Previous studies have established the efficacy of intravenous rt-PA to reduce overall disability when administered within 3–4.5 hours of an acute ischemic stroke. Although rt-PA is the only FDA-approved medical therapy currently available for acute ischemic stroke, it is surprisingly underutilized. It is estimated that less than 2%–5% of patients receive this treatment in most countries, primarily due to delayed admission and the inherent “automatic” exclusion of several patient populations such as the postoperative patient. Furthermore, rt-PA has limited efficacy in achieving recanalization in proximal vessel occlusions.

The endovascular management of acute ischemic stroke circumvents some of these shortfalls because this therapy has proven effective up to 6 hours after the stroke and has demonstrated improvement in recanalization rates. Currently a Class I B level of evidence indication is the use of intraarterial thrombolysis in selected patients with major stroke of 6-hour duration due to an occlusion of the middle cerebral artery.
Current endovascular therapies include local pharmacological infusions (usually of a fibrinolytic such as rt-PA), ultrasound-augmented fibrinolysis, and mechanical manipulation by guide wire, snare, angioplasty balloon, stent, and dedicated clot retrieval systems such as the Merci or Penumbra device. The greatest risks of these therapies are vessel damage, thrombus migration, and possible delays in treatment due to a patient’s need for a specialized stroke center. In fact, currently a Class I A level of evidence indication is that the availability of intraarterial thrombolysis should generally not preclude the intravenous administration of rt-PA in otherwise eligible patients. In addition, the potential benefit of reperfusion decreases with delayed treatment, and there is a corresponding increase in the risk of symptomatic cerebral hemorrhage. Recent evidence suggests that carefully selected patients, chosen based on perfusion imaging, may receive the maximum benefit from intervention.

Northwestern Memorial Hospital, located in the center of Chicago, is a comprehensive stroke center that treated approximately 60 TIA and 242 ischemic strokes in 2008. The purpose of this study is 2-fold: 1) to assess Northwestern Memorial Hospital’s experience in this field as a formal institutional review and 2) to compare our data with major publications.

Methods

Computerized records were reviewed and analyzed for 39 consecutive patients treated between May 2005 and February 2009. All participants provided written and informed consent for release of their clinical data using an institutional review board–approved, Health Insurance Portability and Accountability Act–compliant protocol. Included cases involved strokes of all large-vessel territories that were treated acutely by endovascular methods. Excluded cases were those having central retinal artery occlusions, cerebral venous thrombosis, intracranial angioplasty, stenting done for subacute to chronic cerebral ischemia, any extracranial procedure that did not also choose to report TIMI scores pertaining to the effect on the occluded vessel. A TIMI score of 0/1 was reserved for stump occlusions of the ICA, M1, or basilar system. For example, an M1 superior branch occlusion would be reported as a TIMI score of 2A should the MCA territory be perfused by less than 50%. Improvement after intraarterial treatment to a TIMI score of 2B would be achieved if the MCA territory perfusion improved to greater than 50%. A TIMI score of 3 was reserved for revascularization that included perfusion to all M1 and M2 cortical vessels.

Using the TIMI 2AB classification system, the posterior circulation was scored in a novel way. For instance, a TIMI score of 2A referred to perfusion to the top of the basilar artery and at least one of the PCA branches, whereas a TIMI score of 2B indicated flow involving the basilar tip and both PCA branches. Recanalization was defined as an improvement in grade from TIMI 0/1 to at least a 2A and a TIMI 2A to at least a 2B. The mRS score was recorded as an estimate after reviewing the electronic records of outpatient follow-up visits or readmission notes.

Unless indicated, administration of antiplatelet and anticoagulant agents was prohibited for 24 hours post-intervention. Medical management and acute poststroke care after the procedure were consistent with American Stroke Association guidelines. A CT scan was obtained 24 hours after the procedure to rule out the presence of ICH. An ICH was classified using definitions of hemorrhagic infarction Types 1 and 2 and parenchymal hematoma Types 1 and 2. Progress notes (clinical notes) were reviewed to determine whether ICH was symptomatic. If the notes did not clearly state the impact of ICH clinically, the ICH was assumed to be symptomatic.

