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Histopathological Evaluation of the Anterior Cruciate Ligament in Patients Undergoing Primary Total Knee Arthroplasty

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ABSTRACT

This study assessed gross and histopathological ACL changes in arthritic knees ($n = 174$) undergoing total knee arthroplasty. Histopathological changes were assessed and graded as absent (0), mild (1), moderate (2), or marked (3). These were correlated to demographic and clinical factors, and radiographic evaluations. The ACL was intact in 43, frayed in 85, torn in 15, and absent in 31 knees. Eighty-five percent had histological changes. Overall, there were significant associations between greater age and BMI, and histological changes. Grade IV knees had significantly greater calcium pyrophosphate deposits, microcyst formation, and number of pathologic changes. These correlations may aid decision-making when determining suitability for unicompartmental or bicruciate-retaining arthroplasties, though further studies should correlate these histological findings to mechanical and functional knee status.

It has been postulated that suboptimal functional performance following knee arthroplasty may be due to the inability of certain prostheses to reproduce the native knee kinematic complexity [1,2]. Therefore, one might consider preserving as much of the native knee structures as possible. In particular, preservation of the anterior cruciate ligament (ACL) has been implicated in achieving close to normal kinematics and may play a key role in unicompartmental knee arthroplasty (UKA) and bicruciate-retaining knee arthroplasty [3,4].

In UKA, the ACL preservation restores joint stability and soft-tissue balance and offers the potential to preserve close-to-normal kinematics. It has been suggested in laboratory studies that a deficient ACL may contribute to higher failure rates with sliding between the tibia and femur, resulting in increased polyethylene wear [5,6]. In total knee arthroplasty (TKA), retaining both cruciate ligaments may provide better joint kinematics, improved motion and functional performance, stability, and enhanced proprioception [2,7–12].

However, there has been much debate about the benefits of ACL-retention in knee arthroplasty. There are concerns that this ligament in osteoarthritic knees may not be functional [9,13]. Furthermore, although the ACL may appear normal macroscopically, this does not always correlate with histological integrity [14–16], and up to 97% may have histological changes [13–15,17]. However, there is evidence that degeneration should not be a contraindication to ACL preservation, as long as the ligament remains functional [4]. Upon evaluation of the posterior cruciate ligament (PCL), degenerative patterns have been noted in osteoarthritis (OA), but retention is advocated for PCL-sparing prostheses if the ligament retains its mechanical properties and neural elements [18].

Histologically, degenerative ligaments show varying degrees of chondroid metaplasia, myxoid degeneration, altered collagen fiber arrangement, and cystic changes [15,19,20]. These changes have been reported to correlate with demographic factors and with the extent of knee degeneration [15]. In the assessment of ligament functionality, identifying histological changes is becoming increasingly relevant with the expansion of UKA use and the introduction of bicruciate-retaining prostheses. Specifically, it is important to evaluate these changes in patients who have intact ACLs, as these are the potential candidates for such surgeries. Therefore, the aims of the present study were to: 1) determine in the overall cohort: a) the number and types of gross (macroscopic) and histopathological ACL changes in arthritic knees undergoing TKA; and b) assess effects of patient factors (age, body mass index, gender, and diabetes), clinical factors (range-of-motion), and radiographic findings (Kellgren–Lawrence grade [21] and compartmental involvement) on ACL histological changes; and 2) evaluate the above factors in patients who had intact ACL specimens.

It was hypothesized that certain factors might serve as better predictors of ACL integrity for surgeons treating patients with these devices.

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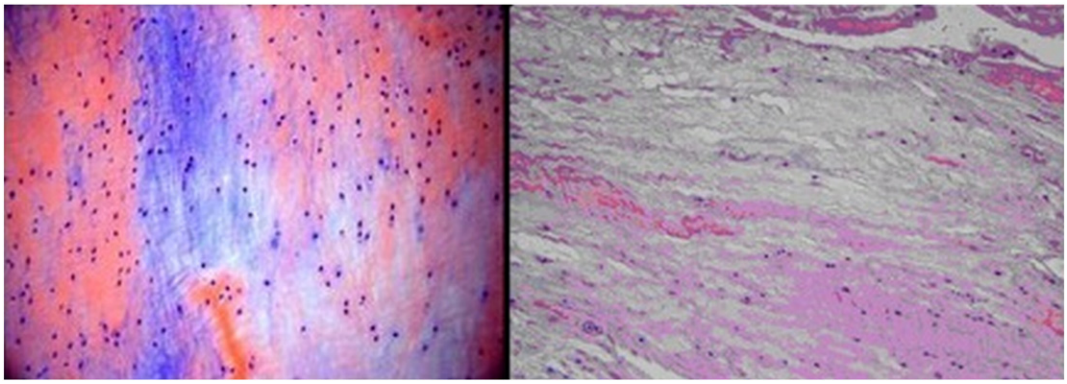

Fig. 1. Specimens stained with hematoxylin and eosin denote myxoid changes. Age was not accounted for. Note background pale staining with increased fibroblast nuclei. The left image denotes high cellularity, more cellular than would be expected in a normal ligament, and nuclei have a very rounded morphology.

