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Postoperative Cardiac Ischemia Detection by Continuous 12-Lead Electrocardiographic Monitoring in Vascular Surgery Patients: A Prospective, Observational Study

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Objectives: Elderly patients undergoing vascular surgery are at major risk for perioperative cardiac complications. The authors investigated continuous electrocardiographic Holter monitoring in a postoperative setting to determine the degree of postoperative ischemic load and its possible associations with perioperative myocardial infarction.

Design: A prospective, observational study.

Setting: One university hospital.

Participants: The study comprised 51 patients aged 65 years or older undergoing peripheral arterial surgery.

Interventions: Continuous electrocardiographic monitoring with a Holter device was started postoperatively and continued for 72 hours or until discharge. Postural changes were recorded using a 3-axis accelerometer. Standard 12-lead electrocardiography, high-sensitive troponin T measurements, and an inquiry of ischemic symptoms were performed 4 times perioperatively.

Measurements and Main Results: The primary outcomes were ischemic load (area under the function of ischemic ST-segment deviation and ischemic time) and perioperative myocardial infarction. During 3,262.7 patient-hours of monitoring, 17 patients (33.3%) experienced 608 transient ischemic events, all denoted by ST-segment depression. Of these 17 patients, 5 experienced perioperative myocardial infarction. The mean ischemic load in all patients was $913.2 \pm 2,797.3 \mu\text{V} \times \text{minute}$. Ischemic load predicted perioperative myocardial infarction, with an area under receiver operating characteristics curve (95% confidence interval) of 0.87 (0.75–0.99). Ischemic changes occurred most frequently during hours 24 to 60 of monitoring. Ischemia was asymptomatic in 14 of 17 patients (82.4%).

Conclusion: Postoperative myocardial ischemia was common in peripheral vascular surgery patients and may progress to perioperative myocardial infarction. Ischemic load was a good predictor of perioperative myocardial infarction. Ambulatory electrocardiographic monitoring solutions for continuous postoperative ischemia detection are warranted in the surgical ward.

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Key Words: vascular surgery; perioperative complications; cardiac ischemia; myocardial infarction; postoperative monitoring; Holter electrocardiography; high-sensitive troponin T

VASCULAR SURGERY PATIENTS are at high risk for adverse postoperative cardiovascular events,^{1–3} the most severe of which is perioperative myocardial infarction (PMI). PMI carries high mortality rates of 12% to 40%.^{4–7} Prolonged perioperative cardiac ischemia is associated with the development of complications,^{8–11} and early detection of ischemia would enable timely treatment.^{12,13}

In current practice, symptomatic PMI is diagnosed using electrocardiographic (ECG) recordings and cardiac enzyme measurements. Protocols of preoperative risk stratification and consequent perioperative ischemia surveillance of patients at risk are not applied systematically. However, because PMI patients rarely experience ischemic symptoms, asymptomatic, yet prognostically significant, myocardial ischemia episodes may go undetected. Continuous ECG recording (cECG) in the ward would permit earlier detection of myocardial ischemia and, consequently, narrow the gap in patient surveillance between the postoperative recovery room or step-down unit and a standard surgical ward.

The authors conducted a prospective, observational study to determine the performance of 12-lead cECG monitoring (Holter) in postoperative cardiac ischemia detection in elderly vascular surgery patients in a standard surgical ward. Furthermore, the authors investigated whether postoperative myocardial ischemia, detected using cECG, had an impact on patient outcome.

Methods

Ethical approval for this study (43/13/03/02/2015) was provided by the Ethics Committee of the Department of Surgery of Helsinki University Hospital, Helsinki, Finland, on March 4, 2015. Data according to the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines for observational studies are reported.¹⁴

Patients

This study comprised 57 patients ages 65 and older who underwent major vascular surgery at the Helsinki University Hospital between March and July 2015. Only patients undergoing elective or urgent/emergency surgeries during office hours were recruited. Written, informed consent was obtained preoperatively from all patients or their proxy. The authors prospectively excluded the following patients: (1) those undergoing redo surgery during the same hospitalization, (2) those who were assigned for treatment in the intensive care unit after surgery, (3) those whose preoperative ECG

included conduction defects that precluded ECG analysis of the ST-segment, and (4) those taking digitalis.

