

Protein levels in extracellular vesicles predict high-risk patients for secondary cardiovascular events: a pilot study

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Disclosure

Speaker name: **Nathalie Timmerman**

I have the following potential conflicts of interest to report:

- Consulting
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other(s)

- I do not have any potential conflict of interest

Introduction

Carotid artery
stenosis
↑ future stroke

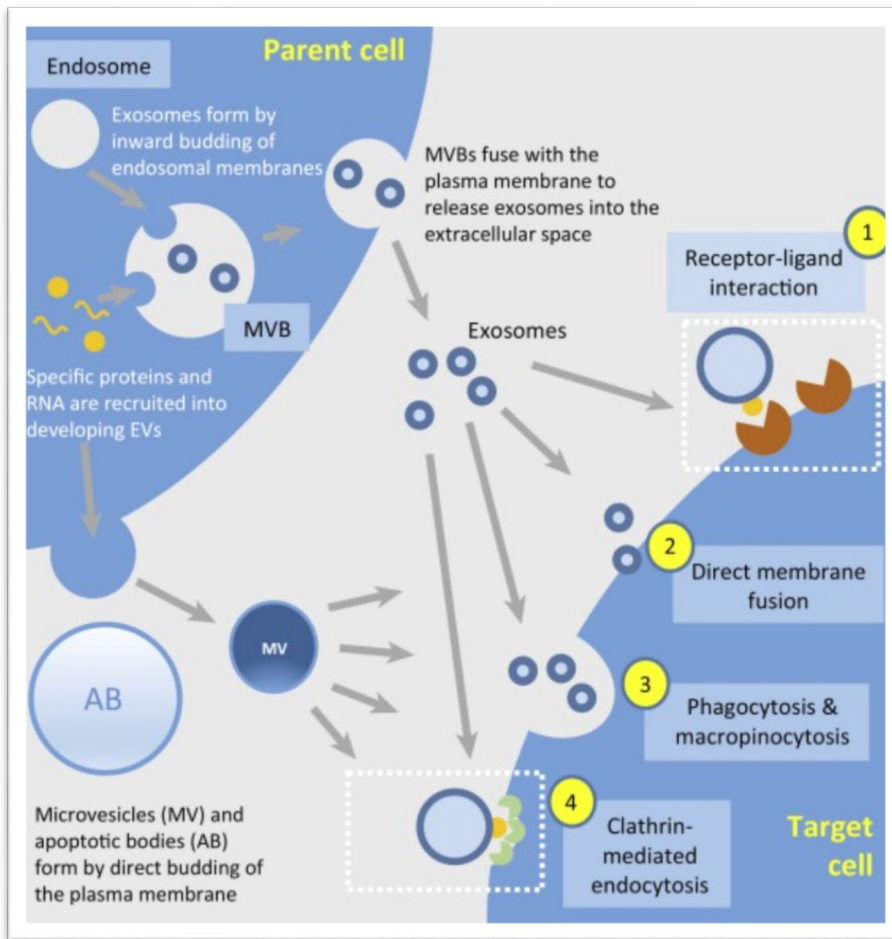
20%
new CVE within
3 years after
CEA

Risk- stratification
tools are lacking

CEA
↓ ipsilateral stroke

Intensify
treatment for
high-risk
patients?

