ± .27 (.08 - .31)
QTA	.07 ± .24 (-.03 - .17)	.04 ± .22 (-.05 - .13)	.2 ± .33 (.07 - .34)
HTA	.05 ± .17 (-.02 - .12)	.1 ± .22 (.02 - .19)	.19 ± .23 (.1 - .28)
Thickness knee cartilage injured side (mm)			
BQTA	0 ± .07 (-.03 - .03)	-.01 ± .12 (-.06 - .05)	0 ± .1 (-.04 - .05)
QTA	-.03 ± .05 (-.05 - -.01)	-.04 ± .1 (-.08 - 0)	0 ± .09 (-.04 - .04)
HTA	-.04 ± .07 (-.07 - -.01)	-.05 ± .09 (-.09 - -.02)	-.02 ± .06 (-.04 - .01)
Thigh girth injured side (cm)			
BQTA	-1.31 ± 2.61[*a-c] (-2.44 - -.18)	-.6 ± 4.05 [*a-c] (-2.35 - 1.15)	.11 ± 4.62 (-1.89 - 2.11)
QTA	-.35 ± 2.59 (-1.4 - .69)	.37 ± 2.99 (-.84 - 1.58)	1.56 ± 3.98 (-.04 - 3.17)
HTA	.42 ± 1.99[*a-c] (-.38 - 1.23)	2.03 ± 2.82[*a-c] (.89 - 3.17)	1.35 ± 3.29 (.02 - 2.67)

Data are shown as Mean ± SD (95% CI) BQTA Bone Quadriceps Tendon Autograft HTA Hamstring Tendon Autograft QTA Quadriceps Tendon Autograft.

*a-b Significant between BQTA and QTAA groups–interaction time (repeated ANCOVA test, $p < .05$), *a-c Significant between BQTA and HTA groups–interaction time (repeated ANCOVA test, $p < .05$), *b-c Significant between QTA and HTA groups–interaction time (repeated ANCOVA test, $p < .05$).

VAS and PPT

The repeated ANOVA analysis of VAS over time x autograft type did not show any significant differences (F = 2.38, P = .10) at 3-, 6-, and 12- months of follow up (**Table 6**). Regarding the results of PPT, the repeated ANOVA analysis over time x autograft type did not demonstrate any significant results for all measured points: epicondyle (F = 1.19, P = .31), vastus lateralis (F = 1.78, P = .11), vastus medialis (F = 1.26, P = .27), patellar tendon (F = 1.82, P = .09), quadriceps tendon (F = 1.6, P = .13), or hamstring tendon (F = 1.9, P = .72) at 3-, 6-, and 12- months of follow up (**Table 6**).

Table 6. Visual Analogue Scale (VAS) and Pressure Pain Thresholds (PPT) at 3-, 6-, and 12- months of follow-up.

Autograft type	Pre - 3 Months Evaluation	Pre - 6 Months Evaluation	Pre - 12 Months Evaluation
VAS			
BQTA	-.86 ± 2.64 (-1.93 - .2)	-1.06 ± 2.26 (-1.97 - -.14)	-1.29 ± 2.13 (-2.15 - -.42)
QTA	-.75 ± 1.98 (-1.55 - .05)	-1.27 ± 2.25 (-2.18 - -.36)	-1.69 ± 1.85 (-2.44 - -.95)
HTA	-.96 ± 2.86 (-2.12 - .19)	-1.08 ± 3.02 (-2.3 - .14)	-1.85 ± 2.27 (-2.77 - -.93)

Epicondyle dominant side (kPa)			
BQTA	32.22 ± 87.91 (-5.79 - 70.24)	69.44 ± 109.24 (22.2 - 116.68)	108.95 ± 102.11 (64.8 - 153.11)
QTA	24.32 ± 96.59 (-14.7 - 63.33)	44.37 ± 123.82 (-5.64 - 94.39)	145.81 ± 139.6 (89.43 - 202.2)
HTA	-24.7 ± 116.62 (-71.8 - 22.41)	20.27 ± 156.71 (-43.03 - 83.56)	105.05 ± 182.03 (31.53 - 178.57)
Vastus lateralis injured side (kPa)			
BQTA	75.29 ± 121.68 (22.67 - 127.91)	102.41 ± 107.09 (56.1 - 148.72)	164.28 ± 111.38 (116.12 - 212.44)
QTA	18.6 ± 142.21 (-38.84 - 76.04)	21.62 ± 145.33 (-37.08 - 80.31)	125 ± 195.61 (45.99 - 204.01)
HTA	-32.91 ± 125.27 (-83.5 - 17.69)	-20.33 ± 156.35 (-83.48 - 42.82)	82.97 ± 183.29 (8.93 - 157)
Vastus medialis injured side (kPa)			
BQTA	62.17 ± 91.46 (22.62 - 101.72)	47.05 ± 116.05 (-3.14 - 97.23)	130.4 ± 152.23 (64.57 - 196.23)
QTA	10.94 ± 134.38 (-43.33 - 65.22)	41.42 ± 140.82 (-15.46 - 98.29)	150.81 ± 142.02 (93.44 - 208.17)
HTA	-4.31 ± 83.48 (-38.03 - 29.4)	51.85 ± 137.97 (-3.87 - 107.58)	140.93 ± 139.27 (84.68 - 197.18)

Patellar tendon injured side (kPa)			
BQTA	60.43 ± 142.15 (-1.04 - 121.9)	107.84 ± 195.6 (23.26 - 192.42)	211.3 ± 159.28 (142.43 - 280.18)
QTA	-13.37 ± 238.31 (-109.63 - 82.88)	-21.6 ± 192.95 (-99.54 - 56.33)	69.89 ± 232.89 (-24.17 - 163.96)
HTA	-51.68 ± 156.16 (-114.75 - 11.4)	13.38 ± 173.81 (-56.82 - 83.58)	102.72 ± 177.29 (31.12 - 174.33)
Quadriceps tendon injured side (kPa)			
BQTA	81.33 ± 128.78 (25.64 - 137.02)	98.54 ± 156.93 (30.68 - 166.41)	217.98 ± 147.37 (154.25 - 281.71)
QTA	-35.33 ± 184.92 (-110.03 - 39.36)	23.13 ± 184.94 (-51.56 - 97.83)	125.64 ± 205.07 (42.81 - 208.47)
HTA	18.21 ± 127.17 (-33.15 - 69.58)	49.59 ± 167.55 (-18.09 - 117.26)	112.05 ± 154.2 (49.77 - 174.34)
Hamstring tendon injured side (kPa)			
BQTA	46.93 ± 113.58 (-2.18 - 96.05)	59.79 ± 106.31 (13.82 - 105.76)	163.8 ± 174.73 (88.25 - 239.36)
QTA	-64.53 ± 159.33 (-128.88 - -0.18)	-45.64 ± 171.94 (-115.08 - 23.81)	176.58 ± 211.8 (91.03 - 262.13)
HTA	-37.3 ± 138.19 (-93.12 - 18.51)	-25.91 ± 144.05 (-84.09 - 32.27)	167.24 ± 216.12 (79.95 - 254.53)

Data are shown as Mean ± SD (95%CI) BQTA Bone Quadriceps Tendon Autograft HTA Hamstring Tendon Autograft QTA Quadriceps Tendon Autograft.

