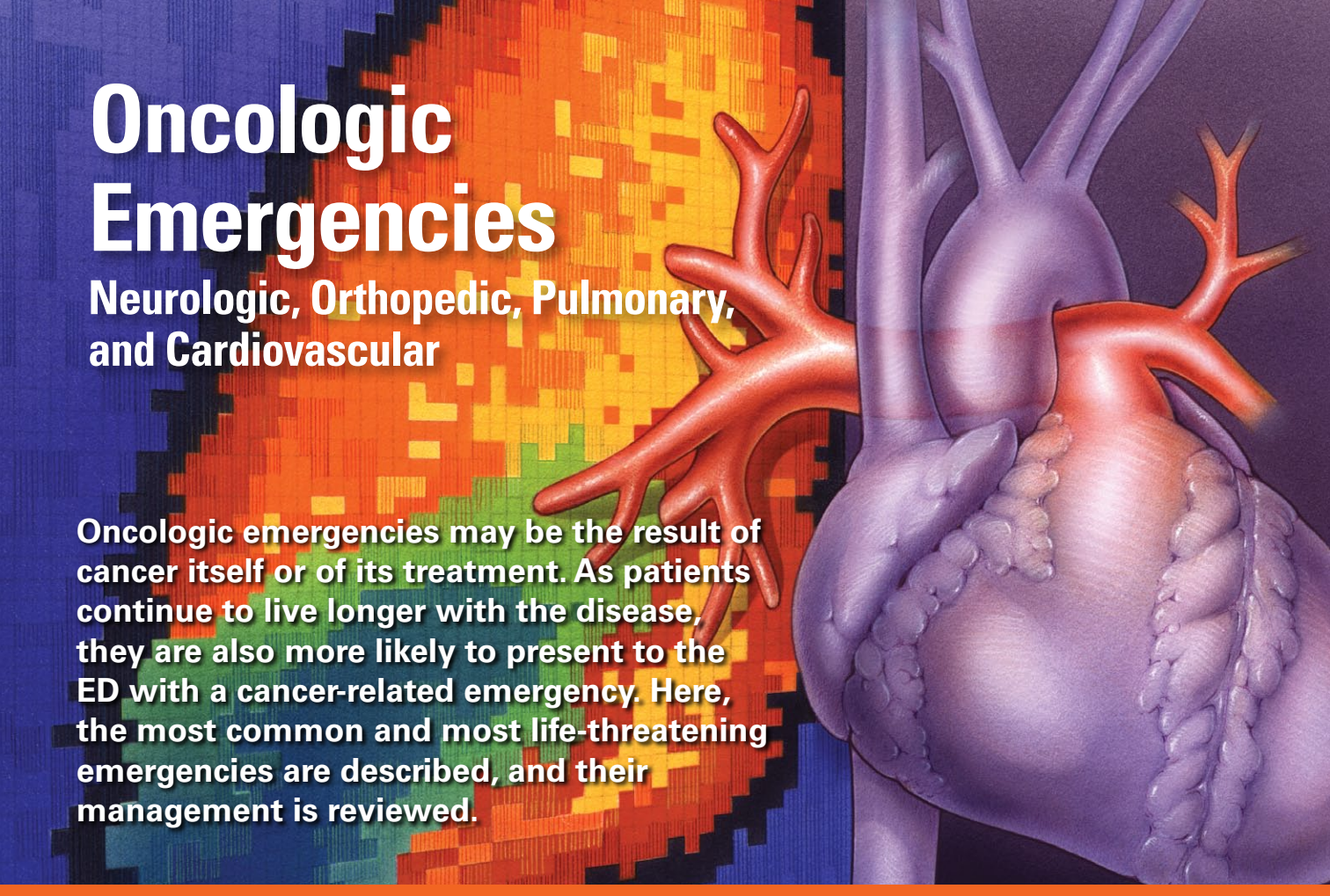
Oncologic Emergencies

Neurologic, Orthopedic, Pulmonary, and Cardiovascular



Oncologic emergencies may be the result of cancer itself or of its treatment. As patients continue to live longer with the disease, they are also more likely to present to the ED with a cancer-related emergency. Here, the most common and most life-threatening emergencies are described, and their management is reviewed.

