Advance preferences regarding thrombolysis in patients at risk for stroke: a cross-sectional study

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Summary

Background: It is difficult to obtain informed consent for thrombolysis in stroke patients given the emergency setting, the need for a speedy decision and the effects of neurological deficits.

Aim: To determine the advance preferences for thrombolysis of patients at risk for stroke following discussion of the potential risks and benefits.

Design: Cross-sectional survey.

Methods: Data on benefits and risks of thrombolysis within 3 h and between 3 and 4.5 h after stroke were presented orally, in writing and pictorially to patients attending geriatric and stroke services in a teaching hospital with specified stroke risk factors and preferences for thrombolysis were recorded.

Results: Of the 121 participants, 108 (89.3%; 95% confidence interval [CI] 82.4–93.7) would opt for thrombolysis within the 3-h period and 100 (82.6%; 95% CI 74.9–88.4) within the 3- to 4.5-h period after acute stroke (P = 0.04, McNemar’s test for correlated proportions). Previous stroke or transient ischaemic attack was more common among those who agreed to thrombolysis (54.1% vs. 30.4%, P = 0.04) and those who opted for thrombolysis were significantly more likely to agree to have their preferences recorded and used in the event of a stroke than those who refused thrombolysis (88.8% vs. 30.4%, P = 0.002).

Conclusion: Advance discussion of the potential risks and benefits of thrombolysis in at-risk patients may improve decision making if thrombolysis is being considered and the patient can no longer make a decision.

Introduction

Thrombolysis with recombinant tissue plasminogen activator (rtPA) within a few hours of an ischaemic stroke reduces long-term disability but at the price of an immediate increased risk of symptomatic and sometimes fatal intracranial haemorrhage.¹ The key aspects of obtaining consent for any intervention include disclosure of the risks, benefits and alternatives, lack of duress and mental competence to make a decision. Conveying complex information about treatment is inherently challenging but, in the context of acute stroke and thrombolysis, this difficulty is exacerbated by the frightening nature of the condition, the effects of neurological deficits, in particular aphasia, and by the need for a speedy decision.²,³

It is unsurprising in view of these factors that difficulties in obtaining consent represent one barrier to thrombolysis in suitable stroke patients.⁴⁻⁷ A retrospective American study suggested that 70% of patients given thrombolysis lacked decision-making capacity at the time the decision was made.⁸ If the patient lacks capacity to make the decision, an alternative in some legal jurisdictions is to seek a proxy consent from someone close to the patient. This is not always possible within an
acceptable time frame. Moreover, proxies may prove reluctant to make important decisions, especially when there is a risk of a poor outcome or may make choices inconsistent with those the patient would have made, especially if there has been no prior discussion regarding the issue.9,10

Many patients who get a stroke have known risk factors. Prior discussion of stroke risk and of the potential risks and benefits of thrombolysis and documentation of patient preferences has the potential to improve the quality of decision making if the issue of thrombolysis arises later and the patient can no longer make a contemporaneous decision. We examined the preferences of patients with stroke risk factors regarding thrombolysis in acute stroke.

Methods

Patients

Potential participants were inpatients and outpatients attending the geriatric and stroke services in Galway University Hospital with one or more of the following stroke risk factors: previous stroke or transient ischaemic attack (TIA), atrial fibrillation (irrespective of antithrombotic treatment), history of myocardial infarction, angina or peripheral vascular disease, hypertension (treated or untreated) and diabetes mellitus. We excluded those stroke patients who had had thrombolysis or whose residual disability was such that they would not be candidates for thrombolysis in the event of another stroke. Those who were unable to correctly identify the year and the month were excluded; this quick test has a sensitivity of 95% and specificity of 87% for the detection of cognitive impairment in older hospital patients.11 We also excluded those who were so ill or had such severe communication difficulties that they were unable to participate and those who were unwilling to participate. Informed consent was obtained from all participants, and the local research ethics committee approved the study.

Methods

Demographic information and details of stroke risks were recorded. We explained to participants that they were at risk for stroke and that thrombolysis—intravenous administration of a clot-dissolving medication—was a treatment option if someone had a stroke that was not caused by a bleed and presented early enough, but that it did carry some risks.

