Intraplaque hemorrhage on carotid mri in stroke patients

SCIENTIFIC AND SOCIAL IMPACT

RELEVANCE

Stroke ranks as the second most prevalent cause of death in the European Union (EU) and stands as a primary contributor to adult disability [1]. Each year, approximately 1.1 million individuals in Europe experience the impact of stroke, with a staggering 440,000 lives lost as a result [2]. This concerning trend is further exacerbated by the aging population, which is expected to contribute to a rise in stroke cases.

The economic impact of stroke on healthcare systems and societies is substantial. In Europe, the provision of informal care alone reached an estimated €1.3 billion, with healthcare costs totaling €27 billion and an additional €12 billion attributed to lost productivity resulting from stroke in 2017 [3].

Approximately 85% of the strokes are ischemic, and approximately 20% of the ischemic strokes are related to carotid artery disease [4]. The rupture of a vulnerable carotid plaque is an important underlying cause of stroke. Therefore, symptomatic patients with severe carotid stenosis are currently treated by carotid endarterectomy (surgical removal of the plaque) or carotid artery stenting to prevent (recurrent stroke). However, relying solely on clinical symptoms and the degree of luminal stenosis to determine the need for surgical intervention or stenting has limitations. The number needed to treat (NNT) was six in patients with 70-99% stenosis, whereas in male patients with stenosis greater than 50%, the NNT was nine, and in female patients, it was thirty-six. This underscores the need to explore alternative plaque characteristics that can identify vulnerable, rupture-prone plaques.

One such characteristic is the presence of intraplaque hemorrhage (IPH), which has been shown to contribute to plaque destabilization and serve as a reliable predictor for recurrent events. Magnetic resonance imaging (MRI) has emerged as a promising tool for noninvasive identification of IPH. However, a comprehensive understanding of the mechanisms underlying the development of IPH is still lacking. The detection and quantification of IPH and other plaque compositions require dedicated carotid plaque MR sequences, which are currently not included in standard imaging protocols for carotid artery disease.

This thesis aims to investigate various factors that may influence the development of IPH. By delving into this area of research, we strive to enhance our understanding of plaque destabilization. Additionally, we seek to validate the efficacy of routine CE-MRA in identifying IPH, as well as introduce a novel carotid MR sequence for the

identification and quantification of carotid plaque composition.
Addressing the burden of ischemic stroke and mitigating its impact on individuals and society is paramount. By uncovering novel insights into the pathophysiology of IPH and advancing novel carotid MRI techniques to facilitate its clinical use, this thesis aims to contribute to the development of more effective strategies for the management and treatment of patients with carotid atherosclerosis, ultimately leading to improved patient outcomes and reduced societal costs associated with stroke.

TARGET GROUPS

These findings have significant implications for clinicians who treat patients with recent ischemic cerebrovascular events. Currently, patients with mild to moderate carotid artery stenosis are not typically referred to vascular surgeons due to previous clinical trials that demonstrated no significant or marginal benefit in this group. However, IPH is a strong independent risk factor for recurrent stroke and can improve risk stratification of patients with carotid artery disease. Also, identifying factors that contribute to IPH occurrence can help clinicians predict the future risk of IPH development and subsequent stroke recurrence. Additionally, the results of this thesis contribute to ongoing research that aims to better stratify patients with carotid artery stenosis, leading to a more personalized treatment approach. Exploring factors that contribute to IPH can also guide the development of medications aimed at modifying these factors, reducing future IPH occurrences, and decreasing ischemic events.

Therefore, the results of this thesis are of interest to various medical professionals, including neurologists, radiologists, and vascular surgeons. The validation of routine CE-MRA as a tool to detect IPH, which is a strong risk factor for future events beyond the degree of carotid stenosis, is particularly significant. These results can be applied in screening procedures. Clinicians and research groups focused on atherosclerosis and carotid artery disease can utilize these findings to further understand the intricate process of plaque destabilization. By addressing these objectives, this research aims to make substantial contributions to the field of carotid artery disease, ultimately improving patient care and outcomes.

PRODUCTS

At present, the analysis of plaque components is conducted using dedicated software packages. This software is currently utilized by experienced observers; however, for broader adoption, a greater number of observers will be required. Moreover, the process of delineating plaque composition on MR images is time-consuming and susceptible to errors introduced by the observers. This indicates the necessity for the development of (semi)-automated software to streamline and enhance this process. Implementing such software would also enable more accurate detection

of changes in plaque composition volume over time. Moreover, it is recommended that MRI vendors prioritize the creation of multi-contrast MRI protocols for assessing plaque composition as a product since these sequences are currently only available for research and not for clinical care.

INNOVATION AND IMPLEMENTATION

In previous research, the presence of leaky plaque microvasculature was suggested as a key contributor to IPH development. However, in this thesis, we conducted a longitudinal study that indicates that erythrocytes can also enter the plaque from the luminal side. Additionally, while the use of standard antiplatelet therapy in the past was associated with IPH in cross-sectional studies, the onset of antiplatelet therapy had no impact on the occurrence of new IPH or the increase in IPH volume over a two-year period.

The findings of this thesis represent a significant advancement towards the integration of carotid atherosclerotic plaque MRI into daily clinical practice by easily and rapidly identifying patients with high-risk plaques as opposed to those with more stable plaques, personalized treatment options can be employed, resulting in improved stratification for surgical interventions compared to the current standard clinical routine.

REFERENCES

[1] Wilkins E, Wilson L, Wickramasinghe K, et al. European cardiovascular disease statistics 2017. 2017.
[2] Oecd. Health at a glance: Europe 2016: state of health in the EU cycle: OECD; 2016.
[3] Luengo-Fernandez R, Violato M, Candio P, Leal J. Economic burden of stroke across Europe: a population-based cost analysis. European stroke journal. 2020;5(1):17-25.
[4] Group PSW, Effectiveness RCoPoLC, Unit E, editors. Stroke in childhood: clinical guidelines for diagnosis, management and rehabilitation2004: Royal College of Physicians.