

## Perioperative Myocardial Ischemia in Patients Undergoing Elective Hip Arthroplasty during Lumbar Regional Anesthesia

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Perioperative myocardial ischemia predicts unfavorable outcomes and occurs in as many as 41% of patients with coronary artery disease or cardiac risk factors undergoing noncardiac surgery. To determine the prevalence of myocardial ischemia, we studied 52 consecutive unselected patients undergoing elective hip arthroplasty during lumbar regional anesthesia. Patients were continuously monitored for 6 days using a three-channel Holter monitor. Ninety-nine episodes of myocardial ischemia occurred in 16 patients (31%), six of whom were considered preoperatively to be at low risk for coronary artery disease. Forty-four percent of the ischemic episodes were preceded or accompanied by a heart rate  $\geq 100$ /min and 56% by a heart rate  $\geq 90$  beats/min. Ninety-six percent of the ischemic episodes were clinically silent, and 82% were not related to patient care events. Thirteen episodes of myocardial ischemia occurred preoperatively, 1 intraoperatively, and 85 postoperatively. The incidence of postoperative ischemic episodes showed a circadian variation: 44% occurred between 6 AM and noon, 33% between noon and 6 PM, 17% between 6 PM and midnight, and 6% between midnight and 6 AM. Six adverse cardiac events occurred during hospitalization (three of the six among patients with perioperative ischemia) and an additional four events during a follow-up period of 12 months (all four events occurred among patients with perioperative ischemia). Patients with perioperative myocardial ischemia had a relative risk of 2.6 (95% confidence interval 1.3-5.2) to develop an adverse cardiac event postoperatively. (Key words: Anesthetic technique: spinal; epidural. Complications: myocardial ischemia. Heart: ischemia. Monitoring: Holter. Surgery: orthopedic.)

PERIOPERATIVE MYOCARDIAL ISCHEMIA detected by Holter monitoring is associated with increased perioperative cardiac morbidity and mortality.<sup>1</sup> The incidence of perioperative ischemia in patients undergoing noncardiac surgery has been determined exclusively among selected patients with either known coronary artery disease or cardiac risk factors. As many as 41% of this population develop perioperative ischemia.<sup>1-4,†,\*\*\*</sup> However, knowledge of the prevalence of perioperative myocardial isch-

emia in unselected patients undergoing a routine operation could help estimate the medical and economic implications of preventive strategies.

Perioperative ischemia has been predominantly determined in patients undergoing general anesthesia. However, regional anesthesia is an option for many operations, and, therefore, more information about the incidence of ischemia in patients receiving regional anesthesia is desirable.

The incidence of ischemic episodes was reported to increase after surgery and to decrease again after reaching maximal levels on the second or third postoperative day.<sup>2-4,†,\*\*\*</sup> However, because the patients studied underwent different operations and postoperative care, specific treatment of subgroups (e.g., early mobilization) could have been the cause of this pattern of perioperative ischemia. The study of a population undergoing similar perioperative management might facilitate the evaluation of postoperative ischemia and its causative factors more precisely.

In patients suffering from osteoarthritis of the hip, hip arthroplasty is routinely performed to restore mobilization and/or to eliminate pain. In our institution, this procedure is routinely performed during regional anesthesia, and the perioperative management is highly standardized. Since hip arthroplasty is performed predominantly in elderly patients, a large prevalence of an underlying coronary artery disease might be expected.<sup>5</sup> Postoperatively, the patients remain immobile and supine in bed for several days, which should minimize misinterpretations of the electrocardiographic (ECG) data caused by changes in position. Furthermore, incidental disconnections of electrodes and cables, as a result of the patient's movements, might occur less frequently.

The aims of this study were to determine the incidence, perioperative distribution, relationship to patient care events, correlation to clinical data obtained preoperatively, and complications of perioperative myocardial ischemia in unselected consecutive patients undergoing elective hip arthroplasty during lumbar regional anesthesia.

### Materials and Methods

#### PATIENTS

The study design was approved by the ethical committee of the University of Basle, and written, informed

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consent was obtained from every patient. During a 6-month period all patients  $\geq 50$  yr of age with coxarthrosis scheduled for elective hip arthroplasty were studied. Exclusion criteria included: contraindications to or rejection of regional anesthesia, digitalis medication, left or right bundle branch block, left ventricular hypertrophy with "strain" pattern, severe deviation of the ST-segment ( $\geq 1.5$  mm in one lead) on the preoperative ECG, and other reasons for arthroplasty than that of coxarthrosis.

#### CLINICAL INVESTIGATIONS

Preoperatively obtained data included the history of any angina, myocardial infarction, coronary bypass grafting, congestive heart failure, claudication, stroke or transient ischemic attack, hypertension, smoking, diabetes mellitus, and intake of nitrates,  $\beta$ -adrenergic blockers, or calcium-channel blockers. A 12-lead ECG was recorded preoperatively and on the 10th postoperative day. Hemoglobin, hematocrit, and potassium levels were measured preoperatively, postoperatively in the recovery room, and thereafter daily during the period of Holter monitoring.

