Failure Rates of Autograft and Allograft ACL Reconstruction in Patients 19 Years of Age and Younger

A Systematic Review and Meta-Analysis

Aristides I. Cruz Jr., MD, MBA, Jennifer J. Beck, MD, Matthew D. Ellington, MD, Stephanie W. Mayer, MD, Andrew T. Pennock, MD, Zachary S. Stinson, MD, Curtis D. VandenBerg, MD, Brooke Barrow, BA, Burke Gao, MD, and Henry B. Ellis Jr., MD

Investigation performed at the Department of Orthopaedic Surgery, Warren Alpert Medical School of Brown University, Providence, Rhode Island

Background: Graft choice for pediatric anterior cruciate ligament reconstruction (ACLR) is determined by several factors. There is limited information on the use and outcomes of allograft ACLR in pediatric patients. The purpose of this systematic review and meta-analysis was to quantify reported failure rates of allograft versus autograft ACLR in patients ≤19 years of age with ≥2 years of follow-up. We hypothesized that there would be higher rates of failure for allograft compared with autograft ACLR in this population.

Methods: PubMed/MEDLINE and Embase databases were systematically searched for literature regarding allograft and autograft ACLR in pediatric/adolescent patients. Articles were included if they described a cohort of patients with average age of ≤19 years, had a minimum of 2 years of follow-up, described graft failure as an outcome, and had a Level of Evidence grade of I to III. Qualitative review and quantitative meta-analysis were performed to compare graft failure rates. A random-effects model was created to compare failure events in patients receiving allograft versus autograft in a pairwise fashion. Data analysis was completed using RevMan 5.3 software (The Cochrane Collaboration).

Results: The database search identified 1,604 studies; 203 full-text articles were assessed for eligibility. Fourteen studies met the inclusion criteria for qualitative review; 5 studies were included for quantitative meta-analysis. Bone-patellar tendon-bone (BTB) represented 58.2% (n = 1,012) of the autografts, and hamstring grafts represented 41.8% (n = 727). Hybrid allografts (autograft + supplemental allograft) represented 12.8% (n = 18) of all allograft ACLRs (n = 141). The unweighted, pooled failure rate for each graft type was 8.5% for BTB, 16.6% for hamstring, and 25.5% for allograft. Allografts were significantly more likely than autografts to result in graft failure (odds ratio, 3.87; 95% confidence interval, 2.24 to 6.69).

Conclusions: Allograft ACLR in pediatric and adolescent patients should be used judiciously, as existing studies revealed a significantly higher failure rate for allograft compared with autograft ACLR in this patient population. Additional studies are needed to improve the understanding of variables associated with the high ACLR failure rate among pediatric and adolescent patients.

Level of Evidence: Therapeutic Level III. See Instructions for Authors for a complete description of levels of evidence.

The incidence of pediatric anterior cruciate ligament (ACL) injury and reconstruction is increasing[1-3]. Many factors likely contribute to this increase including increased participation in, and intensity of, youth sports[4,5]. Attitudes regarding early ACL reconstruction (ACLR) in skeletally immature athletes have also shifted as a result of literature

showing increased risk of meniscal and chondral injuries associated with delayed reconstruction[6-12]. Supporting this shift has been literature showing that pediatric ACLR is relatively safe. A recent meta-analysis identified a <5% rate of growth disturbance, with less than one-third of those cases requiring secondary surgery to address this complication[13]. While reported results of pediatric ACLR are generally favorable[14-16], graft rupture has been consistently shown to occur at higher rates in this young, active population[17,18]. The increased incidence of graft rupture in this group highlights the need to identify and address potentially mitigating factors, including associated injuries (e.g., meniscal tear), postoperative rehabilitation protocols, return to sport clearance/timing, and graft choice[19,20].

Graft choice for pediatric ACLR is determined by several factors, including the amount of skeletal growth remaining, patient size, type of sport played, surgical technique, and surgeon preference. While allograft ACLR has the advantages of eliminating donor-site morbidity, control over the desired graft size, and ease of availability, some studies have shown higher failure rates in younger, more active populations when compared with autograft[13,21,22].

There is limited information on the use and outcomes of allograft ACLR specifically in pediatric patients, as a majority of the literature has evaluated adult populations. The purpose of this systematic review and meta-analysis was to quantify reported failure rates of allograft versus autograft ACLR in patients ≤19 years of age with ≥2 years of follow-up from the primary ACLR. Specifically, we aimed to answer the following: (1) what are the reported failure rates of allograft and autograft ACLR in pediatric/adolescent patients, and (2) do reported graft failure rates differ significantly between allograft and autograft ACLR in pediatric/adolescent patients? We hypothesized that there would be higher rates of failure for allograft compared with autograft ACLR in this patient population.

Materials and Methods

Literature Search

We utilized methods similar to those of a previous investigation[23]. The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines[24] were used to systematically identify literature examining allograft and autograft ACLR in pediatric/adolescent patients. Two university librarians (Brown University, Health Sciences Library) each conducted independent searches of both PubMed (which includes the MEDLINE databases) and Embase databases utilizing search-term combinations described in the Appendix. No time limit ranges were placed on the searches conducted on July 31, 2019, and August 1, 2019.

Eligibility Criteria

All studies found during the initial search were screened by title and abstract. Manuscripts were included in the full-text review if they described autograft and/or allograft ACLR in pediatric patients. If ≥2 studies described the same patient cohort, the most recently published study was included in the final analysis.

Manuscripts were excluded if they primarily described revision ACLR, ACLR + meniscal allograft, primary ACL repair, ACLR + osteotomy, synthetic ACL grafts, nonhuman/animal studies, congenital ACL deficiency, multi-ligamentous knee injury, and imaging studies. Case reports, editorials, nonclinical studies (i.e., basic science, cadaveric, biomechanical), non-English-language articles, technique articles, economic-decision analyses, and meeting abstracts were excluded.

Study Selection

After title/abstract screening, full-text articles were reviewed and included in the final analysis if they met the following criteria: described a cohort of pediatric patients (average age of ≤19 years), had a minimum of 2 years of follow-up, adequately described ACL graft failure as an outcome, and had a Level of Evidence grade of I to III[25]. The average age of ≤19 years was chosen because this age range should be inclusive of those who are high school-aged and younger, an age group that is traditionally thought of as "pediatric/adolescent." Bibliographies of systematic reviews and meta-analyses were manually reviewed for articles not captured by the initial search.

