Prevention and Management of Poststroke Complications

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ABSTRACT

Purpose of Review: This article provides a synopsis of the immediate and delayed medical complications of stroke, with an emphasis on prevention and management of these complications.

Recent Findings: Meta-analysis of the trials for endovascular treatment of acute stroke shows no significant increase in hemorrhagic events. Rehabilitation guidelines published by the American Heart Association and American Stroke Association in 2016 aid in providing the best clinical practice for patients with stroke, from the time of their initial hospitalization to their return to the community.

Summary: Medical complications from stroke are common and are associated with poor clinical outcomes, increased length of hospital stays and higher rates of readmission, increased cost of care, delayed time to rehabilitation, and increased mortality. Being cognizant of the common complications encountered, taking appropriate measures to prevent them, and knowing how to manage them when they do occur are essential to the continued care of patients with stroke.

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INTRODUCTION

Medical complications following acute ischemic stroke are common and are associated with poor clinical outcomes, increased length of hospital stay and higher rates of readmission, increased cost of care, delayed time to rehabilitation, and increased mortality.[1] While the majority of deaths that occur in the first week after stroke are attributed to the direct effects of the ischemic stroke, mortality beyond the first week is largely attributed to medical complications.[2,3] This article discusses measures that should be used to reduce the risk and rate of these complications following acute stroke.

EARLY COMPLICATIONS

Sequelae from acute ischemic stroke occurring in the initial days to weeks following the event are frequently encountered in the hospital setting. These issues can influence the clinician's decision for level of care on admission, duration of hospital stay, and hospital disposition.

Acute Reperfusion Therapy

Orolingual angioedema from IV recombinant tissue plasminogen activator (rtPA) is uncommon, occurring in 1% to 8% of patients, and is often mild and transient. The risk is increased in patients concurrently taking angiotensin-converting enzyme inhibitors and in those with CT findings of ischemia in the frontal or insular cortices.[4] Orolingual angioedema is usually unilateral and affects the tongue and lips contralateral to the ischemic hemisphere. Angioedema and anaphylaxis

KEY POINT

- Angioedema resulting from use of recombinant tissue plasminogen activator often involves the unilateral tongue and lips contralateral to the side of the infarct. It is often mild and transient, but in severe cases, IV recombinant tissue plasminogen activator should be stopped immediately and anaphylaxis appropriately treated.

have been reported up to 2 hours following IV rtPA infusion, and swelling can develop gradually over several hours. In cases of life-threatening angioedema, laryngospasm, and hypotension, the infusion should be stopped immediately and the patient treated with antihistamines, IV corticosteroids, epinephrine, and endotracheal intubation for airway protection as clinically indicated. Favored treatment is 50 mg IV diphenhydramine, 50 mg IV ranitidine, and 10 mg IV dexamethasone. In severe cases or as clinically indicated, 0.3 mg IM epinephrine can be added.[5] Short-term maintenance doses of corticosteroids and antihistamines can be considered in cases of severe edema that fail to promptly respond to the first doses of medications.

In the National Institute of Neurological Disorders and Strokes (NINDS) trial, symptomatic intracranial hemorrhage was defined as hemorrhage seen on CT within 36 hours of treatment, and deemed to be temporally related to neurologic decline.[6] Symptomatic intracranial hemorrhage occurred in 6.4% of patients treated with IV rtPA. The European Cooperative Acute Stroke Study (ECASS) III trial defined symptomatic intracranial hemorrhage as evidence of hemorrhage seen on CT or MRI that was felt to be associated with an increase in the National Institutes of Health Stroke Scale (NIHSS) score of 4 or more points.[7] Symptomatic intracranial hemorrhage occurred in 2.4% of patients treated with IV rtPA in the extended treatment time window of 3 to 4.5 hours.

Figure 5-1 demonstrates the subtypes of hemorrhagic transformation defined by the ECASS I investigators.[8] The four subtypes are: (1) hemorrhagic infarction 1, with scattered heterogeneous petechiae along the margins of the infarct; (2) hemorrhagic infarction 2, with more confluent but still heterogeneous petechiae within the infarct; (3) parenchymal hematoma 1, with a homogeneous hematoma involving less than 30% of the infarct volume and with mild space-occupying effect; and (4) parenchymal hematoma 2, with a dense hematoma involving more than 30% of the infarct volume with significant space-occupying effect (**Table 5-1**). Hemorrhagic infarction 1, hemorrhagic infarction 2, and parenchymal hematoma 1 within the first 36 hours of stroke onset were not associated with a higher risk of neurologic decline when compared to patients without hemorrhagic transformation. Parenchymal hematoma 2 is associated with a significantly increased risk of early deterioration and 3-month mortality.