#### PERIOPERATIVE CARE

Patients continued to take their usual cardiac medication ( $\beta$ -adrenergic blockers, calcium-channel blockers, and nitrates) during hospitalization. Bromazepam (1.5–4.5 mg orally) was given 90 min before surgery. Spinal or epidural anesthesia and the amount of local anesthetics administered were chosen by the anesthesiologist caring for the patient. Spinal anesthesia was performed using isobaric bupivacaine (0.5%). In patients receiving epidural anesthesia, carbonated lidocaine (2.0%) was administered through a catheter followed by bupivacaine (0.5%) at the beginning of the operation. The epidural catheter was removed after the end of surgery. Surgery was performed with patients supine. In all patients, bone cement (methylmethacrylate) was used. The duration of surgery and amount of blood loss were recorded. After surgery, patients were transferred to the recovery room, where they stayed at least 2 h, and afterward were admitted to the ward. Intraoperatively and in the recovery room, blood pressure was measured every 5 min using a noninvasive pressure monitor (Mark III BP-103N) and recorded manually by the attending anesthetist. On the ward, blood pressure was measured and recorded manually by the nurse, every hour during the first postoperative day, and at least every 6 h thereafter. Oxygen was given intraoperatively and postoperatively until the morning of the first postoperative day.

Patients were mobilized by physiotherapists twice daily according to a standardized protocol starting on the morning of the first postoperative day. Apart from mo-

bilization, patients remained supine in bed. Pain was treated with acetaminophen (1,000 mg orally) and methadone ( $0.1 \text{ mg} \cdot \text{kg}^{-1}$  subcutaneously) on demand. Patients received heparin (5,000 IU subcutaneously) twice daily, starting after administration of regional anesthesia. Anticoagulation with oral coumarin was started the third postoperative day. Body temperature was measured at least twice daily during the period of Holter monitoring. During hospitalization, patients were examined and interviewed daily by one of two investigators (S.C.U.M. and I.C.) for signs and symptoms of myocardial ischemia, congestive heart failure, surgical pain, and psychological stress. Nurses, physiotherapists, and physicians noted all manipulations performed and all significant observations in a diary.

#### HOLTER MONITORING

A portable three-channel monitor (Marquette 8500, Marquette, Milwaukee, WI) was attached to the patient 15–20 h preoperatively and removed after 6 days on the afternoon of the 5th postoperative day. Using silver/silver chloride electrodes, three modified bipolar leads (modified CM5, CM3, and modified aVF) were placed according to the user's manual (Marquette): modified CM5—positive electrode on the fifth intercostal space at the left anterior axillary line, negative electrode below right clavicle just lateral to the sternum; CM3—positive electrode on the fourth intercostal space at the left sternal edge, negative electrode on the manubrium; and modified aVF—positive electrode placed on the sixth rib at the midclavicular line, negative electrode just below the left clavicle at the midclavicular line. After removal of the Holter monitor, the tapes containing the ECG data were processed and analyzed by one of the investigators (S.C.U.M.) with a computerized analyzer (Marquette Laser SXP). Classification of beats was controlled and manually corrected when necessary.

For the automatic three-lead ST-trend analysis, an isoelectric point (PQ interval) and the J-point were set manually. The measuring point for the ST-deviation was chosen 60 ms after the J-point. The automatic ST-trend was followed visually on a monitor (Marquette), and the isoelectric point and the J-point were manually adjusted when necessary. If the measuring point fell within the T-wave, it was also manually adjusted to a more appropriate position closer to the J-point (the minimum distance from the J-point was 50 ms). The baseline for the ST-segment was defined as the average of the ST-deviation during a 60-min period preceding an ischemic episode. If a positive baseline was found, depression of the ST-segment was measured from the isoelectric line. Ischemia was defined as either a reversible elevation  $\geq 2$  mm or as a horizontal or downsloping depression of the ST-segment  $\geq 1$  mm

from baseline persisting for 60 s or more at the measuring point. Ischemic episodes were further classified by the degree of ST-segment deviation, *i.e.*,  $\geq 1.5$  mm and  $\geq 2$  mm.

Duration of ischemic episodes, the maximum deviation of the ST-segment, the area under the curve of the deviated ST-segment (millimeters  $\times$  minutes), and the heart rate (at the onset and the highest heart rate during the episode) were measured and recorded automatically. Possible ischemic episodes were printed out (25 mm  $\cdot$  s<sup>-1</sup>, 1 mV = 1 mm) on a laser printer (Marquette) and verified by hand measuring. All ischemic episodes required the independent confirmation of three investigators (S.C.U.M., H.-G.S., and K.S.), two of whom (H.-G.S. and K.S.) were not aware of the patient's characteristics and the clinical course. Heart rate was determined by Holter recording, blood pressure by intraoperative and postoperative protocols, and associations of ischemic episodes with perioperative events from the diary.