Data Extraction

After relevant full-text articles were selected, the study authors met and finalized the criteria for data extraction. Eight authors (A.I.C., J.J.B., M.D.E., S.W.M., A.T.P., Z.S.S., C.D.V., H.B.E.) extracted relevant data from included studies and recorded them into a spreadsheet. After initial data extraction, 2 authors (A.I.C., B.B.) confirmed extracted data points from individual full-text articles prior to final analysis. Study variables recorded included authors, journal, publication year, number of study subjects, sex, average age and range, average follow-up duration and range, graft type (allograft or autograft), and number of failed grafts by type. Hybrid grafts (e.g., autograft + allograft augmentation) were classified as allografts for the purposes of meta-analysis (since only 1 category could be chosen for proper analysis). Because of inconsistent reporting, graft diameter was not analyzed. Graft failure was defined as graft rupture/failure explicitly described in each individual study on the basis of clinical or radiographic criteria or a return to the operating room for failed ACLR. All included studies were assimilated in our qualitative analysis[21,26-38]. All studies included in the qualitative analysis that adequately reported data for our random-effects model were included in our quantitative meta-analysis. These studies presented data on both ACL autograft and allograft reconstruction within the same study cohort[21,28,31,35,38]. Although Razi et al.[26] reported on both autograft and allograft in the same cohort, this study was not included in the meta-analysis because there were 0 events of interest (e.g., graft failure) in either group.

Risk-of-Bias Assessment

The Newcastle-Ottawa Scale (NOS) for assessing quality in nonrandomized studies was used to evaluate the risk of bias within each study[39]. The NOS is an instrument used to assess the quality of eligible prospective and retrospective cohort studies. The NOS assesses study quality within 3 domains:

selection, comparability, and outcome. According to NOS guidelines, stars (0 to 9) were awarded to each study on the basis of methodological quality. Studies with quality scores of 0 to 3 stars, 4 to 6 stars, and 7 to 9 stars were considered to have had high, moderate, and low risk of bias, respectively. Two authors independently assessed study quality (A.I.C., B.B.); any disagreements were resolved by consensus discussion.

Statistical Methods

A random-effects model was created to compare failure events among patients receiving allograft versus autograft in a pairwise fashion. Our model used an inverse variance approach. A random-effects model instead of a fixed-effects model was chosen because there were likely enough underlying differences between study populations (e.g., surgeon characteristics, follow-up duration, postoperative protocols) that it would not be accurate to assume that there was no heterogeneity in the estimates of ACL failure rates in pooled studies[40]. Data analysis was completed using RevMan 5.3 software (The Cochrane Collaboration).

Results

The database search identified 1,604 studies. After the removal of duplicates and title/abstract screening, 203 full-text articles were assessed for eligibility. Fourteen studies remained after the application of inclusion and exclusion criteria, and 5 studies were included in the quantitative meta-analysis. Figure 1 illustrates the search strategy.

Qualitative Analysis

Individual study characteristics are summarized in Tables I and II. The average age of participants in individual studies ranged from 14 years[27] to 19 years[38], and the average duration of follow-up ranged from 24 months[26] to 240 months[34]. The average age of the pediatric/adolescent cohort could not be determined in 3 studies[29,34,36]. Shelbourne et al.[29] stratified patients by age as <18, 18 to 25, or >25 years but did not describe the average age for the subgroups. Thompson et al.[34] stratified patients as ≤18 or >18 years of age and described the average age of the entire study cohort but did not describe the average age of those ≤18
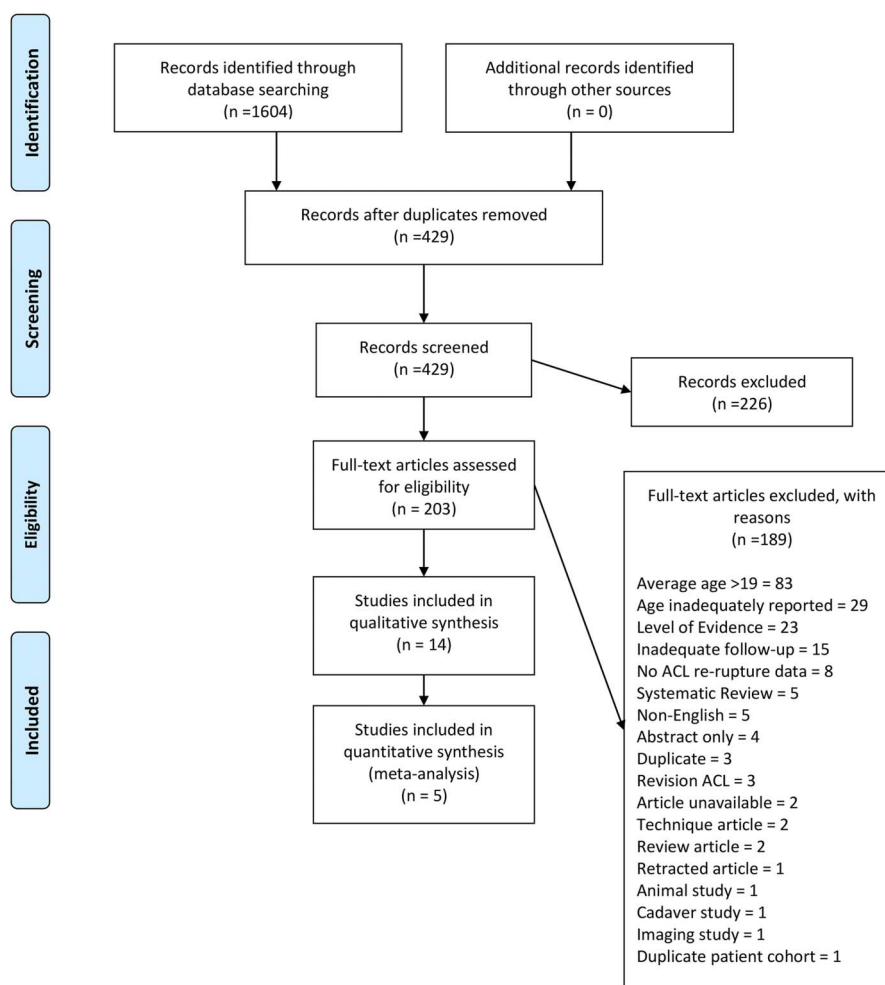

Fig. 1
Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flowchart.

