University of Groningen

Design approach for region-specific improvement of acute stroke care: simulation modeling to enhance organization

Maas, Willemijn

DOI:
10.33612/diss.663809468

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2023

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):
Maas, W. (2023). *Design approach for region-specific improvement of acute stroke care: simulation modeling to enhance organization*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen. https://doi.org/10.33612/diss.663809468

Copyright
Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the “Taverne” license. More information can be found on the University of Groningen website: https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment.

Take-down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Download date: 25-07-2024

CHAPTER 9

General discussion

Regional specific design approach

With the introduction of intravenous thrombolysis (IVT) and endovascular thrombectomy (EVT) for acute ischemic stroke, the organization of stroke care has significantly changed. One of the most important predictors of functional outcome after stroke with large vessel occlusion (LVO) is the time from symptom onset to the start of EVT.[1] In this thesis we learned more about the organization of acute stroke care and related optimization efforts. Insights obtained through our literature review (**Chapter 2**) revealed that no specific organizational model is inherently superior to another. In essence, any optimization effort aimed at improving acute stroke care, will depend on the regional health and transportation infrastructure and appears to be mainly influenced by region-specific characteristics and the stroke onset location. This means that the time span for patient transport from stroke onset location to the most nearby primary stroke center (PSC) and comprehensive stroke center (CSC) plays a crucial role in which organizational model will be applied. For example, direct transport to a CSC at a relatively long travel distance (mothership (MS) model) would not result in significantly improved clinical outcome when compared to routing according to the drip and ship (DS) model, in which the PSC is located more nearby.[2]

In order to further improve current acute stroke care systems, a design approach that assesses current performances of regions and identifies and subsequently analyzes suitable interventions would be helpful as a replacement or precursor for clinical trials. As demonstrated in this thesis, and tested in the northern- and southwest region of the Netherlands, a model-based approach using simulation was successfully used as such a design approach. An advantage of simulation modeling is that it is based on patient-level data collected from a specific region, instead of using probabilistic or meta data, and is therefore better able to reflect current pratice.[3] Data collection of in-hospital processes (using the MR CLEAN Registry), pre-hospital (initial triage and ambulance routing patterns), and inter-hospital transfer data (local emergency medical services (EMSs)) was used to get an accurate and complete overview of the entire acute stroke care pathway from symptom onset to treatment. Using these data we were able to identify regional bottlenecks in pathway performance. Next, promising interventions were tested by simulation to estimate its added value once these interventions would be implemented in real life (**Chapter 3**). We identified several interventions that would appear to qualify for further testing within a certain region. Extension of CSCs, expediting services and processes along the stroke pathway, adaptive patient routing, enabled by pre-hospital triage tools, and the use of other organizational models that bring intravenous thrombolysis (IVT) and/or EVT to the patient instead of transporting the patients are promising options for testing.

Using simulation modeling for testing interventions in the northern Netherlands

For the northern Netherlands region, several interventions such as expediting workflow (**Chapter 4**), adding CSCs to the region (**Chapter 5**), and the implementation of the 'drive the doctor' (DD) organizational model (**Chapter 6**) were tested for its impact on regional pathway performance and patient outcomes.

Firstly, **Chapter 4** showed that both models, the MS and DS model, were both validated, meaning that the collected patient data and model output accurately matched. Expediting workflow by a fast-track routing through the emergency department, pre-alert for inter-hospital transfer, a fast handover from PSC to the ambulance, and a fast workflow from CSC arrival (DS patients) or LVO confirmation (MS patients) to the angiography suite and to groin puncture showed promising results. Onset to groin puncture (OTG) may be reduced by as much as 60 minutes when implementing these interventions, which would result in an additional 6% patients regaining good functional outcome at 90 days (**Chapter 4**).

By modeling one or two CSC(s) added to the northern region of the Netherlands, a time gain of only 15 minutes in OTG may be expected. These modeling results conveniently indicate that adding one or two CSC(s) is probably not a (cost-) effective and an efficient way of optimizing regional acute stroke care. Alternatively, expediting workflow appears to be more promising in order to improve patient outcomes in this region. However, the scenario of adding CSC(s) might be an effective intervention in regions facing longer transportation delays between PSC(s) and CSC(s) (**Chapter 5**).

