

Challenges and ethical issues in the course of palliative care management for people living with advanced neurologic diseases

Varun Sreenivasan, Christa O'Hana S. Nobleza

Department of Neurology, University of Mississippi Medical Center, Jackson, MS, USA

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Correspondence to: Christa O'Hana S. Nobleza, MD. 2500 North State St. Jackson, MS 39216, USA. Email: csanluis@umc.edu.

Abstract: In the recent years, there has been an increase in awareness with regards to the role of palliative care (PC) in management of neurologic diseases. In 1996, the need to incorporate PC in the care for patients with neurologic conditions was recognized by the American Academy of Neurology (AAN) Ethics and Humanities Subcommittee. The gaps in research, education and the ability to deliver adequate PC were then acknowledged by the National Academy of Sciences with their publication of “*Approaching death: improving care at the end of life*” and most recently, continued goals in improving PC was highlighted by another recent publication “*Dying in America: improving quality and honoring individual preferences near the end of life*”. The complexity of managing neurologic patients brings about challenges and ethical issues in this setting. The aim of this review is to discuss and summarize the challenges and ethical issues in the context of PC management of patients with advanced acute, rapidly progressive, slowly-progressive or degenerative neurological conditions that are commonly encountered in practice.

Keywords: Neurology; palliative care (PC); ethical issues

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Introduction

The Institute of Medicine defined palliative care (PC) in their recent report as “*care that provides relief from pain and other symptoms, that supports quality of life (QOL), and that is focused on patients with serious advanced illness and their families*” (1). While the World Health Organization defined it as “*an approach that improves the QOL of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual*” (2). In line with patient- and family-centered care, the Clinical Practice Guidelines for Quality Palliative Care defined PC as “*patient and family-centered care that optimizes QOL by anticipating, preventing, and treating suffering*” (3). A commonly used term interchangeably with PC is hospice

which offers a “*comprehensive, socially supportive, pain-reducing and comforting alternative to technologically elaborate, medically centered interventions*” and is a way by which PC needs of patients at the terminal stage of their illness are delivered (1,4). Traditionally, PC has been utilized among cancer patients however its concepts in management have been applied as early as the late 1980s with the American Academy of Neurology’s (AAN’s) position statement in the management of a persistent vegetative state patient (5). Subsequently, the AAN section on Pain and PC was formed in 1995 to improve on the PC involvement in neurological disorders. PC is important in the management neurological disorders, as very often, these conditions are debilitating, often irreversible, and have significant physical and emotional impact on the patients and their families. Due to the prolonged, fluctuating and unexpected course of some neurologic disease, accompanied by progressive functional

loss of mobility, communication ability and cognition, all of which affects the patient and caregivers, PC should be considered an important part in caring for patients with neurological conditions both in the inpatient or outpatient setting (6). In 1996, the need to incorporate PC in the care for patients with neurologic conditions was recognized by the AAN Ethics and Humanities subcommittee (7,8). In this statement, the duties of neurologists to provide adequate PC and improve education on PC were promoted. The European Academy of Neurology in collaboration with European Association for PC developed recommendations which included early PC integration, incorporation of a multidisciplinary team, open and structured communication with patient and family or caregiver, proactive symptom assessment and management, caregiver support, end-of-life care recognition, assessment and management and training and education of neurologists (9). As the patient goes through the process from diagnosis to the end-stages of their neurological disease, challenges and ethical issues may arise even when the patient is already under palliative level of care. Ethical principles developed by Beauchamp and Childress of respect for autonomy, beneficence, non-maleficence and justice (10) need to be consistently examined.

In this article, we reviewed and summarized the challenges and ethical issues in the context of PC management of patients with advanced acute, rapidly progressive, slowly-progressive or degenerative neurological conditions that are commonly encountered in practice. Acute neurologic conditions included cerebrovascular disorders and vegetative state. Rapidly progressive condition of Creutzfeldt-Jakob disease (CJD), amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), Parkinson's disease and other PD-related disorders, Alzheimer's disease (AD) and other dementias and central nervous system (CNS) malignancies and other tumors are included in the slowly-progressive or degenerative disorders although some CNS malignancies may rapidly progress. Common challenges and ethical dilemmas across all the categories are presented. We also presented neurologic disease-specific considerations in the course of PC management.