Most symptomatic intracranial hemorrhages occur within the first 24 hours following treatment. When intracranial hemorrhage is suspected, the administration of thrombolytics should be stopped until intracranial hemorrhage is excluded. Once intracranial hemorrhage is confirmed on imaging, an initial dose of 10 units of cryoprecipitate should be transfused.[9,10] If cryoprecipitate is contraindicated or unavailable in a timely fashion, consideration can be made to use an antifibrinolytic agent, such as IV tranexamic acid 10 mg/kg to 15 mg/kg over 20 minutes or IV ε-aminocaproic acid 5 g.[10] Fibrinogen levels can be checked after administering reversal agents; if the level is less than 150 mg/dL, additional cryoprecipitate can be given. The benefit of using other agents, such as prothrombin complex concentrate, fibrinogen, platelets, or fresh frozen plasma, is unknown, and further studies are warranted. Surgical intervention can be considered in select patients when the rtPA has been adequately reversed. **Case 5-1** provides an

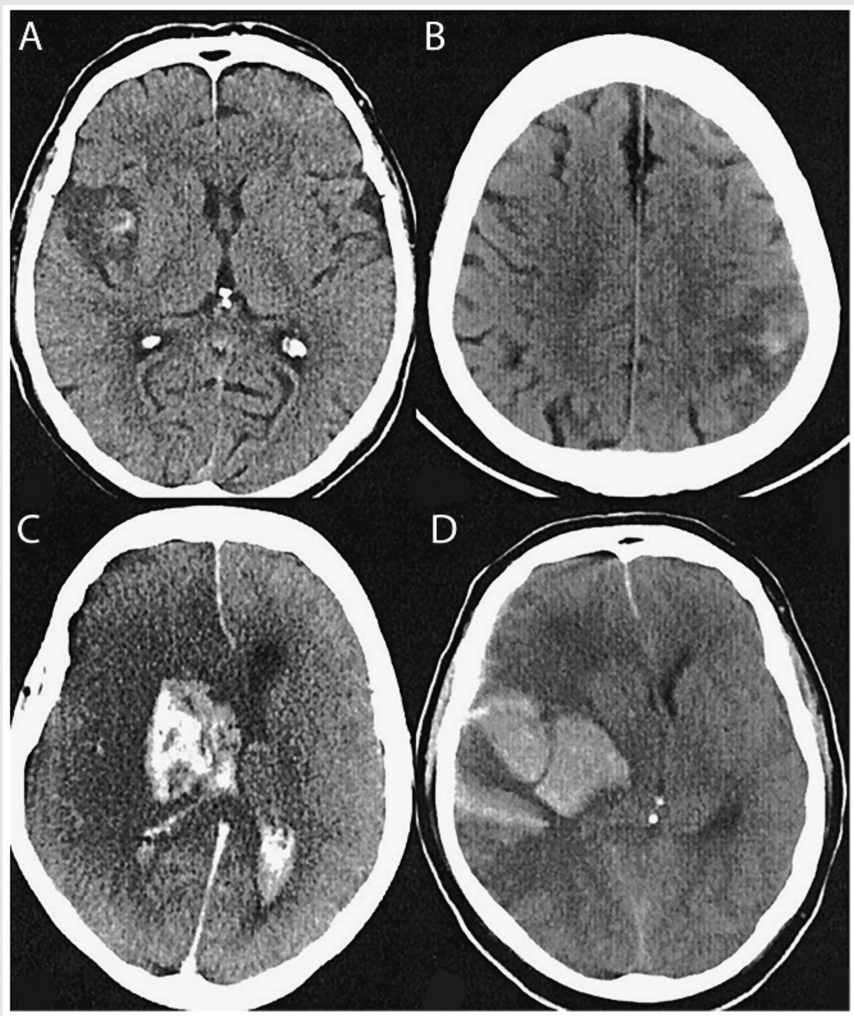

FIGURE 5-1 Subtypes of hemorrhagic transformation. *A*, Hemorrhagic infarction 1, *B*, hemorrhagic infarction 2, *C*, parenchymal hematoma 1, and *D*, parenchymal hematoma 2.

Reprinted with permission from Berger C, et al, Stroke.[8] © 2001 American Heart Association, Inc. *stroke.ahajournals.org/content/32/6/1330.full*.

example of the evaluation and treatment of suspected symptomatic intracranial hemorrhage.

The risk of hemorrhage following administration of IV rtPA is increased in patients with higher stroke severity and older age. Other factors associated with an increased risk of symptomatic hemorrhage include heart failure, ischemic heart disease, atrial fibrillation, hyperglycemia, diabetes mellitus, renal impairment, hypertension in the first 24 hours, preceding antithrombotic use, thrombocytopenia, leukoaraiosis (cerebral white matter disease), and persistent arterial occlusion after IV rtPA infusion.[11] However, given the low rate of hemorrhage and higher potential for improved outcomes with thrombolytic therapy, these factors do not preclude the patient from receiving treatment. Care must be taken to follow posttreatment protocols to minimize the risk of hemorrhage.

The Highly Effective Reperfusion Evaluated in Multiple Endovascular

TABLE 5-1 Hemorrhagic Transformation Subtypes

Subtype		CT Findings
Hemorrhagic infarction	1	Heterogeneous petechiae along the infarct margins
	2	More confluent heterogeneous petechiae within the infarct
Parenchymal hematoma	1	Homogeneous hematoma involving <30% of the infarct volume; mild space-occupying effect
	2	Homogeneous hematoma involving >30% of the infarct volume; significant space-occupying effect

CT = computed tomography.

