Perioperative Myocardial Failure

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Ventricular dysfunction sometimes occurs perioperatively, most often in association with cardiac surgery. This perioperative myocardial failure can often be predicted on the basis of the medical history and selected intraoperative indicators. There are a number of effective drug treatments, and in resistant patients, mechanical assist devices can be life saving.

Characteristics of Patients With Perioperative Heart Failure

Chronic Heart Failure

Several million Americans have been diagnosed with chronic heart failure (CHF), and an additional 400,000 cases are newly diagnosed each year. CHF can be the end result of many conditions. In adult patients, the most common etiologies are ischemic heart disease and hypertension; in children, the most common etiologies are viral infections and congenital heart disease. In cases of CHF intracellular cyclic AMP (cAMP) concentrations decrease as a result of β-adrenergic receptor (βAR) down-regulation and impaired coupling between βARs and adenylyl cyclase. Impaired coupling results from increased intracellular concentrations of the inhibitors $G_{i\alpha}$ and βAR kinase. Patients with CHF respond well to preload reduction with salt restriction and diuretics, preload and afterload reduction with vasodilators, and digoxin. Mortality is increased when positive inotropes (other than digoxin) are administered chronically, even though symptoms may decrease and quality of life may improve (1). Some patients with severe CHF require infusion of positive inotropes, implantation of ventricular assist devices, or both while awaiting cardiac transplantation.

There have been several notable advances in the treatment of CHF in the past decade. Specifically, improved outcome has been conclusively demonstrated with angiotensin-converting enzyme (ACE) inhibitors, β-blockers, and spironolactone. Other types of drugs currently in Phase III clinical trials for heart failure include agents that inhibit both neutral endopeptidase (neprilysin) and ACE, such as omapatrilat, novel sympatholytics such as nomorilole, endothelin receptor antagonists such as bosentan, and cytokine antagonists such as etanercept. There are other agents in earlier stages of clinical investigation, including vasopressin antagonists, positive inotropes, antiarrhythmics, and growth hormone. Finally, novel implantable pulse generators, defibrillators, and assist devices remain in development. Unfortunately, even with current optimal medical management the mortality and hospitalization rates remain unacceptably high (2).

Low Cardiac Output Syndrome

Patients with low cardiac output syndrome (LCOS), particularly those emerging from CPB, demonstrate a peculiar combination of inadequate oxygen delivery to tissues, hemodilution, mild hypocalcemia and hypomagnesemia, kaliuresis, and tissue thermal gradients (3). The underlying pathophysiology may include myocardial "stunning," which is a hypocontractile myocardium in response to ischemia and reperfusion (4). βAR down-regulation has been reported after CPB (5,6). Patients with LCOS receive positive inotropic drug therapy to increase the contractility of normal, hibernating, and "stunned" myocardium, which will in turn increase cardiac output and maintain diastolic blood pressure at levels capable of maintaining adequate oxygen delivery to the myocardium. The LCOS often includes hypotension, and, unlike CHF, responds poorly to vasodilators alone. Diastolic dysfunction, although present in many patients after CPB, is not the most prominent manifestation of LCOS. Increasing age, female gender, decreased left-ventricular ejection fraction (measured before surgery), and increased duration of CPB are all associated with a greater likelihood that inotropic drug support will be administered after coronary surgery. Increased age and reduced left-ventricular ejection fraction are associated with the use of positive inotropic drugs after cardiac valve surgery (7,8). Even patients who do not experience LCOS demonstrate declines in ventricular function after CPB, reaching a nadir some hours after arriving in the intensive care unit. Ventricular function recovers to baseline values over the succeeding 18–24 h (9).

Positive Inotropic Agents

Positive inotropic drugs can be conveniently divided on the basis of their mechanism of action into cAMP-independent and cAMP-dependent agents (Table 1).

cAMP-Independent Agents

Digoxin Digoxin inhibits Na^+, K^+-ATPase, increasing intracellular [Na^+], and indirectly, intracellular [Ca^{2+}]. Intracellular calcium ions may bind to troponin-C, increasing cardiac inotropy. In patients with chronic CHF, digoxin increases left-ventricular shortening and ejection fraction (10). Digoxin is not effective for acute management of LCOS.

