Canstatin, a type IV collagen fragment, is associated with risk of cardiovascular and all-cause mortality in patients with advanced atherosclerosis

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BACKGROUND

Atherosclerosis, a common underlying cause of cardiovascular disease, is defined by the formation of **plaques** in the arterial walls.

Changes in the **ECM composition** impact the risk for plaque rupture, which may cause acute complications (i.e. stroke or myocardial infarction (MI)).

Type IV collagen is primarily known as a major component of basement membranes and has previously been reported to promote plaque stability.

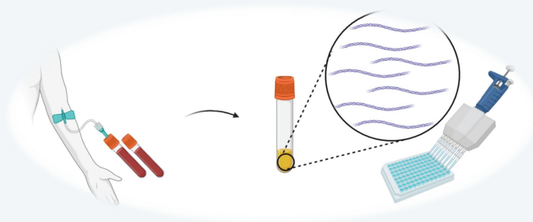
Canstatin is the non-collagenous C-terminal domain of type IV collagen alpha 2 chain. It is not only a by-product of proteolytic activity, but also a **bioactive molecule**.

This study investigated if canstatin was associated with adverse outcomes in patients with advanced carotid atherosclerosis.

Figure 1: Schematic representation of collagen VI a2 chain (Karsdal, Morten. Biochemistry of collagens, laminins and elastin: structure, function and biomarkers. Elsevier, 2023.)

METHODS

Canstatin was quantified in serum from 189 patients who underwent carotid endarterectomy, obtained from the Carotid Plaque Imaging Project biobank (Malmö, Sweden).



Clinical data and outcomes were collected during an average follow-up period of **90 months**.

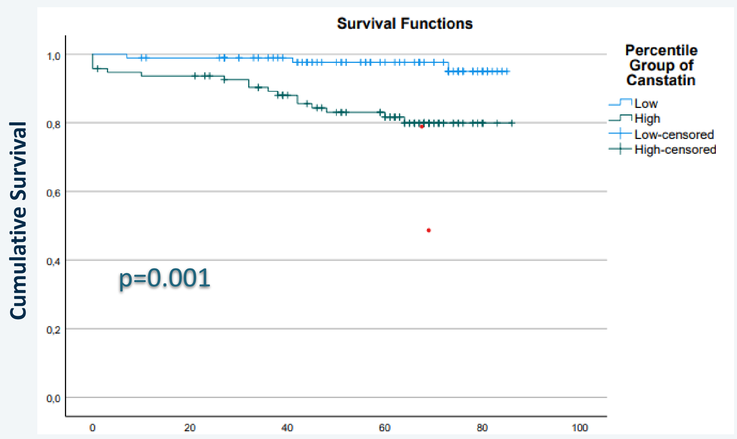
Survival analysis aimed at exploring the association between circulating **canstatin** levels and **cardiovascular mortality** and **all-cause mortality.**

	CPIP (n=189)
Age, years	70 [12]
Female sex	60 (31.7)
BMI, kg/m²	26.1 [4.95]
Current smoker	61 (32.3)
Blood hsCRP, mg/l	3.6 [4.46]
Pre-operative symptoms presence	106 (56.1)

Data are depicted as mean±SD, n (%) or median [IQR]

RESULTS

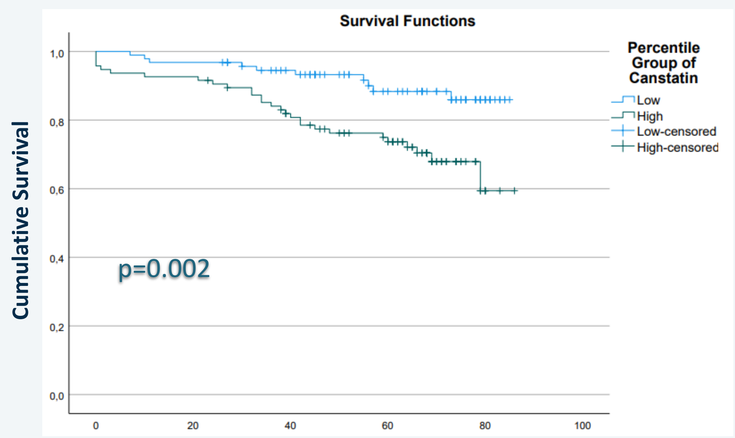
CV mortality



Time to postoperative death (months)

Percentile Canstatin Group	Total N	N of events
Low	94	3
High	95	17

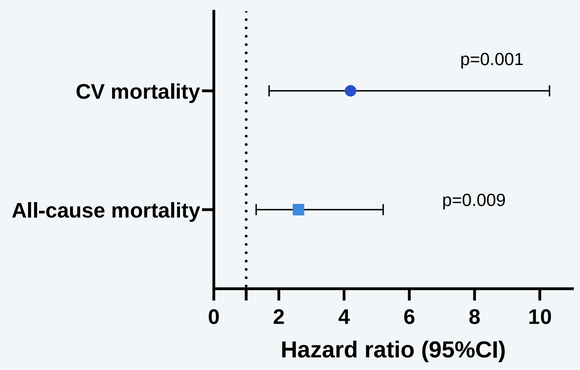
All-cause mortality



Time to postoperative death (months)

Percentile Canstatin Group	Total N	N of events
Low	94	10
High	95	28

Cox regression analysis



Hazard ratio (95% CI) adjusted for age, sex, hsCRP and pre-operative symptoms. Canstatin values were log-transformed.

High levels (above median) of canstatin were associated with an **increased risk** of both future **cardiovascular mortality** (p_{CV}=0.001) and **all-cause mortality** (p_{All}=0.002).

Associations remained **significant after adjustment** for age, sex, hsCRP and pre-operative symptoms (HR_{CV}= 4.2, 95% CI: 1.7 to 10.3, p=0.001, HR_{All}= 2.6, 95% CI: 1.3 to 5.2, p=0.009).

CONCLUSION

Higher circulating **canstatin** levels in patients undergoing carotid endarterectomy predicted **cardiovascular mortality** and **all-cause mortality** over 7.5 years.

Canstatin is a potential novel tool for **risk stratification** in patients with **advanced atherosclerosis**, warranting further studies.

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