Continuous ECG Monitoring and Motion Sensor

A 12-lead continuous ECG Holter recorder (SEER 12; Getemed, Teltow, Germany) and a 3-axis accelerometer (Faros 360° eMotion; Mega Electronics Ltd, Kuopio, Finland) were applied to patients in the recovery room immediately after surgery. Bipolar leads I, II, and III and unipolar leads aVL, aVF, aVR, and V1 to V6 were used. The Holter recordings were analyzed using an EK-Pro analysis program (GE Healthcare, Little Chalfont, United Kingdom) immediately after the patient completed the study. The program stored data on patients' normal QRS-complexes and ST-segments (the average during the stable period) and marked abnormal ST-segment changes compared with baseline. The authors also investigated whether fewer than 12 channels would provide sensitive ischemia detection in this setting. To evaluate ST-segment deviations caused by postural changes and to enhance the reliability of ischemia detection, a 3-axis accelerometer was used. The accelerometer continuously collected data that allowed posture detection of the patient. The device has 3 sensitive axes along which it measures static acceleration (acceleration due to gravity) and dynamic acceleration (acceleration due to the movement of the device). Information about the orientation of the device relative to the gravitational vector and to the patient enabled the determination of the posture of the patient. The accelerometer allowed for the determination of whether the patient was in an upright position (standing/sitting), in a supine position, or lying on either side. During dynamic acceleration, the patient was considered to be moving. The Holter and motion recordings were continued for 72 hours postoperatively¹⁵ or until discharge.

Data

Electronic medical records were used to obtain patients' medical history, characteristics, medication, and physiologic and surgical data (Uranus 8.4.3; CGI Suomi Oy, Helsinki, Finland, and Caresuite 8.2; Picis, Wakefield, MA). These data then were used to prospectively complete a study-specific electronic case record form. Continuous 12-lead ECG monitoring and motion detection were started in the recovery room and continued for 72 hours postoperatively or until discharge. Standard 12-lead ECG recordings and high-sensitive fifth-generation troponin T (hs-TnT) (ECLIA, electrochemiluminescence immunoassay; Roche Diagnostics International Ltd,

Rotkreuz, Switzerland) measurements were obtained at the 4 following times: first preoperatively and then on the first, second, and third postoperative mornings. A trained study nurse visited patients on the first, second, and third postoperative days and inquired about ischemic symptoms (chest pain, neck, jaw or arm discomfort, dyspnea, arrhythmias, and nausea). The estimated perioperative cardiac risk was assessed retrospectively using the Gupta score, with no impact on monitoring or treatment decisions.¹⁶ Additional ECGs or hs-TnT measurements were ordered at the clinicians' discretion. The study did not interfere with the treatment of the patients. However, if signs of perioperative myocardial ischemia occurred, the treating physician was informed and the patients were treated according to the national guidelines.¹⁷

Definitions

PMI

The diagnosis of PMI was based on repeated hs-TnT measurements and either ischemic ECG changes or other ischemic features, which were defined as follows: (1) ischemic symptoms, (2) cardiac imaging evidence of myocardial infarction, or (3) autopsy findings of acute or healing myocardial infarction. To establish the diagnosis of PMI, a rise and/or fall of TnT of at least 1 value above the upper reference limit (14 ng/L) and either ischemic ECG changes or other aforementioned ischemic features were required.^{18–20} Medical conditions potentially causing elevated TnT concentration (sepsis, acute kidney injury, stroke, and pulmonary embolism) were considered when establishing the diagnosis of PMI.