*a-b Significant between BQTA and QTAA groups–interaction time (repeated ANCOVA test, $p < .05$), *a-c Significant between BQTA and HTA groups–interaction time (repeated ANCOVA test, $p < .05$), *b-c Significant between QTA and HTA groups–interaction time (repeated ANCOVA test, $p < .05$).

To answer the fifth objective.

"To compare the difference of FROM (muscle strength and single leg hop tests) between patients following ACL reconstruction with BQTA, QTA, or HTA at three evaluation periods (Pre – 3 months, Pre – 6 months, and Pre – 12 months) after rehabilitation protocols".

Peak Torque (PT)

In relation to the results of isokinetic strength, the analysis of repeated ANOVA interaction time x autograft type showed statistically significant differences for knee extension PT at 300°/s ($F = 4.52$, $P < .001$), 180°/s ($F = 5.79$, $P < .001$), and 60°/s ($F = 5.2$, $P < .001$) at 3-, 6-, and 12- months of follow up. The post hoc analysis displayed statistical differences between the three autografts groups (**Table 4**). However, the analysis did not show any significant difference for knee flexion PT at 300°/s ($F = .76$, $P = .59$), 180°/s($F = .93$, $P = .47$), or 60°/s ($F = 1.4$, $P = .20$) at 3-, 6-, and 12- months of follow up (**Figure 7**).

Regarding the result of knee flexion, the analysis of isokinetic strength PT showed a significant result only for 300°/s ($F = 3.37$, $P = .04$) and no statistical differences for 180°/s ($F = .22$, $P = .80$) or for 60°/s ($F = .73$, $P = .48$) at 3-, 6-, and 12- months of follow up (**Figure 7**). The post hoc analysis of peak torque at 300°/s showed significant differences between BQTA vs. HTA ($P = .04$).

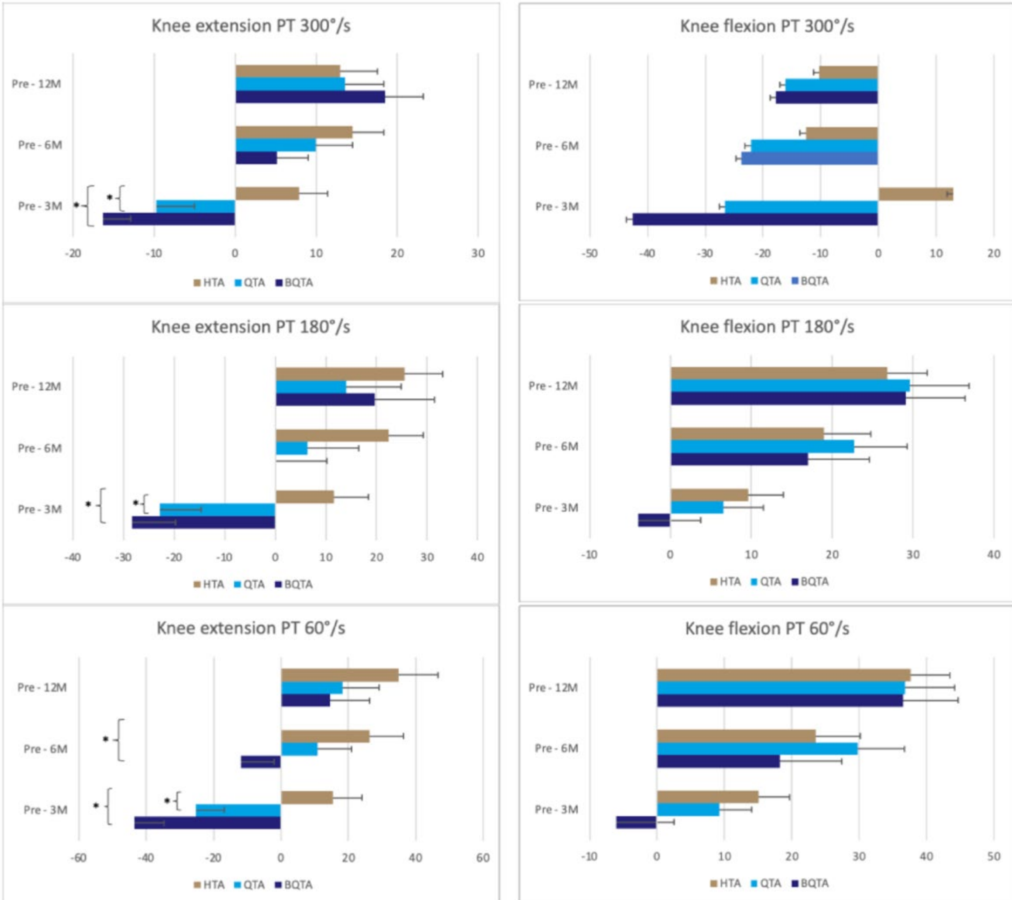


Figure 7. Peak torque of knee extension and flexion for the injured side at 3-, 6-, and 12-months follow-up.

Hamstring/Quadriceps ratio (H/Q ratio).

The statistical analysis of the H/Q ratio examined by isokinetic dynamometry showed a significant difference at 300°/s (F = 4.14, P < .001), 180°/s (F = 7.59, P < .001), and 60°/s (F = 6.74, P < .001) at 3-, 6-, and 12- months of follow up (**Figure 8**). The post hoc analysis demonstrated statistical results between the three autografts groups (**Figure 8**).