Results

At NMH, a total of 40 endovascular procedures were performed in 39 patients for acute large-vessel ischemic stroke between May 2005 and February 2009. One patient suffered a recurrent stroke requiring endovascular intervention for both instances. Nine patients were lost to follow-up after being discharged from the hospital. Table 1 summarizes patient baseline characteristics. Table 2 includes information about the NIHSS scores, locations of vascular occlusions, revascularization rate, and clinical outcomes. The mean baseline NIHSS score was 16.7 (median 15, range 5–36) (Table 2). The estimated median interval from stroke onset to anesthesia prior to endovascular stroke therapy was 265.5 minutes. Overall, 82.5% of the strokes were confined to the anterior circulation. The majority were M1 and M2 occlusions (47.5%), whereas 25% of patients had ICA or carotid-T occlusions. Only 10% of the occlusions were localized to M2.

Endovascular therapies varied, and in most treatment cases more than one modality was applied. The Merci device was used in 22 (55%) of 40 procedures and the Penumbra device in 9 (22.5%) of 40. Angioplasty was performed by the IMS-II authors from an ad hoc scale (TIMI scores of 0/1, 2AB, and 3). Contrary to previous studies, we chose to report TIMI scores pertaining to the effect on cerebral perfusion as a whole rather than reporting a TIMI score specific to the occluded vessel. A TIMI score of 0/1 was reserved for stump occlusions of the ICA, M1, or basilar system. For example, an M1 superior branch occlusion would be reported as a TIMI score of 2A should the MCA territory be perfused by less than 50%. Improvement after intraarterial treatment to a TIMI score of 2B would be achieved if the MCA territory perfusion improved to greater than 50%. A TIMI score of 3 was reserved for revascularization that included perfusion to all M1 and M2 cortical vessels.
Endovascular stroke therapy

TABLE 1: Summary of baseline characteristics*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Median (yrs)†</th>
<th>Female (%)†</th>
<th>Current Smoker (%)‡</th>
<th>Prior Aspirin/ Plavix (%)‡</th>
<th>Prior AC (%)‡</th>
<th>Median INR‡</th>
<th>Known Ac Fib (%)†</th>
<th>Known DM (%)†</th>
<th>Known HL (%)†</th>
<th>Patient History (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>70</td>
<td>59</td>
<td>15.4</td>
<td>41.0</td>
<td>23.1</td>
<td>1.1</td>
<td>38.5</td>
<td>10.3</td>
<td>38.5</td>
<td>TIA/CVA† 15.4</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cardiac Disease† 17.9</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Renal Disease† 5.1</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Past Malignancy† 15.4</td>
</tr>
</tbody>
</table>

* A Fib = atrial fibrillation; AC = anticoagulation; BP = blood pressure; CVA = cerebrovascular accident; DM = diabetes mellitus; HL = hyperlipidemia; INR = International Normalized Ratio.
† Determined in 40 patients.
‡ Determined in 39 patients.
§ Determined in 30 patients.

in 15 (37.5%) of 40 procedures, and intraarterial rt-PA was administered in 23 procedures (57.5%). In 23 cases (57.5%), multiple recanalization methods were used. Three patients required stents (2 with a Neuroform and 1 with Wingspan stent). Two stents were deployed intracranially, whereas the third was deployed at the carotid bifurcation.

The estimated mRS score was available in all surviving patients, except for 9 lost to follow-up; therefore, analysis was confined to 30 patients (Fig. 1 upper). In this group, the mean age was 64.8 years, and the mean and median NIHSS scores were 17.4 and 15.5, respectively. The follow-up period ranged from 1 to 37 months. Outcome in 11 (36.7%) of 30 patients was reflected by the mRS score 0–2. In 4 patients, lack of information in the outpatient records precluded an accurate rating of the mRS score 0–2. In 4 patients, the mortality rate was 26.7% (8 of 30 patients). Five patients died during the initial stroke while being admitted, and 3 died after discharge from the hospital. Of these patients, 1 died of sepsis 2 months after discharge, another was placed in hospice 6 weeks later, and 1 was placed in hospice 2 years later.

