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PREVENTION

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Predictive Value of Preoperative Electrocardiography for Perioperative Cardiovascular Outcomes in Patients Undergoing Noncardiac, Nonvascular Surgery

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ABSTRACT

Background: The utility of routine preoperative electrocardiography (ECG) for assessing perioperative cardiovascular risk in patients undergoing noncardiac, nonvascular surgery (NCNVS) is unclear.

Hypothesis: There would be an association between preoperative ECG and perioperative cardiovascular outcomes in patients undergoing NCNVS.

Methods: A total of 660 patients undergoing NCNVS were prospectively evaluated. Patients age >18 years who underwent an elective, nonday case, open surgical procedure were enrolled. Troponin I concentrations and 12-lead ECG were evaluated the day before surgery, immediately after surgery, and on the first 5 postoperative days. Preoperative ECG showing atrial fibrillation, left or right bundle branch block, left ventricular hypertrophy, frequent premature ventricular complexes, pacemaker rhythm, Q-wave, ST-segment changes, or sinus tachycardia or bradycardia were classified as abnormal. The patients were followed up during hospitalization and were evaluated for the presence of perioperative cardiovascular events (PCE).

Results: Eighty patients (12.1%) experienced PCE. Patients with abnormal ECG findings had a greater incidence of PCE than those with normal ECG results (16% vs 6.4%; $P < 0.001$). Mean QTc interval was significantly longer in the patients who had PCE (436.6 ± 31.4 vs 413.3 ± 16.7 ms; $P < 0.001$). Univariate analysis showed a significant association between preoperative atrial fibrillation, pacemaker rhythm, ST-segment changes, QTc prolongation, and in-hospital PCE. However, only QTc prolongation (odds ratio: 1.15, 95% confidence interval: 1.06-1.2, $P < 0.001$) was an independent predictor of PCE according to the multivariate analysis. Every 10-ms increase in QTc interval was related to a 13% increase for PCE.

Conclusions: Prolongation of the QTc interval on the preoperative ECG was related with PCE in patients undergoing NCNVS.

Introduction

Cardiovascular complications are a major cause of perioperative morbidity and mortality in patients undergoing noncardiac surgery. Surgical procedures are classified to be associated with a low (<1%), intermediate (1%–5%), or high (>5%) risk for the development of perioperative cardiovascular events (PCE) within 30 days after surgery, according to the current American College of Cardiology/American Heart Association (ACC/AHA) Guidelines on Perioperative Cardiac Evaluation.[1] Patients undergoing vascular surgery are generally at a greater cardiac risk than patients undergoing any other type of surgery and defined as high-risk surgery. Most of the studies in the literature evaluating PCE in noncardiac surgery are performed in patients undergoing vascular surgery. However, there is a paucity of clinical data regarding incidence and predictive factors of PCE in patients undergoing major noncardiac, nonvascular surgery (NCNVS). Although widely used, the predictive value of preoperative 12-lead electrocardiography (ECG) for PCE in patients undergoing NCNVS is unclear. We prospectively assessed whether a comprehensive analysis of preoperative ECGs taken before major NCNVS could give prognostic information about in-hospital PCE.

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Methods

Patients

The study included patients age >18 years scheduled for NCNVS with an expected postoperative hospital stay of

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≥2 days. Emergent surgical cases and the patients with an American Society of Anesthesiologists (ASA) classification 5 (moribund, not expected to live 24 hours irrespective of operation) were excluded. Day-case surgical procedures were considered to be very low risk and were not included. Patients fulfilling these criteria who agreed to participate and sign written informed consent in the research study were included as study subjects. After approval of the institutional human investigation committee, 660 consecutive patients (mean age 65.3 ± 14.1 years, 52.8% men) undergoing NCNVS were evaluated. The patients were followed up during hospitalization by the study investigators and were evaluated for the presence of PCE.