Calcium Salts. Contractility of isolated cardiac or skeletal muscle improves with increasing extracellular [Ca^{2+}], particularly when [Ca^{2+}] rises above the normal range. Calcium for muscle contraction derives mostly from the sarcoplasmic reticulum, not from extracellular sources. The IV administration of calcium consistently increases systemic vascular resistance (11,12). Calcium interacts with vasoactive drugs. In patients recovering from coronary artery bypass grafting (CABG), calcium inhibited responses to epinephrine and dobutamine, but not to inamrinone (amrinone) (13,14). Calcium inhibition of βAR agonists likely results from direct inhibition of adenylyl cyclase (15,16). Bolus dosing of calcium has no consistent effect on cardiac output in patients emerging from CPB (11,12).

Thyroid Hormone. Hypothyroidism can cause profound cardiovascular depression. The IV administration of liothyronine (T_3) rapidly restores heart rate, stroke volume index, cardiac index, and peripheral vascular resistance to normal values (17). Patients recovering from CPB usually exhibit low circulating T_3 concentrations and inappropriately low thyrotropin concentrations (18). The routine administration of T_3 to cardiac surgery patients increases contractile function but may not produce an inotrope-sparing effect. How thyroid hormone may increase myocardial contractility remains unclear: T_3 increases myocardial contractile function as potently as isoproterenol, even with overwhelming βAR blockade (19), without increasing cAMP.

Calcium-Sensitizing Drugs. Levosimendan and pimobendan stabilize the calcium-bound conformation of troponin C, and their effects are highly dependent on the intracellular calcium (20). They increase systolic inotropy without impairing diastolic relaxation. Levosimendan also opens K_{atp} channels in cardiac myocytes and vascular smooth muscle. In experimental animals, levosimendan-induced activation of K_{atp} channels reduces myocardial infarct size (21). Levosimendan may be equally effective in the presence and absence of βAR blockers.

Table 1. Positive Inotropic Drugs

cAMP-Independent
Cardiac glycosides (digoxin)
Calcium salts
Thyroid hormone (liothyronine, T_3)
Calcium sensitizers
Levosimendan
Pimobendan
cAMP-Dependent
β-adrenergic agonists
Epinephrine
Norepinephrine
Dobutamine
Isoproterenol
Dopaminergic agonists
Dopamine
Dopexamine
Phosphodiesterase inhibitors
Inamrinone
Milrinone
Enoximone
Olprinone

cAMP-Dependent Agents

βAR Agonists. Catecholamines bind to βAR and activate a membrane-bound guanine nucleotide binding protein. This activates adenyl cyclase, generating cAMP. Increased cAMP increases calcium influx and increases calcium sensitivity of calcium-regulatory proteins. βAR agonists decrease the sensitivity of the contractile myofilaments to calcium, promoting relaxation. This effect is opposite to that of phosphodiesterase (PDE) inhibitors and αAR agonists (22).

Epinephrine binds and activates β_1, β_2, and αARs dose-dependently. Norepinephrine binds α_1, α_2, and β_1 receptors much more readily than β_2 receptors. Compared with norepinephrine, epinephrine produces a significantly greater cardiac output for a comparable increase in mean arterial pressure. Epinephrine is often used as a first-line positive inotrope after CPB (11). The administration of epinephrine into the left (rather than right) atrium offers higher concentrations of epinephrine for action on the heart and peripheral vasculature and reduces the likelihood of pulmonary hypertension. Norepinephrine has also been used as a relatively selective β_1AR agonist, particularly when combined with phentolamine to counteract its potent α_1AR and α_2AR agonist activity, and as a powerful vasoconstrictor to counteract the "vasoplegic syndrome" that sometimes occurs after CPB (23).

Dobutamine binds β_1 and β_2 receptors, producing dose-dependent increases in heart rate and cardiac output, and dose-dependent reductions in filling pressures (24). βAR-mediated reduction of venous capacitance, which increases the effective circulating blood volume, also contributes to the increased cardiac output.

Conventional wisdom, on the basis of studies in patients with CHF and βAR down-regulation, often recommends dobutamine as a "unique" drug that can increase cardiac output without increasing heart rate. This notion is false. Dobutamine increases heart rate more than epinephrine after CABG (24,25). Dobutamine has been used to increase oxygen delivery to tissues in patients with critical illness in the hope that this measure will improve outcome (26–28).

Isoproterenol is a potent, selective βAR agonist. Isoproterenol's current applications include treatment of bradycardia (especially after orthotopic cardiac transplantation), pulmonary hypertension and right-ventricular failure, and heart failure after pediatric cardiac surgery.

