

# State of the art on acute ischemic stroke: Systems of Care and In-hospital Organization

Alejandro Tomasello Weitz<sup>(1)</sup>, Marc Ribó Jacobi<sup>(2)</sup>, Jens Fiehler<sup>(3)</sup>

<sup>1</sup> Head of Interventional Neuroradiology Section, Hospital Universitari Vall d'Hebrón, Barcelona, Catalonia, Spain.

<sup>2</sup> Interventional Neurologists, Hospital Universitari Vall d'Hebrón, Barcelona, Catalonia, Spain.

<sup>3</sup> Director of the Department of Diagnostic and Interventional Neuroradiology, University Medical Center, Hamburg-Eppendorf, Germany.

Received – 30 April 2018; Accepted – 30 May 2018

## A B S T R A C T

This article summarizes a Medtronic-sponsored webinar held on the 19th of March 2018 in Barcelona, Spain. This webinar was moderated by Professor Jens Fiehler. In his introduction to the presentations given by the two speakers, Dr Alejandro Tomasello Weitz and Dr Marc Ribó Jacobi, Professor Fiehler reiterated the axiom familiar to all neurologists: that with a stroke, time lost is brain lost. Professor Fiehler noted that improved organization with associated time savings in the patient transfer process to hospital, and in in-hospital organization, can have a significant beneficial impact in improving patients' treatment outcomes.

This webinar examined the ever-present dilemma faced by stroke neurologists: is it in the best interests of a patient with suspected acute stroke to be despatched the nearest primary stroke-ready hospital, to be stabilized, and if necessary, subsequently transferred to a comprehensive stroke centre, or should the patient be transferred directly to a comprehensive stroke centre? Dr Tomasello provided insights into the process of optimizing in-hospital work flows and demonstrated the significant time-saving that can be achieved in transferring the acute stroke patient via a direct to angio-suite protocol. This event was streamed live, via the Oruen Ltd website, to a wide audience of interventional neuroradiologists and physicians involved in the treatment of acute ischemic stroke. The viewing audience were able to participate in a Questions and Answers session after the speakers' presentations.

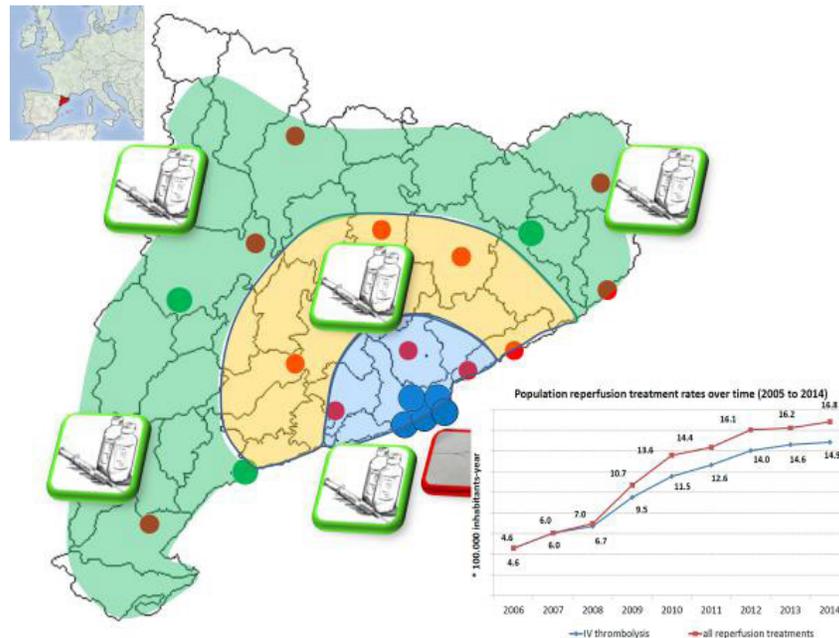
**Key words:** acute stroke, endovascular treatment, hospital transfer, in-hospital work flow.

**Corresponding author:** Marc Ribó – marcriboj@hotmail.com

**Acknowledgements:** The editorial assistance of Mr Rob Goodwin, Oruen Ltd, in the preparation of this article is acknowledged with thanks.

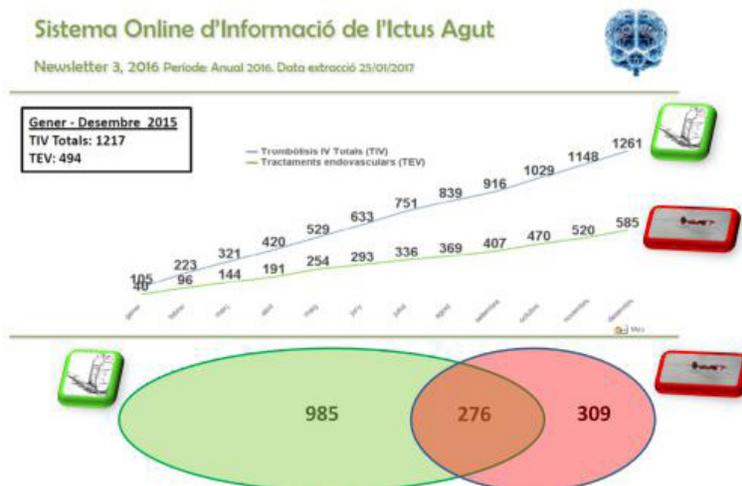
**STROKE PATIENT ORGANIZATION IN CATALONIA - DR MARC RIBÓ .**

TDr Ribó explained that endovascular thrombectomy treatment in Catalonia is currently only available in the Barcelona area; however, i.v. tissue plasminogen activator (tPA ) treatments are administered in 25 primary centres throughout Catalonia. The comprehensive stroke centres with endovascular treatment capability are represented by the blue circles in the following figure.



Since stroke response services and networks were initially established in Catalonia, Emergency Medical Services (EMS) have always transferred the patient to the closest primary stroke centre and then, if necessary, transferred the patient to a comprehensive stroke centre for endovascular treatment. Currently, at comprehensive stroke centres in Barcelona there are three stroke teams on call (two teams for three centres and one team for two centres), and

