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A Between Sex Comparison of Anterior-Posterior Knee Laxity after Anterior Cruciate Ligament Reconstruction with Patellar Tendon or Hamstrings Autograft:

A Systematic Review

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Abstract

Anterior-posterior (AP) knee laxity after anterior cruciate ligament (ACL) reconstruction may differ between sexes for different graft types. Females may experience an increase in AP knee laxity following an ACL reconstruction with a hamstrings graft, which is not seen in males with a hamstrings graft or in males or females with a bone-patellar tendon-bone (BTB) graft. The hypothesis of this review is sex differences in AP knee laxity and this will be identified in patients who undergo an ACL reconstruction with a hamstrings graft, while no sex differences will be observed in patients who have an ACL reconstruction with a BTB graft.

A systematic search was performed in PubMed, CINAHL® and SPORTDiscus™. Inclusion criteria were articles published in the English language that studied human subjects who underwent an ACL reconstruction with a BTB or hamstrings autograft, and the presence of a sex comparison on outcome measures including side-to-side difference in AP knee laxity. Methodological quality was assessed using a Modified Coleman Methodology Score. Eleven cohort studies met the inclusion criteria. Six investigated sex differences in both hamstrings and

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BTB grafts. Three only investigated BTB grafts and two only investigated hamstrings grafts. These studies consistently reported increases in AP knee laxity in females after an ACL reconstruction with a hamstrings graft that was not observed in the other cohorts. This systematic review indicates that female patients have greater AP knee laxity following an ACL reconstruction with a hamstrings autograft compared with males with a similar procedure, and both females and males following an ACL reconstruction with a BTB autograft. These results are derived from lower level evidence, as no randomized control trials have attempted to answer this question. Future studies need to rigorously address this clinical question to confirm the results currently in the literature.

1. Introduction

Each year over 250 000 to 350 000 anterior cruciate ligament (ACL) reconstructions are performed in the US.[1–3] The current literature is replete with evidence indicative of a sex disparity in the incidence and mechanism of ACL injury. Despite this awareness of sex differences related to ACL injury, oftentimes the variable of sex is not investigated relative to outcome following surgical management of an ACL injury.

Several outcome variables are often evaluated after ACL reconstruction. These include mechanical knee stability, functional knee stability, graft failure rate, ability to return to sport, joint range of motion (ROM), strength, anterior knee pain and patient-reported outcomes, such as the International Knee Documentation Committee subjective survey.[1–5] One frequently reported variable after ACL reconstruction used by surgeons to evaluate surgical success is side-to-side differences in anterior-posterior (AP) knee laxity.[6–16] In 1985, Daniel et al.[17,18] assessed AP knee laxity in both healthy and ACL-deficient patients using a KT1000 arthrometer (Medmetric Co., San Diego, CA, USA). These authors suggested that 88–92% of healthy subjects have a <2 mm side-to-side difference in AP laxity using an 89 newton (N) translation force, while 96% of patients with ACL deficiency had >2 mm of AP translation at an 89 N force. Over the last 35 years, several authors have confirmed Daniel et al.’s findings and note an average of <5 mm side-to-side difference in AP knee laxity in healthy individuals.[18–20] Since that time (1985), the assessment of AP knee laxity has been refined with more recent data indicating improved sensitivity at translational forces >89 N,[21] and this continues to be an outcome variable widely used to measure the success of ACL reconstruction. This 2–5 mm of side-to-side difference in AP knee laxity is still used today to define arthrometric failure of the ACL or the reconstructed ACL graft.

One factor that may contribute to AP knee laxity after ACL reconstruction is the strength and integrity of the graft type used to reconstruct the ACL. The debate on optimal graft type choice for ACL reconstruction has been controversial over the last decade. The two most commonly used autogenous grafts include the bone-patellar tendon-bone (BTB) and hamstrings tendon.[22–24] Advantages to BTB grafts include tissue accessibility to graft harvest, strong structural properties, bony fixation (potential for bone-to-bone healing) and a predictable success rate in restoration of knee stability.[25] Conversely, the advantages of a hamstrings graft include less iatrogenic injury to the extensor mechanism and fewer donor-site complications.[25] Some authors suggest that reconstructions with hamstrings graft tend to experience increased anterior laxity over time,[26–28] while others continue to recommend a hamstrings graft as a viable, stable alternative to a BTB graft.[6,8] Though many studies have evaluated AP knee laxity following an ACL reconstruction with both a BTB and hamstrings graft, few studies, and no known reviews, have critically analysed sex differences in AP knee laxity following an ACL reconstruction with a BTB and hamstrings graft.

The purpose of this systematic review was to investigate sex differences in AP knee laxity after ACL reconstruction using autogenous hamstrings tendon and BTB grafts. The clinical hypotheses tested were as follows: (i) there will be no sex differences in AP knee laxity in patients who undergo an ACL reconstruction with a BTB graft; (ii) female patients who have hamstrings graft will demonstrate increased AP laxity compared with males who have a hamstrings graft; and (iii) AP knee laxity asymmetry will be greater in females who have a hamstrings graft than in females who have a BTB graft.

2. Methodology

2.1 Research Questions

1. Is there a side-to-side difference in AP knee laxity after performing an ACL reconstruction with a BTB autograft between males and females?
2. Is there a side-to-side difference in AP knee laxity after performing an ACL reconstruction with a hamstrings autograft between males and females?
3. Is there a sex difference in AP knee laxity asymmetry between an ACL reconstruction with a BTB and hamstrings autograft?

2.2 Literature Search

A literature search was completed using MED-LINE accessed through PubMed, CINAHL® and SPORTDiscus™. The following terms were used in separate searches: ‘ACL reconstruction AND laxity’, ‘ACL reconstruction AND laxity AND gender’, ‘ACL reconstruction AND laxity AND sex’, ‘anterior cruciate ligament reconstruction AND laxity’, ‘anterior cruciate ligament reconstruction AND laxity AND gender’, and ‘anterior cruciate ligament reconstruction AND laxity AND sex’. These search terms yielded 1767 articles from the three databases combined. After removing all duplicates, 980 unique articles remained in the cohort of articles.

