Recurrence of atrial fibrillation is reflected by elevated formation of collagen type III and VI after ablation treatment

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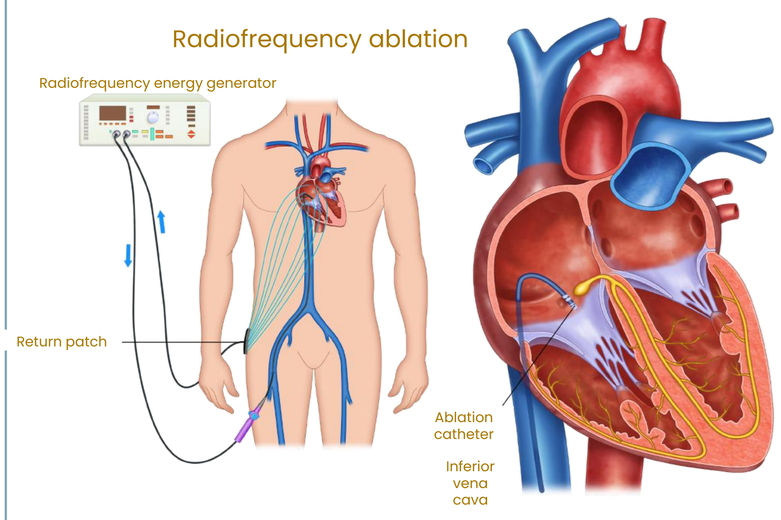
BACKGROUND & AIM



Catheter ablation treatment for atrial fibrillation (AF) induces controlled myocardial injury to the pulmonary veins. This targeted injury initiates a wound healing response involving inflammation, fibroblast activation, and ECM remodelling. Collagen type III remodelling, deposited early during tissue repair, and type VI, which supports ECM organization, may indicate a persistent wound-healing response rather than physiological scar formation.

The aim of this study was to investigate changes in circulating biomarkers of collagen III formation and collagen VI turnover in individuals with AF that underwent ablation to characterize the ECM remodelling response and explore their potential as indicators of post-procedural fibrosis.

Baseline characteristics (n=276)

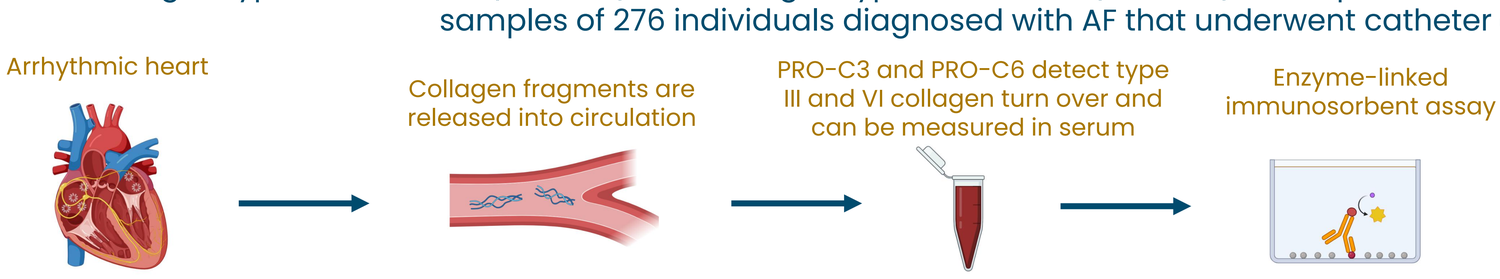
Age	Sex	Hypertension	Diabetes	LVEF
65 years (SD, 11)	72% males	149 (54%)	33 (12%)	60% (IQR, 58-67)

AF duration	Ischemic heart disease	Left atrial volume	Prior AF ablation	AF recurrence
22 months (IQR, 4-60)	19 (7%)	58 mL (IQR, 42-72)	88 (32%)	83 (30%)

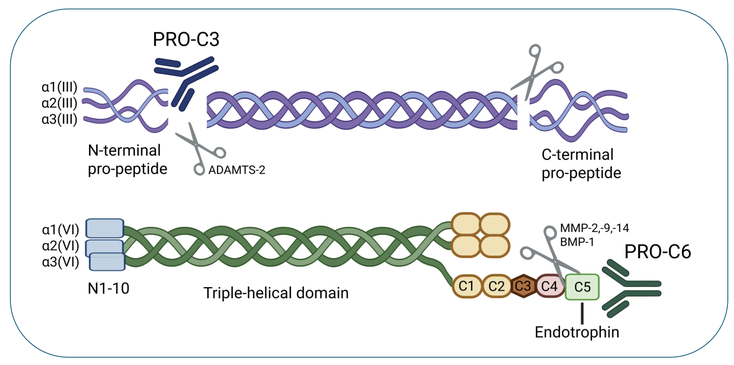
METHODS

Experimental

Levels of collagen type III formation (PRO-C3) and collagen type VI turnover (PRO-C6) were quantified with enzyme-linked immunosorbent assays in serum samples of 276 individuals diagnosed with AF that underwent catheter ablation treatment.



