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Preventing perioperative myocardial ischemia

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Perioperative myocardial ischemia is associated with significant morbidity and mortality. Underlying heart disease, the type of surgical procedure, and postoperative physiological stress all play a role in its physiopathology. Prevention strategies must encompass the entire perioperative period. Very few patients benefit from prophylactic revascularization to decrease short-term postoperative risk. Certain pharmacological agents (eg, beta-blockers and alpha-2 agonists) and certain simple strategies (eg, prevention of hypothermia) have proven to be effective in preventing these complications. More studies are needed in this field and anesthesiologists, as specialists in perioperative medicine, will be called upon to play a greater role in the development and application of these prevention and treatment strategies.

INTRODUCTION

It is estimated that every year, close to 100 million patients worldwide undergo a surgical procedure and this number continues to grow at a steady rate. In the United States, the American Heart Association (AHA) estimates that, by approximately 2018, surgical clientele will exceed medical clientele. An aging hospitalized population is also associated with a greater number of comorbidities, including atherosclerotic heart disease, which affects up to 20%-25% of these patients.[1] Perioperative cardiac ischemia is associated with significant morbidity and mortality; more than half of postoperative deaths are due to cardiac complications, the majority of which are ischemic. While important strides have been made in modern cardiology, the physiopathology, clinical presentation, and treatment of perioperative ischemia and myocardial infarction (MI) have been studied less than MI in the nonsurgical population. This is despite the fact that perioperative MI has a major impact on public health.

PATHOPHYSIOLOGY AND CLINICAL PRESENTATION OF PERIOPERATIVE ISCHEMIA

It is generally accepted that cardiac ischemia is the result of an imbalance between oxygen supply and demand in the myocardium. On the other hand, the traditional notion that fixed stenoses cause limited oxygen intake is probably too simplistic. Indeed, several coronary syndromes are included in the spectrum of myocardial ischemia severity. The unifying physiopathological element seems to be an increase in sympathetic activity in the context of an unstable atheromatous plaque and hypercoagulability – both local and systemic – in the coronary endothelium. Thus, all the elements conducive to cardiac ischemia are present in the context of a surgical procedure.

Therefore, in addition to being associated with a patient's underlying cardiovascular status (hence the development of various point scoring systems to quantify preoperative risk),[2,3] myocardial ischemia also results from phenomena occurring during the procedure. The surgery itself is associated with severe stress, extensive tissue damage, activation of the inflammatory and procoagulant cascade phenomena, and significant

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activation of the hormonal and sympathetic systems.

The type and duration of the procedure and the presence of factors that decrease the oxygen supply to the myocardium during the procedure (eg, tachycardia and hypotension) all have a direct effect on the onset of perioperative myocardial ischemia. On the clinical level, Mangano *et al* observed that the incidence and severity of intraoperative ischemic episodes were comparable to those occurring during hospitalization before the procedure, with even a certain protective effect coming from the anesthesia. Furthermore, this series of studies demonstrated that the severity and duration of ischemic episodes were greater during the stress test than during the operation.[4-6] These same authors demonstrated that in a population of patients who had undergone cardiac surgery, the majority of ischemic episodes occurred without any hemodynamic repercussions. On the other hand, 40% of the episodes of tachycardia were accompanied by ischemia, and postoperative MI was 3 times more frequent in patients with tachycardia.

Moreover, upon recovery from anesthesia and during the immediate postoperative period, there occurs an intense activation of the sympathetic nervous system, exhibited by a significant increase in urine and plasma catecholamines,[7,8] a tendency toward hypercoagulability, and changes in tissue perfusion and body temperature. This postoperative sympathetic system activation occurs even with effective pain control and there is no doubt that it plays a significant role in the etiology of postoperative ischemia.

The implications of ischemia occurring postoperatively were demonstrated in an observational study of 474 coronary patients, or patients at risk of becoming so.[9] After multivariate analysis of several indicators, postoperative ischemia was the only variable associated with 2.8 times more adverse events and 9.2 times more ischemic events. No other variable, be it the cardiac risk score, history of MI or pulmonary edema, or even the onset of ischemia before or during the surgery, was independently associated with the onset of postoperative MI. The authors concluded that in the population of patients at high risk of coronary disease, the early appearance of postoperative ischemia was the most powerful predictive element of postoperative MI.