An initial screening of titles and abstracts using strict inclusion and exclusion criteria was determined by all the authors who identified 90 articles for assessment in full text. Articles were included if they were published in English, used human subjects who underwent ACL reconstructions utilizing BTB or hamstrings autogenous grafts, and made sex comparisons on outcome measures, including a side-to-side difference in AP knee laxity. Those excluded from this review that looked at joints other than the knee used alternate graft sources, such as allograft tissues, iliotibial band or quadriceps tendon grafts, were published in a language other than English; did not make a sex comparison; used nonhuman subjects; or did not measure a side-to-side difference in AP knee laxity. These specific criteria narrowed the search to include eight articles. A hand search through the respective reference list for each article revealed three articles not found from the initial search. In all, 972 articles from the initial search were excluded. Of these, 890 were excluded by title and abstract. The other 82 were excluded after being read in full text. Of these 11 articles, six examined knee laxity considering the variables of graft type and sex, while three examined sex differences only in BTB grafts and two examined sex differences only in hamstrings grafts.

2.3 Data Extraction

A spreadsheet was created and utilized by two of the authors (MVP and AMW) to compile information from each article, including reference, objective, level of evidence, Coleman Methodology Score (CMS), population, laxity assessment tool, time of follow-up, results and conclusion, failure rate and two of the authors comments on each study itself. (table I)

2.4 Quality Appraisal

In order to appraise the relative quality of each study, the CMS[29] was used to appraise each article included in this review. The CMS was designed to assess the methodological quality of surgical outcome studies and consists of 10 criteria, adding to a total score ranging from 0 to 100, with 100 representing a perfect score. Originally designed for surgical management of patellar tendinopathy, the CMS attempts to identify the influence of chance, bias and confounding factors on the results. The development of the CMS was based on the CONSORT (Consolidated Standards of Reporting Trials) statement for randomized control trials. A summary of the mean CMS scores on all 11 citations is in table II.

3. Results

3.1 Bone-Patellar Tendon-Bone (BTB) versus Hamstrings Autograft

3.1.1 Muneta et al., 1998—Muneta et al.[12] conducted a prospective cohort study to assess outcome after ACL reconstruction with a multistrand hamstrings graft versus a BTB graft technique, while considering factors associated with sex. The authors enrolled 110 consecutive patients and 103 were followed up at 20 months post-operative. Fifty-one patients (22 male, 29 female) received BTB grafts and 52 (21 male, 31 female) patients received hamstrings grafts. Side-to-side differences in AP knee laxity at 89 N and manual maximum were assessed using a KT1000 arthrometer. Mean side-to-side differences between the subjects with hamstrings grafts and those with BTB grafts were not significantly different. However, the authors did report a trend ($p = 0.07$) for more patients in the hamstrings graft group to have side-to-side differences in AP laxity >5 mm compared with the BTB graft group, which many consider indicative of clinical failure. The findings of this study were no sex or graft effects on AP knee laxity 20 months after an ACL reconstruction. However, this data did indicate that subjects following a hamstrings graft, regardless of sex, may have a greater likelihood for graft failure than those who have an ACL reconstruction with a BTB graft.

This study was a prospective attempt to analyse differences in outcome based on the source of graft and sex following ACL reconstruction. The authors implemented a consecutive recruitment strategy and the allocation of subjects to each testing group resulted in an equitable apportionment of subjects into each group. However, the authors failed to describe their allocation and randomization methods. Therefore, the reader was unable to determine how the subjects were allocated to each group. Other limitations of this work include a relatively short follow-up, the use of multiple hamstrings graft procedures and a lack of adequate description of the rehabilitation programme. This study was given a CMS of 51 (of 100).

3.1.2 Corry et al., 1999—Corry et al.[8] conducted a prospective cohort study designed to investigate the differences in outcome between a BTB graft and hamstrings tendon autograft at 2 years after an ACL reconstruction. These authors recruited 90 consecutive subjects who received an ACL reconstruction with a BTB graft and then recruited 90 consecutive subjects who received an ACL reconstruction with a four-strand hamstrings graft with similar fixation. Within the first 2 years following an ACL reconstruction with a BTB graft, three subjects suffered a re-rupture of the graft and one subject tore the contralateral ACL. Similarly, in the group following an ACL reconstruction with a hamstrings graft, four subjects suffered a re-rupture of the graft and four suffered a contralateral ACL injury. These subjects were excluded in the 2-year follow-up. Therefore, 77 subjects in each group were potential subjects of the 2-year outcome point.

Assessments of AP knee laxity at 2-years postoperative were collected on 61 patients in the BTB graft group and 75 subjects in the hamstrings graft group using an 89 N force technique on the KT1000. Side-to-side differences in mean (95% confidence interval [CI]) AP knee laxity were significantly greater in the hamstrings tendon graft group (1.7 mm; 95% CI 0.8, 1.2) compared with the BTB graft group (1.0 mm; 95% CI 1.5, 1.9; $p = 0.02$). These differences were associated with sex. The females in the hamstrings graft group presented with significantly greater side-to-side differences in AP knee laxity (2.5 mm; 95% CI 2.2, 2.8) than females in the BTB graft group (1.0 mm; 95% CI 0.7, 1.3; $p = 0.001$), males in the BTB graft group (0.9 mm; 95% CI 0.6, 1.2; $p = 0.0003$) and males in the hamstrings graft group (0.9 mm; 95% CI 0.7, 1.1; $p < 0.0001$). There were no side-to-side differences in mean AP knee laxity in males ($p = 0.99$) between the BTB to the hamstrings graft groups.

