CHEST Postgraduate Education Corner
CONTEMPORARY REVIEWS IN CRITICAL CARE MEDICINE

Acute Left Ventricular Dysfunction in the Critically Ill

Anand Chockalingam, MD; Ankit Mehra, MD; Smrita Dorairajan, MD; and Kevin C. Dellsperger, MD, PhD

Acute left ventricular (LV) dysfunction is common in the critical care setting and more frequently affects the elderly and patients with comorbidities. Because of increased mortality and the potential for significant improvement with early revascularization, the practitioner must first consider acute coronary syndrome. However, variants of stress (takotsubo) cardiomyopathy may be more prevalent in ICU settings than previously recognized. Early diagnosis is important to direct treatment of complications of stress cardiomyopathy, such as dynamic LV outflow tract obstruction, heart failure, and arrhythmias. Global LV dysfunction occurs in the critically ill because of the cardio-depressant effect of inflammatory mediators and endotoxins in septic shock as well as direct catecholamine toxicity. Tachycardia, hypertension, and severe metabolic abnormalities can independently cause global LV dysfunction, which typically improves with addressing the precipitating factor. Routine troponin testing may help early detection of cardiac injury and biomarkers could have prognostic value independent of prior cardiac disease. Echocardiography is ideally suited to quantify LV dysfunction and determine its most likely cause. LV dysfunction suggests a worse prognosis, but with appropriate therapy outcomes can be optimized. ***CHEST 2010; 138(1):198–207***

Abbreviations: ACS = acute cardiac syndrome; BNP = brain natriuretic peptide; LV = left ventricular; NT-proBNP = N-terminal-pro-B-type natriuretic peptide; RWMA = regional wall motion abnormalities

Acute left ventricular (LV) dysfunction occurs in about one-third of critically ill hospitalized patients.[1-4] The increasing incidence of LV dysfunction in ICUs is likely related to both changing patient characteristics (advancing age, increased comorbidities) and practice patterns (widespread troponin, creatine kinase-MB, and brain natriuretic peptide [BNP] testing, as well as more frequent performance of bedside echocardiography).[3,5-8] A determination as to whether the LV dysfunction is the cause, effect, or a coincidental finding has to be made and revisited periodically. Acute medical or surgical plans, ongoing management targets, outcome expectations, and prognosis must be reconciled. Recognizing that all the individual causes and complexities cannot be captured here, we will summarize the most important causes of LV dysfunction in the critically ill (Table 1) and present a unified management approach from the cardiac standpoint.

Manuscript received August 22, 2009; revision accepted December 7, 2009.
Affiliations: From the Division of Cardiovascular Medicine, Department of Internal Medicine (Drs Chockalingam, Mehra, Dorairajan, and Dellsperger), University of Missouri School of Medicine; and the Cardiology Section (Dr Chockalingam), Harry S. Truman VA Medical Center, Columbia, MO.
Funding/Support: This study was funded by Veterans Administration Research award [VISN 15] to Dr Chockalingam.
Correspondence to: Anand Chockalingam, MD, Division of Cardiology, University of Missouri–Columbia, 5 Hospital Dr, CE306, Columbia, MO 65212; e-mail: chockalingama@health.missouri.edu

DOI: 10.1378/chest.09-1996

Diagnosis of LV Dysfunction

Angina, dyspnea, pulmonary crackles, murmurs, tachyarrhythmias, biomarker elevations, or ischemic ECG changes suggest cardiac pathology in hospitalized patients. Because of variability in patient characteristics and study design, predictive values of each cardiac test remain unclear. Several studies suggest routine troponin screening in ICUs may be sensitive in detecting early cardiac involvement among the critically ill.[9,10] Supporting this, 15% to 30% of critically ill noncardiac patients develop troponin elevations and this corresponds with poorer outcomes. Overall

Table 1—*Causes of Acute Left Ventricular Dysfunction in the Critical Care Setting*

Myocardial infarction
Typical acute coronary syndromes
Significant myocardial involvement
Mechanical complications, such as ventricular septal rupture and papillary muscle rupture
Paradoxical venous thromboembolism
Coronary emboli—left atrial myxoma, LV or atrial thrombus
Coronary thrombosis—antiphospholipid antibody syndrome, disseminated intravascular coagulation, thrombotic thrombocytopenic purpura
Aortic dissection—with right coronary occlusion
Stress cardiomyopathy
Apical ballooning ± LV outflow obstruction
Basal cardiomyopathy (apex-sparing)
Focal cardiomyopathy (noncoronary distribution)
Global hypokinesis
Tachyarrhythmias
Hypertensive emergency
Sepsis
Metabolic and multiorgan insults
Post cardiac arrest and resuscitation
Myocardial injury with minor troponin elevations (including supply-demand mismatch)
Myopericarditis—viral, autoimmune, giant cell
Trauma—chest contusion, prolonged resuscitation, bleeding
Congestive heart failure—decompensated, with anemia, shunts
Pulmonary embolism—with right ventricle strain
Sepsis—hypotension, catecholamine drips
Extracardiac stressors—hypertensive crisis, thyrotoxicosis, cocaine, hypothermia, drowning
Prolonged surgery—hypotension, blood loss

LV = left ventricular.

mortality in one study was 27% (58 of 217 patients), but patients with troponin elevation had a much higher mortality (51%) compared with those without (16%).[10] Although routine troponin testing may help identify LV dysfunction early, there is currently no evidence that this improves outcomes in critical care patients.

Significant elevation in plasma levels of N-terminal-pro-B-type natriuretic peptide concentrations (NT-proBNP) and BNP are typically diagnostic of cardiac pathology as cause for dyspnea and heart failure. In critically ill patients with shock, however, BNP tends to be elevated and is thus not reliable for diagnosing heart failure.[11,12] Because BNP is higher in sepsis nonsurvivors (943 pg/mL vs 378 pg/mL in survivors), some believe it may play a prognostic role.[13]

Transthoracic echocardiography, being portable, noninvasive, and easily repeatable, is ideal to evaluate LV dysfunction in critical care settings.[3,5] In addition, right ventricular function, pulmonary pressures, valve disease, and pericardial pathology, along with hemodynamic parameters, such as central volume status and cardiac output, can be quantified and serially monitored.[6] About 8% to 20% of critically ill patients manifest LV dysfunction, although one serial echocardiographic study suggests a higher incidence, up to 30%.[2] Importantly, presence, extent, and location of regional wall motion abnormalities as well as LV dimensions and shape help determine the most likely cause for LV dysfunction and guide further management in most instances.