Data Collection

Major noncardiac surgery was defined by procedures performed in the operating room requiring general, spinal, or epidural anesthesia. The type of surgery was classified and categorized according to the surgical risk, determined using the ACC/AHA classification.[1] High-risk surgeries included vascular surgeries, which have a cardiac risk often >5%. Intermediate-risk surgery is defined as surgery with a cardiac risk of 1%–5%, and included head and neck surgery, intraperitoneal and intrathoracic surgery, orthopaedic surgery, and prostate surgery. In our study patients, major gastrointestinal surgery (laparotomy, advanced bowel surgery, gastric surgery), major gynecological cancer surgery (abdominal hysterectomy and oophorectomy for cancer), major open or transurethral urological surgery (cystectomy, radical nephrectomy, total prostatectomy), head and neck surgery, and hip or knee arthroplasty were included. Intrathoracic surgery is not performed in our institution. Patients requiring emergency surgery (surgery required within 24 hours) or those undergoing minor-grade surgery were excluded. Risk assessment, preoperative preparation and drug therapy, and postoperative follow-up were completed according to current ACC/AHA guidelines.[1]

For each patient, preoperative risk factors of morbidity and mortality, patient characteristics, preoperative medication, and intraoperative data were prospectively evaluated. In the preoperative period, classification of the ASA was used as a composite index of a patient's general status.[2] The Revised Cardiac Risk Index was used for prediction of cardiac risk based on 6 prognostic factors: high-risk type of surgery (defined as intraperitoneal, intrathoracic, or suprainguinal vascular procedures), ischemic heart disease, congestive heart failure, history of cerebrovascular disease, insulin therapy for diabetes mellitus (DM), and preoperative serum creatinine >2.0 mg/dL. Each of the prognostic factors was assigned as 1 point.[3] Anesthetic management, monitoring, and other aspects of perioperative management were at the discretion of the attending physician.

Measurements

Resting 12-lead ECGs recorded at a speed of 25 mm/second were taken 1 day before surgery, on the first 5 postoperative days, and whenever clinically indicated. To avoid interobserver variability, 2 blinded investigators independently analyzed ECG data. All ECGs were analyzed for the Minnesota classification,[4] heart rate, QRS duration, QT interval, and left ventricular hypertrophy (LVH). Atrial fibrillation (AF) was defined by characteristic absolute irregularity of R-R intervals and concurrent loss of identifiable P waves in the ECG recordings.[5] Mean QT-interval duration for 3 consecutive beats in leads II and V_4 was calculated. Each QT interval was measured from the beginning of the QRS complex to visual return of the T wave to the isoelectric line. If U waves were present, the QT interval was measured to the nadir of the curve between the T and U waves. The QT interval was corrected for the heart rate with the use of 2 formulae: (1) Bazett's formula, $QTcB = QT/\sqrt{R\text{-}R}$,[6] and (2) Hodges' formula, $QTcH = QT + 1.75$ (rate $-$ 60).[7] The intra- and interobserver variability were 5% and 6%, respectively, for measurements of QTc. Patients with bundle branch block (BBB; n = 71) and implantable devices (n = 6) were also excluded. ST-segment abnormalities were defined by using the following criteria: ST-J depression of ≥1 mm (Minnesota code 4-1); ST-J depression of 0.5–0.9 mm horizontal or sloping down (Minnesota code 4-2); ST segment sloping down and reaching ≥0.5 mm below baseline in leads I, II, aVL, aVF, and V_1 through V_6 (Minnesota code 4-3); or an ST-segment elevation of ≥1 mm in leads I, II, III, aVL, aVF, V_5, and V_6 or of ≥2 mm in leads V_1 through V_4 (Minnesota code 4-4).

Presence of LVH was defined by means of code 3.1 (Left: R amplitude >26 mm in either V_5 or V_6, or R amplitude >20.0 mm in any of leads I, II, III, and aVF, or R amplitude >12.0 mm in lead aVL measured only on second-to-last complete normal beat) and one of the following codes: 5.1 (T amplitude negative 5.0 mm or more in lead II, or in lead aVF when QRS is mainly upright), 5.2 (T amplitude negative or diphasic with negative phase at least 1.0 mm but not as deep as described in 5.1), or 5.3 (T amplitude flat, negative, or diphasic (negative-positive type only) with <1.0 mm negative phase in lead II; not coded in lead aVF). Frequent premature ventricular complexes were defined as >1 complex in 10 beats. Sinus tachycardia was defined as a heart rate >100 beats per minute, and sinus bradycardia was defined as a heart rate <50 beats per minute.

