

# FIVE-YEAR OUTCOMES FOLLOWING ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION: DOES SEX IMPACT PATIENT-REPORTED OUTCOMES AND RE-OPERATION RATES?

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**BACKGROUND:** Females have been shown to have a two- to eight-times higher risk of anterior cruciate ligament (ACL) injury than their male counterparts. Despite the clear difference in risk, sex-based differences in outcomes following ACL reconstruction are less well understood. The purpose of this study was to compare 5-year outcomes between males and females who were under the age of 26 at the time of enrollment in an ACL registry. We hypothesize that male and female patients will have similar patient-reported outcome scores, but females will have a higher incidence of ACL graft re-injury.

**METHODS:** Patients undergoing ACL reconstruction while under the age of 26 were included if they also had completed five-year follow-up questionnaires. Outcomes were compared between males and females, and the outcomes of interest included the International Knee Documentation Committee (IKDC), Knee Injury and Osteoarthritis Score (KOOS), ACL Return to Sport after Injury (ACL-RSI), and reoperation.

**RESULTS:** Of the 159 patients enrolled in the registry, 35 had complete follow-up (22%). The average difference between postoperative and preoperative IKDC scores for males and females was  $37.9 \pm 21.6$  and  $33.2 \pm 26.6$ , respectively ( $p = 0.600$ ). The average difference between postoperative and preoperative KOOS scores for males and females was  $31.6 \pm 15.4$  and  $29.2 \pm 23.0$ , respectively ( $p = 0.731$ ). The average ACL-RSI for males and females was  $79.8 \pm 47.0$  and  $56.5 \pm 31.1$ , respectively ( $p = 0.088$ ). The incidence of reoperation and ACL re-tear for the entire cohort was 28.6% and 5.7%, respectively.

**CONCLUSION:** Overall, males and females under the age of 26 who underwent ACLR had similar 5-year outcomes regarding outcomes scores after surgical intervention. The ACL-RSI was lower in women, however, failed to reach significance. The reoperation rate for males and females was not statistically significant. ACL reconstruction is a successful operation in young males and females with improvement in knee outcome scores and ability to return to sport.

## INTRODUCTION

Anterior cruciate ligament (ACL) injuries are among the most common orthopedic injuries with roughly 200,000 to 250,000 ACL injuries occurring each year in the United States.<sup>1-3</sup> Females have been shown to have a two- to eight-times higher risk of ACL injury than their male counterparts.<sup>4-6</sup> Despite the clear difference in risk, sex-based differences in outcomes following ACL reconstruction (ACLR) are less well understood. For example, some authors have reported worse outcomes in female patients while others have reported no difference.<sup>7-10</sup> In addition to sex, age and activity level have also

been identified as risk factors for both primary and secondary ACL injury.<sup>11-13</sup> More specifically, young patients who are transitioning from adolescence to young adulthood present a unique challenge given the possibility for open physes and the potential for a dramatic increase in activity level if the patient goes on to participate in collegiate or professional sports. However, there is a paucity of midterm data reporting results of ACLR in the young adult population with an emphasis on sex-based outcomes. With the known increase in the incidence of ACL injuries throughout the past two decades and the increasing emphasis on year-round

sports involvement, the orthopedic community is likely to see ACL injuries continue to increase.<sup>13</sup> The lack of clear data and consensus regarding outcomes between young males and females coupled with the increasing numbers of females participating in sports warrants further investigation into sex based outcomes in the young adult population.

The purpose of this study was to compare 5-year outcomes between males and females who were under the age of 26 at the time of enrollment in an ACL registry. We hypothesize that male and female patients will have similar patient-reported outcome scores, but females will have a higher incidence of ACL graft re-injury.

## METHODS

Institutional Review Board (IRB) approval was obtained to prospectively enroll all patients undergoing ACLR at a single institution since March 2015. This study reports the results of an analysis of the data gathered from this ACL registry database. Patients undergoing ACLR by any one of the 4 fellowship trained orthopedic sports medicine surgeons at this institution were consented and enrolled in the registry prior to their surgery. Each of these surgeons performs an average of about 30-50 ACL reconstructions per year and all 4 surgeons utilize a bone-patellar tendon-bone graft. Demographic data was collected at the time of enrollment including but not limited to age, race, and smoking status. Mechanism of injury and sport participation was also collected. Furthermore, patient-reported outcome scores were gathered prior to injury and yearly following their ACLR. Patient-reported outcome scores (PROs) included: the International Knee Documentation Committee (IKDC) questionnaire, Knee Injury and Osteoarthritis Outcome Score (KOOS), Marx Activity Rating (MARX) scale and ACL Return to Sports after Injury (RSI) scale.<sup>14</sup> In addition to PRO collection, patient re-operation rates and re-injury rates were obtained from patients and electronic medical record review.