Cardiac catheterization provides definitive assessment of coronary disease. CT scan angiography and cardiac MRI may be valuable in specific situations but are limited in ICU settings.[14] Table 2 summarizes key diagnostic advantages and limitations with various cardiac tests in the critical care setting.

Acute Coronary Syndromes

Diagnosis

Plaque rupture resulting in total occlusion of a major coronary artery results in chest pain with ECG evidence of ST elevation. This is associated with a sizable territory of myocardium in jeopardy. This warrants emergent coronary angiography and revascularization. Chest pain with diaphoresis and dyspnea may be reported but classic symptoms may be masked in many ICU patients because of sedation or altered mental status.[3,5] Hemodynamic changes, such as hypotension, low cardiac output, reduced mixed venous saturation, and increasing pulmonary wedge pressures may trigger performing a 12-lead ECG in the sedated or unconscious patient. Increasing ventricular ectopy, ST segment changes, or new bundle branch blocks on telemetry may also be the initial evidence for cardiac ischemia.[1,15] When clinical and ECG findings are equivocal, bedside echocardiography with careful evaluation for regional wall motion abnormalities (RWMA) conforming to typical coronary distributions may help to confirm acute coronary syndrome (ACS).[3,6,9] Mechanical complications of ACS, such as mitral regurgitation or ventricular septal defects, may also be detected with echocardiography.[16]

ACS Without Critical Coronary Artery Disease

Medical, surgical, or trauma intensive care may result in substantial physiologic and mental stress. This may cause alterations in hemodynamics, coagulability, and metabolic parameters. Patients with preexisting significant atherosclerotic stenosis may not be able to increase blood supply commensurate with the increasing demands resulting in supply-demand mismatch. This usually manifests as ACS with ischemic ECG changes and troponin elevations. Although new LV dysfunction is not typical with supply-demand mismatch, it is included in this review because of the relatively higher incidence of supply-demand mismatch in critical care settings.[17-19] This may account

Table 2—*Summary of Various Cardiac Tests Available Highlighting Their Key Characteristics in Critical Care Settings*

Test	Key Diagnosis	Advantages	Limitations
ECG	ST elevation MI Non-ST elevation MI Arrhythmias	Widely available Inexpensive	Stress cardiomyopathy may mimic MI
Troponin	Any myocardial injury	High sensitivity and specificity (> 95%) Quantifies overall muscle damage	Initially, mild elevations are common in MI and stress cardiomyopathy
BNP	Not reliable in determining cardiac cause for pulmonary congestion	May predict ICU outcomes Normal values excludes cardiac disease	Not reliable in obese patients
Echocardiogram	LVD, MI, valve, and pericardial disease vs possible stress cardiomyopathy	Noninvasive, bedside Valuable hemodynamic information	Limited quality images in intubated ICU patients
Catheterization	CAD diagnosis and revascularization	Systolic and diastolic LV function measurement	Invasive Higher risk due to ICU comorbidities Contrast renal injury
Cardiac CT scan	Excludes CAD	Noninvasive	Contrast renal injury. Challenging to perform in critically ill and unstable patients.
Cardiac MR scan	MI, cardiomyopathies and valve disease by scarring pattern	Noninvasive Best test for LV regional wall motion abnormalities and RV function measurement	Challenging to perform in critically ill, unstable, and intubated patients

BNP = brain natriuretic peptide; CAD = coronary artery disease; LVD = left ventricular dysfunction; MI = myocardial infarction; MR = magnetic resonance; RV = right ventricular. See Table 1 for expansion of other abbreviation.

for troponin elevations seen in about one-fourth of critically ill noncardiac patients (Table 1).[9,10]

In instances without angiographic culprit lesions, *in situ* coronary arterial thrombosis due to hypercoagulable conditions, such as thrombocytosis, disseminated intravascular coagulation, thrombocytopenic purpura, and antiphospholipid antibody syndrome, need to be considered.[20,21] Rarely embolic coronary occlusion may be due to left-side heart (atrial or ventricular) mural thrombi, endocarditis, prosthetic valve thrombi, or cardiac myxoma.[22] Paradoxical emboli and thrombi from intracardiac catheters or guidewires have to be considered in patients with a patent foramen ovale.[23] Therapy is mainly supportive and aimed at preventing recurrence by addressing precipitation factors. This might involve surgery for cardiac tumors, percutaneous device closure of patent foramen ovale, or anticoagulation for hypercoagulable states. Cardiac status may potentially improve with antiplatelet (aspirin, clopidogrel, glycoprotein IIb/IIIa antagonists) and anticoagulant therapy (heparin, warfarin). However there are no studies in critical care settings for these therapies because of wide variability in cause for ACS and comorbidities. With the higher bleeding risk in this population, these agents must be used on a case-by-case basis.

Stress Cardiomyopathy

Definition and Epidemiology

Originally described in Japan as takotsubo cardiomyopathy, stress cardiomyopathy by definition implies completely reversible acute LV dysfunction.[24-28] ICU admission because of medical illness, surgical procedure, or traumatic injuries could typically be sufficient stress to cause stress cardiomyopathy.[29] By performing serial echocardiography in consecutive ICU patients, 28% (26 of 92 patients) had stress cardiomyopathy in one series reported from South Korea.[2] This is much higher than we typically encounter and a more recent larger series in which echocardiograms were obtained routinely in the first 24 h of ICU admission detected LV systolic dysfunction in 132 of 704 (18%) patients.[3]

Pathogenesis of Stress Cardiomyopathy

Catecholamine excess in circulation has been identified and possibly mediates the acute cardiac dysfunction in stress cardiomyopathy.[30] This condition typically affects women (in > 80% of most series) in the 62- to 75-year-old age range.[31,32] Severe emotional stress (approximately 27%) or physical illness (approximately 38%), such as sepsis, head trauma, and cerebrovascular accident, may precipitate stress cardiomyopathy in about two-thirds of the instances.[32] In about 60% to 80% of those with this condition the mid and distal segments of the LV are akinetic with a hypercontractile base giving the appearance of "apical ballooning." Stress cardiomyopathy can also affect the base with apical sparing in another 10%. The remainder manifests nonspecific regional wall motion abnormalities or global hypokinesia not conforming to any particular coronary territory.[28,33] This global hypokinesia variant of stress cardiomyopathy is unlikely

to be a separate pathogenic entity from LV dysfunction seen in sepsis. We discuss this with other conditions causing global LV dysfunction in the following section to emphasize the underlying reversible precipitating conditions.