Barry Knapp, MD, FACEP, RDMS, and Melissa L. Williams, MD

In 2006, cancer was the second leading cause of death in the United States. In that year alone, nearly 14 million cases were diagnosed, with almost 560,000 deaths.[1,2] Most cancer patients will experience at least one emergency during the course of their disease, and emergency physicians are increasingly tasked with managing complications related to cancer. A recent study reported about 40% of cancer patients had visited the ED in the last 2 weeks of life.[3] The accurate diagnosis and appropriate treatment of oncologic emergencies can dramatically improve quality of life—or even save a life—in patients with cancer.

Ongoing advancements in the field of oncology are considerable. Patients are benefiting from effective treatment options, higher cure rates, and better long-term survival rates. Chemotherapy regimens are used more broadly now than ever before, and these regimens are more aggressive and effective than their predecessors—thereby causing more adverse effects. There is also a growing trend toward using chemotherapy in elderly patients, who until fairly recently would likely have been deemed "terminally ill" and admitted to hospice. As a result of these factors, cancer patient presentations to the ED are on the rise.

True emergencies related to cancer and its treatment may be the result of local tumor effects, biochemical abnormalities, hematologic abnormalities, renal and urologic syndromes, or cancer treatment itself. In this article, we categorize common cancer-related emergencies according to the body systems affected and the degree of risk, with more serious conditions described first (Table 1).

Dr. Knapp is an associate professor in the department of emergency medicine at Eastern Virginia Medical School in Norfolk. **Dr. Williams** is an emergency physician in the Willis-Knighton Health System in Shreveport, Louisiana.

NEUROLOGIC/ORTHOPEDIC EMERGENCIES

Cerebral Herniation

Cerebral herniation occurs when intracranial pressure (ICP) increases from an expanding mass lesion. The increase in pressure results in a shift of brain tis-

Table 1. Common Oncologic Emergencies

Neurologic/Orthopedic
- Cerebral herniation
- Acute spinal cord compression
- Pathologic fractures

Pulmonary
- Upper airway obstruction

Cardiovascular
- Malignant pericardial effusion with cardiac tamponade
- Superior vena cava syndrome
- Thromboembolism

Endocrinologic/Metabolic
- Adrenal insufficiency
- SIADH
- Tumor lysis syndrome
- Hypercalcemia

Hematologic
- Hyperviscosity syndrome
- Neutropenia and infection

Renal/Urologic

Dermatologic/Immunologic
- Drug extravasation
- Hypersensitivity reactions

Gastrointestinal
- Nausea and vomiting
- Bowel obstruction

Pain

SIADH = syndrome of inappropriate antidiuretic hormone

sue in the direction of least resistance. This occurs in a caudal direction and forces brain tissue through the tentorium and the foramen magnum. Causes of cerebral herniation in cancer patients commonly include primary or metastatic brain tumors and intracerebral hemorrhage. Less common causes include subdural hematoma, brain abscess, acute hydrocephalus, and radiation-induced brain necrosis.[4] Primary brain tumors account for approximately one-half of intracranial tumors. Metastatic brain tumors are seen most commonly in lung, breast, colon, kidney, and testicular cancer and in patients with choriocarcinoma and malignant melanoma.[5,6]

Three distinct herniation syndromes have been described: uncal, central, and tonsillar herniation. Uncal herniation occurs when a lateral mass displaces the temporal lobe, compressing the proximal brain stem. Symptoms include a rapid loss of consciousness along with unilateral pupil dilatation and ipsilateral hemiparesis. Central herniation often results from slowly expanding multifocal lesions that cause a caudal and lateral shift of the thalamus, hypothalamus, and upper pons. Symptoms include a gradually decreasing level of consciousness, small reactive pupils, Cheyne-Stokes respirations, and a lack of focal neurologic signs, which can lead to a misdiagnosis of toxic or metabolic encephalopathy. Tonsillar herniation is caused by a large mass in the posterior fossa that pushes the cerebellar tonsils through the foramen magnum, resulting in compression of the medulla. Symptoms include a rapidly decreasing level of consciousness, occipital headache, vomiting, hiccups, hypertension, meningismus, and abrupt changes in the respiratory pattern.[4-7]