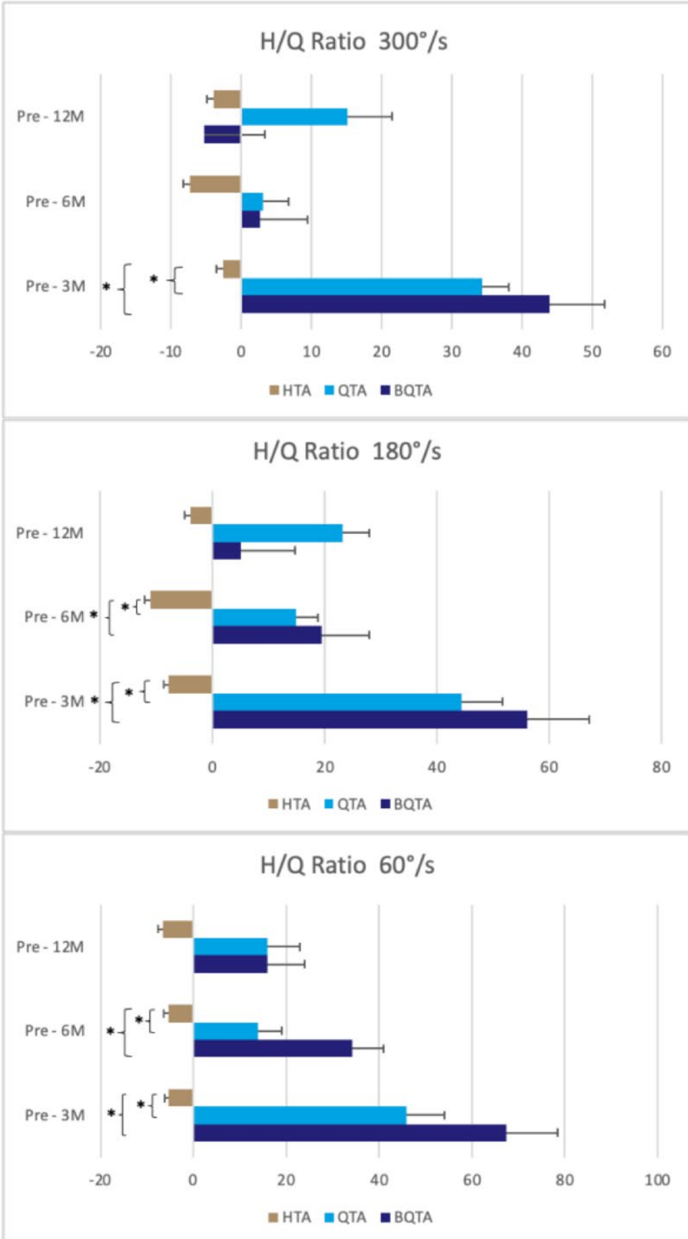


Figure 8. H/Q ratio of the injured side at 3-, 6-, and 12-months follow-up.

Limb Symmetry Index (LSI)

Regarding the result of LSI of peak torque, the repeated ANOVA analysis of knee extension LSI over time x autograft type showed significant results at 300°/s (F = 1.9, P = .07), 180°/s (F = 2.87, P = .011), and at 60°/s (F = 2.8, P = .011) at 3-, 6-, and 12- months of follow up. The post hoc analysis demonstrated statistical results between the three autografts groups (**Figure 9**).

Similarly, the repeated ANOVA analysis of knee flexion LSI over time x autograft type did not show any significant results at 180°/s (F = .86, P = .52) or at 60°/s (F = 1.34, P = .24), except at 300°/s (F = 2.47, P = .026) at 3-, 6-, and 12- months of follow up (**Figure 9**). The post hoc analysis demonstrated statistical results between the three autografts groups (**Figure 9**).

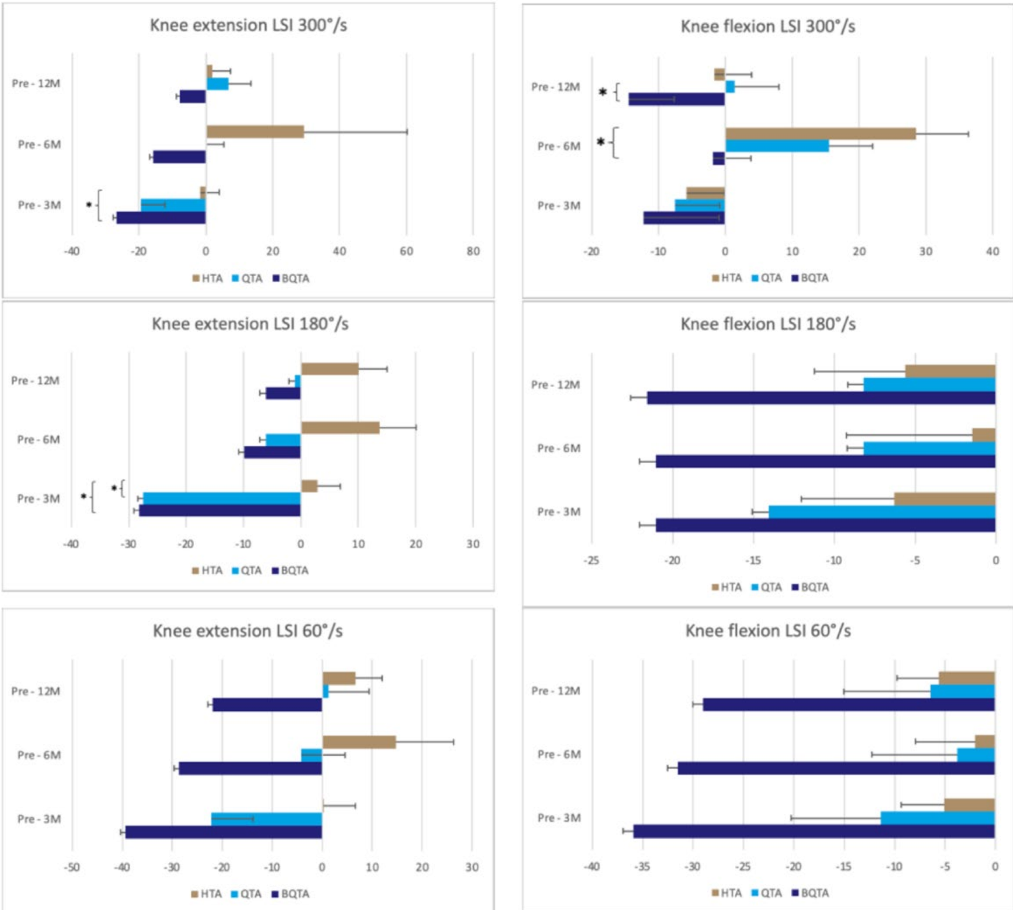


Figure 9. Limb Symmetry Index (LSI) of knee extension and flexion at 3-, 6-, and 12-months follow-up.

