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Development of Automated Algorithms for Epicardial Adipose Tissue Analysis in Computed Tomography and their Application in Population Based Research

Akademisk avhandling som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i sal ”Förmaket”, Sahlgrenska Sjukhuset, Vita Stråket 12, första vån. fredagen den 26 januari 2024 klockan 09.00

av David Molnar

Fakultetsopponent:

Juhani Knuuti, professor
University of Turku, Finland

Avhandlingen baseras på följande delarbeten

I. Norlen, A., Alven, J., Molnar, D., Enqvist, O., Norrlund, R. R., Brandberg, J., Bergstrom, G., & Kahl, F. (2016). Automatic pericardium segmentation and quantification of epicardial fat from computed tomography angiography. *J Med Imaging (Bellingham)*, *3*(3), 34003. https://doi.org/10.1117/1.JMI.3.3.034003

II. Molnar, D., Enqvist, O., Ulén, J., Larsson, M., Brandberg, J., Johnsson Å, A., Björnson, E., Bergström, G., & Hjelmgren, O. (2021). Artificial intelligence based automatic quantification of epicardial adipose tissue suitable for large scale population studies. *Sci Rep*, *11*(1), 23905. https://doi.org/10.1038/s41598-021-03150-w

III. Molnar, D., Björnson, E., Larsson, M., Adiels, M., Gummesson, A., Bäckhed, F., Hjelmgren, O., & Bergström, G. (2023). Pre-diabetes is associated with attenuation rather than volume of epicardial adipose tissue on computed tomography. *Scientific Reports*, *13*(1), 1623. https://doi.org/10.1038/s41598-023-28679-w

IV. Molnar, D., Björnson, E., Hjelmgren, O., Adiels, M., Bäckhed, F., & Bergström, G. Coronary artery calcifications in relation to epicardial adipose tissue volume and attenuation on cardiac computed tomography in a cohort of 1,945 individuals with various degrees of glucose disorders. *Manuscript*.

V. Molnar, D., Bergfeldt, L., Björnson, E., Hjelmgren, O., Adiels, M. & Bergström, G. Vector electrocardiographic QRS-T angle abnormalities are not correlated to epicardial adipose tissue volume or attenuation on cardiac computed tomography in a population sample of 5.571 individuals. *Manuscript*.

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Abstract

The epicardial adipose tissue (EAT), which surrounds the heart and is separated from other tissues only by the thin layers of the pericardium, has enjoyed intense research for the past decades. Increased inflammatory activity in the EAT in coronary artery disease has, together with associated volumetric expansion of the EAT and changes in its radiodensity supported theories that the EAT might play a role in the pathogenesis of coronary atherosclerosis or mirror its progression better than traditional risk factors. Cardiac computed tomography (CT) has been the most frequently used method for in vivo imaging of the EAT, but reliance on labor-intense manual or semi-automated analyses has limited most studies to small cohorts or incomplete EAT data. Lately, new frontiers have been opened by advances in artificial intelligence-based image analysis.

Within the framework of the current thesis, a fully automated model has been developed and validated in CT images from a total of more than 1,400 individuals. The model's performance is equal to that of manual expert measurements, with the capability to handle: a) anatomical variation in an unselected population b) incomplete images c) high noise levels. The relationship between EAT and pre-diabetes was investigated in 1,948 individuals, and an automated quality-control algorithm was added to find unsuccessful analyses (< 1%). In the next paper, EAT data was examined in relation to coronary artery calcifications, while in the final paper, its relation to vector electrocardiographic signs of abnormal QRS-T angles reflecting ventricular de-/repolarization was investigated in 5,571 individuals. Results show that large cohorts can be efficiently analyzed with the model. The co-variation between EAT data and traditional anthropometric and laboratory derived risk factors is substantial and EAT is not superior to these in identifying the presence of coronary artery calcifications or abnormal QRS-T angles in vector electrocardiography indicative of disease.

Keywords: Epicardial adipose tissue, artificial intelligence, automatic analysis, computed tomography, coronary atherosclerosis, pre-diabetes, vector electrocardiography

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