



Title	Articular surface integrity assessed by ultrasound is associated with biological characteristics of articular cartilage in early - stage degeneration
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Citation	大阪大学, 2023, 博士論文
Version Type	
URL	https://hdl.handle.net/11094/92032
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論文内容の要旨

Synopsis of Thesis

氏 名 Name	SHI WEN
論文題名 Title	Articular surface integrity assessed by ultrasound is associated with biological characteristics of articular cartilage in early-stage degeneration (エコーによる関節軟骨表面形状評価は、変性早期の関節軟骨の生物学的性状を反映する)
論文内容の要旨 〔目 的(Purpose)〕 Articular cartilage disorders caused by osteoarthritis (OA) are serious social and medical problems due to the number of patients affected and the impact these disorders on activities of daily living. The early diagnosis of articular cartilage damage and repeated evaluation of treatment efficacy are essential for OA treatment. In this study, we established a simple ultrasound grading system for early degenerative articular cartilage and investigated its relationship with cartilage biological characteristics. 〔方法ならびに成績(Methods/Results)〕 Human osteochondral specimens were obtained from the lateral femoral condyle (LFC) of the patients diagnosed with OA (N = 22; 19 females, 3 males) within 48 h after total knee arthroplasty. The ultrasound grading system were based on surface integrity (S1a: continuous high-echo lines, S1b: discontinuous or weak high-echo lines, S2: surface irregular) and cartilage echogenicity (E1: with >50%, E2: <50% hypoechoic area of total cartilage layer) and verified by surface roughness (Ra; μm) and histological staining. The results showed that Ra was lower in S1 than in S2, and the percentage of hypoechoic and safranin O-stained areas was positively correlated. Then we examined the relationship between ultrasound grade and histopathological evaluation (OARSI grade), gene expression, and protein production in responded to pro-inflammatory cytokine (IL-1β) stimulation. The average OARSI grade (mean $\pm$ SD) for each US grade was as follows: 1.5$\pm$0.7 (S1a), 2.4$\pm$1.0 (S1b), 3.4$\pm$1.0 (S2), 2.5$\pm$1.2 (E1), and 2.5$\pm$1.2 (E2). OARSI grades were significantly related to US grades ($p < 0.0001$). In OA-related gene expression, the superficial part of S1 had higher expression of Collagen10, aggrecan, Sox9, and lower expression of Collagen1 and BMP2 than that of S2. At last, S1 responded more pronouncedly to IL-1β, the concentration differences of IL-6 (2.4-fold, $p = 0.006$), IL-8 (2.0-fold, $p = 0.005$), and CCL2 (2.0-fold, $p = 0.001$) in the supernatant were significantly higher than those in S2. There was no difference among the E-grades. 〔総 括(Conclusion)〕 US assessment focusing on articular cartilage surface integrity reflected the biological characteristics of articular cartilage in the early stages of degeneration, including the OARSI histopathology grading system, gene expression, and response to IL-1β (a pro-inflammatory cytokine). The ability to sensitively delineate the early stages of articular cartilage degeneration may be suitable for screening OA, and for frequent longitudinal assessment of the natural course and after therapeutic intervention. The results of this study suggest that standard ultrasonography can be used as a powerful tool in the field of OA treatment and basic articular cartilage research.	

論文審査の結果の要旨及び担当者

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論文審査の結果の要旨

本研究は、実臨床での運動器エコーの有用性の向上と関節軟骨に関する新知見を目指して、ヒト臨床サンプルを対象として行われた。変形性関節症患者の関節軟骨のエコーによる表面形状評価が、病理組織評価や遺伝子発現・炎症性サイトカインへの反応などの生物学特性を反映する事が示された。エコーを用いて簡便に関節軟骨の生物学的性状評価を評価できることは、関節軟骨損傷の治療の検討への活用はもとより、関節軟骨に関する基礎研究のツールとしても意義が大きい。本研究における成果は、変形性関節症や外傷性関節軟骨損傷などの医療分野の発展において重要な糸口となり得ることから、本論文が博士（医学）の学位授与に値するものと認める。