Early Anterior Cruciate Ligament Reconstruction Delays Secondary Meniscal Injury Compared to Delayed ACLR or Nonoperative Treatment: A Time to Event Analysis using Machine Learning

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INTRODUCTION:
Both surgical and nonoperative management of anterior cruciate ligament (ACL) injuries seek to mitigate the risk of knee instability and chronic degenerative changes, including secondary meniscal injury. However, the associated risk and timing of onset of secondary meniscal tears has not been completely elucidated after these treatments. The purpose of this study was to compare the risk and timing of secondary meniscal injury between matched cohorts of patients treated with ACLR and those treated with nonoperative management, using a machine learning time to event analysis.
METHODS:
An established geographic database of more than 600,000 patients was used to identify patients with a diagnosis of anterior cruciate ligament rupture between 1990 and 2016 with minimum 2-year follow-up. Medical records were reviewed to abstract relevant patient demographic, injury, and treatment information. Patients undergoing ACLR were matched 1:1 to nonoperative controls. The rate and time to a secondary meniscal tear was compared using a random survival forest (RSF) algorithm. Finally, two independent RSF algorithms were developed and internally validated for predicting meniscus-injury free duration in both the ACLR and nonoperative cohorts. Algorithm performance was measured using the out-of-bag (OOB) c-statistic, calibration, and Brier score. Model interpretability was enhanced utilizing global variable importance plots.
RESULTS:
A total of1369 patients who underwent ACLR and 294 patients who underwent nonoperative treatment were included in the study. A matched cohort analysis of 294 ACLR patients and the 294 nonoperatively treated patients identified no significant differences in the rate of secondary meniscal tear (13.3% in the nonoperative cohort compared to 10.5% in the ACLR cohort P=0.373). RSF analysis found that patients undergoing ACLR had the shortest periods of meniscus survival free of injury and were fastest to experience a secondary injury, followed by nonoperatively treated patients, and then early ACLR patients. The RSF algorithm produced for the ACLR cohort achieved an OOB c-statistic of 0.80 and a Brier score of 0.106, while the RSF algorithm for the nonoperative cohort achieved a c-statistic of 0.66 and a Brier score of 0.111; both models outperformed a Kaplan-Meier estimator at long-term follow-up. Significant variables that correlated with secondary meniscal tear in the ACLR cohort model included time to RTS ≤350 days, time to surgery ≥50 days from initial injury, age at injury ≤40, and involvement in high impact rotational landing sports; while those for the nonoperative cohort model included time to RTS ≤200 days, VAS pain >3 at initial consultation, hypermobility, and involvement in a noncontact sport.
DISCUSSION AND CONCLUSION:
Patients undergoing delayed ACLR have the greatest long-term risk of meniscal injury, followed by those who undergo nonoperative treatment and finally those undergoing early ACLR. Risk factors for decreased meniscus survival after ACLR included increase time to surgery, shorter time to RTS, older age at injury, and involvement in a high-impact/rotational landing sport. Two machine learning models outperformed traditional survivorship estimators and, pending careful external validation, may be deployed in the clinical space to provide real-time insights to enhance decision making to prevent and delay degenerative changes of the knee.

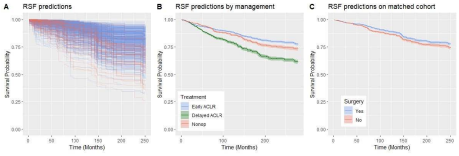

Figure 1: A) individual RSF survival curves from matched cohort of ACLR and nonoperatively treated patients; B) RSF predictions stratified by management with 95% CI; C) RSF predictions stratified by surgery vs nonoperative treatment; no overlap between confidence interval demonstrates significantly extended meniscal survivorship among patients treated with ACLR.

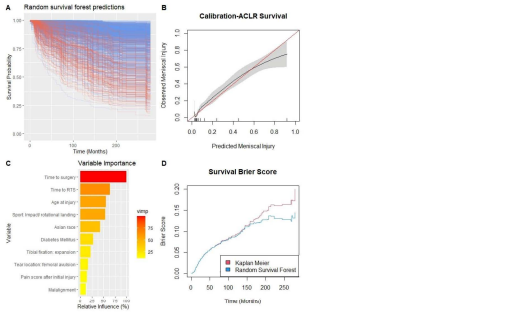

Figure 2: A) individual survival curves predictions from internal validation of all ACLR-treated patients; B) calibration, which plots the sample prevalence of positive cases at every predicted probability; C) global relative variable importance; this plot demonstrates the statistical significance of each variable in the data with respect to its effect on the generated model, as measured on a unitless scale of 0 to 100; D) comparison of Brier score between the RSF and KM estimator predictions over the time period of follow-up demonstrating improved performance of RSF beyond 150 months.