Perioperative myocardial ischaemia

Ian R. Thomson MD

The goal of anaesthetic management in patients with coronary artery disease (CAD) is the prevention of perioperative myocardial ischaemia. This approach is based on the assumption that sustained intraoperative ischaemia may precipitate postoperative myocardial infarction (MI) with its attendant complications. This presentation will review available information regarding perioperative ischaemia, and discuss its possible relationship to postoperative MI.

Detection of ischaemia

Acute myocardial ischaemia caused by coronary occlusion results in a predictable sequence of events known as the ischaemic cascade.[1] The earliest manifestation of ischaemia is diastolic myocardial dysfunction, followed by systolic dysfunction, electrocardiographic (ECG) changes, and angina. The entire sequence develops in less than a minute. Perioperatively, ischaemia is usually diagnosed when either abnormal ventricular contraction or ECG abnormalities are detected.

Ischaemia impairs myocardial contraction and causes ventricular regional wall motion abnormalities (RWMA). These may be detected noninvasively by cardiokymography[2] or radionuclide angiography.[3] Transoesophageal echocardiography (TEE) is relatively noninvasive and may be the most sensitive technique for the detection of intraoperative myocardial ischaemia.[4] Unfortunately, TEE can only be used after the induction of anaesthesia. The specificity of RWMA detected by TEE is unknown. Some new RWMA may reflect altered ventricular loading rather than ischaemia.[5]

The ECG is a relatively insensitive monitor, detecting fewer than 60% of ischaemic episodes.[2,4–9] However, when it is rigorously interpreted, the ECG is a relatively specific index of ischaemia.[10] It has the additional advantage of being inexpensive, noninvasive, and universally available. Recent technological advances, including continuous ambulatory monitoring and computerized ST-segment analysis have facilitated the diagnosis of ischaemia, and broadened our understanding of ischaemic patterns in patients with CAD[11,12]

Ischaemia in nonsurgical patients

The issue of perioperative myocardial ischaemia is best understood in the context of the usual ischaemic pattern in nonsurgical patients with CAD.[13] Continuous ambulatory ECG monitoring reveals that the average patient with CAD experiences several ischaemic episodes daily.[14] These episodes usually last several minutes but occasionally persist for hours. Ischaemia is most frequent after awakening in the morning.[15] This diurnal pattern is relevant in view of the usual timing of CABG. Most ischaemia is not classical effort-related angina. Ischaemia is usually "silent" (i.e. asymptomatic), unrelated to physical exertion, and not preceded by systemic haemodynamic changes which alter myocardial oxygen balance. Silent ischaemia is accompanied by new myocardial perfusion defects, and may reflect acute reductions in myocardial blood flow caused by increased coronary vascular resistance.[14] Frequent or severe silent ischaemia is associated with adverse outcome (e.g. infarction, revascularization, or death) in patients with unstable angina or recent MI.[16,17]

Incidence

During coronary artery bypass grafting (CABG), up to 67 per cent of patients experience an ischaemic episode between induction of anaesthesia and cardiopulmonary bypass (CPB).[2,8,9,11,18-30] The median reported incidence of ischaemia is 22 per cent. Because prebypass ischaemia frequently follows noxious stimuli like intubation and sternotomy, it traditionally has been attributed to the stress of anaesthesia and surgery. However, Knight *et al.* monitored the ECG for 48 hr before and following surgery in patients undergoing CABG.[11] Ischaemia occurred preoperatively in 42 per cent of patients and intraoperatively in 18 per cent. Preoperative ischaemia predicted intraoperative ischaemia, and the frequency of ischaemic episodes in these two periods was not different (0.09 vs 0.11 episodes·hr^{-1}). Thus, prebypass ischaemia may reflect the "preoperative ischaemic pattern," rather than the stress of anaesthesia and surgery. Despite revascularization, ischaemic ECG changes and/or new RWMA occur in 40 per cent of patients following myocardial reperfusion.[11,31] The aetiology of postoperative ischaemia is unclear.

A similar ischaemic pattern occurs during noncardiac surgery in patients with either known CAD or significant

Department of Anaesthesiology, University of Manitoba, Winnipeg, Manitoba, Canada.

risk factors.[4–6,32–43] The median incidence of intraoperative ischaemia is 36 per cent, with frequent episodes during intubation, surgical stimulation, and emergence. Ischaemia is not more frequent intraoperatively than preoperatively,[39,41,42] but may be more frequent postoperatively.[43]

Predictors

Coriat *et al.*[32] noted that, among patients with CAD undergoing noncardiac surgery, ischaemia was more common in those with severe disabling angina (Class III or IV). Patients with poor left ventricular function may also be at increased risk.[19] However, recent studies of patients undergoing noncardiac surgery indicate that ischaemic ECG changes occur as frequently among patients at risk of CAD (i.e. two or more major risk factors) as among those with known CAD.[41–43] However, the specificity of ischaemic ECG changes in the "at risk" group is unclear. Patients at risk of CAD may require more extensive monitoring than they have traditionally received.

