

# Consent Issues in the Management of Acute Ischemic Stroke

## AAN Position Statement

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*Neurology*® 2022;98:73-79. doi:10.1212/WNL.00000000000013040

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## Abstract

This position statement briefly reviews the principle of informed consent, the elements of decisional capacity, and how acute stroke may affect this capacity. It further reviews the role of surrogate decision-making, including advance directives, next of kin, physician orders for life-sustaining treatment, and guardianship. In some cases of acute stroke in which the patient lacks decisional capacity and no advance directives or surrogates are available, consent to treatment may be presumed. The document describes the rationale for this position and various considerations regarding its application to IV thrombolysis, neuroendovascular intervention, decompressive craniectomy, and pediatric stroke. The document also reviews consent issues in acute stroke research.

## Introduction

Despite recent advances in treatment and prevention, stroke remains the second leading cause of death worldwide and the fifth leading cause of death in the United States, with nearly 800,000 strokes occurring each year. There is a rapidly evolving repertoire of treatments that are highly effective in preserving neurologic function after stroke, but only if administered quickly, during a time when patients often lack decisional capacity and surrogate decision-makers may be unavailable. Whereas there are ethical issues surrounding many aspects of stroke prevention and treatment,<sup>1</sup> this position statement, which replaces the American Academy of Neurology's 1999 position paper<sup>2</sup> as well as a 2011 policy statement, focuses specifically on issues of informed consent that arise in the context of acute ischemic stroke treatment.

## Informed Consent and Decisional Capacity

### Elements of Informed Consent

Elements of informed consent include the disclosure of relevant information, recommendation of a plan, and the patient's authorization (or refusal) of the recommended course of action in the absence of coercion.<sup>3</sup> This framework presupposes that the patient has the capacity to understand and decide; such decisional capacity is commonly framed in 4 parts:<sup>4</sup>

1. Understanding—a grasp of the basic facts surrounding a decision, including the nature of the condition, the proposed intervention, and the alternatives, risks, and benefits thereof; understanding may be assessed by asking patients to rephrase provided information in their own words.



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Go to [Neurology.org/N](https://www.neurology.org/N) for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

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This statement was approved by the Ethics, Law, and Humanities Committee, a joint committee of the American Academy of Neurology (AAN), American Neurologic Association (ANA), and Child Neurology Society (CNS), on December 2, 2020; by the AAN on April 22, 2021; by the ANA on May 17, 2021; and by the CNS on May 18, 2021.

## Glossary

EFIC = Exception From Informed Consent; FDA = Food and Drug Administration; mRS = modified Rankin Scale; POLST = Physician Orders for Life-Sustaining Treatment.

2. Appreciation—recognition of how the provided information applies to one’s own case; this may be assessed by asking patients to give a plausible explanation of why a proposed course of action will or will not benefit them.
3. Reasoning—this includes the ability to compare options and consistently infer the consequences of one’s choices; it may be assessed by asking patients how each of the available options will affect their daily lives.
4. Choice—expressing a decision, which should be reasonably stable in the absence of new information.

### Stroke-Related Challenges to the Consent Process

Obtaining informed consent in acute stroke can be encumbered by the sudden, unanticipated, onset of the inability to fulfill one or more of these elements, coupled with the necessity to make decisions rapidly about thrombolysis, thrombectomy, and other high-stakes interventions. For example, understanding of presented information is often impaired in patients with Wernicke aphasia; appreciation may be absent in patients with anosognosia and hemineglect, who do not recognize that they are neurologically impaired; reasoning, particularly about quantitative and probabilistic risks, can be diminished by prefrontal or parietal injury; and patients with Broca aphasia or those with reduced consciousness due to brainstem ischemia may be unable to consistently express a choice.

### Cultural Considerations

In bioethical discourse, informed consent is rooted in the ethical principle of autonomy, which may be viewed more generally as an expression of respect for persons.<sup>5</sup> Self-determination and informed consent have been affirmed as ethical requirements across cultural and national contexts, as in the World Medical Association Declaration of Lisbon on Rights of the Patient<sup>6</sup> and in the Declaration of Helsinki.<sup>7</sup> Medical decision-making in the United States largely emphasizes autonomy, but some cultural traditions within the United States and abroad place greater weight on considerations of community and solidarity. Decisional capacity should be assessed with particular care when such differences are observed, understanding that fully exploring, validating, and applying them to the informed consent process may not be possible in the time-constrained acute stroke setting. In the context of interventions such as hemicraniectomy and research, where time constraints are often not as limiting, cultural perspectives may play a greater role.

