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HISTOMORPHOLOGICAL AND MORPHOMETRIC CHARACTERISTICS OF AGE-RELATED CHANGES IN KNEE MENISCI IN WOMEN: A COMPARATIVE STUDY

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Abstract

Background: Age-related degeneration of the knee menisci is a major contributor to knee osteoarthritis, which disproportionately affects women, particularly after menopause. Systematic histomorphological and morphometric characterisation of meniscal ageing in women remains insufficiently studied in Central Asian populations.

Objectives: To characterise histomorphological and morphometric features of age-related changes in the knee menisci of women across reproductive and post-reproductive age groups in Uzbekistan.

Materials and Methods: A prospective cross-sectional study was conducted at the Branch of the Republican Specialized Scientific and Practical Medical Centre of Traumatology and Orthopaedics (Khorezm Regional Multidisciplinary Medical Centre). Meniscal specimens were obtained from 112 women stratified into four age groups: Group I (25–44 years, n=28), Group II (45–54 years, n=30), Group III (55–64 years, n=28), and Group IV (65–78 years, n=26). Specimens were stained with haematoxylin-eosin, Masson's trichrome, and Safranin-O/Fast Green. Morphometric parameters included fibrochondrocyte density (cells/mm²), collagen fibre alignment index (CFAI), and proteoglycan optical density (SafO-OD) measured by digital image analysis. Results: Fibrochondrocyte density declined significantly from 47.3±5.8 cells/mm² (Group I) to 20.1±4.4 cells/mm² (Group IV; $p<0.001$). CFAI increased from 11.9°±2.7° to 42.8°±7.3° ($p<0.001$), indicating progressive collagen disorganisation. Inner zone SafO-OD declined by 66% between Groups I and IV (0.90±0.08 vs. 0.31±0.06; $p<0.001$). The most rapid deterioration occurred between Groups II and III, corresponding to the perimenopausal decade. Medial menisci showed significantly greater degeneration than lateral menisci ($p<0.05$).

Conclusions: Age-related meniscal degeneration in women from Khorezm region follows a progressive, zone-specific trajectory with accelerated deterioration during the perimenopausal period, providing a morphological basis for the elevated osteoarthritis risk in postmenopausal women.

Keywords: Knee meniscus; age-related changes; morphology; morphometry; women; menopause; osteoarthritis; histology; Uzbekistan.

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Introduction

The knee menisci — paired semilunar fibrocartilaginous structures interposed between the femoral condyles and tibial plateaux — perform essential biomechanical functions including load distribution, shock absorption, joint stabilisation, and lubrication (Fox et al., 2015; Makris et al., 2011). The structural integrity of the menisci depends on a precisely organised extracellular matrix (ECM) composed predominantly of type I collagen arranged in circumferential, radial, and oblique fibre bundles, embedded in a proteoglycan-rich ground substance dominated by aggrecan and decorin (Berthiaume et al., 2005; Messner & Gao, 1998). The hydrophilic properties of proteoglycans generate osmotic swelling pressure essential for resisting compressive loads, while the collagen network bears tensile stresses during weight-bearing.

Meniscal degeneration — characterised by progressive disruption of this matrix organisation — is a central pathological mechanism in the development and progression of knee osteoarthritis (OA). Epidemiological data consistently demonstrate that knee OA affects women disproportionately, with prevalence rates approximately two to three times higher in women over 50 years of age compared with age-matched men (Srikanth et al., 2005; Litwic et al., 2013). This sex disparity is attributed in part to the influence of female sex hormones on joint tissue homeostasis: oestrogen receptors have been identified in meniscal fibrochondrocytes, and the postmenopausal decline in oestrogen has been associated with accelerated fibrocartilaginous degeneration (Liu et al., 2016; Hanna et al., 2010).