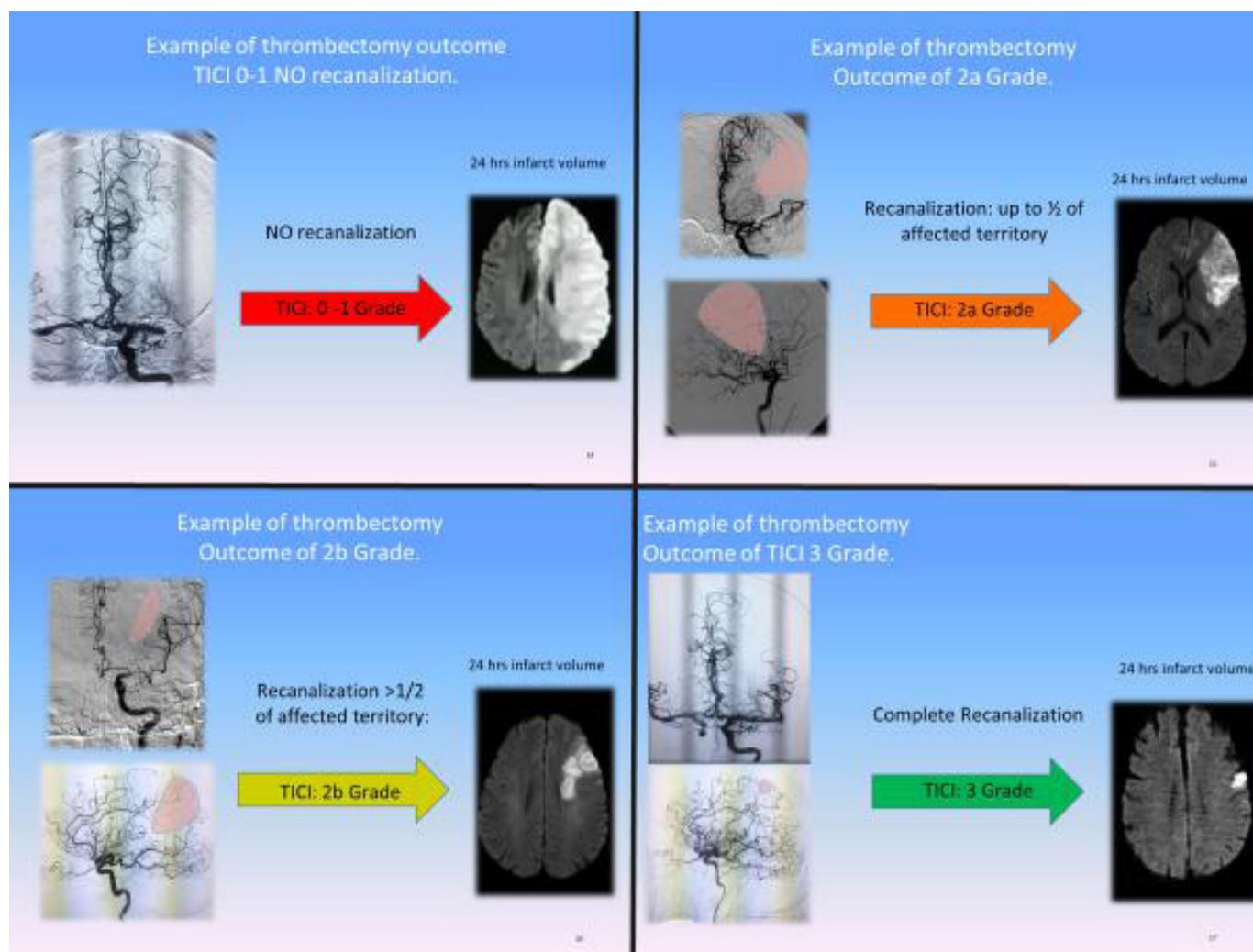
priority is given to transferring interventional stroke teams to the centre where the patient has been admitted. This is considered less problematic than prioritizing transfer of the patient to one or two on-call comprehensive centres. During the 12-month period to December 2015, 1,217 i.v. thrombolysis procedures and 494 endovascular thrombectomy interventions were conducted in Catalonia, as illustrated in the following figure.



Dr Ribó confirmed the use of a prehospital scale by EMS in Catalonia to identify suspicion of large vessel occlusion (LVO) in patients with symptoms of acute stroke. The **R**apid **A**rterial **o**clusion **E**valuation (RACE) scale is a simple tool that correlates well with National Institutes of Health Stroke Scale, (NIHSS) score; it can accurately assess stroke severity, and identify patients with LVO (i.e. score >4) in the prehospital setting by medical emergency technicians.<sup>1</sup> Currently, over 90% of prehospital notification calls from EMS in Catalonia now include a RACE score. About half of these patients will have a RACE score >4.

Dr Ribó described the stroke telenetwork in Catalonia. In his hospital they participate in around 500 consultations with 16 or 17 regional hospitals annually; this telemedicine collaboration involves over 100 i.v. tPA treatment administrations. In addition, highly detailed data on all thrombolysis treatments and thrombectomy interventions conducted by individual hospitals in the Catalonia region are registry-collated, so performance metrics e.g. door-to-needle time (DTN) for individual stroke centres can be compared.

The objective of stroke treatment is to achieve the highest degree of recanalization in the territory affected by the thrombus as soon as possible. Success is currently defined as achieving angiographic Thrombolysis in Cerebral Infarction (TICI) 2b grade or TICI 3 grade recanalization of previously occluded target artery ischemic territory, as illustrated in the following TICI classification.<sup>2</sup>



Administration of i.v. tPA must be carried out as fast as possible to be effective. The impact of time to treatment on resultant revascularization rates is well documented; it drops from around 45% when treatment can be administered within 90 minutes, to around 16% when treatment is administered after 270 minutes.<sup>3</sup> Dr Ribó noted that i.v. tPA treatment was not the best treatment for LVO; it is more suited to small volume clots, but it is widely available in primary stroke centres. In contrast, high revascularization rates can be achieved very quickly with stent-retriever mechanical thrombectomy, but this intervention is not widely available, and can only be performed at comprehensive stroke centres. Unsurprisingly, the best thrombectomy performing centres are those dealing with the greatest volume of patients and with the most experience. Hence, there is an imbalance between the availability of the two types of treatment, and this raises the question of how best to use them, separately or together, to best effect.

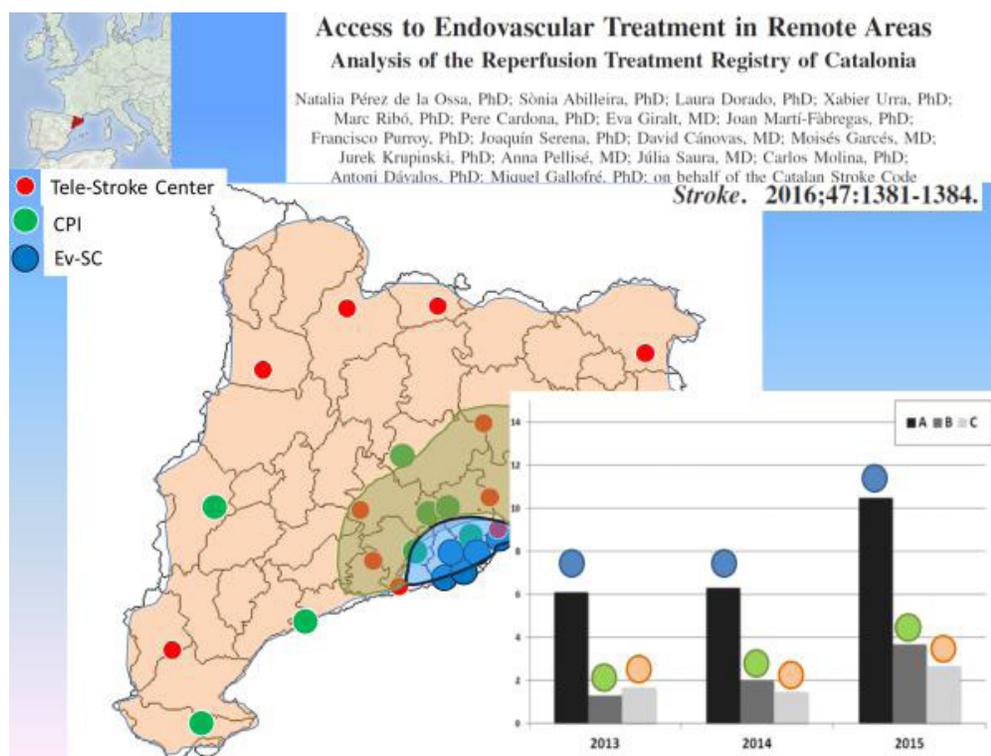
PRIME<sup>7</sup> and REVASCAT<sup>8</sup> reported better revascularization rates following mechanical thrombectomy in LVO compared with i.v. tPA thrombolysis. Furthermore, the available data indicate the combination of i.v. tPA and mechanical thrombectomy is significantly superior to i.v. tPA treatment alone. Dr Ribó felt that when an acute stroke patient has been hospitalized in a comprehensive centre, where both mechanical thrombectomy and i.v. t-PA thrombolysis interventions are available, the patient should receive both treatments. However, complications arise when a patient suffers an acute stroke in a remote area. The dilemma here is: should the patient be dispatched via a shorter transfer to the nearest primary stroke centre for prioritized rapid i.v. thrombolysis, and if necessary, then transferred to a comprehensive stroke centre for endovascular thrombectomy; or, should the primary stroke centre be by-passed, and the patient transferred directly to a comprehensive stroke centre? This, as yet, unsolved dilemma is illustrated in the following figure.