Pathophysiology of perioperative ischaemia

Traditionally, perioperative ischaemia has been attributed to systemic haemodynamic changes which unfavourably alter myocardial oxygen balance (e.g. tachycardia, decreased coronary perfusion pressure). This view is outmoded. For example, Slogoff found that over 50 per cent of prebypass ischaemia was unrelated to tachycardia, hypertension, hypotension, or an acute change in heart rate or blood pressure.[21,22] Knight *et al.* extended those findings to the entire perioperative period.[11] Preoperative ischaemia was usually silent and not associated with abnormal haemodynamics or acute haemodynamic change. Intraoperatively and postoperatively, 50–60 per cent of ischaemia was not haemodynamically related. As in nonsurgical patients, perioperative ischaemia seems to be precipitated most frequently by increased coronary vascular resistance.

The fact that ischaemia is frequently unrelated to abnormal systemic haemodynamics should not cause anaesthetists to abandon the principle of tight haemodynamic control in patients with CAD. Abnormal haemodynamics, particularly tachycardias, remain an important cause of perioperative ischaemia. Prospective studies have demonstrated that anaesthetic regimens which increase heart rate are associated with a higher incidence of myocardial ischaemia than those which prevent tachycardia.[44] Haemodynamically related ischaemia has been particularly common during noncardiac surgery where anaesthetic depth may be less, and intraoperative myocardial revascularization does not occur.[33–37] After noncardiac surgery, postoperative myocardial ischaemia is often associated with tachycardia.[42,43,45]

In patients undergoing CABG, Slogoff noted ischaemia twice as frequently in patients with tachycardia (HR > 90–100 bpm).[22,23] Knight *et al.*[11] achieved better prebypass haemodynamic control than Slogoff, and noted less prebypass ischaemia (18 vs 42 per cent). When the same group administered anaesthesia "under strict haemodynamic control," the incidence of prebypass ischaemia decreased to 2 per cent.[26] Paradoxically, "strict haemodynamic control" may decrease the incidence of ischaemia which is unrelated to haemodynamics. Let us assume that ischaemia results from increased coronary vascular resistance in patients with limited coronary reserve. By optimizing myocardial oxygen balance, haemodynamic control increases coronary reserve, so that ischaemia is less likely to occur when increased coronary resistance decreases oxygen delivery. Simply put, vasospasm might be less likely to provoke ischaemia when heart rate is 50 bpm than when it is 100 bpm.

Prevention

If coronary vasospasm were a frequent cause of perioperative myocardial ischaemia, then drugs which relax vascular smooth muscle might reduce the incidence. Intravenous nitrates have proved effective in some studies,[33,34,46] but not in others.[47,48] Suprisingly, calcium entry blockers (CEB) have proved relatively ineffective. In an uncontrolled study, Slogoff found that patients taking CEB preoperatively had the same incidence of prebypass ischaemia as patients who received no antianginal medication (56 vs 51 per cent).[23] However, patients taking beta-adrenergic blockers (BB) had a significantly lower incidence of tachycardia and ischaemia (37 per cent). Similar studies have confirmed Slogoff's findings.[18,27,36,45] The reason for the inefficacy of preoperative CEB is unclear.[18] Controlled prospective trials are needed. It is also surprising that BB therapy, which theoretically might cause coronary spasm, effectively prevents both haemodynamically related and unrelated ischaemia. These observations suggest an important role for tachycardia in the pathogenesis of perioperative ischaemia whether haemodynamically related or unrelated (see above).

Preoperative beta-blockade may partially explain the differing incidences of ischaemia reported by various authors. In patients undergoing CABG, Slogoff[23] noted a 25 per cent incidence of ischaemia upon arrival in the operating room, whereas Chung[18] noted a four per cent incidence and Knight[11] found none. Only 32 per cent of Slogoff's patients received a BB immediately preoperatively, compared with 75 and 72 per cent in the other studies.

No specific anaesthetic regimen (e.g., volatile vs narcotic) has been demonstrated prospectively to reduce the incidence of perioperative ischaemia.[9,24,26] However, adequate prospective studies have not yet been performed.

Significance of ischaemia

Perioperative myocardial ischaemia, detected by ECG or TEE, predicts adverse cardiac events, including MI, pulmonary oedema, and death, both after CABG, and noncardiac surgery. Slogoff performed a multivariate analysis of data from 1518 patients undergoing CABG.[21,22] Prebypass myocardial ischaemia, detected by ECG, was the most important predictor of postoperative MI (sensitivity 0.68, specificity 0.58), followed by the duration of aortic cross-clamping, and the surgeon's assessment of the quality of revascularization. Infarction was three times more likely in patients with prebypass ischaemia. Cheng *et al.* found that perioperative infarction, detected by positron emission tomography, was predicted by prebypass ischaemic ECG changes (sensitivity and specificity 0.71).[25] Knight *et al.* noted adverse cardiac events in 23 per cent of patients with ECG evidence of perioperative ischaemia, but no adverse outcomes in nonischaemic patients.[11]

