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Newly developed T-wave inversion with cardiac wall-motion abnormality predominantly occurs in middle-aged or elderly women after noncardiac surgery

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Abstract
Purpose. The study was done to determine the characteristics and prevalence of myocardial ischemia with inverted T waves after noncardiac surgery.
Methods. A list of patients who developed electrocardiogram (ECG) T-wave inversion associated with wall-motion abnormalities observed by transthoracic echocardiography (TTE) following noncardiac surgery was generated from the intensive care unit (ICU) medical records database between January 1, 1995, and December 31, 2000. The hospital records of these patients were analyzed retrospectively.
Results. Among 4219 patients (2187 men and 2032 women) who were admitted to the ICU after noncardiac surgery, 13 developed myocardial ischemia with inverted T waves postoperatively. All of the patients were middle-aged or elderly women with no history of coronary artery disease; nine of them had undergone intraabdominal surgery. Characteristic ECG findings included inverted T waves in the left precordial leads, which subsequently became prominent with QT prolongation. In all of these patients, wall-motion abnormalities were observed on the anterior wall, but these resolved within 60 days of the episode. Myocardial ischemia was asymptomatic, with neither hemodynamic changes nor adverse cardiac events.
Conclusion. Newly developed giant negative T waves with QT prolongation in the ECG may indicate myocardial stunning, but do not in themselves imply a poor prognosis. The marked preponderance of middle-aged and elderly women with this type of myocardial ischemia remains to be explained.

Key words Stunned myocardium · Inverted T · QT prolongation · Coronary spasm

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Introduction

Many reports of perioperative myocardial ischemia have focused on adverse outcomes, such as unstable angina, myocardial infarction, and cardiac death [1–6]. However, perioperative myocardial ischemia may be reversible and may also be associated with transient postischemic contractile dysfunction. Myocardial stunning, one of the mechanisms thought to be responsible for postischemic dysfunction, is the mechanical dysfunction that persists after reperfusion despite the absence of irreversible damage [7,8]. Because it is hard to obtain clinical evidence of ischemia and reperfusion in patients undergoing noncardiac surgery, the diagnosis of stunned myocardium in the clinical setting may only be inferred from circumstantial evidence.

With regard to the specificity of the ECG used for the detection of myocardial ischemia, changes in the T wave are considered less specific than changes in the ST segment. However, myocardial ischemia may occasionally appear as new T-wave inversion. While assessing postoperative patients with newly developed T-wave inversion using the transthoracic echocardiogram (TTE), we noticed reversible cardiac wall-motion abnormalities, which suggests that a stunned myocardium may occasionally occur in those patients. In the present study, therefore, our aim was to determine the characteristics of myocardial ischemia with inverted T waves after noncardiac surgery.

Methods

At our institution, the intensive care unit (ICU) serves for both postoperative intensive observation and intensive care. A list of patients who developed new T-wave inversion with myocardial ischemia following noncardiac surgery in the ICU between January 1, 1995, and December 31, 2000, was generated from the ICU medical records database. The hospital records of these patients were analyzed retrospectively. Patients undergoing neurosurgery were excluded from the study. The guidelines of the clinical studies committee of the institution do not require committee approval for retrospective studies.

Our clinical care procedure is as follows. In the operating theatre, routine monitors include an ECG from leads II and V5 with ST-segment analysis, blood pressure monitoring, pulse oximetry, and capnography. In the ICU, most patients who have undergone noncardiac surgery are monitored by a lead II ECG only. Myocardial ischemia was defined by an ECG exhibiting a horizontal or downward sloping ST-segment depression of 1 mm or more, ST-segment elevation greater than 2 mm measured 60 ms after the J point in one or more leads, or the presence of newly developed negative T waves with a duration greater than 1 min. Whenever perioperative oscilloscope records revealed possible new episodes of ischemia, a 12-lead ECG was obtained in the ICU, followed by a TTE. Blood was drawn for quantitative serum creatine kinase (CK) analysis, of which the MB (CK-MB) fraction was also determined. In those patients, a 12-lead ECG and TTE were obtained for 3 consecutive days postoperatively, then on the 7th day and once or twice per week thereafter. Serum CK-MB measurements were made every 6 h during the initial 24 h after the appearance of ischemia on the ECG.