Within the last five years, randomized controlled trials (RCTs), notably: MR CLEAN<sup>4</sup>, ESCAPE<sup>5</sup>, EXTEND-IA<sup>6</sup>, SWIFT



Dr Ribó referred to US 2015 data<sup>9</sup> where the rate of endovascular treatment (EVT) was estimated to be three EVT per 100,000 person-years; however, the number of eligible patients (annual incidence of 24 patients with LVO per 100,000 population) indicates the potential for significant growth of EVT in the USA. These data indicate that the goal for interventional neurologists is to have the capability to perform between 15-20 EVT annually per 100,000 population. In Catalonia (population 7.5 million), up until 2014, and following a protocol of prioritizing initial i.v. tPA, the number of mechanical thrombectomies

performed annually was around 300. Subsequently, following the REVASCAT publication, the number of mechanical thrombectomies performed in Catalonia has increased to between 600-700 per year. Currently, the comprehensive stroke centres in the Barcelona area are performing 10 EVT per 100,000 inhabitants; however, this rate drops to less than two EVT per 100,000 inhabitants for acute stroke patients in more remote areas of Catalonia. The discrepancy in regional EVT rates in Catalonia is illustrated in the following figure.



Data from the STRATIS “real world” registry (**S**ystematic Evaluation of Patients **T**reated with Neurothrombectomy Devices for **A**cu**T**e **I**schemic **S**troke)<sup>10</sup> has allowed a comparison of timings and outcomes associated with US acute stroke patients who were transferred from a peripheral primary hospital to a comprehensive stroke centre, versus patients transferred directly to a comprehensive stroke centre for thrombectomy. Patients; irrespective of whether they had received i.v. tPA or not, who underwent a secondary transfer to the comprehensive centre experienced significant delays in time to revascularization and poorer mRS-assessed outcomes. However, Dr Ribó stressed that this analysis did not include those patients initially transferred to a primary centre, who subsequently did not receive EVT at a comprehensive centre, as they either had shown improvement or presented with a large infarct. Consequently, Dr Ribó considered this analysis does not provide a complete answer to the interventionist’s dilemma of whether to bypass the peripheral centre in favour of direct transfer to a comprehensive centre.

Ideally, triage - the process of determining the priority of patients’ treatments based on the assessment of their condition, and usually conducted at a primary stroke centre, needs to be brought forward to the point where the patient is collected for ambulance transfer. An early decision to transfer the patient to a comprehensive centre, to the CT scan, or even directly to the angio-suite, can typically save up to 60 minutes in the time taken before EVT can be initiated. Important factors to consider in this decision-making process include:

- Triage capability and early identification of LVO versus small volume clots by EMS at the patient collection location.
- The relative distances involved for transfer to nearest primary versus comprehensive centre, and the capability of available EMS to transfer the patient safely, with adequate ambulance support and a low risk of complications.

- The performance of individual primary stroke centres as demonstrated by e.g. DTN time. Poorly performing primary centres should be avoided. Assessment based on neurological symptoms is faster than a long wait for a CT scan.
- However, to avoid futile transfers, there is a contrary argument to wait for the CT scan.
- Organizational consequences: if, increasingly, stroke patients are transferred directly to comprehensive stroke centres, demand for stroke treatment at primary stroke centres will reduce, and available expertise for treating future acute stroke patients will be lost.

### **Methods and approaches to patient transfer decisions**

Dr Ribó explained that one option for making the decision on direct versus indirect patient transfer is to use a pre-hospital scale such as RACE that is predictive for LVO. In a US study,<sup>11</sup> patients assessed by EMS with a RACE score of  $\geq 5$  were taken directly to a comprehensive facility that offered advanced therapy. Patients transferred under the RACE Alert protocol were compared for time to recanalization with patients hospitalized via a standardized stroke alert. The RACE Alert protocol significantly reduced median time to recanalization from 205 minutes in the standard alert cohort to 101 minutes ( $p = 0.001$ ). These results indicate that EMS adaptation of the RA protocol is feasible and effective for early triage and treatment of patients with stroke, and it can significantly improve treatment times for both systemic thrombolysis and mechanical thrombectomy.

Another option for patient transfer decision-making is based on modelling methodology leading to endovascular transport option maps that attempt to define the best transportation option for optimal outcomes for acute stroke patients.<sup>12</sup> Essentially, this involves collating stroke centre performance data: DNT times etc. and the relative distances to individual primary and comprehensive stroke centres to arrive at the best modelled transfer option and outcome.

The American Heart Association (AHA) in conjunction with the American Stroke Association (ASA) has recently proposed a severity-based stroke triage algorithm for EMS when LVO is suspected.<sup>13</sup> Transfer to the nearest primary stroke centres and prioritizing i.v. tPA is recommended, unless direct transport to a comprehensive involves a delay no more than 15 minutes, and the use of i.v. tPA is not precluded. Dr Ribó felt these recommendations are

opinion-based and do not address some of the concerns he had already raised. Dr Ribó emphasized his opinion: that it was not in the best interests of an acute stroke patient with suspicion of LVO, to be transported to a primary stroke centre, if the patient was within a 30-minute transfer window to a comprehensive stroke centre.

A recent further approach, in effect, utilizes the primary stroke centre (PSC) as an extension of a comprehensive stroke centre (CSC). For patients suspected of having emergent LVO who present to a primary stroke centre, a standardized protocol based on: (1) EMS on standby for secondary transfer, (2) early notification to the closest comprehensive centre, and (3) computed tomographic angiography (CTA) at the primary centre but shared cloud-based neuroimaging with the comprehensive stroke centre, is associated with significantly reduced groin-to-puncture time and improved outcomes.<sup>14</sup> When full executed, this protocol was associated with a reduction in median time for PSC arrival to CSC groin puncture from 151 to 111 minutes, and patients were twice as likely to have favourable outcomes.

An increasingly popular approach to the acute stroke patient hospital transfer decision is based on the combination of prehospital scale assessments and novel technology involving mobile tele-stroke systems. This approach allows the EMS physical examination of the patient based on e.g. the RACE scale to be forwarded to comprehensive stroke centres for expert analysis. Instruction to EMS on the best transport option for the patient can then be given by the on-call expert stroke neurologist. However, the best quality evidence to answer the question of whether to by-pass the patient, or not, will be provided by a randomized controlled trial. In this respect, the ongoing RACECAT trial has been designed to compare the **TR**ansfer to the **C**losest local stroke centre vs. direct transfer to **E**ndovascular stroke **C**entre of **A**cute stroke patients with suspected large vessel occlusion in the Catalan **T**erritory. This study will provide specific randomized data that will help decide which transportation option provides the best outcome for acute stroke patients. In particular, the RACECAT study should show whether option B is superior to option A, and also show how these options compare with option C, i.e. acute stroke patients rapidly hospitalized within the local Catalan comprehensive stroke centres area, shaded blue in the following figure.

**RACECAT**

▪**ENDPOINTS:**

Option A Vs Option B ?

Vs

C

▪**SECONDARY ENDPOINTS:**

- Safety / efficacy: according to distance, time from onset
- Safety /efficacy in ischemic / hemorrhagic strokes
- % patients receiving iv-TPA /EVT

As at March 2018, 496 patients have been enrolled in RACECAT. An interim analysis is planned when 700 patients have been enrolled, and the study plans to complete with a total of 1,700 patients. The results and outcomes achieved in this landmark study are eagerly awaited.

**IN-HOSPITAL ISCHEMIC STROKE FLOW - DR ALEJANDRO TOMASELLO WITZ**

Dr Tomasello explained his presentation was based on the experience of in-hospital acute stroke work flows in the Hospital Universitari Vall d’Hebrón, Barcelona, and how these procedures have been optimized. The pace of neural circuitry loss following LVO acute ischemic and the process of accelerated aging are staggering, rapid, and highly time-dependent. The typical patient loses 1.9 million neurons each minute in which stroke is untreated.<sup>15</sup> Put simply: every second counts.