Case 5-1

A 77-year-old man with hypertension, type 2 diabetes mellitus, and obesity presented to the emergency department at 10:38 AM with acute onset of left-sided weakness that occurred at 9:45 AM. Examination revealed a mild left hemiparesis with severe left-sided sensory loss and neglect, with a National Institutes of Health Stroke Scale (NIHSS) score of 9. His wife reported he was taking a daily aspirin 81 mg and had no history of anticoagulant use. Head CT showed no evidence of intracranial hemorrhage or early ischemic changes. His presenting blood pressure was 210/98 mm Hg, which was controlled and maintained below 180/105 mm Hg with a nicardipine infusion. IV recombinant tissue plasminogen activator (rtPA) was administered at 11:17 AM. CT angiogram showed occlusion of a distal left M2 branch of the middle cerebral artery and thrombi in several distal M3 branches, but no proximal large vessel occlusion was identified that would be amenable to thrombectomy. After returning from the CT angiogram, the patient began grimacing and held his head with his right hand. At 11:42 AM , his nurse then noted that his left facial droop had worsened and the patient seemed more confused and lethargic. Upon reexamination, he was noted to have a dense left hemiplegia with right gaze deviation. He was no longer arousable to vocal stimulus, and his repeat NIHSS score was 20. The IV rtPA infusion was stopped and a repeat head CT was performed, which demonstrated a 32 mL intraparenchymal hematoma in the right frontoparietal lobe with mass effect and midline shift. A complete blood cell count, prothrombin time, international normalized ratio (INR), activated partial thromboplastin time, fibrinogen, D-dimer, and type and screen were drawn. The patient was intubated, cryoprecipitate was started, and neurosurgery was called.

Comment. In this case, the patient had neurologic deterioration secondary to suspected intracranial hemorrhage, and the IV rtPA was stopped immediately. Airway, breathing, and circulation must be continuously addressed as a patient's clinical decline can be rapid. Cryoprecipitate is recommended to restore decreased fibrinogen levels, but no study has been conducted to establish the optimal way to treat post-rtPA hemorrhage; further studies are warranted.

Stroke (HERMES) meta-analysis of pooled data of 1287 patients from five randomized trials of endovascular thrombectomy of large vessel occlusions showed no significant difference in rates of symptomatic intracranial hemorrhage between those who underwent thrombectomy and patients who received standard care.[12]

A single-center retrospective study of patients with acute ischemic stroke who underwent thrombectomy with stent retriever between 2010 and 2012 demonstrated that a low baseline Alberta Stroke Program Early CT Score (ASPECTS) independently predicted symptomatic intracranial hemorrhage at 24 hours (5.0 versus 6.9).[13] It also found that the independent factors of atrial fibrillation on admission and hemodynamic instability during the procedure were associated with intracranial hemorrhage at 24 hours.

Malignant Cerebral Edema

An estimated 5% to 10% of patients with ischemic stroke may develop malignant cerebral edema.[14] Neurologic deterioration is often observed within 72 to 96 hours from onset of the stroke.[15] It is important to identify patients who are at high risk of developing this complication to ensure that they are placed under close surveillance at a center with neurologic critical care and neurosurgery services.[16] Frequent neurologic examinations are necessary to monitor for a decreased level of arousal, which may be the earliest clinical change indicating symptomatic cerebral edema and thus necessitating medical and possible surgical treatment.[17] The increased somnolence can precede pupillary changes and worsened motor function and is attributed to tissue swelling and shift of the thalamus and brainstem rather than due to a significant increase in intracranial pressure.[18]

Patients at the highest risk for developing malignant cerebral edema are those who have an identified large vessel occlusion of the terminal internal carotid artery or proximal middle cerebral artery with a large infarct volume (**Case 5-2**).[19–21] Head CT with frank hypodensity within 6 hours of stroke onset, infarct in one-third or more of the middle cerebral artery territory, or midline shift of 5 mm or more in the first 2 days are predictive of malignant edema and poor outcomes.[22–25] Diffusion-weighted MRI volume of 80 mL or more within 6 hours of stroke onset is predictive of a rapid fulminant course toward malignant edema.[20,26]

An NIHSS score greater than 20 in dominant hemispheric strokes or greater than 15 in nondominant hemispheric strokes has been associated with malignant infarction, but the scores alone have low specificity in predicting the development of a malignant syndrome.[22] Other clinical factors associated with edema are early nausea and vomiting, female sex, congestive heart failure, and leukocytosis[22,23] at presentation.

Medical management of patients who are at high risk for progression to malignant cerebral edema includes frequent neurologic examinations to monitor for neurologic deterioration, maintenance of normothermia, avoidance of hypercarbia, maintenance of euvolemia while avoiding hypotonic solutions, control of glucose to between 140 mg/dL and 180 mg/dL, and correction of hyponatremia.[16]

Initiation of osmotic therapy is indicated in patients with clinical and radiographic evidence of swelling. Choosing the appropriate osmotic therapy may depend on individual patient characteristics. Mannitol can be given at 0.5 g/kg to 1 g/kg IV every 4 to 6 hours.[16] Continued

