Consent for Intravenous Thrombolysis in Acute Stroke

Review and Future Directions

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Intravenous thrombolysis with recombinant tissue plasminogen activator is the standard of care for the treatment of acute ischemic stroke within 3 hours after stroke onset. Randomized clinical studies have demonstrated that intravenous thrombolysis improves functional outcomes but is not lifesaving. Complications of intravenous thrombolysis include severe intracranial hemorrhage that may be lethal. As with any therapy, consent cannot be assumed in the decision to use intravenous thrombolysis. Currently, there is no standardized method to estimate the capacity of patients with acute stroke, and empirical data for this patient population are limited. It is our position that candidates for intravenous thrombolysis should be properly assessed for their capacity to give direct consent before another form of consent is sought. We believe this would best be achieved by the development and standardization of a procedure for capacity assessment specifically for use in patients with acute stroke. To this end, we review the elements of informed consent, the legal standards for competence that a candidate for intravenous thrombolysis must meet to consent to treatment, recommendations for assessing capacity to give direct informed consent with attention to difficulties presented by the acute stroke setting, alternatives to direct consent with their inherent moral difficulties, and potential directions for research and discourse on capacity assessment in acute stroke.

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Stroke is the leading cause of disability and the second leading cause of death in the developed world.1 Ischemic stroke, in particular, occurs in approximately 6 million persons per year worldwide.2 Ischemic stroke accounts for 88% of the 700 000 strokes seen each year in the United States.3 Treatment options for acute ischemic stroke were highly limited until 1995 when intravenous recombinant tissue plasminogen activator (hereinafter referred to as IV rtPA), a thrombolytic agent already in use as a therapy for myocardial infarction and pulmonary embolism, was shown to be an effective therapy for acute ischemic stroke,4 a finding supported by the meta-analysis of multiple large, randomized, clinical trials.5 Intravenous rtPA was approved in the United States in 1996 for use in eligible patients within 3 hours of ischemic stroke onset.6 It was later approved for treatment of acute ischemic stroke in Canada (1999)7 and Australia (2003),8 but because of safety concerns was only approved in the European Union (2001)9 contingent on a program of ongoing surveillance through a multinational registry.10

Intravenous rtPA for treatment of ischemic stroke does not improve mortality but significantly reduces disability at 3 months after stroke.5 All trials have shown an increased risk of intracranial hemorrhage in patients treated with IV rtPA compared with placebo. Thrombolysis-induced intracranial hemorrhage usu-
ally has a devastating outcome. Despite the clear evidence of benefit, the number needed to harm has been estimated at 42 patients.\textsuperscript{11} Because of the complex risk-benefit profile of IV rtPA, there is still some resistance in the United States to the use of IV rtPA in acute ischemic stroke. The American Heart Association,\textsuperscript{12} the National Stroke Association,\textsuperscript{13} and the American Academy of Neurology\textsuperscript{14} strongly endorse intravenous thrombolysis for treatment of acute ischemic stroke, whereas the American Academy of Emergency Medicine has officially stated its position that “objective evidence regarding efficacy, safety, and applicability of t-PA for acute ischemic stroke is insufficient to warrant its classification as standard of care.”\textsuperscript{15(p3)}

The American Stroke Association has recommended that patients and their families be informed of the risks and benefits of therapy as with any other approved medical or surgical intervention.\textsuperscript{16} Others have argued that the weight of the decision to use IV rtPA warrants an explicit consent process\textsuperscript{17-19} and capacity assessment.\textsuperscript{20} Some have even pronounced it an ethical obligation to require a higher standard of informed consent than that employed for routine emergency therapies that are universally accepted as standard of care.\textsuperscript{21} Currently, there is no standardized method of obtaining consent for treatment in patients with acute stroke. It is our position that candidates for intravenous thrombolysis should be properly assessed for their capacity to give direct consent before another form of consent is sought. We believe this would best be achieved by the development and standardization of a procedure for capacity assessment specifically for use in patients with acute stroke. To this end, we review the elements of informed consent; the legal standards for competence that a candidate for IV rtPA must meet to consent to treatment; recommendations for assessing capacity to give direct informed consent, with attention to difficulties presented by the acute stroke setting; alternatives to direct consent, with their inherent moral difficulties; and potential directions for research and discourse on capacity assessment in acute stroke.