Single Leg Hop Test (SLHT)

In relation to the result of the SLHT injured side, the repeated ANOVA analysis of SLHT over time x autograft type did not show any significant differences (F = 1.1, P = .36) at 3-, 6-, and 12- months of follow up (**Figure 10**).

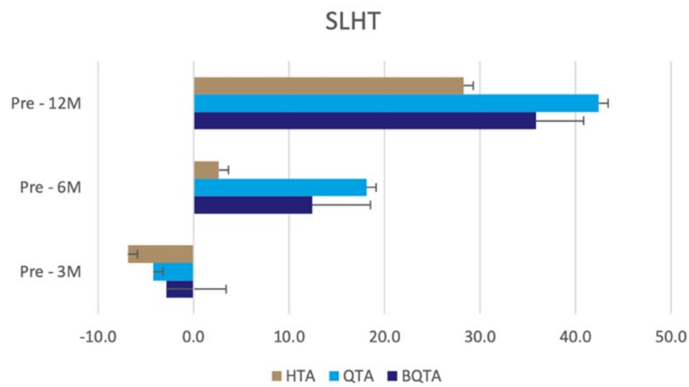


Figure 10. Single Leg Hop Test (SLHT) of injured leg at 3-, 6-, and 12-months follow-up.

Return to Sport (RTS)

Regarding the RTS criteria, the analysis showed a significant difference at six months LSI at 300°/s (P = .048) and LSI at 60 °/s (P = .02), and no significant result at LSI at 180 °/s (P = .28). While the analysis of RTS criteria showed no significant results between autografts groups months LSI at 300 °/s (P = .23), LSI at 180 °/s (P = .51), and LSI at 60 °/s (P = .78) (**Table 7**).

Table 7. Return to Sport (RTS) criteria at 6 and 12 months.

	6 months				12 months			
	BQTA (23)	QTA (26)	HTA (26)	**Total (75)**	BQTA (23)	QTA (26)	HTA (26)	**Total (75)**
LSI at 300°/s (Nm)	11*a-c	18*b-c	21*a-c	50	20	22	18	60
LSI at 180°/s (Nm)	11	14	18	43	18	20	23	61
LSI at 60°/s (Nm)	4*a-c	8	14*a-c	26	11	15	14	40

Data are shown as Mean ± SD (95%CI) BQTA Bone Quadriceps Tendon Autograft HTA Hamstring Tendon Autograft QTA Quadriceps Tendon Autograft.

*a-b Significant between BQTA and QTA groups, *a-c Significant between BQTA and HTA groups., *b-c Significant between QTA and HTA groups.

To answer the sixth objective.

"To compare the difference of CROM and FROM between the injured side and non-injured side of all ACL reconstruction patients at 12 months of follow up".

With respect to the analysis of CROM between the injured and non-injured side at 12 months, there was no significant differences between both sides for knee anteroposterior laxity(F = .17, P= .63), knee echography (quadriceps tendon depth "sagittal view" ; (F = .11, P = .73), quadriceps tendon depth "transversal view" ; (F = .096, P = .75), width of quadriceps ; (F = .19, P = .65), or cartilage thickness ; (F = 2.5, P = .11)), or for PPT (vastus lateralis; (F = .13, P = .71), vastus medialis; (F = .03, P = .84), patellar tendon; (F = .01, P = .91), quadriceps tendon; (F = .04, P = .83) or hamstring tendon; (F = .29, P = .58)) at 12 months follow up (**Table 8**). However, only thigh girth showed statistically significant and better results for the non-injured side (F = 5.46, P = .021) at 12 months (**Table 8**).

The analysis of FROM showed better and more statistically significant results for the non-injured side for knee extension PT at 180°/s (F = 8.28, P = .005), knee extension PT at 60°/s (F = 3.94, P = .049), knee extension PT at 60°/s (F = 18.50, P <.001), and knee flexion PT at 60°/s (F = 4.36, P = .038), and H/Q ratio at 180°/s (F = 7.9, P = .006). However, there were no significant differences between both sides for knee extension PT at 300°/s (F = 3.23, P = .07), knee flexion PT at 300°/s (F = 1.02, P = .31), H/Q ratio at 300°/s (F = 6.8, P = .01), H/Q ratio at 60°/s (F = 2.66, P = .10) (**Table 8**).

Table 8. Side to side comparison at 12 months of follow up.

	Injured side	Non-injured side	P value
Knee anteroposterior laxity (mm)	4.04 ± 1.56 (3.68 ; 4.4)	3.24 ± 1.09 (2.99 ; 3.49)	P =.63

Quadriceps tendon depth "sagittal view"(mm)	.76 ± .33 (.68 ; .84)	.74 ± .33 (.66 ; .82)	P =.73
Quadriceps tendon width (mm)	2.57 ± .62 (2.43 ; 2.72)	2.53 ± .53 (2.41 ; 2.65)	P =.65
Quadriceps tendon depth (mm)	.76 ± .3 (.69 ; .83)	.78 ± .27 (.71 ; .84)	P =.75
Thickness knee cartilage (mm)	.33 ± .07 (.31 ; .34)	.31 ± .08 (.29 ; .33)	P =.11
Thigh girth(cm)	53.85 ± 4.26 (52.87 ; 54.83)	55.44 ± 4.09 (54.5 ; 56.38)	**P =.021**
PPT of vastus lateralis (kPa)	504.93 ± 160.59 (467.99 ; 541.88)	515.2 ± 184.45 (472.76 ; 557.64)	P =.71
PPT of vastus medialis (kPa)	466 ± 168.5 (427.23 ; 504.77)	471.13 ± 159.93 (434.33 ; 507.93)	P =.84
PPT of patellar tendon (kPa)	589.69 ± 179.4 (548.42 ; 630.97)	586.48 ± 179.78 (545.12 ; 627.85)	P =.91
PPT of quadriceps tendon (kPa)	591.24 ± 203.12 (544.51 ; 637.97)	598.2 ± 209.18 (550.07 ; 646.32)	P =.83
PPT of hamstring tendon (kPa)	534.54 ± 218.12 (484.36 ; 584.73)	553.54 ± 212.02 (504.76 ; 602.32)	P =.58
Knee extension peak torque 300°/s (Nm)	83.56 ± 19.32 (79.12 ; 88)	89.54 ± 21.39 (84.62 ; 94.46)	P =.07