Ischemia in cECG

Each minute, the Holter device stores all the ECG complexes and measured the ST-segment deviation in all leads, comparing them with the average of the patient's stable nonischemic ECG complexes. The ST-segment was measured 60 or 80 ms after the J-point, depending on the pulse frequency. An ischemic episode was defined as ST depression ≥ 1 mm or ST elevation ≥ 1 mm. The change had to persist for at least 1 minute and return to the baseline for at least 1 minute.²¹ The data obtained from the accelerometer were combined manually with the Holter data, and the patient's position was taken into account when assessing the significance of the ST-segment changes. A cardiologist (JV) visually analyzed all the ST-segment trends that indicated ischemia; artifacts and false-positive alarms were deleted. The ST-segment trends reflecting ST-segment elevation because of early repolarization or pure upsloping ST-segment depression were not considered to constitute ischemia. If an ischemic change occurred only in 1 lead, the patient's preoperative ECG was reviewed for preoperative ST-segment deviations; if the preoperative deviation exceeded 1 mm, the postoperative change was not considered ischemia. Similarly, a preoperative ST-segment deviation of 0-to-1 mm was subtracted from the postoperative deviation to obtain the exact ischemic change.

Ischemic Load

To quantify and compare the ischemia times, an ischemic load (IL) was calculated for every patient. IL was expressed as an area under the function of ischemic ST-segment deviation and ischemic time.²² The primary outcomes were IL and PMI.

Statistical Analyses

Categorical data are reported as absolute numbers (%) and continuous data as means (standard deviation) when normally distributed or as medians (interquartile range) when not. The chi-square or Fisher exact test was used to compare categorical variables, and a t-test or Mann-Whitney *U*-test was used to compare continuous variables, as appropriate. Areas under receiver operating characteristics curves (AUCs) were calculated with 95% confidence intervals (CIs). An AUC of 0.5 to 0.75 was defined as poor, AUC of 0.75 to 0.9 as good, and AUC of > 0.9 as excellent.²³ The best cutoff points for IL were identified using the Youden method, and these cutoff points were used to calculate sensitivity, specificity, and positive likelihood ratios (LR+). A *p* value of < 0.05 was considered significant.

The sensitivity of the different leads in detecting ischemia was calculated. However, the ischemia-detecting specificity for the leads was not calculated because all the detected ischemic episodes consistent with the study's definition for myocardial ischemia were considered true positive. All statistical analyses were performed using SPSS Statistics, Version 22 (IBM Corp, Armonk, NY).

Results

As the cECG recordings were reviewed, 6 patients were excluded because their recordings could not be analyzed reliably. Thus, 51 patients were included in the final analysis. The patient flowchart is presented in Fig 1. Patient demographics and preoperative clinical findings are summarized in Table 1.

Continuous ECG Monitoring

During 3,262.7 patient-hours of monitoring (64.0 ± 20.2 hours per patient), 17 patients (33.3%) experienced 608 ischemic events (11.9 ± 32.9 events per patient, range 0–184), all denoted by ST-segment depression. The postoperative myocardial ischemia details of patients with or without PMI are shown in Table 2. The mean heart rate during stable, nonischemic stages of monitoring was 90.9 ± 17.6 beats per minute (bpm) in patients with postoperative ischemia and 71.7 ± 12.1 bpm in nonischemic patients ($p < 0.001$). Ischemic events were preceded by an increase in heart rate (Δ heart rate = 3.8 ± 5.7 bpm [range –1.6 to 16.0]). There were no statistically significant differences in pre-ischemic changes in heart rate in patients with or without PMI.

Fig 2 depicts the observed ischemic times in each lead when the monitoring time was divided into 12-hour periods, and the

Fig 1. Patient flowchart.

ischemic time/lead was recorded for each period. Ischemic changes occurred most frequently during the second postoperative day. In all, 82.4% of patients who experienced postoperative ischemia did not experience any ischemic symptoms.

