Intraplaque hemorrhage on carotid mri in stroke patients

CHAPTER 8

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Estimations show that approximately 15% of transient ischemic attacks (TIAs) and ischemic strokes are associated with carotid atherosclerotic plaques. Currently, clinical decision-making in the treatment of stroke patients with carotid artery plaques primarily relies on the degree of stenosis of the internal carotid artery. However, recent findings have highlighted the importance of plaque composition, particularly the presence of intraplaque hemorrhage (IPH) detected on Magnetic Resonance Imaging (MRI), as a strong predictor of stroke risk in patients with carotid plaque.

Despite strong evidence linking IPH to increased stroke risk, the factors contributing to IPH development remain incompletely understood. IPH may originate from the entry of blood from the lumen due to the fissuring or rupture of the fibrous cap. Previous cross-sectional studies have demonstrated an association between the presence of IPH and thin or ruptured fibrous cap (TRFC) detected on MR images, as well as fissured or ulcerated plaque surface observed on computed tomography angiography (CTA) images.

Furthermore, the use of antiplatelet agents, while beneficial in reducing thrombus formation, has been associated with an elevated risk of bleeding complications and IPH. However, the longitudinal changes in IPH volume in relation to these factors have not been investigated before.

Additionally, the identification of IPH relies on advanced MR sequences beyond routine contrast-enhanced MR angiography (CE-MRA) or non-contrast MRA, such as time-of-flight (TOF), for stenosis assessment. However, these additional advanced sequences are often omitted in clinical practice due to time constraints and since they are not yet part of the clinical guidelines. Recently, a novel and fast MR sequence called Multi-contrast Atherosclerosis Characterization (MATCH) has been introduced for imaging carotid atherosclerotic plaque composition.

This thesis aims to explore various factors contributing to changes in IPH volume in symptomatic carotid plaques of stroke patients over a two-year follow-up period. Moreover, it seeks to determine the diagnostic accuracy of identifying IPH using routine carotid MRI (i.e., mask images of CE-MRA and TOF images) and quantifying carotid plaque composition using a novel MR sequence (i.e., MATCH).

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What is the relation between carotid fibrous cap status or plaque surface morphology and the progression of carotid IPH volume on carotid MR imaging?

In Chapter Three of this thesis, we reported that patients with a TRFC or a disrupted plaque surface had a significantly larger IPH volume at baseline than those with a thick cap/smooth plaque surface. During the two years of follow-up, the overall volume of IPH tended to decrease in the patients with TRFC or disrupted plaque surface, indicating plaque healing, while patients with a thick FC or smooth plaque surface showed hardly any IPH at baseline and follow-up. However, patients with TRFC or disrupted plaque surface were still at increased risk of IPH progression. Mainly patients who maintained a TRFC at both baseline and follow-up showed IPH progression. These observations indicate that a TRFC or disrupted plaque surface contributes to the development of IPH.

How does the initiation of antiplatelet therapy after an ischemic cerebrovascular event impact the progression of carotid IPH on MRI over a two-year follow-up period?

In clinical practice, platelet aggregation inhibitors are frequently prescribed as a standard therapeutic approach to reduce recurrent ischemic events in patients diagnosed with TIA or stroke. However, it is important to acknowledge that antiplatelet therapy is also associated with an increased risk of bleeding complications, including IPH. In Chapter Four, we demonstrated that individuals who initiate antiplatelet therapy following an ischemic stroke are not at a higher risk of developing new carotid IPH or experiencing IPH progression on MRI during a two-year follow-up period, in comparison to patients who were already receiving antiplatelet treatment prior to the initial event. No significant association was found between new antiplatelet agent use and the formation of new IPH or IPH volume progression during the two-year follow-up.

What is the sensitivity and specificity of detecting carotid IPH on the mask on TOF images derived from routine CE-MRA compared to the reference standard MPRAGE?

The Magnetization-Prepared Rapid Acquisition Gradient (MP-RAGE) sequence is commonly employed for the detection of IPH. CE-MRA is routinely utilized for the assessment of stenosis and has the potential to be used for IPH identification. In Chapter Five of this thesis, we demonstrated a strong consensus among the observers in detecting IPH on both mask images of CE-MRA and TOF images, particularly when utilizing black blood T1-weighted (T1w) MR images to assess the outer vessel wall. Notably, we observed a high specificity in identifying IPH on both mask and TOF images. Evaluation of the mask images also exhibited a high sensitivity, while TOF images displayed poor sensitivity for IPH identification. Moreover, the

specificity of IPH detection on mask images remained consistent even without the assistance of black blood T1w images while the sensitivity reduced. However, for TOF images, the specificity was moderate, and the sensitivity was found to be poor.

Is the fast novel Multi-contrast Atherosclerosis Characterization (MATCH) MRI sequence able to accurately quantify carotid plaque composition?

In Chapter Six of this thesis, we conducted a validation study to assess the efficacy of the MATCH sequence as a fast imaging method that inherently aligns the images. We used a multi-sequence carotid MRI protocol as a reference standard. Our study findings demonstrated an excellent level of agreement among observers in the detection and quantification of various carotid atherosclerotic plaque components on MATCH images. However, there was fair to moderate agreement for calcifications. Moreover, MATCH images exhibited high sensitivity and specificity in identifying IPH and the lipid-rich necrotic core (LRNC). The quantification of vulnerable carotid plaque components, i.e., IPH and LRNC, on MATCH images showed good to excellent agreement with the quantification obtained using the multi-sequence protocol. However, moderate and poor agreement was observed for the total volume of fibrous tissue and calcifications, respectively. The acquisition and image analysis time of MATCH were significantly less compared to the conventional multi-sequence protocol. These findings underscore the advantages of utilizing MATCH over conventional multi-sequence protocols, as it significantly reduces scanning and image analysis time while maintaining reliable performance in the identification and quantification of the most important carotid plaque components.

Discussion and conclusion

The findings presented in this thesis are discussed in Chapter Seven. This thesis contributes to the understanding of the development of intraplaque hemorrhage over time. Furthermore, our findings aim to facilitate the application of carotid plaque magnetic resonance imaging in clinical practice, providing valuable insights for medical professionals in assessing and managing patients with a carotid plaque. Unlike previous research, which predominantly focused on the association between intraplaque hemorrhage and other risk factors using cross-sectional study designs, in this thesis, longitudinal magnetic resonance imaging studies were performed, indicating the potential involvement of a thin/ruptured fibrous cap, fissures/ulcers on the development and progression of intraplaque hemorrhage. Also, we explored the relationship between the new onset of antiplatelet treatment in the development and

progression of intraplaque hemorrhage. Additionally, we demonstrate that intraplaque hemorrhage, as an independent risk factor for recurrent ischemic stroke, can be accurately identified on the mask images of routine contrast-enhanced MR angiography but not on time-of-flight images. Furthermore, we establish that the novel and fast MATCH MRI sequence can accurately quantify IPH and the LRNC. Large randomized trials to investigate the impact of carotid plaque MRI on patient outcome are warranted.