Failure to predict intraoperative myocardial ischaemia in patients with coronary artery disease

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Patients with severe coronary artery disease were studied to determine if the preoperative assessment or intraoperative haemodynamic monitoring could predict the occurrence of myocardial ischaemia. Thirty-eight patients undergoing coronary artery surgery who had normal electrocardiograms before induction of anaesthesia were included. Leads II and CSS were recorded on a Holter monitor and radial arterial and pulmonary artery catheters were used to measure haemodynamic variables. Eight patients developed ST-segment changes ≥ 0.1 mV before sternotomy. Preoperative factors could not be used to predict which patients would develop ST-segment changes. In all 38 patients haemodynamic determinants of myocardial oxygen supply and demand remained within an optimal range despite evidence of ischaemia in eight. This syndrome of ECG changes in the absence of tachycardia and hypertension resembles the syndrome of silent ischaemia documented in awake patients. Our findings suggest that myocardial ischaemia may be caused by decreases in coronary blood flow not associated with changes in haemodynamic variables.

Key words

ANAESTHESIA: cardiovascular; ARTERIES: coronary;
HEART: blood flow, myocardial ischaemia; MONITORING: electrocardiography, continuous; SURGERY: cardiovascular.

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Prevention of perioperative myocardial infarction is a challenge faced by all anaesthetists caring for patients with ischaemic heart disease. The preoperative assessment is used to identify patients at risk of intraoperative cardiac events. Factors which have been found to be predictive include number of diseased coronary vessels, New York Heart Association class of angina, previous myocardial infarction, left ventricular dysfunction, dysrhythmias, preoperative heart rate (HR) and blood pressure (BP), antianginal therapy, type and site of surgery (emergency, major thoracic or upper abdominal surgery), and duration of surgery beyond five hours.^{1,2}

In the operating room, in those patients at risk of myocardial ischaemia, HR, BP, and pulmonary capillary wedge pressure (PCWP) are controlled to avoid adverse changes in the myocardial oxygen supply/demand relationship. Patients with ischaemic heart disease have limited coronary reserve and so attempts at preventing ischaemia are focused on avoiding increases in myocardial oxygen demand.

Patients with severe coronary artery disease undergoing coronary artery surgery (CABG) were studied to determine if information available before surgery or haemodynamic variables monitored during surgery were useful in predicting which patients would develop ECG evidence of myocardial ischaemia.

Methods

Informed consent was obtained from 100 patients admitted to the Ottawa Heart Institute for elective CABG. All patients were less than 70 years of age and had good left ventricular function (normal contraction of at least 50 per cent of the left ventricle in the right anterior oblique projection). Patients were excluded if they had a previous CABG, a left ventricular aneurysm, diabetes mellitus, cerebrovascular disease, hepatic or renal dysfunction or if they had suffered a myocardial infarction within three months. On the day of surgery all patients received the same premedication: lorazepam $0.06 \text{ mg} \cdot \text{kg}^{-1}$ PO with their usual cardiac medications two hours before surgery,

FIGURE 1 Of 100 consenting patients only the 38 with isoelectric ST-segments before induction of anaesthesia were included in the study. Of these, eight subsequently developed ST-segment changes ≥ 1 mm and are referred to as the ischaemic group. The remaining 30 formed the control group. The number of patients developing ischaemia at each phase is indicated at the bottom of the figure.

followed in one hour by morphine $0.15 \text{ mg} \cdot \text{kg}^{-1}$ and scopolamine $5 \mu\text{g} \cdot \text{kg}^{-1}$ IM. Leads II and CS5 were recorded on a Del Mar Avionics Holter monitor applied one half-hour preoperatively. Following insertion of pulmonary and radial artery catheters anaesthesia was induced with fentanyl $50 \mu\text{g} \cdot \text{kg}^{-1}$. Intubation was facilitated by injecting $0.1 \text{ ml} \cdot \text{kg}^{-1}$ of a mixture containing pancuronium $0.4 \text{ mg} \cdot \text{ml}^{-1}$ and metocurine $1.6 \text{ mg} \cdot \text{ml}^{-1}$. Isoflurane 0.5 per cent was administered to some patients to ensure amnesia. The anaesthetists were instructed to look for and treat myocardial ischaemia detected on either leads II or V₅ on the Electronics for Medicine IM4 patient monitor. Arterial blood gas values were measured immediately before induction of anaesthesia and again after tracheal intubation.

