

CASE REPORTS

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Electrocardiographic Changes during Isoflurane Anesthesia Suggesting Asymptomatic Coronary Artery Disease in Three Patients

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WHETHER isoflurane causes coronary ischemia is controversial. In 1983, Reiz *et al.* provided indirect evidence that isoflurane is a coronary arteriolar dilator capable of inducing myocardial ischemia by the coronary steal mechanism.¹ Others have found that, when hemodynamics are controlled, the incidence of myocardial ischemia during isoflurane anesthesia is similar to that during sufentanil anesthesia.² The finding of Park *et al.* that isoflurane constricts small-diameter rabbit coronary arteries further complicates the problem of understanding the pathogenesis of isoflurane-induced ischemia.³ Regardless of the extensive discussion as to whether isoflurane is a safe anesthetic for patients with coronary artery disease (CAD) and under what conditions,⁴⁻⁶ to the best of our knowledge, only one case report has demonstrated that substituting halothane for isoflurane may improve electrocardiographic signs of myocardial ischemia.⁷

We present results from three elderly patients with electrocardiographic signs of myocardial ischemia, negative T waves, and ST segment depression during isoflurane anesthesia. These changes occurred in otherwise healthy and physically active patients who preoperatively had normal electrocardiogram (ECG) results, reported no history of CAD, and had no intraoperative hypotension or tachycardia. The ECG changes were readily reversible after isoflurane was discontin-

ued or when halothane was substituted. Subsequently, stress testing in two patients confirmed the presence of CAD. These findings suggest that anesthesia with isoflurane can sometimes produce ECG changes that indicate CAD before clinical symptoms develop.

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Our three patients had no history of CAD and had normal preoperative ECG results. The level of their everyday physical activity was normal, unrestricted by cardiovascular limitations (symptoms), and assessed as appropriate for their age. They were not taking any cardiac medications. They received the same type of general anesthesia for colorectal surgeries: induction with thiopental, succinylcholine, and fentanyl and maintenance with isoflurane, 30% O₂ and 70% N₂O, and vecuronium.

Case 1

A 67-yr-old man underwent laparotomy for resection of a colon tumor. His preinduction blood pressure (BP) was 145/75 mmHg, and the heart rate (HR) was 77 beats/min. After anesthetic induction, 1.2% isoflurane was started. Ten minutes later, the patient experienced ST segment depression in the I, II, aVF, and unipolar precordial V5 leads (fig. 1). The BP was 105/78 mmHg, and the HR was 83 beats/min. The anesthetic was changed to halothane, and the ECG returned to normal over 20 min. The BP then was 106/53 mmHg (mean arterial BP 71 mmHg), and the HR was 71 beats/min. Thirty minutes later, isoflurane was substituted for halothane, and the T waves flattened again, particularly in leads II and aVF. The BP at that time was 147/66 mmHg (mean arterial BP 93 mmHg), and the HR was 71 beats/min. After the patient emerged from anesthesia, the 12-lead ECG results were normal, BP was 132/88 mmHg, and HR was 64 beats/min. Postoperatively, serial determination of creatine phosphokinase isoenzyme levels revealed no evidence of myocardial infarction. After full recovery from surgery, the patient underwent cardiac evaluation with exercise stress thallium testing. During testing, 86% of the predicted maximal HR was achieved, and 2.5-3.5-mm ST segment depression occurred in the inferior and lateral leads, but angina was not provoked by the test. Thallium imaging disclosed a reversible perfusion abnormality in the inferior and lateral aspects of the heart. The stress test was considered positive for CAD.

Case 2

A 69-yr-old man with Crohn's disease underwent colectomy to treat an enterovesical fistula. The preinduction BP was 140/75 mmHg,

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Key words: Anesthetics, volatile: halothane; isoflurane. Complications: electrocardiographic ST-T changes. Heart: coronary artery disease.