Ethical dilemmas across neurologic diseases

Timing of PC involvement

There is currently no general guideline on the timing of PC for neurologic disease; however, disease-specific recommendations are emerging. A distinction between a

neurologist with the interdisciplinary team applying PC approach (primary PC) and consulting a specialized palliative care team (specialist PC) should be made. The AAN practice parameter in ALS recommended multidisciplinary team involvement inpatient management which included PC for symptom management most especially in the terminal stages (11); while for stroke, the initial PC management more often comes from primary PC (4,12). The American Heart Association and American Stroke Association however recommends that for more complicated symptom management and decision making, specialty palliative care (SPC) should be involved (4,12). For patients with neurocritical illness, it is recommended that specialist PC be involved earlier in the stage of the disease to establish rapport and trust with the family however, their involvement should not discount the concomitant and continuous primary PC management from the primary neuro-intensive care interdisciplinary team (13). An emerging model of PC particularly applicable in neurologic conditions is "simultaneous care" (14,15) where in early PC integration is done in the disease and throughout the disease process with the aim of improving the quality of care through symptom control, strengthening the support structure to improve patient and caregivers' quality of life and facilitating appropriate resources needed (16). With this approach, PC management is encouraged at the moment of diagnosis (17). Until further prospective studies reveal an optimal disease-specific timing for involvement of PC, applying primary PC and considering an individualized approach to the timing of utilizing SPC is still recommended.

Surrogate decision making and the "Unbefriended" patient

It is common among patients with neurologic disease to have impaired cognition or communication. Both of these affect decision-making capacity (DMC) as it pertains to laws in the United States. The ability to be able to exercise this capacity involve the patient being able to understand the current condition, the testing needed, available management options and the result of not proceeding with testing or management (18,19). The patient must be able to make a decision incorporating the information provided and his or her values and he or she should be able to clearly communicate the decision to the physician (18,19). If the patient lacks DMC, formally appointed surrogates through physicians or lawyers assigning a health-care proxy or durable power of attorney (DPOA) may make decisions in

the patient's best interest (20). In a cohort of 129 patients with neurologic conditions, only 23% of them had a Durable power of attorney (DPOA) appointed prior to the hospitalization (21) which is consistent with another report that only 25% of adults in the United States have advanced directives (22,23). If there is no available legal health-care proxy or DPOA, surrogate consent laws in some states may allow physicians to discuss decisions with an individual or group of people who can potentially express the patient's wishes (24,25). The surrogate consent laws may be based on hierarchy or consensus (25). Among the 44 states that adopted surrogate consent laws two states (Colorado and Hawaii) utilize the consensus statutes requiring all available "interested persons" to have a unified consensus about who will be the decision maker (25). An example of surrogate law based on hierarchy is what is used in Georgia where in legal authority lies with several potential people in the following order spouse, parent of a minor, legal guardian, adult child, parent of an adult child, sibling, grandparent, adult grandchild, adult niece, nephew, aunt or uncle and adult friend (18). In the cases of the "Unbefriended Patients", who are not able to exercise DMC and are alone (26,27), ethics consult are usually warranted according to the American Medical Association (27). While the American Geriatrics Society places the decision making role to the treatment team (28), a court appointed-guardian is what is recommended by the American College of Physicians (29). Institution and state laws vary in terms of patient management in these scenarios (29). In most cases the family makes a united decision, which is acceptable. If the family is unable to agree, a legal process by which a judge assigns a legal guardian or a surrogate may be done. In cases where the patient is under the care of the state, the state serves as the guardian and decision making is done through the state representative. Shared decision-making, the process by which the patient with or without other family members or friends and the health care team share information regarding treatment options, risks and benefits while the patient talks about their preferences according to their beliefs and values, is now a common practice (30).

The role and the process by which the surrogates should approach decision making for the patient should be clearly explained. A common mistake done by inexperienced physicians is asking surrogates "what do you want to do?" The ethical standards by which the surrogates' decisions are made should be based primarily on, the patient's known wishes, followed by substituted judgment and patients' best interest (24,31). When the patient's wishes are completely

unknown, the surrogate should make their best assessment of what the patient may decide under the current situation from how best they know the patient, which is the standard of substituted judgment (32). It is however, important to note, that this has been an area of debate among bioethicists because there is some doubt into how reliable surrogates can be in terms of knowing what the patient would have wanted (33). In cases where in the surrogates are not able to utilize substituted judgment, the best interest standard based on established norms should be used in addition to discussion and analyzing the risk and benefits of the current treatment (33).