All data were stored using research electronic data capture (REDCap) software (Nashville, TN, USA). In October 2023, data from all enrolled

subjects was retrospectively analyzed. Inclusion criteria was age of less than 26 at time of enrollment in the ACL registry, completion of clinic follow up and patient-reported outcome measures of at least five years. The age of 26 was chosen as the cut off age because the study aimed to capture patients in their college aged years. Exclusion criteria included ligamentous injury beyond an isolated ACL injury or ACL injury plus meniscus injury. In addition to PRO comparisons between males and females, number of reoperations and ACL re-injuries were compared between males and females.

Statistical analyses were performed using IBM SPSS statistics software (IBM SPSS Statistics for Windows, version 28.0; IBM, Armonk, NY, USA). The Patient Acceptable Symptom State (PASS) for the IKDC questionnaire was set at 75.9.<sup>15</sup> Continuous variables were analyzed and compared between groups using Student's t-test. Categorical variables were analyzed using Chi-square test. A *p*-value of less than 0.05 was considered statistically significant.

## RESULTS

159 patients enrolled in the ACL registry were less than 26 years old at the time of enrollment in this registry and were five years or more post-ACLR. Of those 159 patients, follow-up data of at least five years was available for 35 (22%) patients. 20 of the 35 were female and 15 were male.

The following data describes the 35 patients with follow up data of five years or more. The average age of females at time of enrollment and data collection was  $18.9 \pm 2.8$  years old, whereas the average age of males was  $19.4 \pm 3.0$  years old ( $p = 0.58$ ). The minimum age was 15 years old, and the maximum age was 25 years old. At the time of enrollment, 2 males and 2 females were presenting for an ACL revision surgery and 31 patients were presenting for a primary ACL reconstruction. The mean follow-up time for all patients was  $73.1 \pm 9.9$  months. 12 males and 14 females ruptured their ACL while playing sports. The mechanism of injury (contact vs non-contact) and the sport played while the injury occurred are summarized in Table 1.

**Table 1.** Mechanism of injury

| <i>Mechanism</i>               | <i>Male</i> | <i>Female</i> |
|--------------------------------|-------------|---------------|
|                                | <i>N</i>    | <i>N</i>      |
| <i>Contact</i>                 | 14          | 20            |
| <i>Non-contact</i>             | 8           | 6             |
| <i>Sport at time of Injury</i> | 6           | 14            |
| <i>Basketball</i>              | 4           | 5             |
| <i>Cheerleading</i>            | 0           | 1             |
| <i>Football</i>                | 3           | 0             |
| <i>Lacrosse</i>                | 1           | 0             |
| <i>Snow Skiing</i>             | 0           | 1             |
| <i>Soccer</i>                  | 4           | 4             |
| <i>Track and Field</i>         | 0           | 1             |
| <i>Volleyball</i>              | 0           | 2             |

Preoperative scores were available for 14 males and 18 females. The average preoperative IKDC score for males and females was  $42.6 \pm 17.0$  and  $43.4 \pm 20.2$ , respectively ( $p = 0.905$ ). The average preoperative KOOS score for males was  $53.3 \pm 12.4$  and for females was  $52.1 \pm 17.3$  ( $p = 0.824$ ). The average preoperative MARX score for males and females was  $13.2 \pm 3.6$  and  $11.7 \pm 5.5$  ( $p = 0.385$ ) (Table 2). The average preoperative KOOS subscale scores are summarized in Table 3. The only statistically significant difference between males and females was seen in the Quality of Life subscale ( $p = 0.050$ ).