Fig. 1. Electrocardiogram (ECG) obtained from patient 1. Preoperative ECG (left column), intraoperative ECG during isoflurane (middle column, upper panel), during halothane anesthetic (middle column, lower panel). These ECG changes were reproduced when the anesthetic was switched to isoflurane (right column, upper panel); the ECG morphology returned to normal after isoflurane was discontinued at the end of anesthesia (right column, lower panel). ECG calibration gain = 10 mm = 1 mV. BP = blood pressure; HR = heart rate.

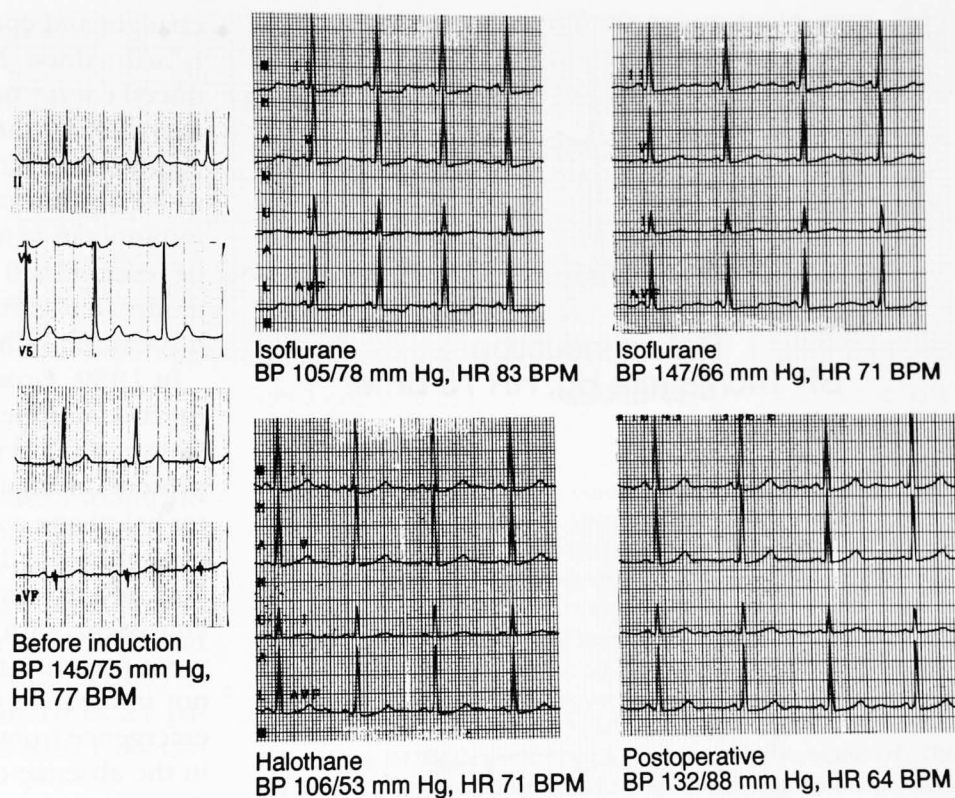
and the HR was 75 beats/min. Intraoperative ECGs were monitored (fig. 2). Soon after anesthetic induction, the ECG morphology was normal. T wave flattened and 1-mm horizontal ST segment depression developed in lead V5, the T wave became upright, and the ST segment depression developed in leads I, II, aVF, and V5. The BP was 108/43 mmHg, and the HR was 68 beats/min. The anesthetic was changed to 0.5% halothane; 20 min later, the ECG morphology returned to normal, whereas the T segment depression was still present. At that time, the BP was 111/43 mmHg and the HR was 71 beats/min. Later in surgery, the patient had significant blood transfusion. We did not test the ECG morphology, which remained normal throughout the anesthesia while the patient received 1.2% isoflurane. The 12-lead ECG was unchanged compared with the preoperative ECG. Serial determination of creatine phosphokinase isoenzyme levels revealed no evidence of myocardial infarction. After full recovery from surgery, the patient underwent cardiac evaluation by exercise stress thallium testing. The predicted maximal HR was achieved, and a retrosternal discomfort and 2.5-3.5-mm ST segment depression occurred in the inferior and lateral leads. Thallium imaging disclosed a reversible perfusion abnormality in the inferior and lateral aspects of the heart, indicating a positive test for CAD.