Dopaminergic Agonists. Dopamine activates dopamine (DA_1 and DA_2) receptors, βARs and αARs dose-dependently. Dopexamine lacks any direct αAR agonist activity but expresses β_2AR and DA_1 receptor agonist activity. Dopexamine also inhibits presynaptic reuptake of norepinephrine. Activation of DA_1 receptors produces vasodilation in renal, mesenteric, coronary, and cerebral arteries. Activation of DA_2 receptors inhibits release of norepinephrine and prolactin. Dopamine A_2 receptor agonists may also produce nausea and vomiting. Traditional teaching is that dopamine activates DA_2 receptors in the dosage range from 0.2 to 0.4 $\mu g \cdot kg^{-1} \cdot min^{-1}$; slightly higher doses (0.5–3.0 $\mu g \cdot kg^{-1} \cdot min^{-1}$) recruit DA_1 receptors. Still higher doses (5–10 $\mu g \cdot kg^{-1} \cdot min^{-1}$) activate βARs and αARs and have been widely used for inotropic support after heart surgery. Low doses of dopamine may increase renal blood flow and modulate corticomedullary distribution of renal blood flow (29) more than they increase cardiac output (30). The relationship between dopamine doses and concentrations is highly variable (31). Dopamine is often infused during periods of renal stress, such as during aortic surgery, sepsis, resuscitation, CPB, and during norepinephrine infusion (30). However, the efficacy of dopamine in this setting is unknown. Dopamine increases splanchnic oxygen consumption in cardiac surgery patients, but decreases splanchnic oxygen consumption in patients with sepsis (32). Dopexamine and dopamine produce a more pronounced increase in jejunal mucosal perfusion than dobutamine (33). After CPB, dopexamine and dobutamine were equally effective at increasing cardiac index; however, tachycardia was more common with dopexamine (24).

Phosphodiesterase Inhibitors. PDE inhibitors block the metabolism of cAMP to 5'-AMP, increasing intracellular cAMP concentrations. They also increase the calcium sensitivity of contractile proteins, increase calcium influx, and antagonize adenosine.

Inamrinone proved more effective than dobutamine with fewer complications during separation from CPB (34). Inamrinone was as effective as epinephrine, but the two drugs combined proved superior to either drug alone (35,36). After CABG, inamrinone increased stroke volume and cardiac index and decreased systemic and pulmonary vascular resistances dose dependently. Inamrinone increased intrapulmonary shunt and decreased Pao_2 (37).

Milrinone has inotropic and vasodilator properties similar to those of inamrinone, but is 15–20 times more potent (38,39). A 50 μg/kg milrinone loading dose is preferable to either 25 or 75 μg/kg in patients emerging from CPB (40). A loading dose of 50 μg/kg plus 0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ infusion maintains effective plasma concentrations >100 ng/mL. In some cases, a simple 50 μg/kg milrinone dose will suffice to facilitate separation from CPB (41). In a randomized comparison of inamrinone with milrinone in adult surgical patients, both drugs significantly increased cardiac index and decreased systemic and pulmonary vascular resistances (42).

Enoximone and olprinone are other PDE inhibitors that have been tested in surgical patients. Enoximone has been widely used in Europe. Olprinone is undergoing development in Japan (43). Both agents' hemodynamic effects resemble those of inamrinone and milrinone. When infused at doses similarly effective at increasing cardiac index, olprinone produced greater increases in hepatosplanchnic blood flow than inamrinone or milrinone (44). Olprinone has vascular capacitance effects opposite to those of dobutamine with capacitance decreasing after dobutamine and increasing after olprinone (45).

Timing and Dosing

There are wide differences of opinion regarding whether positive inotropic drugs should be administered in anticipation of their need (e.g., before separation from CPB) or only after their need has been established (e.g., to increase cardiac output after an unsuccessful attempt to wean from CPB without drug support). Early drug intervention could prevent or ameliorate post-CPB left-ventricular dysfunction and tissue hypoxia from reductions in oxygen transport. In a study of patients with poor left ventricular function, we found that preemptive administration of inamrinone reduced the subsequent need for "rescue" drug support. We also found that inamrinone was as effective as epinephrine in supporting the circulation after CPB (35). Similarly, Kikura and Shigehito (46) found that compared with patients receiving placebo, patients receiving preemptive infusions of either inamrinone or milrinone required significantly less dopamine, and demonstrated lower postoperative concentrations of lactate, LDH, CK, C-reactive protein, and glucose, indicating less stimulation of glycogenolysis and gluconeogenesis. A controlled clinical trial is currently underway to determine whether prophylactic milrinone improves outcomes after cardiac surgery in children (47).

