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Lower Door to Needle Times – Is it the Pace that Kills? [Version 1, 2 Approved with Reservations]

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Abstract

Background: Acute ischemic stroke (AIS) treatment has been revolutionized by the advent of intravenous thrombolysis (IVT) and endovascular treatment (EVT). Both treatment modalities are dependent on the patient arriving promptly at the hospital. There is therefore great emphasis on reducing pre-hospital time consumption and also door-to-needle (DTN) time. We aimed to assess what effect the pursuit of lower DTN had on in-hospital mortality and number of IVT treatments.

Methods: We started systematically working to improve routines around the IVT treatments in 2009. Data were analyzed from 634 AIS patients receiving IVT treatment at our centre from 2009 up to and including 2015.

Results: The median DTN time fell from 64 minutes in 2009 to 29 minutes in 2015 ($p < 0.0001$).
In the same time frame, the number of IVT treatments increased from 45 to 130 ($p < 0.0001$), an increase of almost 290%.
The in-hospital mortality percentage decreased continually from 6.7% in 2009 to 3.0% in 2015 ($p < 0.001$).

Conclusions: Our study showed a dramatic increase in the number of IVT treatments as well as a continual decline in both in-hospital mortality and DTN time. These positive changes are due to continued efforts to educate and update both the patient population and the treatment chain on stroke treatment. As the effects of stroke awareness campaigns inevitably taper off, it is the continued focus on the treatment chain that yields results.

Introduction

The last two decades have seen a revolution in the treatment of acute ischemic stroke (AIS), initially with the advent of intravenous thrombolysis (IVT) [1,2] and later with the use of endovascular treatment (EVT) [3-6]. Outcomes of IVT and EVT are time sensitive, thus the challenge now is getting eligible patients into treatment centres within a suitable timeframe allowing them to benefit from therapy [7].

In the prehospital arena stroke awareness campaigns have been used to get patients to recognize stroke symptoms and promptly contact the emergency medical services (EMS) [8-10]. These campaigns have had varying effect and most evaluative works suggest the need for repeated campaigns and more universal campaign methodology [11-13]. Evaluation of a region wide campaign in our patient catchment area showed a substantial improvement in the numbers of patients being treated, but again a lack of lasting effect; supporting the need for repeated campaigns [14].

After EMS contact: pre- and in- hospital protocols aim to reduce the time elapsed prior to treatment with IVT. These protocols aim to reduce the door – to – needle time (DTN) [15,16] and thus improve clinical outcome [16,17].

These protocols have also shown to be transferrable to other centres providing rapid improvements in DTN [18].

The feasibility and results of DTN reduction have led to the recommendation that DTN be no greater than 60 minutes [19].

This recommendation applies to all centres treating acute stroke patients, but some centres have achieved and sustained a DTN of less than 30 minutes [15,20,21].

In the hyper-acute situation, this emphasis on speed can potentially lead to erroneous treatment and thus increase mortality. Are we pursuing a lower DTN at the expense of patient safety?

Stavanger University Hospital (SUS) started providing IVT treatment in 2003, the same year it was licensed in Europe. It wasn't however until 2009 that we started aggressively working on reducing DTN and increasing the numbers of patients treated for acute onset ischemic stroke. In addition to organizational and educational changes, we ran a month long stroke awareness campaign in May 2015.

Our primary aim was to study what effect, if any, this had on in-hospital patient mortality. Our secondary aims were to monitor DTN times and IVT treatment numbers looking for any changes as a result of our interventions.

Materials and Methods

Population / Catchment Area

SUS serves a population of almost 350 000, receiving all AIS patients in its catchment area. Approximately 200 000 inhabitants live in and around the city of Stavanger; the remainder live in more rural areas of Rogaland County.

All IVT treatments at SUS during the period from 2009 to 2015 (n=634) were included in the study. According to treatment guidelines, IVT was administered within 4.5 hours of symptom onset.

Stroke Database

All patients treated with IVT were retrospectively compiled into a database until 2012, when prospective inclusion into the database started. The database included details from medical records including AIS risk factors, National Institutes of Health Stroke Scale (NIHSS) score on admission and discharge, treatment complications and in-hospital mortality.

Percentage mortality was calculated as the percentage of patients who died before discharge from the hospital in conjunction with acute IVT treatment. Mortality in patients over 90 years of age was excluded due to a significant pre-existing comorbidity. Previously Healthy patients were defined as those living at home without any assistance, without any chronic medical conditions and not using any medications. The remainder of the cohort had varying degrees of pre-existing comorbidity including the most common AIS risk factors (hypertension, hypercholesterolemia, prior TIA/Stroke, etc.).