Cerebral herniation is a neurosurgical emergency. CT of the brain should be performed as soon as the patient is stabilized. Rapid deterioration is likely, and airway management should not be delayed. Intubation with hyperventilation to a Pco_2 level of 25 to 30 mm Hg produces cerebral vasoconstriction and temporarily decreases ICP.[6] This should be avoided if at all possible but may be necessary for brief periods in response to acute neurologic deterioration. Excessive or prolonged hyperventilation is contraindicated, as it can cause paradoxical cerebral vasodilatation. Osmotic diuresis to decrease ICP is accomplished by administering mannitol 1 g/kg IV over 20 to 30 minutes. Repeated dosing may be needed if the patient's clinical condition deteriorates; however, caution is warranted, as the use of repeated doses can lead to a rebound increase in ICP.[6] Corticosteroids reduce cerebral edema associated with neoplastic processes but take hours to exert an effect. Dexamethasone 10 to 20 mg IV should be given early in the ED course. Neurosurgical consultation and prompt admission to the ICU are mandatory.[4,5]

Acute Spinal Cord Compression

Spinal cord compression occurs in 5% of all patients with cancer.[6] That risk increases to 20% when neo-

plastic lesions are present in the vertebral column.[8] The thoracic vertebrae are most commonly involved. Spinal cord compression presents initially as back pain in most patients (96%).[6] The pain is constant and progressive. Unlike back pain caused by most other musculoskeletal causes, pain from spinal cord compression usually worsens when the patient is supine. Eighty percent of patients who are ambulatory at the time of diagnosis retain the ability to walk.[8] Muscle weakness usually presents in the proximal extremities and may progress to complete paralysis.[8] Initial sensory changes can manifest as a band of hyperesthesia around the trunk at the involved spinal level. This can progress to anesthesia distal to the involved level. Urinary retention with overflow incontinence, fecal incontinence, and impotence are late manifestations.[8]

ED evaluation and management of a patient with the possibility of spinal cord compression should center on pain control and imaging of the spine. Plain films may be sufficient to identify the level of vertebral collapse and deformity. MRI is the imaging tool of choice, however, to define the site/degree of cord compression and to identify the presence of additional vertebral lesions. CT with or without myelography is used when MRI is contraindicated or inaccessible.[8]

In cases of acute spinal cord compression, corticosteroids should be initiated early in the ED course. Regimens include dexamethasone 10 mg IV bolus followed by 4 mg PO or IV every 6 hours.[8] Initial pain control is accomplished with IV narcotics. Definitive treatment is accomplished with corticosteroids, radiation therapy, surgery, or a combination of modalities and will depend on the life expectancy of the patient, the extent of disease, and the degree of motor impairment.

Pathologic Fractures

A pathologic fracture is any anatomic disruption of diseased bone resulting from normal but stressful activity. Metastases to bone mainly affect the axial skeleton and the proximal aspect of the limbs, where the red marrow is located. Patients with pathologic fractures due to bone metastases usually present with bone pain and history of a primary cancer. For evaluation in the ED, plain radiographs are usually sufficient for initial imaging. Other imaging modalities can be employed if necessary, including CT, which evaluates the three-dimensional bone integrity and soft-tissue extension, as well as MRI, which delineates soft-tissue and bone marrow involvement.

The goals of treatment in the ED are relief of pain, reduction of displaced fractures, and restoration of ambulation or function. These are accomplished with IV narcotics and fracture immobilization. Historically, surgical treatment of skeletal metastasis was directed primarily at lesions involving the femur. This was likely due to the major morbidity and loss of function associated with metastasis in this location. More recently, improved techniques and equipment have allowed treatment of symptomatic metastases involving not only the femur but other long bones, the pelvis, and the spine.[9] The application of minimally invasive techniques such as vertebroplasty and kyphoplasty has allowed significantly more effective treatment of patients with pathologic vertebral body fractures.[9] Occasionally, nondisplaced fractures in non–weight-bearing bones can be managed conservatively. Specialty consultation with an orthopedist and/or a radiation oncologist is often warranted to determine the best treatment course for pathologic fractures.

PULMONARY EMERGENCIES

Upper Airway Obstruction

Malignancy-related airway obstruction is a gradual process and is rarely an emergent condition. Obstruction of the airway may occur due to tumors arising in the oropharynx, neck, and superior mediastinum. Acute airway compromise may occur due to infection, hemorrhage, or inspissated secretions. The presence of airway obstruction with greater than 50% stenosis of the central airways is associated with stridor and tachypnea. Stridor occurs when erratic air currents pass through the obstructed tracheobronchial tree, resulting in high-pitch breath sounds. Soft-tissue plain films, CT, or direct laryngoscopy may aid in defining the soft-tissue architecture of the neck. As there is often distortion of local anatomy from the tumor, fiberoptic laryngoscopy is frequently necessary to evaluate the airway lumen size. If immediate control of the airway is necessary, options include cricothyrotomy, jet insufflation, or emergency tracheostomy. Longer-term options include surgical "coring-out" of the lesion, laser ablation, and airway stenting.[10]