To summarize, the physiopathology of ischemia and perioperative MI is complex and multifactorial, a consequence of an interaction between the severity of pre-existing coronary disease, the degree of instability of the atheromatous plaque, the type of surgical procedure, and the stress reaction and its consequences during the postoperative period, as well as associated procoagulant and proinflammatory conditions. Strategies to reduce the risk of a perioperative episode of cardiac ischemia must therefore involve these factors.

INTERVENTIONS TO PREVENT PERIOPERATIVE MYOCARDIAL ISCHEMIA

Preoperative period

The purpose of the preoperative visit is to quantify the risk of coronaropathy in patients by stratifying them into low, intermediate, and high-risk groups. To do this, additional testing should be done if necessary. With this assessment, a plan can be developed that encompasses the entire perioperative period. Several organizations have published guidelines on the preoperative assessment of coronary disease. The step-by-step approach of the AHA is based on the evaluation of clinical markers, functional capacity, and the risk associated with the particular type of surgery. It has proven to be effective, with a good cost/benefit ratio. First published in 1996, it was revised in 2002.[10] Once patients at risk of ischemic complications are identified, possible interventions include revascularization (either surgically or by angioplasty) and medical treatment.

Surgical revascularization

Many retrospective studies have demonstrated that patients having already undergone coronary bypass surgery have a perioperative mortality rate equivalent to patients having no clinical markers of coronary disease.[11-13] However, Eagle *et al,* after an analysis of patients registered in the CASS data base,[14] noted that patients undergoing low-risk surgery are at low risk of developing cardiac complications, regardless of whether they have undergone prior revascularization or not. On the other hand, there is a benefit associated with prior revascularization in the context of intermediate or high-risk surgery, especially for patients with more severe coronary disease. However, the morbidity of revascularization will be an added factor in terms of the planned procedure and will erase this benefit except in a very small population of high-risk patients. Therefore, coronary revascularization before elective surgery is only indicated if the patient has revascularization indications,[15] regardless of the perioperative context.

Angioplasty with or without a coronary stent

At present, there is no prospective study that demonstrates beyond a doubt that mortality or morbidity risk is reduced with preoperative angio-

plasty. In the BARI (Bypass Angioplasty Revascularization Investigation),[16] the perioperative risk and duration of hospital stay were similar, whether the means of revascularization was angioplasty or coronary bypass surgery. Even though this study does not identify a population that would benefit from prophylactic angioplasty, it suggests that perioperative mortality is equivalent, regardless of the chosen means of revascularization. While there is no current consensus on the indications for preoperative angioplasty, several retrospective studies have demonstrated a benefit[17] and one multicentre study is now in progress.[18] While we wait for the results, it is recommended that angioplasty be restricted to its usual indications, regardless of the planned surgery.

If preoperative angioplasty is performed, it is recommended that the surgical procedure takes place one week after the angioplasty, the interval of time needed for stabilization of the endothelium, but no longer than three months later, to avoid the restenosis risk peak.

Coronary stents are now inserted during most angioplasty revascularization procedures. One study put the incidence of MI at 18%, major hemorrhage at 28%, and death at 20%, if patients were operated on <2 weeks after coronary angioplasty with insertion of a stent.[19] These high percentages of MI and death ensue mainly from thrombotic events related to the stent. Also, patients take potent antiplatelet drugs following the intervention and, during this period, are at high risk of hemorrhaging if they undergo surgery. Therefore, it is preferable to wait until the antiplatelet treatment is discontinued before operating on a patient, albeit no longer than 6 to 8 weeks, so as to avoid the critical period in terms of restenosis.

MEDICAL TREATMENT

Several studies have examined the impact of pharmacological agents on cardiovascular morbidity and mortality during the perioperative period. These studies looked mainly at beta-blockers, alpha-2 agonists, nitroglycerin, and calcium channel blockers.

Beta-blockers

The most convincing studies are those evaluating the beta-blockers. Three controlled, randomized studies have confirmed their effectiveness during the perioperative period.