TABLE I Study Summary Characteristics						Allograft†			Autograft†		
Study	LOE -Study Type*	No. of Participants	Age† (yr)	% Female	Duration of Follow-up† (mo)	No.	No. Failed	% Failed	No.	No. Failed	% Failed
Razi[26] (2019)	II - PC	31	14.8 (ND)	32%	24 (ND)	13	0	0%	18 (HS)	0	0%
Salem[31] (2019)	III - CS	256	18.4 (15-25)	100%	43 (30-64)	18 (hybrid autograft/ allograft)	4	22%	175 (BTB), 63 (HS)	12 (BTB), 7 (HS)	7% (BTB), 11% (HS)
Salmon[32] (2018)	III - CC	39	16 (14-18)	67%	ND (≥240)	0	0	NA	39 (HS)	15 (HS)	38% (HS)
Webster[33] (2016)	III - RC	316	17.2 (11-19)	37%	60 (36-120)	0	0	NA	316 (HS)	57 (HS)	18% (HS)
Thompson[34] (2016)	II - PC	29	ND (13-18)	ND	240 (ND)	0	0	NA	14 (BTB), 15 (HS)	7§	24%
Engelman[35] (2014)	III - CC	73	15.4 (11-18)	45%	41.3 (ND)	38	11	29%	35 (HS)	4 (HS)	11%
Webster[36] (2014)	III - CC	110	ND (<20)	ND	57.6 (≥36)	0	0	NA	110 (HS)	15 (HS)	14%
Mascarenhas[37] (2012)	III - CC	46	18 (ND)	57%	54 (24-120)	0	0	NA	23 (BTB), 23 (HS)	0	0%
Ellis et al.[21] (2012)	III - RC	79	16 (14-18)	62%	50.4 (24-135.6)	20	7	35%	59 (BTB)	2 (BTB)	3%
Pallis[38] (2012)	II - PC	120 (122 knees)	19 (18-25)	25%	ND (24-48)	16	7	44%	61 (BTB), 45 (HS)	7 (BTB), 6 (HS)	11% (BTB), 13% (HS)
Koizumi[27] (2013)	III - RC	15	14 (13-16)	47%	38# (25-48)	0	0	NA	15 (HS)	2 (HS)	13% (HS)
Barrett[28] (2011)	III - RC	224	17.8 (12-25)	ND	ND (≥24)	24	7	29%	152 (BTB), 48 (HS)	18 (BTB), 12 (HS)	12% (BTB), 25% (HS)
Shelbourne[29] (2009)	II - PC	528**	ND (14-18)	50%	ND (≥60)	0	0	NA	528 (BTB)	46 (BTB)	9% (BTB)
Sankar[30] (2006)	III - RC	12	15.6 (14-17)	50%	64 (30-97)	12	0	0%	0	0	NA

*LOE = level of evidence, PC = prospective cohort, CS = case series, CC = case-control, and RC = retrospective cohort. †The values are given as the mean, with the range in parentheses, unless otherwise specified. ND = no data. ‡NA = not applicable, BTB = bone-patellar tendon-bone, and HS = hamstring. §No data on graft type. #Median. **Patients ≤18 years of age.

years of age. Webster et al.[36] stratified patients as <20 or ≥20 years of age but did not report the average age in the subgroup <20 years of age. This study was not excluded as we postulated that patients <20 years of age in this subgroup still met our inclusion criteria of ≤19 years of age.

The sex of participants in individual studies ranged from 25% female[38] to 100% female[31]. One study described allograft ACLR only[30], 7 studies described autograft ACLR only[27,29,32-34,36,37], and 6 studies described both ACL allograft and autograft reconstruction within the same cohort[21,26,28,31,35,38].

Regarding autograft ACLR, bone-patellar tendon-bone (BTB) or hamstring grafts were the only autograft types described in the included studies. BTB grafts represented 58.2% (n = 1,012) of the autografts, and hamstring grafts represented 41.8% (n = 727). One study described hybrid ACL allografts and represented 12.8% (n = 18) of all allograft ACLRs (n = 141). The overall pooled autograft failure rate was 12.1%. The overall pooled failure rates for each graft type was 8.5% for BTB and 16.6% for hamstring (with the study by Thompson et al.[34] excluded from the calculation because graft failure was not distinguished between BTB or hamstring grafts). This is compared with a pooled allograft failure rate of 25.5% (26.0% if excluding the hybrid grafts; the hybrid grafts had a failure rate of 22.2% [4 of 18]). It should be noted that the graft failure rates

described above are unweighted rates and are presented for descriptive purposes only. Statistical comparisons were limited to our quantitative meta-analysis described below.

Quantitative Analysis
The results of our statistical analysis are summarized in Figure 2. Five studies were included in the quantitative meta-analysis[21,28,31,35,38]. Allografts were significantly more likely than autografts to result in graft failure (odds ratio [OR], 3.87; 95% confidence interval, 2.24 to 6.69; I^2 = 5%; studies = 5).

Bias Assessment
Tables III and IV show the NOS bias assessment for the included studies. All 14 studies received 7 to 9 stars (low risk of bias): 6 studies had 9 stars, 6 had 8 stars, and 2 had 7 stars.

Discussion
The decision between autograft or allograft ACLR is a common topic of discussion between surgeons and patients. The ideal graft would be safe to harvest with minimal morbidity, mimic biomechanical properties of the native ACL, and minimize graft failure rates. Multiple options for grafts are available, each with unique risks and benefits. Allograft tissue has the