Case 3

A 57-yr-old man underwent sigmoid colectomy. The preinduction BP was 130/75 mmHg,

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Fig. 1. Electrocardiogram (ECG) obtained from patient 1. Preoperative ECG (left column), intraoperative ECG during isoflurane (middle column, upper panel), and during halothane anesthetic (middle column, lower panel). These ECG changes were reproduced when the anesthetic was switched to isoflurane (right column, upper panel); the ECG morphology returned to normal after isoflurane was discontinued at the end of anesthesia (right column, lower panel). ECG calibration: gain 1.0 = 10 mm = 1 mV. BP = blood pressure; BPM = beats per minute; HR = heart rate.



and the HR was 75 beats/min. Intraoperatively, ECG leads II and V5 were monitored (fig. 2). Soon after anesthesia was induced and 1.0% isoflurane was begun, the ECG morphology changed: in lead II, the T wave flattened and 1-mm horizontal ST segment depression occurred; in lead V5, the T wave became negative, and 1.5-mm horizontal ST segment depression developed. The BP at that time was 108/43 mmHg, and the HR was 68 beats/min. We changed the volatile anesthetic to 0.5% halothane; 20 min later, the T waves in both leads were normal, whereas the ST segments had become isoelectric. At that time, the BP was 111/44 mmHg, and the HR was 63 beats/min. Later in surgery, the patient had significant bleeding and required blood transfusion. We did not retest the effects of isoflurane on ECG morphology, which remained normal during the remainder of the anesthesia while the patient received halothane. Postoperatively, a 12-lead ECG was unchanged compared to the preoperative ECG, and the creatine phosphokinase isoenzyme levels did not indicate myocardial infarction.

After full recovery from surgery, the patient underwent cardiac evaluation by exercise stress thallium testing. During testing, 65% of the predicted maximal HR was achieved, and the patient experienced a retrosternal discomfort and 2–3-mm ST segment depression in the inferior and lateral leads. Thallium imaging disclosed reversible reduced count activity in the inferior and lateral aspects of the heart, indicating a positive test for CAD.

Case 3

A 57-yr-old man underwent sigmoidectomy for malignancy. The preinduction BP was 130/75 mmHg, and the HR was 56 beats/min.

Anesthesia was induced, and 0.8% isoflurane was started. Soon after, the patient's ECG gradually began to change: the T waves in leads I, II, and V5 flattened (fig. 3), at which time the BP was 126/70 mmHg, and HR was 95 beats/min. We changed the anesthetic from isoflurane to 0.5% halothane, and approximately 25 min later, the flattened T waves became normal. At that time, the BP was 120/79 mmHg, and HR was 86 beats/min. Reintroducing isoflurane induced moderate T wave flattening (fig. 3); the BP was 135/80 mmHg, and the HR was 90 beats/min. Postoperatively, 12-lead ECG and the myocardial band isoenzymes of creatine phosphokinase (CPK-MB) were normal. This patient declined further evaluation.