All the applicable times including; time of stroke onset, when the EMS were contacted, the time of admission and time of IVT administration were taken from a combination of the pre-hospital records (AMIS – acute medical information system) and hospital records. The relevant time durations including DTN could then be calculated, means and medians subsequently calculated.

All these data were compiled into a single database.

Interventions

From 2009 we started to address the treatment chain; both its pre- and in- hospital components.

In the prehospital space we have continued our focus on educating the EMS personnel on AIS using regular seminars. This increased awareness provides a continued focus on AIS leading to a more driven, proactive EMS team. The regular seminars are provided by neurology residents and or consultants interested in acute stroke treatment.

Secondly, the transport of patients to the Emergency Room (ER) was streamlined considerably. This meant that patients were directly admitted by the EMS if an acute onset stroke was suspected. Primary care physicians have also been kept updated on AIS symptoms and treatment at regular intervals.

In-hospital changes began in the ER with the triaging of AIS patients. AIS patients were, prior to 2008, seen as non-acute.

Since then we have implemented a system where the on call registrar in neurology and two ER nurses await the arrival of the patient in an acute suite in the ER. The Computed Tomography (CT) lab is on standby and has been warned of the imminent arrival of the patient by the EMS / ER coordinator.

The ER nurses / personnel are also updated on AIS with regular seminars. The data showing IVT treatment numbers and DTN times are also presented at these seminars as we feel this has a motivational effect.

From 2009 onwards, we have conducted systematic annual reviews of the AIS treatment chain at SUS, looking for any inherent weaknesses and continually trying to improve them.

These changes involving the hyper-acute part of the AIS treatment chain are presented in detail in our earlier work [16].

In 2013 we started a "Stroke School" for all ER and stroke unit personnel involved in the treatment of AIS patients. The Stroke School comprised presentations by stroke physicians and experienced stroke nurses aimed at educating and informing attendees.

In May 2014, we ran a stroke awareness campaign focused at the patient population we serve. The campaign lasted one month and pointed out the importance of contacting the EMS as quickly as possible if stroke symptoms were suspected.

The registrars and consultants working at the department of neurology at SUS have daily morning meetings where patients are presented. All acute admissions are presented including AIS patients and IVT treatments. As well as this daily reminder, there are also regular seminars focusing on AIS treatment where new articles and studies are presented.

With the interventions of the past years (2009 onwards) and the continuing focus on the acute treatment of AIS, we looked for any changes in our primary and secondary end points.

Statistics

Using the Stroke research database, the data for the above mentioned end points was collected and analyzed. Statistical analyses were conducted to determine any changes in the number of EMS admissions as well as the number of treatments with IVT. Statistical analysis was conducted using IBM SPSS version 22. P values were determined using one-way analysis of variance (ANOVA) and Pearson's Chi squared test as appropriate. P values less than 0.05 were considered significant.

Results

Table 1 shows the baseline patient characteristics. Of the total patient population (n=634), 336 were men (53%) with a median age of 70 (range 22 – 89). One hundred and seventy-eight of the (28.1%) were previously healthy individuals. The median NIHSS on admission was 8 (range 1 – 29).

Table 1: Baseline Patient Characteristics.

	Total (n=634)
Men (%)	336 (53.0)
Median Age (Range)	70 (22-89)
Previously Healthy (%)	178 (28.1)
Median Baseline NIHSS (Range)	8 (1-29)

Table 2 shows the In-hospital mortality adjusted for baseline NIHSS. There were 250 patients that had NIHSS 1 – 5 on admission and in this group there were 2 patients that died in-hospital (0.8%). The next group comprised 220 patients having NIHSS 6 – 14 on admission, 6 of them died in-hospital (2.7%). The third group, comprising 130 patients with a NIHSS 15 – 24 on admission, had an in-hospital mortality rate of 7.7% (10 patients). The final group was 34 patients with a NIHSS ≥ 25 of which 12 died in hospital (35.3%).

Table 2: In-hospital Mortality and baseline NIHSS.

NIHSS on Admission	NIHSS 1-5	NIHSS 6-14	NIHSS 15-24	NIHSS ≥ 25
Number of Patients	250	220	130	34
In-hospital Mortality (%)	2 (0.8)	6 (2.7)	10 (7.7)	12 (35.3)

Figure 1 shows the numbers of IVT treatments year on year in the period 2009 – 2015. The number of IVT treatments increases from 45 to 130 ($p < 0.0001$) from 2009 to 2015, an increase of almost 290%. The increment is most pronounced in the first year, between 2009 and 2010, from 45 to 74. There is then a plateauing in number of IVT treatments in 2011, 2012 and 2013, with 86, 84 and 88 treatments respectively. A dramatic increase in the number of treatments is again seen from 2013 to 2014 – a jump from 88 to 127, followed by a modest increase to 130 treatments in 2015.