Withholding and withdrawing treatment

There is neither difference nor legal basis for distinguishing withholding treatment that is life-sustaining versus discontinuing treatment if the patient or the surrogate wishes to do so (20). In neurological conditions there are available prognostic tools that may aid in prognostication and guide the decision to withhold or withdraw life-sustaining treatment (WLST) however; other factors should still be considered before the decision is made such as the patient and family's values, beliefs and current emotional and psychological states. For cardiac arrest, anoxic brain injury in itself do not lead to death as long as supportive ICU care is maintained (34). Death after cardiac arrest occurs in 60–90% after WLST (35–37). The concept of self-fulfilling prophecy, a "*prediction that directly or indirectly causes itself to become true*" also plays a role in most severe acute brain injuries (34). Current recommendations in terms of timing of prognostication, which may in turn affect the timing of WLST is to wait at least 72 hours especially in post anoxic brain injury (38). A retrospective study on intracerebral hemorrhage patients for which WLST was done, compared the median predicted probability of 1-year death and severe disability against the decision to WLST to determine if practitioners were prone to self-fulfilling prophecies when managing ICH (which included subarachnoid, subdural hematoma and intraparenchymal hemorrhage). They found that the patients who underwent WLST still would have died based on probability models which show that in ICH, it is unlikely that WLST lead to a self-fulfilling prophecy (39). It is best to avoid early WLST which has been defined as discontinuation of life sustaining therapy before 72 hours (40) especially in patients with neurologic conditions with an unpredictable course since prediction scores for several neurologic conditions vary in

their accuracy of prediction of death and disability (41–46). For patients with acute onset severe neurologic conditions especially in post-cardiac arrest patients with anoxic brain injury, although early PC involvement is encouraged, it is recommended to not transition to WLST until at least after 72 hours (47–49).

Pain management, palliative sedation (PS) and the principle of double effect

Most commonly, therapy to alleviate pain and discomfort for patients that transitioned to palliative level of care also have adverse effects which most commonly involve respiratory depression and further decrease in level of alertness in the setting of opioid or benzodiazepine use. The principle of double effect is applicable when one uses therapy with an intended beneficial effect but with an unintended foreseen harmful effect (50,51). It is important to note that comorbid pulmonary conditions that may be present in these patients may affect the response of these patients to opioids or sedation in such a way that respiratory depression may occur either in a faster rate or at a more severe degree compared to a patient without pulmonary issues. The physician's act of administering opioids is not intrinsically wrong with an intended good effect even if an adverse effect may have been anticipated however legal fears still may limit its administration (52). To apply the criteria of the Principle of Double effect in this setting the following conditions should be present: the action from which harm results is good, the intention or motivation must be sincerely good and the harmful effect is not intended, the harmful effect must be immediately due to the good effect and the proportion of the reason for the good effect should be serious enough to allow for the side-effect to occur (53–55). The principle of Double Effect also applies to PS which has been defined as the “*intentional reduction of vigilance by pharmacological means up to the point of the complete loss of consciousness with the aim of reducing or abolishing the perception of a symptom that otherwise would be intolerable for the patient despite the implementation of the most adequate means aimed at controlling the symptom itself, which is therefore to be considered refractory*” (56). It has not been shown that sedated patients' survival differs from those not sedated in the terminal phase of their condition (57–63). Indications include dyspnea, delirium (62,64–67), pain, massive bleeding or intractable vomiting (64,68) all of which are applicable to patients with neurologic conditions. Once control of symptoms is achieved, up titration of the medications should stop (69). A survey among neurologists

showed agreement that at the end stage of their disease, the practice of sedation for the terminally ill is acceptable when it was considered refractory to other interventions. However, its use on patients in the earlier stages of their disease and are not imminently dying is still controversial (64).

The use of neuromuscular blockade

Although the use of neuromuscular blockers in the intensive care unit is prevalent, most especially for management of acute respiratory failure, status asthmatics, intra-abdominal or intracranial pressure control (70), its role in PC management has not been widely studied. Even with the intent of decreasing agitation manifesting as violent extremity or truncal movement, paralyzing a patient may mask pain or other symptoms of discomfort (71) especially in patients with primary neurologic dysfunction where in their sole means of expression of pain are movements. It has been proposed however that neuromuscular blockers may be used for patients with persistent agonal respiration in spite of adequate sedation (72). These agonal breaths may be seen in patients with spastic neuromuscular conditions, or central hyperventilation syndromes due to acute brain injuries. Because of the present uncertainty on the association of gasping and the patients' level of pain or discomfort during this period, the principle of “*maximin rule*” may be applied where in a situation of uncertainty, one studies what is the worst possible scenario and what is the appropriate action that will avoid the worst case scenario (72,73). The use of neuromuscular blockers still continues to be debated and is limited and should be further studied due to the sparse availability of data.