New biomarker? Extracellular vesicle proteins

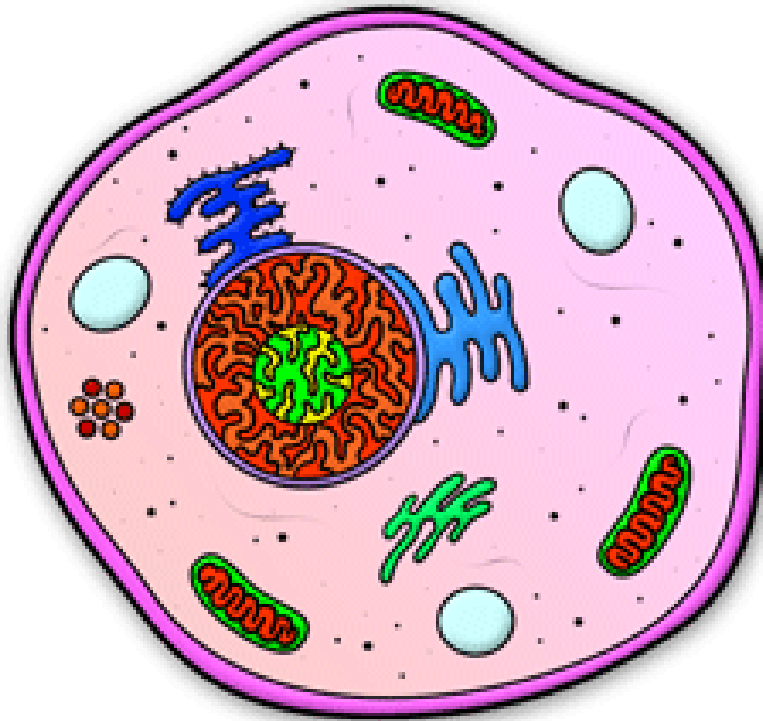


Physiological & pathophysiological processes

- Intercellular communication
- Inflammation
- Coagulation

Bank, *et al.* Exp Rev Mol Diagn (2015)
Boulanger, *et al.* Nature Reviews (2017)

Extracellular vesicles



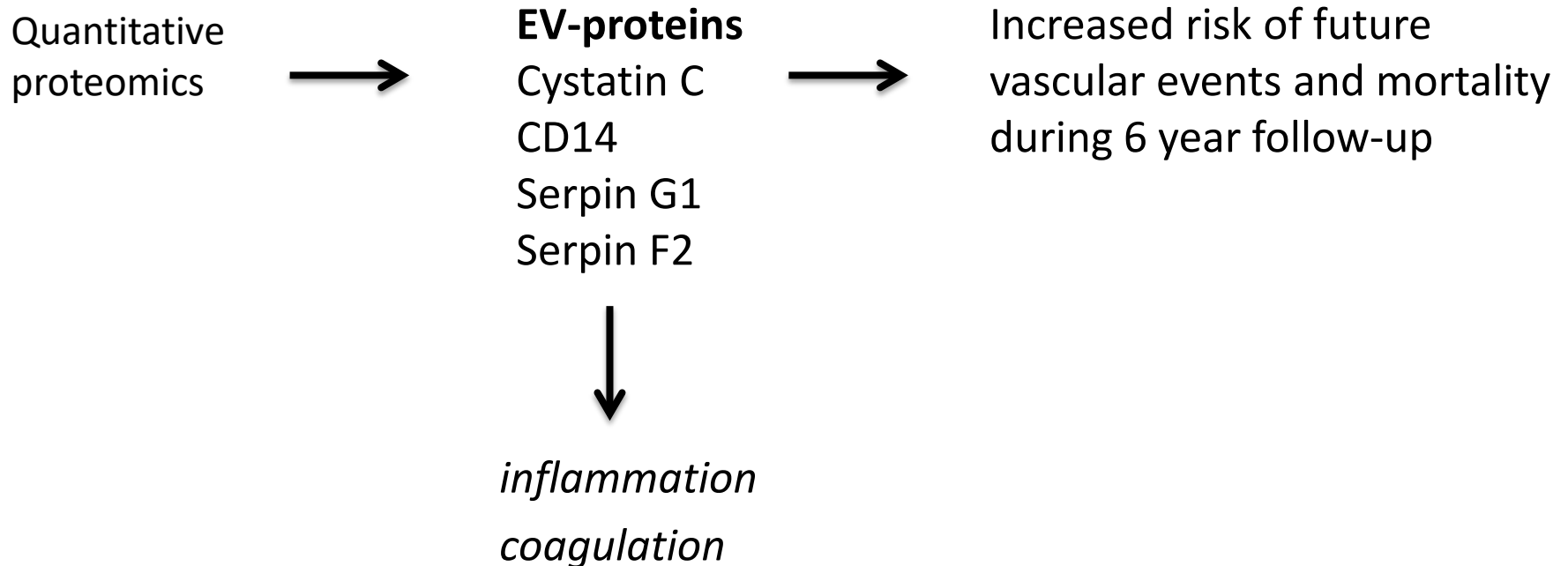
"It's all in the garbage"



