Allograft Augmentation of Hamstring Autograft for Younger Patients Undergoing Anterior Cruciate Ligament Reconstruction: Clinical and Cost-Effectiveness Analyses

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Background: Younger patients and those with smaller hamstring autograft diameters have been shown to be at significantly greater risk of graft failure after anterior cruciate ligament (ACL) reconstruction. To date, there is no information in the literature about the clinical success and/or cost-effectiveness of increasing graft diameter by augmenting with semitendinosus allograft tissue for younger patients.

Hypothesis: Hybrid hamstring grafts are a cost-effective treatment option because of a reduced rate of graft failure.

Study Design: Cohort study (economic and decision analysis); Level of evidence, 3.

Methods: We retrospectively identified patients younger than 18 years who had undergone ACL reconstruction by a single surgeon between 2010 and 2015. During this period, the operating surgeon’s graft selection algorithm included the use of bone–patellar tendon–bone (BTB) autografts for the majority of patients younger than 18 years. However, hamstring autografts (hamstring) or hybrid hamstring autografts with allograft augment (hybrid) were used in skeletally immature patients and in those whom the surgeon felt might have greater difficulty with postoperative rehabilitation after BTB graft harvest. Patient demographics, graft type, graft diameter, the time the patient was cleared to return to activity, and the need for secondary surgical procedures were compared between the hamstring and hybrid groups. The clinical results were then used to assess the potential cost-effectiveness of hybrid grafts in this select group of young patients with an ACL injury or reconstruction.

Results: This study comprised 88 patients (hamstring group, n = 46; hybrid group, n = 42). The 2 groups did not differ in terms of age, sex, timing of return to activity, or prevalence of skeletally immature patients. Graft diameters were significantly smaller in the hamstring group (7.8 vs 9.9 mm; \( P < .001 \)), which corresponded with a significantly greater rate of graft failure (13 of 46 [28.3%] vs 5 of 42 [11.9%]; \( P = .049 \)). As a result of the reduced revision rate, the hybrid graft demonstrated incremental cost savings of US$2765 compared with the hamstring graft, and the hybrid graft was the preferred strategy in 89% of cases.

Conclusion: Driven by increased graft diameters and the reduced risk of revision, hybrid grafts appear to be a more cost-effective treatment option in a subset of younger patients with an ACL injury.

Keywords: ACL; graft failure; complication; adolescent
increasing graft diameter results in increased tensile strength of the graft and reduced anterior laxity. Clinically, this has translated to a significantly lower likelihood of revision ACL reconstruction as graft diameter is increased from 7 to 9 mm.

As such, increasing graft diameter may offer clinicians a potential method to mitigate the increased risk of graft failure for younger patients. In response to the inferior results with small diameter hamstring autografts published in 2012, we began augmenting our hamstring autografts with semitendinosus allografts in select patient populations with the goal of increasing graft diameter. Although these so-called hybrid grafts created using different allograft tissue and graft preparation techniques have demonstrated poor clinical results, our anecdotal clinical experience has been more favorable. Therefore, this study aimed to (1) evaluate the clinical success of increasing graft diameter by augmenting hamstring autografts with semitendinosus allograft tissue and (2) determine whether hybrid hamstring grafts provide a cost-effective alternative to hamstring autografts in this subset of patients. We hypothesized that the initial costs of the allograft tissue with the hybrid graft would be offset by a significant reduction in the need for revision ACL reconstruction, thus providing a cost-effective alternative to hamstring autografts in this subset of younger patients with an ACL injury.

METHODS

Patients

The University of Kentucky institutional review board approved this study (protocol no. 16-0077-P1H). This study included all patients younger than 18 years who had undergone primary ACL reconstruction between 2010 and 2015 with hamstring autograft, either with or without allograft semitendinosus augmentation. Throughout the study period, the operating surgeon’s (D.L.J.) graft selection algorithm involved the use of bone–patellar tendon–bone (BTB) autografts in the majority of patients younger than 18 years. Hamstring autografts were selectively utilized in skeletally immature patients and in those whom the senior author determined to be at high risk of not tolerating the postoperative rehabilitation associated with a BTB autograft. Preoperative factors associated with the patient not being able to tolerate BTB postoperative rehabilitation included failure to achieve adequate range of motion during preoperative physical therapy, demonstrated poor pain tolerance, or poor engagement in preoperative physical therapy. After the inferior results of smaller diameter hamstring autografts published in 2012, hamstring autografts continued to be used in the same patient population. However, beginning in August 2012, these grafts were consistently augmented with semitendinosus allograft tissue to increase the overall graft diameter.