## Surrogate Decision-making

### Advance Directives

When a patient loses decisional capacity, a measure of autonomy can be preserved if care can be directed by

preferences previously expressed by the patient in an advance health care directive. There are 2 broad types of advance directives, although many patients’ directives include elements of both. The first type of advance directive (often called a “living will” or “instruction directive”) specifies particular interventions that patients anticipate that they would accept or reject. The instructions in these documents are often either overly specific or too vague, making it difficult to use them to arrive at treatment decisions in the context of acute stroke. For example, many living wills address end-of-life scenarios—often termed “terminal conditions”—but the documents may not adequately reflect patient preferences in relation to debilitating, but often nonfatal, conditions such as acute stroke.<sup>8</sup>

The second type of advance directive (“durable power of attorney for health care” or “proxy directive”) appoints a surrogate decision-maker (in different states variously termed a health care proxy, agent, representative, or medical decision-maker) to make medically indicated decisions on the patient’s behalf. These documents allow for greater flexibility and for decisions informed by patients’ actual clinical situations, but many surrogates are inadequately prepared for their role in representing patients’ wishes.<sup>9</sup> For these reasons, the neurologist and other clinicians are often put in the position of guiding the patient’s surrogate through the decision-making process:

1. Surrogate decision-makers’ ethical imperative is to give priority to patient preferences expressed premorbidly, when patients retained decisional capacity, such as in an advance directive or a clear oral statement.
2. When no explicit statement of the patient’s preferences exists, surrogates are expected to apply “substituted judgment,” attempting to determine what the patient would have wanted, given their general knowledge of the patient’s values and beliefs. Even when made in good faith, multiple studies have demonstrated that such judgments about patient wishes by family members<sup>10</sup> and clinicians<sup>11</sup> are imperfect.
3. When the patient’s wishes are unknown, surrogate decision-makers and the clinicians counseling them attempt to arrive at treatment decisions based on the patient’s “best interests”—often relying on a prediction of the patient’s likely quality of life with and without the available treatments. One danger in such judgments is that healthy people tend to systematically underrate the quality of life of patients with chronic disabilities, such as those that are often sequelae of stroke.<sup>12</sup>

### Next of Kin

If the patient has not executed an advance directive, or it is not available, some (but not all) states have enacted statutes

authorizing a next of kin to make surrogate decisions for patients who lack decisional capacity. (The family members are hierarchically arranged, usually beginning with the patient's spouse, then proceeding to their adult children, parents, siblings, and so forth.) If no statutorily authorized next of kin is available, some state laws empower hospital ethics committees to designate a willing person sufficiently familiar with the patient's wishes and values to make a substituted judgment, thereby avoiding the need to seek judicial involvement.

### Physician Orders for Life-Sustaining Treatment

Many, but not all, states have passed laws recognizing Physician Orders for Life-Sustaining Treatment (POLST; acronyms and terminology vary across states).<sup>13</sup> Unlike advance directives, POLST are medical orders created by physicians, although in most states they are also signed by the patient (if the patient has capacity) or a legally recognized decision-maker (if the patient lacks capacity). The content of POLST forms varies by state, but they generally address life-prolonging treatments such as cardiopulmonary resuscitation, IV antibiotics, and artificial nutrition and hydration. In acute stroke, reperfusion therapies (discussed below) aim to preserve functional independence rather than prolong life, so the options designated in POLST forms do not directly apply to decisions about these interventions. However, for decisions regarding hemispherectomy for malignant hemispheric stroke (also discussed below), a POLST order for "Full treatments" (i.e., "Attempt to sustain life by all medically effective means") could be action-guiding.

