Determining the Number of Ischemic Strokes Potentially Eligible for Endovascular Thrombectomy

A Population-Based Study

Nicholas H. Chia, MBBS; James M. Leyden, MBBS; Jonathan Newbury, BMBS, PhD; Jim Jannes, MBBS, PhD; Timothy J. Kleinig, MBBS, PhD

Background and Purpose—Endovascular thrombectomy (ET) is standard-of-care for ischemic stroke patients with large vessel occlusion, but estimates of potentially eligible patients from population-based studies have not been published. Such data are urgently needed to rationally plan hyperacute services. Retrospective analysis determined the incidence of ET-eligible ischemic strokes in a comprehensive population-based stroke study (Adelaide, Australia 2009–2010).

Methods—Stroke patients were stratified via a prespecified eligibility algorithm derived from recent ET trials comprising stroke subtype, pathogenesis, severity, premorbid modified Rankin Score, presentation delay, large vessel occlusion, and target mismatch penumbra. Recognizing centers may interpret recent ET trials either loosely or rigidly; 2 eligibility algorithms were applied: restrictive (key criteria modified Rankin Scale score 0–1, presentation delay <3.5 hours, and target mismatch penumbra) and permissive (modified Rankin Scale score 0–3 and presentation delay <5 hours).

Results—In a population of 148 027 people, 318 strokes occurred in the 1-year study period (crude attack rate 215 [192–240] per 100 000 person-years). The number of ischemic strokes eligible by restrictive criteria was 17/258 (7%; 95% confidence intervals 4%–10%) and by permissive criteria, an additional 16 were identified, total 33/258 (13%; 95% confidence intervals 9%–18%). Two of 17 patients (and 6/33 permissive patients) had thrombolysis contraindications. Using the restrictive algorithm, there were 11 (95% confidence intervals 4–18) potential ET cases per 100 000 person-years or 22 (95% confidence intervals 13–31) using the permissive algorithm.

Conclusions—In this cohort, ≈7% of ischemic strokes were potentially eligible for ET (13% with permissive criteria). In similar populations, the permissive criteria predict that ≤22 strokes per 100 000 person-years may be eligible for ET. (Stroke. 2016;47:1377-1380. DOI: 10.1161/STROKEAHA.116.013165.)

Key Words: brain ischemia • endovascular treatment • epidemiology • stroke • thrombectomy

Five pivotal clinical trials recently demonstrated the clinical benefit of endovascular thrombectomy (ET) for acute ischemic stroke in select patients.1–5 Although trial inclusion and exclusion criteria differed, Stentriever therapy in patients with emergent large vessel occlusion has level 1A evidence.

To rationally plan hyperacute services, the proportion of ischemic strokes that may be eligible for ET must be estimated. Previous estimates have not been drawn from population-based studies.6 The objective of this analysis of a recent population-based stroke study was to determine the incidence of ischemic stroke potentially eligible for ET.

Study Data

The Adelaide Stroke Incidence Study (ASCEND) was a population-based stroke study of 148 027 people in the western suburbs of Adelaide, South Australia (July 2009 to July 2010, area 159.5 km2).

Patients were presented to 2 of 3 hyperacute stroke units serving the greater Adelaide region (≈1.2 million). The full methods and primary results have been published previously.7 A high proportion of patients received comprehensive hyperacute neuroimaging. Stroke subtype, pathogenesis, time metrics, and premorbid function data were also collected.

Study Algorithm

Factors influencing eligibility for ET were extracted from medical records and neuroimaging. Two algorithms were prospectively created to discriminate patients potentially eligible for ET—a restrictive algorithm incorporating the most stringent inclusion and exclusion criteria and a permissive algorithm reflecting the greater lenience that may occur in clinical practice (Figure 1 and Table).

Ethics Approval

Ethical approval was obtained from all Adelaide hospitals and from the University of Adelaide (H 155 2008). Informed consent was obtained from patients (or next-of-kin when the patient was unable to consent). No patients (or proxies) declined participation.
Statistics
Incidence rates of eligible emergent large vessel occlusion patients were calculated per 100,000 person-years with confidence intervals (CIs) calculated from the Poisson distribution.

Results
Three hundred and eighteen strokes occurred in the population of 148,027 people in the 1-year study period (crude attack rate 215 per 100,000 person-years). Of 258 definite ischemic strokes, 48 were excluded because of small vessel disease pathogenesis (n=30) or preexisting disability that was unknown (n=6) or severe (modified Rankin Scale score >3; n=12).

Of the remaining 210 nonlacunar ischemic strokes with known modified Rankin Scale score 0 to 3 appropriate for further assessment, 55% were male with median age 78 years (interquartile range 66–85). One hundred and thirty-six patients presented within 24 hours (cumulatively 40%, 52%, 64%, and 83% at 1.5, 3, 6, and 12 hours, respectively). Ninety-one of them received hyperacute vascular imaging and 55 multimodal computed tomography. Median baseline modified Rankin Scale score was 1 (interquartile range 0–1; Figure 2).