CARDIOVASCULAR EMERGENCIES

Malignant Pericardial Effusion With Cardiac Tamponade

Breast and lung cancer are common sources of malignant pericardial effusions; other malignancy-related etiologies include mediastinal radiation, infection, and exposure to certain chemotherapeutic agents. Symptoms of pericardial effusion are related to fluid accumulation rate and total volume. Insidious collections greater than 500 mL may be well tolerated, while sudden accumulation or hemorrhage may cause signs of tamponade, such as dyspnea, chest pain, or hypotension. Pulmonary embolism, congestive heart failure, and pneumonia are misdiagnoses that may be made clinically in patients presenting with pericardial effusion.[11]

Five features occur in the majority of patients with tamponade: dyspnea (88%), tachycardia (77%), pulsus paradoxus (82%), elevated jugular venous pressure (76%), and cardiomegaly seen on chest radiography (89%).[12] The combination of the classic findings known as Beck's triad (hypotension, jugular venous distention, and muffled heart sounds) occurs in only 10% to 40% of patients.[13] Clinical suspicion can be confirmed immediately with bedside transthoracic ultrasound or more formally with consultation for echocardiography. Echocardiographic features consistent with tamponade include pericardial effusion with diastolic collapse of the right ventricle and/or systolic collapse of the right atrium.[14] The absence of sonographic features of pericardial effusion does not exclude tamponade, and the need for emergent pericardiocentesis is based on evidence of inadequate cardiac output.[14] Emergent pericardiocentesis can be a lifesaving procedure in a hemodynamically unstable patient, although blind pericardiocentesis has been associated with a complication rate as high as 50%, and deaths have been reported in many series.[15] Echocardiography-guided pericardiocentesis is safe, effective, and well tolerated. Doppler mode allows evaluation of the hemodynamic effects of the effusion and treatment.[16] For patients who are hemodynamically stable, consultation with an oncologist is prudent. The tumor type, symptom severity, and prognosis are considered in determining a treatment plan that might include systemic chemotherapy, intrapericardial chemotherapy or sclerotherapy, or creation of a pericardial window.

Superior Vena Cava Syndrome

Superior vena cava (SVC) syndrome occurs when a primary tumor or superior mediastinal lymph nodes compress the thin-walled SVC (carrying blood at low

pressure through the nondistensible mediastinum), causing central venous congestion. Up to 90% of patients with SVC syndrome have a malignant cause, with lung cancer and lymphoma accounting for over 90% of cases.[17] Patients with SVC syndrome usually do not die of the syndrome itself but rather from the underlying malignancy.[18] Physical exam findings are classic and easily recognized. The most common and obvious clinical signs are facial swelling with venous engorgement of the trunk, upper extremities, and neck. The skin may have a dusky or violet hue that mimics cyanosis. Common symptoms include dyspnea, orthopnea, and cough. Patients may also present with headache, nausea, dizziness, and visual disturbances. Neurologic involvement with obtundation, seizures, or coma may occur due to metastatic disease and cerebral edema from venous occlusion. The more rapid the onset of SVC compression, the more severe the symptoms will be, due to lack of time for collateral vessel development.

Initial ED management includes elevation of the head, judicious administration of IV fluids, and provision of supplemental oxygen. Steroids are often used as a temporary measure to reduce edema and associated symptoms, but there is an absence of data documenting the effectiveness and dose of steroids in this setting.[17] Most patients with SVC syndrome are treated nonoperatively with radiotherapy, chemotherapy, or both. Other treatment options include vena caval stents, anticoagulants, and surgery.