Figure 1: The number of IVT treatments year on year 2009-2015.

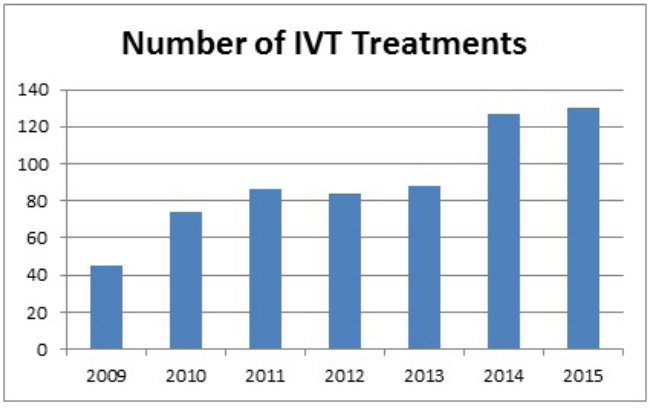


Figure 2 shows the median DTN time year on year in the period 2009 – 2015. There is an overall reduction from a median of 64 minutes in 2009 to a median of 29 minutes in 2015 ($p < 0.0001$). The most significant reductions in median DTN time are of 14 minutes and are seen between 2009-2010 and 2011-2012. From 2012 to 2013 there is an increase in median DTN time from 31 minutes to 35 minutes; falling from 35 minutes to 30 minutes and 29 minutes in 2014 and 2015 respectively.

Figure 2: The Median DTN time year on year 2009-2015.

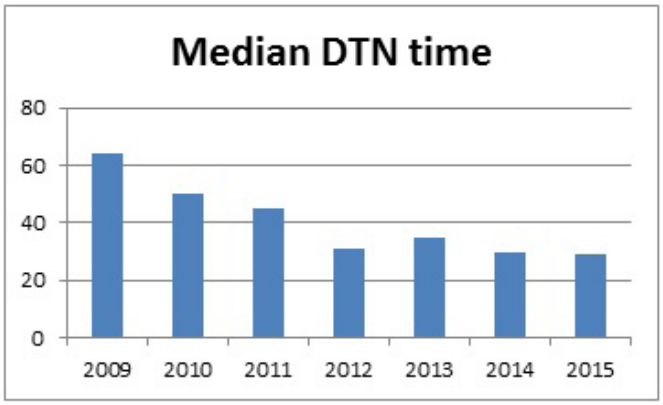


Figure 3 shows the yearly percentage mortality from 2009 up to and including 2015. The percentage mortality decreases from 6.7% in 2009 to 3.0% in 2015 ($p < 0.001$). There is some variation in the in-hospital mortality rates, initially increasing from 6.7% in 2009 to 8.1% in 2010.

Figure 3: The in-hospital mortality rate for those treated with IVT (%) year on year 2009-2015.

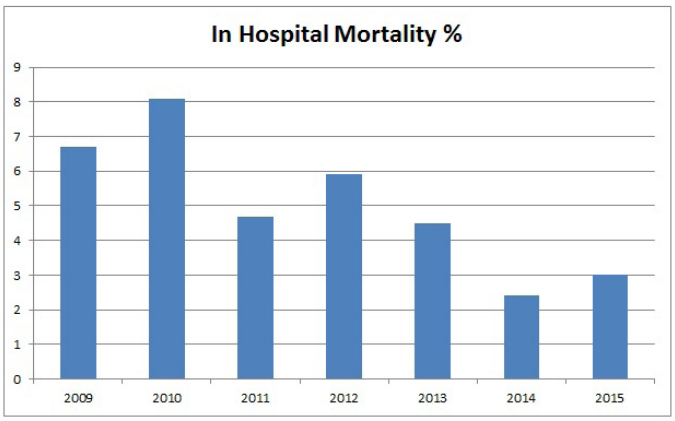
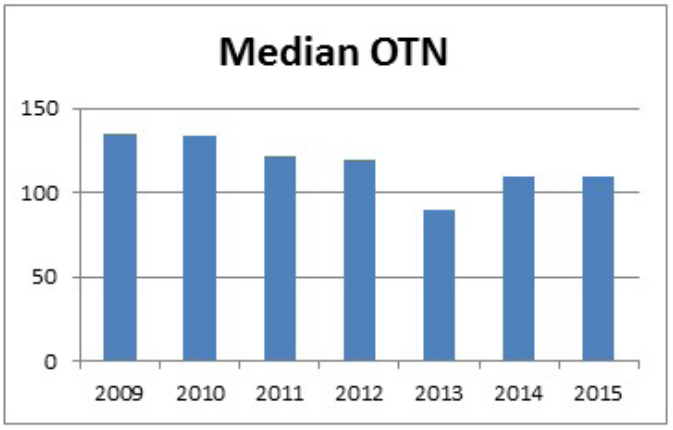


Figure 4 shows the yearly median OTN time in the period 2009 – 2015. The OTN times in 2009 and 2010 are 135 and 134 minutes respectively. There is a fall in OTN to 122 minutes in 2011 and a further fall to 119 minutes in 2012. In 2013 the median OTN is dramatically reduced to just 90 minutes, increasing to 110 minutes in both 2014 and 2015.