Intraoperative haemodynamic variables measured included HR, radial artery systolic, diastolic, and mean BP, PCWP, CVP, and cardiac output. These were taken at six phases: preinduction, one minute postinduction, one minute postintubation, preincision, one minute postincision and one minute poststernotomy. Printouts of the Holter recording were made at these six phases and analyzed by two blinded observers. The ST-segments were measured at 80 msec from the J-point and those with 0.1 mV or greater change persisting for more than one minute were defined as abnormal. Of the 100 patients

entered into the study 76 had Holter recordings technically adequate for interpretation. Of these 38 patients had isoelectric ST-segments in both leads before induction of anaesthesia. Of the remainder one had LBBB, 11 had ST-segment depression $\geq 0.1 \text{ mV}$, 15 had ST-segment elevation $\geq 0.1 \text{ mV}$, and 11 had ST-segment deviations $< 0.1 \text{ mV}$ from the isoelectric line. A 12 lead ECG was recorded two and 24 hours postoperatively. Creatinine kinase-MB fractionation was not available on many of the patients.

Continuous variables were compared using Student's *t* test for unpaired data. Categorical variables were analyzed using a chi-square test or Fisher's exact test as appropriate.

Results

After analysis of the Holter data, only the 38 patients with isoelectric ST-segments on arrival in the OR were included in the study (Figure 1). Thirty patients whose ST-segments remained isoelectric throughout the study will be referred to as the control group. The remaining eight patients later developed 0.1 mV or more change in the ST-segments in one or both leads (three depression and five elevation) and will be referred to as the ischaemic group. The changes occurred postinduction in four, postintubation in one and preincision in three. All ST changes persisted throughout subsequent phases of data analysis. Five of the eight showed ST changes in both leads. These were not recognized on the intraoperative ECG monitor and thus were not treated. Arterial PO₂ was greater than 100 mmHg in all patients. The PCO₂ and pH changed little before and after intubation except in two patients from the ischaemic group. In one, pH decreased from 7.41 to 7.19 while PCO₂ increased from 42 to 76 and in the other pH rose from 7.37 to 7.52 as PCO₂ fell from 45 to 29 mmHg. Four of the eight patients who developed ST-segment changes and 13 of the 30 patients whose ST-segments remained isoelectric received isoflurane 0.5 per cent inspired concentration.

We studied the patient characteristics in each group to look for factors which might predict which patients would become ischaemic. The mean age and range for the control and ischaemic groups were similar: 59 (35–69) and 52 (37–69) respectively. Other characteristics included number of diseased coronary vessels, New York Heart Association class of angina, previous myocardial infarction, left ventricular function, preoperative haemodynamic variables (HR and systolic BP) and previous antianginal therapy. This therapy was divided into those receiving calcium entry blockers, beta-blockers, both, or no treatment. There was no significant difference in the distribution of these factors between the control patients and those who became ischaemic (Table I).

Intraoperative haemodynamic variables are shown in

FIGURE 2 The number inside the bars indicate how many patients were ischaemic at each phase. Phase 1 = preinduction, 2 = 1 min postinduction, 3 = 1 min postintubation, 4 = preincision, 5 = 1 min postincision, 6 = 1 min poststernotomy. Heart rate was not significantly different between the two groups.

Figures 2–4. Figure 2 compares the HR in the ischaemic and control groups at each phase: the bars indicate the number of patients ischaemic at each phase. The HR was maintained at approximately 60 bpm throughout the study period. There was no significant difference between the

TABLE I Patient characteristics

Factor	Control no. (%) n = 30	Ischaemic no. (%) n = 8
Diseased vessels		
1	1 (3)	1 (13)
2	13 (43)	2 (25)
3	16 (53)	5 (63)
NYHA		
Angina class		
1	1 (3)	0 (0)
2	16 (53)	4 (50)
3	12 (40)	4 (50)
4	1 (3)	0 (0)
Previous MI	12 (40)	2 (25)
Antianginal Rx		
BB	7 (23)	2 (25)
CEB	7 (23)	4 (50)
BB + CEB	12 (40)	1 (13)
None	4 (13)	1 (13)

NYHA = New York Heart Association; BB = beta blocker; CEB = calcium entry blocker.