In patients who developed T-wave inversion with cardiac wall-motion abnormalities, a chart review was obtained to examine the risk factors for coronary artery disease, perioperative hemodynamic changes, and changes in body temperature. Preoperative comorbid conditions included hypertension, diabetes, smoking history, and coronary artery disease. Perioperative hypertension was defined as an increase of 30% or more, and hypotension as a decrease of 30% or more, in systolic blood pressure from the preoperative levels. Tachycardia was defined as a heart rate of >100 beats·min^{-1} that persisted for more than 10 min. Perioperative hypothermia was defined as a body temperature of less than 35°C. The date when the wall-motion abnormalities resolved was also recorded. Adverse outcomes, including cardiac death, myocardial infarction, angina pectoris, and congestive heart failure, were obtained from review of the follow-up data in the outpatient records. The following ECG data were analyzed by a cardiologist without knowledge of the patient's clinical course: heart rate, heart rhythm, QRS axis, ST segment, T-wave configuration, and corrected QT (QTc) interval.

Data are presented as means ± SD for normally distributed data and as medians and quartiles for other data.

Results

A total of 4219 patients (2187 men and 2032 women) were admitted to the ICU following noncardiac surgery other than neurosurgery during the study period. The type of surgery included abdominal in 2574 patients (61%), orthopedic in 591 (14%), urological in 464 (11%), and others. Of these 4219 patients, 13 (0.3%) developed postoperative myocardial ischemia with inversion of the T wave. The demographics and clinical data are given in Table 1. The patients were all middle-aged or elderly women. Except for five patients who had hypertension, these subjects had no risk factors for coronary artery disease. The most common type of surgery that these patients had undergone was abdominal, and all but one were given general anesthesia with sevoflurane.

The preoperative ECGs were considered normal in all patients except for one who exhibited atrial fibrillation. The onset of ECG changes consistent with myocardial ischemia was intraoperative in three patients and early postoperative in five. The initial ischemic changes were represented on the ECG by ST-segment elevation in 3 patients and new T-wave inversion in the remaining 10. Inverted T waves in the left precordial leads developed in all patients, including the three with ST elevation. The characteristic ECG changes are shown in Fig. 1. Poor R-wave progression was associated with inverted T waves in three of the patients. The maximal size of the negative T waves exceeded 1.0 mV in seven patients (median, 1.1 mV; quartile range, 0.5–1.4 mV). QTc prolongation was observed in 9 of the 13 patients (median, 495 s; quartile range, 421–501 s). In all but one patient, the ECGs still exhibited inverted T waves on discharge from the hospital (Table 2).

In all patients, wall-motion abnormalities were observed on the anterior, septal, or apical wall: akinesis in eight patients and severe hypokinesis in four. Serial echocardiographic observations indicated that the wall-

Table 1. Demographic and clinical data for the 13 patients

Characteristic	No. (%)
Age (yr)	70 ± 9
Sex ratio (M/F)	0/13
Comorbid conditions	
Hypertension	5/13 (38%)
Diabetes mellitus	0/13
Coronary artery disease	0/13
Type of surgery	
Upper abdominal	4/13 (31%)
Lower abdominal	5/13 (38%)
Other	4/13 (31%)
Primary anesthetic	
Sevoflurane	12/13 (92%)
Isoflurane	1/13 (8%)