Electrocardiographic results showing AF, left or right BBB, LVH, frequent premature ventricular complexes, pacemaker rhythm, Q wave, ST-segment changes, or sinus tachycardia or bradycardia were classified as abnormal.

All patients underwent preoperative transthoracic 2-dimensional echocardiography. Standard parasternal and apical views were obtained in the left lateral decubitus position using available equipment (Vivid 3 Pro; GE Vingmed, Milwaukee, WI). Left ventricular ejection fraction (LVEF) was measured by transthoracic echocardiography using modified Simpson's rule.

Cardiac biomarkers (creatine kinase MB and troponin I) were evaluated 1 day before surgery, on the first 5 postoperative days, and whenever clinically indicated. Perioperative myocardial ischemia was diagnosed if cardiac troponin I was exceeding the 99th percentile of a normal reference population on the first or second day after surgery or if there was a new flat or downsloping ST-segment depression of >0.1 mV that lasted for ≥1 minute in the continuous ECG recording.

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Study Endpoints

Patients were followed up by the consulting physician until discharge after surgery. The PCEs were defined as the occurrence of severe arrhythmias requiring treatment, cardiac death (death caused by acute myocardial infarction [MI], significant cardiac arrhythmias, refractory congestive heart failure, or as a death occurring suddenly without another explanation), acute heart failure, acute coronary syndrome (nonfatal acute MI or unstable angina), pulmonary thromboembolism, nonfatal cardiac arrest, and cardioembolic stroke. Perioperative MI was defined according to the universal definition of MI.[8]

Statistical Analysis

Data were analyzed using SPSS for Windows version 11.5 (SPSS Inc, Chicago, IL). The continuous variables were expressed as mean $\pm$ SD and were compared between groups by 2-tailed Student *t* test. Nonparametric tests were also used when necessary (Mann-Whitney *U* test). The Fisher exact (χ^2) test was used in comparison of categorical variables. For all analyses, $P < 0.05$ was considered statistically significant. Univariate and multivariate logistic regression analyses were applied to determine crude and adjusted odds ratios and 95% confidence interval (CIs) for the relation between ECG abnormalities and PCE.

Results

The mean age of the total 660 patients was 65.3 $\pm$ 14 years (range, 18–97 years), with many patients having a history of associated risk factors. Patient baseline characteristics and comorbidities are described in Table 1. Of the 660 patients, 278 underwent general surgery, 160 underwent orthopedic surgery, 121 underwent urological surgery, 33 underwent gynecological surgery, 32 underwent plastic surgery, 19 underwent neurosurgery, and 17 underwent ophthalmic and ear/nose/throat surgery.

Electrocardiogram Characteristics and Cardiovascular Outcome

Three hundred ninety-four of 660 patients (59.7%) had $\geq$1 abnormality on their preoperative ECG (Table 2). One hundred and twenty-seven patients (19.2%) had a change in preoperative therapy and 30 patients underwent additional preoperative tests. Twelve of the patients who had undergone additional preoperative tests proceeded to their surgery without any delay. However, 21 out of 33 additional cardiologist-ordered preoperative tests (echocardiography, exercise tolerance test, myocardial perfusion scintigraphy, and coronary angiography) resulted in a diagnosis of new or unstable cardiac disease. These patients had their noncardiac surgery after coronary artery bypass operation or coronary stent implantation (n = 15), operation for ascending aortic dilatation (n = 2), aortic valve replacement (n = 2), mitral valve replacement (n = 1), and mitral and aortic valve replacement (n = 1).

The most frequent ECG alterations were Q waves (12.1%), ST-segment abnormalities (12%), AF (12%), and LVH (10.3%). Perioperative cardiovascular events were observed in 80 of 660 patients (12%). The distribution of the PCE is presented in Table 3. There were no significant differences regarding the type of surgical procedure or gender between patients who had PCE or not ($P = 0.53$). However, patients with abnormal ECG results had a higher incidence of PCE than those with normal ECG results. Sixty-three of 394 patients with an abnormal ECG (16%), and 17 of 266 patients with a normal ECG (6.4%) had PCE ($P < 0.001$).