**ELEMENTS OF INFORMED CONSENT**

The concept of informed consent stems from a principle of personal autonomy that allows moral self-determination based on 2 elements: voluntary choice and decisional competence.\textsuperscript{22} As it evolved through a series of court cases in the United States from 1955 to 1972,\textsuperscript{23} the legal doctrine of informed consent incorporated a third element, the disclosure of information, without which voluntary choice and competence cannot be properly exercised. It has been asserted, however, that in both legal and medical circles, excessive emphasis on the disclosure requirement has undermined the implementation of informed consent.\textsuperscript{24} In medicine, this is supported by evidence that medical students are not properly trained to evaluate decision-making capacity,\textsuperscript{25} and house officers and attending physicians are not fully conversant with the standards used for such assessment.\textsuperscript{26,27}

Technically, medical professionals lack the legal authority to determine competence; however, their assessment of decision-making capacity serves not only as a guide for many legal determinations but also as the functional equivalent of such determinations in the absence of legal proceedings.\textsuperscript{28,29} It is the physician’s finding of incapacity that causes alternative forms of consent to be sought and a patient’s legal rights to be temporarily suspended without involvement of the court. It is, therefore, critical that physicians learn to apply those standards to an assessment of decisional capacity that are used to arrive at a legal determination of competence.

**LEGAL STANDARDS FOR COMPETENCE**

*Competence* is the ability to perform a task; a person may be competent in some endeavors but not in others.\textsuperscript{20} As a social construct, *competence* is sufficient ability to make choices\textsuperscript{30} such that personal autonomy remains intact. As a legal construct that evolved along with informed consent, *competence* is a state in which an individual’s decision-making ability is adequate to meet the demands of a clearly specified decision-making task. Based on a review of judicial opinions and case law, the legal standards of competence to consent to treatment were first described by Roth et al\textsuperscript{29} in 1977 and have undergone only minor revision since then.\textsuperscript{30} The standards are framed as abilities, as follows: the ability to understand the information provided, the ability to appreciate one’s own situation in light of the information provided, the ability to reason with the information provided, and the ability to express a choice.\textsuperscript{21} It is important to recognize that state law varies. Only the abilities to understand and to express a choice are universally held as legal standards on which to base a determination of competence, although most jurisdictions also embrace the components of appreciation and reasoning.\textsuperscript{21}

**OBSTACLES TO CONSENT IN ACUTE STROKE**

**Emergency Setting**

Some have questioned whether the cornerstones of informed consent, voluntary choice,\textsuperscript{31} and decisional competence\textsuperscript{31-41} are truly preserved in any medical emergency. Even in patients without cognitive impairment, the emergency context may place a high demand on decisional abilities.\textsuperscript{21} It has been proposed that there are “considerable barriers, conscious and unconscious, intellectual and emotional,”\textsuperscript{28(p282)} to assimilating information in acute illness.\textsuperscript{34} Studies of patients with acute myocardial infarction suggest that psychological and physical stress alone may compromise understanding.\textsuperscript{35,36,38,40} Add to this a new neurologic deficit and it becomes even less clear whether patients with acute stroke can give direct informed consent for treatment, particularly when there is limited time in which to make a treatment decision.\textsuperscript{1} In a recent study, even patients with stroke outside the periacute evaluation and decision-making window were unable to give consent in a large percentage of cases.\textsuperscript{32}

**Neurologic Deficits**

Some have argued that the deficits encountered in acute stroke make direct informed consent nearly impos-
However, those deficits most likely to impair capacity do not occur universally: decreased levels of consciousness occur in fewer than half of the patients; aphasia and anosognosia each arise in fewer than two thirds of the patients; memory deficits, though poorly characterized in acute ischemic stroke, are reported in approximately three fourths of the patients; and comorbid prestroke dementia is noted in one sixth of the patients. It must also be recognized that the presence of impaired cognition does not by itself connote impaired capacity. This "most fundamental, important, and uncontroversial maxim [regarding] the modern concept of legal competence is supported by the results of multiple studies of consent in dementia and psychiatric illness and has formed the basis for discussions of consent in patients with other neurologic deficits.