Postoperative scores were available for 15 males and 20 females. The average postoperative IKDC score for males and females was  $81.6 \pm 16.0$  and  $75.1 \pm 22.5$ , respectively ( $p = 0.344$ ). 67% (10) males achieved a PASS for IKDC compared to 55% (11) females. ( $p = 0.728$ ) The average postoperative KOOS score for males and females was  $85.9 \pm 14.0$  and  $80.3 \pm 17.9$ , respectively ( $p = 0.322$ ). The average postoperative MARX score for males and females was  $7.2 \pm 5.1$  and  $6.6 \pm 4.1$ , respectively ( $p = 0.679$ ). (Table 2)

**Table 2.** Average preoperative IKDC, KOOS, and MARX activity rating scale scores for males and females. Average postoperative IKDC, KOOS, MARX activity rating scale, and ACL-RSI scores for males and females

| <i>Preoperative</i>  | <i>Male</i>     | <i>Female</i>   | <i>p-value</i> |
|----------------------|-----------------|-----------------|----------------|
|                      | <i>N</i>        | <i>N</i>        |                |
|                      | 14              | 18              |                |
| <i>IKDC</i>          | $42.6 \pm 17.0$ | $43.4 \pm 20.0$ | <b>0.905</b>   |
| <i>KOOS</i>          | $53.3 \pm 12.4$ | $52.1 \pm 17.3$ | <b>0.824</b>   |
| <i>MARX</i>          | $13.2 \pm 3.6$  | $11.7 \pm 5.5$  | <b>0.385</b>   |
| <i>Postoperative</i> | 15              | 20              |                |
| <i>IKDC</i>          | $81.6 \pm 16.0$ | $75.1 \pm 22.4$ | <b>0.344</b>   |
| <i>KOOS</i>          | $85.9 \pm 14.0$ | $80.3 \pm 17.9$ | <b>0.322</b>   |
| <i>MARX</i>          | $7.2 \pm 5.1$   | $6.6 \pm 4.1$   | <b>0.679</b>   |
| <i>ACL-RSI</i>       | $79.8 \pm 47.0$ | $56.5 \pm 31.3$ | <b>0.088</b>   |

**Table 3.** Average preoperative and postoperative KOOS Subscale scores for males and females

|                      |  | <i>Male</i>        | <i>Female</i>       | <i>p-value</i> |
|----------------------|--|--------------------|---------------------|----------------|
| <i>Preoperative</i>  | <i>N</i>                               | <b>14</b>          | <b>18</b>           |                |
|                      | <i>Symptoms and Stiffness</i>          | <b>61.0 ± 13.1</b> | <b>65.2 ± 16.3</b>  | <b>0.436</b>   |
|                      | <i>Pain</i>                            | <b>68.4 ± 11.4</b> | <b>68.2 ± 20.8</b>  | <b>0.976</b>   |
|                      | <i>Function: Daily Living</i>          | <b>70.0 ± 15.1</b> | <b>71.3 ± 22.6</b>  | <b>0.850</b>   |
|                      | <i>Function: Sports and Recreation</i> | <b>30.7 ± 23.4</b> | <b>32.5 ± 33.4</b>  | <b>0.866</b>   |
|                      | <i>Quality of Life</i>                 | <b>36.7 ± 21.4</b> | <b>23.4 ± 15.5</b>  | <b>0.050*</b>  |
| <i>Postoperative</i> | <i>N</i>                               | <b>15</b>          | <b>20</b>           |                |
|                      | <i>Symptoms and Stiffness</i>          | <b>82.1 ± 14.7</b> | <b>76.85 ± 20.9</b> | <b>0.410</b>   |
|                      | <i>Pain</i>                            | <b>92.2 ± 9.8</b>  | <b>85.55 ± 17.5</b> | <b>0.195</b>   |
|                      | <i>Function: Daily Living</i>          | <b>95.1 ± 9.9</b>  | <b>93.2 ± 11.6</b>  | <b>0.607</b>   |
|                      | <i>Function: Sports and Recreation</i> | <b>84.0 ± 20.9</b> | <b>78.3 ± 23.1</b>  | <b>0.454</b>   |
|                      | <i>Quality of Life</i>                 | <b>76.3 ± 25.2</b> | <b>66.1 ± 27.2</b>  | <b>0.262</b>   |

**Table 4.** Average difference between postoperative and preoperative scores for IKDC, KOOS, and MARX activity rating scale

|                        |             | <i>Male</i>        | <i>Female</i>      | <i>p-value</i> |
|------------------------|-------------|--------------------|--------------------|----------------|
| <i>Postoperative Δ</i> | <i>N</i>    | <b>14</b>          | <b>18</b>          |                |
|                        | <i>IKDC</i> | <b>37.9 ± 21.6</b> | <b>33.2 ± 26.6</b> | <b>0.600</b>   |
|                        | <i>KOOS</i> | <b>31.6 ± 15.4</b> | <b>29.2 ± 23.0</b> | <b>0.731</b>   |
|                        | <i>MARX</i> | <b>-5.79 ± 5.0</b> | <b>-5.5 ± 6.1</b>  | <b>0.888</b>   |

