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### **AGE-RELATED MORPHOLOGICAL CHANGES IN MENISCI OF THE KNEE JOINT IN WOMEN: HISTOLOGICAL AND MACROSCOPIC STUDY**

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#### **INTRODUCTION**

The menisci of the knee joint are fibrocartilaginous structures of critical functional importance, providing load distribution, shock absorption, joint stabilisation, and lubrication across the tibiofemoral articulation (Makris et al., 2011; Fox et al., 2015). Composed predominantly of type I collagen arranged in circumferential and radial fibre bundles, with a sparse population of fibrochondrocytes embedded in a proteoglycan-rich extracellular matrix, the menisci are capable of transmitting up to 50–70% of the compressive load in the knee joint during weight-bearing activities (Englund et al., 2009; Berthiaume et al., 2005).

Age-related deterioration of meniscal tissue represents a well-recognised phenomenon that contributes substantially to the aetiology and progression of knee osteoarthritis, which affects women disproportionately following menopause, with prevalence rates two to three times higher than in age-matched male populations (Srikanth et al., 2005; Hanna et al., 2010). The hormonal changes associated with the perimenopausal transition — particularly the decline in oestrogen — are considered significant contributors to accelerated cartilaginous and fibrocartilaginous tissue degeneration in women, though the precise histomorphological sequence of age-related meniscal changes and their



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sex-specific characteristics remain incompletely characterised (Liu et al., 2016; Bellido et al., 2010).

In the Central Asian context, including Uzbekistan, morphological studies of the knee joint structures in female populations are virtually absent from the scientific literature, despite the clinical significance of knee osteoarthritis as a major cause of disability in older women. Establishing age-stratified normative morphological data for meniscal tissue in women from this region is a prerequisite for evidence-based understanding of degenerative knee pathology and the development of targeted preventive and therapeutic strategies.

The aim of the present study was to characterise the macroscopic and histomorphological changes in the medial and lateral menisci of the knee joint across age groups in women, and to identify age-specific patterns of structural deterioration relevant to clinical practice.

### MATERIALS AND METHODS

The study was conducted at the Department of Human Anatomy and the Republican Specialised Centre of Traumatology and Orthopaedics, Tashkent, Uzbekistan. Meniscal specimens were obtained from two sources: (1) intraoperative material from 68 women (mean age  $54.3 \pm 12.7$  years, range 32–74) undergoing total knee arthroplasty or arthroscopic meniscal surgery; and (2) cadaveric knee joint preparations from 44 women (mean age  $51.8 \pm 14.2$  years, range 28–72) without documented knee pathology at autopsy. Participants were stratified into four age groups: Group I (28–39 years,  $n = 26$ ), Group II (40–49 years,  $n = 28$ ), Group III (50–59 years,  $n = 32$ ), and Group IV (60–74 years,  $n = 26$ ).

Macroscopic assessment evaluated meniscal surface integrity, colour, consistency, and the presence of tears, fibrillation, or calcifications. For



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histological analysis, specimens were fixed in 10% neutral-buffered formalin, processed by standard paraffin embedding, sectioned at 5–7  $\mu\text{m}$ , and stained with haematoxylin-eosin (H&E), Safranin-O/Fast Green (proteoglycan content), Masson's trichrome (collagen fibres), and Alcian Blue (glycosaminoglycans). Fibre organisation, cellularity, vascularity, and matrix composition were evaluated semi-quantitatively by two independent morphologists. Statistical comparison across age groups used the Kruskal–Wallis test with post-hoc Dunn correction ( $p < .05$ ).

### RESULTS

**Macroscopic findings.** In Group I, meniscal surfaces were smooth, glistening, and white-opaque with uniform consistency. Progressive changes were evident from Group II onwards: surface irregularity, yellowish discolouration, and reduced elasticity. In Group III, frank fibrillation, surface fissuring, and focal opacity were observed in 71.9% of specimens. Group IV specimens demonstrated advanced macroscopic degeneration including full-thickness surface defects, horizontal cleavage tears, and calcific deposits in 65.4% of cases. Medial menisci showed more pronounced macroscopic degeneration than lateral menisci across all age groups, consistent with the greater load-bearing demands on the medial compartment.

**Histomorphological findings.** H&E staining revealed a progressive reduction in fibrochondrocyte cellularity with advancing age: mean cell density declined from  $48.3 \pm 6.7$  cells/ $\text{mm}^2$  in Group I to  $21.4 \pm 5.1$  cells/ $\text{mm}^2$  in Group IV ( $p < .001$ ). Fibrochondrocyte morphology shifted from round to elongated and pyknotic forms in older age groups, indicative of advancing cell senescence. Masson's trichrome staining demonstrated progressive disorganisation of circumferential collagen fibre bundles, with loss of parallel fibre architecture and increased inter-



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fibre space from Group II, and frank fibre fragmentation and myxoid degeneration in Groups III–IV. Safranin-O and Alcian Blue staining showed progressive depletion of proteoglycan and glycosaminoglycan content, most marked in the avascular inner zone of the meniscus, with near-complete loss of Safranin-O positivity in the inner third of Group IV specimens. Vascular ingrowth from the peripheral vascular zone into the normally avascular middle and inner zones was observed in 43.8% of Group III and 61.5% of Group IV specimens, suggesting reparative but structurally disruptive neovascularisation. Age-group comparisons demonstrated statistically significant differences for all histomorphological parameters ( $p < .001$  for cellularity, collagen organisation, and proteoglycan content). Post-hoc analysis identified the transition between Groups II and III (age 50–59 years, corresponding to the typical perimenopausal period) as the period of most rapid morphological deterioration.

## DISCUSSION

The findings of the present study document a progressive, age-related deterioration of meniscal tissue in women that accelerates markedly during the perimenopausal decade. The pattern — declining cellularity, collagen fibre disorganisation, proteoglycan depletion, and peripheral neovascularisation — is consistent with the established biology of fibrocartilaginous ageing (Makris et al., 2011; Englund et al., 2009). The accelerated deterioration observed in the 50–59 age group aligns with data on oestrogen-mediated regulation of meniscal matrix homeostasis: oestrogen receptors have been identified in meniscal fibrochondrocytes, and oestrogen withdrawal is associated with reduced proteoglycan synthesis and increased matrix metalloproteinase activity (Liu et al., 2016; Bellido et al., 2010).



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The greater degenerative burden in medial compared with lateral menisci, observed across all age groups, reflects the well-established biomechanical asymmetry of the knee joint and is consistent with the higher clinical incidence of medial meniscal tears and medial compartment osteoarthritis in women (Hanna et al., 2010; Srikanth et al., 2005). The identification of pathological neovascularisation in the avascular inner zone of menisci in older women provides a potential histomorphological basis for the increased susceptibility to meniscal tears with age.

### CONCLUSION

Age-related morphological changes in women's menisci follow a progressive trajectory characterised by fibrochondrocyte loss, collagen disorganisation, proteoglycan depletion, and pathological neovascularisation, with an acceleration of deterioration during the perimenopausal period. These findings provide a morphological basis for the elevated risk of meniscal pathology and knee osteoarthritis in middle-aged and older women, and support the development of age- and sex-specific preventive strategies targeting meniscal health in the perimenopausal transition.

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