Diagnosis of Stress Cardiomyopathy

Angina, heart failure, arrhythmias, ECG changes (ST elevations or T inversions), and mild troponin elevations are often triggers for performing cardiac catheterization. Typically a culprit coronary artery lesion is not evident.[24-26] Left ventriculography demonstrates significant reduction in LV function and symmetric akinesia involving the mid and apical segments with relative hypercontractility of the cardiac base (Fig 1).

Published guidelines require angiographic proof of absence of coronary artery disease (CAD).[34] In ICU settings, especially where bleeding risk, severe comorbidity, or terminal illness precludes catheterization and revascularization, the following may be useful indicators that the LV dysfunction is due to stress cardiomyopathy and not true ACS:

1. Severe acute LV dysfunction without a significant serum troponin and creatine kinase-MB elevation.
2. Symmetrical mid and apical RWMA by echocardiography—akinesia extending equally in the inferior and lateral walls as the anteroseptum. In ACS of the left anterior descending coronary artery, anteroseptal extent of RWMA from the apex is usually greater than the inferior and lateral walls. Conversely, ACS of the right coronary or left circumflex, if left dominant, usually spares the anteroseptum.
3. Repeat echocardiography in a few days to weeks confirming complete recovery of LV function with normalization of typical apical RWMA (in the absence of lytics and percutaneous coronary intervention).

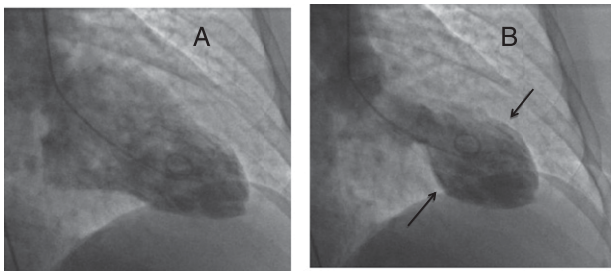

FIGURE 1. Contrast left ventriculography images in diastole (*A*) and systole (*B*). Arrows in the mid anterior and inferior walls point to the area separating the hyperkinetic base from the akinetic apical segments, a typical finding in stress cardiomyopathy.

Atypical forms of stress cardiomyopathy with RWMA involving the base, entire LV, or focal LV areas may be more difficult to identify. Table 3 summarizes salient features of the most common subgroups of LV dysfunction in critically ill patients. Being noninvasive and easy to perform, CT angiography can potentially replace cardiac catheterization in excluding significant CAD especially when the suspicion for CAD is low.[14] However, excellent quality coronary imaging requires patient cooperation (breath holding) and the ability to tolerate β-adrenergic blockade to slow the resting heart rate.

Treatment Options for Stress Cardiomyopathy

In ICU settings, identifying and effectively treating the medical or surgical condition that precipitated stress cardiomyopathy is essential. Supportive treatment includes addressing heart failure and arrhythmias as well as optimizing hemodynamics and metabolic parameters. The prognosis may not be benign, with one review estimating shock (6.5%), LV thrombus formation (3.8%), congestive heart failure (3.8%), and death (3.2%) in patients with stress cardiomyopathy.[35] There are no randomized data on stress cardiomyopathy to guide therapy, but prophylactic anticoagulation with warfarin appears reasonable until LV function recovers.[34,35] Because central sympathetic neurohumoral excess occurs in stress cardiomyopathy,[30] we believe β-adrenergic blockade may be cardioprotective. Because stress cardiomyopathy is a completely reversible condition, if the patient can be sufficiently supported through the acute phase, long-term cardiac prognosis is generally good.[34]

LV Outflow Tract Obstruction in Stress Cardiomyopathy

About 25% of patients with stress cardiomyopathy manifest acute dynamic LV outflow tract obstruction.[36] We have recently reported in depth the pathophysiology and management of LV outflow tract obstruction and this is beyond the scope of this review.[37,38] Briefly, in stress cardiomyopathy the combination of hypercontractile LV base (compensatory for mid and distal akinesia) and a reduction in LV chamber size (due to bleeding, diuretics, trauma, or inotrope infusion) results in systolic anterior motion of the mitral apparatus. This crowding at the LV outflow level causes dynamic obstruction with sudden increase in afterload and LV wall stress manifesting as angina, heart failure, ischemic ECG changes, and cardiac enzyme elevations. Hypotension and a new prominent systolic ejection murmur in the left third parasternal area

Table 3—*Clinical Characteristics That May Help Categorize Common Variants of Acute Cardiac Dysfunction in the Critically Ill*

Clinical Characteristics	Classic Acute Coronary Syndrome	Stress Cardiomyopathy	Global LV Dysfunction	Demand-Supply Mismatch
Risk factors and clinical scenario	Hypertension, diabetes, lipids, smoking and family history of CAD	Acute physiologic or mental stress in about 50%-70% of patients	Severe sepsis, prolonged hypoxia, or recurrent cardiopulmonary arrest and defibrillations	Sepsis, bleeding, trauma, or hypotension requiring inotropes
Symptoms	Typical angina, dyspnea, diaphoresis	Asymptomatic or atypical angina, dyspnea, and palpitations	Predominantly heart failure symptoms: dyspnea, edema, fatigue	Majority asymptomatic from cardiac standpoint
Signs	S4 gallop (S3 with severe cardiomyopathy), mitral regurgitation or pericardial rub uncommon	S3 gallop possible, about 20% develop systolic ejection murmur of LV outflow track obstruction	Pulmonary crackles, dependent edema, some may have cyanosis and cold extremities during peak shock	Tachycardia, depending on the reason the extremities may be warm or cold
ECG	Typical STEMI- or NSTEMI-related ST depressions with deep T inversions	Anterior subtle ST elevations, deep T inversions	Nonspecific ST-T wave changes	Tachycardia, diffuse ST depressions with T inversions
Troponin (normal < 0.04 ng/mL)[a]	Rapid increase, without intervention peak 20-100 ng/mL	Borderline, peak < 5 ng/mL usually	Fluctuating trend, usually peak < 5 ng/mL	Variable, peak < 5 ng/mL
BNP (normal < 100 pg/mL)	100-500 pg/mL	Usually 400-1,000 pg/mL	> 1,000 pg/mL	< 100 pg/mL
Echocardiogram	Regional wall motion abnormality conforming to coronary territory	85% Apical ballooning, 10% Apex sparring basal hypokinesia 5% Focal wall motion abnormality	Global hypokinesia and usually biventricular dilation	Hyperdynamic LV with EF usually > 70%
Coronary angiogram	Culprit lesion amenable to revascularization in majority of cases	Normal coronaries or insignificant CAD	Normal coronaries or insignificant coronary artery disease	Noncritical CAD, stenosis < 70%
Management	ACS protocol, early revascularization	Supportive	Address underlying critical illness	β-blockers or calcium blockers
		Repeat echo in few days to weeks to confirm recovery of LV function. If murmur of LV outflow track obstruction, β-blockers or calcium channel blockers and fluids may be used.	Treat sepsis appropriately Statins may help	Volume and packed RBCs as needed