**Table 5.** Reoperation and ACL re-tear rates for males and females

|                        | <i>Male</i>    | <i>Female</i>  | <i>p-value</i> |
|------------------------|----------------|----------------|----------------|
| <i>N</i>               | <b>15</b>      | <b>20</b>      |                |
| <i>Reoperation (%)</i> | <b>2 (13%)</b> | <b>8 (40%)</b> | <b>0.134</b>   |
| <i>ACL Re-tear (%)</i> | <b>1 (6%)</b>  | <b>1 (5%)</b>  | <b>1.000</b>   |

The average difference between postoperative and preoperative IKDC scores for males and females was 37.9 ± 21.6 and 33.2 ± 26.6, respectively ( $p = .600$ ). The average difference between postoperative and preoperative KOOS scores for males and females was 31.6 ± 15.4 and 29.2 ± 23.0,

respectively ( $p = 0.731$ ). The average difference between postoperative and preoperative MARX scores for males and females was -5.8 ± 5.0 and -5.5 ± 6.1 ( $p = 0.888$ ). (Table 4) The average ACL-RSI for males and females was 79.8 ± 47.0 and 56.5 ± 31.1, respectively ( $p = 0.088$ ). (Table 2)

Two males and eight females reported having additional surgeries on the operative knee, but the difference was not statistically significant ( $p = 0.134$ ). The additional surgeries included scar tissue removal (5), hardware removal (1), meniscus repair (1), meniscectomy (1), and ACL revision (2). One male and one female reported re-tearing of the ACL in their operative knee ( $p = 1.000$ ). (Table 5) The incidence of reoperation and ACL re-tear for the entire cohort was 28.6% and 5.7%, respectively.

## DISCUSSION

In regard to patient-reported outcome scores, reoperations, and ACL reinjuries, the results from this study showed there are no statistically significant differences in five year outcomes between males and females who were under the age of 26 at the time of presentation for either primary ACLR or revision ACLR. There is a growing body of literature investigating sex-based differences in ACLR outcomes, but there is a paucity of literature specifically comparing outcomes between young males and females. Furthermore, few studies have been published reporting five-year outcomes specifically for a young adult population such as this one.

Previous literature has clearly demonstrated an increased risk of ACL injury in females as compared to males, but despite the increased risk of injury there remains unclear data regarding the outcomes following ACLR. For example, females have been reported to have greater laxity on post-operative physical exam, but the clinical significance of this finding is unclear given numerous studies reporting no significant difference in graft rupture or ACL reinjuries.<sup>9,16-18</sup> On the other hand, males have been identified to have a higher incidence of graft failure and rupture following primary ACLR.<sup>10,19-21</sup> Elucidation of risk factors, such as sex, for ACL re-injury are vital for the creation of patient-specific and effective rehabilitation protocols, but the results of this small sample size suggest there is no difference in either reoperation or re-rupture rates between males and females at 5 years post ACLR. It is worth noting, however, that although there was no statistically significant difference between reoperation rates, the ratio of reoperation rates for females to males of 4:1 likely represents a clinically significant difference.

Sex-based differences in patient-reported outcome scores following ACLR are also difficult to adequately characterize, but most evidence seems to suggest lower subjective satisfaction and higher

pain scores in females as compared to males. For example, female sex was identified as a significant predictor for worse outcomes 10 years post ACLR when looking at IKDC, KOOS, and the MARX activity rating scale.<sup>22</sup> Furthermore, Cristiani et al reported that females experienced reduced odds of achieving a PASS on the KOOS pain, activities of daily living, and sport and recreation subscales at 2 years post-ACLR.<sup>23</sup> Similarly, a meta-analysis and systematic review by Mok et al. showed that males were found to have a statistically higher postoperative IKDC score. Ultimately, however, Mok et al. concluded that sex based differences in outcomes after ACLR depend on which measurement method is being reported.<sup>10</sup> Despite the mounting literature suggesting females experience worse subjective outcomes, our results showed no statistically significant difference between males and females when using the IKDC, KOOS, or MARX scales. Additionally, no statistically significant difference was noted in the percent of patients who achieved a PASS on the IKDC, but more a PASS was more commonly seen in the males as compared to the females. Moreover, the ACL-RSI displayed no statistically significant differences between groups, but, similar to the reoperation rate, this difference approached statistical significance. Notably, other research has suggested there is a difference in ACL-RSI between males and females when ACL-RSI is measured at 6 months.<sup>24</sup>

Milewski et al. provide insight into why ACL-RSI scores may be lower in females. Their study reports higher levels of psychological stress as demonstrated by higher PROMIS-PSE scores.<sup>24</sup> These higher levels of stress and anxiety can negatively impact an athlete's feeling of psychological readiness for return to sport. Christino et al. also attempted to explain the difference in ACL-RSI scores by citing kinesiophobia as more psychologically distressing for females as compared to males.<sup>25</sup> Another reason ACL-RSI scores may differ between males and females is because of different societal sex based roles which could alter athletes' willingness to honestly report anxiety, fear of injury, or sport readiness.