Initiating, withholding or discontinuation of artificial nutrition and hydration

Artificial Nutrition includes oral nutritional supplements (ONS), enteral nutrition (EN) delivered through nasogastric (NG), nasogastrojejunal (NGJ), dobhoff tubes (DHT), percutaneous endoscopic gastrostomy (PEG) or jejunostomy (PEG-J) or surgical gastrostomy tubes (GT) or parenteral nutrition delivered via peripheral versus central venous lines. Artificial hydration includes water or electrolyte solutions through feeding tubes or parenteral means (74). It has been advocated by the American Association of Hospice and Palliative Medicine and the Hospice and Palliative Nurses Association that AHN in terminal stages of disease may cause an increased risk of infections, pressure sores,

diarrhea and fluid overload (75,76) supporting withholding AHN during this period. It does not offer benefit during the terminal phase of illness and it has the potential to lead to discomfort especially if feeding tubes are in place, due to the likelihood of requiring restraints for the patient awake (77-80). If able, the patient may have Oral Assisted Comfort Feeding or “food for pleasure” where the goal of adequate nutrition is no longer paramount (81). It enables the patient to once again be part of a familiar social scenario where they are in the table eating with family (82). Patients with stroke, ALS, dementia or other neurologic disorders that allows for the patient to maintain truncal stability are ideal for this routine. The role of the speech and language therapists could not be underestimated as they will assess the likelihood of aspiration to establish expectations for the family. Food modification may be required such as adding thickeners or chopping food into smaller pieces (81). Another option is positioning the patients in their room and feeding them their while the family visits. As needed fluids may be given if the patient expresses thirst (69). Mild fluid administration to avoid excessive dehydration that may contribute to delirium and metabolic intoxication is an option (83,84). For those patients who are in their final stages, a common scenario in the neuro-intensive care unit, administration of intravenous fluids or enteral feeding may result in anasarca, diarrhea and increased secretions that contradict the goals of PC (81,85). This should be clearly explained to the families to avoid unnecessary distress regarding thoughts that the patient is “being starved to death”. Food for pleasure may be continued for as long as the patient is able to without causing discomfort, with the family knowing and understanding the goals, expectations and possible outcomes if oral intake is continued at this stage. In most state laws, the right to refuse artificial hydration and nutrition (AHN) may be relinquished to a surrogate. However, in several states, legislation has been introduced which assumes that a patient in persistent vegetative state would want to continue to receive ANH and if one desires to negate this assumption in court, discontinuation of ANH may only be done when one of the following specific conditions apply: inability to administer ANH, ANH administration would hasten death, ANH cannot be absorbed, there is a specific advance directive authorizing withdrawal applicable to the current clinical condition or if there is clear evidence that the patient expressed and gave informed consent to withdraw ANH as applicable to the current condition (86). Further prospective studies are warranted to delineate limits in ANH, assess its impact on the family and patient and on

healthcare economics, and to analyze the impact of different state laws regarding AHN.

Renal replacement therapy in acute brain injury

Patients on long term dialysis represent a population of patients at risk for acute neurologic injuries including acute ischemic stroke (AIS), intracerebral hemorrhages (ICH), subarachnoid hemorrhage (SAH) and subdural hemorrhage (SDH) (87-90). They are also the same group of people that have a higher risk cardiovascular disease (89,91) that put them at risk of cardiac events that may lead to anoxic brain injuries. There are also patients with brain injury that develop acute kidney injury requiring dialysis in which decisions regarding the utility of dialysis may be in question. In these settings, recommendations from the Renal Physician Association regarding initiating or withdrawing dialysis may be utilized (92). Their most recent published update includes a prognostic model, discussion on the need to assess the patient for DMC and other treatment options and goals for these patients in consideration of their overall prognosis, situation, functional status and personal values (92). Several prognostic scoring systems may aid goals of care discussion for patients on dialysis with neurologic disorders such as iScore, PLAN score and ASTRAL Score in AIS (93); the ICH score and FUNC score for ICH (94,95) and the ALS-SS score for patients with ALS (96). Profound neurologic impairment where in the patient does not have awareness, sensation, purposeful movement or thought process is a situation where dialysis may be withheld or withdrawn (92). There may be a situation that a “time-limited trial” (97) is applicable where dialysis may be withdrawn if clinical improvement does not occur (92). This trial should be explained in terms of goals, outcome measured and duration prior to initiation to draw expectations and not cause further confusion (97,98). Utilization of this guideline, although not universal, is considered standard of care among most nephrologists (99). Further studies on how this guideline is used in the acute and long-term management of patients with neurologic disease both the inpatient and outpatient settings are needed.