- Poldermans *et al* studied the effect of bisoprolol in a group of patients at high risk of cardiac complications undergoing high-risk vascular operations. Bisoprolol was started, on average, 37 days before the surgery, and titrated according to the heart rate. The authors observed a significant reduction in cardiac mortality and the incidence of non-fatal MI.[20]
- In an effort to better define the population to be treated, Boersma monitored the same cohort of patients using a very simple scoring system. He established that all the patients benefited from beta-blockers given perioperatively, except those at very low and very high risk of ischemic cardiac complications (Figure 1).[21]
- Another study randomized 200 patients to receive atenolol or placebo on the day of the operation and during the following 7 days.[22] The two groups showed no differences in terms of the incidence of MI or death in the immediate postoperative period, but the treated group presented fewer episodes of perioperative ischemia. However, a significant difference in cardiovascular morbidity was exhibited in the subsequent months and was maintained for up to 2 years. The study was criticized by some because certain treatments were not equal in the two groups (ACE inhibitors, beta-blockers, and calcium channel blockers).

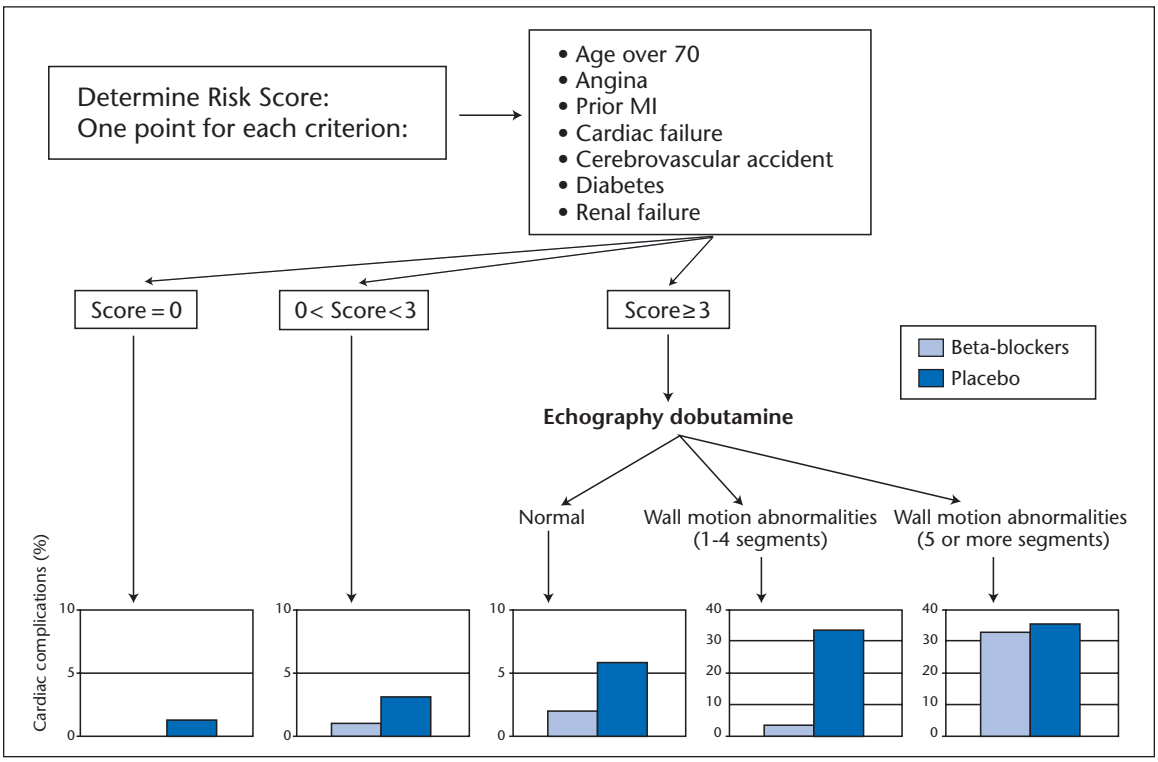
Alpha-2 agonists

Several recent studies have evaluated the role of alpha-2 agonists.[23-26] Oliver *et al* studied 2,854 patients with known coronary disease or significant risk factors. These patients received in random fashion, a continuous infusion of mivazerol or a placebo. The authors noted a significant reduction in cardiac mortality in the treated group. Two other studies also demonstrated a significant decrease in the incidence of myocardial ischemia with clonidine, another alpha-2 agonist.