To compare clinical results of the 2 grafts, we identified patients younger than 18 years who had undergone ACL reconstruction by a single surgeon between 2010 and 2015 with either a hamstring autograft (hamstring) or hybrid autograft with allograft augment (hybrid). Similar surgical technique, pre- and postoperative rehabilitation, and objective return-to-play criteria were used for both groups as directed by the single senior surgeon. Patients undergoing revision procedures, with multiligament injuries, or with follow-up less than 18 months were excluded.

Surgical Technique

Gracilis and semitendinosus autograft harvest was identical between those receiving either hamstring or hybrid grafts. The gracilis and semitendinosus tendons were first harvested via longitudinal incision approximately 4 cm in length, starting 2 cm distal and 2 cm medial to the tibial tubercle. Dissection was continued to the sartorial fascia and the gracilis and semitendinosus tendons were palpated. The sartorial fascia was then incised horizontally between the 2 tendons. The gracilis tendon insertion site was visualized deep to the sartorial fascia and subsequently whipstitched with a nonabsorbable No. 2 TiCron suture (Medline Industries). The insertion was then sharply incised and adhesions around the gracilis tendon were released. A closed tendon stripper was used to perform the harvest. After the gracilis was harvested, the semitendinosus tendon was harvested in a similar manner.

After harvest of the gracilis and semitendinosus tendons was completed, both tendons were brought to the back table. Muscle tissue was removed and a No. 2 TiCron suture was used to whipstitch the proximal ends of both tendons. For those receiving a hybrid graft, the semitendinosus allograft was similarly whipstitched on both ends. The allograft was passed first, then the autograft around the allograft, with the end goal of having as little of the allograft tissue exposed to the knee joint milieu in vivo. Allograft tissue was provided by LifeNet Health Inc, and all grafts were sterilized using the Allowash XG process (LifeNet Health Inc) including 1.2 to 1.9 Mrad irradiation. The allograft strands were then placed in the middle of the autograft strands, and the entire graft was doubled over, forming 6 strands with the semitendinosus allograft in

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One or more of the authors has declared the following potential conflict of interest or source of funding: D.L.J. has intellectual property with, is a paid consultant of, and has received royalties and research support from Smith & Nephew.
A cortical suspension fixation device (Endobutton; Smith & Nephew) was added to the looped end while the free ends were pulled to tension using a graft tensioning device (Graftmaster; Smith & Nephew). Beginning at the looped end of the graft, a Cobraid (Smith & Nephew) suture was used to bundle the tendons together. The suture was run down toward the nonlooped end of the graft, stopping several centimeters from the loose ends, allowing the tendon ends to be separated later for backup tibial fixation. The suture was then run back down the opposite side of the graft. The graft was soaked in mineral oil under tension until ready for insertion into the knee, with the mineral oil acting as a lubricant to help pass the graft.31

For both hamstring and hybrid grafts, the femoral tunnel was drilled using an accessory medial portal, and both tibial and femoral tunnels were reamed to the nearest 0.5 mm equal to or greater than the measured diameter of the graft. Femoral fixation was achieved using an Endobutton as the suspensory fixation, and tibial fixation was achieved using a BioRCI (Smith & Nephew) bioabsorbable interference screw in the tibial tunnel. For backup tibial fixation, the free tendon ends were wrapped around a bicortical 4.5-mm large fragment screw, which was then tightened down with a 20-mm Geofit washer (DePuy Mitek).

Clinical Data Collection and Statistical Analyses

For the current analysis, “graft failure” was operationally defined as patient-reported instability that affected the patient’s ability to perform activities of daily living or sporting activities, pathological laxity during the physical examination (positive Lachman test, marked anterior laxity, or a positive pivot-shift test compared with the healthy knee), or evidence of a failed graft on magnetic resonance imaging or during arthroscopy. Any patient that met these criteria was considered to have a failed graft regardless of whether the patient chose to undergo revision ACL reconstruction.23,32

Patient demographics, graft type, graft diameter, the time the patient was cleared to return to activity, as well as the presence and timing of graft failure were recorded. This information was located by reviewing all orthopaedic clinical notes and operative notes from each patient’s electronic health record. In an attempt to minimize the number of patients lost to follow-up, we also reviewed the Kentucky electronic health information exchange database for any knee-related office visits or surgeries for which the patient’s knee was the primary complaint. The state-based exchange does not contain information on the state’s entire population, but reporting is mandatory for all patients with Medicaid and is optional for all others. The exchange has more than 1300 medical facilities actively submitting and exchanging live data.

