



AMA Journal of Ethics®

October 2021, Volume 23, Number 10: E783-793

CASE AND COMMENTARY: PEER-REVIEWED ARTICLE

When Should Neuroendovascular Care for Patients With Acute Stroke Be Palliative?

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Abstract

Noncurative surgeries intended to relieve suffering during serious illness or near end of life have been analyzed across palliative settings. Yet sparse guidance is available to inform clinical management decisions about whether, when, and which interventions should be offered when ischemic stroke and other neurological complications occur in patients whose survival is extended by other novel disease-modifying interventions. This case commentary examines key ethical and clinical considerations in palliative neuroendovascular care of patients with acute stroke.

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Case

Mr J is a 64-year-old man with metastatic non-small cell lung cancer (NSCLC), who, while eating, abruptly developed right hemiplegia and aphasia. He had been diagnosed 10 months earlier with NSCLC; his estimated life expectancy was approximately 1 year. After a course of chemotherapy with pemetrexed and carboplatin, Mr J started pembrolizumab, an antiprogrammed death-1 immune checkpoint inhibitor offered possibly to extend his life but not as a cure for his cancer.^{1,2} Since diagnosis, Mr J has suffered multiple hematologic complications, including thrombosis and hemorrhage. When brought to an emergency department, he was confirmed as full code and intubated on arrival due to poor mental status and aspiration risk. Computed tomography (CT) imaging of his head and neck revealed normal brain parenchyma and occlusion of the proximal left middle cerebral artery (MCA), which supplies blood to most of the brain's left hemisphere, including areas critical for language and right-side sensorimotor function.³ The mechanism of Mr J's left MCA occlusion was presumed to be thromboembolism, to which he was predisposed by hypercoagulability of malignancy, pembrolizumab,^{4,5,6} and intracardiac hemostasis, given his known low left ventricular ejection fraction.

After discussion of acute stroke as a likely complication of Mr J's cancer, Mr J's health care proxy, GG, consented to Mr J undergoing an emergent thrombectomy. This neuroendovascular procedure is a minimally invasive alternative to more invasive interventions and is the standard method for thrombectomy for acute ischemic stroke with large-vessel occlusion using an endovascular approach. Emergent thrombectomy utilizes femoral artery access to position an intracranial catheter system that permits intracerebral thrombus removal, with the goals of reestablishing blood flow to vascular territory downstream from an occlusion and enabling salvage of the ischemic penumbra to restore neurological function and prevent further impairment.⁷ If thrombectomy is not performed, a large proximal-vessel stroke typically occurs, potentially leading to extended brain tissue infarction, cerebral edema, and other symptoms of elevated intracranial pressure (eg, nausea, vomiting, headache, visual changes, and cranial neuropathies) that can exacerbate a patient's impairment and suffering.^{8,9,10,11}

Mr J's thrombectomy was uncomplicated and resulted in rapid and successful left MCA territory reperfusion. A subsequent brain magnetic resonance (MR) image, however, revealed multifocal infarcts affecting the left and the right hemisphere of Mr J's brain and bilateral cerebellar hemispheres, consistent with his presumed cardioembolic etiology. Mr J was unable to communicate or meaningfully interact. After neurological examination, Dr N informed GG of key findings, including bilateral infarcts expected to produce long-term bilateral weakness, disordered speech, and cognitive impairment. Dr N also explained to GG that Mr J would likely need life support, including tracheostomy, gastrostomy, and rehabilitation if he survived much longer. GG expressed understanding and asked the team to prioritize Mr J's comfort.

Commentary

More than 1 in 10 patients who present with acute ischemic stroke are estimated to have comorbid cancer.^{12,13} As the median survival of patients with cancer improves with **novel targeted therapies**, the frequency of acute stroke and other neurologic complications in this expanding population is expected to rise.^{14,15,16,17,18} Malignancy can predispose patients to ischemic stroke through hypercoagulability, nonbacterial thrombotic endocarditis, systemic treatment effects, or, rarely, tumor embolism or angioinvasion.^{14,19} Since many patients seeking emergency evaluation of acute stroke symptoms might have comorbid cancer, clarifying ethical questions in these patients' stroke care, especially for patients near the end of life, is key. Should clinicians try to preempt or reverse neurological dysfunction when the end of a patient's life is near? When, to what extent, and according to whom should thrombectomy for patients with terminal illness be considered palliative? How should **palliative or comfort care goals** be set in order to guide appropriate neuroendovascular management decisions in the context of end-of-life care?

