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# Insight into Coronary Artery Ectasia

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## Akademisk avhandling

som med vederbörligt tillstånd av Rektor vid Umeå universitet för avläggande av filosofie/medicine doktorsexamen framläggs till offentligt försvar i Major Groove, målpunkt Jo torsdagen den 21 november, kl. 09:00.  
Avhandlingen kommer att försvaras på engelska.

Fakultetsopponent: Professor Corrado Tamurino, Professor i kardiologi, chef för kardiologi, Ferrarotto sjukhus, Policlinico sjukhus och Vittorio Emanuele sjukhus, postgraduate School of Cardiology , universitetet i Catania, Italien.

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Insight into coronary artery ectasia

**Abstract**

**Background and Epidemiology:** Coronary Artery Ectasia (CAE) is a rare condition, defined as a diffuse dilatation of the epicardial coronary arteries exceeding 1.5 folds the diameter of the normal adjacent segment and/or the remaining non-dilated part of the artery. The disease prevalence varies according to many factors; anatomical definition (i.e. localized aneurysm vs. long dilated segment), presence of congenital or systemic inflammatory disorder (e.g. Kawasaki, Takayasu disease, polycystic kidney disease and Ehlers-Danlos syndrome) and as a variant of heavy atherosclerosis and remodeling failure of the coronary arteries intimal wall.

**Aim:** The clinical implication of the presence of the disease and its association with atherosclerosis was much debated. Hence, the purpose of this research is to investigate some aspects of pathogenesis of CAE, short and long-term prognosis as well as similarities with atherosclerosis.

**Methods:** We reviewed 16,464 coronary angiograms performed between 2003 and 2011 at Umeå Heart Centre of Umeå University Hospital, Sweden and Letterkenny University hospital in Ireland. We also reviewed another group of 3200 patients' angiograms that presented with acute coronary syndrome (ACS). Patients with extensive atherosclerosis and with previous history of coronary intervention and those with structurally abnormal hearts were excluded.

**Results:** The CAE prevalence was rare. The short-term outcome and prognosis after acute coronary syndrome (ACS) presentations was not different from non-ectatic arteries and revealed higher acute inflammatory response. On the other hand, long-term prognosis of CAE (not ACS) including CV mortality was higher in CAE than age matched mild coronary artery disease, indicating a worse prognosis. Smoking in CAE is a predictor for worse prognosis.

This thesis also provides distinctive tools for examining the pathophysiology of CAE, using personalized lipid profiling and extended cytokines milieu in CAE. Sixty-five metabolites (27 identified) proved different from non-ectatic controls. The intensities of those metabolites were lower than normal and controls with only mild atherosclerotic coronary disease. Finally, an extended cytokines profile including IL-10, IL-12, IL-23, IL-13, IL-2, IL-4, IL-6, IL-8, IFN- $\gamma$ , IL-1 $\beta$  and TNF- $\alpha$  were investigated in our CAE patients and showed raised systemic levels of INF- $\gamma$ , TNF- $\alpha$ , IL-1 $\beta$ , IL-6, and IL-8 and lower IL-2 and IL-4 than controls, but similar to atherosclerotic CAD. On the other hand, the lower level of IL-2 and IL-4 suggests perturbed TH pathways differentiating it from atherosclerosis.

**Conclusion and reflection:** We, hereto, provided innovative insight on the true form of non-atherosclerotic ectasia, particularly its pathophysiology. Pure or minimal atherosclerotic forms of CAE are not part of atherosclerotic process, which would explain why not all atherosclerotic coronary disease develop CAE and vice versa. CAE patients in acute presentations have aggressive inflammatory response, despite similar short-term prognosis. From the clinical perspective, the outcome and treatment of acute CAE patients may follow the same guidelines as atherosclerotic, non-ectatic, coronary disease. Finally, long-term CAE prognosis including CV mortality was higher than atherosclerotic counterparts, with smoking being an important predictor. These findings support the proposal of CAE having different pathophysiology from that of conventional atherosclerosis.

**Keywords**

Coronary artery ectasia, personalized lipid profiling, cytokines, acute coronary syndrome, short-term outcome, long-term prognosis,

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