Magnetic resonance imaging of carotid intraplaque hemorrhage and microvasculature

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Valorisation

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Relevance

Around 240 000 people in the Netherlands suffer from the consequences of a stroke (REF). Around 25% of all cardiovascular deaths in the Netherlands can be attributed to stroke. Around 4 000 men and 5500 women died in 2016 from a stroke (or the consequences) (REF Hartstichting). The total amount of costs related to stroke patients was almost 2.3 billion in 2011 (CBS). The aging population will only lead to an increase of these numbers.
Occlusion of a supplying artery to the brain due to embolism or thrombosis is the most common type of stroke. 15-20% of these ischemic strokes are the consequence of rupture of an atherosclerotic plaque in the carotid bifurcation or internal carotid artery (Chaturvedi). Currently, the presence of clinical symptoms and the degree of luminal narrowing is used as a decision marker to select patients undergoing surgical removal or stenting of the carotid atherosclerotic plaque. Previous studies have shown that this operation is of benefit to symptomatic patients with a stenosis >70% (number needed to treat = 6). Only a marginal effect of surgical intervention is seen in the group of patients with a lower degree of stenosis (number needed to treat = 22). This implicates that the degree of stenosis is not optimal to stratify patients at risk. Therefore, research focus has shifted towards identification of other plaque characteristics that identify a vulnerable, rupture-prone plaque. The presence of hemorrhage inside the plaque, intraplaque hemorrhage (IPH), has been shown to contribute to plaque destabilisation and has proven to be a good predictor for recurrent events (REF). Magnetic resonance imaging (MRI) has been shown well suited for the identification of the presence of IPH in vivo (REF). However, the mechanism behind the development of IPH are not yet fully understood. This thesis aimed to investigate several factors that could have an influence on development of IPH.

Target groups

Data used in this thesis is derived from the Plaque At RISk study (PARISk). This prospective multicenter cohort study focuses on the identification of patients with mild-to-moderate carotid artery stenosis with an increased risk of recurrent stroke by using non-invasive plaque imaging. The results of this thesis are of interest to all clinicians treating patients with a recent ischemic cerebrovascular event. Ultimately they are the ones that decide which patient will undergo surgery. Currently patients with a mild to moderate carotid artery stenosis are not referred to vascular surgeons because previously performed clinical trials have shown no significant benefit in this group of patients. The results from this thesis are another step forward to introducing plaque imaging into the daily clinical routine, although results from on-going randomised clinical trials relating plaque imaging to clinical outcome will be necessary.

Another target group consists of the patients. The results of this thesis are part of an on-going project to better stratify patients with carotid artery stenosis leading to a more individualized treatment.

Furthermore research groups interested in atherosclerosis, and in particular carotid artery disease can use the results described in this thesis to further unravel the rather complex process of plaque destabilisation.

Products

The analysis of plaque components has been done using a dedicated software package (Vesselmass, Leiden University Medical Center, Leiden, the Netherlands). Assessment is currently being done by experienced observers, but more widespread use will lead to challenges due to an increased number of required observers. Also the delineation of plaque composition on the MR images is currently time consuming. There might be an important role for (semi)-automated software development to implement this software on a broad scale. Future research and product development by vendors of MRI systems will also be focussed on the development and implementation of faster MRI protocols to assess plaque composition.

Innovation and implementation

Previous research has put leaky plaque microvasculature forwards as a vulnerable plaque characteristic and important contributor to IPH development. However, several chapters from this thesis show that IPH is not always associated with plaque microvasculature. This implies that also other factors contribute to the development of IPH and ultimately plaque destabilisation. Additionally, the preferential distribution of IPH at the proximal, upstream side of the plaque implicates a role for plaque biomechanics or hemodynamics to the development of IPH. Furthermore, use of standard antiplatelet therapy might have an influence on IPH. These results bring us a few steps closer towards a better understanding of carotid atherosclerotic plaques, more specifically IPH. Future results will show if patients with a recent ischemic stroke can benefit from plaque imaging in the stratification process of undergoing surgery. Identification of those patients with a high risk plaque compared to those with a more stable plaque, will lead to personalized treatment and better use of surgical interventions compared to the current clinical routine.