### Guardianship

For patients without capacity who do not have advance directives (or whose designated surrogate decision-makers are unable or unfit to make decisions on their behalf), the court may appoint a guardian (in some states called a conservator or a conservator of the person). Unless guardianship happened to be in place already for other reasons, the time required to pursue such would generally be incompatible with the urgency of acute stroke treatments. For patients who are already under guardianship, neurologists should be aware that some states expressly limit the authority of the guardian to withhold or withdraw life-sustaining treatments.<sup>14</sup> As above, acute reperfusion therapies are function- rather than life-preserving, but hemispherectomy might indeed fall under the purview of guardianship laws of this type.

### Institutional Resources

Most situations in acute ischemic stroke require emergent decision-making. When patients lack both decisional capacity and advance directives or surrogates, the treating physicians will have to make clinical decisions on their behalf; the following section reviews ethical considerations regarding various clinical scenarios. For clinical decisions that are less urgent (e.g., when considering hemispherectomy within some hours), many institutions have ethics committees that can aid in decision-making for unrepresented patients.

Although advance directives have been endorsed by the Supreme Court of the United States in *Cruzan*<sup>15</sup> and by Congress in the Patient Self-Determination Act,<sup>16</sup> they are governed by state law and thus vary by jurisdiction, as do POLST and guardianship procedures. Neurologists should be familiar with the laws relevant to these entities in their jurisdictions of practice and, when appropriate, seek legal consultation regarding their application.

## Emergency Treatment for Acute Stroke

What is the neurologist to do in an emergency situation when rapid treatment for acute stroke is indicated, the patient lacks decisional capacity, no determinative advance directive governs the situation, and no authorized surrogates are available? In these situations, interventions may be provided based on the ethical<sup>2,3</sup> and common law<sup>17</sup> presumption of consent; that is, the rationale that reasonable people would consent to treatment if they could be asked. Whereas this presumption of consent is most easily appreciated in life-threatening emergencies, the imminent risk of significant disability—not just death—also justifies emergent treatment in these circumstances.<sup>18,19</sup> Empirical support for this conclusion has been borne out in multiple studies showing that patients consider severe stroke-related disability as undesirable as or worse than death.<sup>20,21</sup> Furthermore, a general population study found that the desirability of thrombolysis for acute ischemic stroke is roughly equivalent to that of cardiopulmonary resuscitation in cardiac arrest, an imminently life-threatening situation in which the presumption of consent is generally accepted.<sup>22,23</sup>

### IV Thrombolysis

IV administration of alteplase (Activase; formerly known as tissue plasminogen activator) was the first acute stroke treatment demonstrated to improve patients' neurologic function. It remains first-line therapy, even for likely endovascular treatment candidates, for selected patients presenting within 3<sup>24</sup> or 4.5<sup>25</sup> hours from stroke onset or the time that the patient was last known to be well. When patients retain decision-making capacity (or surrogates are available), they should be quickly but clearly informed about:

1. The stroke diagnosis and rationale for thrombolytic therapy
2. The patient's prospects for achieving a good functional outcome with and without treatment
3. Risks of treatment, including intracerebral hemorrhage and angioedema

Alteplase treatment within the 3-hour window is approved by the Food and Drug Administration (FDA), whereas treatment of selected patients within the 4.5-hour window is scientifically recommended<sup>26</sup> but remains off-label. The treating neurologist should discuss this, when possible, with the patient or surrogate.

There are numerous contraindications to thrombolytic treatment. Some, such as intracranial hemorrhage, are absolute. Others, such as “minor” deficits, are considered relative contraindications because of uncertainty about their definitions (which neurologic deficits are too minor to warrant treatment?) or about the balance of risks and benefits in a particular circumstance (e.g., treatment in the 4.5-hour window in patients older than 80 years). A review of the scientific evidence behind the various IV thrombolytic contraindications has been published<sup>27</sup> and can inform treatment decisions in cases where relative contraindications exist. With a cognitively intact patient or the help of a family member, the treating neurologist can engage in a careful discussion of individual risks and benefits of treatment in such cases. When the balance of these risks and benefits is uncertain, and the patient lacks decisional capacity and lacks a surrogate, then the neurologist should adhere more closely to guideline-based inclusion and exclusion criteria.<sup>26</sup>

Verbal consent (or refusal) to treatment should be obtained and documented in the medical record by the treating physician. Some institutions and jurisdictions, such as the Veterans Health Administration,<sup>28</sup> require written consent for thrombolysis; acute stroke protocols at such facilities should therefore take into account the potential for treatment delays.