We recommend that in cases in which the evaluation of mental status does not reveal an absolute contraindication to direct consent, which we define as impaired consciousness, substantial Wernicke aphasia, or a striking deficiency in executive function, the physician undertake a full assessment of decisional abilities before a determination of capacity is reached. We expect in less clearcut situations, such as those involving anosognosia or memory or cognitive deficits, that the assessment process will identify those patients for whom alternative means of consent are required. For example, the degree of anosognosia will determine whether a patient can meet the standard of appreciation and the extent of memory or cognitive impairment will determine whether a patient can meet any of the standards of competence. Our goal is the careful and rapid assessment and documentation of capacity in patients with acute stroke so that appropriate forms of consent are sought, protecting patients and physicians alike. Findings of inappropriate consent practices involving IV rtPA and especially involving the overuse of surrogate decision makers support the notion of cautious case-by-case evaluation and the idea that advances in the use of IV rtPA should include improved capacity assessment.

Aphasia

Most discussions of capacity assessment in acute stroke presuppose that the patient does not have aphasia. As it is conceptualized, evaluation by clinical interview or by use of a standardized tool requires prompt feedback from the patient that can be difficult to elicit in the circumstance of acute stroke even from a patient capable of speech. However, patients with Broca aphasia who are otherwise capable of autonomous choice have the same legal right to self-determination as that enjoyed by patients without aphasia. There are techniques for communicating with patients with aphasia to establish treatment choices and it has been suggested that the provision of materials necessary to undertake these techniques is legally mandated by the Americans With Disabilities Act. Whether such techniques can be incorporated into a rapid consent procedure for use of IV rtPA is, at this point, entirely unclear. However, once advances in capacity assessment have been achieved for patients with acute stroke without aphasia, attention might be turned to the possible evaluation of aphasic candidates for treatment.

Time Pressure

Perhaps most limiting to the capacity assessment of patients with acute stroke is the time pressure caused by the narrow therapeutic window of intravenous thrombolysis. Intravenous rtPA for acute ischemic stroke should be used only within 3 hours of stroke onset, and the evidence is clear that better outcomes are obtained with earlier treatment. An involved capacity assessment and consent process in the setting of acute stroke could delay treatment and, therefore, reduce the benefit of intravenous thrombolysis. This is especially true when delays already found along the patient pathway are also considered. A systematic review of the literature identified 9 studies reporting mean delay times from stroke onset to arrival at US or European hospitals and 27 studies worldwide that reported mean delay times from arrival at the hospital to first assessment by a physician; the shortest mean delays reported were 1.9 hours and 0.3 hours, respectively. This suggests that, at best, there is an average delay of 2.2 hours before computed tomography, necessary to make the diagnosis of ischemic stroke, is even undertaken. Although times may be significantly better than average in centers specifically organized to treat stroke, it is, nevertheless, clear that, given the time pressure, many of the strategies used to assess capacity in the cognitively impaired, including multiple repetitions of the disclosure, multiple meetings for the purpose of disclosure, and time-intensive educational strategies cannot be used.

The focus must be to design a brief and straightforward process of capacity assessment that can be systematically incorporated along the patient pathway so that time to treatment is relatively unaffected. At our institution, a 15- to 20-minute interval of unscheduled time between the interpretation of the computed tomographic scan and the return of coagulation study results offers an excellent time frame in which to conduct a streamlined capacity assessment and consent procedure. Similar opportunities may be found along the patient pathway at other institutions.

RECOMMENDATIONS FOR THE CONSENT PROCEDURE

Disclosure

In considering strategies for the efficient disclosure of information in the acute stroke setting, it is useful to draw from previous research on consent. A review of 34 studies of disclosure techniques designed to improve patient understanding found that better understanding was correlated with highly structured oral presentations that made use of brief summaries both of information about to be provided and of information just provided; this is consistent with a previous finding of improved understanding in medically ill elderly persons with the presentation of information in clearly demarcated parts.