Palliative Thrombectomy Goals

Palliative care is defined by the World Health Organization (WHO) as "active total care of patients whose disease is not responsive to curative treatment" that aims to achieve "the best quality of life for patients and their families."²⁰ The Center to Advance Palliative Care (CAPC) conceives of the field as "specialized medical care for people with serious illnesses [that is] focused on providing patients with relief from the symptoms, pain, and stress of a serious illness.... The goal is to improve quality of life ... and [palliative care] can be provided along with curative treatment."²¹ Noncurative surgery intended to relieve symptoms in patients with serious illness or near the end of life has been analyzed in a range of contexts, particularly in surgical

oncology.^{22,23,24,25,26,27,28,29,30,31} However, invasive neurological procedures intended to address indirect complications of terminal illnesses (eg, thrombosis due to hypercoagulability of malignancy) have received little clinical or ethical attention. Especially in clinical neuroscience, little evidence is available to guide neuroendovascular intervention decisions with patients who develop ischemic stroke or other neurological complications near the end of life.

Although in Mr J's case, thrombectomy did not appreciably reduce disability near the end of his life, we argue that Dr N's team's decision to perform thrombectomy was ethically justifiable based on its concordance with Mr J's goals that the team gleaned through conversations with GG. As highlighted by the WHO and CAPC definitions, appropriate palliative care consists not merely of pain control but of the active total care of a patient who strives for the best quality of life. To the extent that neurological symptoms, including sensorimotor dysfunction (eg, weakness and numbness), headache, delirium, aphasia, dysarthria, imbalance, gait disturbance, and cranial neuropathies can detract from quality of life, it is incumbent upon clinicians to diligently address symptoms throughout a patient's illness.^{32,33,34,35} Among patients who experience acute ischemic stroke, more severe neurological impairment has been linked with significantly lower quality of life.^{35,36}

Neuroendovascular approaches, such as thrombectomy, are specifically intended to attenuate or prevent accumulated neurological disability^{37,38,39} and are supported by randomized clinical trials.^{40,41} The location and type of stroke and the extent of salvageable ischemic penumbra must be considered case by case in terms of whether foreseeable benefits of thrombectomy outweigh its risks. Eligibility criteria for late endovascular treatment trials for patient-subjects with acute ischemic stroke have included occlusion of proximal MCA or internal carotid artery on CT imaging or MR angiography, a score greater than 6 on the National Institutes of Health Stroke Scale up to 24 hours from the time the patient was last seen well, significant ischemic penumbra, and factors such as age, baseline modified Rankin Scale score, and life expectancy. Exclusion criteria have varied by trial and have been a source of practice variation across centers.⁴² Another source of complexity is that treatment decisions are typically made emergently.

Minimally invasive neuroendovascular interventions can aptly be considered palliative for a patient with limited life expectancy and should not be withheld based solely on a patient's terminal comorbidity. Even if a patient is expected to live only a few weeks or months, any additional stroke-related neurological impairment could exacerbate their suffering near the end of life. Many patients who undergo thrombectomy experience reversal of neurologic impairment or return to functional independence due to their reduced risk of ischemic penumbra.⁴⁰ Successful reperfusion of ischemic penumbra might forestall development of malignant cerebral edema, cerebral herniation, or other symptoms of increased intracranial pressure, as evidenced by lower rates of decompressive hemicraniectomy since the advent of mechanical thrombectomy.^{43,44,45,46} Following the ethical principles of doing good and avoiding harm^{47,48,49} likely requires clinicians to offer palliative thrombectomy, even when a patient has incurable comorbidity.

Decision Sharing

Patient-centered care requires assessing (1) a patient's functional status at baseline; (2) their preferences, values, and goals, perhaps as expressed by surrogates; and (3) their

prospects for recovery.^{50,51,52,53} Interpreting each stroke not as a discrete new disease but in the context of a patient's broader health state, relevant comorbidities, and **illness narrative** can foster holistic, goal-concordant intervention and might help avoid unnecessary discontinuity or fragmentation in a patient's care.^{54,55,56,57} Clinicians' conversations with patients and surrogates should emphasize that estimates of an intervention's effects are extrapolated from studies in which subjects were drawn not from the unique population of patients with terminal illnesses but from a general population with minimal preexisting disability. Decision sharing and informed consent require conveying uncertainty about how well the available evidence applies to a particular patient.