**Time is Brain**

**Time Is Brain—Quantified**  
Jeffrey L. Saver, MD

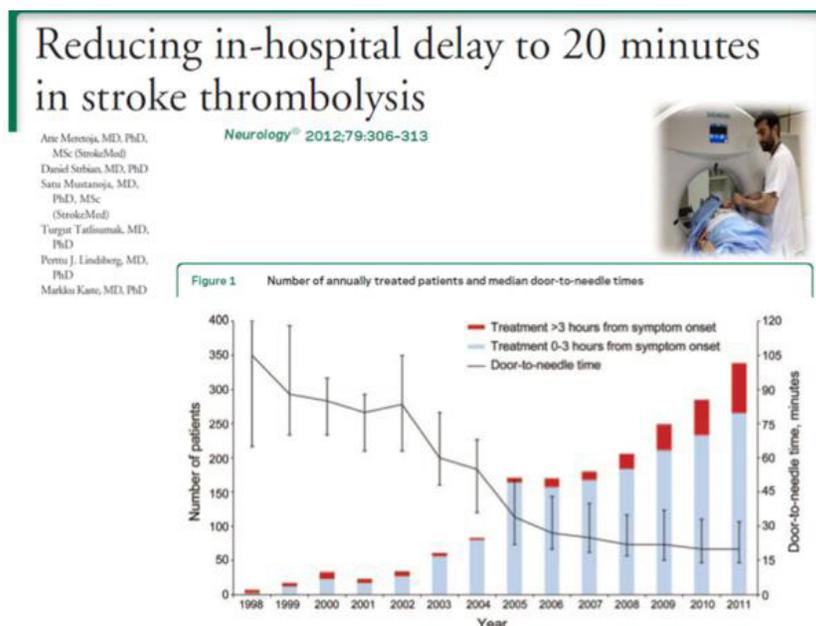
Saver Time Is Brain

**Estimated Pace of Neural Circuitry Loss in Typical Large Vessel, Supratentorial Acute Ischemic Stroke**

	Neurons Lost	Synapses Lost	Myelinated Fibers Lost	Accelerated Aging
Per Stroke	1.2 billion	8.3 trillion	7140 km/4470 miles	36 y
Per Hour	120 million	830 billion	714 km/447 miles	3.6 y
Per Minute	1.9 million	14 billion	12 km/7.5 miles	3.1 wk
Per Second	32 000	230 million	200 meters/218 yards	8.7 h

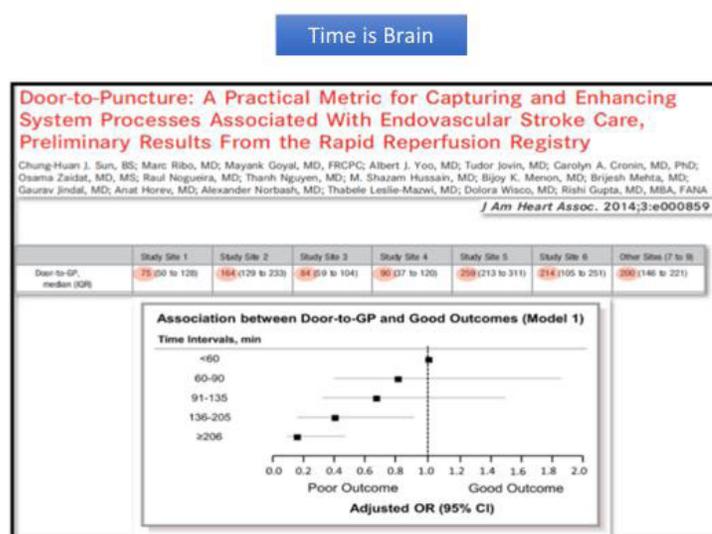
For every 30 minutes lost in stroke onset-to-reperfusion time, the chances of achieving a favourable outcome for the acute stroke patient diminish by 10%,<sup>16</sup> and the increasing negative impact of time to treatment on patients' outcomes has been unequivocally illustrated in collaborative meta-analysis.<sup>17</sup> The motivation of stroke neurologists to reduce timings during in-hospital work flows can be illustrated by the AHA/ASA 2011 recommendations: that comprehensive stroke centres should aim for a goal of two hours for median time from arrival to start of treatment;<sup>18</sup>

yet, within a year, a target of 20 minutes was considered realistic.<sup>19</sup> Door-to-needle (DTN) times have reduced considerably in many stroke centres in recent years. For example, data from the Helsinki Stroke Thrombolysis Registry confirm that a series of interventions to reduce treatment delays, implemented over the years 1998 to 2011, resulted in consistent reductions in annual median DTN times over that period. This is illustrated in the figure below.

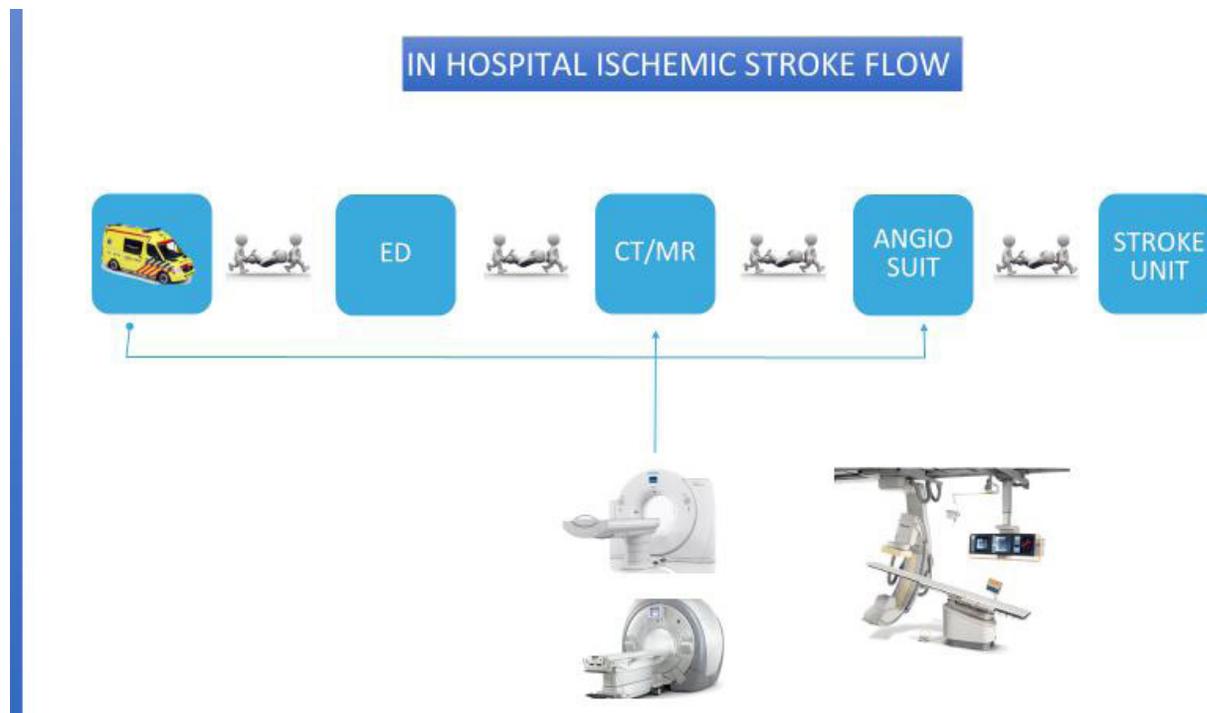


The Helsinki data show that with multiple concurrent time saving strategies in place, it is possible to cut the median in-hospital delay to 20 minutes.<sup>19</sup> Dr Tomasello stressed the relationship between door-to-groin (DTG) puncture time and the likelihood of a good outcome for the patient. The probability of a good

outcome diminishes with increasing time to groin puncture as illustrated in the following figure.<sup>20</sup> Consequently, door to puncture presents a clinically relevant time frame by which system processes can be targeted to streamline the delivery of intra-arterial care in individual hospitals and nationally.