Positive inotropic drugs are often titrated to the "just sufficient" dose to maintain cardiac output. Polonen et al. (48) used dobutamine infusions as necessary to maintain venous oxygen saturation >70% and arterial blood lactate ≤2 mmol/L after heart surgery, and noted a shorter hospital length of stay and reduced mortality in the treatment group.

Drug Synergism/Antagonism

Clinicians often combine two (or more) drugs, hoping to maximize their positive attributes and limit their adverse effects. Two drugs may interact in an additive, synergistic, or antagonistic fashion. We found antagonism between calcium and βAR agonists and between dobutamine and epinephrine (13–16,49). We and others have found combination of PDE inhibitors and βAR agonists to be more effective than either agent alone (35,36).

Complications of Positive Inotropes

Catecholamines may produce local tissue ischemia from subcutaneous infiltration, increase oxygen consumption, enhance lipolysis and gluconeogenesis, alter electrolyte concentrations, activate coagulation, override microvascular control mechanisms, alter distribution of cardiac output, increase myocardial work, and promote cardiac arrhythmias. The PDE inhibitors and β-agonists increase pulmonary shunt after CABG surgery (37). Catecholamine support is associated with critical illness polyneuropathy after heart surgery (50).

Mechanical Assist Devices

Patients with coronary artery disease and LCOS may benefit from intraaortic balloon counter pulsation, which has the advantage of increasing diastolic coronary blood flow without increasing myocardial oxygen consumption. Unfortunately, the 30-day mortality of patients undergoing balloon implantation for LCOS is 34% (51). Patients with severe persisting ventricular dysfunction or cardiomyopathy may require right- or left-ventricular assist devices, or both. Use of these devices is appropriate only for patients who can be expected to have recovery of ventricular function or who are potential candidates for orthotopic heart transplantation.

Summary

Perioperative heart failure, in the forms of acute exacerbation of CHF and LCOS, continues to occur, despite improvements in medical management, myocardial preservation, and surgical techniques. This may be the result of patients now undergoing heart surgery as a routine despite extremes of age and debilitating comorbidities. Fortunately, effective drug treatments are available, and most patients will make a full recovery despite an episode of perioperative heart failure.