Case 5-2

A 62-year-old man with no known medical history was teaching a class when he suddenly became dizzy and collapsed without loss of consciousness. On arrival to the emergency department, his neurologic examination revealed right hemiplegia, left gaze deviation, and mutism. His National Institutes of Health Stroke Scale (NIHSS) score was 26. Head CT within 40 minutes of symptom onset showed a hyperdense left middle cerebral artery sign and early ischemic changes in the left hemisphere. He was given IV recombinant tissue plasminogen activator and transferred to a certified stroke center for potential thrombectomy. Due to local weather conditions, his transfer was delayed, and a repeat head CT 4 hours after symptom onset demonstrated early ischemic changes in a larger area of the left hemisphere. Angiography revealed a distal left M1 occlusion. Postthrombectomy, the M1 was recanalized, but there were multiple M2 branch occlusions. Repeat head CT the following day showed continued evolution of the infarct without significant midline shift (**Figure 5-2A**). His wife was updated with the results, and the possibility of decompressive craniectomy was discussed in detail. The following morning, the patient was difficult to arouse, and the repeat head CT demonstrated 7 mm of midline shift with increasing vasogenic edema (**Figure 5-2B**). He was taken for emergent decompressive craniectomy. The postoperative head CT showed improvement of the midline shift (**Figure 5-2C**).

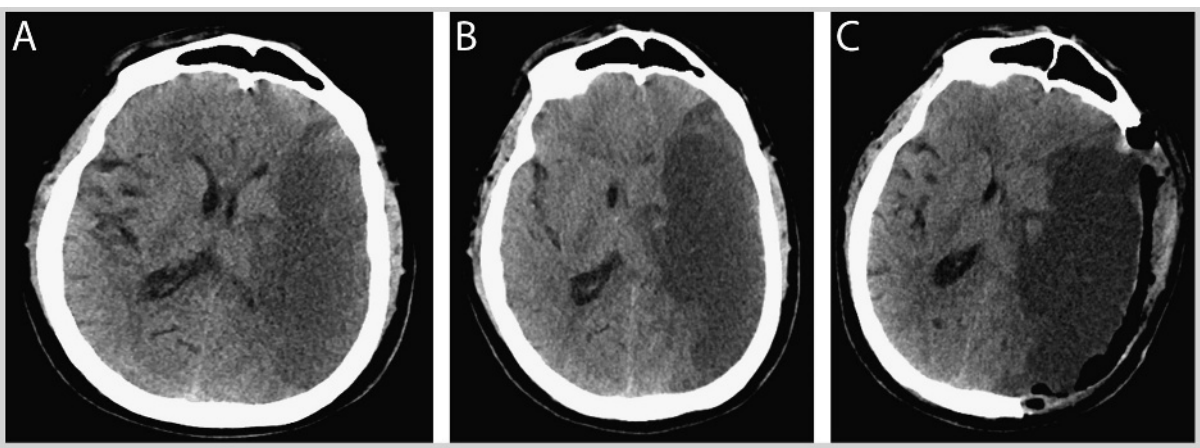

FIGURE 5-2 Imaging of the patient in **Case 5-2**. *A*, Head CT 1 day after stroke shows continued evolution of the infarct without significant midline shift. *B*, Repeat head CT the following day shows 7 mm of midline shift with increasing vasogenic edema. *C*, Head CT following decompressive craniectomy shows improvement of midline shift.

Comment. In this case, the patient had a proximal large vessel occlusion, large infarct volume greater than one-third of the left middle cerebral artery territory, and an NIHSS score greater than 20. The presence of these factors indicated the possibility of progression toward malignant edema, and early discussions with his wife helped to define the goals of care before the patient decompensated the following day.

treatment can be guided by goal serum osmolarity between 310 mOsm/L and 320 mOsm/L or by goal osmolar gap of less than 10. Potential exists for mannitol toxicity to the renal tubular cells, so renal impairment is a relative contraindication. Because of its diuretic effects, mannitol therapy can result in hypotension and hypovolemia. Hypertonic saline can be given in different concentrations, with goal serum sodium of 150 mEq/L to 155 mEq/L. Use of hypertonic saline can cause volume overload, so it should be used with caution in patients with heart failure.

Early discussions should take place with the neurosurgical team and the patient's medical decision maker regarding the potential for a decompressive hemicraniectomy.[16] A pooled analysis of three randomized controlled trials (Decompressive Craniectomy in Malignant Middle Cerebral Artery Infarcts [DECIMAL], Decompressive Surgery for the Treatment of Malignant Infarction of the Middle Cerebral Artery [DESTINY], and Hemicraniectomy After Middle Cerebral Artery Infarction With Life-threatening Edema Trial [HAMLET]) of patients younger than 60 years of age demonstrated that the number needed to treat for survival with a modified Rankin Scale (mRS) score of 4 or less was 2 and for survival with an mRS score of 3 or less was 4.[27] The results demonstrated decreased death and disability, but no patients had complete freedom from disability. DESTINY II evaluated decompressive hemicraniectomy in patients older than 60 years of age,[28] demonstrating a significant increase in survival, but most survivors had significant disability. It is notable that no patients had an mRS score of 2 or less, and outcomes were less favorable when compared to their younger counterparts from the prior studies. The discussion with family and medical decision makers should include realistic expectations for level of disability following surgery. Patients younger than 60 years of age who deteriorate within 48 hours due to malignant cerebral edema despite medical management should be considered for decompressive hemicraniectomy. Outcomes from decompression at a later time are not known, but the procedure should be considered.[16] In patients older than 60 years of age, careful selection of those with excellent prior baseline function and few or no major comorbidities can be considered.

