Multimodal CT imaging for diagnosis, treatment and prognosis in ischemic stroke

Holswilder, G.

Chapter 9

Summary

Summary

Stroke is a prevalent neurological disorder of which transient ischemic stroke (TIA) and ischemic stroke constitute the majority. Ischemic stroke requires acute medical treatment to resolve the blood clot and thereby increase the chance of good clinical recovery. Sophisticated techniques have become available over the years and an increasing number of CT imaging characteristics have been identified and have improved stroke management. The aim of this thesis was to identify novel CT imaging parameters to provide more insight into the diagnosis, prognosis, and treatment selection in patients with TIA or acute ischemic stroke.

In Chapter 2, we evaluated the use of CTA of the heart and aortic arch, in addition to routine diagnostic workup, to detect embolic sources as a possible cause of TIA or ischemic stroke. In addition, we evaluated the implications for secondary preventive management. We identified cardioembolic risk sources in 29 out of 67 patients (43%); most of these were medium or low-risk cardioembolic source, including a complex aortic plaque (n= 16, 24%). A high-risk cardioembolic source was identified in 2 out of 34 (6%) patients with ischemic stroke, both cases involved an intracardiac thrombus. The identification of these high-risk cardioembolic source had consequences for therapeutic management as antiplatelet changed to oral anticoagulation. We concluded that CTA of the heart and aorta has a high yield for the detection of embolic risk sources, with clinical consequences for 6% of ischemic stroke patients. Although the presence of a complex aortic plaque did not carry direct therapeutic implications, the prevalence was relatively high.

In Chapter 3, we evaluated the aortic arch on CTA for the presence of complex aortic plaques in patients with large vessel occlusion ischemic stroke from the MR CLEAN Registry. Subsequently, we investigated the association of a complex plaque with recurrent stroke and functional clinical outcome. We observed a complex plaque in 181 out of 1030 (19%) patients. We did not identify an association between the presence of a complex plaque and recurrent stroke, possibly because of the low number of recurrences in this study (2%), nor did we observe a significant association with functional outcome at 3 months as measured with the modified Ranking scale score after multivariate adjustment. Although both chapter 2 and chapter 3 suggest there is no added benefit of aortic assessment in a general ischemic stroke population, future studies should investigate whether imaging of the aorta might be useful for patients with otherwise no identifiable cause of ischemic stroke.

In Chapter 4 we provided a more detailed assessment of collaterals on dynamic CTA versus single-phase CTA in 61 patients with acute ischemic stroke due to a

proximal MCA occlusion. We measured not only the extent but also the velocity of collateral filling. Poor collateral status assessed on dynamic CTA was more strongly associated with an infarct volume of ≥70 mL with a risk ratio of 1.9 (95% CI, 1.3-2.9) than on single-phase CTA (risk ratio 1.4; 95% CI, 0.8-2.5). This study showed that patients with good and fast collaterals had similar risk ratios for a large infarct volume as patients with good but slow collaterals. This study therefore suggests that the extent of collaterals and thereby the timing of CTA is important for optimal collateral assessment.

In Chapter 5, we investigated whether patients with migraine and acute ischemic stroke have more severe stroke progression and less favorable radiological outcome measures compared to patients without migraine based on CTA and CTP image characteristics. We hypothesized that patients with migraine might have more severe stroke progression due to the increased susceptibility of spreading depolarization in these patients. However, we observed no differences in patients with or without migraine in perfusion characteristics on admission (adjusted Risk Ratio - aRR: 0.98, 95% CI: 0.77 – 1.25), nor for development of malignant edema (0% vs. 5%), hemorrhagic transformation (aRR: 0.26, 95%CI: 0.04 – 1.73), and final infarct volume at 3-months (adjusted Beta: -14.8, 95% CI: -29.9 – 0.2).

In Chapter 6 we identified extracranial vascular characteristics with a prognostic value for EVT procedural outcomes, i.e., procedural duration and revascularization success, in patients with LVO ischemic stroke. In Chapter 7 we developed and validated a prediction model with these extracranial vascular characteristics to predict failure of the transfemoral approach of EVT. For both studies we analyzed pre-intervention CTA images and evaluated the aortic arch configuration, stenosis and tortuosity of the supra-aortic arteries and internal carotid arteries. In Chapter 6, we analyzed CTA images of 828 EVT-treated patients from the MR CLEAN Registry and constructed logistic regression models with baseline variables and extracranial vascular characteristics for procedural duration and revascularization success. Although prediction of revascularization success did not improve after including extracranial vascular characteristics compared with baseline characteristics, we showed that cervical ICA tortuosity and a high-grade stenosis of the cervical ICA improved prediction of procedural duration. Model performance remained limited with an area under the curve of 0.66 (95%CI: 0.62-0.70).

In Chapter 7 we analyzed CTA images of additional patients included in the second phase of the MR CLEAN Registry. With data from a total of 1998 patients, we developed, validated and updated a prediction model including the predictors age, hypertension, severe aortic arch elongation, bovine aortic arch, elongation of the

supra-aortic arteries, cervical ICA elongation and high-grade stenosis of the cervical ICA. This model showed good performance with an intercept of 0.01 (95% CI: -0.15 – 0.20), a slope of 1.02 (95% CI: 0.86 – 1.26) and a c-statistic of 0.75 (95% CI: 0.71-0.79) for prediction of failure to reach the intracranial occlusion by the transfemoral approach.

The findings of this thesis provide valuable additional knowledge for diagnosis, treatment selection and prediction of clinical outcome in patients with acute ischemic stroke. Advances in CT imaging techniques provide an increasing amount of valuable information that can support the neurologist and interventionalist to optimize patient management. Future research should focus on deploying this information more efficiently. This should be done by improving logistics on the level of the data, which can for example be achieved by using automated methods for image processing and analysis, and by improving on the level of the patient, for example by equipping ambulances with advanced neuroimaging.