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Better understanding was also correlated with the use of visual illustrations and simplified consent forms. The introduction of such accessible materials may be helpful, not only to the patient’s understanding but also to the clinician’s assessment of capacity, inasmuch as it has been suggested that the patient’s referral to consent materials throughout the interview can aid the clinician to properly differentiate deficits of understanding and memory. Two of these techniques, the use of a structured oral presentation and the use of illustrations, were used by researchers to facilitate consent in trials of intravenous thrombolysis in acute myocardial infarction, in which time pressure due to a narrow therapeutic window was also an issue.

Given the emergent circumstances of consent for intravenous thrombolysis, the content of the disclosure may also be adjusted to highlight essential points. As recommended for consent procedures in other emergencies, the disclosure should be especially concise and should include an explanation of the diagnosis and proposed treatment but focus on the risks and potential benefits of treatment and its alternative. Above all, the disclosure should make abundantly clear that intravenous thrombolysis in acute stroke is a risky treatment that may be “autonomy saving” but that is not “lifesaving.” It has even been recommended that hospital-specific outcome statistics be supplied to the consent giver, much like New York State community-specific, severity-adjusted cardiac outcome statistics are made available to the public. These are reasonable proposals and should be seriously considered by medical professionals who offer intravenous thrombolysis for treatment of stroke. Such thorough disclosure of the risks would give greater moral credence to a physician’s conclusion that the provider of an informed consent is truly informed.

**Capacity Assessment**

**Requirements.** For the protection of the patient and the physician, any capacity assessment procedure should include several components. These are: clear statements that the patient is being asked to make a treatment choice and that the patient’s ability to make this choice is being evaluated; inquiries into the patient’s self-assessed ability to make a treatment choice; and into the stability of that choice as the interview progresses, and careful documentation of the encounter. With respect to documentation, a highly structured format has been recommended that addresses the patient’s knowledge of the evaluation, the information disclosed, the identity of the participants and of others present, the physician’s assessment of the patient’s decisional abilities, the length of time devoted to this assessment, the possible consequences of the patient’s choice, and the physician’s explicit opinion about the patient’s capacity to make a treatment decision and the likely outcome of any legal inquiry into the patient’s competence.

**Clinical Interview.** In the assessment of capacity by clinical interview, decisional abilities must be approached systematically. Grisso and Appelbaum have provided a useful plan for addressing the 4 legal standards of competence, as follows. First, to evaluate the ability to express a stable choice, the patient should be asked for a treatment decision immediately after the disclosure and again at the close of the assessment interview. Second, to evaluate the ability to understand, the patient should be asked to paraphrase the information provided in the disclosure; if necessary, Roth et al recommend that brief corrections should be offered and understanding reevaluated. Third, to assess the ability to appreciate the personal relevance of the information provided, the patient should be asked directly about personal beliefs about his or her current health status and what the patient foresees as future day-to-day consequences of accepting or rejecting treatment. Fourth, to assess the ability to reason with the information provided, the patient should be asked to describe the flow of thoughts that led to a final decision. Here, it is important for the physician to consider only whether the patient’s decision logically follows from the starting premises. As some have pointed out, the physician must avoid judging the final decision because perception of the various outcomes (death or disability) is highly personal.

**Alternatives to Direct Informed Consent**

When a patient with stroke lacks the capacity to make an emergent treatment choice, the clinician must use alternative means to define a course of action. In this situation, the clinician must attempt to establish whether the patient has drafted an advance directive such as a living will or durable power of attorney. In the absence of an advance directive, the physician must seek the substituted judgment of a proxy authorized by state law. Should the clinician be unable to identify either an advance directive or a legal proxy decision maker, the clinician must choose whether to forgo IV rtPA altogether or to invoke the emergency situation as justification for treatment without consent. None of these alternatives is ideal because each presents an inherent moral problem.

**Living Will.** One form of advance directive, the living will declaration, permits individuals to specify treatments that they would and would not want in the event of incapacity. The practical difficulty with such a document is the need for a patient to anticipate future diagnoses and forms of available treatment. The clinician may not find instructions in a living will that clearly guide a treatment decision about intravenous thrombolysis.