Perioperative Myocardial Infarction

Five of the 51 patients (9.8%) experienced PMI. On the first postoperative day, 2 PMIs were diagnosed; on the second postoperative day, 1 PMI occurred and on the third postoperative day 2 PMIs were diagnosed. Three patients who experienced PMI demonstrated a significant TnT elevation and new ischemic symptoms, and 2 demonstrated new ischemic ECG changes in addition to the enzyme release but were asymptomatic. All the PMIs were diagnosed using the serial standard ECG recordings, and cECG analyses did not reveal any other PMIs. However, the cumulative ischemia duration, the duration of the longest ischemic event, IL, and the preoperative TnT count were greater in PMI patients compared with patients without PMI (see Table 2). IL predicted PMI with an AUC (95% CI) of 0.87 (0.75-0.99). The best cutoff point for IL was $12.5 \mu\text{V} \times \text{minute}$, and sensitivity, specificity, and positive LR (LR+[95% CI]) for that cutoff were 1.0, 0.74, and 3.83 (2.36-6.23), respectively. A similar predictive value of IL was shown

for the longest ischemic event and cumulative ischemia duration (Table 3).

Lead Sensitivity

The sensitivities of the cECG leads and their combinations in detecting postoperative ischemia are shown in Table 4. In this study, the ischemia detection sensitivity of V4 outweighed that of V5, and the best sensitivity was acquired with the combination of the axial leads and leads V4 and V5 (97.2%).

Movement Analysis

Accelerometer data were used in the study to classify the following 7 postures of the patient during the recording: supine, prone, on the right side, on the left side, standing/sitting, half-sitting, and moving. The correlation between the ST values and the corresponding posture with individual patients and in the whole population were analyzed. In addition, the ischemic alarms to which a posture change could be associated were studied. Clear correlation in the ST values and postures could not be found either in the individual patients or in the whole cohort. However, patients did not cycle through all the aforementioned postures, and thus the postural variable was distributed unequally. Six alarms associated with a turn from back to side were found. Those cases

Table 1
Characteristics of All Patients (n = 51) Stratified by the Presence or Absence of Postoperative Ischemia

	Postoperative Ischemia n = 17	No Postoperative Ischemia n = 34
Age	76 [72–79]	73 [69–77]
Sex (male)	8 (47.1)	21 (61.8)
Comorbidity		
CAD	8 (47.1)	16 (47.1)
Heart failure	2 (11.8)	5 (14.7)
Kidney failure	1 (5.9)	6 (17.6)
ASO	16 (94.1)	29 (85.3)
Hypertension	15 (88.2)	31 (91.2)
Diabetes mellitus	6 (35.3)	12 (35.3)
COPD	1 (5.9)	6 (17.6)
Current malignancy	2 (11.8)	4 (11.8)
Prior		
Acute MI	6 (35.3)	10 (29.4)
PCI/CABG	6 (35.3)	8 (23.5)
Stroke/TIA	5 (29.4)	7 (20.6)
ASA classification		
II	0	1 (2.9)
III	11 (64.7)	14 (41.2)
IV-V	6 (35.3)	19 (55.9)
Preoperative medication		
Beta-blocker	12 (70.6)	28 (82.4)
Statin	14 (82.4)	30 (88.2)
Nitroglycerin	3 (17.6)	4 (11.8)
ACEI/AR2B	12 (70.6)	25 (73.5)
CCB	6 (35.3)	16 (47.1)
Acetylsalicylic acid	17 (100)	25 (73.5)
Clopidogrel	5 (29.4)	8 (23.5)
Gupta score	1.63 [0.75–2.98]	1.93 [0.82–3.62]
Urgent/emergency surgery	4 (23.5)	10 (29.4)
Vasopressor load during the day of surgery (mg) ²⁴	1.42 [0.30–1.88]	1.50 [0.69–2.65]
Nadir Hb during hospitalization (g/L)	87 [80–95]	93 [83–114]

NOTE. Data are expressed as n (%) or median [interquartile range].

Abbreviations: A2RB, angiotensin II receptor blocker; ACEI, angiotensin-converting enzyme inhibitor; ASA, American Society of Anesthesiologists; ASO, atherosclerotic disease; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CCB, calcium channel blocker; COPD, chronic obstructive pulmonary disease; Hb, hemoglobin concentration; MI, myocardial infarction; PCI, percutaneous coronary intervention; TIA, transient ischemic attack.

were reviewed in more detail. Combining cECG and body position data suggested that these 6 alarms were due to physical activity provoked by an ischemic episode.