Continuous variables were compared with independent t tests and categorical variables were compared between hamstring and hybrid groups using 1-tailed chi-square or

Figure 1. Augmentation of the hamstring autograft with a semitendinosus allograft. (A) Gracilis and semitendinosus autografts are combined with a semitendinosus allograft (asterisk). The allograft strand is positioned on the interior of the graft. (B) When the graft is doubled, a 6-strand graft is created, with 2 allograft strands on the inside surrounded by the 4 hamstring autografts on the outside, leaving the allograft tissue less directly exposed to the knee joint milieu in vivo. Free tendon ends are visible on the nonlooped side of the graft. These tendon ends are later wrapped around a bicortical 4.5-mm screw and secured with a spiked washer for backup tibial fixation.

Figure 2. The simplified decision tree used to compare the base case cost-effectiveness of hamstring autografts with or without being augmented with semitendinosus allograft tissue. ACL, anterior cruciate ligament.
Fisher exact tests as appropriate. A binary regression (forward entry, Wald method) was used to determine whether a model containing a combination of patient sex, age, body mass index (BMI), duration of follow-up, graft type, or graft diameter could accurately predict graft failure. For all analyses, an alpha level of \( P \leq .05 \) was considered statistically significant.

Cost-Effectiveness Analysis

The clinical results were then used to compare the potential cost-effectiveness and value provided by hybrid grafts. This study made the following assumptions: (1) the subset of patients was similar to the patients included in the clinical portion of this study (ie, patients younger than 18 years who were suspected of potentially not tolerating BTB postoperative rehabilitation), (2) patients underwent equivalent preoperative treatment with equivalent costs, (3) patients did not suffer a contralateral ACL injury during the study period, and (4) those with complications or graft failures occurring after a tertiary surgery remained at the current health state (primary surgery, index ACL reconstruction; secondary surgery, revision ACL reconstruction or reoperation because of infection or arthrofibrosis; and tertiary surgery, second revision ACL reconstruction or second reoperation for infection or arthrofibrosis) (Figure 2).

The base case cost-effectiveness was assessed using Monte Carlo microsimulation of a simplified decision-tree

### TABLE 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline Value</th>
<th>Probabilistic Sensitivity Analysis Distribution</th>
<th>Source</th>
</tr>
</thead>
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<tr>
<td><strong>Probabilities of Complications After Primary ACL Reconstruction</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Revision for graft failure</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Hamstring</td>
<td>0.283</td>
<td>Beta</td>
<td>Current study</td>
</tr>
<tr>
<td>Hybrid</td>
<td>0.119</td>
<td>Beta</td>
<td>Current study</td>
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<tr>
<td>Arthrofibrosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hamstring</td>
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<td>Beta</td>
<td>Current study</td>
</tr>
<tr>
<td>Hybrid</td>
<td>0.048</td>
<td>Beta</td>
<td>Current study</td>
</tr>
<tr>
<td>Instability</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Hamstring</td>
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<td>Beta</td>
<td>Genuario et al\textsuperscript{12}</td>
</tr>
<tr>
<td>Hybrid</td>
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<td>Beta</td>
<td>Genuario et al\textsuperscript{12}</td>
</tr>
<tr>
<td>Infection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hamstring</td>
<td>0.013</td>
<td>Beta</td>
<td>Brophy et al\textsuperscript{4}</td>
</tr>
<tr>
<td>Hybrid</td>
<td>0.013</td>
<td>Beta</td>
<td>Brophy et al\textsuperscript{4}</td>
</tr>
</tbody>
</table>