Defibrillators in acute brain injury

Patients with congestive heart failure or arrhythmias that require them to have implantable cardioverter defibrillators (ICDs) and cardiac resynchronization devices with a pacemaker or defibrillator (CRT-P/CRT-D) are at risk for acute

neurologic injuries such as stroke, anoxic brain injury, ICH for those who are on anticoagulation or traumatic brain injuries for those who suffer a fall due to malfunction of these devices. The approach between the conscious and unconscious differs. The ethical principle of autonomy should be applied as well as the laws of surrogacy for those who are not cognitively intact, which is the more common scenario among patients with neurologic disorders under palliative level care. The reason behind disabling implantable devices such as CRT is that it may activate a shock at the end-stage of the patient's disease that may cause pain, distress, anxiety and decreased quality of life (100,101). Discontinuing a device that acts as a pacemaker or an inotrope may pose as a challenge because stopping these may actually cause death however, it has been recommended to manage these situations just like how one would manage discontinuation of mechanical ventilation for a patient with respiratory failure (101) in that the patient still goes through the natural course of death but the discontinuation of mechanical ventilation is not considered as the direct cause of death. Discussion on deactivation should follow the thorough process of informed consent where options are weighed with risk and benefits. When the decision is made to deactivate the device, a do-not-resuscitate (DNR) status should also be agreed upon (101). Further prospective studies are warranted to gain more information regarding patients with neurological disorders and implantable cardiac devices and how it impacts PC management.

Donation after cardiac death

Patients in the neuro-intensive care unit who don't meet brain death criteria may still be able to donate organs through the process of "donation after cardiac death" or "DCD" (13). Even if the families would want to transition to PC, early involvement of organ procurement organization (OPO) will enable the family to consider this option, especially if the patient is a registered organ donor. It is essential however that organ donation is not brought up by any member of the primary team. Organ donation conversations require specific wording due to the sensitivity and implications of the process. Some members of the primary team may not be familiar with the process and how to answer questions and may cause miscommunication and distress on the family. The decision making on WLST should not be dependent on DCD or vice versa (13) although the involvement of a multidisciplinary team including the OPO staff and PC specialist is encouraged throughout the process to offer support and answer questions. Depending on the institution, immediate family members may

be allowed in the surgical area to witness terminal extubation. The family should be informed that if cardiac death does not occur usually within 60 minutes of extubation, the patient is no longer a suitable donor and will be returned to the ICU for further end-of-life care (102) for which symptom control ensues to make the patient comfortable.

Seizures and status epilepticus

Patients at risk for seizures and status epilepticus include those with primary intracranial pathologies such as AIS, ICH, CNS malignancies, CNS infection or anoxic brain injury. Seizures are a "transient occurrence of signs or symptoms due to abnormal excessive or synchronous neuronal activity in the brain" (103). Status epilepticus is defined as seizures longer than 5 minutes or recurrent seizures without return to baseline (104) while refractory status epilepticus is status epilepticus that require further treatment after not responding to first- and second-line therapy of appropriate doses (104). Seizures may involve only a part or parts of the body while the patient maintains consciousness (focal or partial) or may involve the whole body impairing consciousness (generalized). Seizures may also start partial then progresses to being generalized (partial seizure with secondary generalization). More importantly, they are also classified according to the presence or absence of actual convulsions (Convulsive versus Non-Convulsive). Note that a patient that is in generalized convulsive status epilepticus may progress to a non-convulsive status epilepticus (NCSE) when only subtle twitches are noticeable due to the inability of the body to create strong muscle movements (104) or NCSE may present as delirium or change in mental status (105). The incidence of SE in the PC setting is not well established (106). Once transitioned to palliative level of care, there are limits imposed by the goals of care that will affect diagnostic and therapeutic management that should be discussed with the family especially since the available diagnostic and therapeutic algorithms available do not consider patient under PC (106,107) and the goals of PC largely differs from the curative goal of established guidelines. It is important however to delineate these limits as some families may want to still restore pre-SE baseline which will affect the management of SE (108). Anti-epileptic drugs (AED) should be continued in patients who are already on AEDs prior to transition to palliative level of care as it has been shown in a cohort of patients with high grade glioma that 35% of the patients for which it was tapered, seizures did occur (109)

and this may cause difficulty in symptom management. This may be a common scenario for CNS malignancies (109) or those who were already having seizures before the change in goals of care. The focus of seizure management in PC is on decreasing or alleviating the discomfort caused by seizures and may require medication dosages and routes that are usually not utilized for patients not under PC (109). As management for seizures ensue, concurrent management of other symptoms such as spasticity, increased secretions, pain and respiratory discomfort should continue (110,111). A proposed algorithm for management of patients with status epilepticus in the PC setting is shown in *Figure 1*. Because of the anticipated adverse effects of these medications, underlying principles of PS should be applied. Continued discussion with the family regarding goals of care should be done. The doctrine of double effect may serve as a guide to ethically manage status epilepticus in the PC setting. Further prospective studies should be done to guide management of status epilepticus in the setting of palliative level of care.

