

Studies on carotid plaque vulnerability using contrast enhanced ultrasound

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet, kommer att offentligen försvaras i sal Arvid Carlsson, Medicinaregatan 3, fredagen den 6 november 2015 kl 09:00
av

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Avhandlingen baseras på följande delarbeten:

- I. Hjelmgren O, Holdfeldt P, Johansson L, Fagerberg B, Prahll U, Schmidt C, Bergström G ML. Identification of Vascularised Carotid Plaques Using a Standardised and Reproducible Technique to Measure Ultrasound Contrast Uptake. *Eur J Vasc Endovasc Surg.* 2013;46(1):21-8.
- II. Hjelmgren O, Johansson L, Prahll U, Schmidt C, Fredén Lindqvist J, Bergström G ML. A study of plaque vascularization and inflammation using quantitative contrast-enhanced US and PET/CT. *Eur J Radiol.* 2014;83(7):1184-9.
- III. Hjelmgren O, Johansson L, Prahll U, Schmidt C, Bergström G ML. Inverse Association Between Size of the Lipid-Rich Necrotic Core and Vascularization in Human Carotid Plaques. Submitted.
- IV. Hjelmgren O, Schmidt C, Johansson L, Bergström G ML. Comparison between magnetic resonance imaging and B-mode ultrasound in detecting and estimating the extent of human carotid atherosclerosis. Manuscript.



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ABSTRACT

Background and Aim: Contrast-enhanced ultrasound is a method to examine neovessels that may be present inside the atherosclerotic plaque of the carotid arteries. These neovessels are believed to be involved in the process leading to embolic stroke. The aim of this thesis is to: I /Develop methodology for contrast-enhanced ultrasound examination of carotid plaques and to develop a software program for quantification of the examination. II /Investigate the correlation between neovessels and inflammation in plaques, using PET/CT. III / Investigate the correlation between neovessels and plaque components using MRI. IV / Comparing ultrasound and MRI in detecting and measuring of carotid plaques.

Methods: The papers of this thesis are performed on volunteers recruited through several different databases. The contrast-enhanced ultrasound method has been developed and optimized within the framework of the thesis. For comparison, conventional ultrasound, PET / CT and MRI has been used.

Results: The method we have developed for contrast-enhanced ultrasound is reproducible and reliable. Increased amount of neovessels is more common in subjects with a history of stroke or transient ischemic attack and neovessels are correlated to increased inflammation. Neovessels are less common in plaques with a large lipid-rich necrotic core. Two dimensional imaging using ultrasound does not correctly capture the complex 3D plaque anatomy. MRI is comparable to ultrasound in finding plaque with a height of at least 2.5 mm, but in detection of smaller plaques ultrasound performs better. Multiple plaques seen on ultrasound are usually a misinterpretation of the true anatomy that can be better visualized using MRI. Plaque height measured using ultrasound is slightly more accurate and more feasible than plaque area to estimate the plaque volume measured using MRI.

Conclusion: Contrast-enhanced ultrasound can be used to measure and quantify neovessels in carotid plaques. The quantity of neovessels correlates with the degree of inflammation, a marker for plaque vulnerability. However, the size of the lipid core, another marker of plaque vulnerability, has an inverse correlation to neovessels. Future studies should in more detail examine the exact localization of neovessels in relation to the lipid core. Also, future studies should examine the quality of neovessels since they can have different propensity to cause damage. Small plaques can be undetectable by MRI but in plaques greater than 2.5 mm in height, ultrasound and magnetic resonance imaging have similar sensitivity to detect plaques. If using ultrasound, plaque height is the best way to estimate the volume of the carotid artery plaque.

Keywords: Atherosclerosis, Carotid artery plaque, Contrast-enhanced ultrasound, Positron-emission tomography, Magnetic resonance imaging

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