New approaches continue to be developed to improve patient selection and outcomes; recently reported innovations include the use of alternative medications<sup>29</sup> or multimodal imaging in expanded time windows for selected patients.<sup>30,31</sup> As clinical evidence and practice with respect to IV stroke treatment continue to evolve, neurologists will face more situations in which treatment decisions must be made for patients who lack capacity. When an appropriately designated surrogate decision-maker is present, neurologists should be prepared to engage them in a discussion of the risks and benefits of new interventions. When surrogates are not present, it may be reasonable to proceed with treatment on the presumption of consent when patients’ cases fit extant inclusion/exclusion criteria, contraindications (particularly, absolute contraindications) are absent, and the overall balance of risks and benefits strongly favors intervention.

### Neuroendovascular Intervention

In 2015, several randomized studies demonstrated the benefit of mechanical thrombectomy for large vessel occlusions in the anterior circulation.<sup>32</sup> More recently, 2 additional studies have been published showing that selected patients stand to benefit up to 16–24 hours from stroke onset or from the time that the patient was last known to be well.<sup>33,34</sup> In cases of large hemispheric stroke for which endovascular therapy would be considered, patients are much more likely to be cognitively impaired. Moreover, when patients are evaluated in comprehensive stroke centers remote from their local communities, their families may be in transit or otherwise unavailable at the time a treatment

decision needs to be made. Therefore, many of the ethical issues regarding IV thrombolysis are even more pressing in endovascular treatment. Patients who meet established criteria<sup>26</sup> for endovascular therapy but who lack both decisional capacity and a surrogate decisionmaker should be treated on an emergency basis. The patient or surrogate should later be informed about what was done and how the time-sensitive circumstance precluded the usual consent process. The further outside of published criteria that a patient’s condition falls, the less justified would be emergency treatment absent patient or surrogate consent.

### Decompressive Craniectomy

Malignant brain swelling is a feared and potentially fatal complication of large-territory ischemic stroke. Cerebral edema can lead to compounding injury beyond the originally affected territory via mass effect, herniation, obstructive hydrocephalus, and intracranial hypertension. Decompressive craniectomy is often employed to interrupt this cascade and can be lifesaving. However, most patients in whom decompressive craniectomy is considered will be unable to consent to the procedure, as in both cerebral hemispheric infarction and cerebellar infarction the most reliable indicator of brain tissue swelling is decreased level of consciousness.<sup>35</sup> Large left hemispheric strokes are also often accompanied by aphasia and large right hemispheric strokes are often accompanied by anosognosia, both of which also impair decisional capacity.

When patients with large-territory ischemic strokes are admitted to the hospital, the possibility of developing malignant edema should be anticipated and communicated to patients who retain decisional capacity (as may be the case in cerebellar lesions) or to their surrogates (as will typically be necessary for large hemispheric strokes that impair decisional capacity). Such discussions can prompt earlier consideration about the course of action that will best promote the patient’s values. As with advance care planning, this may help to avoid hasty and emotionally fraught decisions in the setting of a patient’s clinical decompensation.

Discussions with patients or their surrogates should be informed by the likely outcomes of the potential interventions. In malignant cerebellar edema, decompression via suboccipital craniectomy is generally beneficial, often preserving the patient’s life and usually resulting in a modified Rankin Scale (mRS) score of 2 or less.<sup>36</sup> Therefore, in counseling patients with large cerebellar infarcts (or their surrogates), suboccipital craniectomy for cerebellar edema can be generally recommended when necessary in the absence of surgical contraindications or other functionally limiting conditions. In the case of a patient lacking surrogate decision-makers, surgical treatment on the presumption of consent is often justified given the favorable balance of risks and benefits.