### OUTCOMES

Adverse outcomes were: acute myocardial infarction, unstable angina, and onset of atrial fibrillation. Acute myocardial infarction was an elevation of the ST-segment combined with a transient elevation of the serum creatine kinase MB isoenzyme ( $\geq 50$  U/l), a new Q-wave, or clinical evidence of acute myocardial infarction. Unstable angina was either a new onset of typical precordial chest pain or an increase in the frequency of chest pain in a patient with known angina. The diagnosis of congestive heart failure required the new onset of clinical (rales, peripheral edema, or jugular venous distension) and radiologic (cardiomegaly, interstitial, alveolar edema) signs. New atrial fibrillation required ECG confirmation by Holter monitoring or a 12-lead ECG. One of two investigators (S.C.U.M. and I.C.) examined and interviewed the patients and reviewed the medical record daily during the period of Holter monitoring and at the end of hospitalization. A 12-lead ECG was routinely recorded and reviewed on the 10th postoperative day. Further investigations (12-lead ECG, serum creatine kinase) were only performed when clinically indicated. Long-term follow-up was obtained 12 months after surgery by an interview with the patient and his family doctor.

### STATISTICS

Results are expressed as the mean  $\pm$  one standard deviation, unless otherwise stated. Differences between the means of two groups were compared using the unpaired Student's *t* test. Analysis of variance was used to compare the means of more than two groups. Categorical data were analyzed using the chi-square test. A *P*  $\leq 0.05$  was considered to represent statistical significance. Relative risks

with 95% confidence intervals were calculated to determine the relationship between predictor and outcome variables.<sup>6</sup>

## Results

### PATIENTS

During the 6-month period, 65 patients were scheduled for elective unilateral arthroplasty of the hip. Nine patients were excluded according to the preset criteria and four patients did not give informed consent. Thus 52 patients (23 men and 29 women), aged 52–89 yr (mean age 72.4  $\pm$  9.4 yr) were monitored for 16.9  $\pm$  1.7 h preoperatively, 3.4  $\pm$  0.7 h intraoperatively, and 123.9  $\pm$  2.3 h postoperatively (total time monitored 7,422 h). Based on preoperative assessment, patients were assigned to one of three groups: 1) "coronary artery disease" (typical angina, prior infarction revealed by history or preoperative ECG, prior coronary bypass); 2) "coronary risk factors" (no evidence of coronary artery disease but at least one of the following: hypertension, diabetes mellitus, smoking  $\geq 25$  packyears, congestive heart failure, atrial fibrillation, prior stroke or transient ischemic attack, claudication, negative T-waves in the preoperative ECG); 3) "low coronary risk" (no evidence of coronary artery disease, no risk factors, normal preoperative ECG). Patients' clinical data are shown in table 1. All 15 patients with a preoperative cardiac medication ( $\beta$ -adrenergic blockers, calcium-channel

TABLE 1. Clinical Data of 52 Patients Studied

Characteristic	Coronary Artery Disease (n = 11)	Coronary Risk Factors (n = 22)	Low Coronary Risk (n = 19)
Age (yr)	74 $\pm$ 5	76 $\pm$ 9	65 $\pm$ 11
Sex (M:F)	5:6	10:12	8:11
Cardiovascular history			
Typical angina	9	—	—
Myocardial infarction	5	—	—
Coronary bypass	1	—	—
Congestive heart failure	2	2	—
Stroke or transient ischemic attack	1	—	—
Claudication	1	3	—
Cardiac risk factors			
Hypertension	4	13	—
Diabetes mellitus	2	5	—
Smoking	5	15	—
Cardiac medication			
Nitrates	2	—	—
$\beta$ -adrenergic blockers	2	4	—
Calcium channel blockers	1	5	—

Patients were assigned to one of three groups according to the preoperative assessment (see text for further details). Using the unpaired Student's *t* test and the chi-square test, there were no significant differences between the groups with regard to age and sex.

TABLE 2. Characteristics of Perioperative Myocardial Ischemia

	Preoperative	-2-0 h	Intraoperative	0-24 h	24-48 h	48-72 h	72-96 h	96-126 h
Number of patients monitored	52	52	52	52	51	51	50	49
Total hours monitored	878	104	177	1248	1224	1224	1200	1367
Number of ischemic episodes	6	7	1	24	20	11	16	14
Number of patients with ischemia	3	7	1	11	10	5	5	5
Duration of ischemia (min/h monitored)	0.27	1.14	0.03	0.44	0.61	0.47	0.23	0.13
Area under the shifted ST segment (mm × min/h monitored)	0.39	1.79	0.04	0.66	0.99	0.66	0.36	0.19

blockers, nitrates) continued to take their usual medication during their hospitalization.

In 44 patients undergoing spinal anesthesia,  $19.3 \pm 1.7$  mg bupivacaine was administered, resulting in a median sensory level of T8. Spinal anesthesia waned (sensorimotor level below S1) after  $254 \pm 36$  min. In the remaining eight patients undergoing epidural anesthesia,  $326 \pm 38$  mg carbonated lidocaine followed by  $39 \pm 12$  mg bupivacaine was administered, resulting in a median sensory level of T8. Epidural anesthesia waned after  $281 \pm 40$  min. Using the unpaired Student's *t* test and the chi-square test, we found no significant differences between the groups for patients undergoing spinal or epidural anesthesia with regard to sex, age, length of surgery, time until the anesthesia had waned, the occurrence of perioperative ischemia, and adverse cardiac outcomes.

