Δ Collagen X Biomarker Correlates to Canonical Bone Turnover Markers During Fracture Healing and Distinguishes Sex-Related Differences in Soft Callus Formation

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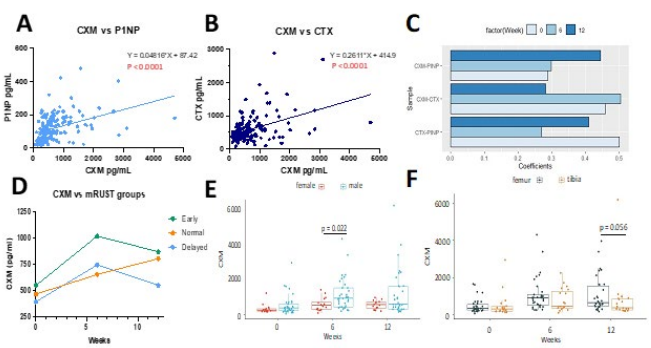
Purpose: To date there remain no rigorously characterized biomarkers for fracture repair. In this study we correlate our novel collagen X biomarker (CXM), which measures the transient matrix protein in the soft callus, to the canonical bone turnover markers CTX (bone resorption) and P1NP (bone formation) in a cohort of tibia and femur fracture patients. We then evaluate changes in CXM expression according to vitamin D3 (VitD3) treatment group, healing rate, sex, and fracture location.

Methods: Patients receiving an intramedullary nail for a tibial or femoral shaft fracture (IRB approval, age 18-50 years) were enrolled in a randomized controlled trial comparing various VitD3 supplementation protocols to placebo. Serum CXM expression was compared to CTX and P1NP (total procollagen type 1 N-terminal <g-bubble jscontroller="QVaUhf" data-ci="" data-du="200" data-tp="5" jsaction="R9S7w:VqIRre;" jsshadow="">propeptide) </g-bubble>concentrations (injury, 6 and 12 weeks post-injury). Longitudinal radiographs were scored (blinded mRUST [modified Radiographic Union Score for Tibial Fractures). Groups were defined by time to mRUST = 12: early (<12 weeks), normal (13-26 weeks), delayed (>27 weeks).

Results: Consistent with previously reported study results, CXM expression patterns did not support VitD3 supplementation resulting in different healing outcomes. However, for the first time, we show strong correlations between CXM and both CTX (P<0.001) and P1NP (P<0.001) (Fig, 1A-C). Furthermore, we find a statistically significant peak in CXM at 6 weeks, consistent with presumed formation of the soft callus, and show that early healers (<12 weeks) present with higher CXM values (Fig. 1D). Regarding sex, there was no difference in unfractured control patients; men presented higher CXM values than women at 6 weeks (Fig. 1E, P = 0.02). As for location, CXM values trended higher in femur than tibia fractures at 12 weeks (Fig. 1F, P = 0.056).

Conclusion: CXM correlates with traditional bone turnover markers and may provide early information about extent of fracture healing.



Δ OTA Grant