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Intra-arterial treatment in acute ischemic stroke

Rozeman, A.D.

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English summary

Stroke is one of the leading causes of mortality and morbidity in the world. Stroke can be divided in ischemic stroke and hemorrhagic stroke. Ischemic stroke is most often caused by an acute occlusion of one of the cerebral arteries. Acute stroke treatment aims at resolving these acute artery occlusions. This can be done with intravenous thrombolysis or with locally applied therapy, i.e. intra-arterial, with thrombolytics or mechanical thrombectomy.

This thesis focuses on the evolution of intra-arterial stroke treatment in the Netherlands. It captures the period before publication of the large randomized controlled trials that would eventually lead to implementation of intra-arterial treatment as standard treatment for patients with acute ischemic stroke caused by large cerebral artery occlusion. The first part of this thesis contains two studies on patients treated with intra-arterial treatment in the period before the start of the Dutch nationwide MR CLEAN trial (2010-2014). In chapter 2 we studied a cohort treated with intra-arterial therapy in the period 2009-2011. During this period newer devices became available, the so-called stent-retrievers. A stent-retriever achieves recanalisation by deploying itself into the thrombus and relocating the thrombus against the blood vessel wall. The deployed stent then incorporates the thrombus that is retrieved with the removal of the stent-retriever. We were able to show that recanalisation rates were higher with the use of stent-retrievers, with a trend towards higher rates of favourable outcome after three months. In chapter 3 we describe a national cohort containing all patients treated with intra-arterial treatment from 2002 to the start of the MR CLEAN trial in 2010. We showed that, over the years, door to groin times reduced, intra-arterial treatment was more often combined with intravenous treatment and mechanical thrombectomy was more often used instead of intra-arterial thrombolysis. In addition, a shift in type of device used for mechanical thrombectomy was seen with more stent-retrievers being used in the later period. Together, this resulted in a trend towards higher rates of favourable outcome at discharge and after three months. In addition, recanalisation rates tended to improve.

In the second part of this thesis, we focus on specific treatment groups. In chapter 4 we studied the effect of age on outcome after intra-arterial treatment. We found that higher age was inversely related to favourable clinical outcome. In addition, risk of non-neurological adverse events was higher with increasing age. However, there was no increased risk of treatment related adverse events nor an increase of neurological adverse events. Hence, we concluded that increasing age lessens chances of favourable outcome after stroke but does not seem to interact with

treatment effect of intra-arterial treatment. In chapter 5 we describe a cohort with prolonged bleeding times ($\text{INR} > 1.7$) treated with intra-arterial treatment. Patients with prolonged bleeding times are considered prone to bleeding complications. We compared these patients with patients with normal bleeding times treated with intra-arterial treatment and found no increased risk of intracerebral hemorrhage (RR 0.49, 95% confidence interval 0.07-3.13). Our meta-analysis on risk of symptomatic intracerebral hemorrhage in patients on oral anticoagulants suffering from acute ischemic stroke treated with intra-arterial treatment showed a first week bleeding risk of 8.1%. This bleeding risk is comparable with the percentage of symptomatic intracerebral hemorrhage found in a large Cochrane review on thrombolytic therapy for acute ischemic stroke. We therefore concluded that there was no increased risk of symptomatic intracerebral hemorrhage in patients with prolonged bleeding times treated with intra-arterial treatment. In the most recent Dutch national guideline on acute stroke treatment, the use of oral anticoagulants is no longer mentioned as contra-indication for the use of intra-arterial treatment.

In the third part of this thesis we focus on diagnostics in ischemic stroke and intra-arterial treatment. We studied the feasibility of duplex ultrasonography for screening of extracranial vertebral artery stenosis (chapter 6). To this end, we compared duplex sonography with CT angiography in patients with posterior circulation stroke or TIA. We found that duplex sonography was able to detect significant stenosis quite adequately (AUC-ROC 0.73, 95% confidence interval 0.63-0.83). However, due to anatomic difficulties, adequate assessment of the most proximal segment of the vertebral artery was often not possible rendering duplex sonography less useful in daily practice.

Furthermore, we studied variations in Circle of Willis anatomy on CT angiography and its relation to outcome in acute stroke patients given intra-arterial treatment (chapter 7). We hypothesized that a complete Circle of Willis would result in better (primary) collateral circulation and hence better outcome. In addition, we studied the number of carotid arteries supplying the Circle of Willis and its influence on clinical outcome. Circle of Willis was regarded complete if the A1 segment contralateral to the occluded side, the posterior communicating artery ipsilateral to the occluded side and the anterior communicating artery were fully developed. Contrary to our expectation, completeness of Circle of Willis was not related to clinical outcome. However, chances of good clinical outcome tended to improve with the number of carotid arteries supplying the cerebral circulation. In the last part of this thesis the results of the aforementioned studies are discussed (chapter 8).