Univariate Analysis

The incidence of major in-hospital PCE was higher in patients who had AF, pacemaker rhythm, ST-segment changes, and QTc prolongation on the preoperative ECG ($P = 0.019$, <0.001, 0.019, and 0.001, respectively). However, Q waves ($P = 0.053$), conduction defects such as left and right BBB ($P = 0.124$ and 0.120, respectively), LVH ($P = 0.52$), frequent premature ventricular complexes ($P = 0.52$), or sinus tachycardia ($P = 0.55$) or bradycardia ($P = 0.52$) on the preoperative ECG were not associated with PCE. Univariate analysis also showed a significant association between age, DM, coronary artery disease, preoperative AF, ASA status, Revised Cardiac Risk Index, LVEF, and in-hospital PCE.

Multivariate Analysis

Only DM (odds ratio [OR]: 2.28, 95% confidence interval [CI]: 1.08–4.82, $P = 0.03$), LVEF (OR: 0.96, 95% CI: 0.93–0.99, $P = 0.03$), and QTc prolongation on the preoperative ECG (OR 1.15, 95% CI: 1.06–1.2, $P < 0.001$) were independent predictors of PCE (Table 4).

After adjustment for age, gender, comorbidity, pharmacological treatment, QRS duration, and clinical risk indicators, QTc prolongation was remained as a significant variable associated with PCE. Patients with PCE had a significantly longer mean QTc interval (436.6 ms; SD, 31.4) compared with patients who did not have PCE (413.3 ms; SD, 16.7). Every 10-ms increase in QTc interval was related to a 13% increase for PCE.

Discussion

The current study shows that preoperative ECG provides prognostic information in patients undergoing NCNVS. Prolonged QTc interval was an independent predictor of PCE, and every 10-ms increase in QTc interval was related to a 13% increase for PCE.

Patients undergoing noncardiac surgery are at risk of major PCEs.[1] The major determinants of PCE are the nature of surgery and patients' risk scores. Guidelines for perioperative cardiovascular evaluation in noncardiac surgery include history, physical examination, and performance of a 12-lead ECG to identify patients at increased risk for PCE.[1] However, although preoperative ECGs are routinely performed in patients scheduled for noncardiac surgery, whether patients with abnormal ECGs have an increased probability of developing PCEs is questionable.

The cardiac risk index of Goldman was the first multifactorial model specifically for perioperative cardiac complications in a noncardiac surgical population.[9] Two of the 9 independent risk factors correlated with postoperative cardiac complications were >5 premature ventricular

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Table 1. Baseline Clinical/Demographic Characteristics and Risk Scores