TABLE II Summary of Concomitant Meniscal Procedures, Associated Ligament Injuries, and Definition of Graft Failure				
	Graft Type* (no. [%])			
Study	Meniscal Repair	Meniscectomy	Associated Ligament Injury	Definition of Graft Failure
Razi[26] (2019)	Allo, 4 (30.8%) Auto, 6 (33.3%)	Allo, 2 (15.4%) Auto, 5 (27.8%)	Allo: LCL, 1 (7.7%) MCL, 0 (0%) Auto: LCL, 0 (0%) MCL, 1 (5.6%)	Not explicitly defined
Salem[31] (2019)	BTB, 42 (24%) HS, 29 (46%)	BTB, 32 (18.3%) HS, 15 (23.8%)	Not reported	"Graft rupture" not explicitly defined
Salmon[32] (2018)	HS, 20 (10%)†	HS, 20 (10%)†	Not reported‡	"Graft rupture" not explicitly defined
Webster[33] (2016)	Not reported	Not reported	Not reported	"Medical records… were initially checked to identify patients who had sustained a second ACL injury…"; "… structured questions regarding any further injuries to the ACL-reconstructed knee or the contralateral knee"
Thompson[34] (2016)	HS, 10 (11.1%)† BTB, 7 (7.8%)†	HS, 9 (10%)† BTB, 6 (6.7%)†	Not reported‡	"Graft rupture" not explicitly defined
Engelman[35] (2014)	Allo, 2 (5.3%) Auto, 4 (11.4%)	Allo, 24 (63.2%) Auto, 12 (34.3%)	Not reported	Need for revision ACL surgery and/or MRI (magnetic resonance imaging) confirmation of ACL graft failure
Webster[36] (2014)	Not reported	HS, 207 (36.9%)†	Not reported	Patient self-report. "[They] answered structured questions regarding any further injuries to the ACL-reconstructed knee or the contralateral knee"
Mascarenhas[37] (2012)	BTB, 3 (13%) HS, 5 (21.7%)	BTB, 5 (21.7%) HS, 3 (13%)	None reported (Grade-III collateral ligament injuries excluded)	Not explicitly defined
Ellis[21] (2012)	Not reported	Not reported	Not reported	Patient self-report. "Subjects were also asked if they had sustained a reinjury to the respective knee or if they had undergone revision ACL surgery"
Pallis[38] (2012)	Not reported	Not reported	Not reported	ACL injury verified through MRI and/or diagnostic arthroscopy
Koizumi[27] (2013)	HS, 4 (26.7%)	HS, 2 (13.3%)	Not reported	"Rerupture" not explicitly defined
Barrett[28] (2011)	Not reported	Not reported	Associated collateral ligament injuries excluded	Reconstruction failure defined as 2+ Lachman, positive pivot shift, and KT-1000 results >5 mm side-to-side difference
Shelbourne[29] (2009)	Not reported	Not reported	Not reported	"ACL injury was counted if it had been confirmed by physician examination or if the patient reported the ACL injury on a subjective survey or by phone"
Sankar[30] (2006)	Not reported	Not reported	Allo: MCL, 12 (100%)	Not explicitly defined

*Allo = allograft, Auto = autograft, LCL = lateral collateral ligament, MCL = medial collateral ligament, BTB = bone-patellar tendon-bone autograft, and HS = hamstring. †Percentages of overall cohort (i.e., inclusive of pediatric and adult-aged subgroups). ‡Exclusion criteria = "associated ligament injury requiring surgical treatment."

advantage of less donor-site morbidity and possibly, quicker postoperative recovery. While allograft ACLR has been shown to be relatively safe in adult patients, its use in pediatric patients remains debatable[41,42].

With the present systematic review and meta-analysis, we aimed to assess and compare ACL graft failure rates in pediatric/adolescent patients. Among the included studies, we found failure rates of 8.5% for BTB autograft, 16.6% for hamstring autograft, 22.2% for hybrid autograft/allograft, and 25.5% for allograft ACLR. Our meta-analysis found an almost 4-fold increased risk (OR, 3.87) of failure for allograft compared with autograft (BTB/hamstring) ACLR. These findings are consistent with others in the literature. Kaeding et al. examined results of autograft versus allograft ACLR from the MOON (Multicenter Orthopaedic Outcomes Network) cohort, finding the highest risk of graft failure within the age group of 10 to 19 years in those who received allograft reconstruction[22]. Given these results, the potential benefits of allograft ACLR, compared with autograft
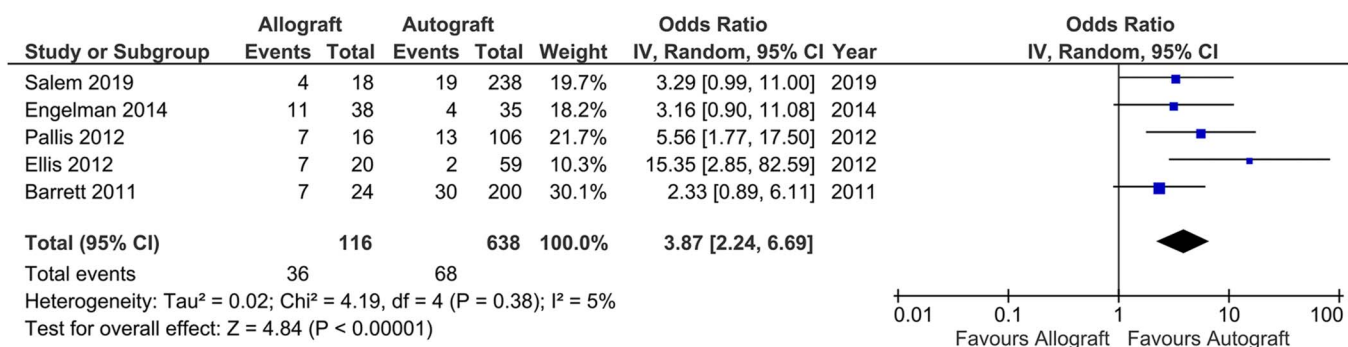
Fig. 2

Forest plot examining the 5 studies that were included in the quantitative meta-analysis. The plot shows that allografts were significantly more likely to result in graft failure compared with autografts (odds ratio, 3.87; 95% confidence interval [CI], 2.24 to 6.69). IV = inverse variance, and df = degrees of freedom.

reconstruction, in pediatric/adolescent patients are outweighed by the risks of graft failure.

Shanmugaraj et al. also performed a systematic review of allograft use in pediatric patients[43]. In their review of the literature, the authors found a 7.9% rate of retear following allograft ACLR, nearly double the reported autograft failure rate (4.2%). That study, however, focused only on skeletally immature patients, and as the rates of ACLR have been shown to be highest among older, high school-aged children[3,44], this limits the generalizability of their findings to younger patients and not necessarily those most at risk for rerupture as a whole. Shanmugaraj et al. concluded that the reported pooled graft failure rate of 7.9% following allograft ACLR in skeletally immature patients was acceptable[43]. On the basis of our findings in the current study,

however, we caution against concluding that allograft ACLR in those ≤19 years of age has acceptable rates of graft failure compared with autograft. Rather, we conclude that the consistently higher reported rate of allograft failure is unacceptable in this young, active population and would advocate for the limited use of allografts in pediatric/adolescent ACLR.