Venous Thromboembolism

The estimated incidence of pulmonary embolism in the first few months following a stroke is between 1% and 3%,[29] but up to 13% to 25% of early deaths after stroke are due to pulmonary embolism.[30] Fatal pulmonary embolism is uncommon in the first week following an acute stroke and most commonly encountered in weeks 2 to 4.

The development of a deep venous thrombosis (DVT) may take place as early as day 2 after stroke onset, with a peak incidence between days 2 and 7.[30] The incidence of DVT in immobile patients with stroke was between 11% and 15% of patients within the first month of stroke in the Clots in Legs or Stockings After Stroke (CLOTS) observational study.[31] Risk factors for the development of DVT include severity of impaired mobility, dehydration, advanced age, malignancy, prior history of DVT, and clotting disorders.[32] Early mobilization is encouraged in patients who can tolerate activity to decrease the risk of venous thromboembolism.

In patients with stroke with restricted mobility, chemical DVT prophylaxis should be initiated at the time of presentation if they do not receive thrombolytic therapy. Either subcutaneous low-molecular-weight heparin or subcutaneous unfractionated heparin should be started immediately in patients without significant risk for bleeding. A systematic review of randomized controlled trials comparing administration of either low-molecular-weight heparin or unfractionated heparin with controls suggested that low-dose low-molecular-weight heparin provided the best benefit to risk ratio for venous thromboembolism prophylaxis, reducing the risk of DVT and pulmonary embolism with no significant increase in risk of major hemorrhagic events.[33] The PREvention of

KEY POINTS

- The peak incidence of deep venous thrombosis formation is in the first week after stroke, while pulmonary embolism is most commonly seen in weeks 2 to 4. Prevention of deep venous thrombosis and pulmonary embolism starts with early initiation of venous thromboembolism prophylaxis.
- Patients with stroke who are at high risk of developing deep venous thrombosis and pulmonary embolism include those who are immobilized, dehydrated, or elderly and those who have a history of malignancy, previous deep venous thrombosis, or clotting disorders.

KEY POINT

- Contraindications to unfractionated heparin or low-molecular-weight heparin for deep venous thrombosis prophylaxis or therapy for symptomatic deep venous thrombosis or pulmonary embolism include intracranial hemorrhage, recent thrombolytic therapy, and active extracranial hemorrhage. Alternatives include intermittent pneumatic compression or aspirin for prophylaxis and inferior vena cava filter or surgical embolectomy for symptomatic deep venous thrombosis or pulmonary embolism.

VTE [venous thromboembolism] After Acute Ischemic Stroke With LMWH [low-molecular-weight heparin] Enoxaparin (PREVAIL) study demonstrated a significantly lower rate of venous thromboembolism without a significant increase in major hemorrhagic events in patients treated with 40 mg/d enoxaparin versus 5000 IU unfractionated heparin 2 times a day.[34] A meta-analysis of three randomized trials demonstrated that low-molecular-weight heparin was superior to unfractionated heparin for venous thromboembolism prevention without a significant difference for rates of intracranial hemorrhage, overall hemorrhage, or mortality.[35]

In patients receiving IV rtPA, the initiation of heparin prophylaxis should be delayed until 24 hours after thrombolytic therapy, and the therapy is recommended to be continued during the hospitalization or until the patient regains mobility.[9]

For patients presenting with an intracerebral hemorrhage, intermittent pneumatic compression devices should be used on the day of admission. Once the cessation of bleeding is confirmed, a low dose of low-molecular-weight heparin or unfractionated heparin can be considered for patients with restricted mobility after 1 to 4 days following the event.[36] **Table 5-2** provides examples of DVT prophylaxis in different clinical scenarios.

For patients with contraindications for heparin use, intermittent pneumatic compression devices can be used. The use of intermittent pneumatic compression has been demonstrated to be effective in DVT prevention in immobilized patients with stroke.[31] Contraindications to intermittent pneumatic compression include peripheral vascular disease causing leg ischemia, leg ulcerations, dermatitis, and severe leg edema. Aspirin is also reasonable for DVT prophylaxis in patients who cannot receive heparin or intermittent pneumatic compression.[9]

Therapeutic anticoagulation is recommended for patients who are found to have a symptomatic proximal DVT, since pulmonary embolism can occur in 50% of patients if untreated. Untreated acute pulmonary embolism has a 30% mortality rate, with most deaths occurring within the first few hours after the initial event due to recurrent pulmonary embolism. Risks associated with anticoagulation include hemorrhagic transformation of ischemic stroke, hematoma expansion or recurrent bleeding in patients with intracranial hemorrhage, or extracranial hemorrhage. These risks must be carefully weighed against the benefits when considering therapeutic anticoagulation.

In patients who are not suitable candidates for anticoagulation, inferior vena cava filter placement is an option. For large or severe acute pulmonary embolism in patients unable to receive anticoagulation, catheter or surgical embolectomy is also a treatment option. For symptomatic distal DVTs, anticoagulation can be considered in patients who are felt to be at high risk for proximal extension of the thrombus. If anticoagulation is not pursued, serial noninvasive vascular imaging can be performed to assess for proximal extension of the DVT in the first 2 weeks.