Discussion

Several mechanisms have been proposed to explain how isoflurane affects the myocardial circulation of patients with CAD.^{1,8–10} Isoflurane is a coronary vasodilator capable of inducing coronary steal if steal-prone anatomy exists: (1) complete occlusion of one or more coronary arteries, (2) collateral blood flow into the zone previously supplied by the occluded vessel, and (3) a hemodynamically significant stenosis of the artery that supplies the collateral vessels.¹⁰ Such anatomy is encountered in 19–23% of patients with CAD.^{8,9} The effects of BP on isoflurane-induced myocardial ischemia are controversial: disagreement exists regarding whether ischemic changes caused by coronary steal can

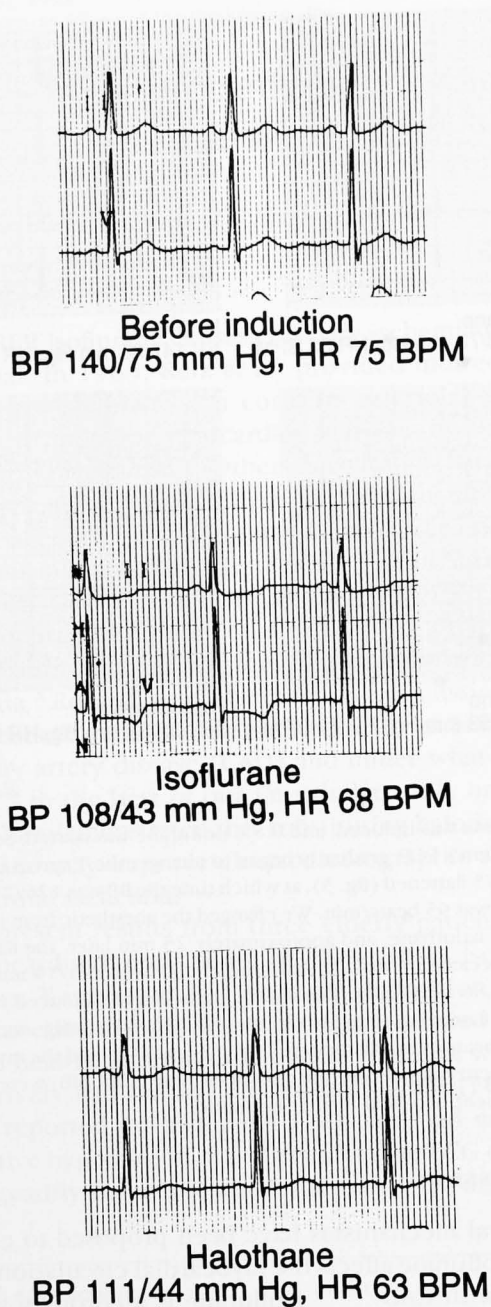


Fig. 2. Electrocardiogram (ECG) obtained from patient 2. ECG before the anesthetic induction (upper panel), after exposure to isoflurane (middle panel), and 15 min after switching the anesthetic to halothane (lower panel). ECG calibration: gain 1.0 = 10 mm = 1 mV. BP = blood pressure; BPM = beats per minute; HR = heart rate.

be prevented or reversed by increasing perfusion pressure across the stenotic area. Tatekawa *et al.* showed in dogs that maintaining mean arterial pressure at 80 mmHg was sufficient to prevent myocardial ischemic

changes and concluded that, when perfusion pressure is maintained, blood flow remains at or above the reduced energy needs of the myocardium despite induction of transmural steal.⁴ Leung *et al.* found that, under conditions of strict hemodynamic control, the presence of steal-prone anatomy does not increase the risk of intraoperative myocardial ischemia,⁵ whereas Diana *et al.* determined that, even with strict control of hemodynamic variables, isoflurane is associated with more myocardial ischemia than is enflurane.⁶

In 1989, Gross described a patient who was asymptomatic preoperatively for CAD but intraoperatively showed ECG evidence of myocardial ischemia that was present during isoflurane administration and absent after halothane was substituted for isoflurane.⁷ Similarly, our patients had no history of cardiac disease, but while anesthetized with isoflurane, they showed ECG changes consistent with myocardial ischemia. These changes were present only during exposure to isoflurane and not immediately after anesthetic induction or during emergence from anesthesia. The ECG changes occurred in the absence of tachycardia and hypotension. When the anesthetic was switched from isoflurane to halothane, the ECG reverted to normal over approximately 20 min while all hemodynamic variables were reasonably stable, with values similar to those seen during isoflurane. This pattern suggests that isoflurane was responsible for the ECG changes consistent with myocardial ischemia that had developed *via* a mechanism that was independent of HR or BP. Intraoperatively, we tested the reproducibility of ECG changes in two patients and were able to reinduce the T wave and ST segment changes by switching the inhalational anesthetic from halothane to isoflurane. In patients 1 and 2, a postoperative stress thallium test was positive for CAD.