ACS = acute coronary syndrome; EF = ejection fraction; LVOTO = LV outflow tract obstruction; NSTEMI = non-ST elevation myocardial infarction; STEMI = ST elevation myocardial infarction. See Tables 1 and 2 for expansion of other abbreviations.
[a]Normal ranges from the University of Missouri clinical laboratories.

imply hemodynamically significant LV outflow tract obstruction.[34,37,38]

Transthoracic echocardiography can provide the diagnosis, correlating the systemic BP with Doppler gradients in the LV outflow while also estimating the mitral regurgitation, LV dysfunction, and pulmonary hypertension.[38] Aggressive volume resuscitation and IV β-blockade targeting heart rate reduction to the 60 to 70 bpm range is central to management of LV outflow tract obstruction. Diltiazem or verapamil may offer sufficient negative inotropy, lusitropy, and hemodynamic benefits when bronchospasm contraindicates aggressive β-blockade. With appropriate treatment over the course of few hours to days, the hypotension, systolic ejection murmur, dynamic LV outflow gradient, mitral regurgitation, and stress cardiomyopathy-related apical RWMA all resolve.[37,38]

Global LV Dysfunction

Diagnosis

Although heart failure and hemodynamic instability warrant further cardiac testing, routine echocardiography is increasingly advocated for all ICU patients.[5] Often, the entire LV is significantly hypokinetic with variable cavity dilation and ejection fraction in the 30% range.[3] Echocardiography also excludes severe valvular heart disease, ACS-related RWMA, stress cardiomyopathy, and pericardial effusion with tamponade features. It is crucial to identify previously undiagnosed dilated cardiomyopathy with detailed history about preceding functional status, excessive alcohol intake, and heart failure-related symptoms. Echocardiographically, presence of LV chamber dilation and globular contour with significant mitral annular and left atrial

dilation would suggest longstanding LV dysfunction and underlying chronic dilated cardiomyopathy.[3,39]

Tachycardia-Induced Cardiomyopathy

Tachycardia-induced cardiomyopathy implies global systolic LV dysfunction secondary to atrial or ventricular tachyarrhythmias that reverses with rate and rhythm control.[40] Ventricular rate in atrial fibrillation is typically controlled with IV β-blockers or calcium channel blockers. IV digoxin is often used for rate control, although there is little literature concerning ICU settings with heightened sympathetic tone. Amiodarone may be the drug of choice for atrial and ventricular tachyarrhythmias because it does not adversely affect survival and may actually reduce cardiovascular events by an estimated 20% in LV dysfunction.[41] LV function generally normalizes in a few days to weeks of controlling heart rate in these situations.[42] Catheter ablation may be required for some tachyarrhythmias but this would typically require stabilization of other critical medical issues first. Animal studies demonstrate that the progression of heart failure is determined by faster heart rate, longer duration, as well as type of tachycardia (ventricular > atrial).[40] Thyroid abnormalities, electrolyte deficits (potassium and magnesium), hypoxia, and cardiac stimulant medications (β-agonist inhalers and inotropes) may contribute to the LV dysfunction. Addressing sepsis, volume depletion, and pain may control sinus tachycardia and potentially improve LV dysfunction. Although sinus tachycardia is prevalent in ICU settings, providers must realize there is no literature relating it directly to LV dysfunction, and rate-reducing medications (β-blockers and calcium channel blockers) may significantly worsen hemodynamics when cardiac output is heart rate dependent.[38]

Hypertensive LV Dysfunction

Patients with uncontrolled hypertension, especially with LV hypertrophy, often have subendocardial wall stress sufficient to cause ACS-like symptoms, mild troponin elevations, ischemic ECG changes, and acute heart failure.[4,43] Multiple stressors in ICU settings, such as hypovolemia, hypoxia, and infection, interact to precipitate acute global LV dysfunction. Importantly, the volume loss related to critical illness or development of LV dysfunction may normalize BP in the hospital. Recent home recordings suggesting elevated BP, poor compliance with medications, funduscopic changes, LV hypertrophy, and left atrial dilation on echocardiography are valuable clues toward establishing significance of preceding hypertension. Nitroprusside and nitroglycerin infusions are indicated for hypertensive emergencies and heart failure when rapid BP lowering is required. ACE inhibitors and angiotensin receptor antagonists may be first-line oral agents for BP lowering in the presence of LV dysfunction. After pulmonary congestion and overt heart failure are stabilized, β-blockade may offer cardioprotection in LV dysfunction settings. Home BP monitoring and compliance with dietary salt restriction are important to prevent recurrence.

Sepsis

Septic cardiomyopathy, implying impairment of the heart within the scope of systemic sepsis, was demonstrated more than 20 years ago.[44] Although the pathogenesis is still debated and probably multifactorial, LV dysfunction implies a worse prognosis in sepsis.[44-47] Various systemic inflammatory response syndrome- and sepsis-related substances in circulation, such as tumor necrosis factor-α, interleukin-1β, and interleukin-6, cause myocardial depression. Pulmonary or systemic infections are a precipitating factor in 12% to 20% of overall acute heart failure admissions.[4,43,48,49] Bacterial endotoxins, microvascular dysfunction, and catecholamines administered for shock could also mediate cardiotoxicity.[50,51] Among medical ICU admissions, one-fifth manifest clinical cardiac dysfunction.[9] In septic shock up to 50% of patients manifest LV dilation or systolic dysfunction, but there is evidence to suggest this may be an adaptive response with survival advantage.[44]