Dysphagia and Nutritional Considerations

Many patients cannot receive fluids or nutrition orally because of dysphagia or impaired mental status. Dysphagia is commonly encountered following stroke, and the risk is increased in patients who are male; are older than 70 years of age; have had severe stroke; or have impaired pharyngeal

TABLE 5-2 **Deep Venous Thrombosis Prophylaxis in Patients With Stroke**

Clinical Scenario	Timing of Initiation	Therapy
Stroke without thrombolysis	On admission	Unfractionated heparin 5000 IU every 8–12 hours *OR* low-molecular-weight heparin Enoxaparin 40 mg/d SC Dalteparin 5000 units/d SC Fondaparinux 2.5 mg/d SC
Stroke with IV recombinant tissue plasminogen activator	1 day after thrombolytic therapy	Mechanical prophylaxis with intermittent pneumatic compression devices on admission until chemical prophylaxis can be started, then: Unfractionated heparin 5000 IU every 8–12 hours *OR* low-molecular-weight heparin Enoxaparin 40 mg/d SC Dalteparin 5000 units/d SC Fondaparinux 2.5 mg/d SC
Intracranial hemorrhage	1 to 4 days after bleeding cessation is demonstrated	
Contraindication to anticoagulation	On admission	Mechanical prophylaxis with intermittent pneumatic compression devices and chemical prophylaxis with aspirin 325 mg/d orally

IV = intravenous; SC = subcutaneous.

response, incomplete oral clearance, or palatal weakness or asymmetry.[37]

Prevention of aspiration pneumonia begins with proper identification of patients with dysphagia, and every patient with stroke should have a swallow evaluation before initiating a diet or oral medication intake in the hospital. A prospective multicenter study demonstrated that the use of a formal screening protocol for dysphagia with a water swallow test significantly decreased the risk of aspiration pneumonia in patients admitted with acute stroke.[38] A wet voice or spontaneous cough after swallowing are predictors of high aspiration risk. For patients at high risk, a videofluoroscopic evaluation of swallow or a fiberoptic endoscopic evaluation of swallow may be performed.

In patients who are unable to take anything by mouth, adequate hydration with isotonic fluids should be maintained to prevent DVT. Early placement of a nasogastric or nasoduodenal tube can facilitate administration of nutrition and medications in patients at high risk for aspiration. Patients who receive early nasogastric tube feeding have a significantly reduced risk for death. If long-term tube feeding is anticipated, a percutaneous endoscopic gastrostomy tube should be placed.

KEY POINTS

- Aspiration may be prevented with early dysphagia screening.
- Provide adequate hydration and early nutrition in patients who are unable to take anything by mouth. Dehydration carries an increased risk of deep venous thrombosis, while early nutrition through a nasogastric tube is associated with improved survival.

KEY POINTS

- Up to 70% of patients with stroke will have a fall, thus all patients with stroke should have a formal fall prevention program.
- Fractures in patients who are poststroke often occur on the paretic side and are secondary to accidental falls.

Infection

Fever after a stroke should prompt evaluation for common sources, including pneumonia and urinary tract infection. Prophylactic antibiotic use is not recommended. The most common cause of fever in the first 48 hours after acute stroke is pneumonia, which is attributed to aspiration in 60% of cases.[3] In addition to aspiration, immobility and atelectasis can lead to development of pneumonia. Early mobilization and good pulmonary care should be encouraged in the hospital to prevent pneumonia. For patients who are intubated, preventive measures include ventilation in a semirecumbent position, appropriate airway positioning, suctioning of secretions, and daily assessments for potential extubation. Nausea should be addressed and treated to prevent vomiting.

Urinary tract infections occur in 11% to 15% of patients with stroke, and are often seen during the first 5 days of the hospitalization, but they can occur up to 3 months poststroke. Urinary tract infection is an independent predictor of worse outcomes and prolonged hospitalizations.[1,39] Indwelling catheters should be avoided to reduce the risk of catheter-associated urinary tract infection. However, they may be required in certain circumstances, such as in cases of acute urinary retention or obstruction or when strict monitoring of urinary output is needed in patients who are critically ill. The catheter should be removed as soon as possible, and intermittent catheterization can be implemented to decrease infection risk.

LATE COMPLICATIONS

Many late complications of stroke can be seen in the acute setting, but issues such as falls, seizures, sleep-disordered breathing, and depression become more apparent following the acute hospitalization.

Falls

All patients with stroke should be provided with a formal fall prevention program during hospitalization.[40] A fall prevention program includes identifying the patient at high risk for falls, counseling the patient and family about the risk, encouraging the patient and family to seek assistance if needed, preventing delirium, minimizing the use of mechanical restraints, using bed and chair alarms, using ceiling lifts to facilitate transfers, and effectively communicating the patient's care plan with the team with shift changes. Patients at high risk for falls include those with cognitive impairment, neglect, anosognosia, and polypharmacy. In the acute setting, most falls are observed during the day in the patient's room or restroom, often associated with transfers or attempts at activities without supervision. Once the patient returns to the community, the rate of falls associated with transfers decreases, and subsequent falls are most commonly associated with ambulation.[41] A retrospective study showed that 5% of patients with stroke fell during their acute hospitalization, and these falls were associated with greater stroke severity and history of anxiety.[42] In the first 6 months after hospitalization, up to 70% of patients with stroke will have a fall.[43]