In malignant hemispheric edema due to middle cerebral or internal carotid territory infarctions, decompression via

hemicraniectomy can be lifesaving while also leaving patients with significant functionally limiting deficits. In many cases, this effectively averts death in favor of survival with major dependency. In a pooled analysis of 3 trials in patients age 60 and below, hemicraniectomy was considered to be beneficial on the assumption that survival with an mRS score of 4 (moderately severe disability, unable to walk without assistance, and unable to attend to own bodily needs without assistance) was a favorable outcome.<sup>37</sup> In a trial of patients over age 60, no surviving patients had an mRS score of 2 or less and only 7% had an mRS score of 3.<sup>38,39</sup>

Thus, decision-making is more difficult for malignant cerebral hemispheric edema, as (particularly for older patients) hemicraniectomy involves a tradeoff between mortality and major dependency. Prospectively, many people rate severe disability as undesirable as or worse than death<sup>20,21</sup> and most people consider an mRS score of 3 to be the maximum acceptable outcome score.<sup>40-43</sup> However, retrospectively, long-term survivors of hemicraniectomy, including older patients, reported acceptable quality of life and agreed with their treatment.<sup>44,45</sup> This discrepancy may reflect “response shifts” in which patients recalibrate and reprioritize their assessments of health-related quality of life after stroke and other disabling events.<sup>46</sup> In decisions concerning hemicraniectomy, it remains controversial whether the prospective or retrospective perspective should be given priority, and thus how clinicians should advise surrogates or proceed when surrogates are unavailable. This is a challenging decision that must be guided as much as possible by consideration of the patient’s own health-related values. The patient’s premorbid functional status and life expectancy may be informative. Surrogates and clinicians faced with such decisions may take some comfort in the observation that most patients do not retrospectively regret having undergone surgery, even when this results in major disability.

### Pediatric Stroke

Acute arterial ischemic stroke occurs in children at a rate of 1.2–8/100,000 person-years and 1 per 2,500–4,000 live births for neonates.<sup>47</sup> Children typically present later than adults; because of diagnostic challenges and a high rate of mimicking conditions, the median time to diagnosis is 24 hours from symptom onset.<sup>48,49</sup> Therapeutic options for stroke management are similar to those for adults, although there is a lack of data on efficacy and safety for children. This leads to challenges in counseling families about the risks and benefits of a potential therapy.

Many therapies, including alteplase and mechanical thrombectomy, are not FDA-approved in children and are used off-label. Parents or legal guardians are the legally authorized decision-makers for children and are expected to use the best interest standard when making medical decisions for them. The time constraints of obtaining informed consent for acute stroke therapies make this process challenging, especially given the lack of data for these high-risk procedures.

To aid with this process, institutions should create acute stroke treatment protocols and involve the appropriately

qualified clinicians, namely physicians with experience and expertise in treating children with stroke. In the absence of a strong body of empirical data, physicians should rely on these opinion-based institutional standards and published guidance documents<sup>50</sup> to counsel families and treat children with acute strokes. Additional supportive data from well-designed trials are required before establishing standards for treatment with thrombolysis or thrombectomy for young children and for children whose stroke severity or time to treatment fall outside of established adult guidelines.

## Consent Issues in Acute Stroke Research

Just as stroke-related deficits can interfere with patients’ capacity to consent to medical treatment, the same deficits may render patients incapable of consenting to clinical research. While this poses ethical challenges, the inclusion of patients with impaired decisional capacity in research is itself an ethical priority. Limiting clinical trials only to patients able to consent for themselves would restrict the generalizability of research by excluding patients with more severe strokes.<sup>51,52</sup> These are the patients for whom new therapies and improved systems of stroke care are most urgently needed.

In case of incapacity, few patients’ advance directives include specific instructions about what types of research they would consent to in advance. As with state laws about advance directives in a purely clinical context, laws governing surrogate decision-making for clinical research vary by jurisdiction. Many states lack explicit provisions for surrogate research consent; the 2017 revised Common Rule clarifies that in these states, individuals empowered to make clinical care decisions for patients can also serve as surrogate decision-makers for research.<sup>53</sup> Still, designated surrogate decision-makers may have more difficulty in extrapolating from the patient’s known wishes and beliefs to decisions about clinical research than to decisions about medical treatment, leading to greater reluctance to enroll.<sup>54</sup> Enrollment of patients generally cannot be justified purely by appeal to patients’ “best interests,” as clinical trials typically involve exposing participants to unproven interventions in the interest of producing generalizable knowledge.<sup>55</sup>