The results of this study indicate no effect of sex or graft on failure rate. However, there does appear to be an increase in AP knee laxity in females after ACL reconstruction with a hamstrings graft, when compared with females who had a BTB graft and males who had either graft source. This study had a strong methodological design with a CMS score of 54. The authors appropriately attempted to minimize bias by matching the groups, using one surgeon, matching the graft placement and fixation, and matching rehabilitation. Limitations to this study were the consecutive recruitment strategy and coincidental change, by the surgeon of his technique, from BTB grafts to hamstrings grafts. Specifically, the authors recruited all the subjects in the BTB group and then recruited all of the subjects in the hamstrings graft group. This, potentially, significantly biases the study findings, as the BTB graft cohort may have benefited from the surgeon’s skills, whereas the hamstrings graft cohort would be the initial patients on whom the surgeon executed this procedure, or the surgeon may have become more skilled or accumulated greater resources over time. This may bias the BTB versus hamstrings graft comparison, but it would not explain the sex differences seen in this study.

3.1.3 Gobbi et al., 2003—Gobbi et al.[11] conducted a prospective cohort study to compare outcomes after an ACL reconstruction with a BTB graft versus a quadrupled bone-semitendinosis (hamstrings) graft. The authors enrolled 40 subjects for the BTB graft group (26 male, 14 female) and 40 subjects for the hamstrings graft group (22 male, 18 female). Each subject had their AP knee laxity assessed with a computerized knee motion analyser (OSI CA4000; Orthopaedic System, Hayward, CA, USA) at 36 months post-operative at 20 N of force.

In their presentation of AP knee laxity, the authors categorized their results into percentages of patients with a <3 mm side-to-side difference in AP translation, a 3–5 mm side-to-side difference and a >5 mm of side-to-side difference. The authors reported no significant side-to-side difference in mean AP knee laxity between the BTB group and the hamstrings graft group ($p = 0.166$). However, the authors did note an increase in the mean side-to-side difference in AP knee laxity in females in the hamstrings graft group (2.3 mm) compared with males in the hamstrings group (1.7 mm) These differences were both greater than those seen in the males (1.3 mm) and females (1.3 mm) in the BTB graft group. Statistical significance was not reported. The authors did not report any graft ruptures during the 36 months following surgery.

The results of this study indicate an increase in AP knee laxity in females after an ACL reconstruction with a hamstrings graft compared with females who had a BTB graft and males who had either graft source. This study represents a prospective study design with one surgeon, an adequate follow-up period, consistent surgical procedures in each group, similar rehabilitation and standardized outcome measures. There was one major potential design flaw related to group allocation. Patients were assigned to a group based on their choice of hospital location for the surgical procedure, as all patients at one institution received a BTB graft, while the second facility conducted ACL reconstructions with hamstrings graft. The authors noted this choice was influenced by economic factors, as one institution was a private facility, while the other was a social medicine facility. This represents a major potential confounding problem related to homogeneity of the groups, which may have affected the results when comparing the BTB with the hamstrings graft groups. However, it would not have influenced the sex differences seen within each group. The study was given a CMS of 53.

3.1.4 Gobbi et al., 2004—Gobbi et al.[10] published a second study that more specifically examined sex differences in outcome after an ACL reconstruction with a BTB and hamstrings autograft. The authors again prospectively examined the outcome of 80 patients of a potential 287 who were cared for at their institution over a 7-year span. The author's, again, evaluated 40 patients with a BTB graft (26 male, 14 female) and 40 patients with a hamstrings graft (22 male, 18 female). AP knee laxity was assessed at 36-months post-operative using a 200 N force on a computerized knee motion analyser (OSI CA4000). With respect to graft failure, one male in the BTB graft group suffered a re-injury of his graft and one female in the hamstrings graft group suffered a partial injury of her ACL reconstruction graft.

The authors reported mean side-to-side differences in AP knee laxity in all groups. In the BTB graft group, they noted no significant differences (p = 0.19) in side-to-side comparisons of AP knee laxity between the males (1.61 mm) and the females (1.04 mm). Conversely, in the hamstrings graft group, the female patients presented with significantly greater side-to-side differences in AP knee laxity (1.7 mm) when compared with the male patients who had a hamstrings graft ACL reconstruction (1.14 mm) [p = 0.035]. The authors noted the hamstrings graft diameter in the male patients was significantly greater than in the female patients and noted this may contribute to the difference in AP knee laxity. This theory is difficult to assess, as the graft diameter was not normalized to the size of the patient.

The results of this study indicate no sex differences in AP knee laxity after an ACL reconstruction with a BTB graft. However, a significant increase in AP knee laxity was observed in female patients following an ACL reconstruction with a hamstrings graft that was not noted in the males. No difference in graft failure was reported. Gobbi et al.[10] again presented a prospective cohort study with a consistent surgical procedure, rehabilitation course and outcome measures. With respect to group assignment, there was a nonrandomized allocation of subjects to each group and the inclusion criteria were not clearly outlined by the authors. This may result in bias within the groups. Finally, this article received a CMS score of 53.

3.1.5 Bizzini et al., 2006—Bizzini et al.[7] published a comparative case series with the purpose of analysing ligamentous instability and strength after an ACL reconstruction with either a BTB graft or a quadruple semitendinosis/gracilis tendon (hamstrings) graft. The authors consecutively recruited 153 subjects who met the inclusion criteria. Three surgeons participated in this study. Surgeon selection was based on referral and by minimizing selection bias. Conversely, graft selection was based on surgeon preference as two surgeons preferred BTB grafts while one preferred hamstrings grafts. Eighty-seven patients (54 male, 33 female) received a BTB graft and 66 patients (45 male, 21 female) received a hamstrings graft, Similar fixation and rehabilitation was implemented in all patients. Follow-up assessment of AP knee laxity occurred at a mean of 11-months postoperative. AP laxity was assessed with a KneeLax arthrometer (Gatso Products, Overveen, NL, USA) at 133 N of force.

