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Novel tissue turnover biomarkers are associated with prolonged QTc and pulmonary arterial hypertension in patients with systemic sclerosis

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BACKGROUND

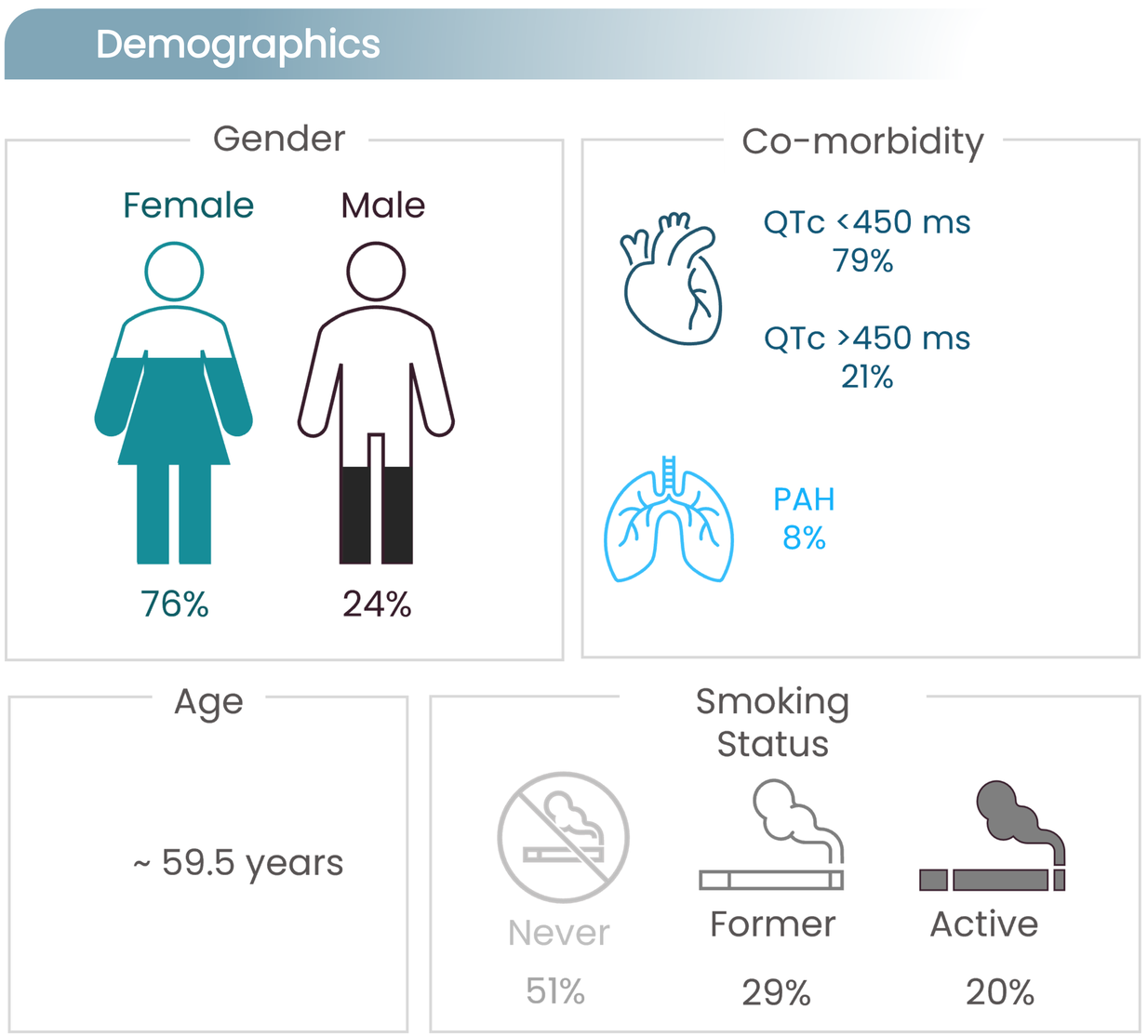
Systemic sclerosis (SSc) is characterized by vasculopathy and fibrosis of the skin and internal organs. Cardiovascular involvement is a frequent and significant contributor to morbidity and mortality in SSc. They can develop clinically silent and be difficult to detect. Novel tissue turnover biomarkers hold the potential to detect the manifestations before clinical overt disease, identify risk patients and monitor the disease course as well as improve our understanding of the pathophysiology in SSc.