To better compare our results to outcomes in major clinical trials, we performed subgroup analysis to compute 3-month outcomes (Fig. 1 lower). Of the 39 patients, 9 were lost to follow-up and because 6 were followed up for less than 3 months, their data were excluded from the analysis. For this remaining subgroup of 24, the mean age was 63.1 years, while the mean and median NIHSS scores were 18.45 and 17, respectively. Good outcome was achieved in 37.5% of patients (9 of 24), whereas the overall mortality rate was 29.1% (7 of 24 patients).

Hospital discharge locations were available for all 39 patients: 5 (12.8%) went home, 22 (56.4%) went to acute inpatient rehabilitation, 1 (2.6%) to long-term acute care, 1 (2.6%) to an in-network hospital, 5 (12.8%) for subacute nursing care, and 5 (12.8%) died while in the hospital.

At baseline, 70% of patients had a TIMI score of 0 or 1, and the other 30% had a TIMI score of 2A/2B. After the procedure, 60% of patients achieved a TIMI score of 2AB or 3. In cases of proximal stump occlusion, recanalization from a TIMI score of 0/1 to 2AB occurred in 71.4% (20/28) of the patients, and recanalization from a TIMI score of 0/1 to 3 occurred in 7.1% (2/28) of the patients. For this subgroup of patients, the mean and median NIHSS scores on presentation were 18 and 17, respectively.

Patients with successful revascularization tended to have better outcomes than those in whom revascularization was not successful. In this case series analysis, excluding patients with inadequate follow-up, 9 (47.4%) of 19 patients with successful recanalization had good outcome (mRS score ≤ 2), whereas only 2 (16.7%) of 12 patients without successful recanalization had a good outcome. Similarly, the mortality rate was lower in the revascularized group than in its counterpart, at 26.3% and 33.3%, respectively.

The impact of revascularization of proximal stump occlusions was also evaluated for clinical outcome. Similar conclusions prevailed. Among the 71.4% of the cases that were successfully revascularized (20 of 28 patients), an mRS score of ≤ 2 was achieved in 7 (43.7%) of 16 patients, whereas among those in the nonrevascularized group, an mRS of ≤ 2 was only achieved in 1 (14.3%) of 7 patients. Correspondingly, the revascularized groups had a lower mortality rate, 25% (4 of 16 patients), compared with 42.8% (3 of 7 patients) in the nonrevascularized cases. (Note: 4 patients in the revascularized group and 1 patient in the nonrevascularized group were lost to follow-up, respectively [Table 3].)

TABLE 2: Summary of perioperative data*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Median NIHSS Score†</th>
<th>Circulation of the ICH</th>
<th>Segment/Artery of Occlusion</th>
<th>Revascularization Rate†</th>
<th>Index TIMI Score 0/1†</th>
<th>Revascularization Rate in TIMI Score 0/1 Cases‡</th>
<th>mRS Score &lt;2§</th>
<th>Mortality Rate§</th>
<th>SICH by 24 hrs†</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of pts</td>
<td>15</td>
<td>82.5</td>
<td>17.5</td>
<td>47.5</td>
<td>10</td>
<td>25</td>
<td>60</td>
<td>70</td>
<td>71.4</td>
</tr>
</tbody>
</table>

* All values are presented as percentages except NIHSS scores. Abbreviations: pts = patients; SICH = symptomatic ICH.
† Determined in 40 patients.
‡ Determined in 28 patients.
§ Determined in 24 patients.
In 17 patients (42.5%), 24-hour CT scanning revealed ICH; 3 patients (7.5%) were symptomatic (Table 2). Of these 3 patients, 1 developed ICH and SAH after intravenous rt-PA. In this patient, endovascular methods were palliative to decrease clot burden, and subsequently, the patient underwent surgical evacuation of the hematoma and died during the index hospitalization (Fig. 2A). The second patient suffered an intraprocedural perforation, underwent decompressive craniectomy, and was lost to follow-up (Fig. 2B). The third patient suffered a contralateral parenchymal hematoma Type 2 ICH after a skull base carotid stenting procedure was performed for acute stroke. Prior to the emergence of the ICH, postprocedure MR imaging revealed an interval development of a new infarction contralateral to the original stroke. This patient was also lost to follow-up (Fig. 2C).

