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Characteristics of Patients With Acute Coronary Syndrome and Normal Electrocardiogram

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ABSTRACT

Background: Patients with acute coronary syndrome (ACS) and normal electrocardiogram (ECG) may have an increased risk of late diagnosis and complications of the disease. **Objective**: To study the demographic, angiographic and echocardiographic characteristics of patients hospitalized for ACS in whom the ECG was normal on admission to the hospital. **Methods:** This retrospective study included patients who were hospitalized for ACS without ST-elevation between 2015 and 2023 and who had coronary artery disease (CAD) confirmed by coronary angiography. By further inspection of the electronic databases, patients with ACS who had a normal ECG on admission were filtered out and analyzed separately. **Results:** Of the total 3137 patients with suspected ACS without ST-elevation, 129 patients (4.1%) were diagnosed as having ACS with a normal ECG. In three patients a non-atherosclerotic cause for the ACS was found. A significantly higher proportion of patients had single-vessel (54.3%) compared to two-vessel (29.5%) and three-vessel (14%) CAD. In addition to a normal ECG, 5.7% of patients with single-vessel CAD and 3.5% of patients with multi-vessel CAD had normal troponin levels and normal regional LV systolic function on echocardiography. **Conclusion:** Less than 5% of hospitalized patients with ACS without ST-elevation had a normal ECG on admission. The majority of these patients have single-vessel CAD. In about 5% of patients with single-vessel CAD, neither elevated troponin levels nor LV asynergy are detected.

Keywords: acute coronary syndrome, normal electrocardiogram, coronary disease, left ventricular asynergy.

1. BACKGROUND

In patients with acute coronary syndrome (ACS), the electrocardiogram (ECG) provides important information about the presence, extent and severity of myocardial ischemia (1). However, a normal ECG does not rule out the presence of ACS (2, 3), and patients with ACS and normal ECG represent an important group as they are at higher risk of delayed diagnosis and complications of the disease (2, 4). After ruling out clinical and ECG signs suggestive of ST-elevation myocardial infarction (STEMI) or high-risk non-ST-elevation (NSTE) ACS, cardiac biomarkers play an important role in the diagnosis, risk stratification and treatment of patients with suspected ACS (5). In clinical practice, they are of great help in identifying patients with ACS who are at high risk and in identifying patients who will benefit from early invasive diagnostics (6). Echocardiography is one of the most important tools in emergency departments and intensive care units and it is essential for the diagnosis in patients with acute cardiovascular disease (7). Early echocardiographic examination of patients with suspected NSTE ACS can reveal left ventricular (LV) wall motion abnormalities (WMA) and indicate significant coronary artery stenosis but may also detect other conditions associated with chest pain. However, the proportion of patients with NSTE ACS and normal ECG who have echocardiographic abnormalities, particularly LV asynergy, has not been fully investigated.

2. OBJECTIVE

The aim of this retrospective, observational study is to investigate the demographic, angiographic and echocardiographic characteristics of patients with ACS diagnosed with coronary artery disease (CAD) who had a normal ECG on admission to hospital.

3. MATERIAL AND METHODS

The study was conducted at the Clinical Hospital Centre Zemun (CHCZ). Patients with ACS were identified through a search in the electronic health information system based on the discharge diagnosis of NSTE ACS between 2015 and 2023. After identifying all patients treated under the above diagnoses, a selection of patients with ACS, normal ECG on admission and angiography-proven CAD was made. Demographic data, data on risk factors for CAD (dyslipidemia, arterial hypertension, smoking, diabetes mellitus, family history of CAD), data on previous myocardial infarction (MI), previous revascularization procedures (percutaneous coronary intervention or aortocoronary bypass), data on maximum troponin levels and echocardiographic and coronary angiography findings were collected by reviewing the discharge lists of these patients.