There are no established guidelines for managing LV dysfunction in sepsis but the importance of effectively addressing the source of infection cannot be overemphasized. Cardiovascular support with fluids and inotropes (such as dopamine) helped optimize outcomes in dog model of sepsis.[47,52] One case cohort study suggests chronic statin therapy for CAD may reduce incidence of sepsis by about 20%.[53] Statins may reduce myocardial inflammatory mediators, thereby potentially improving LV dysfunction and survival in sepsis.[54-58] These pleiotropic effects show promise, but large placebo-controlled randomized trials are needed to establish the role of statins in acutely ill patients with multiple comorbidities.[59]

Metabolic and Multiorgan Insults

LV dysfunction in the critical care setting could be related to severe hypoxia, hypothermia, drowning, anemia, pheochromocytoma, thyrotoxicosis, ARDS, systemic inflammatory response syndrome, and multiorgan dysfunction.[46,60] Cardiac arrest survivors have reduced cardiac output 4 to 8 h later due to cardiac dysfunction, and this normalizes typically by 24 h.[61] Systolic LV dysfunction was demonstrated in 28% of adult patients following electroconvulsive therapy

but was transient in all patients.[62] Elegant animal studies demonstrate reproducible LV dysfunction in anaphylactic shock. The mechanism appears to be direct cardio-inhibition by the mediators of anaphylaxis.[63]

Diastolic Dysfunction in the Critically Ill

The available literature is limited and suggests diastolic dysfunction may worsen outcomes in sepsis; an in-depth review of this topic is beyond the scope of this review.[39,64,65] Importantly, about 50% of acute heart failure occurs in the absence of systolic cardiac dysfunction and the term heart failure with normal ejection fraction (HFNEF) is more appropriate.[66] This is because Doppler transmitral flow velocity has many limitations and not all HFNEF patients manifest echocardiographic characteristics of diastolic dysfunction. Direct measurement of pulmonary capillary wedge or LV diastolic pressure may offer definitive proof of HFNEF but is not routinely performed because of its invasive nature. Clinical signs and symptoms of heart failure as well as radiographic pulmonary congestion are often sufficient to make the diagnosis of HFNEF. ICU therapy involves IV loop diuretics, restriction of fluid intake, and optimization of heart rate and BP control for symptom relief, systemic arterial oxygen saturation, and radiographic improvement.[67] Long-term management requires particular attention to optimal BP control, cardiovascular risk factor reduction, and lifestyle measures.[68]

LV Dysfunction Management Principles in the Critically Ill

During the initial evaluation and with significant changes in the clinical condition, two specific questions should be addressed:

1. How is the LV dysfunction contributing to the critical illness?
2. How is the critical illness contributing to the LV dysfunction?

A careful review of all available clinical and hemodynamic information, level and trend of troponin elevation, as well as echocardiographic features of the LV dysfunction determine the likelihood of ACS and amount of myocardium at risk. Medical management, including aspirin, anticoagulation with heparin, β-adrenergic blockade, statins, and nitrates should be initiated if ACS is suspected. Figure 2 outlines broad indications for urgent catheterization, which is typically reserved for ST elevation myocardial infarction and CAD with hemodynamic instability, heart failure, or arrhythmias refractory to medical management. Diagnosing ACS is challenging in the critical care setting because of atypical presentations and sedation. If and when percutaneous coronary intervention is performed, only the culprit lesions corresponding to an RWMA should be intervened upon to minimize anticoagulation and bleeding-related morbidity.

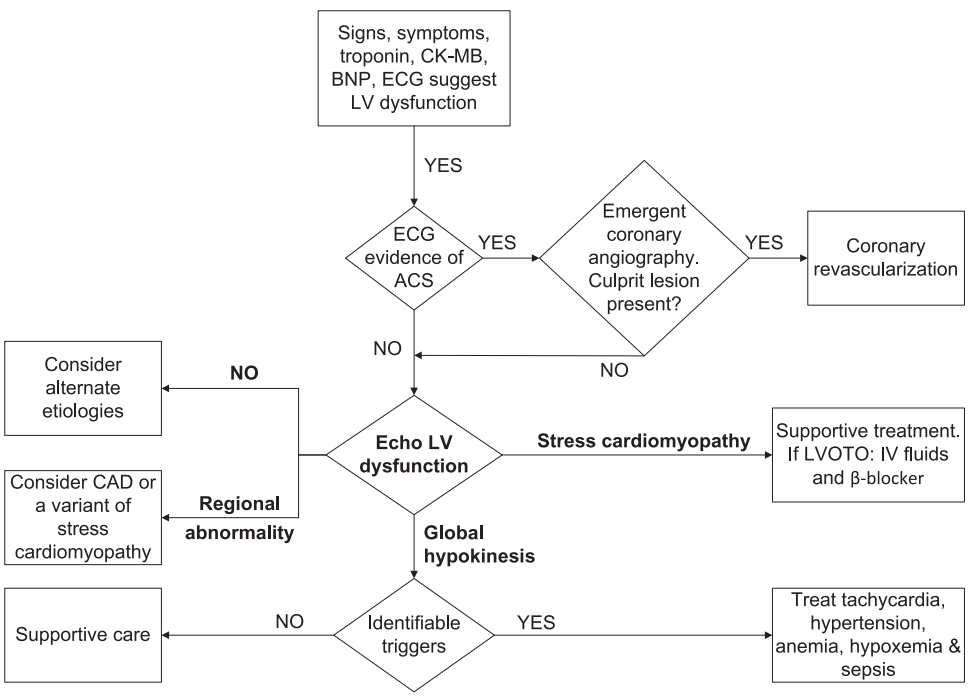

Figure 2. Algorithm for management of LV dysfunction in the critically ill based on clinical presentation and cause of cardiac pathology. ACS = acute coronary syndrome; BNP = brain natriuretic peptide; CAD = coronary artery disease; CK-MB = creatine kinase-MB fraction; LV = left ventricular; LVOTO = LV outflow tract obstruction.

Stress cardiomyopathy has a relatively better prognosis compared with ACS if the patient responds adequately to supportive treatment of heart failure, arrhythmias, and hypotension. LV outflow tract obstruction requires adequate β-blockade and aggressive IV fluid replacement. Repeat echocardiography documenting recovery of RWMA may be the only "proof" of this diagnosis when catheterization is not possible because of comorbidities or patient wishes.