Nitrates

The use of nitrates is more controversial. There is no doubt that nitroglycerin can treat cardiac ischemia, but administered prophylactically, it is probably useless. Only one study,[27] conducted in a population of patients undergoing carotid endarterectomy, demonstrated a reduced incidence of ischemia, but there was no effect whatsoever on cardiac morbidity and mortality. Furthermore, nitroglycerin used with anesthetic agents can induce or aggravate ischemia through vasodilatation, leading to reflex tachycardia. Finally, the hypotension associated with nitrates can reduce the room to maneuver when it comes to using treatments proven to be effective, such as beta-blockers. It is therefore advisable to use intravenous nitrates solely for the treat-

FIGURE 1: Evaluation of the risk of cardiac complications



ment of myocardial ischemia in normotensive or hypertensive patients. The transcutaneous route should be avoided because absorption is too uncertain in the perioperative period.

Calcium channel blockers

The few studies that have examined the potential role of calcium channel blockers in the perioperative period are either too small to allow any firm conclusions or did not demonstrate any benefit.[28,29]

THE PEROPERATIVE PERIOD

The intraoperative early detection of myocardial ischemia, followed by effective treatment, should logically lead to a reduction in cardiovascular mortality and morbidity. However, thus far no study has managed to demonstrate this, and because of ethical considerations, it is impossible to conduct a controlled randomized study to prove it.

Monitoring and diagnosing intraoperative ischemia, either through ST-segment analysis, transesophageal echography, or intrapulmonary artery catheter, is too broad a subject to discuss in detail here. Nonetheless, the appearance of intraoperative ischemia is definitely a coronary disease marker and associated with a greater probability of morbidity. It is therefore logical to treat these episodes aggressively, especially in patients at higher risk of coronary disease. To this end, the agents mentioned above are used to optimize the balance between oxygen demand and supply to the myocardium. To accomplish this, adequate coronary perfusion pressure and optimal oxygenation must be maintained and factors that increase oxygen consumption must be minimized.

Given our current knowledge, it is not possible to recommend one anesthetic technique over another. Some physicians suggest that the decreased sympathetic response associated with regional anesthesia can produce a benefit – both in terms of cardiac and thrombotic complications – by attenuating the hypercoagulability associated with the postoperative period. But the findings of studies are contradictory. For example, Tuman observed a reduction in cardiovascular morbidity with the combined use of regional and general anesthesia.[30] In the same year, however, Baron *et al* failed to reproduce these results in a population of 176 patients.[31] Since no study suggests an increase in complications, while some demonstrate benefits, and considering the advantages of postoperative analgesia they offer, regional techniques, (particularly the epidural)

should be part of the anesthetic plan in patients at risk of ischemic complications.

Hypothermia frequently occurs during major surgery and may be accentuated by the combination of general and epidural anesthesia. Two studies have demonstrated a decrease in cardiac morbidity in patients where normothermia was maintained. In addition, one of these studies cited hypothermia as an independent risk factor for cardiac complications after multivariate analysis, with a decrease of about 55% in cardiac complications when normothermia was maintained in the patient.

Finally, the absence of an ischemic episode during the procedure and emergence constitutes an excellent negative prediction of cardiac complications. This seems to be true regardless of the patient's underlying disease and type of surgery. On the other hand, patients who present with myocardial ischemia during a surgical procedure or emergence have a 9-fold greater risk of a cardiac event during hospitalization and double the risk of dying in the 6 months following surgery.[9,32] These patients likely require closer postoperative supervision.

POSTOPERATIVE PERIOD

Despite all of our efforts, a certain number of patients will present with an acute coronary syndrome during the perioperative period, with an associated mortality of 40% to 70%. This mortality stems, in part, from comorbidities, but also from the fact that certain therapeutic options are limited during the perioperative context. For obvious reasons, patients having recently undergone surgery were excluded from large-scale studies on thrombolysis. Some specialists prefer rapid angiography and coronary dilatation, since the risk of hemorrhage is considered lower with invasive strategies than with thrombolysis. The patient would, nonetheless, be exposed to anticoagulants such as heparin and antiplatelet drugs, which could be dangerous following certain types of surgery. However, it is important to administer the usual treatments for an acute MI, eg, aspirin, beta-blockers, and ACE inhibitors. The latter have not been studied in the perioperative context, but they have proven their usefulness in the treatment of MI, especially when it is associated with left ventricular dysfunction or located in the anterior wall.[33]

Even if the majority of MIs are induced by thrombosis or an acute coronary occlusion, there is no doubt that a significant number of perioperative MIs are caused by an increase in demand to deal with perioperative stress, in conditions when the supply of oxygen is limited. In these cases, decreasing demand through aggressive management of tachycardia, hypotension, fever, and hyperadrenergic stimulation is essential.