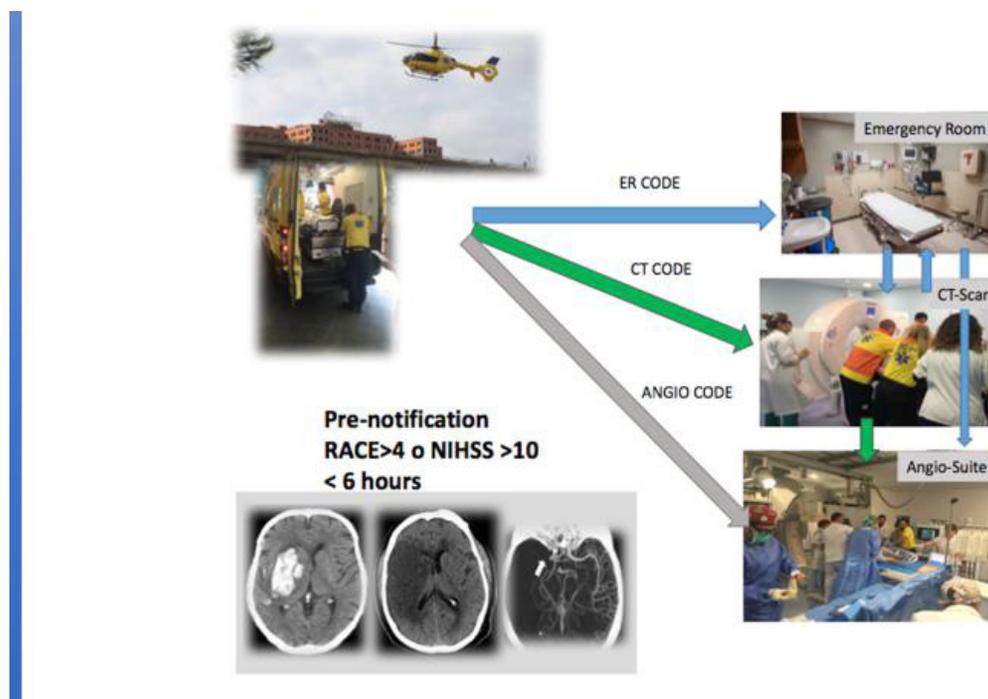
A typical in-hospital acute ischemic stroke work flow is shown in the following figure. Several patient transfers are involved. Dr Tomasello confirmed the 2015 mean DTG time at the Hospital Universitari Vall d'Hebrón was 92 minutes.



**In-hospital flow optimization**

Dr Tomasello pointed out that, in reality, there are several different in-hospital ischemic stroke work flows. The clinical situation is different for individual patients. Dealing with a patient referred from a primary stroke centre is different from a patient transferred directly to the hospital. At Vall d'Hebrón three key work flows or stroke

codes are utilized: direct transfer to emergency room (DTER), direct transfer to the CT room (DTCT), and direct transfer to the angio-suite (DTAS).



Dr Tomasello explained that in 2010 almost all acute stroke patients at Vall d’Hebrón were hospitalized with a DTER stroke code; however, by 2016, the majority of patients were hospitalized with more time-efficient DTCT or DTAS codes. Improved pre-notification communication from EMS, with more specific diagnostic information on the in-coming patient’s status, has allowed the hospitalization stroke code to be decided in advance of the patient’s arrival, and has been increasingly responsible for the switch from DTER to DTCT and DTAS stroke codes.

In attempting to optimize in-hospital work flow, Dr Tomasello suggested an analysis based on deconstruction of the linear process involved, separating each individual step, the actions assigned at each step, and the professional(s) involved with each step.

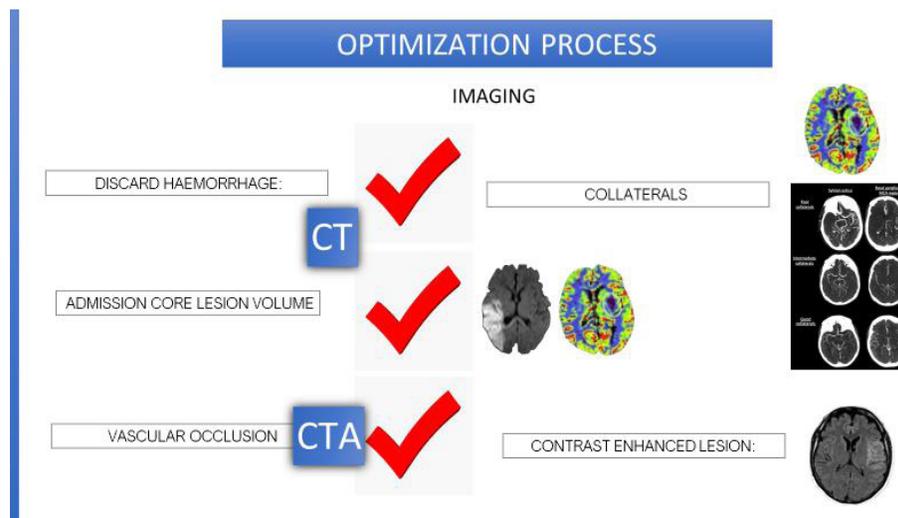
Other factors to take into consideration are whether it is decided to treat the patient aggressively and the recommendations provided in recent guidelines for the early management of patients with acute ischaemic stroke.<sup>21</sup>



**Neuroimaging**

All patients suspected of having a stroke should receive neuroimaging; however, Dr Tomasello raised the question: what neuroimaging should be mandatory? He noted that additional imaging beyond CT and CTA or MRI and magnetic resonance angiography (MRA), such as perfusion studies for selecting patients for mechanical thrombectomy within a 6-hour time window, is not recommended in

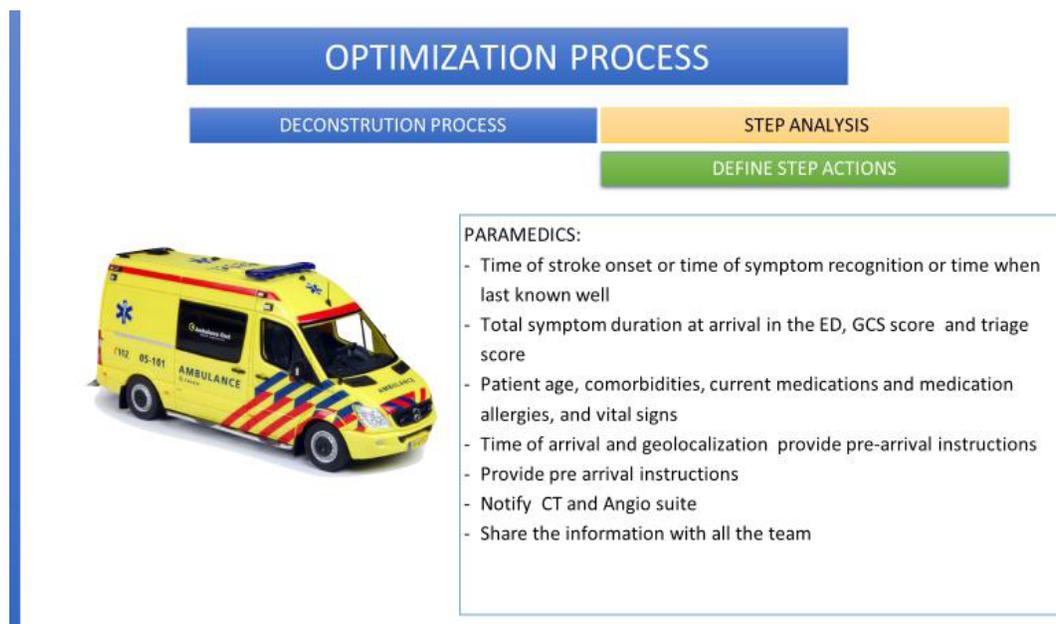
recent AHA/ASA guidelines.<sup>21</sup> Dr Tomasello felt a CT scan is mandatory to rule out haemorrhage and to quantify admission core lesion volume, and CT angiography is mandatory to identify vascular occlusion and will help with assessment of collaterals. However, specific neuroimaging for collaterals and other contrast enhanced lesions are probably not required.



