Newer mechanical devices have resulted in faster and better recanalization in patients with acute ischemic stroke.1-5 This improvement is reflected in better clinical outcome in studies such as Solitaire With the Intention for Thrombectomy (SWIFT), Thrombectomy Revascularization of Large Vessel Occlusions in Acute Ischemic Stroke (TREVO)-2, and Solitaire FR Thrombectomy for Acute Revascularization (STAR).6-9 This enthusiasm for newer mechanical devices is tempered by results of Interventional Management of Stroke (IMS) 3, Synthesis Expansion: A Randomized Controlled Trial on Intra-Arterial Versus Intravenous Thrombolysis in Acute Ischemic Stroke (SYNTHESIS), and Mechanical Retrieval and Recanalization of Stroke Clots Using Embolectomy (MR Rescue) that demonstrate no added advantage of endovascular therapy compared with intravenous tissue-type plasminogen activator (tPA).10-12 Of the many reasons discussed about the inability of these latter trials to show any additional benefit in the endovascular arm, prolonged time to revascularization stands out.8,13,14 Time is of critical importance in the management of acute ischemic stroke.15-17 Time saved at every stage, including reaching the hospital, initial patient evaluation, transfer to imaging, the imaging time, imaging postprocessing and interpretation, and finally initiation of treatment is critical.
and achieving revascularization, has the potential to improve clinical outcome.\textsuperscript{5,18–22} Despite the importance of reducing time to treatment in improving outcome, inefficiencies continue to exist.\textsuperscript{22–24} These inefficiencies could be because of patient, hospital, and health system characteristics and varying physician practices. By recognizing reasons for these inefficiencies, we can formulate strategies to reduce them.\textsuperscript{19}

The STAR study was an international, prospective, multicenter, single-arm study using stent retrievers and conducted in dedicated high-volume stroke centers with extensive experience on stroke interventions, per-procedural management, and stroke recovery.\textsuperscript{9} Using data from this study, we analyze patient, hospital, health system, and all other characteristics that are associated with increase in each interval time, focusing our attention on workflow from arrival in hospital to final digital subtraction angiography (DSA) run or revascularization. Finally, we assess the effect of these various characteristics and interval times on final clinical outcome.

**Methods**

A total of 202 patients were enrolled in the STAR study across 14 comprehensive stroke centers in Europe, Canada, and Australia. Patients were eligible if they presented within 8 hours after onset of an acute ischemic stroke and had a documented proximal intracranial anterior circulation arterial occlusion. Other inclusion criteria were age (>18 and <85 years), National Institutes of Health Stroke Scale score of 8 to 30, and a baseline-modified Rankin score <2. Study methodology is previously published.\textsuperscript{9} The following time intervals were measured: stroke onset to hospital arrival, hospital arrival to baseline imaging, baseline imaging to groin puncture, groin puncture to first stent deployment, and groin puncture to final DSA run (or TICI 2b/3 revascularization) using Student $t$-test for continuous data, Wilcoxon rank test for nonparametric data, and Fischer’s test for categorical data. Multivariable linear regression was then used to assess variables associated with increase in each of the prespecified interval times. Only those variables considered clinically relevant and statistically significant ($P \leq 0.05$) in univariable analyses were included in these models. We also did similar analysis on the composite time interval stroke onset to final DSA run (or TICI 2b/3 revascularization). Finally, we built a multivariable logistic regression model assessing the effect of time from stroke onset to final DSA (or TICI 2b/3) on primary clinical outcome (modified Rankin score, 0–2 at 90 days). In all models, we report main effects after adjustment for other significant variables. Statistical analysis was performed in SAS version 9.3 (SAS Institute, Cary, NC).