The authors reported that the patients with a BTB graft had a significantly less mean side-to-side difference in AP knee laxity (1.9 ±0.7 mm) than patients with a hamstrings graft (2.7 ±0.7 mm; $p < 0.001$). Both males (2.4 ±0.5 mm) and females (3.5 ± 0.5 mm) in the hamstrings graft group demonstrated increased laxity ($p < 0.001$) compared with the males (1.9 ±0.7 mm) and females (1.9 ± 0.7 mm) in the BTB graft group. Finally, females in the hamstrings graft group demonstrated the greatest laxity, as they were significantly greater than the males in the hamstrings graft group ($p < 0.001$). Data on graft failure rate was not reported by the authors.

The results of this study indicate that ACL reconstructions with hamstrings grafts tend to have greater AP laxity than those with BTB grafts, and females who have hamstrings grafts tend to have greater laxity than males who have hamstrings grafts. This cohort study represented early, objective outcome data of a relatively large sample that underwent ACL reconstruction and performed similar rehabilitation. There were several limitations to this study. Regarding patient allocation, a nonrandomized method was used to assign patients to each group and three different surgeons were included. Among these surgeons, two exclusively performed ACL reconstructions with BTB grafts, while the third utilized hamstrings grafts. These methodological limitations in this study resulted in a relatively low CMS score of 41.

3.1.6 Pinczewski et al., 2007—Pinczewski et al.[14] published a 10-year outcome of their patients following ACL reconstruction in 2007. In this prospective cohort study, the authors originally enrolled 180 patients following ACL injury. The first 90 patients received an ACL reconstruction with a BTB graft and then the following 90 patients received an ACL reconstruction with a four-strand semitendinosis/gracilis (hamstrings) graft. After 10 years, seven patients in the BTB group ruptured their reconstructed graft and 20 had suffered a contralateral ACL injury. Similarly, in the hamstrings graft group, 12 patients ruptured their reconstructed graft and nine suffered a contralateral ACL injury. This reduced the number of patients available for objective assessment at 10-years post-operative to 74 patients who had a BTB graft and 78 patients who had a hamstrings graft.

The authors reported mean side-to-side differences in AP knee laxity at 10-years postoperative using a KT1000 testing device with a manual maximum technique. The authors reported that the greatest mean side-to-side difference in AP knee laxity was observed in female patients who received a hamstrings graft (1.7 mm) with the smallest difference seen in both males and females in the BTB graft group (1.2 mm). The authors also noted that the females who had a hamstrings graft presented with the smallest percentage of patients with <3 mm difference between limbs (66%); the males in the BTB graft group had the largest percentage of patients with <3 mm difference in side-to-side AP knee laxity (81%). Statistical significance was not reported in these measures. The authors did report that regression analysis identified a significant relationship between laxity at 10-years postoperative and laxity at 2-years post-operative.

This study represents a strong prospective cohort design that compared outcomes of ACL reconstructions with BTB grafts, with ACL reconstructions with hamstrings grafts. It received a CMS ranking of 57. The authors reported a high incidence of second ACL injury (ipsilateral and contralateral) in both the hamstrings and BTB graft cohorts. The presentation of the AP knee laxity data results in several unanswered questions. The authors noted at a 2-year follow-up that females in the hamstrings graft group had the greatest mean side-to-side difference in AP knee laxity (2.4 mm) and they had the lowest percentage of patients with side-to-side differences in AP knee laxity <3 mm (54%). They noted that this was significantly different than the male patients in the hamstrings tendon graft group (1.2 mm; 84%) and the females (0.8 mm; 94%) and males (0.9 mm; 83%) in the BTB graft group. This represented a significant difference ($p = 0.004$). Interestingly, at the 10-year follow-up, female patients in the hamstrings tendon graft group now had a mean side-to-side difference of 1.7 mm, and 66% of the patients had <3 mm of asymmetry; this was not significantly different than the other three groups. This improvement in outcome is likely explained by the dropout of subjects from the study who suffered graft rupture or contralateral injury. The authors did note in their discussion that asymmetry in AP knee laxity >3 mm was correlated with graft failure, indicating those with greater asymmetric laxity at 2-years post-operative, ultimately went on to fail and were excluded from objective analysis at 10-years post-operative, thus biasing the results. Through a careful analysis of the longitudinal data presented in this study, it appears that females who undergo an ACL reconstruction with a hamstrings graft tend to have significantly greater asymmetry in AP knee laxity than males who have a hamstrings graft and greater asymmetry than all patients who have a BTB graft.

3.2 BTB Grafts

Three studies were identified in the literature that investigated sex differences in AP knee laxity and failure rate after ACL reconstruction using a BTB graft.[6,9,16] Each of these studies reported various outcome variables after ACL reconstruction, inclusive of AP knee laxity and graft failure.

Two of the three studies[6,16] reported no significant sex differences in AP knee laxity as assessed in the KT1000 arthrometer at 26–38-months postoperative. Ferrari et al.[9] noted a significant side-to-side sex difference in AP translation ($p = 0.014$) using a manual maximum technique on the KT1000, as the males presented with a 0.77 ± 2.77 mm side-to-side difference, while the females presented with a 1.73 ± 2.16 mm side-to-side difference.

With respect to graft failure, each study had a unique operational definition. Wiger et al.[16] identified patients who had suffered a re-injury to the ACL reconstructed knee prior to follow-up testing and noted there was no sex difference in the re-injury rate (3% males; 3% females). Ferrari et al.[9] and Barber-Westin et al.[6] reported arthrometric graft failure after follow-up assessment. Ferrari et al.[9] defined graft failure as >5 mm of AP translation and Barber-Westin et al.[6] defined graft failure as >5.5 mm of AP translation. Using these independent definitions, both authors reported no sex differences in graft failure rate after ACL reconstruction using a BTB graft.

