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ORIGINAL PAPER

Correlation of Cruciate Ligament Histological Findings with Coronal Plane Deformities and Characteristics of Patients Undergoing Total Knee Arthroplasty

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ABSTRACT

Introduction: *Osteoarthritis (OA) is a leading cause of disability in older adults. The majority of cruciate ligament injuries progress to OA through numerous mechanisms. The aim of this study was to identify the histological changes of cruciate ligaments in OA knees from patients undergoing total knee arthroplasty (TKA) as well as possible correlations with coronal plate deformities and patients' characteristics.*

Methods: *A total of 50 consecutive patients with knee OA undergoing TKA with posterior stabilized prosthesis were included in the study. Demographics, preoperative range of flexion, the flexion contracture, Visual Analogue Scale (VAS) score, coronal plane deformity, Kellgren and Lawrence radiological degree of OA and Beguin-Locker classification of intraoperative degree of OA were recorded. The histopathological changes evaluated in specimens from both cruciate ligaments included myxoid and mucoid degeneration, chondroid metaplasia and orientation of collagen fibers.*

Results: *A total of 24 males (48%) and 26 females (52%) with a mean age of 71 years (SD 5.93) participated in our study. The mean preoperative duration of pain was 3.62 years (SD 2.2). The K-L scale mean score was 2.60 (SD 0.64) and the mean VAS score 6.38 (SD 1.1). The mean varus deformity was 10.14 degrees (SD 3.7). Knee flexion/flexion contracture were recorded at 95.76±6.183 and 16.14±4.914 degrees, respectively. Intraoperatively, the B-L scale mean score was 2.02 (SD 0.77). Mucoid degeneration in ACL was the most common histopathological feature (15.7%) (SD 12.9), followed by chondroid metaplasia in both ACL and PCL [14.3% (SD12.5) and 14.3% (SD 13.2), respectively]. A negative correlation between BMI and myxoid*

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ACL (p=0.01) as well as between varus deformity and mucoid ACL (p=0.05) was found, while a negative correlation between height and myxoid ACL (p=0.05) has been also revealed.

Conclusions: *Degeneration of cruciate ligaments is associated with degenerative joint disease and OA should be considered a disease involving the whole joint including ligaments, menisci, synovium and joint capsule. However, the correlation between degeneration of cruciate ligaments and OA is not yet fully understood and more research is needed.*

Keywords: osteoarthritis, cruciate ligament, total knee arthroplasty, varus, valgus deformity, histology, mucoid degeneration.

INTRODUCTION

Osteoarthritis (OA) is the most prevalent chronic joint disease, while it represents a leading cause of disability in older adults (1). Articular cartilage loss, typically recognized on plain radiographs as reduction in joint space, is the main pathologic feature of OA (2). Loss of cartilage and joint disruption are associated with attempts of new bone formation as well as the development of subchondral sclerosis and osteophytes. With the advent of more detailed imaging studies, particularly magnetic resonance imaging (MRI), OA has been found to affect the whole joint including ligaments, menisci, synovium (synovitis) as well as joint capsule (2).

It has been documented that the majority of anterior cruciate ligament (ACL) injuries progress to OA (3, 4). Following ACL injury, grade III or IV radiologic changes in the Kellgren–Lawrence classification system are nearly five times more likely than in the contralateral knees without history of ACL injury (5). A number of factors may contribute to increased risk of OA following ACL injury, such as gender (female), age, high body mass index (BMI), obesity, physical activity level, smoking, low education level, subsequent surgery, time interval between injury and surgery, and varus alignment of the uninjured knee (3, 6, 7, 8).

Although accumulating evidence demonstrates that patients with ACL injury have predisposition to develop OA, the precise mechanism remains unclear. Structural, biological, mechanical and neuromuscular factors are believed to participate in this process (9, 10).

The aim of this study was to identify the histological changes of the anterior, as well as posterior cruciate (PCL) ligament in OA knees from patients undergoing total knee arthroplasty (TKA) and to identify possible correlations between these histological characteristics of ACL and PCL and bone, cartilaginous, as well as mechanical features of each case. ❑

PATIENTS AND METHODS

In a period of two years, 50 consecutive patients suffering from knee OA and undergoing total knee arthroplasty with posterior stabilized prosthesis at the Orthopedics Department of the University General Hospital of Ioannina, Greece, were included in the study. Patients' demographics, the preoperative range of flexion, the flexion contracture as well as the preoperative Visual Analogue Scale (VAS) score for pain, the degree of coronal plane deformity (varus-valgus), the Kellgren and Lawrence radiological degree of OA (K-L Classification) and the Beguin and Locker classification of intraoperative degree of OA (B-L Classification) were prospectively recorded.