The occurrence of nonhemodynamic-related myocardial ischemia, as seen in our patients, may be consistent with ischemia induced by coronary steal mechanism. However, in patient 1, after isoflurane was substituted for halothane, the ECG evidence of myocardial ischemia reoccurred despite increased MAP to 93 mmHg; as shown in the dog model, this finding is not expected if steal-induced ischemia was an underlying cause.⁴ Isoflurane-induced vasoconstriction of small coronary vessels³ also seems a plausible explanation for myocardial ischemia in our patients. Finally, the possibility exists that the myocardial oxygen supply/demand ratio was less with isoflurane than with halothane anesthesia because isoflurane results in less myo-

Fig. 3. Electrocardiogram obtained from patient 3. Superposition of ST and T changes (ST segment analysis) during isoflurane and halothane anesthesia. Flattening of the T wave is evident during isoflurane anesthesia; after isoflurane was changed to halothane, the T wave morphology normalized. ECG calibration: gain 1.0 = 10 mm = 1 mV.

cardial depression.¹⁰ Nathanson and colleagues reported increased lactate production but decreased lactate production in swine hearts during isoflurane anesthesia that ischemic metabolism was not seen with halothane or enflurane.¹¹ Similar metabolic evidence (increased lactate) of myocardial ischemia have been reported in patients with CAD who were anesthetized with isoflurane.¹

In conclusion, isoflurane may be associated with myocardial ischemia in asymptomatic patients with CAD. If these changes are seen, the patient should undergo further evaluation.

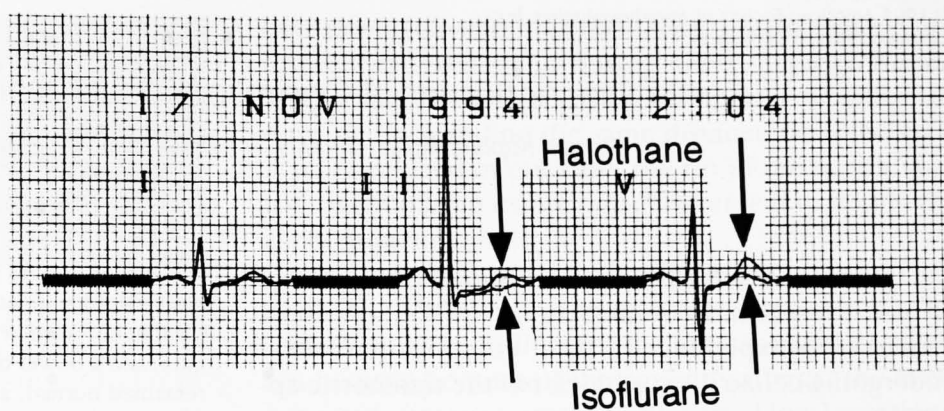
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cardial depression.¹⁰ Nathan and Smallman found increased lactate production but no coronary steal in swine hearts during isoflurane anesthesia, suggesting that ischemic metabolism was worse as compared to halothane or enflurane.¹¹ Similar results of ECG and metabolic evidence (increased lactate production) of myocardial ischemia have been seen in 10 of 21 patients with CAD who were anesthetized with 1.0% isoflurane.¹

In conclusion, isoflurane may induce ECG changes consistent with myocardial ischemia in previously asymptomatic patients with CAD. When such changes are seen, the patient should undergo further cardiac evaluation.

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