References

1. Packer M, Carver JR, Rodeheffer RJ, et al. Effect of oral milrinone on mortality in severe chronic heart failure. The PROMISE Study Research Group. N Engl J Med 1991;325:1468–75.
2. McMurray JJV. Heart failure in 10 years' time: focus on pharmacological treatment. Heart 2002;88(Suppl II):ii40-ii46.
3. Butterworth JF IV. Therapeutic choices in separation from cardiopulmonary bypass. J Drug Development 1991;4(Suppl 2): 16–21.
4. Bolli R. Myocardial stunning in man. Circulation 1992;86: 1671–91.
5. Schwinn DA, Leone BJ, Spahn DR, et al. Desensitization of myocardial β-adrenergic receptors during cardiopulmonary bypass: evidence for early uncoupling and late downregulation. Circulation 1991;84:2559–67.
6. Booth JV, Landolfo KP, Chesnut LC, et al. Acute depression of myocardial β-adrenergic receptor signaling during cardiopulmonary bypass. Anesthesiology 1998;89:602–11.
7. Royster RL, Butterworth JF IV, Prough DS, et al. Preoperative and intraoperative predictors of inotropic support and long-term outcome in patients having coronary artery bypass grafting. Anesth Analg 1991;72:729–36.
8. Butterworth JF IV, Legault C, Royster RL, Hammon JW Jr. Factors that predict the use of positive inotropic drug support after cardiac valve surgery. Anesth Analg 1998;86:461–7.
9. Breisblatt WM, Stein KL, Wolfe CJ, et al. Acute myocardial dysfunction and recovery: a common occurrence after coronary bypass surgery. J Am Coll Cardiol 1990;15:1261–9.
10. Kulick DL, Rahimtoola SH. Current role of digitalis therapy in patients with congestive heart failure. JAMA 1991;265:2995–7.
11. Royster RL, Butterworth JF IV, Prielipp RC, et al. A randomized, blinded, placebo-controlled evaluation of calcium chloride and epinephrine for inotropic support after emergence from cardiopulmonary bypass. Anesth Analg 1992;74:3–13.
12. Johnston WE, Robertie PG, Butterworth JF IV, et al. Is calcium or ephedrine superior to placebo for emergence from cardiopulmonary bypass? J Cardiothorac Vasc Anesth 1992;6:528–34.
13. Zaloga GP, Strickland RA, Butterworth JF IV, et al. Calcium attenuates epinephrine's β-adrenergic effects in postoperative heart surgery patients. Circulation 1990;81:196–200.
14. Butterworth JF IV, Zaloga GP, Prielipp RC, et al. Calcium inhibits the cardiac stimulating properties of dobutamine but not of amrinone. Chest 1992;101:174–80.
15. Prielipp RC, Hill T, Washburn D, Zaloga GP. Circulating calcium modulates adrenaline induced cyclic adenosine monophosphate production. Cardiovasc Res 1989;23:838–41.
16. Abernethy WB, Butterworth JF IV, Prielipp RC, et al. Calcium entry attenuates adenylyl cyclase activity: a possible mechanism for calcium-induced catecholamine resistance. Chest 1995;107: 1420–5.
17. Klemperer JD. Thyroid hormone and cardiac surgery. Thyroid 2002;12:517–21.
18. Ririe DG, Butterworth JF, Hines M, et al. Effects of cardiopulmonary bypass and deep hypothermic circulatory arrest on the thyroid axis during and after repair of congenital heart defects: preservation of deep hypothermia? Anesth Analg 1998;87: 543–8.
19. Ririe DG, Butterworth JF IV, Royster RL, et al. Triiodothyronine increases contractility independent of beta-adrenergic receptors or stimulation of cyclic-3', 5'-adenosine monophosphate. Anesthesiology 1995;82:1004–12.
20. Cleland JG, McGowan J. Levosimendan: a new era for inodilator therapy for heart failure? Curr Opin Cardiol 2002;17:257–65.