Knee flexion peak torque 300°/s (Nm)	89.13 ± 18.21 (84.94 ; 93.32)	92.16 ± 18.55 (87.9 ; 96.43)	P =.31
Knee extension peak torque 180°/s (Nm)	112.21 ± 28.27 (105.71 ; 118.72)	125.11 ± 26.59 (119 ; 131.23)	P <.01
Knee flexion peak torque 180°/s (Nm)	119.69 ± 30.48 (112.67 ; 126.7)	129.28 ± 28.67 (122.69 ; 135.88)	P <.05
Knee extension peak torque 60°/s (Nm)	135.77 ± 40.93 (126.36 ; 145.19)	164.11 ± 39.74 (154.97 ; 173.26)	P <.001
Knee flexion peak torque 60°/s (Nm)	142.78 ± 39.34 (133.73 ; 151.83)	155.44 ± 34.71 (147.46 ; 163.43)	**P <.05**
H/Q ratio 300°/s (Nm)	113.82 ± 25.77 (108.01 ; 119.63)	134.35 ± 63.87 (119.65 ; 149.04)	**P <.05**
H/Q ratio 180°/s (Nm)	110.72 ± 26.19 (104.69 ; 116.74)	134.21 ± 67.31 (118.72 ; 149.7)	**P <.01**
H/Q ratio 60°/s (Nm)	104.95 ± 28.11 (98.49 ; 111.42)	98.68 ± 17.75 (94.6 ; 102.77)	P =.10

Data are shown as Mean ± SD (95%CI). H/Q ratio: Hamstring /Quadriceps ratio PPT: Pressure Pain Thresholds SLHT single leg hop test.

DISCUSSION

Thesis Main Findings And General Consideration.

The main findings of the first phase of this doctoral thesis were adding further quantitative analysis to previous systematic reviews and including more studies than previously published studies. In total, 754 patients were assessed from 10 studies, and 5 of 10 studies were included in the meta-analysis. The results suggest that QTA showed better isokinetic strength results in the short term (e.g., 3 and 6 months) than HTA and PTA. Additionally, they showed similar isokinetic strength results in the long term (e.g., 12 and 24 months). Finally, our findings showed similar results in functional outcomes and knee anteroposterior laxity during short- and long-term evaluations between QTA and HTA or PTA.

Regarding the second phase, the main findings were;

1. The BQTA showed the major disadvantage in terms of surgery failure due to intraoperative patella fracture. However, this result could not be generalised due to the low number of patients. Similarly, all patients underwent a single orthopaedic surgery.

2. All of the groups showed a similar result in terms of PROM during all of the follow-up evaluation times. However, all patients showed great improvement from pre-surgical to the final follow-up.

3. The three autograft groups demonstrated similar results for knee anteroposterior laxity, sonographic measurements, PPT, and VAS. However, the HTA group showed better improvement of thigh girth measurements during the 3- and 6-months follow-up test. Moreover, all patients showed great improvement during the 3- and 12-months follow-up period in CROM.

4. The HTA group had greater improvement of knee extension during the first 6 months compared to BQTA and QTA. However, the three groups demonstrated similar results at 12 months. Knee flexion and SLHT results were similar for all groups. The three groups showed a serious improvement between the 3- and 12-months follow-up period. The RTS criteria was in favour of HTA at 6 months and similar between all groups at 12 months. Furthermore, both sides showed an improvement regarding the isokinetic strength data.

5. The side-to-side comparison showed similar results regarding knee anteroposterior laxity, sonographic measurements, PPT, and VAS. However, the non-injured side had better improvement in terms of thigh girths measurements, and knee flexion and extension isokinetic tests compared to the injured side, due to improvement of both sides during the rehabilitation process.

The results of the second part of the thesis showed some differences between autograft groups at 3 and 6 months of follow-up and similar recovery at 12 months of follow-up. However, the BQTA group showed the major disadvantage, which is surgery failure (11%) due to intraoperative patella fracturing during the harvest of the quadriceps tendon. All of the three patients had a new ACL reconstruction surgery with HTA and they did not participate with the follow-up evaluations. The fracture of the patella was fixed with an internal screw. Similarly, a recent study from Fu F. et al 2019 reported a total of 5 (8.8%) patient with patella fractures occurring at two years post-reconstruction. Two patients had (3.5%) intraoperative and were detected with computed tomography and only fracture occurred during strength testing[20]. The mentioned study harvested a length of 18 to 20 mm and a width of 10 mm while, in our study, the diameters of the harvested bone were 20 to 25 long and 10 width. The comparison between both studies could indicate more patella fracture with the larger bone size [104].

Although, the BQTA autograft had its biomechanical advantage over that of QTA and similar to HTA[104]. Still, the consequences of patella bone fracture affect the primary aims of ACL reconstruction and delay the process to return to sport and competitions. More studies about BQTA are recommended to generate further understanding of the patella bone fracture.

The present thesis has been carried out on 78 ACL injured football players divided randomly into three groups (BQTA, QTA, and HTA). However, 17 patients did not participate in the final follow-up. Three of them were excluded due to patella fracture, and 12 patients were missing due to the Covid-19 pandemic situation during the evaluation period of 2020 and 2021. The missing patients refused to attend to the evaluation session due to their personal fear of viral exposure and infection. Therefore, multiple imputations were incorporated for the data type Missing at Not Random (MNAR), and do not include any categorical data and only continuance data were imputed[132].

Patient Reported Outcomes Measurement (PROM)

Through the first phase of this thesis, the present systematic review and meta-analysis compared PROM between QTA vs. HTA or PTA and found no differences between groups. However, it was not possible to quantitatively combine data due to the use of different PROM such as LKS, Cincinnati, IKDC, and KOOS. Previous meta-analyses[137] focused mainly on PROM which included QTA (N = 804) patients compared to HTA (N = 14761) patients and found no significant differences between both groups. These results were in the same direction as our review results, as well as recent published studies, which confirmed the same results[68,77,138].

