Avoiding Thrombolysis In Patients With Mild Stroke

Is It SMART?

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There is increasing evidence that the commonly used intravenous recombinant tissue-type plasminogen activator (IV rtPA) eligibility criteria are unnecessarily restrictive and limit the use of thrombolysis in acute stroke. A number of recent studies have reported that treatment of patients possessing common IV rtPA exclusion criteria does not result in an increased complication rate or in worse outcomes.1–6 The recently described SMART (Simplified Management of Acute Stroke using Revised Treatment) criteria have distilled this viewpoint and resulted in a far less complex algorithm for IV rtPA use. This has resulted in an overall IV thrombolysis rate of nearly 20%, well above the current treatment rate of approximately 1% to 5%, and with outcomes comparable to those treated with more conventional criteria.7

One of the most common exclusions is due to mild or rapidly improving symptoms. Approximately 30% to 40% of patients with acute stroke are excluded from treatment because of symptoms that are “too mild” at the time of initial emergency department evaluation.8,9 However, approximately 25% to 30% of these patients are disabled at the time of discharge raising the question of the reason for, and the appropriateness of, avoiding therapy in this group. A recent discussion of this subject raised numerous areas of concern, including unclear definition of “mild stroke” both in guidelines and in practice and the insensitivity of the National Institutes of Health Stroke Scale to mild stroke symptoms.10

In this issue of Stroke, this question of who is “too mild to treat” is more carefully examined, particularly in relation to National Institutes of Health Stroke Scale subscore and clinical syndrome.11 The investigators analyzed the results of the TOAST (Trial of ORG 10172) study, a well-described clinical syndrome.11 The investigators analyzed the results of the TOAST (Trial of ORG 10172) study, a well-described clinical syndrome.11 The investigators analyzed the results of the TOAST (Trial of ORG 10172) study, a well-described clinical syndrome.11 The investigators analyzed the results of the TOAST (Trial of ORG 10172) study, a well-described clinical syndrome.11 The investigators analyzed the results of the TOAST (Trial of ORG 10172) study, a well-described clinical syndrome.11 The investigators analyzed the results of the TOAST (Trial of ORG 10172) study, a well-described clinical syndrome.11

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The authors report that regardless of the combination of variables used, there was no significant relationship between the initial National Institutes of Health Stroke Scale score or syndrome subtype and patient outcome. These data refute the commonly held belief that specific neurological characteristics may accurately predict good neurological prognosis in patients with mild stroke. Based on these observations, it is more difficult to justify withholding therapy in patients with mild stroke solely based on a clinician’s prediction of patient outcome. The importance of this observation could be substantial given the large proportion of patients with mild stroke presenting soon after symptom onset.

This study reflects a growing consensus challenging the conventional wisdom of excluding patients from thrombolytic therapy based on specific patient subgroups.2,7,10,12,13 Clearly, many of the eligibility criteria used for IV thrombolysis unnecessarily excludes a significant proportion of patients from treatment. In the SMART study, for example, 90% of treated IV rtPA patients possessed at least 1 common IV rtPA exclusion criterion by conventional standards.7 Without these restrictions, a much higher percentage of patients could be eligible for thrombolytic therapy.

Some may question whether a formal clinical trial is necessary to determine definitively whether patients with mild stroke benefit from IV rtPA treatment. In an ideal world, this would certainly be desirable. Realistically, however, given the known difficulty of enrolling sufficient patients with acute stroke in clinical trials, it likely would take a long time to enroll sufficient patients with mild deficit. This is particularly true because the benefit in mild patients could be reduced by the ceiling effect, requiring a substantially larger sample size to detect a statistically significant difference between treated and untreated patients. There may also be ethical reluctance by some clinicians to enroll patients, especially at aggressive stroke centers that already routinely provide IV thrombolysis to mild patients. Similarly, it may be unrealistic to consider formal randomized clinical trials for other IV thrombolysis patient subgroups due to small group size and other analogous practical reasons.13

In any event, until additional data become available, we must decide whether the overall risk/benefit ratio favors treatment based on our current imperfect information. Because few if any studies of specific IV rtPA patient subgroups report OVERALL harm from treatment, it seems reasonable to at least strongly consider patients with mild stroke for IV thrombolytic therapy.

It also appears that current thrombolysis guidelines need revision. This would not only better reflect the current state of scientific knowledge, but also give support to the clinician who may be interested in providing the option of IV
thrombolysis to a specific patient but is reluctant to treat outside current published guidelines. Clarification of the precise meaning of existing thrombolysis exclusion criteria is also needed. The definition of mild symptoms, rapidly improving symptoms as well as other common thrombolysis eligibility criteria in current published guidelines is vague and subject to major misinterpretation. Fortunately, with adequate education, this can probably be remedied. In one study in which intensive education regarding thrombolytic inclusion criteria was instituted, IV rtPA treatment rates increased substantially.14

Conclusions

IV thrombolysis remains the only proven effective acute ischemic stroke treatment. Streamlining of treatment criteria might substantially increase the number of patients qualifying for treatment. It is imperative that this important aspect of IV thrombolytic treatment be addressed and efforts made to clarify the appropriateness of common eligibility criteria for treatment. Only in this way may we more safely and effectively increase the use of this approach and better achieve the ultimate goal of improved patient outcome.

Disclosures

Dr Tong is a consultant and on the speakers bureau for Genentech.

References


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