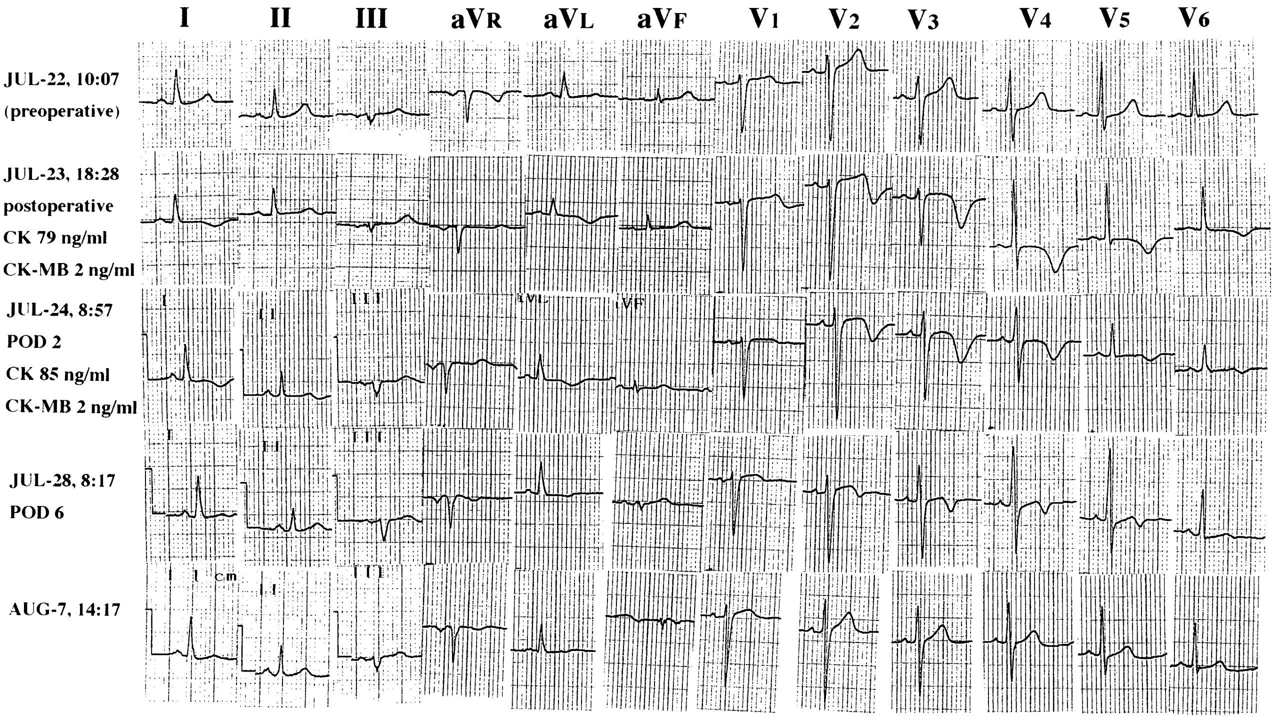

Fig. 1. Sequential ECG changes in case 4. The preoperative ECG obtained on the day before surgery was within normal limits. In this case, inverted T wave developed in the V5 lead 1 h before the end of operation. The ECG at 18:28 on July 23 was taken on admission to the ICU postoperatively, and showed deep symmetrical negative T waves. The cardiac isoenzyme of creatine kinase (CK-MB) was minimally elevated. The ECG of August 7 was almost normal

Table 2. Perioperative electrocardiographic (ECG) changes

Case	Onset (h)*	Initial ECG changes	Maximum negative T (mV)	Maximum QTc (s)
1	0	Inverted T in I, II, V4–V6	0.8 in V5	501
2	Intraoperative	ST elevation in I, III, aVF, V3–V6	1.2 in V5	484
3	12	Inverted T in V4–V6	1.9 in V4	522
4	Intraoperative	Inverted T in V5	0.7 in V3	529
5	18	Inverted T in I, II, V3–V6	1.3 in V3	495
6	0	Inverted T in I, II, V3–V6	0.4 in V4	496
7	18	Inverted T in II, V3–V5	1.2 in V4	485
8	Intraoperative	ST elevation in V5	0.8 in V4	421
9	0	Inverted T in V5, V6	0.4 in V4	418
10	8	Inverted T in I, II, aVF, V2–V6	2.8 in V3	501
11	13	Inverted T in I, II, III, V2–V6	0.4 in V3	421
12	0.5	ST elevation in V1–V3	1.4 in V3	419
13	6	Inverted T in V2–V6	1.1 in V3	495
Median			1.1	495
Quartile (25%, 75%)			0.5, 1.4	421, 501