Equity and Evolving Therapies

Further research on the efficacy of palliative neuroendovascular care is essential, although the practical and ethical problems of conducting clinical research in patient-subjects with advanced illnesses deserve careful consideration.^{58,59,60,61} In one study of persons with metastatic NSCLC, newly diagnosed patients whose care plans integrated early palliative care experienced improved quality of life and mood,⁶² and the challenges of ensuring goal-concordant palliative care given the growth of novel interventions in the past decade are actively being studied.^{63,64} Equity as an organizational ethical value requires inclusion of all key stakeholders' perspectives and goals—curative and palliative—when crafting policy and evaluating downstream implications of decisions to administer or withhold neuroendovascular interventions in individual cases.

In the case, Mr J had an acceptable health-related quality of life and—assuming his comparability to otherwise healthy patients with acute stroke—a higher chance of making a functional recovery with treatment than without it, at very low procedural risk.⁶⁵ While caution must be exercised in generalizing from studies of acute stroke patients who did not have cancer, the data indicate that patients treated with thrombectomy for acute proximal MCA occlusion stroke lived the remainder of their lives with fewer neurologic impairments than if untreated and with reduced need for aggressive care and institutionalization following a sentinel cerebrovascular event.^{64,66,67,68}

While not a factor in this Mr J's case, do-not-intubate (DNI) orders are common and worthy of mention here. DNI orders should not independently influence stroke care decisions “unless otherwise explicitly indicated,” as emphasized by an American Heart Association/American Stroke Association statement (Class IIa recommendation).⁶⁹ Generally, clinicians should express respect for patients' right to decline interventions⁷⁰ but should recognize that such interventions can have palliative roles by preventing debilitating neurological impairment and concomitant end-of-life suffering.^{71,72} Palliative radiotherapy, including stereotactic radiosurgery for patients with advanced cancer with brain metastases, has been pursued,^{73,74,75,76} as have deep brain stimulation for Parkinson disease management near the end of life⁷⁷ and palliative decompressive spinal surgery for patients with metastatic spinal cord compression.^{78,79,80,81}

Care Planning

Unlike decisions about specific palliative interventions, decisions about stroke care are typically made quickly, given the urgency of acute stroke, its impact on patients' capacity to participate in decision making, and the exquisite time sensitivity of implementing acute stroke interventions. Although outcomes data for specific palliative neuroendovascular interventions are limited, advance care planning should include

surrogate designation and discussion of minimally invasive intervention preferences, which could help safeguard value-concordant goal setting and decision sharing later.^{71,82}

Ethically appropriate palliative neuroendovascular care for patients with acute stroke includes more than pain control and extends to management of distressing physical, spiritual, emotional, and psychosocial symptoms.^{83,84} Recognizing the relatively high frequency of neurological complications among patients with terminal illnesses,^{12,85,86,87,88,89} clinicians can implement patient-centered palliative neuroendovascular care with guidance from the ideas in the Table.

Table. Elements of Ethically Appropriate Palliative Neuroendovascular Care

Recognize palliative care as more than pain control; extend it to management of potentially disabling, distressing neurologic symptoms.^{83,84,90}

Clarify the patient's (or surrogate's) values and goals of care.⁹¹

Avoid assumptions about a patient's values, preferences, or goals.⁹²

Discuss intended aims, prospective benefits, and possible risks of a neuroendovascular intervention with a patient or surrogate.

Explain the range of possible postprocedural outcomes to motivate transparency.

Discuss likely outcomes of no neuroendovascular intervention or alternative interventions.

Ensure that decision making is sensitive to patient preferences, values, and goals.

Clearly document and communicate decisions to colleagues and care team members.

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Citation

AMA J Ethics. 2021;23(10):E783-793.

DOI

10.1001/amajethics.2021.783.

Acknowledgements

This work was supported by Northwestern University Feinberg School of Medicine Department of Neurology's Physician-Scientist Training Program, National Institutes of Health R25 CA190169 for Meaning-Centered Psychotherapy research and training at Memorial Sloan Kettering Cancer Center, National Institute of Neurological Disorders and Stroke of the National Institutes of Health Cooperative Agreement F32MH123001, the Tiny Blue Dot Foundation, and a Scientific Projects to Accelerate Research and Collaboration award from the Henry and Allison McCance Center for Brain Health, Massachusetts General Hospital.

Conflict of Interest Disclosure

Dr Sokol serves as an ad hoc consultant for Tikvah for Parkinson and is an ad hoc reviewer for the *Journal of Geriatric Psychiatry and Neurology*, *Pilot and Feasibility Studies*, and *Palliative Medicine Reports*. The other authors had no conflicts of interest to disclose.

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