In terms of imaging, OA has been classified into four subcategories according to the Kellgren and Lawrence classification: grade 0 = no presence of OA; grade 1 = ambiguous narrowing of the joint space and possible appearance of osteophytes; grade 2 = occurrence of osteophytes possible narrowing of the joint space; and grade 3 = moderate narrowing of the joint space, multiple osteophytes, mild hardening of joint surfaces, possible deformity of the capsule (11). Intraoperatively, Beguin and Locker criteria have been commonly used for visual evaluation of cartilage and classification of its lesions, and four grades were described as follows: grade 1 = normal cartilage; grade 2 = edema or soft cartilage; grade 3 = appearance of surface fibrils; and grade 4 = appearance of deep fibrils up to the bone (12).

In all cases, specimens of ACL and PCL were removed during surgery and then sent for histological analysis. The pathology findings were categorized as: a) myxoid degeneration; b) mucoid degeneration; c) chondroid metaplasia; and d) orientation of collagen fibers.

The present study has been approved from the institution's bioethical committee and written consent was given by all participants.

Testing of all hypothesis comparisons between trials was performed using the SPSS 20 (SPSS Inc. Chicago, IL, USA) statistical package for personal computers. Correlations were made using the Spearman correlation coefficient (positive or negative values of "rho" exhibit positive or negative correlation between the studied variables). A correlation was considered low when rho value was between 0.1–0.3, moderate when rho was between 0.31–0.5, and high when rho>0.5. The level of significance was set to 0.05. ❑

RESULTS

The studied population, comprising 24 males (48%) and 26 females (52%), had a mean age

TABLE 1. Statistical data of examined parameters

	Number of patients		Mean	Median	Standard deviation (SD)	Min.	Max.
	Valid	Invalid					
Age (years)	50	0	71.00	72.0	5.94	51	80
Height (cm)	50	0	162.04	160.0	7.55	145	176
Weight (kg)	50	0	72.10	71.0	6.64	59	90
Body mass index (kg/m^2)	50	0	27.5	27.4	2.22	23	33.3
Duration of pain (years)	50	0	3.62	3.0	2.20	1	10
K-L scale (grade)	50	0	2.60	3.0	0.64	2	4
B-L scale (grade)	50	0	2.02	2.0	0.77	1	4
VAS scale (score)	50	0	6.38	7.0	1.11	4	8
Varus deformity (°)	50	0	10.14	10.0	3.70	5	20
Flexion/extension (°)	50	0	95.76	95.0	6.18	80	110
Stiffness (°)	7	43	16.14	20.0	4.91	10	20
Myxoid ACL (%)*	50	0	6.14	5.0	7.82	0	30
Myxoid PCL (%)*	50	0	3.90	0.0	5.37	0	20
Mucoid ACL (%)*	50	0	15.70	15.0	12.94	0	50
Mucoid PCL (%)*	50	0	13.10	10.0	10.54	0	40
ACL chondroid metaplasia (%)*	50	0	14.30	10.0	12.54	0	60
PCL chondroid metaplasia (%)*	50	0	14.30	10.0	13.25	0	70
ACL fiber orientation: parallel (%)**	50	0	60.50	70.0	26.33	0	100
ACL fiber orientation: irregular (%)**	50	0	34.50	30.0	19.57	0	70
PCL fiber orientation: parallel (%)**	50	0	60.30	70.0	24.11	0	90
PCL fiber orientation: irregular (%)**	50	0	33.90	30.0	19.75	0	80
ACL cystic changes (%)*	50	0	13.20	10.0	10.39	0	40
PCL cystic changes (%)*	50	0	12.5	10.0	9.96	0	30

*Percentage of histological lesions in the examined specimen (by microscope field of view at magnification x10)

**Percentage ratio of the number of fibers in the relative orientation to the total fibers in the examined specimen (by microscope field of view at magnification x10)

of 71 years (SD 5.93). The mean duration of pain was 3.62 years (SD 2.2) prior to surgery. The K-L scale mean score was estimated at 2.60 (SD 0.64), while the mean preoperative VAS score was 6.38 (SD 1.1). The average varus deformity was 10.14 degrees (SD 3.7) and none of the study participants had valgus deformity. Knee flexion and flexion contracture were recorded at 95.76±6.183 and 16.14±4.914 degrees, respectively. During surgery, the B-L scale mean score was 2.02 (SD 0.77).