The distribution of factors between the two groups was not significantly different.

FIGURE 3 Systolic blood pressure was similar in both groups at all phases.

FIGURE 4 Before induction of anaesthesia PCWP was significantly higher in the ischaemic group, however, this difference disappeared before any patient showed ST-segment changes.

groups at any phase. The bars show that no patient was ischaemic preinduction, four became ischaemic one minute postinduction, one more became ischaemic one minute postintubation, and three more became ischaemic preincision. All eight patients remained ischaemic during later phases. Although there seems to be a trend toward a higher HR in the ischaemic group following intubation (phase 3) (mean heart rate = 69 in the ischaemic and 62 in the control group, $P = 0.08$ by unpaired t test), four of the patients had become ischaemic before this. Only one additional patient first showed ST segment changes at this point.

TABLE II Haemodynamic variables at onset of ischaemia

	Mean	Minimum	Maximum
HR	62	34	72
SBP	115	96	147
PCWP	15	10	23
RPP	7186	3570	9555
PRQ	1.4	1.0	2.0

HR = heart rate; SBP = systolic blood pressure; PCWP = pulmonary capillary wedge pressure; RPP = rate-pressure product ($SBP \times HR$); PRQ = pressure-rate quotient (MAP/HR). $N = 8$.

At onset of ischaemia haemodynamic values suggested an adequate myocardial oxygen supply/demand ratio.

In Figure 3, systolic BP is displayed for the two groups at each phase of data collection. Systolic BP remained between 120 and 125 mmHg in both groups and the smooth curves are almost superimposed.

The PCWP measured in the ischaemic and control groups is shown in Figure 4. Although the initial value for the ischaemic group was higher (22 for ischaemic and 17 for control, $P < 0.05$), this difference disappeared after induction of anaesthesia and the two curves were similar from this phase onward. The bars show that no significant change in PCWP was associated with the onset of ischaemia.

Cardiac index, rate-pressure product ($SBP \times HR$), and pressure-rate quotient (MAP/HR) were analyzed in the same manner. There was no significant difference between the two groups for any variable.

In each of the eight patients who developed ischaemic ST-segment changes, we noted the phase at which this began and called this the time of onset of ischaemia. We averaged the haemodynamic values measured at this time in these eight patients (see Table II). These values were within a range considered optimal for patients with coronary artery disease. There was no significant change when comparing these with the values measured at the phase immediately preceding ischaemia. The values at onset of ischaemia were also not different from the values in the control group during any phase of data collection.

No patient developed a new Q-wave following the surgery.

Discussion

In a group of patients with severe coronary artery disease, all of whom had a normal ECG before induction of anaesthesia, we compared those who developed ECG evidence of ischaemia with those whose ST-segments remained isoelectric. Information available from the preoperative assessment did not predict the occurrence of ST-segment changes. Intraoperative haemodynamic vari-

ables measured also gave no indication or warning of myocardial ischaemia.

There is lack of agreement on what ECG criteria should be used to define intraoperative myocardial ischemia.³⁻⁶ We included only patients with an isoelectric baseline to simplify the interpretation of subsequent ST-segment changes and reduce the number of false positive diagnoses of ischaemia. Using criteria similar to those of the present study Smith *et al.*⁷ found that of 24 patients showing new segmental wall motion abnormalities detected with two-dimensional transoesophageal echocardiography only six had ST-segment changes. All patients with ST-segment changes had new wall motion abnormalities.

Recently it has been suggested that the use of three leads, V_2 , V_5 , AVF ⁸ or V_4 , V_5 , II ⁴ is necessary if the majority of ischaemic events are to be detected. Other methods, not available to us, including assessment of myocardial lactate extraction, regional wall motion, and thallium perfusion scanning, would have been useful to confirm the significance of the ST-segment changes observed in the present study.⁷⁻⁹

Patients received their usual antianginal medication until two hours before surgery. The small number of patients diagnosed as ischaemic in our study make it difficult to draw conclusions about the effect of previous antianginal therapy on intraoperative ischaemia. However, a recent study by Slogoff and Keats⁵ using a large number of patients looked at the effect of preoperative calcium entry blockers (CEB) on perioperative myocardial ischaemia. Their results also suggest a lack of benefit from CEB in the prevention of ischaemia.