Thromboembolism

Venous thromboembolism (VTE), as manifested by deep venous thrombosis (DVT) and pulmonary embolism (PE), is identified in as many as 15% of patients with cancer. The overall incidence of cancer-related VTE in postmortem studies is much higher, ranging between 35% and 50%.[19] It may occur in all cancers but is most commonly associated with four distinct cancer types: adenocarcinoma of the lung, stomach, pancreas, and colon. Symptomatic DVT occurs in approximately 15% of all patients with cancer and up to 50% of those with advanced malignancies.[20] Factors that increase thromboembolism risk include a hypercoagulable state caused by intimal injury from neoplastic cells and chemotherapy; decreased levels of protein C, protein S, and antithrombin III; the effect of metastases on activation of the coagulation pathway; invasive procedures; venous stasis from obstructive tumors and decreased mobility; and long-term venous catheterization.[21]

Patients may present with fever, dyspnea, cough, hemoptysis, dyspnea on exertion, pleuritic chest pain, or lower leg pain/swelling. Physical findings may include tachycardia, tachypnea, pleural rub, or unilateral leg swelling. A common ECG change is nonspecific T-wave inversion. Chest radiography may reveal local infiltrates, ipsilateral diaphragm elevation, and Westermark sign (decreased lung markings from oligemia) or Hampton hump (wedge infiltrate). D-dimer assay is sensitive but not specific for PE. Pulmonary angiography is the gold standard for diagnosis but is an invasive procedure. CT angiography (CTA) of the chest is growing in favor as the diagnostic test of choice, as it is noninvasive and has high specificity and sensitivity for PE. V/Q scans are an option for those patients who cannot tolerate the dye load required for CTA.[22]

A hemodynamically stable patient with a PE is treated with weight-based unfractionated heparin or a low-molecular-weight heparin (LMWH) such as enoxaparin (1 mg/kg SC twice daily). Contemporary evidence on the risk of anticoagulation-related hemorrhage in cancer patients remains conflicting; findings from retrospective studies support a greater bleeding risk in cancer patients, while results of prospective cohort studies suggest the risk is no greater than that in patients who do not have cancer.[23] Clear indications for PE thrombolysis are debated. Thrombolysis has been demonstrated to improve survival in patients with massive PE plus shock and is probably indicated in these patients regardless of cancer status.[23] Thrombolysis is contraindicated in any cancer patient with significant transfusion-refractory thrombocytopenia, active bleeding, and CNS lesions.[23] Of the available thrombolytics currently available, no agent or dosing range has currently been shown to be superior to another. Stable and marginally unstable patients should not receive thrombolytic therapy, as major bleeding can occur and there is no proven reduction in mortality in these patients.[24] Treatment with LMWH or unfractionated heparin as a bridge to chronic warfarin therapy is appropriate for most newly diagnosed cases of DVT, although some recommend the use of LMWH in view of data suggesting a survival advantage for cancer patients.[25] More frequent monitoring of the INR (international normalized ratio) is required,

because the anticoagulation effects of warfarin are more difficult to control in cancer patients than in other patients.[20]

Use of inferior vena cava (IVC) filters can be considered in patients with significant anticoagulation risks, including active bleeding, thrombocytopenia, or CNS malignancy. Filters placed in the IVC convey a significant short-term benefit (within the first several weeks), but their long-term benefits are not proven. It has also been shown that prophylactic IVC filter placement may increase the long-term DVT recurrence rate.[26]

Operative venous thrombectomy and catheter-directed thrombolysis (CDT) are also options in the acutely symptomatic patient. In selected patients with extensive acute proximal DVT (eg, iliofemoral DVT, symptoms for <14 days, good functional status, life expectancy ≥1 year) who have a low risk of bleeding, CDT may be used to reduce acute symptoms and postthrombotic morbidity if appropriate expertise is available. Thrombectomy should be considered for those who are not candidates for CDT.[27] □

COMING NEXT MONTH

The following cancer-related emergencies will be considered: endocrinologic/metabolic, hematologic, renal/urologic, dermatologic/immunologic, gastrointestinal, and pain.