"Liquid biopsy"

EV-proteins & cardiovascular events

SMART cohort: 1060 patients with first cardiovascular event (MI, PAD, AAA, stroke)



Kanhai, *et al.* Int J Cardiol (2013)

Research aim

plasma EVs-proteins

- Cystatin C
- CD14
- Serpin G1
- Serpin F2



*inflammation
coagulation*

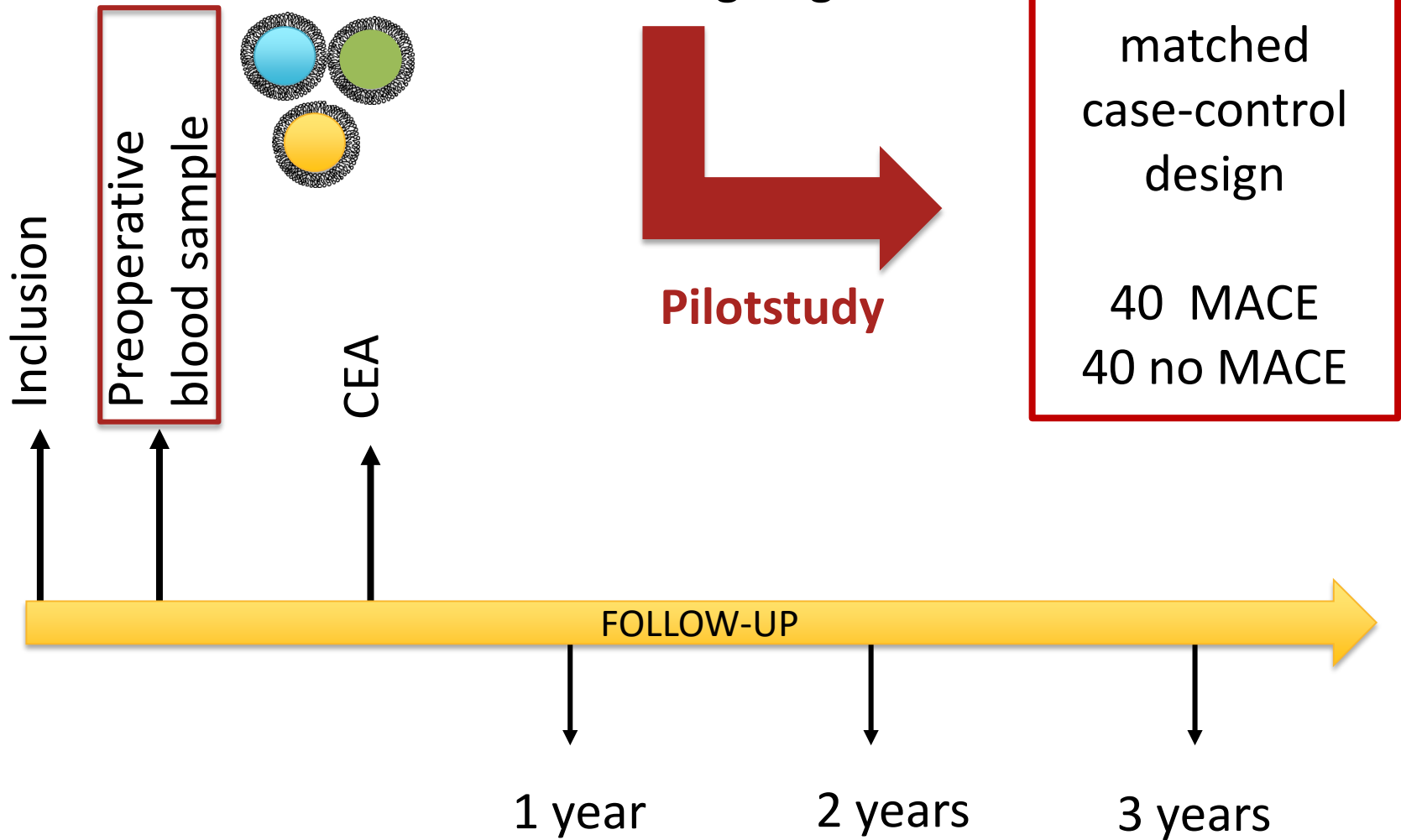
Predictor?