Methods

From August 2011 to April 2012, 192 patients who underwent a primary TKA were identified. Patients were included if they had primary or traumatic osteoarthritis, as diagnosed clinically and radiographically. Those who had a diagnosis of osteonecrosis ($n = 4$) or rheumatoid arthritis ($n = 17$), or varus/valgus deformities > 10 degrees ($n = 11$) were excluded. After eliminating exclusions, 160 patients (174 knees) were prospectively evaluated. There were 104 women and 56 men who had a mean age of 59 years (range, 26 to 84 years) and a mean body mass index (BMI) of 34.9 kg/m^2 (range, 17.6 to 58.0). Institutional review board approval and patient consent were obtained.

The ACL was evaluated intra-operatively at primary TKA macroscopically and was classified as: 1) intact; 2) frayed; 3) torn; or 4) absent [22]. If the ACL was present, the specimen was sent for histopathological analysis (143 specimens).

Specimens were processed in their entirety, with transverse and longitudinal slices obtained at both the proximal one-third and ligament center. For histopathologic evaluation, samples were fixed in formalin, dehydrated, and paraffin-embedded. The 4 micrometer sections were cut and stained with Hematoxylin and Eosin. The following were evaluated: 1) myxoid change (material rich in proteoglycan, hydrophilic in nature with abundant water content); 2) cystic myxoid or microcyst formation (matrix pools without synovial lining, similar to myxoid change but more advanced); 3) chondroid metaplasia (rounded cells lying within lacunae containing proteoglycan, similar to cartilage); 4) acellular zones (loss of fibroblast nuclei); 5) vascular proliferation (increased capillaries); 6) fibroblast proliferation (increased fibroblast nuclei); 7) calcium pyrophosphate deposits; and 8) presence of gout. Using a modification of previous grading systems [15,23,24], each finding was graded as absent (0 points), mild (1 point), moderate (2 points), or marked (3 points) and was scored based on the extent of histological degenerative changes. A total histological degeneration score was generated by summating each individual microscopic change score, with minimum score of 0 and a maximum of 24 [24]. The samples were analyzed and scored by a bone pathologist, who was blinded to any patient clinical or radiographic factors.

Demographic factors assessed were age, BMI, gender, a medical diagnosis of diabetes mellitus, and pre-operative range-of-motion. Association of these factors with ACL macroscopic and histological findings was performed.

Radiographic factors and ACL findings were correlated by first determining the osteoarthritis severity and location of changes (uni-, bi-, or tricompartmental). Osteoarthritis degree was determined on anteroposterior and lateral radiographs using the Kellgren and Lawrence system [21], which consists of five grades: 0) no x-ray changes; 1) doubtful joint space narrowing; 2) minimal narrowing and osteophytes; 3) moderate narrowing with multiple osteophytes; and 4) severe narrowing. All patients had grade III ($n = 94$) or IV ($n = 49$) osteoarthritis. Two readers (M.A.M., B.H.K.) independently evaluated radiographs to assess intra- and inter-observer reliability. They were blinded to patient age, gender, and ACL histological scores.

Each factor was correlated with macroscopic and histological findings. The sum of histological changes for each patient was determined and a total degeneration score was deduced. Using multivariate regression analysis, the association between secondary endpoints and total degeneration scores was determined. Means and standard deviations of values were calculated, and GraphPad Prism software (version 5.0 for Windows; GraphPad Software, San Diego, California) was used for statistical analysis. Assuming a Gaussian distribution, the significance of associations between the factors and ACL changes was evaluated using one-way analysis of variance (ANOVA) for continuous variables (such as patient BMI), Kruskal–Wallis tests for ordinal variables (such as extent of histological change), and Fisher's exact test for dichotomous categorical values (such as patient gender). Correlation statistics were performed using Pearson's correlation coefficient. A P value < 0.05 determined significance.

Results

Overall

Of 174 knees evaluated, the ACL was present in 143 (82%; 98 female, 45 male). Macroscopically, the ACL was intact in 43 knees (30%), frayed in 85 (59%), and torn in 15 (11%). Histopathologic changes were detected in 85% (121/143), with 22 having no changes. None of the specimens had significant inflammation and no necrotic cells were observed. The most common histological change was myxoid degeneration (63%, 90

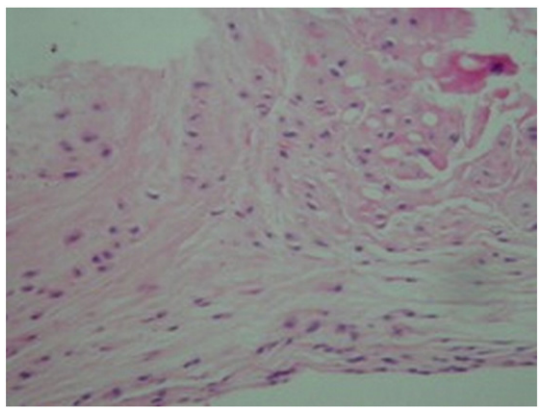

Fig. 2. ACL specimens with Hematoxylin and Eosin staining. Note disorientation of collagen fibers. Right upper quadrant denotes area of chondroid metaplasia.