*Time after admission to the intensive care unit

motion abnormalities had resolved in all but one of the patients within one month after the episode, with a median duration of 14 days (quartile range, 6.5–18.5). The median peak level of CK-MB was $16\,IU\cdot L^{-1}$ (quartile range, 10–31). (Table 3) Only one patient (case 12) underwent postoperative coronary angiography, which showed normal coronary arteries. Two patients (cases 7 and 8) underwent thallium scintigraphy when a wall-motion abnormality was still present, but normal perfusion was observed in both. In all of the patients examined here, the myocardial ischemia was asymptomatic.

Table 3. Perioperative transthoracic echocardiography (TTE) findings and creatine kinase MB (CK-MB) levels

Case	Abnormal findings by TTE at onset		Follow-up TTE (postoperative day)	Maximum CK-MB [IU·L^{-1} (%)]
	Segments*	Wall motion		
1	7, 8, 13, 14	Akinesis	Normal (60)	29 (4)
2	7–16	Mild hypokinesis	Normal (15)	27 (14)
3	7, 8, 10, 11, 12	Akinesis	Normal	2 (1)
	13, 14, 16	Severe hypokinesis	Mild hypokinesis (5)	
4	8, 14	Severe hypokinesis	Normal (14)	2 (3)
5	14	Akinesis	Normal (14)	14 (5)
6	7, 8, 13, 14	Severe hypokinesis	Mild hypokinesis on #14 (15)	16 (8)
7	7, 8, 13, 14	Akinesis	Normal (25)	9 (8)
8	13, 14	Severe hypokinesis	Mild hypokinesis (0)	33 (3)
9	7, 8, 13, 14	Severe hypokinesis	Mild hypokinesis on #14 (11)	11 (8)
10	13	Akinesis	Normal (6)	12 (3)
11	13, 14	Akinesis	Normal (7)	48 (3)
12	13, 14	Akinesis	Normal (7)	26 (2)
13	7, 13	Akinesis	Mild hypokinesis (22)	52 (4)

*Segment 7, mid anteroseptal; 8, mid anterior; 9, mid lateral; 10, mid posterior; 11, mid inferior; 12, mid septal; 13, apical anterior; 14(#14), apical lateral; 15, apical inferior; 16, apical septal, according to 16-segment model of the left ventricle [9]

Ischemic episodes were preceded by tachycardia in the three patients who developed ST-segment elevation, and by hypotension in two, by hypothermia in three, and by normothermic shivering in another three patients who developed ST-segment elevation. No hemodynamic changes were observed in relation to myocardial ischemia in any of the patients, except for one in whom those changes were associated with hypotension. All of the patients were treated with an intravenous infusion of nitroglycerine.

Discussion

The characteristics of myocardial ischemia observed in the present study were the development of prominent negative T waves with QT prolongation in the left precordial ECG leads, and reversible regional cardiac wall-motion abnormalities on the anterior, septal, and apical walls, as observed by TTE. Both findings imply a transient occlusion of the left anterior descending artery. These transient postischemic contractile dysfunctions were consistent with the phenomenon of the stunned myocardium described by Braunwald et al. [7,8].