#### ISCHEMIC EPISODES

No significant elevation of the ST-segment was observed. Ninety-nine episodes of significant depression of the ST-segment occurred in 16 (10 women, median number of ischemic episodes 4.5, range 2-19) of the 52 patients (31%). Only four episodes (4%) were accompanied by typical angina.

The characteristics of myocardial ischemia are shown in table 2. Seventy-five percent of the ischemic episodes had a ST-depression of  $\geq 1.5$  mm, and 51% exhibited a ST-depression of  $\geq 2.0$  mm. ECG characteristics of the 99 ischemic episodes are shown in table 3.

Figure 1 shows the heart rates at the onset of the ischemic episodes and the maximal heart rates during ischemic episodes. No ischemic episode was preceded or accom-

TABLE 3. Electrocardiographic Characteristics of 99 Episodes of Perioperative Myocardial Ischemia in 16 Patients

	Preoperative	-2-0 h	Intraoperative*	0-24 h	24-48 h	48-72 h	72-96 h	96-126 h
Duration of episodes (min)								
Mean	32 ± 23	18 ± 15	5	25 ± 39	36 ± 43	48 ± 52	17 ± 34	12 ± 13
Median	30	18		10	15	33	3	6
Range	10-75	2-40		2-181	2-134	2-172	2-86	2-44
Maximal ST deviation (mm)								
Mean	1.9 ± 0.6	1.8 ± 0.4	1.2	1.8 ± 0.7	2.3 ± 0.6	2.5 ± 0.4	1.9 ± 0.6	2.2 ± 0.4
Median	2.0	2.0		1.5	2.3	2.3	2.0	2.2
Range	1.2-2.7	1.2-2.2		1.1-4.0	1.3-4.2	1.9-3.1	1.1-3.0	1.7-3.1
AUC (mm × min)								
Mean	46 ± 37	29 ± 28	6	37 ± 39	58 ± 63	74 ± 82	27 ± 43	19 ± 21
Median	37	25		13	33	39	7	15
Range	6-97	3-75		3-247	3-234	3-264	3-137	3-65

Using analysis of variance, no significant differences were found between the time periods with regard to duration of ischemic episodes, AUC, and electrocardiographic extent.

AUC, and electrocardiographic extent.

AUC = area under the shifted ST segment.

\* n = 1.

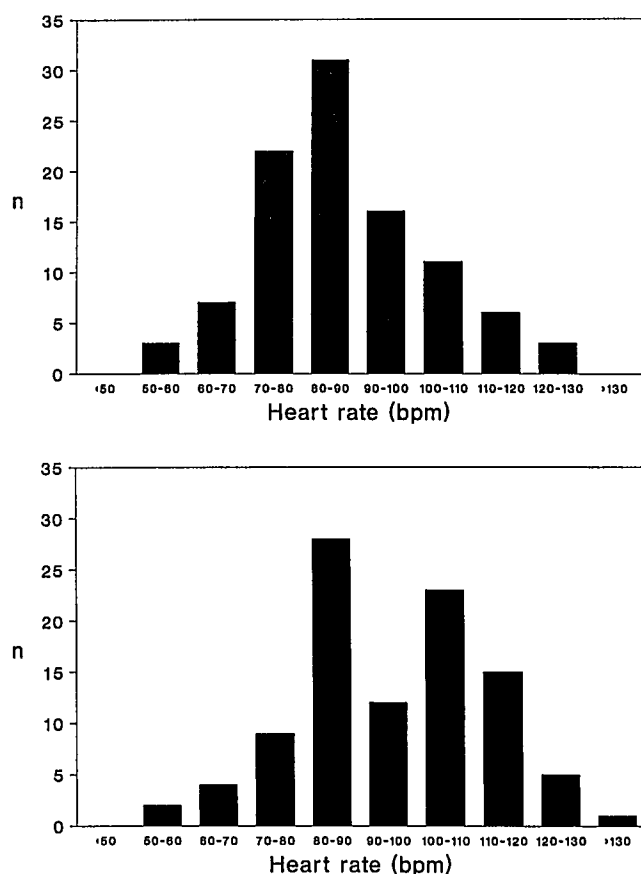


FIG. 1. Relationship between heart rate and 99 episodes of perioperative myocardial ischemia in 16 patients. *Top*: Heart rate at the onset of ischemic episodes. *Bottom*: Maximal heart rate during ischemic episodes. *n* = number of ischemic episodes.

panied by a bradycardia (heart rate  $\leq 50$ /min), whereas 44 ischemic episodes were preceded or accompanied by a heart rate  $\geq 100$ /min and 56 ischemic episodes by a heart rate  $\geq 90$  beats/min. Since blood pressure was not continuously measured during the 6-day perioperative period, we are not able to relate myocardial ischemia to changes in blood pressure.