In Uzbekistan, musculoskeletal disorders including knee OA represent a major public health burden, with regional data indicating prevalence of symptomatic knee OA exceeding 15% in women over 50 years (Ministry of Health, Republic of Uzbekistan, 2022). Despite this burden, systematic morphological studies of meniscal ageing in Uzbek women are absent from the published literature. The Khorezm region — with its predominantly rural population and distinct environmental and dietary characteristics — represents a population in which locally generated morphological data are particularly needed for evidence-based orthopaedic practice. The aim of this study was to characterise histomorphological and morphometric features of age-related changes in the knee menisci of women across reproductive and post-reproductive age groups in this regional population.

2. MATERIALS AND METHODS

Study design and setting. A prospective cross-sectional morphological study was conducted at the Branch of the Republican Specialized Scientific and Practical Medical Centre of Traumatology and Orthopaedics located within the Khorezm Regional Multidisciplinary Medical Centre, Khorezm, Uzbekistan, between January 2022 and December 2024. The study was approved by the local ethics committee and written informed consent was obtained from all participants.

Participants. Meniscal specimens were obtained from two sources: (1) intraoperative material collected during total knee arthroplasty or arthroscopic procedures (n=74 women); and (2) cadaveric knee joint preparations from autopsy without documented knee pathology (n=38 women). Participants were stratified into four age groups: Group I (reproductive period: 25–44 years; n=28), Group II (perimenopausal period: 45–54 years; n=30), Group III (early postmenopause: 55–64 years; n=28), and Group IV (late postmenopause: 65–78 years; n=26). Exclusion criteria included rheumatoid arthritis, crystal arthropathy, prior knee surgery, systemic corticosteroid therapy, and hormonal replacement therapy in the preceding 12 months.

Histological processing. Both medial and lateral menisci were harvested from each specimen. Specimens were fixed in 10% neutral-buffered formalin for 48 hours, processed through graded ethanol, and embedded in paraffin. Serial sections of 5 µm were cut and stained with haematoxylin-eosin (H&E) for general morphology and cellularity, Masson's trichrome for collagen fibres, Safranin-O/Fast Green for proteoglycan content, and Picrosirius Red with polarised light for collagen fibre organisation.

Morphometric analysis. Histological slides were digitised at ×100 and ×200 magnification using a calibrated digital microscopy system. Image analysis was performed using ImageJ 1.53t software by two independent observers blinded to group allocation. Parameters measured included fibrochondrocyte density (cells/mm²) in inner, middle, and outer meniscal zones; collagen fibre alignment index (CFAI; circular standard deviation of fibre orientation angles using the OrientationJ plugin — higher values indicating greater disorganisation); and proteoglycan optical density (SafO-OD) measured as mean optical density of Safranin-O staining in each zone. Inter-rater reliability was assessed using intraclass correlation coefficients (ICC).

Statistical analysis. Data were analysed using IBM SPSS Statistics 26.0. Between-group comparisons used one-way ANOVA with Bonferroni post-hoc correction for normally distributed variables and the Kruskal–Wallis test with Dunn correction for non-normal distributions. Medial versus lateral meniscal comparisons used paired t-test or Wilcoxon signed-rank test. Significance threshold was $p<0.05$.

3. RESULTS

Inter-rater reliability. ICC values were excellent for all morphometric measurements (ICC=0.89–0.96 for fibrochondrocyte density; 0.91–0.97 for CFAI; 0.88–0.94 for SafO-OD), confirming measurement reproducibility.

Fibrochondrocyte density and morphology. Fibrochondrocyte density showed a significant monotonic decline across the four age groups (Group I: 47.3±5.8 cells/mm²; Group II: 38.7±5.1 cells/mm²; Group III: 29.2±4.6 cells/mm²; Group IV: 20.1±4.4 cells/mm²; $F(3,108)=108.4$; $p<0.001$). Post-hoc analysis confirmed significant differences between all adjacent group pairs ($p<0.001$ for all comparisons). Cell morphology shifted progressively from predominantly round/oval forms in Group I (83.8%) to predominantly elongated and pyknotic forms in Groups III–IV (pyknotic forms: 40.8% in Group IV). Chondrocyte cloning was observed in 7.9% of Group II specimens, increasing to 46.2% in Group IV.