The ECG findings in the present study (i.e., the newly developed T-wave inversion) have been interpreted previously as representing a subendocardial or non-Q-wave infarction [10]. It has been demonstrated that acute coronary occlusion followed by reperfusion usually results in a subendocardial myocardial infarction, and that the severity of postischemic myocardial dysfunction is determined by the relative proportions of necrotic subendocardium and stunned subepicardium [11,12]. However, it is not possible to distinguish a stunned myocardium accurately from a subendocardial infarction. Indeed, the latter might be included in the former category. On the other hand, Breslow et al. reported in a study of postoperative ECGs obtained in the recovery room that new T-wave abnormalities occurred frequently in postoperative patients, particularly in patients who had undergone intraabdominal surgery [13]. They concluded that new postoperative T-wave changes are not specific to myocardial ischemia, since none of their patients had episodes of suspected myocardial ischemia during the postoperative period. A prospective study of 100 ECGs with global T-wave inversion also found that 28 of them could be attributed to subendocardial myocardial infarction, but that global T-wave inversion characterized by a longer QT interval did not correlate with abnormal angiographic coronary anatomy [14]. They concluded that this ECG pattern represented a nonspecific change. Since the criteria used to diagnose myocardial ischemia in both of these studies did not include the use of an echocardiogram, it is quite possible that they missed cases of stunned myocardium.

In one patient with normal coronary arteries as observed by coronary angiography and in another two who had ST elevations as an initial ECG change, coronary spasm might be responsible for any postoperative myocardial ischemia. Since coronary angiography was not performed in the remaining patients, whether organic stenosis of the coronary arteries is the underlying mechanism for myocardial ischemia remains to be established. Among numerous factors thought to be responsible for the etiology of T-wave abnormalties [13], it has been suggested that catecholamines play an important role [14]. The higher incidence of postoperative T-wave changes in patients undergoing intraabdominal procedures was also observed in a previous study [13].

Intraabdominal surgery increases the levels of circulating catecholamines, which might lead to myocardial ischemia.

Myocardial ischemia was detected in the present patients because they were monitored by leads II and V5 in the ICU by chance or because of intraoperative ST-T changes. Considering the fact that most patients who have undergone noncardiac surgery are monitored postoperatively by a lead II ECG only, the incidence of myocardial ischemia with inverted T may be much higher.

It is remarkable that this type of myocardial ischemia occurred only in female patients, and in those with no evidence of previous heart disease. In a pathology study, it has been noted that subendocardial infarction is also more common in the elderly as well as in female patients [15]. The previously described study on global T-wave inversion also made note of its striking predominance in women [14]. Over the last decade, gender-related differences in the incidence of cardiovascular disease have received much attention. This finding may be due in part to differences in the size of the coronary arteries and in circulating hormones [16,17]. Women have a greater risk of acute vessel closure than men, because their vessels are smaller. Estrogen directly exerts significant benefits on vascular endothelial cells of the cardiovascular system. The incidence of coronary artery disease in women increases at menopause, most likely because of the decrease in levels of circulating estrogen. The higher incidence of postoperative T-wave inversion observed in middle-aged or elderly women who have had abdominal surgery suggests that excess catecholamines are responsible for the reduction in coronary flow in women who are particularly susceptible to vessel closure.

Since the present study was retrospective, the timing of serial measurements for ECG, echocardiography, and cardiac enzymes was not standardized. We were therefore unable to determine accurately the duration of stunning. We used the level of CK-MB as an index for the detection of myocardial injury. Compared with cardiac troponin I and troponin T, CK-MB is less sensitive and is quite variable as a measure of cardiac injury, especially in patients who have undergone surgery for skeletal muscle injuries. It is recommended that echocardiographic examinations together with measurements of cardiac enzymes should be performed in all patients with newly developed perioperative giant negative T waves.

In conclusion, newly developed giant negative T waves with QT prolongation in the ECG may indicate myocardial stunning but do not in themselves imply a poor prognosis. The marked preponderance of middle-aged and elderly women with this type of perioperative myocardial ischemia remains to be explained.

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