| **Probabilities of Secondary Complications** |               |                                               |        |
| (Assumed to Be Similar for Both Hamstring and Hybrid) |               |                                               |        |
| After revision ACL reconstruction              |                |                                               |        |
| Rerevision for graft failure                   | 0.095          | Beta                                          | Reinhardt et al\textsuperscript{26} |
| Arthrofibrosis                                 | 0.068          | Beta                                          | Nwachuwku et al\textsuperscript{24} |
| Instability                                    | 0.095          | Beta                                          | Reinhardt et al\textsuperscript{26} |
| Infection                                      | 0.022          | Beta                                          | Leroux et al\textsuperscript{16} |
| Second reoperation for arthrofibrosis          | 0.151          | Beta                                          | Nwachuwku et al\textsuperscript{24} |
| Second infection                               | 0.286          | Beta                                          | Calvo et al\textsuperscript{7} |
| Utility (QALY)                                 |                |                                               |        |
| Well state                                     | 1              | Normal                                        | Genuario et al\textsuperscript{12} |
| Arthrofibrosis                                 | 0.770          | Normal                                        | Genuario et al\textsuperscript{12} |
| Instability                                    | 0.790          | Normal                                        | Genuario et al\textsuperscript{12} |
| Infection                                      | 0.965          | Normal                                        | Genuario et al\textsuperscript{12} |
| Well after revision                            | 0.98           | Normal                                        | Genuario et al\textsuperscript{12} |
| Secondary complication                         | 0.700          | Normal                                        | Genuario et al\textsuperscript{12} |
| Cost, US$\textsuperscript{4}                  |                |                                               |        |
| Hamstring                                      | 4072           | Gamma                                         | Genuario et al\textsuperscript{12} |
| Hybrid                                         | 5273.56        | Gamma                                         | Current study |
| Infection                                      | 9805           | Gamma                                         | Genuario et al\textsuperscript{12} |
| Arthrofibrosis                                 | 3000           | Gamma                                         | Genuario et al\textsuperscript{12} |
| Revision                                       | 20,000         | Gamma                                         | Genuario et al\textsuperscript{12} |

\textsuperscript{a}Hamstring indicates hamstring autografts, whereas hybrid indicates hybrid hamstring autografts with allograft augment. ACL, anterior cruciate ligament; QALY, quality-adjusted life-year.

\textsuperscript{b}Probability parameters were assigned beta distributions about the baseline value, with the standard deviation assumed to be 20% of the mean.\textsuperscript{9}

\textsuperscript{c}Utility parameters were assigned normal distributions about the baseline value.\textsuperscript{9}

\textsuperscript{d}Cost parameters were assigned gamma distributions about the baseline value.\textsuperscript{9}
model created with 1000 theoretical patients assigned equally to hamstring or hybrid cohorts (Figure 2). These treatment arms were divided into outcome arms based on probabilities, utilities, and costs derived from both the current clinical results and from the literature (Table 1). Specifically, we included the probabilities of a successful outcome as well as revision owing to graft failure, persistent instability, arthrofibrosis requiring reoperation, and infection. These values were taken directly from our clinical results or literature published on patients younger than 18 years when possible, but we used adult values if adolescent-specific references could not be identified (Table 1). The incremental cost of the hybrid graft was US$1201.56 greater than the hamstring graft based on pricing at our facility. All other costs were consistent with the previous study by Genuario et al.12 Terminal outcomes were assigned a health state/utility score and a societal cost, and the threshold for cost-effectiveness was set as an incremental cost-effectiveness ratio of $50,000/quality-adjusted life-year (QALY).12

To better estimate uncertainty within each model, probabilistic sensitivity analysis of 1000 first-order cases was used to vary probabilities, utilities, and costs within the 2 models. Similar to the methods of Crall et al.,9 probability parameters were assigned beta distributions, utility parameters were assigned normal distributions, and cost parameters were assigned gamma distributions. All parameter distributions were centered about the baseline value and standard deviations were assumed to be 20% of the mean. We also determined the percentage of cases in which each strategy (hamstring or hybrid graft) would be the preferred strategy based on the willingness to pay of $50,000.

### RESULTS

#### Clinical Results

This study included a total of 88 patients: 46 in the hamstring group and 42 in the hybrid group (Table 2). The 2 groups did not differ in terms of age, sex, or the prevalence of skeletally immature patients. However, BMI was significantly greater in the hybrid group and the duration of follow-up was significantly greater in the hamstring group. Graft diameters were significantly smaller in the hamstring group (median 7.8 vs 9.9 mm; \(P < .001\)), which corresponded with a significantly greater rate of graft failure (13 of 46 [28.3%] vs 5 of 42 [11.9%]; \(P = .049\)). Neither the timing of when the patient was cleared to return to activity nor the time to graft failure differed between groups (Table 2). The logistic regression results indicated that a model containing graft type, BMI, and follow-up duration explained 58% of the variability in the graft failure rates (Nagelkerke \(R^2 = 0.58\), \(P < .001\)). Both BMI and follow-up duration were inversely related to graft failure,
suggesting that patients with a lower BMI in the hamstring group were more likely to fail, and that these failures tended to occur sooner after surgery and not later.