Ongoing assessment of sepsis, systemic inflammatory response syndrome, hemodynamics, electrolyte and metabolic parameters, pulmonary function, and nutritional support are required on a daily basis in patients with global LV dysfunction. Optimal systolic BP is probably < 140 mm Hg and resting heart rate < 85 bpm from a cardiac standpoint. LV outflow tract obstruction may respond to lowering the heart rate to < 65 bpm.[37,38]

Inotropes and Vasopressors

Selection of inotropic agents can be quite difficult in the ICU setting, especially if conditions favor a stress cardiomyopathy and LV outflow tract obstruction. By taking many factors into consideration, the likely cause of LV dysfunction can be ascertained. Depending on regional perfusion to many critical vascular beds and the total cardiac output, the practitioner can determine which inotropic agent or pressors may assist in providing hemodynamic support. The choice of inotropic agent is reviewed in detail elsewhere.[69] The deleterious effects of these agents, namely increasing cardiac workload, arrhythmias, tachycardia, supply-demand mismatch, and direct myocardial toxicity should be carefully considered when evaluating using these agents in patients with LV dysfunction.[30,70]

Patients with acute decompensated heart failure with renal insufficiency or diuretic resistance may benefit from ultrafiltration. This is an effective method of fluid removal with advantages that include adjustable fluid removal volumes and rates, no effect on serum electrolytes, and decreased neurohormonal activation. Ultrafiltration is associated with significant increases in fluid removal at 24 h and fewer heart failure rehospitalizations without impacting renal function.[71,72]

Circulatory Assist Devices

When associated with refractory pump failure and hypoperfusion-related organ dysfunction, cardiogenic shock carries a significant mortality. There are no clearly defined indications for mechanical circulatory assist devices, but recent technical advances have made them a potential tool for circulatory failure refractory to conventional medical therapy and resuscitation.[60] The choice of a particular device is based on patient characteristics, operator preference, and expected length of support. Venoarterial extracorporeal membrane oxygenation can generally be initiated as temporary life support for severe acute respiratory or cardiac failure if it is potentially reversible.[73] Newer portable modular extracorporeal membrane oxygenation systems may expand the use of mechanical assist devices to improve persistent cardiogenic shock prehospital in the ambulance, disaster areas, air, sea, and battlefields, and can provide effective hemodynamic support for at least 6 months.[74,75]

Conclusions

LV dysfunction is common in critically ill patients. It is imperative to consider the clinical, hemodynamic, biochemical, and imaging data as well as their temporal trends to determine if the LVD is the cause, effect, or a coincidental finding. Coronary angiography and revascularization should be judiciously performed because of the additional morbidity in the critically ill. Adequately addressing the critical illness and optimizing LV dysfunction management through a concerted team effort is needed to maximize patient outcomes.

Acknowledgments

Financial/nonfinancial disclosures: The authors have reported to *CHEST* the following conflicts of interest: Dr Chockalingam has received VISN Research Awards in the last 2 years. Dr Dellsperger has received a 10% salary supported by the NIH. Drs Mehra and Dorairajan have reported no potential conflicts of interest with any companies/organizations whose products or services may be discussed in this article.

References

1. Lim W, Qushmaq I, Cook DJ, Crowther MA, Heels-Ansdell D, Devereaux PJ; Troponin T Trials Group. Elevated troponin and myocardial infarction in the intensive care unit: a prospective study. *Crit Care*. 2005;9(6):R636-R644.
2. Park JH, Kang SJ, Song JK, et al. Left ventricular apical ballooning due to severe physical stress in patients admitted to the medical ICU. *Chest*. 2005;128(1):296-302.
3. Marcelino PA, Marum SM, Fernandes AP, Germano N, Lopes MG. Routine transthoracic echocardiography in a general intensive care unit: an 18 month survey in 704 patients. *Eur J Intern Med*. 2009;20(3):e37-e42.
4. Zannad F, Mebazaa A, Juillière Y, et al; EFICA Investigators. Clinical profile, contemporary management and one-year mortality in patients with severe acute heart failure syndromes: The EFICA study. *Eur J Heart Fail*. 2006;8(7):697-705.
5. Melamed R, Sprenkle MD, Ulstad VK, Herzog CA, Leatherman JW. Assessment of left ventricular function by intensivists using hand-held echocardiography. *Chest*. 2009;135(6):1416-1420.
6. Feinberg MS, Hopkins WE, Davila-Roman VG, Barzilai B. Multiplane transesophageal echocardiographic doppler