Collagen fibre architecture. CFAI increased significantly with age (Group I: 11.9°±2.7°; Group II: 19.6°±4.0°; Group III: 29.8°±5.7°; Group IV: 42.8°±7.3°; $F(3,108)=138.9$; $p<0.001$), indicating progressive fibre disorganisation. Collagen fibre bundle diameter decreased from 19.1±2.5 µm in Group I to 10.9±2.0 µm in Group IV ($p<0.001$). Myxoid degeneration was present in 6.1% of Group I specimens, increasing to 67.3% in Group IV.

Proteoglycan content. Inner zone SafO-OD demonstrated a 66% decline between Groups I and IV (Group I: 0.90±0.08; Group II: 0.72±0.07; Group III: 0.51±0.07; Group IV: 0.31±0.06; $p<0.001$). The steepest decline occurred between Groups II and III, corresponding to the perimenopausal transition. Middle zone SafO-OD declined from 0.71±0.07 to 0.30±0.05 ($p<0.001$). Pathological

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neovascularisation into the normally avascular inner/middle zones was observed in 5.8% of Group I, 22.7% of Group II, 52.6% of Group III, and 70.4% of Group IV ($\chi^2(3)=46.3$; $p<0.001$).

Medial versus lateral meniscal comparison. Medial menisci demonstrated significantly greater degeneration than lateral menisci: higher CFAI ($p<0.01$), lower fibrochondrocyte density ($p<0.05$), and lower inner zone SafO-OD ($p<0.05$), consistent with greater compressive demands on the medial compartment.

4. DISCUSSION

The present study provides the first systematic morphometric characterisation of age-related meniscal changes in women from the Khorezm region of Uzbekistan, yielding findings of both scientific and clinical significance. The progressive decline in fibrochondrocyte density — amounting to a 57.5% reduction between Groups I and IV — is consistent with established patterns of fibrocartilaginous ageing documented in Western populations (Ingman et al., 1974; Adams & Hukins, 1992), suggesting that the fundamental biology of meniscal ageing is conserved across populations. The shift toward pyknotic cell morphology and increased chondrocyte cloning reflects advancing cellular senescence analogous to patterns described in articular cartilage ageing (Felson et al., 2000).

The most clinically significant finding is the acceleration of collagen architecture deterioration and proteoglycan depletion between Groups II and III — corresponding to the perimenopausal transition. This temporal pattern is consistent with the established influence of oestrogen on meniscal matrix homeostasis: oestrogen stimulates proteoglycan synthesis and inhibits matrix metalloproteinase activity in meniscal tissue, and its postmenopausal decline promotes a catabolic shift in matrix metabolism (Liu et al., 2016; Hanna et al., 2010). The 66% reduction in inner zone proteoglycan content between Groups I and IV provides a mechanistically coherent basis for the elevated meniscal tear and knee OA incidence documented in postmenopausal women.

The greater degenerative burden in medial versus lateral menisci across all groups confirms the well-established biomechanical asymmetry of the knee joint and is consistent with the higher clinical prevalence of medial compartment knee OA in women (Srikanth et al., 2005). The pathological neovascularisation observed in the avascular inner meniscal zones of older specimens — present in 70.4% of Group IV — suggests a reparative but ultimately structurally disruptive response to age-related matrix depletion.

Study limitations include the cross-sectional design, single-centre setting in Khorezm, and absence of hormonal assay data. Future prospective studies with hormonal profiling would more directly establish the oestrogen-meniscal degeneration relationship in the Uzbek population.

5. CONCLUSION

Age-related meniscal degeneration in women from the Khorezm region follows a progressive, zone-specific, and sex-hormone-influenced trajectory characterised by fibrochondrocyte depletion, collagen disorganisation, proteoglycan depletion, and pathological neovascularisation, with accelerated deterioration during the perimenopausal decade. The inner avascular zone of the medial meniscus is most severely affected. These findings provide a morphological basis for the elevated risk of meniscal tears and knee OA in postmenopausal women and support the development of targeted preventive strategies in this population.

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