Tracheostomy placement

Tracheostomies are commonly done in several neurologic disorders. In the neuro-intensive care unit, this procedure is usually indicated for those patients who are unable to protect their airway due to the underlying brain injury and those who are unable to wean from the ventilator but require long-term mechanical ventilation (112). These patients include but are not limited to stroke (112), traumatic brain injuries (113), spinal cord injuries and neuromuscular disorders such as myasthenia gravis (114) or Guillain-Barré Syndrome (115). In the outpatient setting among patients with ALS, certain parameters such as a forced vital capacity of $\leq 50\%$ trigger discussion regarding tracheostomy with invasive ventilation that has been shown to prolong survival but also are associated with more expense and an increased caregiver burden (116). There is no consensus regarding the timing of discussing tracheostomy placement in these disorders however various predictors have been published to guide physicians in discussing the likelihood of tracheostomy (112,115,117). Multiple factors eventually play a role in the final decision to proceed with a tracheostomy including the providers' own views, the hospital's practice, financial incentive, but most importantly the patients' wishes expressed through the family (118). PC involvement is encouraged as early as possible to be part of the decision making even after tracheostomy. A retrospective study among TBI patients

under PC showed that 65% of the patients under PC received a tracheostomy (119). This indicates that even with tracheostomy placement, PC involvement should continue. On the other hand, it has been shown that involvement of PC decreased performance of tracheostomy (118,120). The approach to the decision making should be balanced with what we know of the outcome of the underlying condition, patient comorbidities, what is uncertain regarding the prognosis, the risk and benefits of tracheostomy and how it may affect the patient and caregiver quality of life.

Feeding tube placement

Feeding tube placement among patients with neurological disorders are common most especially when dysphagia results from the disease. It encompasses several tubes including an NGT, DHT which are usually not for long-term use and , PEG tubes or PEG-J tubes or surgical GT which may be used long-term and in the outpatient setting. For a patient to be able to have oral nutritional intake, they have to have intact level of consciousness, a learned ability to eat, adequate truncal and axial tone, proper coordination of neural mechanisms for swallowing, intact oral and nasal passage with a functional oro-digestive and respiratory tract. Neurologic disorders can potentially affect any of these key requirements for safe oral intake. Intracranial lesions can affect the level of consciousness to make it unable for patients to open their mouth, follow commands or use their basic known skills to eat, patients with spinal cord injuries in the acute phase may not be adequately be able to position themselves, patients with neuromuscular disorders have impaired tone that affect their oro-digestive tract. It has been shown that dysphagia is a predictor of transitioning to palliative level of care among stroke patients (121). The interaction between the ability to swallow, the decision to place a feeding tube and the decision to transition to palliative level of care has not been studied well. It has been shown that GT was an independent predictor of increased length of stay in a PC center (122). It has been shown as well that mortality after GT placement is high, although not directly related to GT placement, that PC involvement is strongly encouraged to discuss goals of care prior to GT placement (123). Decision making on PEG tube placement is not straightforward especially in patients with ALS where GT placement is recommended to stabilize weight and prolong survival (11) although the timing is still unclear. A recent report on GT placement for patients with prion disease was done and found that their tolerance of the procedure is similar to what has been published in literature for other