imaging accurately determines cardiac output measurements in critically ill patients. *Chest*. 1995;107(3):769-773.
7. Bossone E, DiGiovine B, Watts S, et al. Range and prevalence of cardiac abnormalities in patients hospitalized in a medical ICU. *Chest*. 2002;122(4):1370-1376.
8. Ruiz Bailén M, Aguayo de Hoyos E, López Martnez A, et al. Reversible myocardial dysfunction, a possible complication in critically ill patients without heart disease. *J Crit Care*. 2003; 18(4):245-252.
9. Kollef MH, Ladenson JH, Eisenberg PR. Clinically recognized cardiac dysfunction: an independent determinant of mortality among critically ill patients. Is there a role for serial measurement of cardiac troponin I? *Chest*. 1997;111(5): 1340-1347.
10. Quenot JP, Le Teuff G, Quantin C, et al. Myocardial injury in critically ill patients: relation to increased cardiac troponin I and hospital mortality. *Chest*. 2005;128(4):2758-2764.
11. Januzzi JL, Morss A, Tung R, et al. Natriuretic peptide testing for the evaluation of critically ill patients with shock in the intensive care unit: a prospective cohort study. *Crit Care*. 2006;10(1):R37.
12. Rudiger A, Gasser S, Fischler M, Hornemann T, von Eckardstein A, Maggiorini M. Comparable increase of B-type natriuretic peptide and amino-terminal pro-B-type natriuretic peptide levels in patients with severe sepsis, septic shock, and acute heart failure. *Crit Care Med*. 2006;34(8):2140-2144.
13. Tung RH, Garcia C, Morss AM, et al. Utility of B-type natriuretic peptide for the evaluation of intensive care unit shock. *Crit Care Med*. 2004;32(8):1643-1647.
14. Mowatt G, Cook JA, Hillis GS, et al. 64-Slice computed tomography angiography in the diagnosis and assessment of coronary artery disease: systematic review and meta-analysis. *Heart*. 2008;94(11):1386-1393.
15. Lim W, Qushmaq I, Cook DJ, et al. Reliability of electrocardiogram interpretation in critically ill patients. *Crit Care Med*. 2006;34(5):1338-1343.
16. Kishon Y, Iqbal A, Oh JK, et al. Evolution of echocardiographic modalities in detection of postmyocardial infarction ventricular septal defect and papillary muscle rupture: study of 62 patients. *Am Heart J*. 1993;126(3 pt 1):667-675.
17. Scirica BM, Cannon CP, McCabe CH, et al; Thrombolysis in Myocardial Ischemia III Registry Investigators. Prognosis in the thrombolysis in myocardial ischemia III registry according to the Braunwald unstable angina pectoris classification. *Am J Cardiol*. 2002;90(8):821-826.
18. Braunwald E. Unstable angina. A classification. *Circulation*. 1989;80(2):410-414.
19. Noel B. Cardiovascular complications of cocaine use. *N Engl J Med*. 2001;345(21):1575, author reply 1576.
20. Cheitlin MD, McAllister HA, de Castro CM. Myocardial infarction without atherosclerosis. *JAMA*. 1975;231(9): 951-959.
21. Lockshin M, Tenedios F, Petri M, et al. Cardiac disease in the antiphospholipid syndrome: recommendations for treatment. Committee consensus report. *Lupus*. 2003;12(7):518-523.
22. Namazee MH, Rohani-Sarvestani HR, Serati AR. The early presentation of atrial myxoma with acute myocardial infarction. *Arch Iran Med*. 2008;11(1):98-102.
23. Rovner A, Valika AA, Kovacs A, Kates AM. Possible paradoxical embolism as a rare cause for an acute myocardial infarction. *Echocardiography*. 2006;23(5):407-409.
24. Tsuchihashi K, Ueshima K, Uchida T, et al; Angina Pectoris-Myocardial Infarction Investigations in Japan. Transient left ventricular apical ballooning without coronary artery stenosis: a novel heart syndrome mimicking acute myocardial infarction. Angina Pectoris-Myocardial Infarction Investigations in Japan. *J Am Coll Cardiol*. 2001;38(1):11-18.
25. Abe Y, Kondo M, Matsuoka R, Araki M, Dohyama K, Tanio H. Assessment of clinical features in transient left ventricular apical ballooning. *J Am Coll Cardiol*. 2003;41(5):737-742.
26. Kurisu S, Sato H, Kawagoe T, et al. Tako-tsubo-like left ventricular dysfunction with ST-segment elevation: a novel cardiac syndrome mimicking acute myocardial infarction. *Am Heart J*. 2002;143(3):448-455.
27. Seth PS, Aurigemma GP, Krasnow JM, Tighe DA, Untereker WJ, Meyer TE. A syndrome of transient left ventricular apical wall motion abnormality in the absence of coronary disease: a perspective from the United States. *Cardiology*. 2003;100(2):61-66.
28. Desmet WJ, Adriaenssens BF, Dens JA. Apical ballooning of the left ventricle: first series in white patients. *Heart*. 2003;89(9):1027-1031.
29. From AM, Prasad A, Pellikka PA, McCully RB. Are some false-positive stress echocardiograms a forme fruste variety of apical ballooning syndrome? *Am J Cardiol*. 2009;103(10):1434-1438.
30. Wittstein IS, Thiemann DR, Lima JA, et al. Neurohumoral features of myocardial stunning due to sudden emotional stress. *N Engl J Med*. 2005;352(6):539-548.
31. Ako J, Sudhir K, Farouque HM, Honda Y, Fitzgerald PJ. Transient left ventricular dysfunction under severe stress: brain-heart relationship revisited. *Am J Med*. 2006;119(1):10-17.
32. Gianni M, Dentali F, Grandi AM, Sumner G, Hiralal R, Lonn E. Apical ballooning syndrome or takotsubo cardiomyopathy: a systematic review. *Eur Heart J*. 2006;27(13):1523-1529.
33. Kurowski V, Kaiser A, von Hof K, et al. Apical and midventricular transient left ventricular dysfunction syndrome (takotsubo cardiomyopathy): frequency, mechanisms, and prognosis. *Chest*. 2007;132(3):809-816.
34. Bybee KA, Prasad A. Stress-related cardiomyopathy syndromes. *Circulation*. 2008;118(4):397-409.
35. Donohue D, Movahed MR. Clinical characteristics, demographics and prognosis of transient left ventricular apical ballooning syndrome. *Heart Fail Rev*. 2005;10(4):311-316.
36. El Mahmoud R, Mansencal N, Pilliére R, et al. Prevalence and characteristics of left ventricular outflow tract obstruction in tako-tsubo syndrome. *Am Heart J*. 2008;156(3):543-548.
37. Chockalingam A, Tejwani L, Aggarwal K, Dellsperger KC. Dynamic left ventricular outflow tract obstruction in acute myocardial infarction with shock: cause, effect, and coincidence. *Circulation*. 2007;116(5):e110-e113.
38. Chockalingam A, Dorairajan S, Bhalla M, Dellsperger KC. Unexplained hypotension: the spectrum of dynamic left ventricular outflow tract obstruction in critical care settings. *Crit Care Med*. 2009;37(2):729-734.
39. Bouhemad B, Nicolas-Robin A, Arbelot C, Arthaud M, Féger F, Rouby JJ. Acute left ventricular dilatation and shock-induced myocardial dysfunction. *Crit Care Med*. 2009; 37(2):441-447.
40. Umana E, Solares CA, Alpert MA. Tachycardia-induced cardiomyopathy. *Am J Med*. 2003;114(1):51-55.
41. Piccini JP, Berger JS, O'Connor CM. Amiodarone for the prevention of sudden cardiac death: a meta-analysis of randomized controlled trials. *Eur Heart J*. 2009;30(10):1245-1253.
42. Jeong YH, Choi KJ, Song JM, et al. Diagnostic approach and treatment strategy in tachycardia-induced cardiomyopathy. *Clin Cardiol*. 2008;31(4):172-178.
43. Nieminen MS, Brutsaert D, Dickstein K, et al; EuroHeart Survey Investigators; Heart Failure Association, European Society of Cardiology. EuroHeart Failure Survey II (EHFS II): a survey on hospitalized acute heart failure patients: description of population. *Eur Heart J*. 2006;27(22):2725-2736.
44. Parker MM, Shelhamer JH, Bacharach SL, et al. Profound but reversible myocardial depression in patients with septic shock. *Ann Intern Med*. 1984;100(4):483-490.