Discussion

This study was designed to investigate the degree of postoperative IL and its possible associations with PMI, using the latest PMI definition and hs-TnT generation.¹⁸ Continuous ambulatory ECG monitoring detected postoperative ischemic episodes in one-third of the high-risk patients undergoing peripheral arterial surgery. Of the 51 monitored patients, 5 (9.8%) experienced PMI. The cumulative IL detected using cECG was strongly predictive of PMI. The combination of

Table 2
Postoperative Myocardial Ischemia Details of All Patients Stratified by the Presence of PMI

	All Patients n = 51 mean (SD)	PMI n = 5 mean (SD)	No PMI n = 46 mean (SD)	p Value
Longest ischemia duration (min)	7.2 (20.4)	22.6 (27.4)	5.6 (19.1)	0.001
Cumulative ischemia duration (min)	42.9 (127.0)	224.0 (311.1)	23.3 (72.7)	0.001
Ischemic load ($\mu\text{V} \times \text{min}$)	913.2 (2,797.3)	4,475.6 (6,241.8)	526.0 (1,915.1)	0.001
Preoperative TnT (ng/L)	32.7 (70.1)	112.2 (200.9)	24.0 (33.1)	0.002
Highest TnT (ng/L)	54.9 (107.5)	244.2 (278.7)	34.4 (38.9)	0.16

Abbreviation: PMI, perioperative myocardial infarction; SD, standard deviation; TnT, troponin T.

axial leads and leads V4 and V5 yielded the best ischemia-detecting sensitivity (97.2%). Lead V4 outweighed V5 in ischemia detection.

In light of this and previous studies,^{8–10,25} it seems evident that prolonged ST-depression-type postoperative ischemia predisposes to PMI and an adverse postoperative outcome. This study demonstrated that IL's performance was good in predicting PMI with an AUC (95% CI) of 0.87 (0.75–0.99) and a positive LR (95% CI) of 3.83 (2.36–6.23). The sensitivity was excellent, ensuring that prognostically significant ischemia was not missed. However, an association between IL and a rising/falling TnT level could not be found, suggesting that transient, short-duration ischemic events are insufficient to cause myocardial injury and cardiac enzyme release. Additional studies are needed to determine which preoperative and

Fig 2. Ischemic time (min) in the leads. Monitoring time is divided into 12-hour units, and the ischemic time/lead is recorded for each unit.

Table 3

Ischemic Load, Longest Ischemic Event, and Cumulative Ischemia Duration in the Prediction of PMI in All Study Patients (n = 51)

	Sensitivity	Specificity	AUC (95% CI)	Cutoff Value	LR +
Ischemic load ($\mu\text{V} \times \text{min}$)	1.00	0.74	0.87 (0.75-0.99)	12.5	3.83 (2.36-6.23)
Longest ischemic event (min)	1.00	0.76	0.87 (0.76-0.98)	1.34	4.18 (2.50-7.00)
Cumulative ischemia duration (min)	1.00	0.74	0.88 (0.76-0.99)	1.25	3.83 (2.36-6.23)

Abbreviations: AUC, area under receiver operating characteristics curve; LR +, positive likelihood ratio; PMI, perioperative myocardial infarction.

postoperative factors increase the IL and cause perioperative ischemia to develop into PMI and how this could be prevented.^{13,26–28} This study showed that the postoperative heart rate level was significantly higher in patients with postoperative ischemia compared with those without ischemia. Furthermore, an increase in heart rate preceded the ischemic events. These findings suggested that timely postoperative heart rate control in high-risk patients may protect from myocardial ischemia. In a previous Holter study by Raby et al,¹³ 26 ischemic postoperative vascular surgery patients were assigned randomly to receive either esmolol or placebo to reach a predefined individual ischemic threshold. Their results suggested that the treatment group experienced fewer ischemic episodes, which also were of a shorter duration. The study, however, was flawed because of the use of alternative β -blocker therapy in the control group.