**Results**

Median age was 72 years, 60\% were female patients, and the median National Institutes of Health Stroke Scale score was 17. Other baseline demographics are in the published article.\textsuperscript{9} CT±computed tomography angiography at baseline was used in 81 patients, CT perfusion in 67, and MRI in 51 patients. Distribution of interval times is illustrated in Figure 1. Half of patients achieved a hospital arrival to baseline imaging time of 24 minutes, baseline imaging to groin puncture time of 86 minutes, and groin puncture to final DSA (or TICI 2b/3) time of 34 minutes. Successful revascularization was achieved in 79.2\% of patients and good clinical outcome in 57.9\%.
Variables Affecting Interval Times
Using multivariable linear regression, we found that hospital arrival to baseline imaging time was on average 11 minutes shorter for women than men ($P=0.013$). Time from baseline imaging to groin puncture was on average 32 minutes more in patients administered intravenous tPA and 54 minutes less in patients taking warfarin. In multivariable analysis, time from baseline imaging to groin puncture was on average 18 minutes less when using CT-based imaging versus MRI. Time from groin puncture to first stent deployment was on average 25 minutes longer for patients with extracranial carotid disease. Other variables associated with prolonged groin puncture to first stent deployment time included male sex and increase in prestroke modified Rankin score. Time from groin puncture to final DSA run (or TICI 2b/3) was on average 13 minutes longer for patients administered GA. On-hours versus off-hours presentation and weekday versus weekend presentation did not influence any interval time. Transfer in to the IA facility from a primary facility (n=29) increased the time from stroke symptom onset to final DSA run (or TICI 2b/3) compared with direct transfer (n=157) to IA facility (median time, 332 versus 276 minutes; $P=0.02$). In multivariable linear regression modeling, these variables did not affect any interval time. Finally, the composite time from stroke onset to final DSA run (or TICI 2b/3) was on average 13 minutes longer in patients who were administered GA. On-hours versus off-hours presentation and weekday versus weekend presentation did not influence any interval time.

Effect of Time on Clinical Outcome
Each 1-hour increase in stroke onset to final DSA (or TICI 2b/3) time decreased the odds of good clinical outcome by 38% even after adjusting for reperfusion status, age, baseline National Institutes of Health Stroke Scale, noncontrast computer tomography Alberta Stroke Program Early CT score, and other relevant baseline characteristics (Table 2; Figure 2).

Discussion
Data from the STAR study are a reflection of the recent experience (after September 2010) of dedicated high-volume comprehensive stroke centers (across 3 different continents) at IA therapy using stentriever. We have identified several patient, hospital, and health system characteristics associated with delay in workflow/interval times. Among these, intravenous tPA administration, the modality of imaging at baseline (CT versus magnetic resonance), and difficulty in endovascular access could represent opportunities for improvement. We are also able to show that shorter time from stroke onset to revascularization has a significant effect in improving final clinical outcome even in this era of stentriever.

A median door to needle time of <60 minutes is now considered an established metric for which stroke centers aim. Similar metrics have been proposed recently for IA therapy but have not gained wide acceptance. Based on a widely accepted metric used in cardiology (door to balloon time <90 minutes), the Society for Vascular and Interventional Neurology proposed a door to groin puncture time <90 minutes. Other metrics proposed include baseline imaging to groin puncture (picture to puncture) time <90 minutes and a door to treatment time <120 minutes. Our results show that baseline imaging to groin puncture time

| Table 1. Final Multivariable Linear Regression Models Reporting Characteristics Associated With Delay in Each Prespecified Interval Time |
|-------------------------------------------------|-----------------|-----------------|-----------------|
| Interval Times                                  | Significant Variable | Parameter Estimate (Multivariable) | SE  | $P$ Value |
| Hospital arrival to baseline imaging            | Female sex       | −10.75           | 4.25           | 0.013       |
| Time from stroke onset to hospital arrival (in hours) | −2.44            | 1.22             | 0.047          |
| Baseline imaging to groin puncture              | Warfarin use     | −53.68           | 16.76          | 0.002       |
|                                                   | Intravenous tissue-type plasminogen activator use | 31.88            | 8.73           | <0.001  |
|                                                   | CT±CTP (vs MRI)  | −18.06           | 8.86           | 0.043       |
| Groin puncture to first stent deployment        | Female sex       | −4.92            | 2.25           | 0.031       |
|                                                   | Extracranial carotid disease | 24.53         | 9.99           | 0.015     |
|                                                   | Prestroke mRS    | 3.37             | 1.54           | 0.031       |
| Groin puncture to final DSA (or TICI 2b/3)      | GA use           | 12.54            | 5.68           | 0.029       |