	All Patients, n = 660	Without PCE, n = 580	With PCE, n = 80	*P* Value
Age, y	65.3 ± 14	64.7 ± 14.5	70.3 ± 9.6	0.001
Male sex	348 (52.8)	296 (51.1)	42 (52.5)	0.45
BMI	28.4 ± 12.4	28.5 ± 13.1	27.8 ± 5.5	0.478
ASA status				<0.001
I	117 (17.7)	111 (19.1)	6 (7.5)	
II	339 (51.4)	308 (56.9)	31 (38.8)	
III	161 (24.4)	129 (18.8)	32 (40)	
IV	43 (6.5)	31 (2.5)	12 (15)	
Systemic hypertension	360 (54.6)	315 (54.3)	45 (56.2)	0.45
Current smoking	77 (11.7)	70 (12.1)	7 (8.8)	0.63
HF	63 (9.6)	44 (7.6)	19 (23.8)	<0.001
AF	79 (12)	63 (10.9)	16 (20)	0.019
DM	166 (25.2)	129 (22.3)	37 (46.3)	<0.001
CAD/PAD	167 (25.3)	134 (23.1)	33 (41.3)	<0.001
History of cerebrovascular disease	62 (9.4)	52 (9)	10 (12.5)	0.312
METs				<0.001
1–4 METs	57 (8.6)	46 (7.9)	11 (13.7)	
4 METs	237 (36)	199 (34.3)	38 (47.5)	
4–10 METs	297 (45)	268 (46.2)	29 (36.3)	
>10 METs	69 (10.4)	67 (11.5)	2 (2.5)	
Revised cardiac risk index				
0	94 (14.3)	91 (15.7)	3 (3.8)	
1	311 (47.2)	287 (49.6)	24 (30)	<0.001
2	186 (28.2)	150 (25.9)	36 (45)	
3	61 (9.3)	46 (7.9)	15 (18.8)	
4	7 (1.1)	5 (0.9)	2 (2.5)	
LVEF	58.8 ± 8.6	59.5 ± 7.8	53.9 ± 11.9	<0.001
Preoperative medication				
β-Blocker	149 (22.6)	127 (21.9)	22 (27.5)	0.265
Calcium inhibitor	97 (14.7)	85 (14.7)	12 (15)	0.940
ACEI	173 (26.3)	153 (26.4)	20 (25)	0.595
Furosemide	20 (3)	16 (2.8)	4 (5)	0.274
Thiazid diuretic	18 (2.7)	15 (2.6)	3 (3.8)	0.551
Spironolactone	18 (2.7)	16 (2.8)	2 (2.5)	0.892
Aspirin	141 (21.4)	114 (19.7)	27 (33.8)	0.004
Anticoagulants	31 (4.7)	25 (4.3)	6 (7.5)	0.208
ARB	58 (8.8)	50 (8.6)	8 (10)	0.686
Statin	66 (10)	57 (9.8)	9 (11.3)	0.695
Digoxin	25 (3.8)	19 (3.3)	6 (7.5)	0.064

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin II receptor blocker; ASA, American Society of Anesthesiologists; BMI, body mass index; CAD, coronary artery disease; DM, diabetes mellitus; HF, heart failure; LVEF, left ventricular ejection fraction; MET, metabolic equivalent; PAD, peripheral artery disease; PCE, perioperative cardiovascular events. Values are given as mean ± standard deviation or n (%).

Table 2. Baseline Electrocardiographic Characteristics of Patients With and Without Perioperative Cardiovascular Events

	All Patients, n = 660	Without PCE, n = 580	With PCE, n = 80	*P* Value
Electrocardiography				<0.001
Normal	266 (40.3)	249 (42.8)	17 (21.2)	
Abnormal	394 (59.7)	331 (57.2)	63 (78.8)	0.019
ST-T changes	79 (12)	63 (10.9)	16 (20)	0.124
Left BBB	28 (4.2)	22 (3.8)	6 (7.5)	0.120
Right BBB	43 (6.5)	41 (7.1)	2 (2.5)	<0.001
Pace rhythm	6 (0.9)	1 (0.2)	5 (6.3)	0.52
Premature ventricular contraction	39 (5.9)	33 (5.7)	6 (7.5)	0.51
Sinus bradycardia	15 (2.3)	14 (2.4)	1 (1.3)	0.55
Sinus tachycardia	45 (6.8)	40 (8.3)	5 (6.3)	0.52
LVH	68 (10.3)	58 (12.1)	10 (12.5)	0.053
Q wave	80 (12.1)	65 (11.2)	15 (18.8)	0.019
AF	79 (12)	63 (10.9)	16 (20)	<0.001
QTc interval (ms)	416.1 ± 20.5	413.3 ± 16.7	436.6 ± 31.4	

Abbreviations: AF, atrial fibrillation; BBB, bundle branch block; LVH, left ventricular hypertrophy; PCE, perioperative cardiovascular event; QTc, corrected QT interval. Values are given as mean ± standard deviation or n (%).

Table 3. Distribution of Perioperative Complications

Complications	N (%)
ACS	24 (30)
Acute HF	17 (21.3)
Severe arrhythmia	12 (15)
Cardioembolic stroke	10 (12.5)
PE	7 (8.8)
Nonfatal cardiac arrest	5 (6.3)
CV death	5 (6.3)
Total	80 (12.1)

Abbreviations: ACS, acute coronary syndrome; CV, cardiovascular; HF, heart failure; PE, pulmonary embolism.