In patients without decisional capacity who also lack available surrogates at the time when enrollment decisions must be made, US regulations recognize 2 conditions in which patients may be enrolled in research without the patient’s or surrogate’s consent. First, institutional review boards may waive the requirement of informed consent for research with minimal risks, generally defined as risks similar in magnitude and probability to those encountered in daily life.<sup>56</sup> This threshold may be met by some systems-level interventions or qualitative studies of care delivery processes, but is unlikely to be met by physiologic interventions directed at reperfusion or neuroprotection.

Second, investigators may apply to the US FDA for an Exception From Informed Consent (EFIC), introduced in 1996 to permit research involving human subjects in need of emergency interventions whose ability to consent is impaired due to life-threatening conditions.<sup>57</sup> These exceptions involve additional safeguards that may add to the cost and difficulty of conducting clinical trials, such as the requirement for public disclosure and community consultation. Moreover, recent research has raised concerns about equitable burdens in research in EFIC trials, as African Americans are overrepresented in EFIC trials.<sup>58</sup>

Of note, while the requirement of informed consent has been described by some as the “rate-limiting step” of acute stroke trials,<sup>59</sup> waivers of consent are not generally associated with more rapid trial recruitment for controlled trials of clinical therapies delivered in traditional settings.<sup>60</sup> However, such waivers may be of value in enabling novel trial designs, particularly of systems-level studies addressing the speed and efficiency with which standard therapies are delivered.

## Conclusion

Decision-making for acute stroke, which is often complex in itself, can be complicated by patients’ lack of either decisional capacity or an advance directive offering guidance applicable to this usually unanticipated situation. In pediatric stroke, the patient will usually have a parent or other surrogate available; a common challenge is the paucity of clinical data to guide decisions. The Federal Common Rule, state law, and individual trial protocols all govern enrollment in clinical trials. The Table summarizes a basic approach to ethical decision-making in these situations; neurologists also need to be familiar with the relevant laws in their jurisdictions of practice.

**Table** Consent Guidance for Major Categories of Acute Ischemic Stroke Treatment

Type of treatment	Example	Guidance
<b>Generally accepted treatment</b>	IV thrombolysis fitting all inclusion/exclusion criteria	Proceed with treatment on the presumption of consent, if necessary.
<b>Treatments requiring heightened consideration of risk/benefit tradeoffs</b>	Endovascular treatment for distal vascular occlusions	Consider how far from published standards the case falls; the decision whether to proceed should be informed by how closely the facts of the case match current guidelines.
<b>Treatments for which evidence is lacking</b>	Pediatric stroke	Work with institutional stakeholders to develop local treatment protocols.
<b>Investigational treatment</b>	Enrollment in an acute treatment trial	Laws regarding surrogate consent vary by state, and research protocols vary as well. The Federal Common Rule does allow lawful surrogates to consent.

## Acknowledgment

The authors thank the members of the Ethics, Law, and Humanities Committee and other experts who contributed to this manuscript by reviewing and offering suggestions, including Gabrielle deVeber, MSc, MD (Senior Scientist, Child Health Evaluative Sciences, The Hospital for Sick Children, Toronto, on behalf of the Child Neurology Society); Larry B. Goldstein, MD (Professor and Chair of Neurology, University of Kentucky); Lori Jordan, MD, PhD (Director, Pediatric Stroke Program, Vanderbilt University Medical Center, on behalf of the Child Neurology Society); and Barney J. Stern, MD (Professor of Neurology, Johns Hopkins University); as well as Sarah Bird Nelson, JD (Associate Counsel, American Academy of Neurology) for her support in this project and for her longstanding commitment to the Ethics, Law, and Humanities Committee.

## Study Funding

The authors report no targeted funding.

## Disclosure

The authors report no disclosures relevant to the manuscript. Go to [Neurology.org/N](http://Neurology.org/N) for full disclosures.

## Publication History

Received by *Neurology* June 16, 2021. Accepted in final form October 25, 2021.

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*Neurology* 2022;98;73-79

DOI 10.1212/WNL.0000000000013040

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