The objective of this study is to measure a panel of collagen biomarkers in SSc and explore associations to cardiac involvement detected by ECG and to PAH.

METHODS

One-hundred and two patients fulfilling the 2013 ACR/EULAR criteria for SSc were included in the study (mean age 59, 77% female, disease duration 0.5-30 years). At study visit, participants completed a questionnaire concerning co-morbidities (confirmed by medical records review), current medication, family history of CV events, heart symptoms, and smoking habits. Systolic and diastolic blood pressures and standard 12-lead electrocardiogram (ECG) were measured. Biomarkers of type III and VI collagen formation (PRO-C3 and PRO-C6) and degradation (C3M and C6M) were measured in serum by competitive ELISAs.
Differences between biomarker levels in SSc patients with myocardial involvement presented as the prolongation of the corrected QT (QTc) interval (QTC<450ms or QTC>450ms), and with or without PAH, were calculated by Mann-Whitney U test.

Demographics



RESULTS

Patients with SSc and prolonged QTc (>450 ms) have higher levels of PRO-C3 and PRO-C6

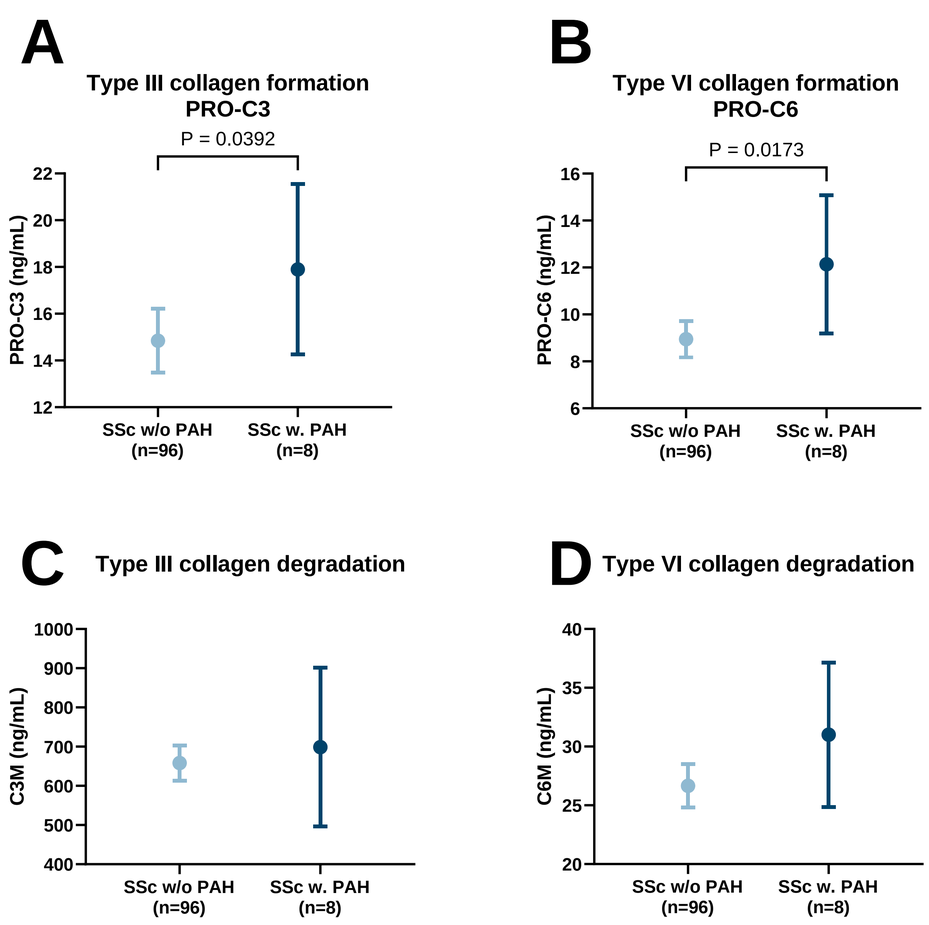


Figure 1. **Levels of ECM biomarkers in SSc patients with QTc<450 ms (n=81) vs. QTc>450ms (n=21).** Serum levels of: A) type III collagen formation (PRO-C3); B) type VI collagen formation (PRO-C6); C) type III collagen degradation (C3M); and D) type VI collagen degradation. Differences between groups were calculated by a non-parametric Mann-Whitney t-test, and data are presented as Mean with 95% CI.