Table 4. Predictive Variables of Perioperative Complications

			OR (95% CI)	
	P Value	OR	Lower	Upper
DM	0.031	2.283	1.080	4.827
QTc (ms)	0.000	1.043	1.028	1.058
LVEF (%)	0.038	0.966	0.935	0.998

Abbreviations: CI, confidence interval; DM, diabetes mellitus; LVEF, left ventricular ejection fraction; OR, odds ratio; QTc, corrected QT interval.

contractions per minute documented at any time before operation, and rhythms other than sinus rhythm or the presence of premature atrial contractions on preoperative ECG. Lee et al developed the largest and currently most widely used model of risk assessment, the Revised Cardiac Risk Index, in 1999.[3] This index identifies 6 predictors of major cardiac complications without any ECG variable. However, pathological Q waves were found in 17% of patients, with a 2.4-fold increased risk of perioperative events in 4315 patients age ≥50 years undergoing elective major noncardiac procedures. Landesberg et al evaluated 405 patients scheduled for vascular surgery.[10] Left ventricular hypertrophy and ST-segment depression on preoperative 12-lead ECGs were identified as important markers of increased risk for MI or cardiac death after major vascular surgery.

Schein et al evaluated the use of routine ECG in 18 189 patients who underwent low-risk cataract surgery.[11] Detailed analysis of preoperative routine ECGs revealed no prognostic information for short-term outcome. Liu et al evaluated 513 patients age ≥70 years undergoing noncardiac surgery.[12] Although 75.2% of the patients had ≥1 abnormality on their preoperative ECGs, it was not associated with an increased risk of postoperative cardiac complications.

Noordzij et al retrospectively studied 23 036 patients who underwent 28 457 surgical procedures.[13] They showed that the addition of a simple classification of preoperative ECG (ie, normal or abnormal) improved the predictive value of the combination of clinical cardiac risk factors and type of surgery. Patients with abnormal ECG findings had a higher incidence of 30-day cardiovascular death compared with

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patients with a normal ECG (1.8% vs 0.3%; adjusted OR: 3.4, 95% CI: 2.4–4.5).

However, in patients who underwent low-risk or low- to intermediate-risk surgery, the absolute difference in the incidence of cardiovascular death between those with and without ECG abnormalities was only 0.5%. Although this study has several limitations, such as the retrospective design and not analyzing nonfatal cardiac events, it suggests routine preoperative ECG testing should be abandoned in patients who undergo lower-risk types of surgery.

To the best of our knowledge, there are no studies investigating the role of preoperative QTc interval on PCE in patients undergoing noncardiac surgery. There is an ongoing debate on the clinical significance of a prolonged QTc interval in general population. The Framingham study failed to show an association of baseline QTc prolongation with total mortality or sudden death, or coronary mortality.[14] However, in the Rotterdam Study[15] and Strong Heart Study,[16] QTc prolongation was associated with an increased risk of total and cardiovascular mortality. The results of these studies show that prolongation of the QTc interval has been associated with an increased risk of ventricular arrhythmias, which may trigger ventricular fibrillation and cardiac death. Cardiac arrhythmias are believed to be responsible for one-third of all perioperative cardiac complications.[17] In the current study, prolonged preoperative QTc interval, which is a marker of subclinical cardiac disease and a surrogate marker of myocardial ischemia, was identified as an independent predictor of PCE in patients undergoing NCNVS.

Study Limitations

This study was performed at single center and only patients who had undergone formal preoperative cardiovascular consultation were included. Patients undergoing high-risk surgery (vascular surgery) were not included. Long-term follow-up after discharge was not performed.

Conclusion

The preoperative 12-lead ECG of patients undergoing major NCNVS contains important prognostic information to in-hospital PCE. The results of our study show that QTc prolongation on the preoperative ECG should be viewed as an independent risk factor for PCE after NCNVS. The QTc obtained from the ordinary 12-lead ECG may identify high-risk individuals among the general surgical population.

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