Practical problems aside, the concept of a living will declaration, though legally valid, has been challenged on ethical grounds. The dominant argument is that one’s reaction to disability cannot be predicted. Studies have demonstrated a tendency among the nondisabled to view a disabling stroke as tantamount to death, and researchers, in designing treatment studies, have frequently collapsed severe disability and death into a single outcome measure. However, it has been aptly pointed out that the views of those with completed strokes have not been properly explored. This is particularly important in light of the high quality of life reported by some patients with motor impairments so severe that they require mechanical ventilatory assistance. Such is the trans-
forming potential of a phenomenon called “response shift,” in which an individual comes to redefine personal values and the sense of self in reaction to disability. It follows that the static nature of the living will may not be ideally suited to the goal of self-determination when the perceptions that guide one’s chosen moral course may change. In the case of acute stroke, when faced with a possibility of disability or death from stroke or a fatal complication from intravenous thrombolysis, it is difficult to predict how fears of future disability will ultimately alter the predefined preferences of an individual patient.

Substituted Judgment. Another alternative to direct informed consent is informed consent by an authorized surrogate decision maker. Whether the patient’s appointee by advance directive (specifically, by a durable power of attorney or a health care proxy) or an appropriate family member identified by state law, the surrogate is expected to make the same decisions as the patient would if the patient’s capacity were intact. This idea of substituted judgment is widely accepted as a valid means of respecting patient preferences. However, the several practical problems with substituted judgment undermine the ethical basis for its use. First, studies have shown that in the absence of previous discussion between the proxy and patient about a given treatment, the proxy’s ability to predict the patient’s wishes is poor or no better than random chance. Second, even when a proxy is well informed of the patient’s views about a particular treatment, the proxy is no more able to know than the patient before the event whether a response shift would alter treatment preferences. Third, perhaps because of moral uneasiness with making treatment choices for another person, proxies can be reluctant participants in the consent process; this is demonstrated by the results of one large study of potential surrogates in which fewer than half consented across communities, with fewer than half of the attendees expressing approval of the surrogate and by the World Medical Association would support the emergent use of IV rtPA in patients lacking capacity when an alternative form of consent could not be obtained within the treatment window.

Although a physician may have adequate legal grounds on which to invoke an exception to informed consent, one important question remains: On what ethical grounds is a physician qualified to make the decision for intravenous thrombolysis? What certifies a physician to do this moral calculus for another person? The assumption that physicians are appropriate decision makers by virtue of holding medical degrees has been deemed, perhaps quite properly, a revival of paternalism. One means of shifting the ethical choice away from physicians has been the use of community consultation to establish community preferences. This approach was adopted by the Food and Drug Administration as something of an external safeguard and moral argument for permitting exceptions to informed consent in emergency research.

Community consultation for the design of trials evaluating IV rtPA was used by several groups, both in and outside of the United States, as were focus groups to assess community support of research in the emergency setting. As expected, results have varied across communities, with fewer than half of the attendees to all attendees of a given meeting expressing approval of subject enrollment without consent. Based on this experience, it might seem that positive feedback from such consultations could bolster the case for using IV rtPA when consent is unobtainable. However, the moral grounds for community consultation have also been a subject of keen debate. It has been questioned what real protection community consultation affords, given that communities have no veto power over decisions made by hospital ethics committees. Further, and most important, it has been pointed out that community consensus is by no means a substitute for informed consent provided by the individual. Ultimately, neither the individual’s physician nor the individual’s neighbors are possessed of the moral authority to dictate that individual’s fate.

Emergency Exception to Informed Consent. When there are no readily available sources of consent, a legal exception to the rule of informed consent may be invoked if the situation is emergent, in which case consent of a reasonable person to appropriate treatment is implied. As an approved therapy endorsed by evidence-based guidelines, IV rtPA may be emergently administered under US regulations by implied consent. Recourse to implied consent is permitted when it is established that the patient cannot provide direct consent and that another form of consent cannot be obtained in time to avert death or, more relevant to candidates for IV rtPA therapy, severe health impairment. Regulatory precedents set by the Food and Drug Administration and the Department of Health and Human Services in the United States and by the World Medical Association would support the emergent use of IV rtPA in patients lacking capacity when an alternative form of consent could not be obtained within the treatment window.