Table 2. Final Multivariable Logistic Regression of Variables Associated With Good Clinical Outcome (Modified Rankin Scale, 0–2 at 90 Days)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time from stroke onset to final digital subtraction angiography run (or TICI 2b/3) in hours</td>
<td>0.62</td>
<td>0.48–0.80</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TICI 2b/3 within 3 passes</td>
<td>3</td>
<td>1.11–8.10</td>
<td>0.03</td>
</tr>
<tr>
<td>Age (every 10 y)</td>
<td>0.49</td>
<td>0.34–0.72</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline NIHSS</td>
<td>0.92</td>
<td>0.84–1.00</td>
<td>0.04</td>
</tr>
<tr>
<td>ASPECTS score on baseline NCCT</td>
<td>1.37</td>
<td>1.05–1.78</td>
<td>0.02</td>
</tr>
</tbody>
</table>

ASPECTS indicates Alberta Stroke Program Early CT score; CI confidence interval; NCCT, noncontrast computer tomography; NIHSS, National Institutes of Health Stroke Scale; and TICI, thrombolysis in cerebral infarction scale.
<90 minutes and a door to treatment time <120 minutes can be achieved (Figure 3). A door to groin puncture time <90 minutes is, however, difficult to achieve except in a minority of patients.

Unique patient, hospital, health system, and clinical practice variables influence each interval time. Hospital arrival to imaging time can be reduced if prior information on patient is available, patient is transferred directly from door to scanner, and a quick, focused clinical assessment is done in parallel. Other variables that may affect this interval time are nonmodifiable and include patient characteristics such as age, stroke severity, and respiratory and hemodynamic status. Interestingly, in the STAR data, hospital arrival to imaging time is slower, on average, by 13 minutes in men compared with women; this is possibly because men are sicker at presentation than women. Nonetheless, we did not find a significant effect of any other patient characteristics on this interval time.

Imaging to groin puncture time could be influenced by numerous variables. These include the availability and speed of access to scanner, type of imaging modality used, efficiency of the picture archival and retrieval system, workflow for intravenous tPA administration, method of activation of neurointerventional team, time of workday (on-hours versus off-hours or weekday versus weekend), use of GA, consent for intervention, and so on. In addition, this interval time can be prolonged if the workflow involves imaging at a primary hospital followed by transfer to the IA facility versus direct transfer to IA facility. In the STAR data, the variable that influenced this metric most was workflow around intravenous tPA administration. In many institutions, workflow around intravenous tPA administration is such that patients are imaged and administered the drug in a primary care facility followed by transfer to the IA facility. Even when directly transported to the IA facility, intravenous tPA is administered in a dedicated unit away from the angiography suite and patients assessed for clinical improvement before being moved to the angiography suite. Activation of the neurointerventional team may also be delayed pending this assessment. Proponents of this workflow highlight patients

Figure 2. Estimated probability of good clinical outcome (modified Rankin score, 0–2 at 90 days) based on time from stroke onset to final digital subtraction angiography (DSA) run (or thrombolysis in cerebral infarction [TICI] 2b/3).

Figure 3. Metrics in the Solitaire FR Thrombectomy for Acute Revascularization (STAR) trial that are a reflection of current practice in high-volume comprehensive stroke centers in comparison with metrics in the Interventional Management of Stroke (IMS) 3 study. DSA indicates digital subtraction angiography; and TICI, thrombolysis in cerebral infarction.
who either have no proximal occlusion or have clinically improved that result in a resource-intensive process such as IA therapy being mobilized and not used. Nonetheless, the number of such false-negatives is small in patients with disabling strokes and proximal occlusions; early recanalization rates with intravenous tPA are also low.31 Moreover, use of CT angiography at baseline can help identify proximal artery occlusions.32 A workflow that offers intravenous tPA administration in parallel to rapid activation of the neurointerventional team and transfer to angiography suite has the potential to reduce time from imaging to groin puncture. Shorter imaging to groin puncture time in patients on warfarin in the STAR study is also probably because they bypass intravenous tPA.