Cost-Effectiveness Results

The hybrid graft was the dominant strategy in the base case because it provided an incremental cost savings of $2765.49 and was slightly more effective (0.94 QALY vs 0.92 QALY). Probabilistic sensitivity analysis results were similar, with the hybrid graft demonstrating mean costs of $8259.51 ± $1289.55 and effectiveness of 0.94 ± 0.13 compared with $10,736.31 ± $1975.85 and effectiveness of 0.92 ± 0.11 of the hamstring graft (Figure 3). The hybrid graft was the preferred treatment strategy in 86% of the simulated cases. The cost advantage of the hybrid graft was driven by the reduced revision rate compared with the hamstring group in the current study; however, if the revision rate for the hamstring graft could be reduced from 28% to 12% in this subset of younger patients, the hamstring graft would become the dominant strategy because of the added cost associated with the allograft tissue.

DISCUSSION

The rate of reinjury after ACL reconstruction is alarmingly high in the young athlete who returns to level 1 sports, suggesting that the standard of care may not be sufficient in this high-risk patient population. Although primary ACL reconstruction has been demonstrated to be cost-effective,13,14,27 revision ACL reconstruction leads to worse outcomes29,35 and higher costs.5 As such, cost-effective alternatives during primary ACL reconstruction must be explored to better protect long-term knee health for this subset of high-risk patients. Although there are many modifiable factors that can potentially improve graft survivorship for younger patients (eg, improved injury prevention and screening, biologic interventions, development of evidence-based return to play criteria), optimizing the biomechanical characteristics of the graft is one area that warrants continued evaluation. As such, this study aimed to (1) evaluate the clinical success of increasing the graft diameter by augmenting hamstring autografts with semitendinosus allograft tissue and (2) determine whether hybrid hamstring grafts provide a cost-effective alternative to hamstring autografts in this subset of patients. The results supported our hypothesis that the initial costs of the allograft tissue with the hybrid graft would be offset by the value provided by the significant reduction in the need for revision ACL reconstruction.

As previously discussed, there are biomechanical advantages to increased graft diameter, including increased tensile strength of the graft,2 with the potential for reduced meniscal stress, decreased joint laxity, and less articular cartilage contact stress.34 Clinically, larger hamstring graft diameters have been associated with reduced risk of graft failure and the need for revision ACL reconstruction.8,30 In the current study, the use of the hybrid graft resulted in consistently greater graft diameters compared with treatment with hamstring autograft tissue alone, and the hybrid group also demonstrated a reduced need for revision ACL reconstruction.

Although incorporating allograft tissue within a hamstring autograft can provide surgeons with the ability to consistently increase graft diameter,1 results of hybrid grafts have been mixed.6 In contrast with our findings, previous authors have reported increased failure rates when augmenting hamstring autografts with allograft tissue. Interestingly, the number of graft failures did not dramatically differ between studies, with 5 of 42 (11.9%) requiring revision for graft failure in the current study compared with 4 of 29 (13.8%) in the study by Burrus et al.6 However, Burrus et al reported that an additional 8 of 29 hybrid grafts (28%) became structurally compromised or incompetent. There were several methodological differences between the 2 studies that may explain, at least in part, the discordance in clinical results (Table 3). First, the current study used a more homogeneous patient population in terms of allograft tissue used, femoral tunnel drilling technique, and femoral and tibial fixation utilized. Furthermore, the final location of the allograft tissue in vivo differed between studies. In the current study, allograft tissue was folded within the graft, whereas not standardized, Burrus et al reported that the surgeons attempted to rotate the graft so that the allograft tissue was anterior to the autograft tissue. We cannot speculate as to whether there was an individual effect or combined effects of the different patient populations, fixation methods, tunnel locations, or anterior location of the allograft tissue, which may be related to the increased rate of clinical failures reported by Burrus et al. Future studies in this area are certainly warranted. Furthermore, we restricted the use of the hamstring or hybrid graft to a selected subset of our ACL reconstructions, as discussed below.

This study was not without limitations. First, the sample size of this retrospective study was fairly small and did not include patient-reported outcomes. Larger prospective
Hybrid Hamstring Grafts in Younger Patients

CONCLUSION

Augmenting hamstring autographs with semitendinosus allograft tissue resulted in a significantly reduced rate of graft failure in a subset of patients with ACL injury who were younger than age 18 years. The value associated with the decreased revision rate translated into an overall cost savings of $22765 per patient, suggesting that hybrid grafts offer a cost-effective alternative to hamstring autographs in this subset of high-risk patients. However, if the failure rate of hamstring autographs can be reduced to 12% in this subset of patients, hamstring autographs would provide the more cost-effective treatment option. Future studies are therefore needed to determine whether other surgical techniques or perioperative interventions can provide such a reduction.

REFERENCES