CONCLUSIONS

With an aging population and an ever-growing surgical clientele, we will increasingly face perioperative myocardial ischemic complications. Thus far, the knowledge in this field is too vague to determine the ideal strategy for preventing and treating these complications. Anesthesiologists are acutely aware of the physiological response to surgical stress and are in a particularly good position to implement and administer optimal anti-ischemic measures. Their role should not be confined to the operating room, but should extend from preoperative assessment to the postoperative period, and include collaboration with other caregivers.

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References

1. Mangano DT. Perioperative cardiac morbidity—epidemiology, costs, problems, and solutions. *West J Med* 1994;161:87-9.
2. Goldman L, Caldera DL, Nussbaum SR, et al. Multifactorial index of cardiac risk in noncardiac surgical procedures. *N Engl J Med* 1977;297:845-50.
3. Detsky AS, Abrams HB, Forbath N, Scott JG, Hilliard JR. Cardiac assessment for patients undergoing noncardiac surgery. A multifactorial clinical risk index. *Arch Intern Med* 1986;146:2131-4.
4. Knight AA, Hollenberg M, London MJ, et al. Perioperative myocardial ischemia: importance of the preoperative ischemic pattern. *Anesthesiology* 1988;68:681-8.
5. Mangano DT, Wong MG, London MJ, Tubau JF, Rapp JA. Perioperative myocardial ischemia in patients undergoing noncardiac surgery—II: Incidence and severity during the 1st week after surgery. The Study of Perioperative Ischemia (SPI) Research Group. *J Am Coll Cardiol* 1991;17:851-7.
6. Mangano DT, Hollenberg M, Fegert G, et al. Perioperative myocardial ischemia in patients undergoing noncardiac surgery—I: Incidence and severity during the 4 day perioperative period. The Study of Perioperative Ischemia (SPI) Research Group. *J Am Coll Cardiol* 1991;17:843-50.
7. Udelsman R, Norton JA, Jelenich SE, et al. Responses of the hypothalamic-pituitary-adrenal and renin-angiotensin axes and the sympathetic system during controlled surgical and anesthetic stress. *J Clin Endocrinol Metab* 1987;64:986-94.
8. Plunkett JJ, Reeves JD, Ngo L, et al. Urine and plasma catecholamine and cortisol concentrations after myocardial revascularization. Modulation by continuous sedation. Multicenter Study of Perioperative Ischemia (McSPI) Research Group, and the Ischemia Research and Education Foundation (IREF). *Anesthesiology* 1997;86:785-96.

