Collagen type I degradation biomarkers are associated with risk of mortality after ST-elevated myocardial infarction.

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PURPOSE

After **ST-elevated myocardial infarction (STEMI)**, collagen type-I (COL1), the myocardium's main constituent, is acutely degraded from cardiac tissue. **Destabilisation** of the cardiac tissue by **extracellular matrix remodelling** post-STEMI could increase the risk of further adverse events.

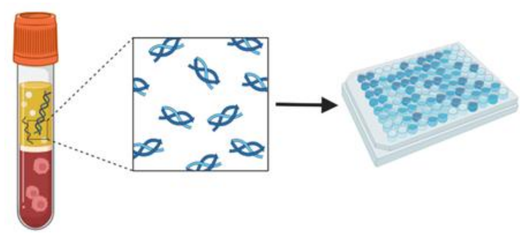
We aimed to **quantify COL1** using specific plasma biomarkers, including a **novel signalling fragment** of COL1 (**C1SIG**) and a more established **COL1 degradation** marker (**C1M**).

We also evaluated their use in risk prediction for all-cause mortality after STEMI event.

METHODS

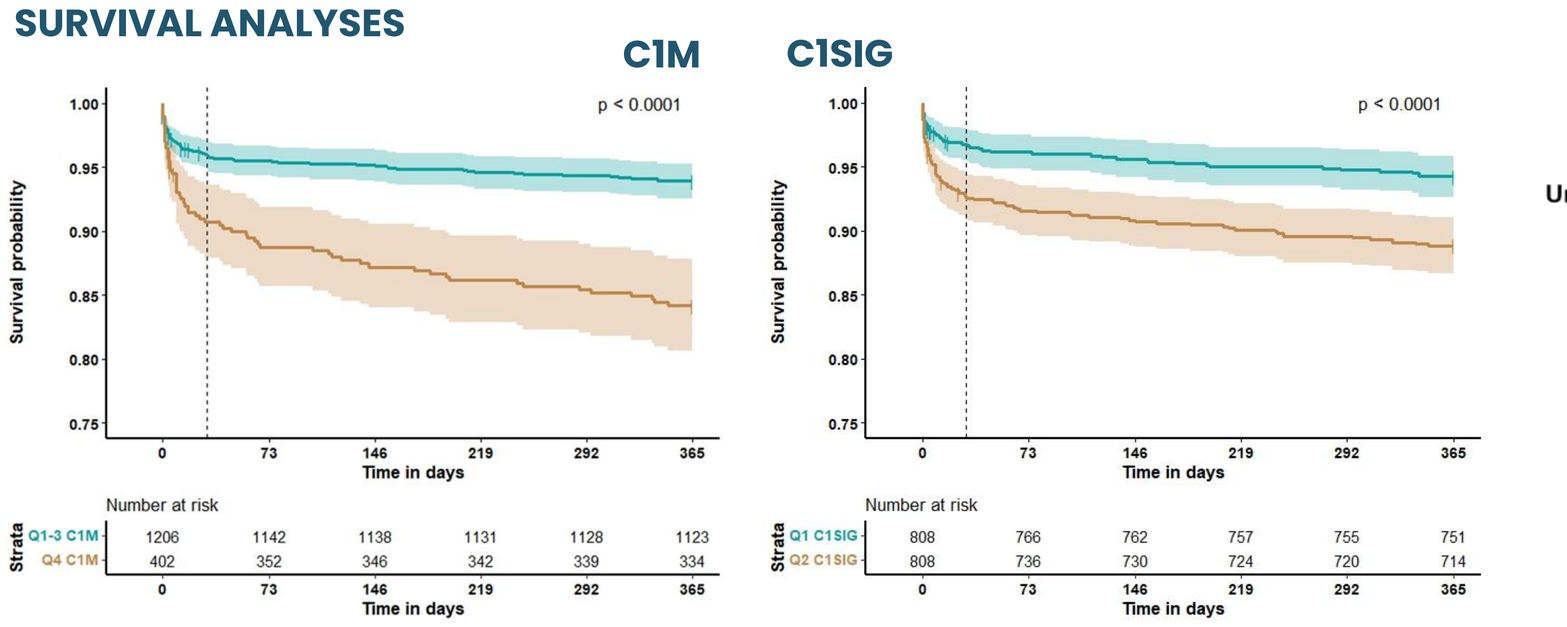
The **novel ELISA-based biomarker** targeting a **signalling fragment** of COL1 (C1SIG) was **technically developed and evaluated** before measuring in the plasma of **1,616 verified STEMI patients**. The plasma COL1 degradation marker, C1M, was measured in all STEMI patients.

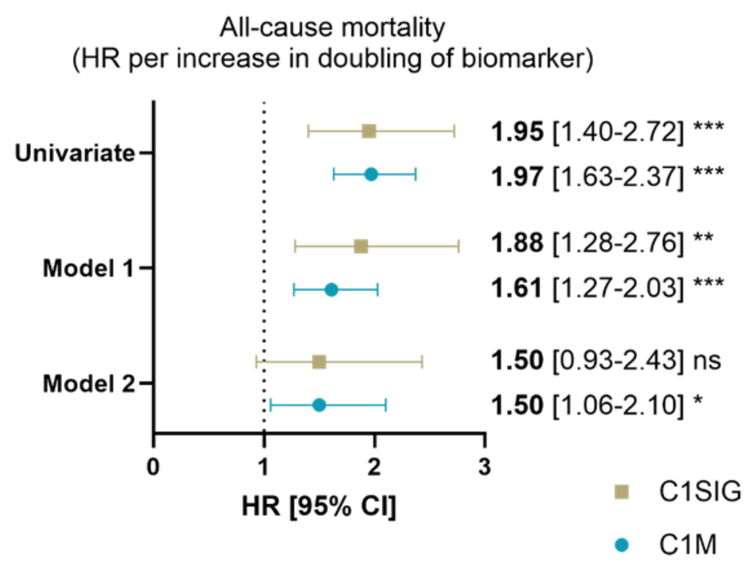
	Overall (n=1,616)
Sex (male)	73.0%
Age (years)	64.0 [19] Median [IQR]
C1M (ng/ml)	20.7 [10.6] Median [IQR]
C1SIG (ng/ml)	30.4 [9.50] Median [IQR]
Death (n)	100 / 136 (30 / 365 days)



