

Collagen X Longitudinal Fracture Biomarker Expression Demonstrates Similar Endochondral Activity in Intra and Extra-articular Fractures

Caellagh D Catley 1, Catherine E Hutchison 1, Tasha McKibben 1, Talia Trapalis 1, Colby Curtis 1, Dane J. Brodke 1, Graham J. DeKeyser 1, Darin M. Friess 1, Chelsea Bahney 1, Zachary M Working 1
1Oregon Health and Science University Portland, Oregon

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INTRODUCTION: A biologic method to quantify fracture healing remains elusive. Growing evidence supports Collagen X as an experimental yet validated marker of endochondral ossification in fracture healing through a cartilaginous intermediate (validated assay: "CXM"). We hypothesized CXM would demonstrate increased expression in intra-articular fractures when compared to extra-articular fractures given the hypothesized contribution of cartilage damage to circulating CXM levels.

METHODS: This study was approved by the Ethics Committee. Patients presenting to a single level 1 trauma center (2019 -2023) within 14 days of isolated fractures were consented and observed, patients were treated via standard of care. Blood was collected at all clinical encounters and analyzed for CXM. Maximum CXM expression (peak) and time to peak (days from injury to peak) were compared between pelvic ring vs. acetabular fractures, femoral shaft vs. distal femur fractures, and tibial shaft vs. pilon and plateau fractures. A pooled analysis of all intra-articular fractures was compared against extra-articular fractures using t tests.

RESULTS SECTION: 113 patients sustaining fractures of the pelvis (15 acetabulum/8 pelvic ring) femur (14 femoral shaft/3 distal femur) or tibia (28 tibial shaft/9 pilon fractures/36 tibial plateau) were enrolled. The average age was 43.4 years (range 18-82). The majority of patients were male (57%) with a high energy mechanism (71%) with similar proportions present in both intra and extra-articular groups. An average of 4.6 samples were collected per patient. Peak CXM and time to peak CXM did not significantly differ between any of the comparison groups ($p>0.1$ in all groups). Pooled comparison of all intra-articular and extra-articular fractures similarly did not demonstrate a difference in expression ($p>0.1$). Critical subanalyses demonstrate that peak CXM and time to peak by biological sex similarly did not demonstrate effect on expression. Elderly patients (>65) demonstrated higher peak CMX ($1,536 \pm 700\text{pg/mL}$ vs. $1085.1 \pm 527 \text{pg/mL}$, $p=0.024$) but no difference in time to peak expression ($p=0.2$)

DISCUSSION: Endochondral ossification did not differ significantly between fractures sparing adjacent joint surfaces and those which were intra-articular with cartilage injury. This conclusion is limited by use of experimental CXM blood testing, but is an important translational stepping stone, allowing for analysis of multiple fracture types together in future research on endochondral fracture healing.

SIGNIFICANCE/CLINICAL RELEVANCE: A clinical measure of fracture healing remains elusive but CXM as a promising marker demonstrates no difference in expression during articular vs nonarticular fractures. This exploratory study intends to build on orthopedic knowledge to allow surgeons to identify how to promote optimal fracture healing depending on location.

REFERENCES:

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