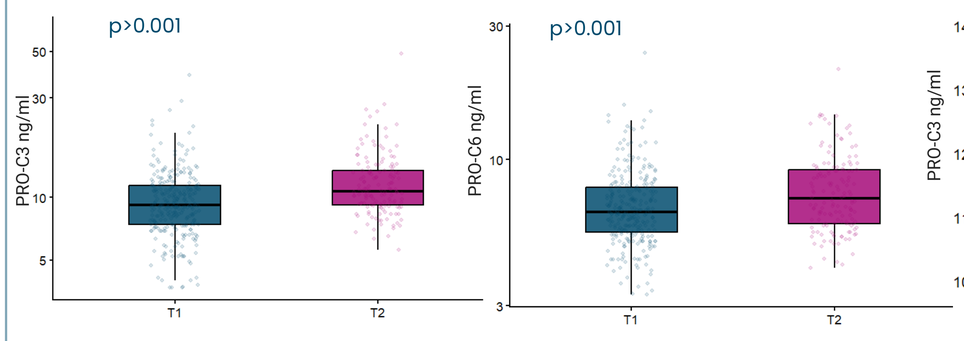
PRO-C3 and PRO-C6 ELISA are based on the competitive binding of the monoclonal antibody specific to the N-terminal propeptide of type III and C- terminal of VI collagen, respectively.



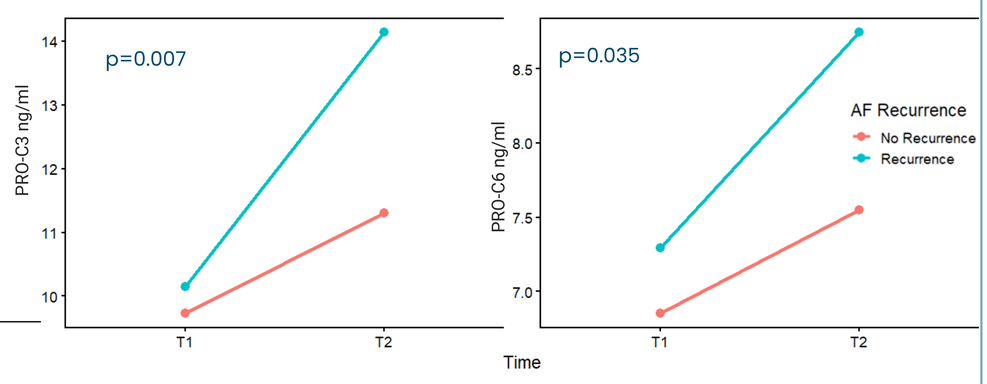
Statistical

Wilcoxon signed-rank test was used to assess differences in groups. Biomarker changes from baseline to follow-up were compared using linear mixed models. The associations with AF recurrence were evaluated using unadjusted and multivariable-adjusted logistic regression models.

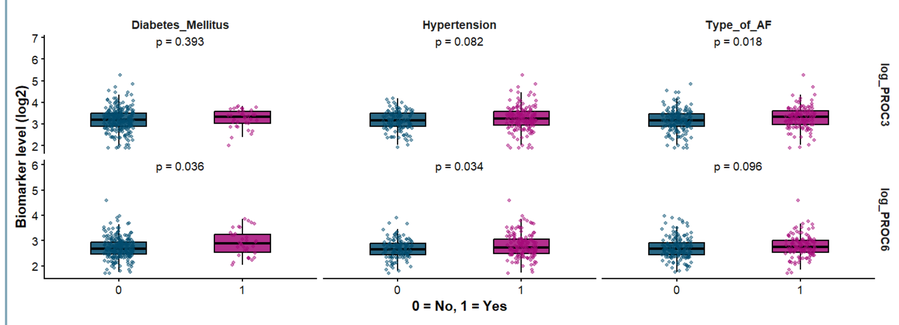
RESULTS



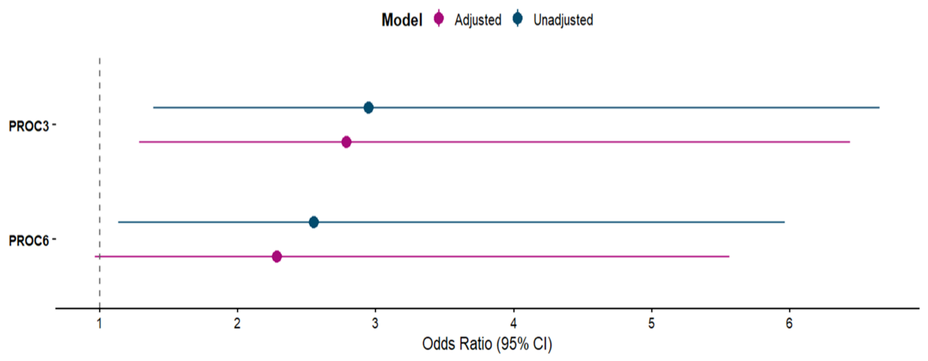
Levels of circulating PRO-C3 and PRO-C6 increased significantly post ablation. p<0.001 for PRO-C3 and PRO-C6.



Individuals who experienced AF recurrence had higher increase in post-ablation PRO-C3 and PRO-C6 levels from baseline compared to those without AF recurrence (p = 0.007 and p = 0.035, respectively)



PRO-C3 levels were more elevated in individuals with persistent AF (p=0.018). PRO-C6 levels were more elevated in individuals with hypertension (p=0.04) and diabetes (p=0.03). There were no other significant differences observed. In type of AF, 0=paroxysmal AF and 1= persistent.



Post-ablation levels of both PRO-C3 and PRO-C6 were associated to AF recurrence (HR per doubling of PRO-C3: 2.95, [1.39-6.65], p= 0.006 and PRO-C6: 2.55 [1.13-5.96], p=0.026). After adjustment for age and sex, only PRO-C3 levels remained associated to AF recurrence (HR per doubling of PRO-C 3: 2.79 [1.29-6.44], p= 0.012).

CONCLUSION

The findings suggest that PRO-C3 and PRO-C6 may reflect excessive activation of fibroblasts following the ablation, and although physiological scarring is necessary, AF recurrence might be driven by overactive fibrosis. These biomarkers could potentially assist in identifying patients who develop excessive scarring and could benefit from antifibrotic treatment after their ablation therapy

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