21. Kersten JR, Montgomery MW, Pagel PS, Warltier DC. Levosimendan, a new positive inotropic drug, decreases myocardial infarct size via activation of K(ATP) channels. Anesth Analg 2000;90:5–11.
22. Endoh M. Mechanisms of action of novel cardiotonic agents. J Cardiovasc Pharmacol 2002;40:323–328.
23. Kristof AS, Magder S. Low systemic vascular resistance state in patients undergoing cardiopulmonary bypass. Crit Care Med 1999;27:1121–7.
24. MacGregor DA, Butterworth JF IV, Zaloga GP, et al. Hemodynamic and renal effects of dopexamine and dobutamine in patients with reduced cardiac output following coronary artery bypass grafting. Chest 1994;106:835–41.
25. Butterworth JF IV, Prielipp RC, Royster RL, et al. Dobutamine increases heart rate more than epinephrine in patients recovering from aortocoronary bypass surgery. J Cardiothorac Vasc Anesth 1992;6:535–41.
26. Shoemaker WC, Appel PL, Kram HB. Oxygen transport measurements to evaluate tissue perfusion and titrate therapy: dobutamine and dopamine effects. Crit Care Med 1991;19:672–88.
27. Shoemaker WC, Appel PL, Kram HB, et al. Comparison of hemodynamic and oxygen transport effects of dopamine and dobutamine in critically ill surgical patients. Chest 1989;96: 120–6.
28. Hayes MA, Timmins AC, Yau EHS, et al. Elevation of systemic oxygen delivery in the treatment of critically ill patients. N Engl J Med 1994;330:1717–22.
29. Frishman WH, Hotchkiss H. Selective and nonselective dopamine receptor agonists: an innovative approach to cardiovascular disease treatment. Am Heart J 1996;132:861–70.
30. Richer M, Robert S, Lebel M. Renal hemodynamics during norepinephrine and low-dose dopamine infusions in man. Crit Care Med 1996;24:1150–6.
31. MacGregor DA, Smith TE, Prielipp RC, et al. Pharmacokinetics of dopamine in healthy male subjects. Anesthesiology 2000;92: 338–46.
32. Jakob SM, Ruokonen E, Takala J. Effects of dopamine on systemic and regional blood flow and metabolism in septic and cardiac surgery patients. Shock 2002;18:8–13.
33. Thorén A, Elam M, Ricksten S-E. Differential effects of dopamine, dopexamine, and dobutamine on jejunal mucosal perfusion early after cardiac surgery. Crit Care Med 2000;28:2338–43.
34. Dupuis JY, Bondy R, Cattran C, et al. Amrinone and dobutamine as primary treatment of low cardiac output syndrome following coronary artery surgery: a comparison of their effects on hemodynamics and outcome. J Cardiothorac Vasc Anesth 1992;6:542–53.
35. Butterworth JF IV, Royster RL, Prielipp RC, et al. Amrinone in cardiac surgical patients with left-ventricular dysfunction: a prospective, randomized placebo-controlled trial. Chest 1993; 104:1660–7.
36. Royster RL, Butterworth JF IV, Prielipp RC, et al. Combined inotropic effects of amrinone and epinephrine after cardiopulmonary bypass in humans. Anesth Analg 1993;77:662–72.
37. Prielipp RC, Butterworth JF IV, Zaloga GP, et al. Effects of amrinone on cardiac index, venous oxygen saturation and venous admixture in patients recovering from cardiac surgery. Chest 1991;99:820–5.
38. Levy JH, Bailey JM, Deeb GM. Intravenous milrinone in cardiac surgery. Ann Thorac Surg 2002;73:325–30.
39. Bailey JM, Levy JH, Kikura M, et al. Pharmacokinetics of intravenous milrinone in patients undergoing cardiac surgery. Anesthesiology 1994;81:616–22.
40. Butterworth JF IV, Hines RL, Royster RL, James RL. A pharmacokinetic and pharmacodynamic evaluation of milrinone in adults undergoing cardiac surgery. Anesth Analg 1995;81: 783–92.
41. Lobato EB, Florete O Jr, Bingham HL. A single dose of milrinone facilitates separation from cardiopulmonary bypass in patients with pre-existing left ventricular dysfunction. Br J Anaesth 1998; 81:782–4.
42. Rathmell JP, Prielipp RC, Butterworth JF, et al. A multicenter, randomized, blind comparison of amrinone with milrinone after elective cardiac surgery. Anesth Analg 1998;86:683–90.
43. Orime Y, Shiono M, Hata H, et al. Post-operative effects of olprinone after coronary artery bypass grafting. Ann Thorac Cardiovasc Surg 1998;4:340–6.
44. Iribe G, Yamada H, Matsunaga A, Yoshimura N. Effects of the phosphodiesterase III inhibitors olprinone, milrinone, and amrinone on hepatosplanchnic oxygen metabolism. Crit Care Med 2000;28:743–8.
45. Tanoue Y, Morita S, Nagano I, et al. Effect of phosphodiesterase III inhibitor on contractility, afterload, and vascular capacitance during right heart bypass preparation. Jpn J Thorac Cardiovasc Surg 2001;49:607–13.
46. Kikura M, Shigehito S. The efficacy of preemptive milrinone or amrinone therapy in patients undergoing coronary artery bypass grafting. Anesth Analg 2002;94:22–30.
47. Hoffman TM, Wernovsky G, Atz AM, et al. Prophylactic intravenous use of milrinone after cardiac operation in pediatrics (PRIMACORP) study. Prophylactic Intravenous Use of Milrinone After Cardiac Operation in Pediatrics. Am Heart J 2002; 143:15–21.
48. Pölönen P, Ruokonen E, Hippeläinen M, et al. A prospective, randomized study of goal-oriented therapy in cardiac surgical patients. Anesth Analg 2000;90:1052–9.
49. Prielipp RC, MacGregor DA, Royster RL, et al. Dobutamine antagonizes epinephrine's biochemical and cardiotonic effects. Results of an in vitro model using human lymphocytes and a clinical study in patients recovering from cardiac surgery. Anesthesiology 1998;89:49–57.
50. Thiele RI, Jakob H, Hund E, et al. Sepsis and catecholamine support are the major risk factors for critical illness polyneuropathy after open heart surgery. Thorac Cardiovasc Surg 2000;48: 145–50.
51. Hausmann H, Potapov EV, Koster A, et al. Prognosis after the implantation of an intra-aortic balloon pump in cardiac surgery calculated with a new score. Circulation 2002;106(Suppl I):I-203–6.