Overall, 3 (7.5%) of 40 patients had definite procedure-related SAH. One had a concomitant ICH and was discussed in the previous paragraph. The other 2 patients had asymptomatic SAH. An mRS score of 4 was estimated in 1 patient at 2-month follow-up, and an mRS score of 0 was estimated in the other patient at 4-month follow-up.

**Discussion**

In our population overall, 36.7% of the patients had an outcome represented by an mRS score of ≤2 at various follow-up times; 37.5% of the patients had an outcome represented by an mRS score of ≤2 at the 3-month follow-up. These results exceed the outcomes of the Penumbra Phase 2 trial7 (25.0%) and the MERCI Trial,27 but they are similar to those reported in the Multi MERCI trial (36.0%).24 Of note, our mRS ≤2 rate was less favorable than those of PROACT II (40.0%),10 MELT (Middle Cerebral Artery Embolism Local Fibrinolytic Intervention Trial [49.1%]),23 and IMS-II (46.0%),15 all of which disallowed direct mechanical means of thrombolysis.24 Patients with successful revascularization tended to have better outcomes, as measured by an mRS score ≤2, than those without revascularization. Outcome reflected by an mRS score of ≤2 was achieved in 47.4% of the patients with revascularization, which exceeded the outcome in the Penumbra trial (29%),7 and was comparable to rates in the MERCI (46.0%),27 Multi MERCI (49.1%),26 and IMS-II (45.6%)15 trials.

The overall mortality rate in our study was 26.7%, and the 3-month mortality rate was 29.1%. On the one hand, this rate is consistent with that in the PROACT II Trial (25.0%) but is exceeded by the rates reported by MERCI/Multi MERCI (43.5% and 34.0%, respectively) and Penumbra (32.8%)24 investigators. On the other hand, the mortality rate was lower in the IMS-I/IMS-II14,15 (16.0%) and MELT studies (5.3%). The encouraging mortality rate seen in the latter trial may be attributed to a lower baseline NIHSS score of 14. Based on the location of the target vessels, the highest mortality rate in our cas-

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**Table 3: Outcome in patients with and without successful recanalization**

<table>
<thead>
<tr>
<th>Index TIMI Score &amp; Outcome</th>
<th>Percentage of Patients*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>w/ Recanalization</td>
</tr>
<tr>
<td>all TIMI scores</td>
<td></td>
</tr>
<tr>
<td>mRS score ≤2</td>
<td>47.4</td>
</tr>
<tr>
<td>mortality rate</td>
<td>26.3</td>
</tr>
<tr>
<td>w/ TIMI scores 0/1</td>
<td></td>
</tr>
<tr>
<td>mRS score ≤2</td>
<td>43.7</td>
</tr>
<tr>
<td>mortality rate</td>
<td>25.0</td>
</tr>
</tbody>
</table>

* Four patients in the revascularized group and 1 patient in the nonrevascularized group were lost to follow-up.
Endovascular stroke therapy

es series was associated with the MCA (62.5% [5 of 8]) and the basilar artery (37.5% [3 of 8]). A literature review indicated expected mortality rates ranged from 27% to 78% for the MCA and nearly 90% in the basilar artery. Although our data set is limited, it is worth noting that the mortality rate for basilar artery occlusion was less than half (42.8% [3 of 7]) in our case series.

Seventeen patients (42.5%) were found to have ICH on 24-hour postoperative CT scans; 3 patients (7.5%) were symptomatic. This rate has been exceeded by all major endovascular trials to date except for the IMS-I (6.3%). The definition of symptomatic ICH varies across the stroke studies: NINDS (National Institute of Neurological Disorders and Stroke) defined symptomatic ICH as any neurological decline as a result of ICH, whereas the ECASS (European and Australian Cooperative Stroke Study II), ECASS III, PROACT II, ECASS III, MERCI, Multi MERCI, and Penumbra trials defined it as a 4-point increase or higher on the NIHSS. In our study, the impact of ICH on clinical status was determined by review of the clinic notes.