The main characteristics of pathological findings of ACL and PCL are summarized in Table 1. More specifically, the mean percentage of myxoid ACL and PCL degeneration was 6.14% (SD 7.8) and 3.9% (SD 5.4), respectively. Mucoid degeneration was also present in both ACL and PCL, with a mean percentage of 15.7% (SD 12.9) and 13.1% (SD 10.5), respectively. Chondroid metaplasia lesion was reported in ACL and PCL, with a mean percentage of 14.3% for both ligaments (SD 12.5 and 13.2, respectively). Furthermore, the percentage ratio of the number of fibers in the relative orientation to the total fibers in the examined specimen was reported. Regarding ACL, the parallel fibers orientation was recorded with mean percentage=60.5% (SD 26.3), while the irregular fibers were 34.5% (SD 19.6). As far as PCL is concerned, the parallel fibers orientation was recorded with mean percentage=60.3% (SD 24.1), while the irregular fibers were 33.9% (SD 19.8). Cystic changes were also present in both ACL and PCL specimens, with a mean percentage of 13.2% (SD 10.4) and 12.5% (SD 10), respectively.

Table 2 exhibits the correlation between the histological findings of the ligaments (ACL and PCL) and examined variables. The analysis showed positive correlation between both BMI and muxoid ACL (rho=0.35, p=0.01), and varus deformity and mucoid ACL degeneration (rho=-0.25, p=0.05). A positive correlation has been also found between height and myxoid ACL, (rho=0.28, p=0.05). In addition, marginally negative correlations between VAS scale (pain scale) and myxoid ACL (rho=-0.25, p=0.08) as well as between the duration of pain (in years) and myxoid ACL (rho=-0.25, p=0.08) were revealed.

The analysis has also shown negative correlation between B-L scale and myxoid ACL (rho=-0.24, p=0.09), as well as between duration of pain and myxoid PCL (rho=-0.28, p=0.06). Furthermore, significant negative correlation between varus deformity and mucoid ACL (rho=-0.27, p=0.05) were noted. ❑

TABLE 2. Correlation between cruciate ligaments histological lesions and examined variables

Variables		Myxoid ACL	Myxoid PCL	Mucoid ACL	Mucoid PCL
Age	rho	-0.09	-0.13	-0.01	-0.05
	p-value	0.52	0.37	0.94	0.76
BMI	rho	0.35	-0.06	-0.23	-0.1
	p-value	**0.01**	0.70	0.11	0.50
Height	rho	0.28	-0.03	0.06	0.20
	p-value	**0.05**	0.82	0.70	0.17
B-L scale	rho	-0.13	-0.24	0.04	-0.02
	p-value	0.38	0.09	0.79	0.90
Varus deformity	rho	-0.25	0.04	0.27	-0.18
	p-value	0.07	0.80	**0.05**	0.22
Flexion/flexion contracture	rho	0.23	0.13	0.16	0.22
	p-value	0.10	0.36	0.27	0.12
VAS scale	rho	-0.25	-0.10	-0.06	-0.18
	p-value	0.08	0.51	0.67	0.21
Duration of pain	rho	-0.25	-0.27	-0.03	-0.08
	p-value	0.08	0.06	0.84	0.57

DISCUSSION

Osteoarthritis (OA) is the most common form of arthritis and represents a complex interplay between mechanical, cellular, and biomechanical factors, leading to an end-stage pathology. Multiple risk factors have been associated to the pathogenesis of OA. Risk factors for OA include age, joint injury, obesity, genetics, anatomical factors including joint shape and alignment and gender (13).