45. Muller-Werdan U, Buerke M, Ebelt H, et al. Septic cardiomyopathy—A not yet discovered cardiomyopathy? *Exp Clin Cardiol*. 2006;11(3):226-236.
46. Merx MW, Weber C. Sepsis and the heart. *Circulation*. 2007;116(7):793-802.
47. Parrillo JE, Parker MM, Natanson C, et al. Septic shock in humans. Advances in the understanding of pathogenesis, cardiovascular dysfunction, and therapy. *Ann Intern Med*. 1990;113(3):227-242.
48. Opasich C, Rapezzi C, Lucci D, et al; Italian Network on Congestive Heart Failure (IN-CHF) Investigators. Precipitating factors and decision-making processes of short-term worsening heart failure despite "optimal" treatment (from the IN-CHF Registry). *Am J Cardiol*. 2001;88(4):382-387.
49. Cohen-Solal A, Desnos M, Delahaye F, Emeriau JP, Hanania G. A national survey of heart failure in French hospitals. The Myocardiopathy and Heart Failure Working Group of the French Society of Cardiology, the National College of General Hospital Cardiologists and the French Geriatrics Society. *Eur Heart J*. 2000;21(9):763-769.
50. Hinshaw LB. Sepsis/septic shock: participation of the microcirculation: an abbreviated review. *Crit Care Med*. 1996; 24(6):1072-1078.
51. Steiner S, Speidl WS, Pleiner J, et al. Simvastatin blunts endotoxin-induced tissue factor in vivo. *Circulation*. 2005; 111(14):1841-1846.
52. Natanson C, Danner RL, Reilly JM, et al. Antibiotics versus cardiovascular support in a canine model of human septic shock. *Am J Physiol*. 1990;259(5 pt 2):H1440-H1447.
53. Hackam DG, Mamdani M, Li P, Redelmeier DA. Statins and sepsis in patients with cardiovascular disease: a population-based cohort analysis. *Lancet*. 2006;367(9508):413-418.
54. Liappis AP, Kan VL, Rochester CG, Simon GL. The effect of statins on mortality in patients with bacteremia. *Clin Infect Dis*. 2001;33(8):1352-1357.
55. Buerke U, Carter JM, Schlitt A, et al. Apoptosis contributes to septic cardiomyopathy and is improved by simvastatin therapy. *Shock*. 2008;29(4):497-503.
56. Wallace CK, Stetson SJ, Küçüker SA, et al. Simvastatin decreases myocardial tumor necrosis factor alpha content in heart transplant recipients. *J Heart Lung Transplant*. 2005;24(1):46-51.
57. Merx MW, Liehn EA, Graf J, et al. Statin treatment after onset of sepsis in a murine model improves survival. *Circulation*. 2005;112(1):117-124.
58. Almog Y, Shefer A, Novack V, et al. Prior statin therapy is associated with a decreased rate of severe sepsis. *Circulation*. 2004;110(7):880-885.
59. Merx MW, Weber C. Statins: a preventive strike against sepsis in patients with cardiovascular disease? *Lancet*. 2006;367(9508):372-373.
60. Koerner MM, Jahanyar J. Assist devices for circulatory support in therapy-refractory acute heart failure. *Curr Opin Cardiol*. 2008;23(4):399-406.
61. Laurent I, Monchi M, Chiche JD, et al. Reversible myocardial dysfunction in survivors of out-of-hospital cardiac arrest. *J Am Coll Cardiol*. 2002;40(12):2110-2116.
62. McCully RB, Karon BL, Rummans TA, et al. Frequency of left ventricular dysfunction after electroconvulsive therapy. *Am J Cardiol*. 2003;91(9):1147-1150.
63. Correa E, Mink S, Unruh H, Kepron W. Left ventricular contractility is depressed in IgE-mediated anaphylactic shock in dogs. *Am J Physiol*. 1991;260(3 pt 2):H744-H751.
64. Munt B, Jue J, Gin K, Fenwick J, Tweeddale M. Diastolic filling in human severe sepsis: an echocardiographic study. *Crit Care Med*. 1998;26(11):1829-1833.
65. Poelaert J, Declerck C, Vogelaers D, Colardyn F, Visser CA. Left ventricular systolic and diastolic function in septic shock. *Intensive Care Med*. 1997;23(5):553-560.
66. Paulus WJ, Tschöpe C, Sanderson JE, et al. How to diagnose diastolic heart failure: a consensus statement on the diagnosis of heart failure with normal left ventricular ejection fraction by the Heart Failure and Echocardiography Associations of the European Society of Cardiology. *Eur Heart J*. 2007;28(20):2539-2550.
67. Hamlin SK, Villars PS, Kanusky JT. Shaw AD. Role of diastole in left ventricular function, II: diagnosis and treatment. *Am J Crit Care*. 2004;13(6):453-468.
68. Smart N, Haluska B, Jeffriess L, Marwick TH. Exercise training in systolic and diastolic dysfunction: effects on cardiac function, functional capacity, and quality of life. *Am Heart J*. 2007;153(4):530-536.
69. Dellinger RP, Levy MM, Carlet JM, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. *Intensive Care Med*. 2008;34(1):17-60.
70. Akashi YJ, Nakazawa K, Sakakibara M, Miyake F, Sasaka K. Reversible left ventricular dysfunction "takotsubo" cardiomyopathy related to catecholamine cardiotoxicity. *J Electrocardiol*. 2002;35(4):351-356.
71. Bart BA, Boyle A, Bank AJ, et al. Ultrafiltration versus usual care for hospitalized patients with heart failure: the Relief for Acutely Fluid-Overloaded Patients With Decompensated Congestive Heart Failure (RAPID-CHF) trial. *J Am Coll Cardiol*. 2005;46(11):2043-2046.
72. Costanzo MR, Guglin ME, Saltzberg MT, et al; UNLOAD Trial Investigators. Ultrafiltration versus intravenous diuretics for patients hospitalized for acute decompensated heart failure. *J Am Coll Cardiol*. 2007;49(6):675-683.
73. Hemmila MR, Rowe SA, Boules TN, et al. Extracorporeal life support for severe acute respiratory distress syndrome in adults. *Ann Surg*. 2004;240(4):595-605.
74. Midla GS. Extracorporeal circulatory systems and their role in military medicine: a clinical review. *Mil Med*. 2007;172(5): 523-526.
75. Miller LW, Pagani FD, Russell SD, et al; HeartMate II Clinical Investigators. Use of a continuous-flow device in patients awaiting heart transplantation. *N Engl J Med*. 2007;357(9):885-896.