Using the unpaired Student's *t* test and the chi-square test, there were no significant differences between the groups for patients with and without perioperative ischemia with regard to sex, age, length of operation, blood loss, lowest postoperative hemoglobin, and the difference between the preoperative value and the lowest postoperative value of hemoglobin.

Distribution of ischemic activity during the perioperative period is shown in figures 2 and 3. All of the 13 preoperative ischemic episodes (eight patients) were clinically silent. The median duration of the preoperative episodes was 19 min (range 2–75 min). Seven patients had myocardial ischemia during the 2 h before arrival in the operating room. None of these patients expressed anxiety

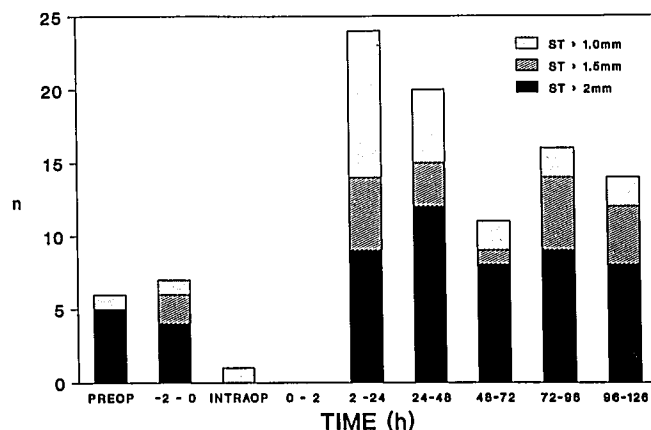


FIG. 2. Distribution during the perioperative period and electrocardiographic extent of 99 episodes of perioperative myocardial ischemia in 16 patients. PREOP = preoperative period; -2-0 = 2 h before arrival in the operating room; INTRAOP = between arrival in operating room and arrival in recovery room; 0-2 = 2 h after arrival in recovery room. *n* = number of ischemic episodes.

or any other unpleasant feelings upon arrival in the operating room.

The intraoperative period lasted  $166 \pm 34$  min and was defined as time under the direct care of the anesthesiologist, beginning with the arrival of the patient in the operating room and ending in the recovery room. Only one patient developed myocardial ischemia during this time: a clinically silent episode occurred following a decrease in blood pressure after the onset of epidural anesthesia (duration of ischemia 3 min).

Postoperatively, 15 patients had 85 ischemic episodes. Of the 15 patients with postoperative ischemia, only eight

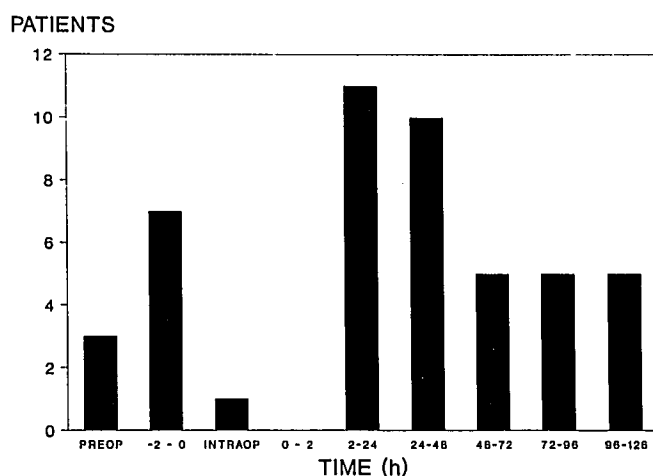


FIG. 3. Number of patients developing myocardial ischemia during the perioperative period. PREOP = preoperative period; -2-0 = 2 h before arrival in the operating room; INTRAOP = between arrival in operating room and arrival in recovery room; 0-2 = 2 h after arrival in recovery room. *n* = number of patients.

had preoperative ischemia. No single postoperative ischemic episode occurred before regional anesthesia waned (sensorimotor level below S1). The median duration of the postoperative episodes was 11 min (range 2–181 min). Four episodes were accompanied by typical angina, and one by nausea, whereas the remaining 81 (94%) were clinically silent.

Forty-four percent of the postoperative ischemia occurred between 6 AM and noon, 33% between noon and 6 PM, 17% between 6 PM and midnight, and 6% between midnight and 6 AM (fig. 4).

#### POSTOPERATIVE CARE

In 49 patients the 12-lead ECG performed on the 10th postoperative day was identical with the preoperative recording. In one patient a 12-lead ECG confirmed the diagnosis of an acute myocardial infarction, and in the remaining two, new atrial fibrillation was present. Serum potassium remained in the normal range in all patients. Transient anemia (hemoglobin < 100 g/l) occurred in 10 patients. One patient developed four episodes of myocardial ischemia while anemic. Three patients developing perioperative ischemia had no ischemic episodes while anemic. Intermittent fever ( $\geq 38^{\circ}\text{C}$ ) occurred in eight patients. Three patients developing perioperative ischemia had no ischemic episodes while they had a fever.