At Vall d’Hebrón for patients arriving within a 6-hour window since their symptom onset, a CT or angio-CT scan is performed; sometimes CT perfusion is carried out, but not as a mandatory procedure. For patients presenting later, from 6-8 hours up to 24 hours from symptom onset, Dr Tomasello stressed CT perfusion imaging (RAPID software, iSchema View) is mandatory, with the stroke team following the DAWN study<sup>22</sup> protocol.

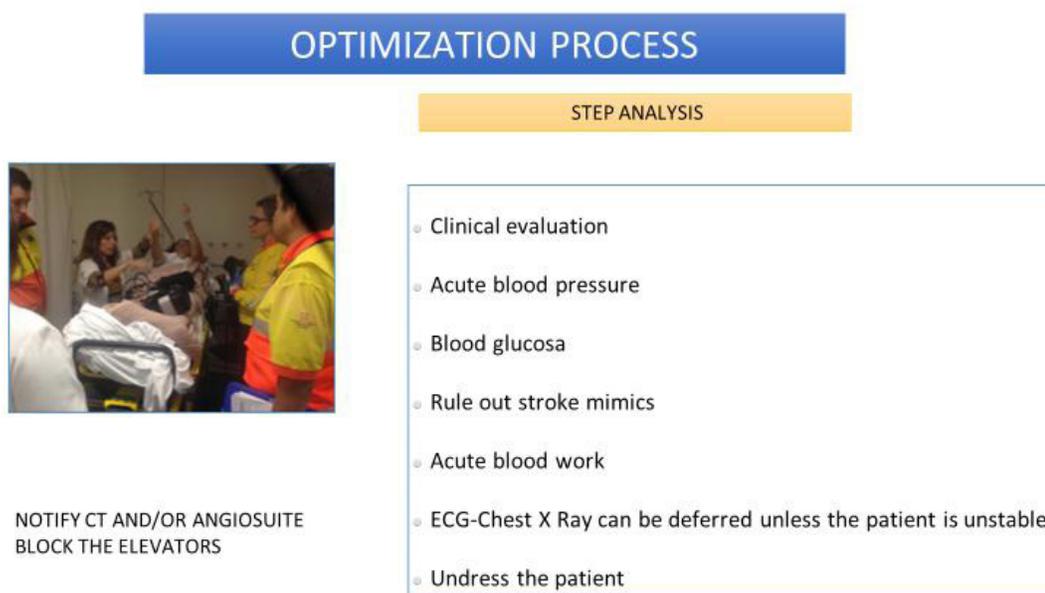
with a detailed step-by-step analysis that identifies the individual actions that have to be performed, and the individuals that perform them. During this process it is important to identify any unnecessary activities that can be avoided, and any activities that can be delayed so priorities can be established. For example, in the pre-hospital phase, the following steps and key information has to be recorded and coordinated by EMS and forwarded to the receiving stroke team, so the most efficient in-hospital work flow can be prepared in advance of the patient’s arrival.

To recap, Dr Tomasello explained the work flow optimization process is based on a deconstruction process,



ED = Emergency department; GCS = Glasgow Coma Scale

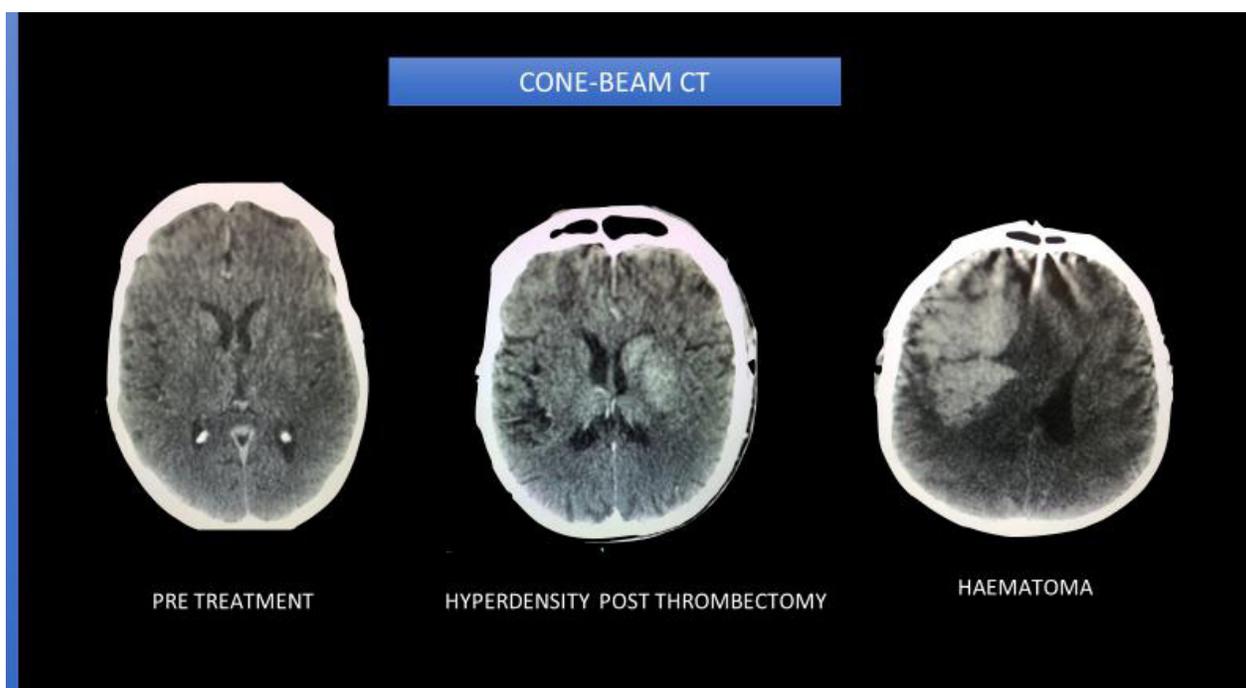
Similarly, once the patient has been hospitalized the following steps and activities and checks have to be coordinated rapidly and efficiently.



As an example of optimization of work flow steps to reduce procedural times, Dr Tomasello referred to a pilot study conducted by Aghaebrahim and colleagues.<sup>23</sup> In this investigation, by introducing initiatives such as: continuous feedback, improving communication between the emergency department and the stroke intervention team, prenotifications from EMS, minimizing diagnostic testing, direct transport to the CT scanner, and direct transport from the CT scanner to the angiography suite, the median door-to-puncture time was reduced from 105 to 67 minutes. This study shows relatively simple workflow improvements to streamline in-hospital triage and perform critical workup at the receiving hospital can result in highly significant reductions in door-to-puncture time.

The STEPS-T program (**S**troke **T**riage **E**ducation, **P**rocedure **S**tandardization, and **T**echnology) consists of stroke triage education and a standardized workflow; it was developed to manage the acute stroke patient as efficiently as possible on arrival to the hospital. STEPS-T relies on the team dividing up responsibilities and tasks and running preparation and activities in parallel. In a recent investigation,<sup>24</sup> implementation of STEPS-T improved time-

to-treat in patients undergoing mechanical thrombectomy for AIS. Over a 5-year period, significant reductions in median intervention time (from 121 to 52 minutes), and recanalization times (from 83 to 36 minutes), were achieved. Additionally, across the study period, patients' modified Rankin Score (mRS) 0-2 increased from 36-59%. At Vall d'Hebrón, Dr Ribó and colleagues have compared the impact of their three principal workflow protocols i.e. direct transfer to emergency room (DTER), direct transfer to the CT room (DTCT), and direct transfer to the angio-suite (DTAS) in 201 patients who were scheduled for endovascular treatment (EVT) over a 12-month period.<sup>25</sup> Those patients transferred directly to the angio-suite had NIHSS scores of <9, a time of onset of symptoms of <4.5 hours, and underwent cone-beam CT. Dr Tomasello reported that cone-beam CT produces good results in his hospital and provides adequate imaging for evaluating acute stroke patients received within the 4.5 -hour time window. The example scans below show pre-treatment status, hyperdensity evident post-thrombectomy, and haematoma.