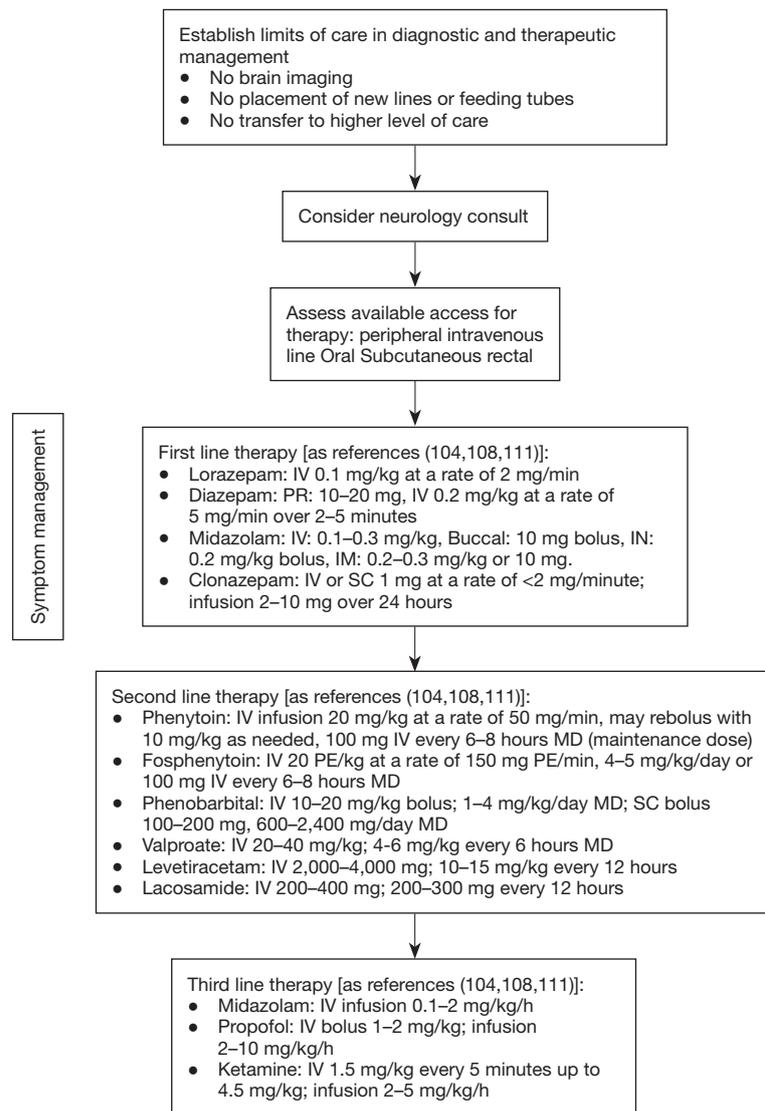


Figure 1 Palliative care approach to status epilepticus (104,108,111).

conditions (124). It is important to be clear what is the effect or lack thereof of gastrostomy tube placement on the outcome of the disease based on evidence and to be transparent with potential complications. PC involvement should be continued even after GT placement because these patients will still require continued support through the course of their disease.

Disease specific considerations in PC management of patients with neurologic disorders

Several disease specific considerations are worth noting

(Table 1). Patients with a focal neurologic lesion such as an ischemic stroke will have specific neurologic deficits that may pose as a challenge in management under PC. More importantly, there are stroke syndromes by which the level of consciousness and ability to communicate are directly affected. Several examples of these stroke syndromes are presented in Table 1 of note however; “stroke-like” syndromes with a similar presentation may be seen if the intracranial lesion affects a similar area compared to the vascular territory of the stroke. The patient in a vegetative and minimally conscious state is specifically shown due to the implications in PC management. It is

Table 1 Disease specific considerations in palliative care management of patients with neurologic disorders

Neurologic disorder	Special considerations
Malignant left middle cerebral artery ischemic stroke	<p>Aphasia specifically makes these patients unable to effectively communicate their needs nor responses to simple questions. They are usually unable to follow commands. They have the tendency to be agitated due to frustration about the inability to communicate</p> <p>Right sided hemiplegia in the acute phase may be flaccid and may progress to spastic hemiplegia</p> <p>Right homonymous hemianopia should be considered when the patient is not attending towards the right side. Attempts to communicating with the patient should be done from the left visual field</p>
Malignant right middle cerebral artery ischemic stroke	<p>Hemispatial neglect may cause the patient to not be aware of the position of their extremities which should be considered when evaluating for pain (125) source or pressure sores</p> <p>Silent aspiration risk is higher in these patients and their trigger for a cough reflex is decreased. An increased awareness of pooling of secretions is warranted</p> <p>Left sided hemiplegia in the acute phase may be flaccid and may progress to spastic hemiplegia</p>
Vertebra-basilar artery stroke	<p>If complete or extensive, may involve bilateral thalamus and midbrain impairing consciousness. These patients will not be able to communicate their needs</p> <p>For anterior pontine or midbrain involvement only with spared reticular activating system, these patients are considered “locked-in” and may be able to communicate by using vertical eye movements. Their higher cortical functions are intact which make them able to feel and interpret pain compared to comatose patients</p> <p>They will have impaired secretion management and may have weak to no cough</p> <p>Quadriplegia may initially be flaccid then progress to spastic</p> <p>Prominent dysphagia is highly likely that early tracheostomy and gastrostomy are usually done</p>
Posterior cerebral artery stroke	<p>Visual cortex involvement makes the patient prone to hallucinations or seizures that present as hallucinations</p> <p>Hemi-visual field cut may make difficulty looking at the caregiver. Modifications in positioning oneself should be done during conversations or when asking the patient to move on one side</p>
Vegetative state	<p>Patient may be awake with eyes open but is not aware of self or environment and electroencephalography may reveal sleep-wake cycles (125)</p> <p>“Persistent” is used if vegetative for more than a month and “permanent” if vegetative for more than 3 months</p> <p>May evolve into minimally conscious state especially if the patient is not yet in “permanent vegetative state” (125-127)</p> <p>Important to consider etiology, i.e., traumatic brain injury is more favorable than anoxic injury in terms of outcome (128)</p>
Minimally conscious state	<p>Patient able to attend, track, speak intermittently and have purposeful behaviors, follow commands inconsistently but repeatedly (125-127)</p> <p>May feel pain compared to vegetative state (126)</p>
Creutzfeldt-Jakob disease (CJD)	<p>Most common type is sporadic CJD for which patients are found to have progressive dementia, visual and cerebellar abnormalities, myoclonus then eventual akinetic mutism</p> <p>Median survival times range from 4.6 to 17.4 months (129)</p> <p>Requires very close collaboration with Psychiatry and Neurology due to prominence of psychiatric and neurologic symptomatology such as severe dementia, rigidity and myoclonus (130)</p> <p>Gastrostomy placement in these patients have been reported (124)</p>