Although these three studies present similar results, they each suffer from methodological limitations that limit their generalizability and threaten the external validity of the results. Most notable is the retrospective cohort design by Ferrari et al.,[9] the inconsistent procedures associated with the AP laxity assessment and the variability in the experience of the tester. The CMS ranking for each article demonstrated in the articles by Barber-Westin et al.[6] (CMS 64) and Ferrari et al.[9] (CMS 55) had a stronger research design, while the study by Wiger et al.[16] (CMS 25) was a weaker study. In summary, the results appeared to support the findings of the prior studies that compared the hamstrings graft with the BTB graft. Specifically, there does appear to be a sex effect on AP knee laxity after an ACL reconstruction with a BTB graft.

3.3 Hamstrings Tendon Autografts

Two prospective cohort studies were identified in the literature that investigated sex differences in AP knee laxity and failure rate after ACL reconstruction using hamstrings graft.[13,15] Noojin et al.[13] examined sex differences in outcomes after ACL reconstruction using quadruple-loop semitendinosus and gracilis tendons. Sixty-five (39 females, 26 males) of a possible 690 patients qualified, enrolled and were assessed at a mean of 39.0–40.9

months after ACL reconstruction. During the follow-up period, 9 female patients (23%) had graft ruptures, while one male (4%) patient had an athrometrically-defined clinical failure with a 7 mm side-to-side difference, which was statistically significant. Mean side-to-side differences in AP knee laxity, assessed with a manual maximum technique on the KT1000 arthrometer, was 1.88 mm (range 0–6.5) for females, and 1.25 mm (range 0–7) for males.

Salmon et al.[15] examined the effects of sex on AP ligament laxity after ACL reconstruction. Two hundred patients (100 male, 100 female) received an ACL reconstruction with a four-bundle hamstrings graft and were enrolled in the study. During the 7-year follow-up, 21 (11%) patients had graft ruptures and 12 (8 males, 4 females; 6%) had contralateral ruptures. No significant difference was observed in the rate of graft rupture between males[12] and females.[11] All patients with a graft rupture or contralateral tear were excluded from further analysis. At the 7-year follow-up, 70 female and 73 male patients were evaluated. KT1000 testing was completed on 125 of the patients, including 62 females and 63 males. The mean side-to-side difference was 1.9 mm and 1.3 mm for females and males, respectively. This difference was significant (p = 0.02). There were two additional females with an AP knee laxity of 6 mm that was described as arthrometric failure.

Together, these studies demonstrate a high graft failure rate in females following an ACL reconstruction with a hamstrings graft and support the tested study hypotheses related to AP knee laxity in hamstrings grafts. Specifically, female patients who undergo an ACL reconstruction with a hamstrings graft tend to have greater asymmetry in AP knee laxity when compared with males who have a similar procedure. Both of these studies have comparable study designs with CMS rankings of 55. However, each has methodological limitations. Noojin et al.[13] failed to report how the patients were enrolled in their study, which may have resulted in a selection bias. In addition, the surgical procedure utilized endobutton fixation, which was unique in this study. Salmon et al.,[15] also suffered from methodological flaws, particularly related to patient recruitment, randomization and follow-up. In summary, the results appear to support the findings of the prior studies that compared the hamstrings graft with the BTB graft. Specifically, there appeared to be a sex effect on AP knee laxity after an ACL reconstruction with a hamstrings graft.

4. Discussion

Assessment of AP knee laxity is often considered the gold standard in the determination of outcome after ACL reconstruction.[30] The studies identified in this systematic review appear to support our hypothesis that female patients who receive an ACL reconstruction with a hamstrings autograph tend to have increased AP knee laxity compared with males who have a similar procedure, and both males and females with a BTB graft after an ACL reconstruction. The inclusion of sex as an independent variable in this case, may alter the findings of many authors who suggest no differences exist in AP knee laxity when comparing a hamstrings graft with a BTB graft after an ACL reconstruction.

4.1 Anterior Cruciate Ligament (ACL) Reconstruction With a Hamstrings Graft: Males versus Females

Four of the six studies[7,8,10,11] that examined sex differences in AP knee laxity between hamstrings and BTB grafts reported that females who had a hamstrings graft had significantly greater AP knee laxity than males who had an ACL reconstruction with a hamstrings graft. Muneta et al.[12] did not report mean side-to-side differences in AP laxity; however, they noted that patients who received a hamstrings graft were the greatest percentage of patients who had >5 mm of asymmetric AP knee laxity. In addition, there were more females who had >5 mm of asymmetry in AP knee laxity than males. Finally, although the study by Pinczewski et al.[14] did not report mean side-to-side differences in AP knee laxity at 10-years post-operative, the authors did note that females who had a hamstrings graft ACL reconstruction had a significantly greater AP translation, and there were significantly fewer of these patients who had >3 mm of asymmetry than that of male patients who had an identical procedure at 2-years post-operative. The change in their outcome at 10 years when compared with the 2-years post-operative, may be related to their patient dropouts due to re-injury and contralateral injury. Therefore, all six studies presented data supporting our hypothesis. In addition to the studies examining patients with both hamstrings and BTB grafts, the two studies that investigated only subjects with hamstrings grafts, also presented similar results. Salmon et al.[15] and Noonjin et al.[13] noted greater AP translation in females when compared with males after an ACL reconstruction with a hamstrings graft.

4.2 ACL Reconstruction with a BTB Graft: Males versus Females

None of the six studies that investigated the influence of sex and graft source on outcomes after ACL reconstruction reported significant sex differences in asymmetric AP knee laxity after an ACL reconstruction with a BTB graft. In addition, only one of the three studies that evaluated sex differences in AP laxity after only an ACL reconstruction with a BTB graft noted any significant difference. Ferrari et al.[9] noted that the mean side-to-side difference in AP knee laxity of male patients who received an ACL reconstruction with a BTB graft was significantly less than that of females. However, there was no difference in the percentage of patients who had >5 mm of asymmetry in AP laxity. This represented one of the weaker study designs, as it was a retrospective case review and only achieved a CMS rank of 32. The remaining studies, which were of a much stronger methodological design, reported no significant difference in AP knee laxity between sexes following an ACL reconstruction with a BTB graft. These results are consistent with other studies in the literature that reported no sex differences in AP knee laxity[31,32] or graft failure[33,34] after an ACL reconstruction with a BTB graft.