Two scenarios were presented: presentation within 3 h and presentation within 3–4.5 h. The interviewer read the information while respondents were encouraged to read along on their own copy. For each scenario, the potential benefits and harms and the medical recommendation were provided (Supplementary data). Risk information was derived using the data from the 2012 American College of Chest Physicians guidelines.1 Data on benefits and risks with and without thrombolysis were presented as absolute percentage risks and as numbers needed to treat and to harm. The same information was presented in pictorial fashion.12

For each scenario, participants were asked to make a decision whether or not to have thrombolysis as they thought they would in real life. ‘Don’t know’ responses were discouraged. A number of follow-up questions were also asked:

1. Would you be happy for the preference you have given to be recorded in your medical notes—rather than just recorded anonymously for this research project—and used to assist decision-making in the event that you did have a stroke and were unable to speak for yourself?

2. If you did have a stroke and couldn’t speak for yourself and you hadn’t made your views known in advance, would you prefer (i) that we go ahead with thrombolysis if we believe it in your best interest or (ii) that we ask a close family member for permission to give treatment and adhere to their agreement or refusal?

After observing the spontaneous comments made by those in the first 30 subjects who had refused thrombolysis, subsequent subjects who refused in either time window were told: ‘We are interested in understating why some people agree and some people don’t agree to treatment in these situations’. They were asked: (1) ‘do you agree with being involved in decision making about a treatment that needs to be given urgently when you have just had a stroke?’ and (ii) ‘do you think that the treatment we described sounds too risky?’ Any spontaneous comments were recorded verbatim.

Analyses

The primary outcome measures were the proportion of respondents opting to have thrombolysis for each scenario. Demographic and clinical features of those agreeing to and those refusing thrombolysis were compared; refusal to choose was classified as a decision not to proceed. We hypothesized that (i) fewer patients would opt for thrombolysis in the 3- to 4.5-h scenario than in the <3-h scenario and (ii) patients with actual experience of a stroke or TIA would be more likely to opt for thrombolysis than those with other risk factors. Based on results from the first 30 subjects, we calculated that a sample size of 120 would be required to show a reduction of 12.5% in the proportion choosing thrombolysis from the <3-h to the 3- to 4.5-h scenario.
**Results**

Of the 189 potential participants, 43 (22.8%) were excluded because of one or more of the following: cognitive impairment (24), severe acute illness (10), severe disability after stroke (10), communication difficulties (5) or previous stroke thrombolysis (3). Of the remaining 146 eligible subjects, 13 (8.9%) refused to participate and 12 (8.2%) withdrew after starting. Of the 12 who withdrew, 4 noted that the study seemed too difficult for them, 3 felt it was stressful to consider having a stroke, 3 withdrew because of time constraints and no reason was given by 2 subjects. There were no significant differences in age, sex or risk factor profile between those who participated and those who refused or withdrew.

Of the 121 participants in the study, 108 (89.3%; 95% confidence interval [CI] 82.4–93.7) would opt for thrombolysis within the 3-h period and 100 (82.6%; 95% CI 74.9–88.4) within the 3- to 4.5-h period after acute stroke \(^{P} = 0.04\), McNemar’s test for correlated proportions). Ninety-eight (81.0%) would have thrombolysis in both scenarios, 10 (8.3%) in the <3-h scenario but not in the 3- to 4.5-h scenario and 11 (9.1%) in neither scenario. Two (1.7%) subjects made the illogical choice of refusing thrombolysis for the <3-h scenario and agreeing to it in the 3- to 4.5-h scenario; these subjects are included because exclusion did not influence the overall results.

Details of those who agreed to and refused thrombolysis (in either scenario) are shown in Table 1. Previous stroke or TIA was significantly more common among those who agreed to thrombolysis; thus, 53 (54.1%) of 60 subjects with previous stroke or TIA opted for thrombolysis in both scenarios compared with 45 (73.8%) of 61 subjects who did not have previous stroke or TIA as a risk factor. Those who opted for thrombolysis were significantly more likely to agree to have their preferences recorded and used in the event of a stroke than those who refused thrombolysis (in either time window). Other demographic and clinical data did not differ between the groups.

Responses regarding their reasons were obtained from 18 subjects who refused thrombolysis. Eight (44.4%) agreed, 9 (50.0%) disagreed and 1 (5.6%) was undecided about being involved in decision making about urgent treatment of acute stroke. Three (16.7%) agreed, 5 disagreed (27.8%) and 10 (55.6%) were unsure whether the treatment described was too risky. Comments recorded included the following:

- ‘I’d want to know what was going on if I could but I wouldn’t want to decide something like this. That’s your job.’

| Age (years) | 71 (42–90) | 73 (61–92) |
| Female sex | 56 (57.1%) | 11 (47.8%) |
| Risk factors | | |
| Previous stroke/TIA | 53 (54.1%) | 7 (30.4%)* |
| Atrial fibrillation | 28 (26.6%) | 8 (34.8%) |
| MI/Angina/PVD | 20 (20.4%) | 5 (21.7%) |
| Hypertension | 62 (63.3%) | 16 (69.6%) |
| Diabetes mellitus | 20 (20.4%) | 7 (30.4%) |
| Willing to have preference recorded | 87 (88.8%) | 7 (30.4%)** |
| Decision maker if no preference recorded | | |
| Doctor decides | 74 (75.5%) | 17 (73.9%) |
| Family decides | 24 (24.5%) | 6 (26.1%) |

*MI = myocardial infarction; PVD = peripheral vascular disease.