Regarding the second phase of this thesis, no significant differences were found between BQTA, QTA, and HTA in the three follow-up periods. All the autograft's groups showed an improvement between the pre-surgical evaluation and 3-, 6-

, and 12-months follow-up. Moreover, our RCT results confirm the findings of the first phase of this doctoral thesis. However, the final follow-up at 12 months demonstrated a different percentage of patients who achieved more than 90% for LSK (BQTA: 87%, QTA: 85%, HTA: 92%) and for CKRS (BQTA: 69%, QTA: 76% , HTA: 92%). Previous studies have compared BQTA vs. HTA and QTA vs. HTA and showed no significant results between compared groups [68,77,135,138] Therefore, our result confirms the previous published studies and compared BQTA vs. QTA in terms of PROM which, to our knowledge, is the first time to compare these three autografts in the same study. The finding of no significant difference between the groups could be explained by the PROM, considering it is a general questionnaire and a subjective evaluation. Therefore, in our study, we have supplemented the personal subjective questionnaire with objective evaluations (CROM and FROM) to ensure a complete comparison between all groups.

Clinical Reported Outcomes Measurement

Knee anteroposterior laxity

For knee anteroposterior laxity, both phases of the thesis confirmed the same results: no differences were found between QTA, HTA, and PTA in the first phase, and between BQTA, QTA, and HTA either in the second phase of the thesis. However, in our systematic review, it was not possible to do the meta-analysis since there was no homogeneity of tools used in any of the follow-up time periods. Regarding the clinical RCT study, the three groups showed an improvement between pre-surgical and the final evaluations. However, QTA patients showed more improvement between pre-surgical (BQTA = 6.47 , QTA = 5.42 , HTA = 6.12 mm) and post-12 months follow-up (BQTA = 4.38, QTA = 3.67 , HTA = 4.11 mm). Our results were similar to results in previous published articles from Horstmann X.[138] et al. and Johnston P.[139] et al. Both studies compared BQTA vs. HTA and QTA vs. HTA, respectively, and indicated no significant result between the mentioned groups. Both studies included 51 and 74 patients, respectively. However, the study of Johnston P. 2021 et al. did not include equal groups[139]. On the other hand, the study of Cavaignac E.[58] showed the QTA group had better stability compared to HTA at 3 and 6 years [58]. However, this study was an observational study with 45 QTA and 41 HTA, which could affect the level of evidence [58]. All of the mentioned studies have used the same instrument (i.e., the KT-1000 arthrometer), while in our study we used the KT-2000 arthrometer. Both arthrometers have shown robust knee anteroposterior laxity results [27,140].

Finally, our results do not only confirm the published results, but also supplement the comparison between BQTA, QTA, and HTA. To our knowledge, the previous published studies always compared QTA with HTA or BQTA with HTA and did not include the three autograft groups in the same study. We have ensured a lower possible risk of bias in our RCT, which produces a more specific conclusion related to knee anteroposterior laxity, through using a highly valid instrument at the same follow-up times. This instrument was not accurately controlled in the previous recorded studies, making our study novel and valuable[58,65,139].

Sonographic measurements.

For sonographic measurements, our results indicated no differences between the three groups except for quadriceps tendon width. The BQTA group showed a slightly lower improvement compared to QTA and HTA. However, no significant results were found between groups with Bonferroni correction for quadriceps tendon width due to the small differences between groups. Our result was similar to the study of Martin-Alguacil et al. 2019[24], which included 56 patients, compared QTA vs. HTA, and reported no differences between both groups. Nevertheless, an improvement was noticed for cartilage and tendon thickness measured by ultrasound. Moreover, these results were similar to our results through the evolution of 12-months follow-up. The mentioned study only includes QTA and HTA groups, which led to lower comparisons in the mentioned data. And, in our study, we included BQTA, QTA, and HTA groups. On the other hand, a study by Akkaya S. et al[141] mentioned a significantly higher strain ratio for the injured side compared to a non-injured knee. However, in our results, there were no differences between both sides at the 12-month follow-up[141]. The sonographic measurement has not been widely studied, and further studies are required to allow the comparison of sonographic measurements between different autografts.

Muscle girth

For muscle girth, a small improvement was observed between pre-surgical and 12-months evaluation for both QTA and HTA, and almost no improvement was recorded for BQTA (53.0 to 53.1 cm). A slightly higher improvement of thigh girth was observed for the non-injured side, specifically with BQTA (53.2 to 55 cm) and QTA and HTA. This improvement was explained by the inclusion of both legs during the rehabilitation protocol. These observations were similar to the study of Martin-Alguacil et al. 2019[78], which compared QTA with HTA, showed no significant differences between groups, and illustrated an improvement between injury pre-surgery and post 12-months follow-up[78]. In the mentioned study, the muscle thickness was measured using the same reference point but also applied the use of ultrasound. In our study, we measured thigh girth using tap measurements. Both methods are considered a valid method to evaluate the change in quadriceps diameter in the rehabilitation process[78,125]. The possible explanation of slow improvement of BQTA in muscle girth would be due to grafting the autografts of the quadriceps tendon with bone, that did not allow the patients to progress rapidly through the rehabilitation protocol. Therefore, the muscle enlargement and muscle girth could have been affected. Finally, further studies with larger muscle samples are recommended to explain the retention between autografts and muscle girth.

VAS and PPT

Regarding the general pain patients endured, which was evaluated with VAS, all of the patients experienced low pain (VAS < 3) in the four evaluation times. This result could be explained by the fact that we did not evaluate the pain immediately after the surgery. On the contrary, the study of Lind M. et al.[142] mentioned slightly higher pain with QTA group compared to HTA, but still without significant results. The mentioned study had evaluated the pain at 24 months follow-up and did not mention data from before the surgery[142].

For knee pain and donor site morbidity, which were evaluated in our study by algometry in five different points, no significant differences were found between the three groups. Although no significant differences were reported, the QTA group showed better results compared with BQTA at 6- and 12-months follow-up. Similarly, a previous study which compares QTA with HTA found similar results of our study with no significant results for both autografts. The mentioned study used the algometer to evaluate PPT around the knee[78].

The result of VAS and PPT confirmed the same conclusion. In parallel, our results and the results of the previous studies led to the same conclusion, which is that there are no differences in knee pain and PPT between the three groups during the follow-up. All of our results together with the previous studies suggest that VAS and PPT have the same results at 3-, 6-, and 12- months follow-up. Further studies are recommended to evaluate VAS and PPT during the first three months after surgery to ensure if there are any differences as it was reported in the study of Lind M [142].