3-years risk of MACE
after CEA

MACE: “major adverse cardiovascular event”
stroke, myocardial infarction or cardiovascular death

Athero-Express Biobank

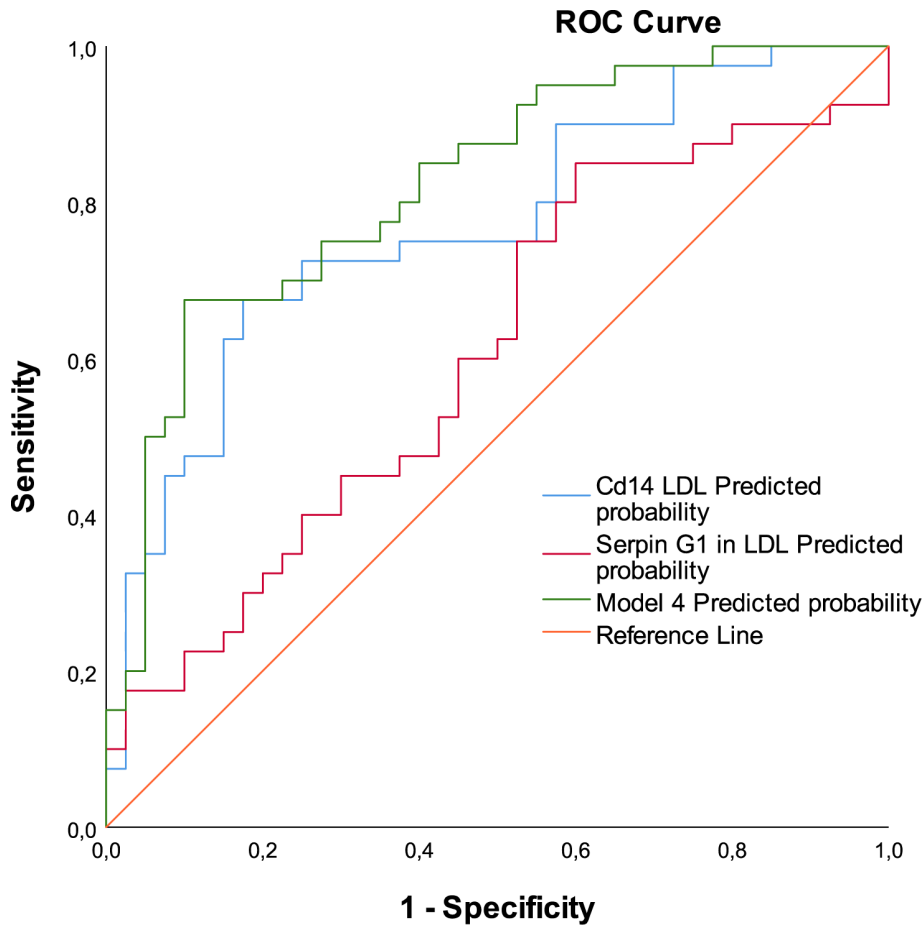
2002-ongoing



Patient characteristics (n=80)

Male gender	52 (65%)
Age (years), mean [SD]	71 [8]
Body Mass Index (kg/m ²), mean [SD]	28 [5]
Diabetes mellitus	27 (34%)
Hypertension	62 (78%)
Hypercholesterolemia	57 (71%)
Current smoker	24 (30%)
eGFR (ml/min/1.73m ²), mean [SD]	72 [22]
<u>Ipsilateral stenosis</u>	
▪ 50-70%	11 (14%)
▪ 70-99%	69 (86%)
Contralateral stenosis >50%	35 (44%)
<u>Index symptom</u>	
▪ Stroke	23 (29%)
▪ TIA	35 (44%)
▪ Ocular	17 (21%)
▪ Asymptomatic	4 (5%)
<u>Medical history</u>	
▪ Stroke	28 (35%)
▪ Coronary artery disease	43 (54%)
▪ Peripheral artery disease	25 (31%)
<u>Medication use</u>	
▪ Antihypertensive	63 (79%)
▪ Lipid-lowering	74 (93%)
▪ Antiplatelet	70 (88%)