Figure 4: The Median OTN time year on year 2009-2015.



Discussion

Our study demonstrates a significant increase in the number of IVT treatments along with a decline in DTN time as a result of our interventions. A simultaneous decrease in the rate of in-hospital mortality for those patients with AIS being treated with IVT is also seen.

Our primary endpoint, in-hospital mortality rate for AIS patients treated with IVT, decreased from 6.7% in 2009 to 3.0% in 2015. This is particularly noteworthy as other recent studies from specialized stroke units report rates of around 8.0% [22,23]. When we factor in the baseline NIHSS (Table 2), the mortality rates in our study are still very low. Comparing our results to those from the SITS-ISTR registry, mortality rates for patients with a baseline NIHSS 15 – 25 and NIHSS ≥ 25 are significantly lower in our cohort 26.9% vs. 7.7% and 50.4% vs. 35.4% respectively [24,25]. Again, it has to be emphasized that our cohort included octogenarians, a subset which is excluded in most works including the SITS-ISTR registry.

A significant factor in the low in-hospital mortality seems to be time frame within which IVT was administered after the onset of stroke symptoms – the onset to needle (OTN) time. In all the years of our study the median OTN has been relatively low; always being below 140 minutes and from 2012 onwards lower than 120 minutes. This is supported by the work of Gumbinger et al where the retrospective analysis of over 10,000 patients treated with IVT for AIS showed that better outcome was strongly associated with shorter treatment times [26]. This is also reflected by the work of Strbian et al; where a prospective analysis of almost 7000 patients showed that early treatment was both strongly and independently correlated with good outcome [27].

It is however important to point out that the OTN isn't continually decreasing and any correlations between OTN and DTN are difficult to establish. In our study, despite the decreasing DTN times, there is at best a sporadic fluctuation in OTN in

the same period. This lack of direct correlation is supported by the work of Strbian et al where a prospective pooled analysis of over 6500 patients showed that there is a weak inverse correlation between onset to door time and DTN time. The sum of the onset to door time and the DTN time (OTN time) was therefore almost arbitrary [28].

The quest for lower DTN times is a challenge the world over, with specialized stroke units still struggling to achieve times lower than 60 mins [29-31] despite their attempts at streamlining the stroke treatment chain. These studies showed however that a significant improvements in DTN times were achieved when both the pre- and in- hospital treatment chain were addressed. This finding is also strongly supported by our study and we strongly advocate targeting the treatment chain. The importance of patient volume in the reduction in DTN is emphasized by our study where a strong positive correlation is seen. These findings are supported by the work of Groot et al in a retrospective analysis of almost 2000 IVT treated patients [32].

Other factors that seem to play a role in reduced in-hospital mortality are the "Stroke School" and the ongoing focus on AIS treatment at departmental meetings. Increased awareness amongst the treating physicians, nurses and the rest of treatment chain leads to improved in-hospital follow up and therefore reduced in-hospital mortality. Similar findings are suggested in other studies backing up the need for well-informed specialists in the care of AIS patients [33,34].

The main limitation of our study is the retrospective data collection in the earlier years; relying on the accuracy of medical records has the potential to give inaccurate information. However, from 2012 onwards we had the means to include patients prospectively thus dramatically improving data collection. A confounding variable is the physician's level of comfort with IVT treatment. The number of IVT treatments has increased year on year and each physician on staff has become more comfortable with this treatment modality. A higher level of comfort in decision making is an important factor in reducing erroneous treatment thus potentially reducing in-hospital mortality. It is however difficult to ascertain exactly how this variable influences our primary end point. The merits of our study are the number of patients included, the number of years of data collection, subsequently giving good validity of results.

Lower DTN times can be safely achieved, resulting in the possibility of improved patient outcomes without an increase in in-hospital mortality. Such results however, require a continued and ongoing effort in order to be sustained and can only be achieved through repetition. It is this continued emphasis on stroke management throughout the treatment chain that serves to facilitate better treatment of AIS patients from admission to discharge.

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