Modeling DD in the northern region of the Netherlands (**Chapter 6**) required additional effort to design this organizational model, due to various design options, e.g. use of several suitable transport modalities. Several design options were tested, which is also fairly straightforward by using simulation modeling. Using Randomized Control Trials (RCTs) to test all these design options would certainly have higher costs and increase the time needed for research. Design choices for DD model that were tested included the choice of upgrading suitable PSC(s) to thrombectomy capable stroke centers (TSCs), patient routing strategy, notification time of the mobile interventionalist (MI) and the use of different transport modalities. Results indicated that a design implementing 3 TSCs, patient routing using the Rapid Arterial Occlusion Evaluation (RACE) Scale (cut-off score > 4), MI's notification after LVO confirmation, and ground ambulance as transport modality might be the most realistic and feasible option for implementing the DD model in the northern Netherlands region. Testing this scenario indicated that, OTG may be reduced by approximately 50 minutes. A novelty of our simulation study is that this is the first time that a DD model was hypothetically tested in a rural area, whereas previous studies focused on urban settings. A recent (non-simulation) study from Germany showed also promising results for flying an interventional team in a non-urban region.[4]

Re-use of simulation models for acute stroke care

While regional differences require an efficient design approach for optimizing acute stroke care systems, similarities between acute stroke systems made it easy to re-use our in-house developed northern Netherlands models in the southwestern Netherlands (**Chapter 7**). Re-use was a straightforward and pragmatic way to identify suitable interventions for optimization in southwestern Netherlands, even revealing that multiple interventions could be tested simultaneously for this region. Promising results were found for the implementation of the DD model and use the RACE scale cut-off score > 4 to triage patients directly to a CSC. The time to EVT treatment could be reduced up to 1 hour. Future research is needed to study whether re-use of this model can be applied to other national- and international regions and whether a model extension is needed due to the current acute stroke care developments, for example, alternative approaches in diagnostic work-up such as MRI diagnostics.

In addition, future research should extend our developed simulation models with data input from other stroke patients such as non-LVO patients or intracerebral hemorrhage patients. For example, some interventions, such as pre-hospital routing, could have a major impact on the time from onset to thrombolysis for non-LVO patients, which we did not measure in our studies. Ideally, simulation models would be comprehensive including all patients and health infrastructure affected by proposed interventions.

Economic evaluation of suitable interventions using simulation modeling

Another important issue in improving the organization of acute stroke care is the cost-effectiveness of suitable interventions in certain regions. Our systematic review (**Chapter 8**) showed that most interventions aiming to reduce the time to treatment for IVT and EVT are cost-effective. Nevertheless, one study showed that DD is only cost-effective in one specific region compared to six other regions.[5] Again, a certain improvement in acute stroke care does not fit in every region, meaning that interventions cost-effective for one region are not necessarily cost-effective for another region. Cost-effectiveness analysis should be performed per region to support local policymakers, clinicians, and other stakeholders in deciding what will efficiently improve the acute stroke system. Another advantage of using simulation modeling as a design approach for improving regional-specific acute stroke care is that our developed simulation models can easily be extended to allow performing cost-effectiveness analyses.[6] Extending simulation models for cost-effectiveness analysis is a logical next step in region-specific optimization efforts for acute stroke care.

Future directions

The main conclusion of this thesis is that organizational improvement of acute stroke care requires a region-specific design approach. An RCT is a costly and time-consuming manner to analyze interventions suitable for a specific region. We showed that simulation modeling, based on patient-level data, is useful to assess and test several interventions in specific regions. The use of simulation modeling as a design approach or precursor for an RCT appears unknown, underestimated, and therefore underused by many clinicians, managers, policymakers and even by editors of clinical journals. Future research may implement a promising intervention, identified by the use of simulation modeling, to show the accuracy of the expected time gains estimated by simulation modeling. This likely will add more value to the use of simulation modeling in studying the organization of acute stroke care. Also the extension and use of simulation models for cost-effectiveness studies of promising interventions may guide policy makers. Beyond model re-use, a long term objective would be the development of a generic model, allowing for its easy tailoring to regional stroke systems by local stroke physicians, further lowering thresholds for simulation use and reaping its benefits.

Future research should focus on the extension of our current simulation model, as stated before. Extension of the model will be necessary for an optimal organization of the whole acute stroke population, including those patients without LVO. With the addition of data from these non-LVO patients to the current model, time to treatment effects for those patients can be calculated as well. Another advantage of such a model is that interventions, suitable for this group, can also be tested, resulting in the calculated time to treatment effects of all patient groups affected by organizational interventions.