No temporal association with postoperative events was found in 71 (82%) of the 85 postoperative ischemic episodes. A total of 151 mobilizations were performed in the 16 patients with perioperative ischemia. Nine mobilizations (6%) in six patients were associated with myocardial ischemia. Two ischemic episodes were associated with nocturnal confusion, one with surgical pain, and one with the intake of a meal; one occurred during adminis-

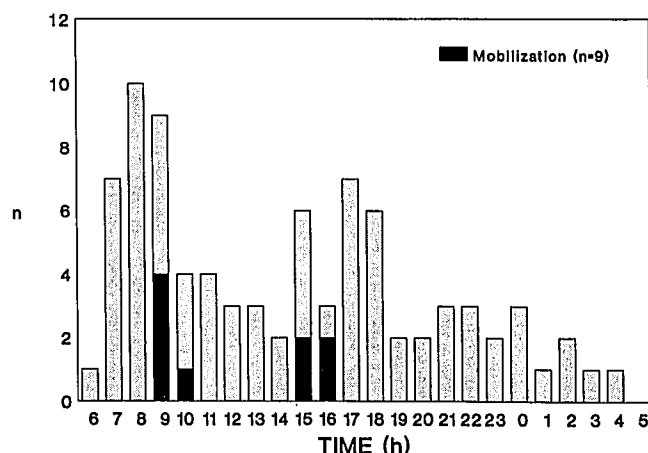


FIG. 4. Circadian variation of the onset of 85 episodes of postoperative myocardial ischemia in 15 patients. n = number of ischemic episodes.

TABLE 4. Preoperative Assessment *versus* Relative Risk of the Occurrence of Perioperative Ischemia and Postoperative Cardiac Outcomes

Preoperative Assessment	Perioperative Ischemia: Relative Risk (95% confidence interval)	Cardiac Outcomes: Relative Risk (95% confidence interval)
Coronary artery disease	1.9 (0.7–5.2)	3.5 (1.3–9.2)
Coronary risk factors	0.7 (0.3–1.5)	0.4 (0.1–1.5)
Low coronary risk	1.0 (0.5–2.2)	0.8 (0.5–1.3)

tration of an enema, and one occurred immediately after the start of a blood transfusion.

#### OUTCOMES

During the period of Holter monitoring ventricular dysrhythmias  $\geq$  Lown class IIIb occurred in eight patients; six of the eight patients (75%) also had perioperative ischemia.

Table 4 shows the relative risks for patients with coronary heart disease, for patients with coronary risk factors, and for patients considered to be at a low coronary risk for developing perioperative myocardial ischemia and adverse cardiac events. During hospitalization six adverse cardiac outcomes occurred and included one myocardial infarction, three unstable angina, and two atrial fibrillation. In three of the six patients (50%) with adverse outcomes, perioperative ischemia was observed, and five of the six had known coronary artery disease or at least two major risk factors. Thus, patients with perioperative myocardial ischemia had a relative risk of 1.8 (95% confidence interval 0.7–4.5) for developing an adverse cardiac event during hospitalization.

From the end of hospitalization until 12 months after surgery, an additional four adverse cardiac outcomes occurred and included one lethal myocardial infarction, two unstable angina, and one ventricular dysrhythmia leading to recurrent syncope. All four adverse outcomes occurred in patients with perioperative ischemia (relative risk 4.0, 95% confidence interval 2.5–6.5).

Thus, during a period of 12 months, seven adverse cardiac outcomes occurred among the 16 patients (44%) with perioperative ischemia and three among the 36 patients (8%) without perioperative ischemia. In patients with perioperative myocardial ischemia this results in a relative risk for postoperative adverse cardiac outcomes of 2.6 (95% confidence interval 1.3–5.2). Preoperative ischemia was present in only 3 of the 10 patients with adverse events.

#### Discussion

Our results demonstrate that: 1) nearly one third of our elderly orthopedic patients developed perioperative

ischemia; 2) a substantial amount of ischemia occurred in patients considered to be at low coronary risk; 3) the intraoperative ischemic activity was less than that in the preoperative period; 4) perioperative ischemia appeared to predict adverse cardiac events beyond the immediate perioperative period; 5) the circadian pattern of myocardial ischemia present during normal daily activity was preserved during the postoperative period; 6) the incidence of ischemic episodes was greatest during the first 48 h following surgery and declined thereafter; and 7) most of the ischemic episodes were asymptomatic and unrelated to patient care events.

Because there is no absolute reference for myocardial ischemia, not all ST-deviations detected might really reflect ischemic episodes. Deviation of the ST-segment, however, has been found to be correlated with impaired coronary perfusion.<sup>7-10</sup> Our study design favored the elimination of false positive results because we studied old patients, excluding those with conditions interfering with the interpretation of the ST-segment, and because immobility and continuous supine position during the postoperative period with short and well-defined mobilizations (physiotherapy) minimized the risk of misinterpretations provoked by changes in position. The ECG extent of most ischemic episodes exceeded the criteria normally applied. In addition, adverse coronary events occurred in the later course of 44% of the patients with perioperative depression of the ST-segment. We found it reasonable to assume, therefore, that most if not all episodes of ST-depression detected represent true myocardial ischemia.