Functional Reported Outcomes Measurement (FROM)

Isokinetic strength test

The FROM is considered to be the main criteria to evaluate patient progress and return them to sport after ACL reconstruction and rehabilitation. Therefore, the differences of FROM between autograft groups will directly affect the return to sport and later the return to performance[75]. Our results of the systematic reviews and meta-analysis were similar to previous systematic reviews[65,77,108]. Additionally, our results were similar to a previous meta-analysis by Johnston et al.[65], where QTA showed better isokinetic strength results during the short-term evaluation and similar results during the long-term evaluation. The study from Johnston et al.[65] compared the isokinetic strength test using the categorical angular velocity (low: 60°/s–90°/s; moderate: 160°/s–180°/s) and categorical follow-up periods (5–8, 9–15, 24, and 36–60 months). We compared a determined angular velocity (60°/s or 180°/s) and determined follow-up time points (3-, 6-, 12-, and 24-months). Also, no functional outcomes or knee stability were reported in the mentioned meta-analysis. Furthermore, we could not compare the heterogeneity between the mentioned meta-analysis and our study because it was not reported. Additionally, they also compared only the peak torque of the LSI and did not compare it with that of the injured limb. In our RCT study, we compared the peak torque from the injured limb and that of the LSI, revealing that the peak torque results for the uninjured limb contrast the peak torque results of the LSI[65].

The studies from Martin-Alguacil et al.[68] and Undheim et al.[94] have shown that the use of different angular velocity led to statistically different results, which were not considered by the author of the previous meta-analysis[65]. Moreover, the mentioned meta-analysis has used downs and black scales to evaluate the risk of bias of the selected studies. This tool has been considered a numerical quality assessment scale and, in our study, we have used RoB 2 and ROBINS-I from the Cochrane Handbook for Systematic Reviews of Intervention. Five studies were excluded in the meta-analysis[42,47,58,135,136]. The main reasons were that Pigozzi et al.[136] did not report the isokinetic test angular velocity and Cavaignac et al.[58] reported the isokinetic angular velocity at 90°/s, preventing the formation of a meta-analysis group with other studies. Three studies were excluded because their follow-up time points did not form any meta-analysis group[42,47,135]. Finally, no meta-analysis subgroup comparing QTA vs. PTA was introduced because of the variations in the testing protocols or follow-up time points.

In the second part of the thesis, muscle strength was reported as peak torque, H/Q ratio, and LSI. Both peak torque and LSI results were in the same direction which reported a significant result in knee extension. The HTA group showed better knee extension peak torque and LSI at the 3- and 6-months evaluation. However, at the 12-months evaluation, a similar result of the peak torque and LSI was observed between different groups. Contrastingly, the LSI for knee flexion differences between groups related similar results between groups for knee flexion peak torque.

The result of LSI for all groups together did not show high differences between different pre-surgery, 3-, 6-, and 12-months follow-up for knee extension (87.4, 67.4, 81.6, and 83.1 Nm) and for knee flexion (104.0, 87.9, 92.7, and 91.7 Nm), respectively. Through a direct interpretation, all patients did not see improvement during the process of rehabilitation; however, this similarity of LSI refers to the improvement of the injured and non-injured sides. As it is reported, the peak torque of 60°/s for all patients is improving for the injured side knee extension (113.2, 95.3, 122.2, and 135.7 Nm) and flexion (106.1, 112.0, 130.7, and 142.9 Nm). In parallel, there was similar improvement of the non-injured side for knee extension (209.0, 208.9, 224.9, and 225.3 Nm) and knee flexion (163.1, 185.2, 201.4, and 214.0 Nm). This interpretation for both sides shows the effect of the rehabilitation program on both sides. Accordingly, the study of Hughes D J et al.

2018[143] showed similar results for knee flexion and knee extension LSI. The mentioned study compared 39 QTA patients with 19 HTA patients. Even though, we achieved similar results, the mentioned study showed higher LSI values for all groups compared to our study groups using the exact same isokinetic protocols[143]. We were not able to compare further details between both studies because the study did not mention angular velocity of the test with the data for the injured and non-injured side[143].

On the contrary, a recent study reported better knee flexion LSI for QTA at 60°/s and 180°/s tests compared to HTA[27]. In our study, we showed similar results between the three groups. The mentioned study included 111 patients divided into QTA (N = 37) and HTA (N = 74). Comparatively, we have similar patient characteristics such as age and gender. However, this was different post six months. There was no data reporting 12 months follow-up to compare and only 6 months follow-up. Beside the significance, the mentioned study showed an average effect side of .52 for 60°/s and .58 for 180°/s. We summarise the needed RCT which included different autografts to ensure better comparison of LSI[139].

Different articles Adams D. et al[75] and Ardren C. et al[24] reported the importance of knee extension LSI to return to sport decision and recommended a special criterion concerning knee extension muscle strength[24,75]. During the application of this criteria, we showed 57% and 35% of the total patients had met more than 80% of knee extension LSI at 180°/s and 60°/s respectively. Specifically, each autograft group showed a different percentage of patients who met the criteria at 6 months follow-up with BQTA (48% and 17%), QTA (54% and 31%), and HTA (69% and 53%) at 180°/s and 60°/s respectively. However, at a 12 months test, 81% and 53% of the total patients had met the mentioned criteria at 180°/s and 60°/s, respectively. All three groups showed more similarity than the follow-up of 6 months with BQTA (78% and 48%), QTA (77% and 58%), and HTA (88% and 53%) for LSI at 180°/s and 60°/s, respectively. As we explained in the last section, all patients showed great improvement in both legs. Therefore, a good percentage of the patients did not meet the recommended criteria in order to return to their sport.

Regarding the H/Q ratio, we have found significant results in favour of HTA compared to BQTA and QTA. However, all groups showed a massive improvement between pre-surgical evaluation and 12-month evolution. Both BQTA and QTA showed high reduction between pre- and post-three months evolution: BQTA (94.3 to 161.8 Nm) and QTA (93.4 to 139.4 Nm), compared to HTA (102.3 to 97 Nm). This reduction could be explained by the direct effect of harvesting the quadriceps tendon on knee extension peak torque which directly affected the H/Q ratio[34]. These results do match with a recent published study of a randomised control trial comparing QTA vs. HTA and found significant differences in favour of the HTA group. This study included athletic evaluation[24]. However, a recently published cohort study compared BQTA vs. HTA and showed similar H/Q ratio results between both groups. This did not match with our results. The explanation of these results was that the HTA group showed a lower knee extension peak torque compared to our results in the same group[43]. Therefore, in the mentioned study, the H/Q ratio was similar between both groups. Moreover, in the mentioned study, pre-surgery data in order to make further comparisons and to ensure that the patients did not have a baseline difference in terms of muscle strength was missing[43]. Another meta-analysis from Tan T. et al.[137] reported no differences between QTA and HTA in terms of H/Q ratio with (P = .16) but with high heterogeneity (1^2= .85%), which impacts the accuracy of the conclusion[137].