FUTURE DIRECTIONS FOR RESEARCH AND DISCOURSE

Given the moral difficulties inherent in alternative forms of consent, it is incumbent on the physician, whenever possible, to obtain direct informed consent from the candidate for IV rtPA therapy. To aid in this endeavor, we recommend the establishment of a standardized means for assessing the patient’s capacity to consent to intravenous thrombolysis. The existence of a validated and widely accepted method could substantially improve the rates and quality of capacity assessment for intravenous thrombolysis and could bolster the ethical case for administering this controversial therapy in patients providing informed consent.
The Problem With Screening

From a practical standpoint, it would seem ideal to have a simple, validated method of screening for capacity, especially if it were already used in the medical assessment of acute stroke. The Mini-Mental Status Examination has received fair attention in this regard. Studies have shown it to predict decisional difficulties in the elderly and capacity impairment to various degrees in patients with acute stroke. It has been suggested that the use of such a tool can help to identify patients whose cognitive impairment may threaten their capacity. However, as has been widely recognized, the evaluation of cognitive deficits cannot replace the direct observation of a patient’s decision-making abilities and cannot yield capacity-specific information. Perhaps even more important, the idea of a screening tool is problematic because it suggests that those identified as being at greater risk for incapacity should be assessed more rigorously when, in the context of acute stroke, all patients without striking contraindications should receive the same rigorous assessment. Therefore, rather than focusing on the establishment of a screening measure, attention should be turned to the idea of standardizing a capacity-specific instrument.

Standardized Capacity-Specific Instrument

There is no dearth of instruments for measuring decisional abilities. For example, in a review of 24 studies of capacity in the cognitively impaired elderly, the authors found that 18 different tools had been developed to assess patients according to the 4 legal standards of competence. However, the problem is that most structured assessments are tailored to a specific patient population or decisional crossroads. To date, there is no validated instrument for measuring capacity in the patient with acute stroke or for assessing treatment decisions about intravenous thrombolysis. The establishment of a tool for these purposes is an area of potentially important research. Given the narrow therapeutic window of IV rtPA, time does not permit the use of an instrument composed of hypothetical vignettes, such as the Hopkins Competency Assessment Test (the content of which, in any event, is not decision specific). Possible candidates might include the MacArthur Competence Assessment Tool for Treatment and the Capacity Assessment Tool. One advantage of using the MacArthur Competence Assessment Tool for Treatment might be the facilitated and explicit documentation of patient responses that is built into the capacity assessment and consent procedure. In any case, the introduction of a valid standardized means of evaluating treatment decisions in the acute stroke setting could represent a major advance in the ethical and medicolegal use of IV rtPA.

Lack of Standardization of Legal Standards

One issue perhaps needing consideration is the lack of nationwide standardization of the legal standards of competence. Only 2 of the 4 legal standards of competence are recognized by every state; these are the ability to express a choice and the ability to understand the disclosure. The abilities to appreciate the personal relevance of a disclosure and to reason with information provided are variably sanctioned though not explicitly rejected, with one exception; appreciation as a standard of competence has been legally rejected by the State of Wisconsin. It has been suggested that state competence laws have evolved in such a patchwork fashion because of reliance on case law. In other words, the courts have had to see it to recognize it. This has led to the recommendation that all 4 legal standards be used for any capacity assessment because historically, but for a single instance, the abilities to appreciate and to reason have been accepted once brought before a state court.

CONCLUSIONS

The current lack of a standardized protocol for capacity assessment in acute stroke leaves both patient and physician vulnerable in a climate of ethical and medicolegal controversy about the use of intravenous thrombolysis. The need for proper capacity assessment is imperative, given that all forms of consent to treatment presuppose an adequate evaluation of the patient’s decisional ability about such treatment. Development of a validated and reliable instrument for capacity assessment in acute stroke would facilitate clinical decision making and is an important frontier for ethical discourse and future stroke research.

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