Patients with SSc-PAH have higher levels of PRO-C3 and PRO-C6

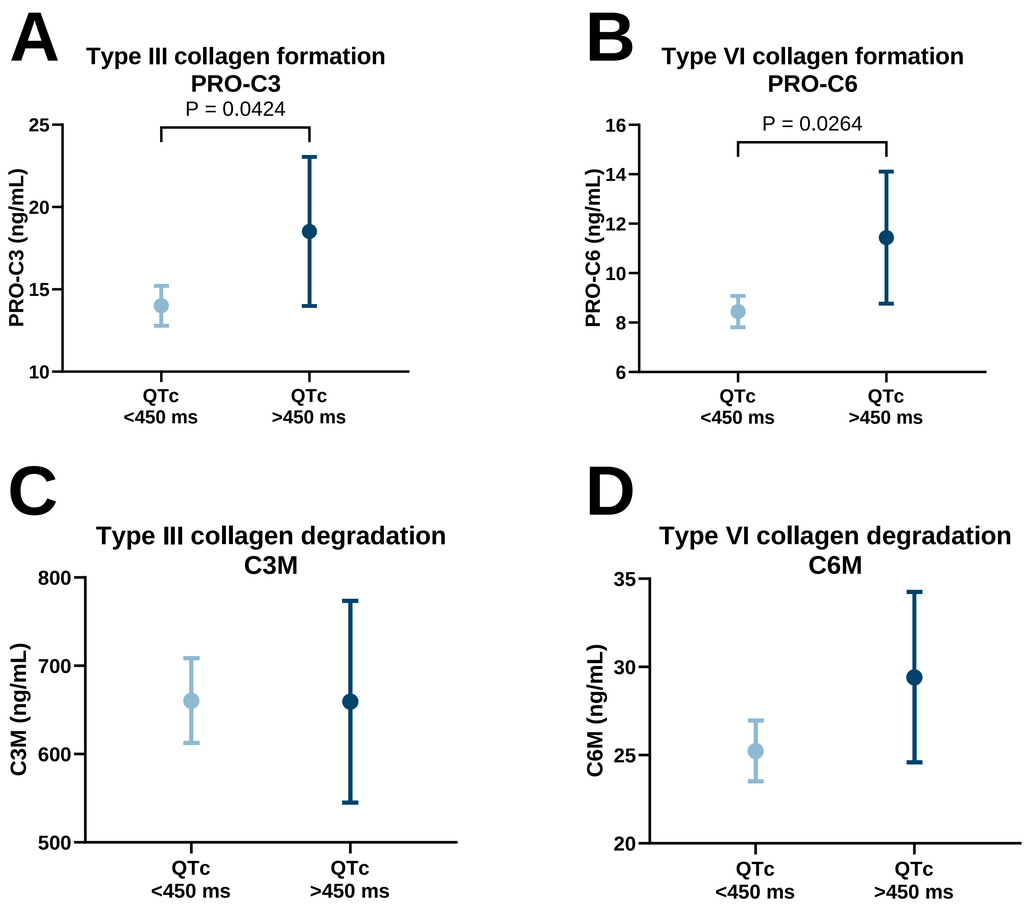


Figure 2. **Levels of ECM biomarkers in SSc patients with PAH (n=8) and without PAH (n=94).** Serum levels of: A) type III collagen formation (PRO-C3); B) type VI collagen formation (PRO-C6); C) type III collagen degradation (C3M); and D) type VI collagen degradation. Differences between groups were calculated by a non-parametric Mann-Whitney t-test, and data are presented as Mean with 95% CI.

CONCLUSION

Patients with SSc and prolonged ECG presented an altered tissue turnover, by an increased level of PRO-C3 and PRO-C6. In addition, SSc patients with presence of PAH had increased levels of PRO-C3 and PRO-C6 as well. presented an altered tissue turnover in presence of PAH, and with a QTc>450 ms. Our study indicates that they could serve as biomarkers of these manifestations and warrant further studies in cardiac disease in SSc.

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