4.3 Female Patients with ACL Reconstruction: Hamstrings versus BTB

Two of the six studies[7,8,10] that reported females who had a hamstrings graft ACL reconstruction, demonstrated significantly greater side-to-side differences in AP translation than a cohort of females patients who underwent an ACL reconstruction with a BTB graft. Two additional studies[10,11] reported greater values in mean AP knee laxity asymmetries in females who had a hamstrings graft when compared with a BTB graft ACL reconstruction;

however, they did not report if the difference was statistically significant. Finally, Pinczewski et al.[14] noted at their 10-year follow-up that there was no difference in mean AP laxity between the hamstrings and BTB graft groups; however, in their 2-year data, there was a significant difference between the groups. Collectively, this data indicates females experience greater asymmetries in AP knee laxity after an ACL reconstruction with a hamstrings graft than with a BTB graft.

4.4 AP Knee Laxity after ACL Reconstruction: Females versus Population

The evidence that asymmetries in AP knee laxity are greater following a hamstrings graft ACL reconstruction than with a BTB graft ACL reconstruction appears to be unique to the female sex. There are a plethora of studies currently published in the literature that indicate there are no differences in AP knee laxity between an ACL reconstruction with a hamstrings graft and an ACL reconstruction with a BTB graft.[25,30,34–41] The findings of the current systematic review indicate that because of sex differences in AP laxity after ACL reconstruction, a re-evaluation of the results of these studies is needed. If the study populations in these studies are skewed towards one sex, the mean results may be affected. Considering the mean differences in many of these studies are <1 mm,[10,11,14] inequities in sex within the sample may significantly skew the results. In addition, comparisons between studies may be invalid if the male to female ratio within each study population is not similar. As a result, much of the data in these high level, randomized controlled trials will need to be re-evaluated, controlling for sex, to determine if the results are consistent.

4.5 Clinical Significance

The issue of statistical significance versus minimal clinical significance could be brought to question in these studies. Although many of the studies presented highly significant sex differences in AP knee laxity after an ACL reconstruction with a hamstrings graft,[7,8] the mean difference between the groups was small; typically between 1.0–1.5 mm. One could argue that this is much less than the 2–5 mm required to diagnose a knee as ACL deficient [17] and greater than what has been described as typical measurement error with a KT1000.[42] However, in this example, the mean difference described in each study represents a trend towards greater laxity. This trend indicates that females experience a greater increase, although small, in AP knee laxity with a hamstrings graft than with a BTB graft after an ACL reconstruction. The mechanism of this increase could be related to histological properties of the graft, issues with fixation or other sex-specific variables related to the hamstrings graft that would tend to increase AP knee laxity. This is consistent with the work of Biau et al.,[43] who suggested that knee instability was more common after an ACL reconstruction with a hamstrings autograft and the work of Salmon et al.,[15] who noted that the female sex was the best predictor of laxity outcomes after an ACL reconstruction with a hamstrings graft. Considering this evidence, in future studies, an appropriate analysis of AP knee laxity results would report both mean side-to-side differences as well as a sub-classification of laxity data. Some of the current studies have reported this data, using 0–2 mm, 3–5 mm and >5 mm, as clinically significant categories.[12,14] This may allow the sports medicine community to better understand the implications of these subtle differences in AP knee laxity and their relationship to outcome.

The relationship between mechanical stability and functional outcomes also needs to be addressed. Current evidence indicates that AP knee laxity (or mechanical stability) does not correlate well with patient-reported outcomes,[44] or functional disability.[45] These studies report that increases in AP knee laxity may not predict patient satisfaction or functional abilities. However, Pinczewski et al.[14] have shown that AP knee laxity >3 mm at a timepoint of 2 years after surgery, was correlated with graft failure. In consideration of this relationship between early AP laxity and ultimate graft failure, early knowledge of increased AP knee laxity could be used as an indicator to modify rehabilitation or implement unique interventions previously shown to be efficacious in an ACL-deficient population,[46] in hopes of enhancing dynamic stability and reducing the incidence of graft failure. Furthermore, if females are experiencing increased AP knee laxity after an ACL reconstruction with a hamstrings graft, it is important to consider if this is an appropriate graft choice for female athletes, knowing this relationship between laxity and graft failure.

4.6 Limitations

The current systematic review had limitations in its design. Only three databases, MEDLINE, CINAHL® and SPORTDiscus™ were used for the literature search. Many of the journals included in these databases are published in the US, limiting the possible inclusion of some world literature.[47] Only articles published in English were included. Also, no randomized control trials were included, as none were available in the literature that met the inclusion criteria. Therefore, the literature included within this review, which represents the highest available level of evidence on this topic, is classified overall as lower level evidence. With respect to patient group assignment, none of the six studies that directly compared patients who had BTB grafts to patients who had hamstrings grafts randomly assigned their patients to each group. Primarily, the patients were consecutively recruited into a group and then secondarily into the other cohort. This type of recruitment represents a convenience sample and creates significant potential for bias.[48] A more appropriate randomization into each group would have improved the quality of each of these studies. Finally, there is inconsistent methodology used between these studies related to the means to assess AP knee laxity. Although all utilized an objective tool to assess laxity, three different types of units were used, introducing the potential for difficulty in comparison between studies. In addition, there was variability in the technique used within the KT1000. Notably, some recorded side-to-side differences at 89 N, 133 N or with a manual maximum technique. With respect to data presentation, some studies reported mean side-to-side differences in AP knee laxity, while others classified results into subgroups. Consequently, direct comparisons between studies were difficult. Despite this limitation, one could assume that even if mean AP translations were different between units, the side-to-side differences should be comparable and allow for an equitable comparison of asymmetry in AP laxity.