Systematic reviews examining allograft ACLR in adult populations have found different results than those reported in the current study. Mariscalco et al. performed a systematic review and meta-analysis of autograft versus nonirradiated allograft ACLR in patients with an average age of 24.5 to 32 years[41]. They found no differences in the graft failure rate, laxity, or patient-reported outcome scores between the 2 groups. Cvetanovich et al. also performed a systematic review

TABLE III Quality Assessment of the Included Cohort Studies by the Newcastle-Ottawa Scale†								
	Selection				Comparability	Outcome		
Study	Represen-tativeness of Exposed Cohort	Selection of Non-Exposed Cohort	Ascertainment of Exposure	Demonstration That Outcome of Interest Was Not Present at Start of Study	Comparability of Cohort on the Basis of Design or Analysis	Assessment of Outcome	Was Follow-up Long Enough for Outcomes to Occur?	Adequacy of Follow-up of Cohorts
Razi[26] (2019)	*	*	*	*	**	*	*	*
Salem[31] (2019)	*	*	*	*	*	*	*	*
Webster[33] (2016)	*	*	*	*	**	*	*	*
Thompson[34] (2016)	*	*	*	*	**	*	*	*
Ellis[21] (2012)	*	*	*	*	X	*	*	*
Pallis[38] (2012)	*	*	*	*	*	*	*	*
Koizumi[27] (2013)	*	*	*	*	*	*	*	*
Barrett[28] (2011)	*	*	*	*	*	*	*	*
Shelbourne[29] (2009)	*	*	*	*	**	*	*	*
Sankar[30] (2006)	*	*	*	*	X	*	*	*

†Star (*) = item present, and X = item absent. A maximum of 1 star is possible for the Selection and Outcome domains, and a maximum of 2 stars for the Comparability domain.

TABLE IV Quality Assessment of the Included Case-Control Studies by the Newcastle-Ottawa Scale†							
	Selection				Comparability	Exposure		
Study	Adequacy of Case Definition	Representativeness of Cases	Selection of Controls	Definition of Controls	Comparability of Cases and Controls on the Basis of the Design or Analysis	Ascertainment of Exposure	Same Method of Ascertainment for Cases and Controls	Non-response Rate
Salmon et al.[32] (2018)	*	*	*	*	**	*	*	X
Engelman et al.[35] (2014)	*	*	*	*	**	*	*	X
Webster et al.[36] (2014)	*	*	*	*	**	*	*	*
Mascarenhas et al.[37] (2012)	*	*	*	*	**	*	*	*

†Star (*) = item present, and X = item absent. A maximum of 1 star is possible for the Selection and Exposure domains, and a maximum of 2 stars for the Comparability domain.

and meta-analysis of randomized controlled trials, comparing hamstring autograft and soft-tissue allograft in patients with a mean age of 29.9 years, and found no differences in outcomes[42]. It is worth noting, however, that the authors of the above studies cautioned against extrapolating their data to younger patient populations.

There was variability in allograft failure rates across the studies evaluated in our investigation, with rates ranging from 0% to 44%. This is likely multifactorial, but the choice of allograft type or allograft sterilization may play a role. Allograft types include all-soft-tissue grafts and soft-tissue-with-bone-block grafts. Our review did not find any studies directly comparing these different allograft types. It has also been shown that irradiated allografts and allografts treated with certain chemical sterilization techniques have poorer outcomes compared with autograft ACLR[41,45-47], which may be because of delayed graft incorporation or diminished structural integrity of the graft itself[47,48]. The studies that reported on allograft use in our analysis inconsistently reported the allograft type, and only 1 study reported on the specific sterilization process[21]. Because of this, we were unable to elucidate the influence of specific allograft type or sterilization technique on graft failure rates.

Failure rates after ACLR among pediatric/adolescent patients, in general, are higher than those reported for adults, with studies of pediatric ACLR outcomes noting failure rates of 6% to 25%[9,17,27,49-54], whereas failure rates of 1% to 8% have generally been found in studies in the adult literature[53,55-60]. Potential reasons for the higher failure rates among pediatric patients include a return to higher baseline levels of activity, continued musculoskeletal and neuromuscular development, and poorer adherence to activity restrictions during the post-operative rehabilitation period. Given the inherent differences between adult and pediatric/adolescent ACLR outcomes, it is important to distinguish these 2 populations when consolidating and critically evaluating the literature. ACLR in pediatric/adolescent patients should aim to reduce the risk of graft failure in this already vulnerable population, and we believe that this includes avoiding the use of allograft reconstruction, if possible.

Limitations
Limitations of this study include the inherent limitations of systematic reviews and meta-analyses, including the relative paucity of high-quality, nonbiased literature and detailed description of the data reported. We evaluated the included studies with a validated bias-assessment tool[39] and found a low risk of bias. Despite the large number of pediatric ACLRs performed each year[2], there were limited data meeting our inclusion criteria for final analysis. We included only Level-III or higher evidence in an attempt to improve data quality; however, there were only 4 Level-II studies and no Level-I studies available for inclusion. We pooled allograft data in our analysis because of the variability of allograft types used in individual studies. We therefore cannot comment on variations between allograft types or sterilization techniques, or whether certain allografts could be more desirable in pediatric ACLR. The effect on graft failure rates of other variables, such as surgical technique, graft preparation technique, fixation type, postoperative rehabilitation protocols, duration of follow-up, and return to sport evaluations/timing, could not be analyzed given the variable reporting of these data. Additionally, no weighting or adjustment was performed for autograft type (BTB versus hamstring) in our meta-analysis. These are all important considerations when evaluating the risk of ACLR failure, and authors of primary research studies should strive to consistently report these variables. Additionally, we did not specifically examine other clinical outcomes, such as postoperative radiographic changes or patient-reported outcome measures, and therefore cannot comment on these outcomes. Finally, we were required to rely on the age data presented within each study's methods section, but we were unable to reliably pool age data given heterogeneous reporting. We could not, therefore, stratify risk of graft failure on the basis of age within this younger population. Additionally, because we included studies with an average patient age of ≤19

years, there may have been some individual patients who were >19 years of age[28,31,38]. This could have biased the results toward a decreased risk of rerupture in those studies.

Conclusions

Existing studies on ACLR in pediatric/adolescent patients revealed a significantly higher failure rate after allograft reconstruction compared with autograft reconstruction. Allograft ACLR in pediatric/adolescent patients should therefore be used judiciously. Additional studies are needed to improve the understanding of variables associated with the high ACLR failure rate in pediatric/adolescent patients.