Most fractures in patients who are poststroke occur on the paretic side and are secondary to accidental falls. Of all poststroke fractures, hip fractures represent 45% and are 2 to 4 times more common in the stroke community when compared with the age-matched population.[44] Patients who ambulate early after stroke appear to lose bone mineral density on the paretic side only, as opposed to those who are not ambulatory, who lose bone mineral density on both sides.[44,45] Bone mineral density can decrease by more than 10% in the paretic leg in patients who are nonambulatory within the first year after stroke, as opposed to a reduction of 3% in patients who are ambulatory.[46,47] Ambulating at 2 months is associated with less decrease of bone mineral density compared to patients who are wheelchair dependent.[47] A cross-sectional study showed that poststroke hip fractures were prevalent in the first 2.4 years after stroke in women with dementia, a history of transient ischemic attack, hypertension, coronary artery disease, low vitamin D levels, secondary hyperparathyroidism, high bone resorption, higher serum vitamin B_{12}, or increased disability.[48]

Because of the high incidence of poststroke falls and because of the high morbidity associated with hip fractures, it is recommended that patients with stroke participate in exercise programs with balance training to reduce falls when discharged from the hospital. It is also reasonable to assess a patient's fall risk on an annual basis and to provide patients and their caregivers with information to reduce falls at home. Additionally, it is recommended that patients with stroke residing in long-term care facilities be evaluated for calcium and vitamin D supplementation.[40]

Seizures

Stroke is the most common cause of seizures in adults older than 35 years of age.[49] Most seizures are focal at onset and may have secondary generalization. Less than 10% of patients with ischemic stroke develop seizures.[50,51] The incidence of seizures appears to be higher in those patients who have had hemorrhagic transformation of the stroke. In a large prospective study, poststroke seizures occurred in 8.9% of patients after hemispheric ischemic or hemorrhagic stroke. Of those patients, 43% had their seizure within 24 hours of the stroke. Early-onset seizures are postulated to be due to ion shifts and release of excitotoxic neurotransmitters in the ischemic cascade.[52]

Late-onset seizures occur at least 2 weeks after a stroke and are commonly encountered 6 months to 2 years after stroke but can occur several years later.[53] The development of chronic epilepsy is higher in patients with late-onset seizures. Late-onset seizures are believed to be due to the permanent lesion causing an alteration in neuronal excitability. A population-based study demonstrated an incidence of poststroke epilepsy in 1.5%, 3.5%, 9.0%, and 12.4% of patients at 3 months, 1 year, 5 years, and 10 years, respectively.[54]

No studies have shown a benefit to starting prophylactic antiepileptic drugs after acute stroke, and routine seizure prophylaxis is not recommended.[40] Characteristics such as stroke severity, hemorrhagic lesion, and cortical location are associated with an increased risk of developing seizures.[54] Future trials are needed to stratify patients who may benefit from prophylactic antiepileptic drug use. Until then, the management of seizures after stroke should be similar to the management of seizures that can complicate other neurologic illnesses.[40]

Sleep-disordered Breathing

The prevalence of obstructive and central sleep apnea/hypopnea is increased in patients with stroke, occurring in up to 70% of patients when defined as an apnea-hypopnea index of five or more events per hour.[55] Patients commonly have preexisting obstructive sleep apnea or central sleep apnea, which is often undiagnosed at the time of the

KEY POINTS

- Decreased mobility is associated with decreased bone mineral density.
- Balance training can help to reduce falls.
- Patients with stroke in long-term care facilities should be assessed for calcium and vitamin D supplementation.
- Seizures after stroke are often focal in onset and can have secondary generalization. They may have early or late onset; late-onset seizures are associated with a higher rate of developing chronic epilepsy.
- Prophylactic antiepileptic drugs are not recommended after stroke.

stroke. These breathing patterns can worsen following a stroke, especially when the level of consciousness is impaired. Some sleep-disordered breathing is a consequence of brain injury from the stroke. Patients with stroke to the medullary respiratory centers can have obstructive sleep apnea, central sleep apnea, or a combination of the two. Bihemispheric strokes can result in Cheyne-Stokes respiration.

Early complications encountered as the result of sleep apnea include early neurologic deterioration in the acute setting. The reversed Robin Hood syndrome has been described as a possible mechanism for early neurologic deterioration, in particular in patients with proximal large vessel occlusions and sleep apnea.[56] In this syndrome, compensatory vasodilatation during hypercapnia increases blood flow velocity in the unaffected intracranial vessels. This creates a steal phenomenon that decreases the blood flow velocity in the vessels supplying the ischemic territory, thus causing a decline in neurologic status.