Histopathological degenerative changes in cruciate ligaments have a high prevalence in knees with severe osteoarthritis (14-16). Histologically, degeneration of ligaments causes varying levels of cartilage metaplasia and myxoid degeneration as well as changes in the collagen fiber alignment and cystic lesions (15-17). In particular, reported histopathological degenerative features in cruciate ligaments include: a) myxoid change (material rich in proteoglycan, hydrophilic in nature with abundant water content);

b) cystic myxoid or microcycystic formation (matrix pools without synovial lining, similar to myxoid change but more advanced); c) chondroid metaplasia (rounded cells lying within lacunae containing proteoglycan, similar to cartilage); d) acellular zone (loss of fibroblast nuclei); e) vascular proliferation (increased capillaries); f) fibroblast proliferation (increased fibroblast nuclei); g) calcium pyrophosphate deposits; h) presence of gout; and i) orientation of collagen fibers (14, 15, 18, 19).

A total number of 50 subjects – including 24 (48%) males and 26 (52%) females – with a mean age of 71±5.93 years participated in the present study, which evaluated the following histopathological changes: myxoid degeneration, mucoid degeneration, chondroid metaplasia and orientation of collagen fibers. Mucoid degeneration in ACL was the most commonly found histopathological feature (15.7%) (SD 12.9), followed by chondroid metaplasia in both ACL and PCL, with mean value of 14.3% (SD 12.5) and 14.3% (SD 13.2), respectively.

The analysis showed negative correlation between BMI and myxoid ACL (rho=-0.35, p=0.01) as well as between varus deformity and mucoid ACL (rho=-0.27, p=0.05), while a negative correlation was revealed between height and myxoid ACL (rho=0.28, p=0.05). It has already been documented that an increased BMI represents a risk factor for OA (20). Excess weight leads to increased load on the joint as well as metabolic contribution to OA progression. Cytokines associated with obesity may promote low-grade, systemic, proinflammatory state that could contribute to the development of OA, while leptin has been proposed to have direct effects on joint tissues that promote OA development (20). In similar studies in the available literature, higher BMI score has not been associated with ACL macroscopic changes nor histopathological lesions. This could be attributed to the possibility that obese patients require surgical intervention at younger age, and as a result, age-related ligament degeneration may not be present (15, 21).

The positive correlation between varus deformity and mucoid ACL is in line with other studies (22-24). In particular, in a recent study, several OA findings were worse in participants with ACL mucoid degeneration compared to those with normal ACL (24). Knee alignments (varus and valgus deformities) were also evaluated, and a statistically significant correlation in participants with varus deformity and ACL mucoid degeneration was shown.

Previous research showed that both histological changes in the ACL and PCL of patients with knee OA are similar due to inflammation; however, they are more severe in ACL (15, 24, 25). Both degenerative and traumatic changes occur to the cruciate ligaments in knee OA and there is evidence that damage to ACL from osteophytes or previous direct injury may induce degeneration in PCL as well (25).

With the increasing histological degeneration grade, disruption of the parallel collagen fibers is reported to be more severe, including increased cellularity and fibroblast nuclei. Secondary degenerative changes such as calcifications, cystic degeneration, and myxoid lesions are also reported to be more prominent. Mucoid degeneration and irregular fiber orientation is almost always present when the clinical OA is of grade V, with lesser grades of radiological changes reflecting lesser degrees of degeneration on histology (26).

Despite the fact that no correlation between histopathological lesions and age was found in the present study, it has been reported that ligament degeneration, including myxoid degeneration, chondroid metaplasia and fiber disorganization, are mostly present in the higher age groups (15, 19). The earliest age-related lesions of ACL include collagen fiber disorientation and mucoid degeneration, while calcification is reported to be the latest change (27). Unlike the pattern of changes seen with OA progression, ACL and PCL degeneration has a similar severity throughout aging (15, 26). ❑

CONCLUSION

The present study has shown that mucoid degeneration in ACL was the most common histopathological change among patients undergoing total knee arthroplasty due to OA. Moreover, a negative correlation between BMI and myxoid ACL, varus deformity and mucoid ACL as well as between height and myxoid ACL was revealed. It seems that degeneration of cruciate ligaments is associated with degenerative joint disease and OA should be considered a disease involving the whole joint, including liga-

ments, menisci, synovium (synovitis) as well as joint capsule. The correlation between degeneration of cruciate ligaments and OA or vice versa, although already documented, is not yet fully understood. Thus, more data and research are needed for elucidating these mechanisms, as well as clarifying all risk factors of OA that may lead to possible establishment of prevention strategies, especially in high-risk patients. ❑

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