Appendix

(eA) Supporting material provided by the authors is posted with the online version of this article as a data supplement at jbjs.org (http://links.lww.com/JBJSOA/A239). ∎

Aristides I. Cruz Jr., MD, MBA[1,2]
Jennifer J. Beck, MD[3]
Matthew D. Ellington, MD[4]
Stephanie W. Mayer, MD[5]
Andrew T. Pennock, MD[6]
Zachary S. Stinson, MD[7]
Curtis D. VandenBerg, MD[8]
Brooke Barrow, BA[1]
Burke Gao, MD[9]
Henry B. Ellis Jr., MD[10]

[1]Department of Orthopaedic Surgery, Warren Alpert Medical School of Brown University, Providence, Rhode Island

[2]Hasbro Children's Hospital, Providence, Rhode Island

[3]Orthopaedic Institute for Children, David Geffen School of Medicine at UCLA, Los Angeles, California

[4]Dell Medical School, The University of Texas at Austin, and Central Texas Pediatric Orthopedics, Austin, Texas

[5]Sports Medicine Center, Department of Orthopaedic Surgery, Children's Hospital Colorado, University of Colorado, Denver, Colorado

[6]Rady Children's Hospital, University of California San Diego, San Diego, California

[7]Nemours Children's Hospital, University of Central Florida, Orlando, Florida

[8]Children's Hospital of Los Angeles, Keck School of Medicine of USC, Los Angeles, California

[9]Department of Orthopaedic Surgery, University of Iowa Hospitals and Clinics, Iowa City, Iowa

[10]Texas Scottish Rite Hospital for Children, University of Texas Southwestern, Dallas, Texas

Email address for A.I. Cruz Jr.: aristides_cruz@brown.edu

ORCID iD for A.I. Cruz Jr.: 0000-0003-0368-9731
ORCID iD for J.J. Beck: 0000-0001-9235-6407
ORCID iD for M.D. Ellington: 0000-0002-2289-205X
ORCID iD for S.W. Mayer: 0000-0002-9432-8191
ORCID iD for A.T. Pennock: 0000-0002-8628-5603
ORCID iD for Z.S. Stinson: 0000-0003-2431-797X
ORCID iD for C.D. VandenBerg: 0000-0003-1131-4227
ORCID iD for B. Barrow: 0000-0002-2947-1506
ORCID iD for B. Gao: 0000-0002-6877-1659
ORCID iD for H.B. Ellis Jr.: 0000-0001-5444-094X

References

1. Buller LT, Best MJ, Baraga MG, Kaplan LD. Trends in anterior cruciate ligament reconstruction in the United States. Orthop J Sports Med. 2014 Dec 26;3(1): 2325967114563664.

2. Tepolt FA, Feldman L, Kocher MS. Trends in pediatric ACL reconstruction from the PHIS database. J Pediatr Orthop. 2018 Oct;38(9):e490-4.

3. Dodwell ER, Lamont LE, Green DW, Pan TJ, Marx RG, Lyman S. 20 years of pediatric anterior cruciate ligament reconstruction in New York State. Am J Sports Med. 2014 Mar;42(3):675-80. Epub 2014 Jan 29.

4. Jayanthi NA, LaBella CR, Fischer D, Pasulka J, Dugas LR. Sports-specialized intensive training and the risk of injury in young athletes: a clinical case-control study. Am J Sports Med. 2015 Apr;43(4):794-801. Epub 2015 Feb 2.

5. Frank JS, Gambacorta PL. Anterior cruciate ligament injuries in the skeletally immature athlete: diagnosis and management. J Am Acad Orthop Surg. 2013 Feb; 21(2):78-87.

6. Lawrence JTR, Argawal N, Ganley TJ. Degeneration of the knee joint in skeletally immature patients with a diagnosis of an anterior cruciate ligament tear: is there harm in delay of treatment? Am J Sports Med. 2011 Dec;39(12):2582-7. Epub 2011 Sep 14.

7. McCarroll JR, Rettig AC, Shelbourne KD. Anterior cruciate ligament injuries in the young athlete with open physes. Am J Sports Med. 1988 Jan-Feb;16(1):44-7.

8. Dumont GD, Hogue GD, Padalecki JR, Okoro N, Wilson PL. Meniscal and chondral injuries associated with pediatric anterior cruciate ligament tears: relationship of treatment time and patient-specific factors. Am J Sports Med. 2012 Sep;40(9): 2128-33. Epub 2012 Jun 22.

9. Anderson AF, Anderson CN. Correlation of meniscal and articular cartilage injuries in children and adolescents with timing of anterior cruciate ligament reconstruction. Am J Sports Med. 2015 Feb;43(2):275-81. Epub 2014 Dec 12.

10. Ekås GR, Moksnes H, Grindem H, Risberg MA, Engebretsen L. Coping with anterior cruciate ligament injury from childhood to maturation: a prospective case series of 44 patients with mean 8 years' follow-up. Am J Sports Med. 2019 Jan; 47(1):22-30. Epub 2018 Nov 26.

11. Crawford EA, Young LJ, Bedi A, Wojtys EM. The effects of delays in diagnosis and surgical reconstruction of ACL tears in skeletally immature individuals on subsequent meniscal and chondral injury. J Pediatr Orthop. 2019 Feb;39(2):55-8.

12. Ramski DE, Kanj WW, Franklin CC, Baldwin KD, Ganley TJ. Anterior cruciate ligament tears in children and adolescents: a meta-analysis of nonoperative versus operative treatment. Am J Sports Med. 2014 Nov;42(11):2769-76. Epub 2013 Dec 4.

13. Wong SE, Feeley BT, Pandya NK. Complications after pediatric ACL reconstruction: a meta-analysis. J Pediatr Orthop. 2019 Sep;39(8):e566-71.

14. Cruz AI Jr, Fabricant PD, McGraw M, Rozell JC, Ganley TJ, Wells L. All-epiphyseal ACL reconstruction in children: review of safety and early complications. J Pediatr Orthop. 2017 Apr/May;37(3):204-9.

15. Kocher MS, Heyworth BE, Fabricant PD, Tepolt FA, Micheli LJ. Outcomes of physeal-sparing ACL reconstruction with iliotibial band autograft in skeletally immature prepubescent children. J Bone Joint Surg Am. 2018 Jul 5;100(13):1087-94.

16. Cordasco FA, Black SR, Price M, Wixted C, Heller M, Asaro LA, Nguyen J, Green DW. Return to sport and reoperation rates in patients under the age of 20 after primary anterior cruciate ligament reconstruction: risk profile comparing 3 patient groups predicated upon skeletal age. Am J Sports Med. 2019 Mar;47(3):628-39. Epub 2019 Jan 15.

