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Triage of stroke patients in the chain of acute stroke care

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Chapter 9

Summary
Samenvatting

SUMMARY

By advancing existing stroke triage systems, diagnosis and timely access of stroke patients to specialized care can be improved, which in turn can have a tremendous impact on current clinical practice.

The overall aim of this thesis was to assess various ways to improve stroke triage in the chain of acute stroke. To begin with patient triage by assessing the patient's entrance into the chain of acute stroke care (**Part I**), identifying and validating prehospital triage tools to improve patient selection in the ambulance (**Part II**) and to finalize with investigating in-hospital factors that are known to have an adverse effect on patient outcome in the final part of the chain of acute stroke care (**Part III**).

Part I. Patient triage

The first part of this thesis focuses on the patient's alarm choice after stroke onset. The choice of health care provider that is contacted first by the patient (or bystander) after acute stroke, determines the entrance into the chain of acute stroke care and appears to be an important factor that causes delay. In **Chapter 2**, we assessed differences between stroke patients who first alarmed the general practitioner (GP) and patients who directly alarmed the emergency medical services (EMS) after onset of stroke with data from a questionnaire. Most patients alarmed the GP (64%) and median onset-to-door times were longer (466 min, [95% CI, 149-1586]) compared with patients who directly called the EMS (90 min, [95% CI, 45-286]). Our results showed that patients who alarmed the GP first instead of the EMS differed in several factors that are potentially modifiable. Patients who first alarmed the GP experienced a threshold to burden the EMS or underestimated their symptomatology compared with patients who directly alarmed the EMS. Moreover, three-quarters of the patients who initially alarmed the GP were also first examined by the GP before the EMS was involved for transportation to the hospital. Stroke diagnosis was less apparent in these patients, as they more often presented with non-FAST symptoms compared to patients for whom the GP directly called the ambulance. Strategies to achieve reduction of vital prehospital time delays and to improve patient outcome are optimizing public awareness campaigns and GP triage along with adjusting current guidelines by enabling and focusing on immediate involvement of the EMS once acute stroke is suspected.

Part II. Prehospital triage by EMS paramedics

The second part focuses on identifying stroke code patients with large anterior vessel occlusion (LAVO) in the ambulance. In **Chapter 3**, we described a systematic review on prehospital scales to predict LAVO in stroke code patients. We identified seven scales, validated these scales externally with data from the Dutch acute stroke study (DUST), assessed these scales in terms of feasibility and developed a new scale: the Gaze, facial Asymmetry, level of Consciousness, Extinction/inattention (GACE) decision tree. We found that the FAST-ED (0.83, [95% CI, 0.80–0.85]) and RACE scale (0.82, [95% CI, 0.79–0.84]) had the highest accuracies to predict LAVO. The GACE can predict LAVO in 61% of patients with assessment of only two clinical items, and for all patients with a maximum of only four items, yielding a high feasibility.

These prehospital scales need to be validated in the setting where such a scale would be ideally used: in the field (i.e. applied by EMS paramedics in the ambulance). Therefore, in **Chapter 4**, we performed external validation of the seven prehospital scales identified in Chapter 3. External validation of these scales in the field showed moderate to good scale performance for the prediction of LAVO, with the LAMS and RACE scales showing the highest accuracies (0.89, [95% CI, 0.87–0.90] and 0.88, [95% CI, 0.86–0.89], respectively). Head-to-head comparison showed that both scales significantly outperformed the other scales (P<0.05). Feasibility was relatively high for all scales and ranged between 78%-88%. Furthermore, our results indicate that the use of a prehospital scale in the field can reduce inter-hospital delays (median of 53 minutes) to reperfusion treatment in a large urban area with relatively small distances between a primary stroke center and a comprehensive stroke center.

Another approach to improve patient selection in the ambulance is to develop a diagnostic tool to accurately differentiate patients with acute ischemic stroke from intracerebral hemorrhage. In **Chapter 5**, we reported on a preplanned discovery analysis of the MIRAS (MicroRNA in Acute Stroke) study, an ongoing observational cohort study including suspected stroke patients presented to the emergency department within 6 hours of symptom onset. We investigated whether tRNA-derived fragments (tRFs) can be used as early biomarkers in stroke diagnosis using small RNA-sequencing in plasma in a discovery cohort (N=26). We discovered that tRFs are a promising novel class of biomarkers. An important finding was that combinations of four to five tRFs showed diagnostic accuracies up to 0.99, [95% CI, 0.95-1.00] for intracerebral hemorrhage vs. ischemic stroke and stroke mimic in the discovery cohort. We validated our results in an independent cohort of ischemic stroke patients and healthy controls, which yielded similar diagnostic accuracies.

Part III. In-hospital triage, treatment and patient outcome

In the last part of the chain of acute stroke care, in-hospital factors that are associated with an adverse effect on patient outcome were investigated. In **Chapter 6**, we described the association between mode of weight assessment to titrate recombinant tissue plasminogen activator (rt-PA) dose for intravenous thrombolysis and several outcomes. In a large patient sample (n=4801) from 11 hospitals, we found that weight modality was not associated with symptomatic intracranial hemorrhage or clinical outcome. We showed that patients with estimated body weight had longer door-to-needle times compared to patients with measured body weight. While previous prospective studies have shown that estimated body weight leads to dosing errors, our results indicated that this does not translate into a different safety and efficacy profile of intravenous rt-PA.

Another factor that is associated with worse functional outcome is hyperglycemia on hospital admission. In **Chapter 7**, we performed an analysis with real world data from the MR CLEAN Registry, a prospective nationwide registry of consecutive patients who received endovascular treatment in routine clinical practice. We showed that hyperglycemia was associated with worse functional outcome, increased mortality, and an increased risk of symptomatic intracerebral hemorrhage after endovascular treatment (EVT). There were no differences in the rates of successful reperfusion, nor did we find that successful reperfusion modified the association between admission glucose and functional outcome. Studies are warranted to determine whether tight control of glucose improves efficacy of EVT after large vessel stroke.

In conclusion, this thesis addresses several ways to improve stroke triage in the chain of acute stroke care. To improve patient triage, the focus should be to directly involve the ambulance once stroke is suspected. Furthermore, prehospital triage tools that can help identify patients who are more likely to have LAVO or can differentiate between patients with acute ischemic stroke and intracerebral hemorrhage, will improve patient selection in the ambulance and thereby result in earlier initiation of EVT, thereby improving patient outcomes. Finally, continued efforts need to be made to further reduce in-hospital delays by identifying factors that have an adverse effect on patient outcome.