The ischemia-detecting sensitivity increases as more leads are used in monitoring. The 12-lead system, however, is too complex for routine perioperative monitoring of elderly patients at ordinary wards. When the number of leads is reduced, the choice of the precordial leads has important implications on detecting perioperative myocardial ischemia. In this study, lead V4 was the most sensitive in detecting postoperative ischemia, both at the beginning of and at peak ischemia. This study demonstrated that V4 was superior to V5, which traditionally has been used most commonly in 3-lead ECG systems (at the beginning of ischemia [51.4% v 24.7%] and at peak ischemia [45.7% v 17.4%]; see Table 4). The best ischemia-detecting sensitivity was acquired with the combination of the axial leads and leads V4 and V5 (97.2%). These findings further supported the observation that lead V4 rather than V5 is the most appropriate precordial lead for the detection of postoperative ischemia. These results also

emphasized the need for a re-evaluation of the optimal 3-lead ECG combination.⁷

Myocardial ischemia leading to an infarction can evolve after an atherosclerotic coronary plaque rupture and following a coronary thrombosis (type I) or because of a decreased coronary blood flow (type II). The majority of PMIs are type II,^{29,30} although in an angiography study by Gualandro et al,³¹ 45% of PMI patients experienced a plaque rupture. In the study presented here, all detected postoperative ischemic episodes were of ST-depression type, indicating that perioperative physiologic factors such as tachycardia, stress, hypotension, and anemia may have caused stable multivessel coronary artery disease to become unstable. Stress-induced ST-depression-type ischemia usually affects a large portion of subendocardium.³² This explains the incongruence among the ECG leads with ST-segment depression during ischemia. Only leads V1, V2, aVL, and aVR did not demonstrate any ischemia in this study.

The 12-lead Holter device used in this study was not optimal for postoperative ischemia monitoring in a surgical ward. To be better-suited for large-scale use in a low-acuity setting, the device should be lighter, smaller, and easier to assemble and disassemble. The number of leads should be reduced to the minimal number that offers adequate sensitivity and specificity in detecting myocardial ischemia. These features would enable efficient mobilization of postoperative patients. In clinical use, the batteries should hold their charge for the entire monitoring period, which in recent studies has been 72 hours.³³ The data also should be available on a timely basis, and an alarm should be triggered by prognostically significant ischemia. The Holter technology allows for mobilization and is an established method for diagnosis of arrhythmias and ischemia, but the information is available only after the monitoring period. An integrated motion sensor would improve accuracy in ST-segment analysis because changes in body position are the most common cause of false-positive ST-segment monitor alarms.³⁴ The motion sensor algorithm used for this study, however, needs more validation.

This study had some important limitations. First, the study was designed to investigate the accuracy and usability of a Holter device in postoperative continuous ischemia monitoring. A 33% incidence of postoperative myocardial ischemia and a good prediction of PMI using IL were observed, but because of the small cohort size, this study was statistically underpowered to build a model that would adequately support a cumulative IL trigger for an automated ischemia alarm.

Table 4

Sensitivity of cECG Leads and Lead Combinations in the Detection of Postoperative Ischemia

Lead	At the Beginning of Ischemia (%)		p Value
V4	51.4		
II	39.4	II v V4	0.096
aVF	33.8	aVF v V4	< 0.001
V5	24.7	V5 v V4	< 0.001
	At Peak Ischemia (%)		
	45.7V4		
	25.2II	II v V4	< 0.001
V5	17.4	V5 v V4	< 0.001

Abbreviation: cECG, continuous electrocardiogram.

Second, in this study, the cECG monitoring was initiated after surgery. Therefore, it was possible that preoperative and intraoperative ischemia periods were not included in the cumulative parameters. However, it has been shown that postoperative cardiac ischemia is more common than is preoperative or intraoperative ischemia, and it is associated mostly with postoperative cardiac complications.¹⁵

In conclusion, one-third of the high-risk vascular surgery patients experienced postoperative cardiac ischemia, and PMI was a common complication in these patients. Cumulative IL detected by continuous postoperative Holter monitoring was a strong predictor of PMI. The best ischemia-detecting sensitivity was reached by a combination of axial leads and leads V4 and V5. V4 outweighed V5 in the detection of ischemia. New solutions are needed for continuous ambulatory ischemia monitoring in the postoperative surgical ward.

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