Late complications as a result of sleep apnea include those seen in the general population in addition to increased hospital length of stay, functional impairment, and mortality.[57,58] The risk of stroke has a strong independent association with sleep apnea in the general population. Additionally, a prospective cohort study demonstrated an increased risk for recurrent stroke in patients with stroke with moderate to severe obstructive sleep apnea who could not tolerate continuous positive airway pressure (CPAP) when followed over 7 years.[59]

Because of the increased prevalence of sleep-disordered breathing in patients with stroke, a high index of suspicion and a low threshold to pursue formal sleep testing should be upheld. **Table 5-3** provides clinical

TABLE 5-3 Clinical Features Associated With Increased Risk of Sleep-Disordered Breathing

▶ History
High stroke severity
Early neurologic deterioration
Stroke occurring at night
Stroke associated with diabetes mellitus
Stroke due to macroangiopathy
Hemorrhagic stroke
History of prior stroke
Cor pulmonale
Obesity
▶ Sleep Review of Systems
Loud snoring
Daytime sleepiness
Gasping or choking
Nonrestorative sleep
Witnessed apnea during sleep
Frequent nighttime awakenings
Morning headache
Nocturia
Irritability
Cognitive impairment
▶ Physical Examination and Clinical Findings
Systolic hypertension
Nocturnal desaturation
Hypercapnia
Cardiac arrhythmias
Pulmonary hypertension
Increased body mass index
Crowded airway
Increased neck circumference
Dysphagia or dysphonia
Floppy eyelid syndrome

features that are associated with an increased risk for sleep-disordered breathing. In the acute hospital setting, if patients have nocturnal desaturations, they can be treated with supplemental oxygen, CPAP, or bilevel positive airway pressure. Emerging evidence suggests that auto-titrating CPAP has diagnostic validity and may be feasible in patients with nonsevere stroke or transient ischemic attack.[60–62] Polysomnography can be arranged as an outpatient evaluation and should be considered as a necessary part of the management of secondary stroke prevention.[63]

Depression

Poststroke depression affects up to one-third of stroke survivors at any given time after stroke, with the highest frequency in the first year and a cumulative incidence of 55%.[64–66] It is associated with increased mortality and poor functional outcomes. Risk factors include stroke severity, severe disability, cognitive impairment, prestroke depression, previous stroke, family history of psychiatric disorder, and female sex.[40] Studies have not demonstrated a relationship between depression and stroke size or location.[67] The cause of poststroke depression is poorly understood but is likely a combination of psychological and biological factors.

Evidence is lacking with regard to treatment of depression and stroke outcomes. In a prospective study, patients who were depressed at 3 months were found to have poorer functional outcomes at 1 year.[68] It is notable that patients who were depressed had more neurologic impairments; thus, it is unclear whether the depression was due to the patient being significantly disabled or if the depression had an impact on stroke recovery. Another study of patients with poststroke depression showed that patients with improved mood at follow-up had significantly greater recovery in their activities of daily living than patients whose mood did not improve.[69] Again, it is notable that these results were observational, and causality cannot be inferred. The Fluoxetine for Motor Recovery After Acute Ischaemic Stroke (FLAME) trial showed significant improvement in motor function as well as lower rates of poststroke depression in patients given fluoxetine compared to placebo.[70] Further studies are needed to assess antidepressant treatments in poststroke depression.

While no clear evidence indicates that improvement of poststroke depression is independently associated with functional improvement, untreated depression can negatively impact the patient's ability to participate in rehabilitation (**Case 5-3**).[71,72] In addition, fatigue can be significantly disabling. Poststroke fatigue can occur in the

Case 5-3

A 74-year-old woman presented to clinic for follow-up 1 month after a left middle cerebral artery territory stroke. She had a residual moderate mixed aphasia and right hemiparesis but was able to ambulate with a walker. During her hospitalization, she was identified to be at risk for obstructive sleep apnea; this was confirmed on polysomnography in the sleep clinic. Continuous positive airway pressure therapy had been initiated, and she noticed significantly improved sleep and a moderate improvement of her daytime sleepiness. However, she continued to have difficulty getting out of bed in the mornings and struggled with persistent daytime fatigue since her

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hospitalization. Upon further questioning, her husband endorsed that she appeared withdrawn and had been avoiding social contact with family and friends. She no longer enjoyed her prior activities of watching films, picking fruit from her mango trees, or playing with her great-grandson. She missed multiple outpatient therapy appointments because of lack of motivation and significant fatigue. She denied suicidal or homicidal ideation but reported a history of a suicide attempt in her teenage years.

Comment. This patient's untreated depression is preventing her from optimizing her stroke recovery through therapy and is associated with poor functional outcome. She would likely benefit from starting antidepressant therapy. With adequate treatment of her depression, she may also experience improvement of her daytime fatigue.

absence of depression and can be difficult to treat. However, fatigue associated with depression can potentially be alleviated when the depression is treated[73]; thus, a standard approach to treating depression with nonpharmacologic and pharmacologic treatment options should be offered to patients with poststroke depression. Screening tools such as the Center of Epidemiological Studies-Depression Scale (CES-D), Hamilton Depression Rating Scale (HDRS), and Patient Health Questionnaire (PHQ-9) have demonstrated high sensitivity for detecting depression.[74] A 2016 scientific statement by the American Heart Association/American Stroke Association acknowledged that further research is needed to determine whether screening and subsequent treatment improve outcomes in the general stroke population.[75]

CONCLUSION

A heightened awareness of commonly encountered early and late medical complications of stroke along with knowledge of how to prevent and manage them can help to improve patient outcomes, decrease the length of hospital stays and readmission rates, and decrease overall health care costs. Further studies are needed to identify patients at risk for seizures, sleep-disordered breathing, and depression after stroke. Until then, patients should be screened for sleep apnea and depression in both the hospital and outpatient settings, as these can have implications for their functional outcomes. Patients should also be regularly assessed for fall risk beginning with their initial hospitalization and continuing in the clinic setting during follow-up visits.

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