4.7 Future Studies

The reviewed studies, which evaluated sex differences after ACL reconstructions with hamstrings and BTB grafts, are primarily retrospective and prospective cohort studies. Although the results of the current literature appear to be consistent, inherent bias within the disparate study designs may result in the reader questioning the validity of the overall findings. Therefore, the current results should be validated in the future with strong randomized controlled trials to potentially confirm the results and allow greater confidence in the findings. A second variable that is often overlooked in relation to outcome is rehabilitation. Few of the current studies clearly outlined the rehabilitation programme of their patients. This variable could have an effect on AP laxity after surgery and needs to be rigorously investigated. Finally, other variables that historically predict a poor outcome should be investigated to determine their relationship to AP knee laxity. This will help determine the influence of AP knee laxity on various outcome measures currently being developed, to determine readiness to return to activity after ACL reconstruction. Unbiased results of outcome measures post-ACL reconstruction will lead to more appropriate and efficacious outcome measures prior to return to activity.

5. Conclusion

This review utilized the highest available evidence in order to identify sex and graft-dependent variability in the outcome of AP knee laxity following ACL reconstruction. Females who undergo ACL reconstruction utilizing hamstrings grafts demonstrate increased AP knee laxity over time than males undergoing the same procedure. These differences were not seen in patients who received an ACL reconstruction with a BTB grafts. Therefore, with current surgical interventions, ACL reconstruction with a BTB graft appears to offer the most mechanical stability for both sexes, while less mechanical stability is noted in females following ACL reconstruction with a hamstrings autograft. The clinical significance of this finding in relation to the ability to return to activity and the long-term outcome after ACL reconstruction requires further investigation.

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Table I

Summary of CMS on all 11 studies

Study (y)	Modified Coleman (n)	Objective	Sample size		F/u (mean range)	Laxity tool and force	Results/conclusion	Failure rate	Comments
			HSG	BTBG					
Barber-Westin et al.[6] (1997)	55	To determine whether differences existed between the sexes in complications and outcomes	NI	M = 47	26 mo (22–42)	KT2000 arthrometer	Chronic BTB: M laxity = F laxity	2 BTB in a M	Specific inclusion/exclusion criteria
				F = 47		20° flex	Acute BTB: M laxity = F laxity	3 BTB in a F	M randomly selected and matched with F
				F/u M = 45		89 N and 134 N		>5.5 mm diff	KT2000 arthrometer performed by experienced technician
				F/u F = 38					One surgeon for all procedures Comparison of chronic vs subacute Interference screw fixation
Bizzini et al.[7] (2006)	41	Analyse ligamentous stability and isokinetic strength of knee extensor and flexor muscles after ACLR with two different autografts with identical fixation in consecutive pts undergoing a similar rehabilitation programme	M = 45	M = 54	11 mo (9–13)	Kneelax	HSG AP > BTBG AP laxity	Unknown	Specific inclusion/exclusion criteria
			F = 21	F = 33		30° flex	BTBG: M = F laxity		Consecutive pts, no randomized method
						132 N	HSG: F > M laxity		Three surgeons used One PT completed testing for study, reliability unknown Semitendinosus/gracilis quadrupled tendon used Femoral endobutton fixation and tibial blauth screw fixation
Corry et al.[8] (1999)	54	To evaluate any diff in outcome between the patellar and hamstrings tendon autografts, controlling as far as possible all other variables. To show that the outcome after arthroscopic reconstruction with either	M = 47	M = 48	2 y	KT1000 arthrometer	HSG AP > BTBG AP laxity	3 BTBG in a M	Consecutive pts used, no randomized method
			F = 43	F = 42		89 N	BTBG: M = F laxity	4 HSG	One surgeon, same surgical technique
			F/u 82	F/u 85		89 N	HSG: F > M laxity	5/64 BTBG >5 mm	One experienced technician completed KT1000, reliability of tester unknown
			77 tested	77 tested				5/79 HSG >5 mm	Semitendinosus and gracilis quadrupled tendons used for HSG
			M = 47 / KT f/u 75	M = 48 / KT f/u 61	2 y	KT1000 arthrometer	HSG AP > BTBG AP laxity	3 BTBG in a M	Consecutive pts used, no randomized method / Interference screws used to fix graft

Study (y)	Modified Coleman (n)	Objective	Sample size HSG	Sample size BTBG	F/u (mean range)	Laxity tool and force	Results/conclusion	Failure rate	Comments
		graft reaches acceptable standards graft reaches acceptable standards graft reaches acceptable standards							
Ferrari et al.[9] (2001)	32	To determine whether diffs existed between M and F in the outcome of ACLR using autogenous BTBG.	N = 43 / F = 43 F/u 82 77 tested KT for 75	M = 42 / N = 137 F/u 83 77 tested KT for 61	M = 59.5 mo F = 52 mo	KT1000 arthrometer / 89 N 89 N, 133 N man max	BTBG: M = F / F > M laxity HSG: F > M laxity / No diff in M >5 mm	4 BTBG in a M / 3 HSG 2/84 BTBG / 5/61 in a F >5 mm >5 mm diff 5/79 HSG >5 mm	Specific inclusion/exclusion criteria / One surgeon, same surgical technique Not randomized method / One experienced clinician completed KT1000, reliability of tester unknown Single surgeon completed all procedures Semitendinosus and gracilis quadrupled tendons used for HSG / Independent experienced examiner for KT, reliability of tester unknown Interference screws used to fix graft Interference screw fixation
Gobbi et al.[11] (2003)	53	To compare the results of ACLR in athletes with two diff graft types, both using healing: BTBG and a bone-to-bone quadrupled bone-semitendinosus graft	M = 22 F = 18	M = 26 F = 14	3 y	OSI CA4000 200 N Max static	BTBG: M = F laxity HSG: F laxity > M laxity	1 HSG in a F partial	Specific inclusion/exclusion criteria Consecutive pts, two places, BTBG at one, HSG at the other No randomized method One surgeon performed all surgeries Independent examiner for CA4000, reliability of tester unknown Quadrupled semitendinosus graft Tibial bone plug press-fit and fastlok, femoral endobutton for HSG Tibial fixation with metal wire tied over bicortical screw post-BTBG
Gobbi et al.[10] (2004)	53	Determine whether the results of ACLR using PT or HSG techniques are equivalent in M and F	M = 22 F = 18	M = 26 F = 14	3 y	OSI CA4000 200 N 20° flex	BTBG: M laxity = F laxity HSG: F laxity > M laxity	1 BTBG M 1 HSG F partial	Specific inclusion/exclusion criteria No randomized method One surgeon Independent examiner at 3 y f/u reliability of tester unknown Semitendinosus only quadrupled grafts Graft fixation diff between BTBG and HSG BTBG metal wire tied over 'ortical screw 'post' in tibia Femoral fixation with endobutton, tibial fixation with fastlok device
Muneta et al.[12] (1998)	51	To assess the outcome of reconstruction using multistranded	M = 21	M = 22	HSG = 31 ± 8	KT1000	More pts showed >5 mm	Unknown	Consecutive patients with ≥20 month f/u included