The sensitivity of ECG ischemia detection depends on the selection of leads. Using a 12-lead ECG, the most sensitive leads are V5, V4, V6, and II.<sup>11-13</sup> In the present study, modified bipolar leads had to be adapted to an immobile patient undergoing continuous Holter monitoring during a period of 6 days: all electrodes of the leads used (modified CM5, CM3, and modified aVF) are located close together in the anterior part of the thorax which provides optimal comfort for the patient (no impairment of the upper extremities by cables and electrodes) and easy access for the control of attachment and correction of incidental disconnections. Nevertheless, the selected leads allowed the recording of anterolateral (modified CM5), inferior (modified aVF), septal (CM3), and posterior forces (CM3).

All our patients received heparin and coumarin as deep venous thrombosis prophylaxis. Since coumarin was begun on the third postoperative day, an effective decrease in prothrombin activity was not achieved before the end of the study period. However, the low-dose heparin treatment, which was started on the day of operation, could have affected the postoperative myocardial ischemia.

In addition to its well-established ability to control

postoperative hypercoagulability and to prevent related thromboembolic phenomena, heparin has been shown to enhance the exercise-induced development of coronary collaterals to jeopardized myocardium<sup>14</sup> and to decrease the frequency of anginal attacks and silent ischemic episodes in patients with unstable angina.<sup>15</sup> The reduction in frequency of spontaneous anginal episodes was also observed after administration of low doses of heparin by the subcutaneous route and was accompanied by a reduction in fibrinopeptide A levels, an index of *in vivo* thrombin generation and fibrin formation.<sup>16</sup>

Consequently, the low-dose heparin treatment that our patients received may have had beneficial effects on myocardial ischemia, and in its absence the incidence of ischemic episodes may have been even higher.

To our knowledge, this is the first study of perioperative ischemia in unselected patients. Our results thus may give an estimate of the prevalence of myocardial ischemia in an unselected elderly population undergoing routine noncardiac surgery and of the medical and economic implications of future preventive strategies. We found perioperative ischemia in 31% of elderly patients undergoing elective hip arthroplasty. This incidence is within the range of perioperative ischemia in patients with known coronary artery disease or major risk factors undergoing vascular, thoracic, abdominal, or other major surgery, which was reported to be 27-41%.<sup>1-4,¶,\*\*\*</sup> The unexpectedly large incidence of perioperative ischemia might be partly explained by a longer duration of monitoring and the use of a three-channel monitor (instead of a two-channel monitor in the other studies). Our results confirm prior observations showing that during the perioperative period the majority of myocardial ischemia occurs without typical angina and therefore is difficult for the clinician to detect.<sup>2-4,¶,\*\*\*</sup>

Not surprisingly, the incidence of perioperative ischemia was greatest among the patients with established coronary artery disease. However, a substantial amount of perioperative ischemia occurred among patients without known coronary artery disease or major risk factors. This finding cannot necessarily be extrapolated to patients undergoing other kinds of surgery, since in patients with coxarthrosis, immobility and/or chronic intake of analgesics might mask an otherwise symptomatic coronary artery disease. Currently, patients with restricted mobility without evidence of cardiac disease are not considered to require further preoperative diagnostic testing. Further work is required to determine whether we have to modify this policy. However, orthopedic patients are often unable to undergo treadmill exercise testing, and dipyridamole-thallium scintigraphy might be of reduced value in the absence of clinical or ECG signs of cardiac disease.<sup>17</sup> In patients undergoing vascular surgery, the absence of preoperative myocardial ischemia was reported to be an in-

indicator of very low risk.<sup>18</sup> However, in 70% of our orthopedic patients with adverse events, no preoperative ischemia was found, which might be partly explained by the shorter duration of the preoperative monitoring. Until more data are available, we find it reasonable to suspect an undiagnosed coronary artery disease in elderly patients with restricted mobility.

Only one episode of myocardial ischemia occurred during the intraoperative period, following a decrease in blood pressure after the onset of epidural anesthesia. Ischemic activity was thus less intraoperatively than preoperatively. This is in contrast to previous studies including patients undergoing various kinds of surgery during general anesthesia, which reported that the incidence of intraoperative ischemia equals that in the preoperative period.<sup>2,3,19</sup> Furthermore, in our patients, postoperative ischemia occurred only after the regional anesthesia had waned. This might be related to the high standard of care during the intraoperative period and in the recovery room. However, the possibility exists that regional anesthesia, once established, has a beneficial effect on ischemic activity. Conversely, in a nonrandomized study including high-risk patients undergoing peripheral vascular surgery, the incidences of perioperative myocardial ischemia and myocardial infarction were found to be significantly greater among patients undergoing regional anesthesia compared with those undergoing general anesthesia.<sup>20</sup> However, whether different anesthetic techniques have a different effect on perioperative ischemic activity needs to be determined using prospective randomized trials.