Data are expressed as number (percent) or median (range).

\(P = 0.04\), **\(P < 0.002\).

- ‘I don’t think it’s fair to put the responsibility on someone who’s had a stroke’
- ‘The doctor needs to decide if it’s too risky. You have to trust them if you’re very sick’
- ‘It’s bad enough to have a stroke but there’s no point in risking making it worse’

**Discussion**

In this study, 10% of subjects said they would not have thrombolysis within 3 h and 17% within 3–4.5 h of stroke. These are substantially greater refusal rates than those found in actual practice, where our experience is consistent with the finding in most studies that the refusal rate is between 0% and 3%.

Also, it is likely that refusal has become less common in recent years: a Texan study which found that 4.2% of potential recipients refused tPA over a 7.5-year period reported that refusal rates of over 8% in 2004 dropped to about 2% in 2010–2011. This might have resulted from greater public awareness of the potential benefits of thrombolysis in acute stroke or from more confident recommendations for thrombolysis from clinicians in response to the growing evidence base for treatment.

Concerns have been raised regarding the adequacy or validity of consent for thrombolysis. Interviews with patients after recovery suggest that many were not aware of the severity of their problem. A detailed analysis of videotaped telestroke consultations with candidates for thrombolysis found acceptable understanding in only...
three-quarters of patients or families. The average duration of consent discussion in the latter study was <3 min. In contrast, although not formally measured, the information provision in this study took about 15 min. Our impression was that the pictorial presentation of the risk information was particularly helpful in this study. Further evaluation of educational interventions to facilitate speedy and effective communication regarding stroke thrombolysis is required.

It could be argued that the preferences expressed by our patients following presentation of more detailed information than is possible in an emergency might better reflect their genuine views. However, refusal was less common among those with experience of a stroke or TIA, and this suggests that the hypothetical nature of the study for many subjects was an important factor. Furthermore, a striking finding was the greater reluctance of those who did not agree to thrombolysis to have that decision documented and acted upon in comparison to those who agreed to thrombolysis. This finding and the responses to direct questioning suggest that a reluctance to make the decision themselves may have been a more important factor than risk aversion in those who would not agree to thrombolysis, especially since many were willing to allow the doctor to proceed with thrombolysis if no preference had been recorded.

When thrombolysis (or other) decisions arise in actual emergencies, not only is there less time for discussion than in this study but doctors will usually take the lead in recommending—and even urging—thrombolysis if they feel it is the best option for a patient. The comments from the (admittedly small number of) participants who did not agree to thrombolysis to have that decision documented and acted upon in comparison to those who agreed to thrombolysis. This finding and the responses to direct questioning suggest that a reluctance to make the decision themselves may have been a more important factor than risk aversion in those who would not agree to thrombolysis, especially since many were willing to allow the doctor to proceed with thrombolysis if no preference had been recorded.

A strength of this study is that it was conducted in those at risk for, and who were told they were at risk for, stroke. One criticism is that we did not assess subject understanding of the information provided. However, although two subjects provided illogical choices, the overall pattern of lesser enthusiasm for thrombolysis in the later time window clearly reflects an understanding of the relative risks and benefits.

Recording individual patients’ preferences regarding thrombolysis for future reference might be helpful in some cases. However, the relatively low likelihood of stroke in any individual, uncertainty regarding the stability of preferences and the practical difficulties in maintaining a record of preferences and of accessing such a record in an emergency, would be major barriers to this approach. Nevertheless, having a prior discussion about thrombolysis with appropriate patients and encouraging them to think about it and to discuss it with those close to them has the potential to expedite decision making in the event of an acute stroke (and might improve compliance with preventative measures). Also, the finding that a considerable majority of potential stroke victims would agree to thrombolysis and would want that preference respected may also be helpful in discussions with proxy decision makers or in deciding whether or not to proceed if a stroke patient lacks capacity and no alternative decision maker is available.

**Supplementary material**

Supplementary material is available at *QJMEDI* online.

**Conflict of interest:** None declared.

**References**