In patients undergoing vascular surgery, Smith *et al.* noted a significant association between new RWMA, detected by TEE, and postoperative MI.[4] In high-risk patients undergoing major noncardiac surgery, London noted a 26 per cent incidence of adverse cardiac events among patients who developed new intraoperative RWMA, and a one per cent incidence among those without TEE evidence of new ischaemia.[5]

Based on Slogoff's work, it has been suggested that prebypass myocardial ischaemia causes postoperative MI in patients undergoing CABG.[49] Supporting this hypothesis is experimental evidence indicating that repeated episodes of myocardial ischaemia provoke sustained ventricular dysfuntion and/or infarction in animals.[50,51] This suggestion also agrees with the traditional bias of anaesthetists, and is attractive to investigators whose funding is based on the assumption that preventing perioperative ischaemia will reduce postoperative morbidity. However, there are cogent arguments against uncritical acceptance of the suggestion that prebypass ischaemia causes infarction.

Continuous ambulatory ECG monitoring indicates that ischaemia is no more frequent or severe intraoperatively, than it was preoperatively.[11,26,30] It seems illogical that transient prebypass ischaemic events which do not lead to infarction in ambulatory patients would cause infarction after CPB. A transient episode of subendocardial ischaemia is a minor insult compared with the prolonged period of total ischaemia and surgical manipulation occurring during revascularization on CPB. In this regard, Knight *et al.* reported that although the preoperative ischaemic pattern predicted prebypass ischaemia, it did not predict ischaemia after myocardial reperfusion.[11]

A review of the literature reveals significant uncoupling of ischaemia and infarction in various studies.[52] For example, Slogoff noted a very high incidence of prebypass ischaemia, but a low incidence of infarction (43 and 4.2 per cent respectively).[21,22] In contrast, Knight *et al.* reported a lower incidence of ischaemia but a higher incidence of infarction (18 and 12 per cent respectively).[11] If ischaemia caused infarction, then elimination of perioperative ischaemia ought to reduce the incidence of postoperative MI. Yousif *et al.* randomly assigned 100 CABG patients to receive a continuous infusion of either isosorbide dinitrate or placebo for 24 hours prior to surgery.[46] The incidence of ischaemia, detected by continuous ECG recording, was reduced by isosorbide infusion (0 vs 18 per cent), but the incidence of postoperative MI was not affected (18 vs 22 per cent).

A statistically significant relationship between two variables (e.g. ischaemia and infarction), does not prove cause and effect. It is equally possible that both are causally related to another variable (e.g. severity of CAD) which is responsible for the coincidental relationship. This is the most likely explanation of the association between ischaemia and infarction in CABG. Preoperative and/or prebypass ischaemia probably defines a population of patients with severe, diffuse, CAD. These same patients may present the surgeon with technical difficulties which lead to prolonged ischaemia, inadequate myocardial protection, and incomplete revascularization during bypass. It is possible that optimal anaesthetic management can reduce the incidence of prebypass ischaemia to zero without influencing the incidence of postoperative infarction.[26]

High-risk patients undergoing noncardiac surgery are a different population in which prevention of perioperative ischaemia might ultimately prove useful. Recent studies indicate that the postoperative period is associated with sustained tachycardia and an increased frequency and duration of ischaemia.[39,41,43,45] Anecdotal reports indicate that morbid cardiac events may be preceded by a crescendo of silent ischaemia.[53,54] Careful monitoring and treatment of postoperative ischaemia could conceivably reduce morbidity. However, it is not necessary to postulate a causal relationship between ischaemia and infarction to explain their association.

In noncardiac surgery, perioperative ischaemia which simply recapitulates a preoperative ischaemic pattern seems intuitively unlikely to cause postoperative infarction. This is especially true with regard to preoperative or

intraoperative ischaemia which is temporally separated from postoperative infarction by several days. It seems more likely that perioperative ischaemia identifies a population of patients with severe CAD who are also at increased risk of postoperative infarction. However, the ischaemia may not cause the infarction. In the nonsurgical population acute MI is caused by coronary thrombosis. If this is the case after noncardiac surgery, then stress-related changes in blood coagulability which lead to thrombosis in patients with severe coronary artery stenosis are a more likely cause of infarction. Techniques such as epidural analgesia which produce sustained perioperative stress reduction may reduce the incidence of adverse cardiac events in high-risk patients undergoing noncardiac surgery.[55]

Conclusions

Techniques which detect the mechanical and electrical manifestations of ischaemia are defining the incidence and temporal pattern of perioperative ischaemia. Preoperative ischaemia is more common than previously thought, tends to be silent, and is unrelated to systemic haemodynamic changes. Intraoperative ischaemia is often unrelated to haemodynamics, and may reflect the preoperative ischaemic pattern more than the stress of anaesthesia and surgery. Postoperative ischaemia in noncardiac surgery is also silent and may be prolonged and severe. Perioperative ischaemia is associated with adverse postoperative cardiac events both after CABG and noncardiac surgery. The possibility that perioperative ischaemia may cause postoperative infarction has not been ruled out. However, it is more likely that ischaemia and infarction are two unrelated manifestations of severe underlying coronary artery disease. Further investigations are needed to resolve this intriguing controversy.

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