Table 1 (continued)

Table 1 (continued)

Neurologic disorder	Special considerations
Amyotrophic Lateral Sclerosis (ALS)	Chronic, irreversible motor neuron disease Cognitive dysfunction may be seen for those with concomitant Fronto-Temporal-Dementia (131) Tracheostomy and gastrostomy has been found to prolong survival (11,116)
Multiple sclerosis (MS)	Chronic, progressive, inflammatory, autoimmune process primarily affecting the CNS white matter (132) Timing of palliative care (PC) involvement not well established, however it has been recommended that for patients with Expanded Disability Status Scale (133) of >6 and when nursing care is required, PC involvement should be started Patients will eventually progress to advanced stages where the patient is cognitively impaired with multi-organ failure (134)
Parkinson's disease (PD) and parkinsonian syndromes	Progressive irreversible disease Motor (bradykinesia, cogwheel rigidity and resting tremor) and non-motor symptoms (autonomic dysfunction, depression, fatigue and pain) Prominent visual hallucinations for patients for Lewy Body Dementia (135) Parkinsonian syndromes have little or no response to dopaminergic agents, thus will have a much more rapid neurologic decline compared to PD (136,137)
Alzheimer's disease and other dementia	Probability of patient with AD to suffer at least one episode of pneumonia is >40% (138) Gastrostomy tube placement have been associated with higher mortality (123)
Central nervous system malignancies	Propensity for seizures and status epilepticus Neurologic deficits based on location of tumor Brain tumors may have a high risk of hemorrhage Palliative resection, stereotactic surgery and brain radiation have a role (139-141)

CNS, central nervous system; PC, palliative care involvement.

important to emphasize that patients who are minimally conscious may have intact pain sensation (126). Note that several mechanisms of injury that lead to these states have implications on outcome which are beyond the scope of this review however as an example, a vegetative state due to TBI may have a better outcome than a patient with an anoxic brain injury (128). Although uncommon, CJD may pose as a challenge in PC management due to its fatal course, staff unfamiliarity with the disease and its transmission and the prominence of severe psychiatric and neurologic symptoms towards its terminal stages (130). ALS is one of the well-studied neurologic conditions in terms of PC management although similar to MS, PD and AD; the timing of PC involvement is still unclear. Unique to this group however is that it has been recommended that they undergo tracheostomy and gastrostomy for prolonged survival (11,116). This recommendation is not applicable to

other chronic neurodegenerative or progressive disorders. Common to these conditions is cognitive impairment either as a part of the progression of disease (MS) or as a variant of the disease (ALS with Fronto-Temporal-Dementia or parkinsonian syndrome with Lewy Body Dementia) (131,134). These have implications on limitations of communication and expression of pain or discomfort. The challenge in managing AD, a chronic progressive cognitive disorder is that they usually have comorbidities that make them prone to multiple hospitalizations. Proactive discussion and early involvement of PC teams may play a role in improving their overall quality of life (138). Aside from the general challenges experienced in the PC management of patients with CNS malignancies, one specific consideration for these patients are steroid and AED tapering at the end-stage of their illness. If steroids are tapered, it may be helpful to increase the dose of the

AED. If the patient develops seizures or progress to status epilepticus, they should be managed accordingly as part of PC (Figure 1). Neurology consult may be warranted.

Conclusions

There is an overall increase in awareness and research on the role of PC in the management of patients with neurologic disorders. There are however unique challenges and ethical issues that are important to consider in the management of these patients. Further prospective studies are warranted to examine the effect of PC management on patient and family outcome as well as studies to systematically analyze other means to improve PC utilization among patients with neurologic conditions.

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Footnote

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