Seventeen patients were eligible for ET by the restrictive algorithm (7% of all ischemic strokes; 95% CI 4%–10%). Two of these had thrombolyis contraindications. This equates to 11 ischemic strokes per 100,000 person-years (95% CI 4–18) that would be eligible for ET applying strict selection criteria.

Thirty-three patients (6 with thrombolyis contraindications) were eligible for ET by the permissive algorithm (13% of all ischemic strokes; 95% CI 9%–18%), equating to 22 ischemic strokes per 100,000 person-years (95% CI 13–31).

Twenty-nine patients received thrombolysis and 8, ET (12% and 3% of all ischemic strokes, respectively). Thirteen additional cases potentially eligible for thrombolysis were identified retrospectively (in total, 18% of all ischemic strokes).

Discussion
Application of the algorithms to this stroke study population enabled calculation of patients potentially eligible for ET—around 7% of ischemic strokes or 13% with the less stringent permissive criteria.

A small proportion of patients eligible for ET had thrombolysis contraindications (1% of ischemic strokes by restrictive and 2% by permissive criteria). This small subset may yield the greatest functional benefit (compared with no treatment).

The permissive algorithm may provide a firmer basis for system planning. The ET trials were stricter than real-world clinical practice, in which more marginal interventions are performed (in particular, for patients with preexisting

Table. Definitions

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<thead>
<tr>
<th>Criterion</th>
<th>Definition</th>
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<tr>
<td>Presentation delay</td>
<td>Last known well time to emergency triage</td>
</tr>
<tr>
<td>Nondisabling stroke</td>
<td>No significant functional impairment*</td>
</tr>
<tr>
<td>Large infarct</td>
<td>&gt;1/3 of MCA territory on CT or MRI</td>
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<tr>
<td>Retrievable thrombus</td>
<td>Occlusive thrombus on CT or MR angiography occurring in extra- or intracranial internal carotid artery, M1 MCA, proximal M2 MCA, basilar or dominant vertebral arteries or Clear hyperdense artery sign on noncontrast CT or Baseline NIHSS&gt;12</td>
</tr>
<tr>
<td>Target mismatch penumbra</td>
<td>As per EXTEND-IA criteria† or Assumed positive in permissive group</td>
</tr>
</tbody>
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CT indicates computed tomography; EXTEND-IA, Extending the Time for Thrombolysis in Emergency Neurological Deficits — Intra-Arterial; MCA, middle cerebral artery; MR, magnetic resonance; MRI, magnetic resonance imaging; and NIHSS, National Institutes of Health Stroke Scale.

*Judged by the 2 stroke neurologists.
†Judged by the EXTEND-IA author (Dr Kleinig).
mild–moderate disability). The algorithms were designed to provide proof-of-concept in a population with the highest chance of benefit, rather than to determine the range of patients that may benefit. Given the large treatment effect, it is highly probable that additional populations such as wake-up stroke and patients with milder neurological symptoms will also benefit.

Despite the upfront cost, ET for patients similar to those enrolled in the landmark trials likely reduces long-term healthcare expenditure by reducing disability and length of stay. In this population of 1.2 million, cost-effectiveness is probably maximized by a single 24/7 endovascular center. In small population centers, where rapid drip and ship transfer to larger centers is not feasible, cost-effectiveness may be marginal; however, this study will aid health providers in modeling cost-benefit analyses in varied populations and health systems.

The strength of this study was the application of a prespecified algorithm to a well-characterized and heavily investigated cohort of ischemic stroke patients in a population-based study. The use of 2 algorithms allowed estimation of 2 poles of ET eligibility that may guide system development depending on regional variations in evidence interpretation and reimbursement approaches.

Figure 2. Application of algorithms depicting exclusion criteria. mRS indicates modified Rankin Score.
A potential weakness of this analysis is that eligibility assessment was retrospective. Clinical factors that might have precluded patients from treatment in real time may not have been apparent on review. Additionally, not all patients had hyperacute National Institutes of Health Stroke Scale scores or assessment of baseline disability. Further, data were collected when ET was not the standard-of-care; thus, patients ineligible for thrombolysis (because of contraindication or late presentation) did not receive comprehensive neuroimaging. In such cases, determining emergent large vessel occlusion from the baseline National Institutes of Health Stroke Scale is imperfect; however, the cut off of 12 was conservative (positive predictive value 64%).

It is difficult to anticipate future practice evolution. This study was based on average time metrics (door-to-needle and door-to-reperfusion) assuming futile reperfusion beyond 7 hours, but some may benefit beyond this after selection by multimodal imaging. The pool of eligible patients will inevitably enlarge as stroke-to-door and door-to-reperfusion times improve. New devices and techniques will likely improve speed and quality of reperfusion, further broadening eligibility.

Despite these limitations, this study is timely because population-based data are urgently needed to design services capable of providing broad access to this effective treatment. A modern population-based study in a cohort with continuous access to multimodal imaging in patients with presentation delay <12 hours would be needed for a more precise estimate.

Conclusions
In this cohort, ≈7% of ischemic strokes were potentially eligible for ET or 13% using permissive criteria. In similar stroke populations, the permissive algorithm predicts that 22 patients per 100,000 person-years may be eligible for ET, a number that may expand as practice evolves.

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Disclosures
None.

References
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