REFERENCES

1. American Cancer Society. Cancer Facts and Figures 2006. Atlanta, GA: American Cancer Society; 2006.
2. Heron M, Hoyert DL, Murphy SL, et al. Deaths: final data for 2006. *Natl Vital Stat Rep*. 2009;57(14):1-134.
3. Barbera L, Taylor C, Dudgeon D. Why do patients with cancer visit the emergency department near the end of life? *CMAJ*. 2010;182(6):563-568.
4. Cascino TL. Neurologic complications of systemic cancer. *Med Clin North Am*. 1993;77(1):265-278.
5. DeAngelis LM, Posner JB. Neurologic complications. In: Holland JF, Bast RC, Morton DL, et al, eds. *Cancer Medicine*. 4th ed. Baltimore, MD: Williams & Wilkins; 1997:3117-3139.
6. Quinn JA, DeAngelis LM. Neurologic emergencies in the cancer patient. *Semin Oncol*. 2000;27(3):311-321.
7. Jeyapalan SA, Batchelor TT. Diagnostic evaluation of neurologic metastases. *Cancer Invest*. 2000;18(4):381-394.
8. Manglani HH, Marco RA, Picciolo A, Healey JH. Orthopedic emergencies in cancer patients. *Semin Oncol*. 2000;27(3):299-310.
9. Levine AM, Aboulafia AJ. Pathologic fractures. In: Browner BD, Jupiter JB, Levine AM, eds. *Skeletal Trauma*. 4th ed. Philadelphia, PA: WB Saunders; 2008:453-512.
10. Theodore PR. Emergent management of malignancy-related acute airway obstruction. *Emerg Med Clin North Am*. 2009;27(2):231-241.
11. Ugras-Rey S, Watson M. Selected oncologic emergencies. In: Marx J, Hockberger R, Walls R, eds. *Rosen's Emergency Medicine*. 7th ed. Philadelphia, PA: Mosby; 2009:1590-1603.
12. Roy CL, Minor MA, Brookhart MA, Choudhry NK. Does this patient with a pericardial effusion have cardiac tamponade? *JAMA*. 2007;297(16):1810-1818.
13. Jacob R, Grimm RA. Pericardial disease. In: Carey WD, ed. *Cleveland Clinic: Current Clinical Medicine*. 2nd ed. Philadelphia, PA: Saunders/Elsevier; 2009:171-179.
14. Klein LW. Diagnosis of cardiac tamponade in the presence of complex medical illness. *Crit Care Med*. 2002;30(3):721-723.
15. Tibbles CD. Procedural applications of ultrasound. *Emerg Med Clin North Am*. 2004;22(3):797-815.
16. Tsang TS, Seward JB, Barnes ME, et al. Outcomes of primary and secondary treatment of pericardial effusion in patients with malignancy. *Mayo Clin Proc*. 2000;75(3):248-253.
17. Wan JF, Bezjak A. Superior vena cava syndrome. *Emerg Med Clin North Am*. 2009;27(2):243-255.
18. Wudel LJ Jr, Nesbitt JC. Superior vena cava syndrome. *Curr Treat Options Oncol*. 2001;2(1):77-91.
19. DeSancho MT, Rand JH. Bleeding and thrombotic complications in critically ill patients with cancer. *Crit Care Clin*. 2001;17(3): 599-622.
20. Ornstein DL, Zacharski LR. Cancer, thrombosis, and anticoagulants. *Curr Opin Pulm Med*. 2000;6(4):301-308.
21. Lee AY. Treatment of venous thromboembolism in cancer patients. *Thromb Res*. 2001;102(6):V195-208.
22. Kline JA, Runyon MS. Pulmonary embolism and deep vein thrombosis. In: Marx J, Hockberger R, Walls R, eds. *Rosen's Emergency Medicine*. 7th ed. Philadelphia, PA: Mosby; 2009:1127-1135.
23. Deitcher SR. Diagnosis, treatment, and prevention of cancer-related venous thrombosis. In: Abeloff MD, Armitage JO, Niederhuber JE, eds. *Abeloff 's Clinical Oncology*. 4th ed. Philadelphia, PA: Churchill Livingstone; 2008:693-716.
24. Konstantinides S, Geibel A, Heusel G, et al; Management Strategies and Prognosis of Pulmonary Embolism-3 Trial Investigators. Heparin plus alteplase compared with heparin alone in patients with submassive pulmonary embolism. *N Engl J Med*. 2002;347:1143-1150.
25. Lee AY, Levine MN, Baker RI, et al; Randomized Comparison of Low-Molecular-Weight Heparin versus Oral Anticoagulant Therapy for the Prevention of Recurrent Venous Thromboembolism in Patients with Cancer (CLOT) Investigators. Low-molecular-weight heparin versus a coumarin for the prevention of recurrent venous thromboembolism in patients with cancer. *N Engl J Med*. 2003;349(2):146-153.
26. Decousus H, Leizorovicz A, Parent F, et al. A clinical trial of vena caval filters in the prevention of pulmonary embolism in patients with proximal deep-vein thrombosis. Prévention du Risque d'Embolie Pulmonaire par Interruption Cave Study Group. *N Engl J Med*. 1998;338(7):409-415.
27. Kearon C, Kahn SR, Agnelli G, et al; American College of Chest Physicians. Antithrombotic therapy for venous thromboembolic disease: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest*. 2008;133(6 suppl):454S-545S.