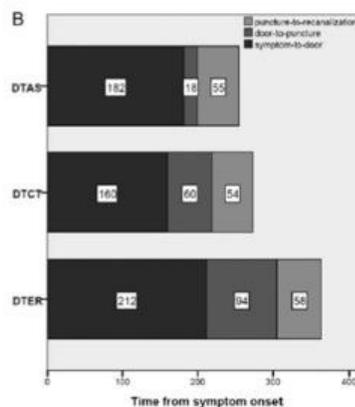
Of the study's 40 DTAS patients, 10 (25%) did not receive EVT due to evidence of intracranial haemorrhage (n = 3), or they did show an occlusion on angiography (n = 7); these patients were not included in the comparative analyses. Mean door-to puncture (D2P) time was significantly

shorter in DTAS patients (17 minutes), compared with DTCT (60 minutes) and DTER (90 minutes). These results are illustrated in the following figure, with the mean D2P times shown in the mid-grey shading.

## DIRECT THROMBECTOMY

Ischemic stroke  
ORIGINAL RESEARCH *J NeuroIntervent Surg* 2017

Direct transfer to angiosuite to reduce door-to-puncture time in thrombectomy for acute stroke



Notably, although there were no significant differences in NIHSS scores at 24 hours between the three workflow protocols, the rate of dramatic clinical improvement, defined as a drop of 10 NIHSS points over 24 hours, was significantly higher in DTAS patients (48.6%), compared with DTER (24.1%) and DTCT (27.4%) patients. These analyses support the direct transfer and triage of acute

ischaemic stroke patients in the angio-suite as feasible; it appears to be safe and achieves significant reduction in hospital work flow timings.

## OTHER THINGS YOU SHOULD CONSIDER



..... about

- CREATE THE OPTIMIZATION PROCESS WITH CONSENSUS
- CONTINUE TO WORK WITHIN THE PROCESS AND WITH YOUR PEOPLE
- REDUCE THE STEPS THROUGH USE OF TOOL-BASED AUTOMATION
- USE INFORMATICS TOOLS
- SHARE THE INFORMATION WITH YOUR TEAM
- USE TECHNOLOGY
- FEEDBACK TO YOUR TEAM
- CONSIDER SETTING UP STROKE SIMULATIONS ESPECIALLY WHEN YOU START

## QUESTIONS AND ANSWERS

Professor Fiehler consolidated questions received from the webinar audience and relayed them to Dr Ribó and Dr Tomasello for response.

**Jens Fiehler:** *How many endovascular stroke specialists do you think need to be available in the stroke centre?*

**Marc Ribó:** In our setting we cover the department with three specialists. This is feasible; however, ideally, we would like to have four. Three would be the minimum to cover a hospital like ours.

**Alejandro Tomasello:** I agree. For a hospital which provides endovascular treatment for over 200 acute ischaemic stroke patients a year, you need four stroke physicians. Remember, we also treat haemorrhagic stroke and paediatric patients as well.

**Jens Fiehler:** *What is your assumption of the number of thrombectomies required per 100,000 inhabitants? One webinar participant suggests 10-15 per 100,000. Does this apply in the light of your Catalonia experience?*

**Marc Ribó:** In the best areas of Catalonia we are at around 10 per 100,000, but available published data indicate we should really be aiming to achieve between 15 and 20, especially since we have widened the time window for endovascular treatment beyond six hours and up to 24 hours post-onset.

**Jens Fiehler:** *What is your expectation of the rate of large vessel occlusion in ischaemic stroke?*

**Marc Ribó:** In our experience the rate of stroke code activations that have large vessel occlusion is in the region of 35-50%.

**Jens Fiehler:** *With respect to the RACECAT study, how far away is the most remote hospital in your trial?*

**Marc Ribó:** In some cases, we may have transfers taking almost three hours to get the patient to a comprehensive stroke centre, during which time there will be no direct physician supervision and limited or no treatment for the patient. In the RACECAT study we are hoping to identify if there is a time point in the direct transfer to the comprehensive centre, beyond which, there is no benefit to be gained over transfer to the nearest primary stroke centre.

**Jens Fiehler:** *Do you think the RACECAT study may provide answers and solutions for patient transfer options that are relevant for Catalonia, but necessarily for the rest of the world?*

**Marc Ribó:** We hope the RACECAT study will provide information and pointers that can be applied to patient transfer decisions in other countries. I am convinced there are distinctive differences and peculiarities between different regions; however, there will be similarities and parallels and we should concentrate on these.

**Jens Fiehler:** *How do you train new physicians to do thrombectomies? Do you have specific ways to include new colleagues for them to become endovascular treatment specialists?*

**Alejandro Tomasello:** At the moment we are not training new interventionalists, but we know in the future will face this problem very soon. Most likely we will have to develop greater expertise with more neurological radiologists and interventionalists outside the Barcelona area.

**Marc Ribó:** We are currently working at a European level to standardize the capability criteria and relevant credentials for physicians who, on qualification, will be able to offer and perform this endovascular treatment.

**Jens Fiehler:** *We have a question about combined occlusions in the internal carotid artery (ICA) and MCA. What are your experiences here, and if you do ICA stenting, do you do this before or after recanalization i.e. on the way up or down?*

**Marc Ribó:** This is a controversial topic. I can tell you what we are doing, but this might not be a solution for all interventional neurologists. We don't have a definitive answer about whether we should do stenting in the acute setting or not. It probably depends on the ASPECTS score, whether the patient can tolerate dual antiplatelet therapy, and the kind of stent you are going to place. We prefer to avoid acute stenting and perform angioplasty; however, if we sense there is acute re-occlusion following angioplasty we would then use a stent.

**Alejandro Tomasello:** For most patients with these occlusions we cross the occlusion and perform the thrombectomy in the MCA, and then we treat the ICA occlusion. There is one exception: when you have a dissection of the ICA with CT imaging showing a large clot evident in the vessel, under these circumstances, I sometimes prefer to stent first and then go to the thrombectomy to avoid re-occlusion and new embolization in the artery.

**Jens Fiehler:** *After the DAWN and DEFUSE-3 studies, what is your opinion about CT perfusion? You indicated in your presentation that you differentiate between 0-6 and 6-24 hours. What is your current opinion about this?*

**Marc Ribó:** According to the latest AHA/ASA guidelines there is not much point in taking the endovascular treatment decision based on CT perfusion within six hours. We can argue you should not take into account a CT perfusion scan within six hours because we are not really sure of what we are seeing, and this may result in avoiding treatment for some patients that can still benefit. For centres which have the capability, I would suggest CT perfusion beyond six hours is mandatory; however, if there is no opportunity to perform CT perfusion, it should not preclude endovascular treatment for a patient after six hours. If the ASPECTS score is reasonable i.e. >5, I would not deny a patient thrombectomy after six hours.

**Alejandro Tomasello:** I think CT perfusion may be useful in patients within the 0-6 or 0-8-hour windows who have low NIHSS scores and are carotid symptomatic.

**Jens Fiehler:** *In Columbia, the insurance companies need to move patients to other stroke units regardless of their quality and experience. The most important thing is the contracted deals the insurance companies have with the hospitals. In some cases, they send patients long distances. Is this system similar to yours?*

**Marc Ribó:** This is a completely different setting to ours. Our patients are treated in public hospitals which are driven by completely different interests. Here we prioritize time and use of the closest hospital – either primary or comprehensive centres – there are no other interests other than these.

**Jens Fiehler:** *Do you use balloon catheters and in what percentage of cases?*

**Alejandro Tomasello:** In most of our cases at our hospital we have been using the Solumbra aspiration technique; however, in the light of positive reports in the literature, I have recently moved back to the balloon guide catheter, and now I estimate I currently use the BGC in around 50% of cases.

**Marc Ribó:** I am not a balloon guide catheter lover, but I acknowledge the available literature that supports its use. If you do not use the BGC, you definitely need to use a distal access catheter in conjunction with the stent-retriever and guide catheter.