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Study (y)	Modified Coleman (n)	Objective	Sample size HSG	Sample size BTBG	F/u (mean range)	Laxity tool and force	Results/conclusion	Failure rate	Comments
		semitendinosus tendon compared with the BTBG technique using aggressive early rehabilitation	F = 31	F = 29	BTBG = 28 ± 5	89 N	Anterior laxity in HSG group than BTBG		No randomized method
					≥20 mo	Man max	(p = 0.07)		Results not statistically significant Unknown who completed KT testing, or reliability of their KT testing Semitendinosus and gracilis needed for four pts Triple or quadruple mutlistrand graft Nonabsorbable sutures over button, staple or screw for HSG at 30° Interference screw BTBG at 30° flex
Noojin et al.[13] (2000)	55	To determine whether the results of ACLR using quadruple-looped semitendinosus and gracilis tendons are equivalent in M and F at short- to medium-range f/u	M = 26	NI	41 mo (24–81)	KT1000 arthrometer 25° flex Man max	HSG: F > M laxity	1 HSG in a M	Specific in/exclusion criteria
			F = 39	NI			HSG: F > M failure	9 HSG in a F >5 mm diff	No randomized method One surgeon for all procedures, all procedures the same Semitendinosus and gracilis quadrupled tendon used Endobutton fixation femoral, button or post tibial
Pinczewski et al.[14] (2007)	57	To report on long-term outcomes of ACLR on knee function using an endoscopic technique, as well as a prospective comparison of isolated effects of one extrinsic variable (graft choice)	M = 47	M = 48	10 y	KT1000 arthrometer man max	Laxity diff at 2 y, not 5, 7, 10	12 HSG at 50 mo	Specific inclusion/exclusion criteria
			F = 43	F = 42			2 y HSG: F > M laxity	7 PT at 63 mo	No randomized method
			F/u = 53	F/u = 58			2 y: HSG laxity > BTBG laxity	Not significant >5 mm diff	Single surgeon, changed to HSGs after BTBGs
							2 y BTBG: F = M laxity		Semitendinosus and gracilis quadrupled graft BTBG significant experience, HSG beginning experience Independent examiner 6, 12 mo, 5, 7 and 10 y, reliability of tester unknown Pts and examiners not blinded Interference screws proximal and distal for both graft types

Study (y)	Modified Coleman (n)	Objective	Sample size		F/u (mean range)	Laxity tool and force	Results/conclusion	Failure rate	Comments
			HSG	BTBG					
Salmon et al.[15] (2006)	55	To examine the effect of gender on clinical ligament laxity, and perceived and functional outcomes. To examine the relationship between laxity and self-reported outcomes	M = 100	NI	1, 2 and 7 y	KT1000 arthrometer	No significant diff HSG M/HSG F for failure rate	12 HSG, M	Specific inclusion/exclusion criteria
			F = 100	NI		30° flex	HSG > BTBG laxity (1, 2 and 7 y)	10 HSG, F	Consecutive pts
			F/u M = 63			Man max	HSG: F > M laxity (7 y)	>5 mm diff	No randomized method
			F/u F = 62					2 HSG, F >5 mm	One surgeon performed all procedures PT or clinical researcher completed KT1000 arthrometer, reliability unknown Semitendinosus and gracilis quadrupled tendon grafts Interference screw fixation
Wiger et al.[16] (1999)	25	To compare the results after ACLR in a large population of F and M competitive athletes. Special emphasis on gender-specific diffs, such as objective laxity, function and return to competitive sports	NI	M = 296	M = 39 mo	KT1000 arthrometer	BTBG: F = M laxity	8 BTBG in a M (3%)	No randomized method
			NI	F = 133	F = 37 mo	Unknown		4 BTBG in a F (3%)	Six surgeorns performed all procedures Independent examiner at f/u Interference screw fixation

ACLR = anterior cruciate ligament reconstruction; **AP** = anterior-posterior; **BTBG** = bone-pateller tendon-bone graft; **CMS** = Coleman methodology scores; **diff(s)** = different/difference(s); **F** = female; **F(f)/u** = F(f)ollow-up; **flex** = flexion; **HSG** = hamstrings graft; **M** = male; **man max** = manual maximum, technique; **N** = Newtons; **NI** = not included in study; **PT** = physical therapist; **pt(s)** = patient(s);

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Table II

Summary of Coleman methodology scores

	Question (maximum score)	Mean score
Part A		
1	Study size (10)	8.6
2	Mean follow-up (5)	4
3	Number of surgical procedures (10)	8.2
4	Type of study (15)	7.3
5	Diagnostic certainty (5)	0.5
6	Description of surgery (5)	0.05
7	Description of rehabilitation (5)	0.5
Part B		
1	Outcome criteria (10)	3.7
2	Procedure for assessing outcome (15)	9.6
3	Description of subject selection (18)	3.2
Mean total score – sum of all scores (out of 100)		**49.1**