Use of the appropriate imaging modality is also an important workflow issue.21,22 The STAR data suggest that using a CT-based paradigm takes less imaging to groin puncture time compared with a magnetic resonance–based imaging paradigm without any comparable improvement in clinical outcome. Making imaging quickly and easily accessible to the treating physician 24×7 through use of efficient picture archiving and communication system and simple imaging paradigms is also an important element in improving workflow. The STAR data suggest that with improvement in the above-mentioned processes, a median imaging to puncture time of 60 minutes is an achievable metric (Figure 3).

Groin puncture to first stent deployment and final DSA (or TICI 2b/3) are indicators of IA procedural efficiency.20 Patient’s condition (including hemodynamic and respiratory status, state of agitation or calmness), access issues (at the groin and supra-aortic segment including type of arch and large artery tortuosity), experience and efficiency of the interventional team, and type of mechanical device all influence this metric.23,33 In the STAR data, median time from groin puncture to first stent deployment was 23 minutes and to final DSA run (or TICI 2b/3) was 34 minutes. Nonetheless, presence of carotid disease (access issue) and use of GA prolonged puncture to final DSA (or TICI 2b/3) time. CT angiography head and neck at baseline could help the interventionist select beforehand catheters and tools to facilitate access.32 Of note, our results show patients receiving GA had shorter overall time from stroke onset to final reperfusion, although these same patients had prolonged time from groin puncture to final reperfusion. We think this is because some patients were intubated on route to hospital or at emergency room before imaging; in such patients, workflow may have improved significantly after intubation. In other patients who were intubated in the angio-suite to reduce agitation, interval time from groin puncture to final reperfusion may have increased. We do not have data on indication and timing of intubation/GA administration to confirm this. Nonetheless, in our opinion, GA use could be restricted to patients who need it for medical reasons and not used for reducing patient movement during intervention; in the latter case, conscious sedation may be tried.29 Finally, teamwork and familiarity between the interventionist, stroke physician, and nurses are essential to increase efficiency within the groin puncture to final reperfusion metric. With improvement in efficiency, a groin puncture to final DSA (or TICI 2b/3) time of <30 minutes is achievable (Figure 3).

The STAR data show that reducing time from stroke onset to reperfusion improves clinical outcome (Figure 1). Workflow metrics in the IMS 3 trial show prolonged times compared with the STAR study (Figure 3).10 This improvement in workflow in the STAR study reflects in an improved rate of good clinical outcome (modified Rankin score, 0–2 at 90 days) of 57.9% compared with 41% in the endovascular arm of IMS 3 (with evident proximal occlusion on CT angiography).4,10,30 The use of stentriever and an effort toward improvement in workflow metrics across board are anticipated to be key outcome determinants in future trials of endovascular stroke therapy.

Our study has limitations. The STAR registry is a single-arm study. The lack of a randomly assigned control arm raises concerns of biases that might have influenced the results. Data on indications for GA, workflow details around intravenous tPA administration, time taken for study consent, and the nature of difficulty in access to target occlusion was not available. The small number of patients who were transferred in from a primary stroke center versus those who were transferred directly to the IA center reflect practice of the enrolling centers, thus limiting our ability to comment on the relative merits of these paradigms. Nonetheless, the STAR data shed light on workflow metrics that can be achieved in dedicated stroke centers. In addition, our results show that there is potential for further improvement in each of these metrics if workflow is designed in a parallel process framework with various intermediate steps from patient arrival to final recanalization happening simultaneously whenever possible. Even in high-volume centers such as those in the STAR study, many patients did not achieve an imaging to groin puncture time <90 minutes. Finally, our results show that an improvement in each metric has a cumulative effect on improving clinical outcome. A focus on these individual metrics has the potential to benefit future endovascular trials in addition to improving efficiency and outcomes in comprehensive stroke centers.

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Dr Davalos is a consultant for Covidien; Dr Chapot is a consultant for Covidien, Microvention, and Balt; Dr Gralla, global PI STAR, is a consultant for Covidien; Dr Pereira, global PI STAR, is a consultant for Covidien; Dr Goyal is a consultant for Covidien; and the other authors report no conflicts.

References


Optimal Workflow and Process-Based Performance Measures for Endovascular Therapy in Acute Ischemic Stroke: Analysis of the Solitaire FR Thrombectomy for Acute Revascularization Study

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