Accelerated collagen turnover in women with angina pectoris without obstructive coronary artery disease: An iPOWER substudy - DTU Orbit (20/10/2019)

**Aim:** Collagens are major cardiac extracellular matrix components, known to be actively remodelled and accumulated during diffuse myocardial fibrosis. We evaluated whether accelerated collagen turnover described by neo-epitope biomarkers reflecting collagen formation and degradation separates patients with diffuse myocardial fibrosis from asymptomatic controls.

**Methods and results:** Seventy-one women with angina pectoris without significant coronary artery disease assessed by invasive coronary angiogram were included. Competitive enzyme-linked immunosorbent assays (ELISAs) measuring circulating protein fragments in serum assessed the formation and degradation of collagen type III (Pro-C3, C3M and C3C), IV (P4NP7S and C4M), V (Pro-C5 and C5M) and VI (Pro-C6 and C6M), and degradation of collagen type I (C1M). Serum samples from 32 age-matched asymptomatic women were included as controls. Symptomatic women presented significantly elevated levels of Pro-C6, C3C, C3M, C4M and C8-C ($p<0.0001–0.0058$) and significantly decreased levels of Pro-C3, C5M and C6M ($p<0.0001–0.041$), reflecting accelerated collagen turnover and an imbalanced collagen formation and degradation compared to controls. Cardiac magnetic resonance T1 mapping was performed to determine extracellular volume fraction and thus diffuse myocardial fibrosis. A significant association was identified between C5M and extracellular volume fraction by cardiac magnetic resonance ($p=0.01$).

**Conclusion:** Women with angina pectoris, but without significant obstructive coronary artery disease, showed an imbalanced collagen turnover compared to asymptomatic controls. The examined biomarkers are tools to monitor active collagen remodelling in patients with angina pectoris, in risk of developing myocardial fibrosis.