The narcotic technique used to anaesthetize our patients produced very stable haemodynamic conditions. We were thus able to avoid ischaemic events secondary to changes in myocardial oxygen demand. Slogoff and Keats⁵ defined hypertension as $SBP \geq 180$ and tachycardia as $HR \geq 90$. In contrast, our patients had values at onset of ischaemia which were much lower (see Table II). This again may account for the lower incidence (21 per cent) of ischaemia seen in our study compared with that seen in other studies (37-55 per cent).^{5,6,10}

Silent ischaemia, or asymptomatic ischaemia usually not associated with large changes in haemodynamic values, has been described in the cardiology literature and more recently in the anaesthetic journals. Deanfield's description^{11, 12} of silent ischaemia seen on Holter monitoring and corresponding to perfusion defects on rubidium-82 positron emission tomograms of outpatients shows characteristics similar to the ischaemia seen in our study. Kleinman *et al.*¹³ studied a group of patients undergoing coronary artery surgery and found new postintubation thallium perfusion defects not associated with significant changes in haemodynamic variables.

Slogoff and Keats also described patients with ischaemic ECG changes not associated with a marked change in HR or BP.^{10, 14} These data suggest that such ischaemic changes in anaesthetized patients may be due to a primary reduction in coronary blood flow.¹⁵ Thus, in a group of patients with severe CAD, we detected a significant number who developed "haemodynamically silent ischaemia." This occurred despite excellent control of haemodynamic determinants of myocardial oxygen supply and demand. The ischaemia was also not detected or treated by the attending anaesthetists despite a protocol which encouraged vigilant intraoperative ECG monitoring.

Should this type of ischaemia be ignored by anaesthetists? Gottlieb documents unfavourable outcomes in patients who suffer episodes of silent ischaemia.¹⁶ We did not detect new Q-wave myocardial infarctions. However, these patients subsequently underwent coronary revascularization thereby likely decoupling outcome from early intraoperative events. In patients with CAD undergoing non-cardiac surgery such ischaemia may be more likely to lead to an unfavourable outcome.¹⁷

The hypothesis that prevention of "haemodynamically silent ischaemia" in the perioperative period will reduce the incidence of perioperative cardiac events needs to be tested. Thomson⁶ was unable to prevent intraoperative myocardial ischaemia with intravenous nitroglycerin. However, most of the ischaemic events were associated with haemodynamic changes and a low dose of nitroglycerin was used. Slogoff and Keats⁵ as well as Chung³ have observed that the preoperative administration of CEBs does not prevent intraoperative ischaemia. These drugs may, however, be more efficacious if given continuously IV during the operative period. Further studies are required to determine if agents such as nitroglycerin or calcium entry blockers can, in adequate doses, reduce the incidence of haemodynamically silent intraoperative myocardial ischaemia.

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Résumé

Nous avons tenté de voir si l'évaluation pré-opératoire ou la mesure intra-opératoire de variables hémodynamiques pouvait permettre de détecter dans un groupe de 38 coronariens sévèrement atteints, ceux qui auraient de l'ischémie myocardique. Ces patients, dont l'électrocardiogramme était normal, devaient subir une revascularisation coronarienne. Nous avons enregistré avec un "Holter" les dérivations D₂ et CS₅ et avons mesuré les variables hémodynamiques via des cathéters placés dans les artères radiale et pulmonaire. Avant la sternotomie, les segments ST étaient abaissés d'au moins 1 mm chez huit patients. Nous n'avons pu identifier aucun facteur pré-opératoire prédisposant à cette altération du segment ST. De plus, le ratio apport/demande en oxygène au myocarde, établi sur la foi des variables hémodynamiques semblait adéquat pour chacun des 38 patients. Ces altérations électrocardiographiques sans tachycardie ou hypertension rappellent le syndrome d'ischémie silencieuse déjà décrit chez des patients conscients. Il semble donc qu'une baisse du débit coronarien sans modification des variables hémodynamiques puisse être à l'origine d'ischémie myocardique.