Acute stent procedures were performed in 3 patients. Inclusion of these procedures makes our study unique in that previous studies excluded patients with arterial stenosis because it prevented safe passage of a microcatheter. Stenting was not designed to be performed in MERCI, Multi MERCI, or Penumbra trials. A case example of a supraclinoid dissection treated with stent placement is shown in Fig. 3. Additionally, unlike other intraarterial trials, we included patients with tandem stenosis as long as the extracranial carotid artery was successfully revascularized, which occurred in 10 (25%) of the 40 procedures. Thus, our patients had a mixture of cardioembolic and atherosclerotic occlusions for the treatment of tandem stenosis and an artery-to-artery embolus.

As mentioned earlier, our methods also differ by the definition we used for TIMI revascularization. To our knowledge, all major prior endovascular trials commented on TIMI scores in reference to effect on target vessel treated. In PROACT II, the investigators defined successful recanalization as TIMI Score 2 flow in at least one of the M segments (should M be treated vessel). The same definition was followed in the IMS-II and Penumbra trials. Both MERCI and Multi MERCI trials were unique in this regard as recanalization was defined as TIMI Score 2 flow in both M segments when treating a more proximal target.

Our institution is capable of undertaking diffusion/perfusion imaging; however, quantifiable measurement of mismatch is pending. As noted in the DEFUSE (Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution) study and subsequent analysis, perfusion-weighted imaging can greatly help in selecting the most appropriate patients for intervention. In our series, perfusion-weighted imaging was used in 25 (62.5%) of 40 cases, and we determined that there was a mismatch in 17 (68%) of these 25 patients. Unfortunately, a large proportion of our patients lost to follow-up were in this category, precluding any meaningful analysis.

Fig. 2. Imaging studies in different patients. A: Intracerebral hemorrhage after intravenous rt-PA followed by endovascular mechanical thrombolysis, surgical evacuation, and craniectomy. The patient died 5 days later. B: Perforation of the MCA during intraarterial treatment, followed by surgical evacuation and craniectomy. The patient had a 3-week hospital stay, was discharged to acute rehabilitation, and was thereafter lost to follow-up. C: Contralateral parenchymal hematoma Type 2 ICH after right skull base carotid artery angioplasty in which Wingspan stenting was used. The patient had a 2-week hospital stay, was discharged to a subacute facility, and was thereafter lost to follow-up.

Fig. 3. Right ICA supraclinoid dissection treated with Neuroform stent. At 8-months’ follow-up the patient’s outcome was reflected by an mRS score of 1.
The other 15 patients, who did not undergo perfusion imaging, were selected for endovascular therapy based on several factors and findings including elapsed intravenous treatment window, clinical decision making, noninvasive angiography, flow void interpretation from MR imaging, or dense artery signs on head CT scanning. There was only one use of combined intravenous plasminogen activator dense artery signs on head CT scanning. There was angiography, flow void interpretation from MR imaging, treatment window, clinical decision making, noninvasive several factors and findings including elapsed intravenous of endovascular cases with standardized medical history it is not easily comparable to prior studies, in which our approach resembles most practices at stroke centers, endovascular modalities or devices were applied. While lar therapies varied, and in most treatment cases different endovascular modalities or devices were applied. While our approach resembles most practices at stroke centers, it is not easily comparable to prior studies, in which one treatment modality was used at a time.

Conclusions

Our center is performing endovascular stroke therapy with a safety and efficacy profile that is consistent with other major endovascular studies. To successfully continue with future analysis, we have established a registry of endovascular cases with standardized medical history forms, follow-up scales, and standardized follow-up.

Disclosure

Dr. Bernstein reports a financial relationship with Boehringer Ingelheim.

Author contributions to the study and manuscript preparation include the following. Concept and design: Bendok, Day, Hurley, Alberts, Bernstein, Dabus, Shaibani. Acquisition of data: Bendok, Day, Hurley, Dabus, Shaibani. Analysis and interpretation of data: Bendok, Day, Rahme, Alberts, Bernstein, Dabus, Shaibani. Drafting the article: Bendok, Day, Chmayssani, Rahme. Critically revising the article: Bendok, Chmayssani. Reviewed final version of the manuscript and approved it for submission: all authors. Statistical analysis: Day, Hurley. Study supervision: Bendok, Day, Alberts.

References

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