Perioperative myocardial ischemia is associated with unfavorable perioperative outcomes.<sup>1</sup> Our results, as well, suggest that perioperative ischemia predicts the occurrence of adverse cardiac events beyond the immediate perioperative period. This finding might reflect the fact that silent myocardial ischemia is a marker for poor outcomes under various circumstances.<sup>18,21,22</sup> The long-term predictive value of perioperative ischemia, however, has to be determined in further studies.

During the postoperative period, the ischemic activity was greatest in the morning and least during the night. The distribution of ischemic events was not significantly influenced by mobilization or other manipulations performed at a specific time. Therefore, we assume that the circadian rhythm of myocardial ischemia present during normal daily activity<sup>23</sup> was preserved in the postoperative period. All our patients underwent regional anesthesia, and thus the amount of anesthetic administered was small. This might be of concern since sleeping disorders following administration of various drugs and nocturnal decreases in hemoglobin oxygen saturation, partly as a result of residual effects from administered anesthetics, have been proposed as a cause of perioperative ischemia.<sup>24</sup> However, a circadian variation of postoperative ischemia

similar to that in ambulatory subjects was also recently reported to occur after general anesthesia.<sup>25</sup>

The number of ischemic episodes and patients developing ischemia was greatest in the early postoperative period (0–48 h postoperatively) and decreased thereafter. A similar pattern of postoperative ischemia was reported in previous studies.<sup>2,4,11,26</sup> In contrast to these studies, however, all our patients underwent standardized operations and postoperative care. Thus, the asymmetric distribution of postoperative ischemia was not caused by different managements in different subgroups. Due to economic reasons, we were unable to prolong preoperative Holter monitoring to establish a baseline of myocardial ischemic activity. Therefore, we cannot definitely relate the postoperative ischemic pattern to the preoperative one. We assume, however, that the ischemia occurring in the late postoperative period approximated the ischemic baseline and that the ischemia that occurred in the early postoperative period represented a real increase.

Forty-four percent of the patients with perioperative ischemia had an ischemic episode during the 2 h before arrival in the operating room. All episodes were clinically silent and all patients denied experiencing fear or anxiety upon arrival in the operating room. We do not know if the ischemia observed in the 2 h prior surgery exceeded the true baseline ischemic activity. The time necessary to recover from myocardial ischemia may exceed the time of normalization of the ST-segment.<sup>26,27</sup> Anesthesiologists must thus be aware of the possibility that they may induce anesthesia while their—asymptomatic—patients are recovering from previous myocardial ischemia or may even suffer from ongoing ischemia. Whether this is of clinical relevance is not known. In our study, however, two of the six postoperative cardiac events occurred in patients who had developed ischemia during the 2 h before arrival in the operating room.

Little is known about the causative factors of perioperative myocardial ischemia. Prior studies revealed that the majority of perioperative myocardial ischemia is not related to hemodynamic abnormalities.<sup>1,2,19,28</sup> In the present study most of the ischemic episodes were neither preceded nor accompanied by a tachycardia ( $\geq 100$  beats/min). Because blood pressure was not measured continuously during the perioperative period, we are not able to relate myocardial ischemia to changes in blood pressure. Our results demonstrate that only a minority of the ischemic episodes is related to patient care events. Although ischemia occasionally occurred during or immediately after mobilization, most periods of mobilization were not accompanied by ischemia. Surprisingly, only one ischemic episode was related to the onset of surgical pain. Anemia was reported to be a cause of perioperative ischemia.<sup>29,30</sup> In one of our patients, episodes of myocardial ischemia occurred while hemoglobin was less than 100 g/l, and



there was no further ischemia after transfusion. However, in four other patients occasionally developing perioperative ischemia, intermittent anemia (hemoglobin < 100 g/l) was not associated with ischemic episodes. Psychological stress can provoke myocardial ischemia.<sup>31</sup> In our patients no single ischemic episode was preceded or accompanied by anxiety, fear, or other unpleasant experiences. This might reflect the absence of psychological stress in our elderly patients. However, elderly patients in our cultural environment are not accustomed to talking about their feelings and the daily interview may not have disclosed feelings of psychological stress. In conclusion, hemodynamic abnormalities, surgical pain, and usual patient care events are not related to the majority of perioperative ischemic events. The influence of psychological factors and of biochemical or physiologic alterations provoked by surgery and anesthesia to the ischemic activity remains to be determined.

In summary, we found electrocardiographically defined myocardial ischemia in 31% of unselected patients undergoing elective hip arthroplasty. Most of the ischemic episodes were clinically silent, were not preceded or accompanied by tachycardia ( $\geq 100$  beats/min), and were not associated with events related to the patient's care. A substantial amount of ischemia occurred in patients considered to be at low risk for coronary artery disease. The occurrence of perioperative ischemia appears to predict unfavorable outcomes beyond the immediate perioperative period. The circadian variation of myocardial ischemia usually seen in normal life was preserved during the postoperative period. Ischemic activity was greatest immediately preoperatively and in the 48 h following surgery, while a low ischemic activity was found intraoperatively.

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