Predictionmodel for the 3-years risk of MACE

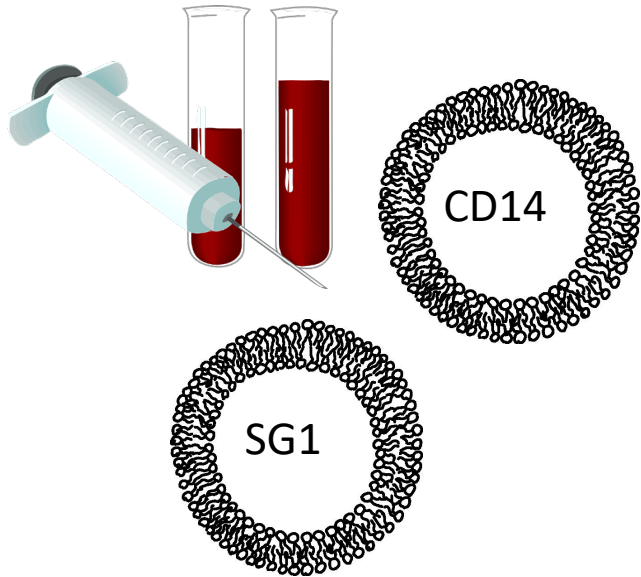


	AUC
CD14	0.77 (0.67-0.87)
Serpin G1	0.60 (0.48-0.73)
Combined	0.82 (0.73-0.91)

EV-protein	HR (95% CI)	p-value
CD14	5.52 (2.72-11.22)	p<0.01
Serpin G1	0.28 (0.14-0.55)	p<0.01

Conclusion

Preoperative blood test



Postoperative

3-years risk of MACE
after CEA

Discussion

Pathophysiological mechanism?

Hypothesis

↑ *Inflammation* ↑ *progression atherosclerosis*

- CD14: innate immune response
- Serpin G1: C1 inhibitor



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Thank you for your attention!



It's all in the garbage...

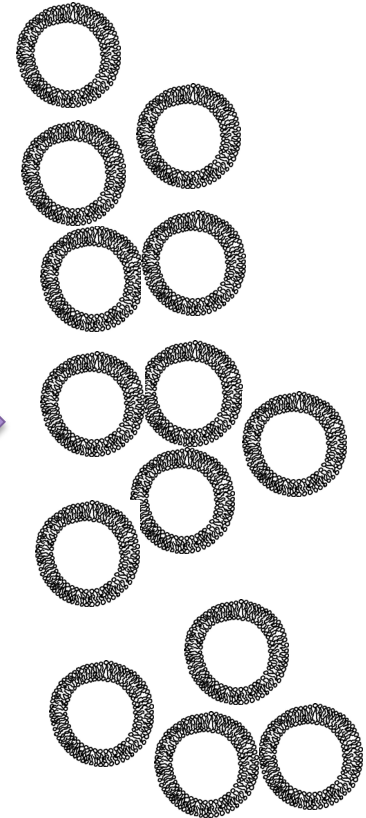
- **SERPINF2**
 - Alpha 2-antiplasmin → inactivation of plasmin → inhibition of **fibrinolysis**
- **SERPING1**
 - C1-inhibitor → inhibition **complement system**
 - Also inhibitor **fibrinolytic** and **clotting** system
- **CD14**
 - **innate immune system**, co-receptor Toll-like receptor (detection bacterial LPS)
- **CYSTATIN C**
 - Inhibitor of lysosomal proteinases and extracellular inhibitors of cysteine proteases
 - Marker for decreased renal function
 - **Biomarker for CVD**

Subpopulations

Blood



EVs



Wang, *et al.* Int. J. Mol. Sci (2017)
Zang, *et al.* Plos One (2016)

Subpopulations

Blood



Wang, *et al.* Int. J. Mol. Sci (2017)
Zang, *et al.* Plos One (2016)