Furthermore, the development of an accurate triage tool for LVO patients is another direction of future research for the optimization of acute stroke care organizations. Until now the RACE Scale (cut-off score > 4) seems to be the best performing pre-hospital stroke scale for ambulance personnel to identify suspected LVO patients for direct transfer to a CSC.[7] A recent RCT that included patients with suspected LVO patients in a nonurban area in Catalunya that were routed based on the RACE scale (cut-off score > 4) showed no significant difference in clinical outcome after 90 days compared to suspected LVO patients routed to the nearest IVT facility.[2] Delay in time to IVT for non-LVO patients (out of the suspected LVO patients group) might be a reason for this non-significant result. A more accurate triage tool might reveal the benefit of direct routing to a CSC for (suspected) LVO patients. Simulation modeling is also suitable for cost-effectiveness analyses of such a tool and thus may be used for full fledged (early) Health Technology Assessment prior to implementation.

In addition to organizational simulation models, the development of a prediction tool for clinical outcomes, based on a combination of patients characteristics, diagnostics and the stroke onset location plus routing options, could be promising topic for future research. Ambulance personnel might use such a prediction tool to decide whether to transfer a suspected stroke patient directly to a CSC or to the nearest IVT facility, i.e. according to the MS – or DS model. THRIVE-c[8] and MR PREDICTS[9] are prediction models for EVT using patient characteristics and diagnostics with imaging.[10] Development of a prediction model/tool without imaging diagnostics and with GPS location to PSC and CSC could be the next step in regional and patient-specific pre-hospital routing. The idea of a previously developed probabilistic model[11] might help to build such a tool but the use of patient-level data should provide a more accurate tool for a specific region. With the use of simulation modeling, the time-to-treatment effects of such a tool can be tested before implementation.

References

1 Mulder MJHL, Jansen IG, Goldhoorn RJB, et al. Time to endovascular treatment and outcome in acute ischemic stroke: MR CLEAN registry results. *Circulation* 138.3 (2018): 232-240.

2 de la Ossa N P, Abilleira S, Jovin T G, et al. Effect of Direct Transportation to Thrombectomy-Capable Center vs Local Stroke Center on Neurological Outcomes in Patients With Suspected Large-Vessel Occlusion Stroke in Nonurban Areas: The RACECAT Randomized Clinical Trial. *JAMA*, 2020;327(18), 1782-1794.

3 Holodinsky JK, Willianson TS, Kamal N, et al. Drip and ship versus direct to comprehensive stroke center: conditional probability modeling. *Stroke* 48.1 (2017): 233-238.

4 Hubert GJ, Hubert ND, Maegerlein C, et al. Association between use of a flying intervention team vs patient interhospital transfer and time to endovascular thrombectomy among patients with acute ischemic stroke in nonurban Germany. *JAMA* 327.18 (2022): 1795-1805.

5 Morii Y, Osanai T, Fujiwara K, et al. Analyzing Cost-Effectiveness of Allocating Neurointerventionist for Drive and Retrieve System for Patients with Acute Ischemic Stroke. *Journal of stroke and cerebrovascular diseases*. 2021, 30(8):105843.

6 Lahr MMH, van der Zee DJ, Luijckx GJ, et al. Centralising and optimising decentralised stroke care systems: a simulation study on short-term costs and effects. *BMC medical research methodology* 17.1 (2017): 1-12.

7 Duvekot MHC, Venema E, Rozeman AD, et al. Comparison of eight prehospital stroke scales to detect intracranial large-vessel occlusion in suspected stroke (PRESTO): a prospective observational study. *Lancet Neurol*. 2021; 20:213.

8 Flint AC, Rao VA, Chan SL, et al.. Improved ischemic stroke outcome prediction using model estimation of outcome probability: the THRIVE-c calculation. *Int J Stroke*. 2015; 10:815–821. doi: 10.1111/ijs.12529

9 Venema E, Mulder MJHL, Roozenbeek B, et al.. Selection of patients for intra-arterial treatment for acute ischaemic stroke: development and validation of a clinical decision tool in two randomised trials. *BMJ*. 2017; 357:j1710. doi: 10.1136/bmj.j1710

10 Kremers F Venema E, Duvecot M, et al. Outcome Prediction Models for Endovascular Treatment of Ischemic Stroke: Systematic Review and External Validation. *Stroke* 29.2 (2022): 825-836.

11 Holodinsky JK, Williamson TS, Demchuk AM, et al.. Modeling stroke patient transport for all patients with suspected large-vessel occlusion. *JAMA Neurol*. 2018; 75:1477–1486. doi: 10.1001/jamaneurol.2018.2424