RESULTS

SURVIVAL ANALYSES

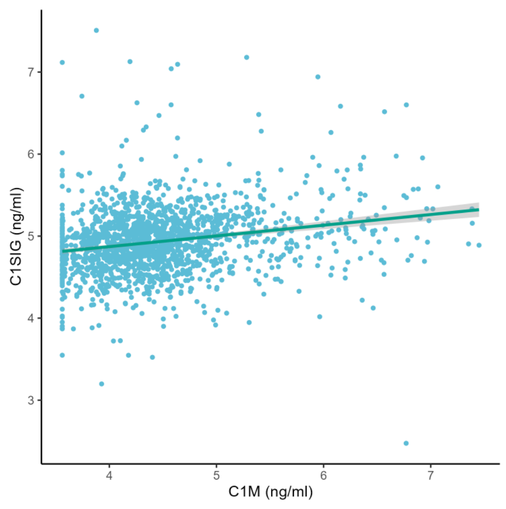




High C1M and **high C1SIG**, as the highest quartile and above the median, respectively, were **independently and significantly associated with all-cause mortality** in verified STEMI patients at 1-year post-admission. C1M and C1SIG are **risk predictors** for all-cause mortality **at 1-year post-STEMI** in univariate and **multivariate** cox regression analysis when adjusted for a model based on the **Framingham score**.

Model 1 was based on the Framingham Score (age, sex, diastolic blood pressure (BP), systolic BP, hypercholesterolemia, diabetes, smoking) and time to blood sampling. Model 2 was model 1 plus clinically used and emerging cardiac biomarkers (mid-regional pro-adrenomedullin, copeptin, pro-atrial natriuretic peptide, ST2 and C-reactive protein).

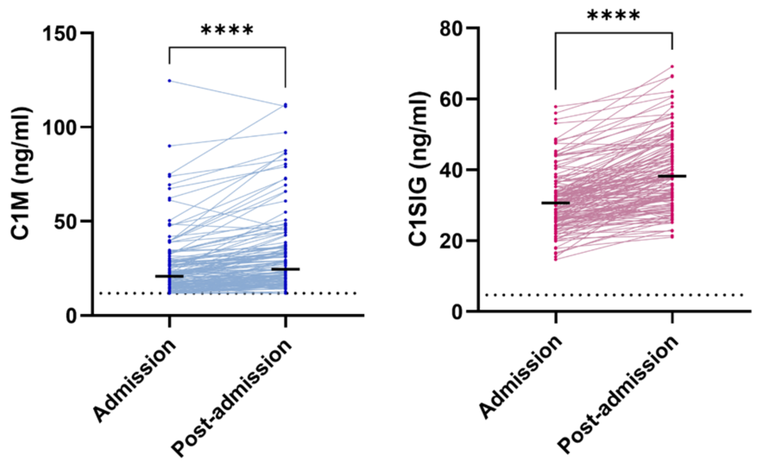
CORRELATION OF C1SIG and C1M



C1SIG and C1M are **poorly correlated** in patient plasma at admission with STEMI

r = 0.227, p < 0.001,
n = 1,607

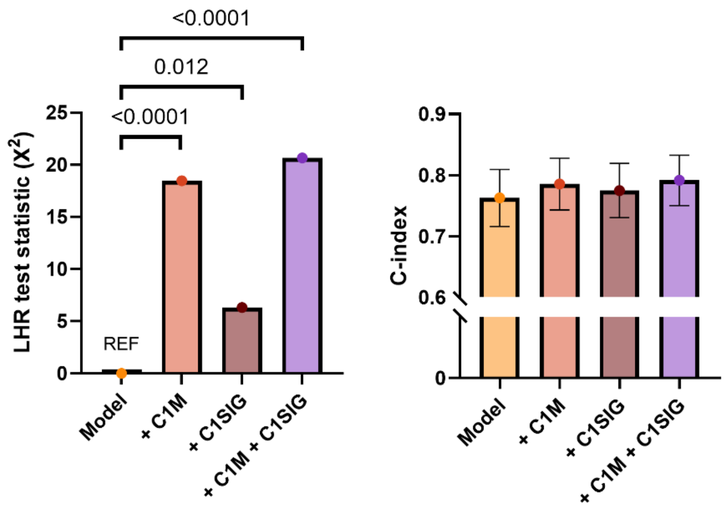
SUBSET ANALYSIS – EARLY BIOMARKER CHANGES



C1SIG and C1M show **dynamic changes** with increases in plasma concentrations from samples taken at admission to 6-12 hours post-admission.

Both, p < 0.0001, n = 140 pairs

DOES C1M OR C1SIG ADD VALUE TO THE FRAMINGHAM RISK SCORE?



The likelihood ratio test statistic suggests that C1M and C1SIG independently (but also together) improve the fit of the Framingham risk score. Other analyses may support some added value C1M biomarker to the Framingham score.

CONCLUSION

C1M and C1SIG are independently prognostic for mortality in STEMI patients after 1 year, in a multivariate model based on the Framingham Score. Assessing acute extracellular matrix processing in STEMI patients using COL1 biomarkers could be beneficial for predicting mortality and identifying a patient subset at increased risk of long-term outcome.

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