In addition to measuring the impact of sex on ACLR outcomes, this study also aimed report ACL-RSI and rates of reoperation and re-injury in a young adult population based on sex. This age demographic is of particular interest given the significant increase in physical demand that can



occur if patients go on to play collegiate and/ or professional sports between the ages of 18-22. Furthermore, this patient population may include patients who still have open physes which presents significant challenges due to the risk of physeal damage and growth arrest.<sup>26,27</sup> In a young adult patient population, return to sport is often used as a defining metric for successful ACLR, and psychological readiness, as measured by the ACL-RSI, has been shown to influence when patients return to sport or previous activity level.<sup>24,28</sup> Moreover, higher ACL-RSI scores correlate with clinical outcomes.<sup>29</sup> Previous literature investigating the impact of age on 6 month ACL-RSI scores reported an average ACL-RSI of  $61.5 \pm 20.4$  in adolescents (15-18 years old) and  $52.5 \pm 19.8$  in young adults (19-30 years old).<sup>24</sup> The average ACL-RSI scores in this study of  $79.79 \pm 46.95$  and  $56.54 \pm 31.14$  for males and females respectively, falls within a similar score range, but the comparison of 5 year ACL-RSI scores to 6-month ACL-RSI scores may not be clinically relevant. Therefore, more research is necessary to better characterize ACL-RSI scores at 5 years.

Previous literature has cited younger age as a risk factor for ACL rupture with estimates of re-injury rates in patients under the age of 25 ranging from 29-40%.<sup>21,30-32</sup> Moreover, the Multicenter Orthopaedic Outcomes Network (MOON) consortium cohort reported that patients between the ages of 10-19 had an 8.2% chance of re-rupture versus 4% in patients between the ages of 20-29 years old.<sup>33</sup> The results from this study demonstrate an ACL re-injury rate of 5.71% which is much lower than 29-40%, but the small sample size of this study must be taken into consideration when comparing our re-injury rates to other previously cited estimates. In terms of ipsilateral re-operation rates, this study revealed a rate of 28.57% which is similar to a previously cited reoperation rate of 34.7%, however, this estimate was derived from a study of patients who were 16 at the time of ACLR and included reoperations on both the contralateral and ipsilateral knee.<sup>34</sup> Of note, the surgeons included in this analysis are aggressive in their treatment of arthrofibrosis which helps to explain the 5 cases of scar tissue removal in this cohort. Overall, there has been an increase in published manuscripts reporting outcomes in the adolescent and pediatric population following ACLR, but there remains a paucity of literature, especially mid-term and long-term, available for patients between the ages of 18-26.<sup>35,36</sup> Therefore emphasizing the need for further

investigation of ACL outcomes in the young adult patient.

#### *Limitations*

This study is not without limitations. First and foremost is the small sample size of 35 patients. The study is likely underpowered and the small sample size limits the validity and generalizability of our findings. Despite the small sample size and its impact on the strength of this study's conclusions, this study provides clinically useful information and presents a basis for further analysis of sex-based outcomes in the young adult population. Secondly, this study relied upon patient recall which predisposes these findings to recall and observer bias. These biases were attempted to be lessened by corroborating electronic medical records with the patient reports. Finally, patients included in this analysis received surgery from multiple orthopedic surgeons, therefore presenting possible confounders outside of patient age and sex.

#### **CONCLUSION**

Overall, males and females under the age of 26 who underwent ACLR had similar 5-year outcomes with regard to patient-reported outcomes scores after surgical intervention. Reoperation rate for males and females also demonstrated no statistically significant difference. The results of this study suggest ACLR is effective in males and females. Further research is necessary however to better understand the role of sex and young age on ACLR outcomes.

#### **Conflict of Interest Statement**

Brian M. Grawe, MD, reports being a board/committee member for the American Orthopaedic Society for Sports Medicine, American Shoulder and Elbow Surgeons, and Journal of Shoulder and Elbow Surgery, and being a paid consultant for Mitek and Zimmer.

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