**Jens Fiehler:** *Do you think artificial intelligence and robotic technology will be able to contribute to stroke management - to make endovascular treatments faster?*

**Marc Ribó:** We are facing times where, increasingly, new technologies can help us. For example, I am collaborating with a start-up company which is developing an application that will assess and provide an NIHSS score based on a recording of the patient. This, potentially, has great value in the pre-hospital phase. Soon paramedics may be able to determine if their patient is having a stroke, or not, and include the patient's NIHSS score in pre-notification calls; however, this technology will have to be properly validated before we can embrace it. Original ideas like this will help us for sure.

**Jens Fiehler:** *Is there a specific algorithm to define how a developing region should organize itself, and indicate where a patient should be sent from a specific location after the pre-hospital assessment? What would be your recommendation for a region without interventional stroke care? How would you start?*

**Marc Ribó:** There is no "one size fits all" answer here. You cannot blindly apply the policy and procedures that have worked in one region to a completely different region. The best way forward is to become familiar with different approaches that have been taken and adapt those features and ideas that fit best with the specific challenges faced by the developing region. There are some common points and considerations that are relevant to all regions irrespective of their stroke management capabilities. You should use pre-hospital scales; these are very useful. You should try

to concentrate and consolidate endovascular treatment in one or two centres, to build expertise, volume of patients, and knowledge, rather than attempting very few endovascular interventions in numerous centres. These basic principles are applicable to all regions; however, as far as I am aware, there is no published compendium or review of these stroke managements organizational models that we have discussed.

**Jens Fiehler:** *Finally, when will the results of your RACECAT study be published?*

**Marc Ribó:** We need some results first. The first chance to stop the study will be in October or November 2018 following the first interim analysis; there will be further interim analyses 6-monthly after that.

## REFERENCES

1. Pérez de la Ossa N, Carrera D, Gorchs M, et al. Design and validation of a prehospital stroke scale to predict large arterial occlusion: the rapid arterial occlusion evaluation scale. *Stroke*. 2014 Jan; 45(1): 87-91. doi: 10.1161/STROKEAHA.113.003071
2. Zaidat OO, Yoo AJ, Khatri P, et al. Recommendations on angiographic revascularization grading standards for acute ischemic stroke: A consensus statement. *Stroke*. 2013 Sep; 44(9): 2650-2663. doi:10.1161/STROKEAHA.113.001972
3. Mucha M, Rodriguez-Luma D, Pagola J, et al. Impact of time to treatment on tissue-type plasminogen activator-induced recanalization in acute ischemic stroke. *Stroke* 2014; 45: 2734-2738. doi: 10.1161/STROKEAHA.114.006222
4. Berkhemer OA, Franzen PS, Beemer D, van den Berg LA, Linesman HF, Yoo AJ, et al; MR CLEAN Investigators. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med*. 2015; 372: 11-20. doi: 10.1056/NEJMoa1411587.
5. Goyal M, Demchuk AM, Menon BK, Elsa M, Rempel JL, Thornton J, et al; ESCAPE Trial Investigators. Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Engl J Med*. 2015; 372: 1019-1030. doi: 10.1056/NEJMoa1414905.
6. Campbell BC, Mitchell PJ, Kleinig TJ, Dewey HM, Churilov L, Yassi N, et al; EXTEND-IA Investigators. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med*. 2015; 372: 1009-1018. doi: 10.1056/NEJMoa1414792.
7. Saver JL, Goyal M, Bofo A, Diener HC, Levy EI, Pereira VM, et al; SWIFT PRIME Investigators. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. *N Engl J Med*. 2015; 372: 2285-2295. doi: 10.1056/NEJMoa1415061.
8. Jovin TG, Chamorro A, Cobo E, de Miquel MA, Molina CA, Rovira A, et al; REVASCAT Trial Investigators. Thrombectomy within 8 hours after symptom onset in ischemic stroke. *N Engl J Med*. 2015; 372: 2296-2306. doi: 10.1056/NEJMoa1503780
9. Rai AT, Seldon AE, Boo S, et al. A population-based incidence of acute large vessel occlusions and thrombectomy eligible patients indicates significant potential for growth of endovascular stroke therapy in the USA. *J NeuroIntervent Surg* 2016; 0:1-5. doi:10.1136/neurintsurg-2016-012515
10. Froehler MT, Saver JL, Zaidat OO, et al. Interhospital Transfer Before Thrombectomy Is Associated with Delayed Treatment and Worse Outcome in the STRATIS Registry (Systematic Evaluation of Patients Treated with Neurothrombectomy Devices for Acute Ischemic Stroke). *Circulation* 2017; 136(24): 2311-2321. doi.org/10.1161/CIRCULATIONAHA.117.028920
11. Zaidi SF, Shawver J, Morales AE, et al. Stroke care: data from a county-based bypass protocol for patients with acute stroke. *J NeuroIntervent Surg* 2016; 0:1-5 doi:10.1136/neurintsurg-2016-012476
12. Milne MSW, Holodinsky JK, Hill MD, et al. Drip 'n Ship versus Mothership for endovascular treatment: modelling for the best transportation options for optimal outcomes. *Stroke* 2017; 48: 791-794. doi.org/10.1161/STROKEAHA.116.015321.

13. American Heart Association and American Stroke Association Consensus Algorithm for severity-based stroke triage for EMS, March 2017. Available at: [https://www.scribd.com/document/340862215/Severity-Based-Stroke-Algorithm#from\\_embed](https://www.scribd.com/document/340862215/Severity-Based-Stroke-Algorithm#from_embed) Accessed on 05 April 2018.
14. McTaggart RA, Yaghi S, Cutting SM, et al. Association of a primary stroke center protocol for suspected stroke by large-vessel occlusion with efficiency of care and patient outcomes. *JAMA Neurol* 2017; 74(7): 793-800. doi: 10.1001/jamaneurol.2017.0477
15. Saver JL. Time is brain – quantified. *Stroke* 2006; 37: 263-266. doi: 10.1161/01.STR.0000196957.55928.ab
16. Mazighi M, Chaudhry SA, Ribó M, et al. impact of onset-to-reperfusion time on stroke mortality. *Circulation* 2013; 127: 1980-1985.
17. Saver JL, Goyal M, van der Lugt A, et al. Time to treatment with endovascular thrombectomy and outcomes from ischemic stroke: a meta-analysis. *JAMA* 2016; 316(12): 1279-1288. doi: 10.1001/JAMA.2016.13647
19. Meretoja A, Subian D, Mustanoja S, et al. Reducing in-hospital delay to 20 minutes in stroke thrombolysis. *Neurology* 2012; 79: 306-313. doi: 10.1212/WNL.0b013e31825d6011.
20. Sun CH, Ribó M, Goyal M, et al. Door-to-puncture: a practical metric for capturing and enhancing system processes associated with endovascular stroke care, preliminary results from the rapid reperfusion registry. *J Am Heart Assoc.* 2014; 3(2): e000859. doi:10.1161/JAHA.114.000859
21. Powers WJ, Rabinstein AA, Ackerson T, et al. 2018 Guidelines for the early management of patients with acute ischemic stroke a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2018; 49: e46– e110. doi: 10.1161/STR.0000000000000158
22. Nogueira RG, Jadhav AP, Haussen DC, et al. Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct. *N Engl J Med* 2018; 378:11-21. doi: 10.1056/NEJMoa1706442
23. Aghaebrahim A, Streib C, Rangaraju S, et al. Streamlining door to recanalization processes in endovascular stroke therapy. *J Neurointerv Surg.* 2017 Apr;9(4):340-345. doi: 10.1136/neurintsurg-2016-012324.
24. Hassan AE Sanchez C, Johnson AN. Endovascular treatment outcomes using the Stroke Triage Education, Procedure Standardization, and Technology (STEPS-T) program. *Interv Neuroradiol.* 2018 Feb;24(1):51-56. doi: 10.1177/1591019917740100
25. Ribó M, Boned S, Rubiera M. Direct transfer to angiosuite to reduce door-to-puncture time in thrombectomy for acute stroke *Journal of NeuroInterventional Surgery*, 2018;10(3): 221-224. doi.org/10.1136/neurintsurg-2017-013038