SLHT

Single leg hop tests are considered the second functional outcomes after ACL reconstruction. They are also one of the simple criteria applied for patients to return to sport. For its evaluation, no differences were found between the results.

The three groups showed no improvement of the SLHT distance between pre-surgery and 3 months of follow-up with BQTA (83.8 ; 82.8 cm), QTA (87.8 ; 83.6 cm), and HTA (98.2 ; 91.2 cm). However, massive improvement of SLHT distance was noted between pre-surgery and 12 months of follow-up with BQTA (83.8 ; 121.5 cm) and QTA (87.8 ; 130.2 cm) and only HTA (98.2 ; 126.5 cm). In a recent meta- analysis, which compared QTA vs. HTA and included 105 vs. 108 patients, respectively and reported no significant result between both groups. However, the mentioned review did not specify if the QTA patients were harvested with bone or without bone. In our study, we have confirmed a similar result but we have observed a slightly better results for BQTA and QTA compared to HTA. And in the mentioned meta-analysis, HTA showed slightly better results[22]. In contrast, an RCT from Lind M. et al. [142] reported different results which indicate that the HTA group had better results than with the BQTA group, which were not according to our results. The mentioned study only reported SLHT at 12 months follow-up; therefore, we were not able to compare the progression from time before the surgery to time after the surgery[142]. Another RCT from Johnson P. et al reported similar results between QTA and HTA six months after the surgery. There was no data for a 12 months follow-up to compare with our results[139].

We can summarise that both FROM showed different results at 6 months follow-up. However, at 12 months follow-up, both isokinetic strength test and SLHT showed the same result and confirmed that the three (BQTA, QTA or HTA) achieved the same final results without significant differences.

LIMITATIONS AND STRENGTH

This doctoral thesis has some limitations that need to be articulated. In the first phase of the thesis, the systematic review and meta-analysis indicated some limitations. Only five studies were included in the meta-analysis because of their methodological differences. All the studies were included in the review despite their methodological characteristics. The database search was limited to English and Spanish languages only, leading to a potential publication bias. Some ACL reconstruction outcomes were not analysed, such as the one-legged hop test or graft failure, because of the high variation among the studies.

The second phase of the study presented some limitations as well. All of the surgeries were done by a single surgeon, which could have affected the generalisation of the results. The sample did not include matching criteria of sociodemographic characteristics between autograft groups and the only randomisation factor was type of autograft. The follow-up period only included the first 12 months after the surgery and did not include 24 or either five years of follow-up. However, the first 12 months is considered the most important period for return-to-sport decision-making. Our ultrasound examination did not include any hamstring tendon sonographic measurements and only quadriceps tendon and knee cartilage were measured. A considerable number of patients did not participate in the follow-up due to the mentioned reason.

On the other hand, this thesis showed points of strength too. It was reported according to the PRISMA guidelines. A risk of bias assessment was included, and a meta-analysis with low statistical heterogeneity was obtained because of the inclusion of determined subgroups. The methodological design was prospective and randomised with standardised follow-up points, which reduced the predictable risk of bias of the results. The three groups were treated by the same surgeon, received the same rehabilitation protocol, and examined by the same researcher. This implies a strong sense of consistency in design. The study included four evaluation times in order to control the progression of the patient during the rehabilitation. The study achieved a power higher than 85% regarding the calculation of sample size.

CONCLUSION

1. The first phase of the thesis adds further quantitative data analysis to previously published systematic reviews. The QTA showed better and significant results in knee flexion strength compared with HTA and similar results to PTA at 3-, 6-, and 12- months. HTA showed better and significant results in knee extension strength at 6 months and similar results at 12 months compared to QTA. This review showed similar results between QTA and HTA or PTA in functional outcomes and knee anteroposterior laxity. Furthermore, a standardised isokinetic strength test must be followed to achieve a more specific conclusion and better clinical comparison among participants.

2. The BQTA showed the major disadvantage in terms of surgery failure due to intraoperative patella fracture and therefore the delay of rehabilitation process and return to sport. However, this result could not be generalised due to the low number of patients.

3. All of the three groups (BQTA, QTA, and HTA) showed a similar result in terms of PROM during all of the evaluation times. However, all patients showed massive improvement between pre-surgery and the final follow-up.

4. All of the three groups (BQTA, QTA, and HTA) showed a similar result in terms of knee anteroposterior laxity, sonographic measurements, PPT, and VAS. However, the HTA group showed better improvement of thigh girth measurement during the 3 - and 6-months follow-up test. Moreover, all patients showed huge improvement between 3 - and 12-months follow-up.

5. The HTA group showed better improvement of knee extension muscle strength during the first 6 months. The three groups showed similar knee extensions muscle strength results at 12 months follow-up. A similar result was found for all groups in terms of knee flexion muscle strength and SLHT. The RTS criteria was in favour of HTA at 6 months and similar between all groups at 12 months. Furthermore, both sides showed an improvement regarding the FROMs.

6. The side-to-side comparison showed similar results regarding knee anteroposterior laxity, sonographic measurements, PPT, and VAS. However, the non-injured side had better results in terms of thigh girths measurements and knee flexion and extension isokinetic test.

CLINICAL IMPLICATION

Regarding the clinical implication of this doctoral thesis. We propose a standardized isokinetic strength test to ensure the comparison between further studies, as previous authors have recommended[94]. Such tests included five repetitions for knee flexion and another five for knee extension with one minute of rest between each test. Two angular velocities should be applied starting at 60◦/s and then 180◦/s. Additionally, patients should be seated with 85 degrees of hip flexion and 90 degrees of knee flexion. Furthermore, to ensure the comparison between testing protocols, standardized time points for evaluation (6, 12, and 24 months after surgery) may be useful. Indeed, all the tests may be applied to injured and uninjured limbs, allowing the examiner to report data on one limb and LSI. We recommend future studies including more specific rehabilitation programs adjusted specifically to each autograft and patient strength and physical conditioning level before the surgery. Moreover, future descriptive studies are recommended of surgery failure with BQTA to clarify and explain the risk factors related to patella fracture.

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It always seems impossible until it's done.

Nelson Mandela

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