17. Dekker TJ, Godin JA, Dale KM, Garrett WE, Taylor DC, Riboh JC. Return to sport after pediatric anterior cruciate ligament reconstruction and its effect on

subsequent anterior cruciate ligament injury. J Bone Joint Surg Am. 2017 Jun 7; 99(11):897-904.

18. Dekker TJ, Rush JK, Schmitz MR. What's new in pediatric and adolescent anterior cruciate ligament injuries? J Pediatr Orthop. 2018 Mar;38(3):185-92.

19. King E, Richter C, Jackson M, Franklyn-Miller A, Falvey E, Myer GD, Strike S, Withers D, Moran R. Factors influencing return to play and second anterior cruciate ligament injury rates in level 1 athletes after primary anterior cruciate ligament reconstruction: 2-year follow-up on 1432 reconstructions at a single center. Am J Sports Med. 2020 Mar;48(4):812-24. Epub 2020 Feb 7.

20. Webster KE, Feller JA, Kimp AJ, Whitehead TS. Revision anterior cruciate ligament reconstruction outcomes in younger patients: medial meniscal pathology and high rates of return to sport are associated with third ACL injuries. Am J Sports Med. 2018 Apr;46(5):1137-42. Epub 2018 Jan 30.

21. Ellis HB, Matheny LM, Briggs KK, Pennock AT, Steadman JR. Outcomes and revision rate after bone-patellar tendon-bone allograft versus autograft anterior cruciate ligament reconstruction in patients aged 18 years or younger with closed physes. Arthroscopy. 2012 Dec;28(12):1819-25. Epub 2012 Oct 24.

22. Kaeding CC, Aros B, Pedroza A, Pifel E, Amendola A, Andrish JT, Dunn WR, Marx RG, McCarty EC, Parker RD, Wright RW, Spindler KP. Allograft versus autograft anterior cruciate ligament reconstruction: predictors of failure from a MOON prospective longitudinal cohort. Sports Health. 2011 Jan;3(1):73-81.

23. Gao B, Dwivedi S, Milewski MD, Cruz AI Jr. Lack of sleep and sports injuries in adolescents: a systematic review and meta-analysis. J Pediatr Orthop. 2019 May/ Jun;39(5):e324-33.

24. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ. 2009 Jul 21;339:b2700.

25. Durieux N, Pasleau F, Howick J; OCEBM Levels of Evidence Working Group. The Oxford 2011 levels of evidence. Oxford Centre for Evidence-Based Medicine. 2012. Accessed 2020 Oct 16. https://www.cebm.ox.ac.uk/resources/levels-of-evidence/ocebm-levels-of-evidence

26. Razi M, Moradi A, Safarcherati A, Askari A, Arasteh P, Ziabari EZ, Dadgostar H. Allograft or autograft in skeletally immature anterior cruciate ligament reconstruction: a prospective evaluation using both partial and complete transphyseal techniques. J Orthop Surg Res. 2019 Mar 21;14(1):85.

27. Koizumi H, Kimura M, Kamimura T, Hagiwara K, Takagishi K. The outcomes after anterior cruciate ligament reconstruction in adolescents with open physes. Knee Surg Sports Traumatol Arthrosc. 2013 Apr;21(4):950-6. Epub 2012 May 16.

28. Barrett AM, Craft JA, Replogle WH, Hydrick JM, Barrett GR. Anterior cruciate ligament graft failure: a comparison of graft type based on age and Tegner activity level. Am J Sports Med. 2011 Oct;39(10):2194-8. Epub 2011 Jul 22.

29. Shelbourne KD, Gray T, Haro M. Incidence of subsequent injury to either knee within 5 years after anterior cruciate ligament reconstruction with patellar tendon autograft. Am J Sports Med. 2009 Feb;37(2):246-51. Epub 2008 Dec 24.

30. Sankar WN, Wells L, Sennett BJ, Wiesel BB, Ganley TJ. Combined anterior cruciate ligament and medial collateral ligament injuries in adolescents. J Pediatr Orthop. 2006 Nov-Dec;26(6):733-6.

31. Salem HS, Varzhapetyan V, Patel N, Dodson CC, Tjoumakaris FP, Freedman KB. Anterior cruciate ligament reconstruction in young female athletes: patellar versus hamstring tendon autografts. Am J Sports Med. 2019 Jul;47(9):2086-92. Epub 2019 Jun 24.

32. Salmon LJ, Heath E, Akrawi H, Roe JP, Linklater J, Pinczewski LA. 20-year outcomes of anterior cruciate ligament reconstruction with hamstring tendon autograft: the catastrophic effect of age and posterior tibial slope. Am J Sports Med. 2018 Mar;46(3):531-43. Epub 2017 Dec 15.

33. Webster KE, Feller JA. Exploring the high reinjury rate in younger patients undergoing anterior cruciate ligament reconstruction. Am J Sports Med. 2016 Nov; 44(11):2827-32. Epub 2016 Jul 7.

34. Thompson SM, Salmon LJ, Waller A, Linklater J, Roe JP, Pinczewski LA. Twenty-year outcome of a longitudinal prospective evaluation of isolated endoscopic anterior cruciate ligament reconstruction with patellar tendon or hamstring autograft. Am J Sports Med. 2016 Dec;44(12):3083-94. Epub 2016 Aug 4.

35. Engelman GH, Carry PM, Hitt KG, Polousky JD, Vidal AF. Comparison of allograft versus autograft anterior cruciate ligament reconstruction graft survival in an active adolescent cohort. Am J Sports Med. 2014 Oct;42(10):2311-8. Epub 2014 Jul 31.

36. Webster KE, Feller JA, Leigh WB, Richmond AK. Younger patients are at increased risk for graft rupture and contralateral injury after anterior cruciate ligament reconstruction. Am J Sports Med. 2014 Mar;42(3):641-7. Epub 2014 Jan 22.

37. Mascarenhas R, Tranovich MJ, Kropf EJ, Fu FH, Harner CD. Bone-patellar tendon-bone autograft versus hamstring autograft anterior cruciate ligament reconstruction in the young athlete: a retrospective matched analysis with 2-10 year follow-up. Knee Surg Sports Traumatol Arthrosc. 2012 Aug;20(8):1520-7. Epub 2011 Nov 3.

38. Pallis M, Svoboda SJ, Cameron KL, Owens BD. Survival comparison of allograft and autograft anterior cruciate ligament reconstruction at the United States Military Academy. Am J Sports Med. 2012 Jun;40(6):1242-6. Epub 2012 Apr 24.

39. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality if nonrandomized studies in meta-analyses. 2012. Accessed 2020 Oct 16. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp

40. Riley RD, Higgins JPT, Deeks JJ. Interpretation of random effects meta-analyses. BMJ. 2011 Feb 10;342:d549.

41. Mariscalco MW, Magnussen RA, Mehta D, Hewett TE, Flanigan DC, Kaeding CC. Autograft versus nonirradiated allograft tissue for anterior cruciate ligament reconstruction: a systematic review. Am J Sports Med. 2014 Feb;42(2):492-9. Epub 2013 Aug 8.

42. Cvetanovich GL, Mascarenhas R, Saccomanno MF, Verma NN, Cole BJ, Bush-Joseph CA, Bach BR. Hamstring autograft versus soft-tissue allograft in anterior cruciate ligament reconstruction: a systematic review and meta-analysis of randomized controlled trials. Arthroscopy. 2014 Dec;30(12):1616-24. Epub 2014 Aug 6.

43. Shanmugaraj A, de Sa D, Skelly MM, Duong A, Simunovic N, Musahl V, Peterson DC, Ayeni OR. Primary allograft ACL reconstruction in skeletally immature patients-a systematic review of surgical techniques, outcomes, and complications. J Knee Surg. 2019 Jul;32(7):673-85. Epub 2018 Jul 10.

44. Beck NA, Lawrence JTR, Nordin JD, DeFor TA, Tompkins M. ACL tears in school-aged children and adolescents over 20 years. Pediatrics. 2017 Mar;139(3): e20161877.

45. Zeng C, Gao SG, Li H, Yang T, Luo W, Li YS, Lei GH. Autograft versus allograft in anterior cruciate ligament reconstruction: a meta-analysis of randomized controlled trials and systematic review of overlapping systematic reviews. Arthroscopy. 2016 Jan;32(1):153-63.e18. Epub 2015 Oct 21.

46. Tian S, Wang B, Liu L, Wang Y, Ha C, Li Q, Yang X, Sun K. Irradiated hamstring tendon allograft versus autograft for anatomic double-bundle anterior cruciate ligament reconstruction: midterm clinical outcomes. Am J Sports Med. 2016 Oct; 44(10):2579-88. Epub 2016 Jul 27.

47. Lansdown DA, Riff AJ, Meadows M, Yanke AB, Bach BR Jr. What factors influence the biomechanical properties of allograft tissue for ACL reconstruction? A systematic review. Clin Orthop Relat Res. 2017 Oct;475(10):2412-26.

48. Malinin TI, Levitt HL, Bashore C, Temple HT, Mnaymneh W. A study of retrieved allografts used to replace anterior cruciate ligaments. Arthroscopy. 2002 Feb;18(2):163-70.

49. Aichroth PM, Patel DV, Zorrilla P. The natural history and treatment of rupture of the anterior cruciate ligament in children and adolescents. A prospective review. J Bone Joint Surg Br. 2002 Jan;84(1):38-41.

50. Magnussen RA, Meschbach NT, Kaeding CC, Wright RW, Spindler KP. ACL graft and contralateral ACL tear risk within ten years following reconstruction: a systematic review. JBJS Rev. 2015 Jan 20;3(1):01874474-201501000-00002.

51. Nelson IR, Chen J, Love R, Davis BR, Maletis GB, Funahashi TT. A comparison of revision and rerupture rates of ACL reconstruction between autografts and allografts in the skeletally immature. Knee Surg Sports Traumatol Arthrosc. 2016 Mar;24(3): 773-9. Epub 2016 Feb 9.

52. Peterson DC, Ayeni OR. Pediatric anterior cruciate ligament reconstruction outcomes. Curr Rev Musculoskelet Med. 2016 Dec;9(4):339-47.

53. Sanders TL, Pareek A, Hewett TE, Levy BA, Dahm DL, Stuart MJ, Krych AJ. Long-term rate of graft failure after ACL reconstruction: a geographic population cohort analysis. Knee Surg Sports Traumatol Arthrosc. 2017 Jan;25(1):222-8. Epub 2016 Aug 13.

54. Kay J, Memon M, Marx RG, Peterson D, Simunovic N, Ayeni OR. Over 90 % of children and adolescents return to sport after anterior cruciate ligament reconstruction: a systematic review and meta-analysis. Knee Surg Sports Traumatol Arthrosc. 2018 Apr;26(4):1019-36. Epub 2018 Jan 13.

55. Kaeding CC, Pedroza AD, Reinke EK, Huston LJ, Hewett TE, Flanigan DC, Spindler KP; MOON Knee Group. Change in anterior cruciate ligament graft choice and outcomes over time. Arthroscopy. 2017 Nov;33(11):2007-14. Epub 2017 Aug 26.

56. Wright RW, Dunn WR, Amendola A, Andrish JT, Flanigan DC, Jones M, Kaeding CC, Marx RG, Matava MJ, McCarty EC, Parker RD, Vidal A, Wolcott M, Wolf BR, Spindler KP; MOON Cohort. Anterior cruciate ligament revision reconstruction: two-year results from the MOON cohort. J Knee Surg. 2007 Oct;20(4):308-11.

57. Spindler KP, Wright RW. Clinical practice. Anterior cruciate ligament tear. N Engl J Med. 2008 Nov 13;359(20):2135-42.

58. Wright RW, Dunn WR, Amendola A, Andrish JT, Bergfeld J, Kaeding CC, Marx RG, McCarty EC, Parker RD, Wolcott M, Wolf BR, Spindler KP. Risk of tearing the intact anterior cruciate ligament in the contralateral knee and rupturing the anterior cruciate ligament graft during the first 2 years after anterior cruciate ligament reconstruction: a prospective MOON cohort study. Am J Sports Med. 2007 Jul;35(7): 1131-4. Epub 2007 Apr 23.

59. Wright RW, Magnussen RA, Dunn WR, Spindler KP. Ipsilateral graft and contralateral ACL rupture at five years or more following ACL reconstruction: a systematic review. J Bone Joint Surg Am. 2011 Jun 15;93(12):1159-65.

60. Maletis GB, Chen J, Inacio MCS, Love RM, Funahashi TT. Increased risk of revision after anterior cruciate ligament reconstruction with soft tissue allografts compared with autografts: graft processing and time make a difference. Am J Sports Med. 2017 Jul;45(8):1837-44. Epub 2017 Mar 16.