9. Mangano DT, Browner WS, Hollenberg M, London MJ, Tubau JF, Tateo IM. Association of perioperative myocardial ischemia with cardiac morbidity and mortality in men undergoing noncardiac surgery. The Study of Perioperative Ischemia Research Group. *N Engl J Med* 1990;323:1781-8.
10. Eagle KA, Berger PB, Calkins H, et al. ACC/AHA guideline update for perioperative cardiovascular evaluation for noncardiac surgery—executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1996 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). *J Am Coll Cardiol* 2002;39:542-53.
11. Crawford ES, Morris GC, Jr., Howell JF, Flynn WF, Moorhead DT. Operative risk in patients with previous coronary artery bypass. *Ann Thorac Surg* 1978;26:215-21.
12. Nielsen JL, Page CP, Mann C, Schwesinger WH, Fountain RL, Grover FL. Risk of major elective operation after myocardial revascularization. *Am J Surg* 1992;164:423-6.
13. Reul GJ Jr, Cooley DA, Duncan JM, et al. The effect of coronary bypass on the outcome of peripheral vascular operations in 1093 patients. *J Vasc Surg* 1986;3:788-98.
14. Eagle KA, Rihal CS, Mickel MC, Holmes DR, Foster ED, Gersh BJ. Cardiac risk of noncardiac surgery: influence of coronary disease and type of surgery in 3368 operations. CASS Investigators and University of Michigan Heart Care Program. Coronary Artery Surgery Study. *Circulation* 1997;96:1882-7.
15. Eagle KA, Guyton RA, Davidoff R, et al. ACC/AHA guidelines for coronary artery bypass graft surgery: executive summary and recommendations: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to revise the 1991 guidelines for coronary artery bypass graft surgery). *Circulation* 1999;100:1464-80.
16. Hassan SA, Hlatky MA, Boothroyd DB, et al. Outcomes of noncardiac surgery after coronary bypass surgery or coronary angioplasty in the Bypass Angioplasty Revascularization Investigation (BARI). *Am J Med* 2001;110:260-6.
17. Gottlieb A, Banoub M, Sprung J, Levy PJ, Beven M, Mascha EJ. Perioperative cardiovascular morbidity in patients with coronary artery disease undergoing vascular surgery after percutaneous transluminal coronary angioplasty. *J Cardiothorac Vasc Anesth* 1998;12:501-6.
18. McFalls EO, Ward HB, Krupski WC, et al. Prophylactic coronary artery revascularization for elective vascular surgery: study design. Veterans Affairs Cooperative Study Group on Coronary Artery Revascularization Prophylaxis for Elective Vascular Surgery. *Control Clin Trials* 1999;20:297-308.
19. Kaluza GL, Joseph J, Lee JR, Raizner ME, Raizner AE. Catastrophic outcomes of noncardiac surgery soon after coronary stenting. *J Am Coll Cardiol* 2000;35:1288-94.
20. Poldermans D, Boersma E, Bax JJ, et al. The effect of bisoprolol on perioperative mortality and myocardial infarction in high-risk patients undergoing vascular surgery. Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography Study Group. *N Engl J Med* 1999;341:1789-94.
21. Boersma E, Poldermans D, Bax JJ, et al. Predictors of cardiac events after major vascular surgery: Role of clinical characteristics, dobutamine echocardiography, and beta-blocker therapy. *JAMA* 2001;285:1865-73.
22. Wallace A, Layug B, Tateo I, et al. Prophylactic atenolol reduces postoperative myocardial ischemia. McSPI Research Group. *Anesthesiology* 1998;88:7-17.
23. Perioperative sympatholysis. Beneficial effects of the alpha 2-adrenoceptor agonist mivazerol on hemodynamic stability and myocardial ischemia. McSPI—Europe Research Group. *Anesthesiology* 1997;86:346-63.
24. Oliver MF, Goldman L, Julian DG, Holme I. Effect of mivazerol on perioperative cardiac complications during non-cardiac surgery in patients with coronary heart disease: the European Mivazerol Trial (EMIT). *Anesthesiology* 1999;91:951-61.
25. Ellis JE, Drijvers G, Pedlow S, et al. Premedication with oral and transdermal clonidine provides safe and efficacious postoperative sympatholysis. *Anesth Analg* 1994;79:1133-40.
26. Stuhmeier KD, Mainzer B, Cierpka J, Sandmann W, Tarnow J. Small, oral dose of clonidine reduces the incidence of intraoperative myocardial ischemia in patients having vascular surgery. *Anesthesiology* 1996;85:706-12.
27. Coriat P, Daloz M, Bousseau D, Fusciardi J, Echter E, Viars P. Prevention of intraoperative myocardial ischemia during noncardiac surgery with intravenous nitroglycerin. *Anesthesiology* 1984;61:193-6.
28. Godet G, Coriat P, Baron JF, et al. Prevention of intraoperative myocardial ischemia during noncardiac surgery with intravenous diltiazem: a randomized trial versus placebo. *Anesthesiology* 1987;66:241-5.
29. Chung F, Houston PL, Cheng DC, et al. Calcium channel blockade does not offer adequate protection from perioperative myocardial ischemia. *Anesthesiology* 1988;69:343-7.
30. Tuman KJ, McCarthy RJ, March RJ, DeLaria GA, Patel RV, Ivankovich AD. Effects of epidural anesthesia and analgesia on coagulation and outcome after major vascular surgery. *Anesth Analg* 1991;73:696-704.
31. Baron JF, Bertrand M, Barre E, et al. Combined epidural and general anesthesia versus general anesthesia for abdominal aortic surgery. *Anesthesiology* 1991;75:611-8.
32. Mangano DT, Browner WS, Hollenberg M, Li J, Tateo IM. Long-term cardiac prognosis following noncardiac surgery. The Study of Perioperative Ischemia Research Group. *JAMA* 1992;268:233-9.
33. Ryan TJ, Antman EM, Brooks NH, et al. 1999 update: ACC/AHA guidelines for the management of patients with acute myocardial infarction. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Acute Myocardial Infarction). *J Am Coll Cardiol* 1999;34:890-911.

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