An ECG with sinus rhythm, without changes in the ST-segment and in the T-wave, without atrial or ventricular arrhythmias was considered a normal ECG finding. The presence of a physiological Q-wave in lead III or incomplete right bundle branch block was also considered a normal finding. Significant coronary artery stenosis determined by invasive or computed tomography (CT) coronary angiography was defined as stenosis of the left main stem ≥50% or stenosis ≥70% in any other coronary artery. Patients were also included in the study if a non-atherosclerotic cause of ACS (coronary vasospasm, myocardial bridge, etc.) was documented by coronary angiography or other diagnostic procedures.

According to the standard CHCZ protocol, all patients underwent an echocardiographic examination within 24 hours of admission and prior to invasive procedures. In this study, we analyzed LV end-diastolic diameter, LV ejection fraction (LVEF) and assessed regional LV systolic function. LV end-diastolic diameter was measured at the end of diastole in a parasternal long-axis view using a two-dimensional technique (8). LVEF was determined using Simpson's disc summation method from the apical 4- and 2-chamber views (9). Regional LV systolic function was assessed visually using the 18-segment LV model (3 segments per wall) and grading for each segment according to the following scale: normokinesia, hypokinesia, akinesia, and dyskinesia. Regional LV systolic dysfunction (asynergy) was defined as the presence of hypokinesia, akinesia or dyskinesia in any two neighboring LV segments.

High-sensitivity troponin I levels were measured in all patients as part of routine care. Any value above the reference range was considered elevated. The study was approved by the Institutional Ethics Committee.

Statistical analysis

Continuous variables are presented with mean values and standard deviations, while categorical variables are presented with absolute numbers and proportions. The differences in frequencies between the groups were tested using the chi-square test. The statistical analysis was performed using commercially available software (PASW Statistics, version 18, SPSS, Inc., Chicago, IL, USA).

4. RESULTS

During the study period, a total of 3137 patients were hospitalized with suspected NSTE-ACS. Of these, 129 patients (4.1%) had a normal ECG on admission. After excluding patients without significant CAD, 126 patients (4%) with CAD and a normal ECG on admission were registered, whose basic demographic, clinical and echocardiographic characteristics are shown in Table 1. In 98% of patients with normal ECG, ACS was the result of atherosclerotic CAD; in three patients, a non-atherosclerotic cause of ACS was found (myocardial bridge, coronary vasospasm and coronary-pulmonary fistula). Most patients had arterial hypertension, dyslipidemia and were active or former smokers. Less than 10% of patients had a previous coronary event or myocardial revascularization. Although most patients had LV asynergy (74%), LVEF was preserved (≥50%) in 90% of patients. Elevated high-sensitivity troponin I values were found in 79% of patients. The data on coronary artery lesions are shown in Table 2. A significantly higher proportion of patients had single-vessel CAD (55%) compared with two-vessel (30%) and three-vessel CAD (15%) (p<0.001 for the difference between groups).

The extent of CAD, LV asynergy and elevated troponin levels

The majority of patients with single- and multi-vessel CAD had elevated troponin levels during hospitalization (79%). However, 4 patients (3.2%) with single-vessel

Parameter	All patients (n=126)
Age, years	60±10
Male patients, n (%)	93 (74)
Arterial hypertension, n (%)	124 (98)
Diabetes mellitus, n (%)	30 (24)
Dyslipidemia, n (%)	113 (90)
Smokers*, n (%)	66 (52)
Family history of coronary artery disease, n (%)	49 (39)
Previous myocardial infarction, n (%)	9 (7)
Previous percutaneous coronary intervention, n (%)	8 (6)
Elevated troponin levels, n (%)	100 (79)
Left ventricular end-diastolic diameter, mm	48±5
Left ventricular ejection fraction, %	55±7
Left ventricular ejection fraction <50%, n (%)	12 (9.5)
Left ventricular asynergy , n (%)	93 (74)

Table 1. Demographic, clinical and echocardiographic characteristics of patients included in the study

	All patients (n=126)
Single-vessel coronary artery disease, n (%)	70 (55)
Two-vessel coronary artery disease, n (%)	38 (30)
Three-vessel coronary artery disease, n (%)	18 (15)
Left anterior descending coronary artery, n (%)	27 (39)
Left circumflex coronary artery, n (%)	24 (34)
Right coronary artery, n (%)	19 (27)

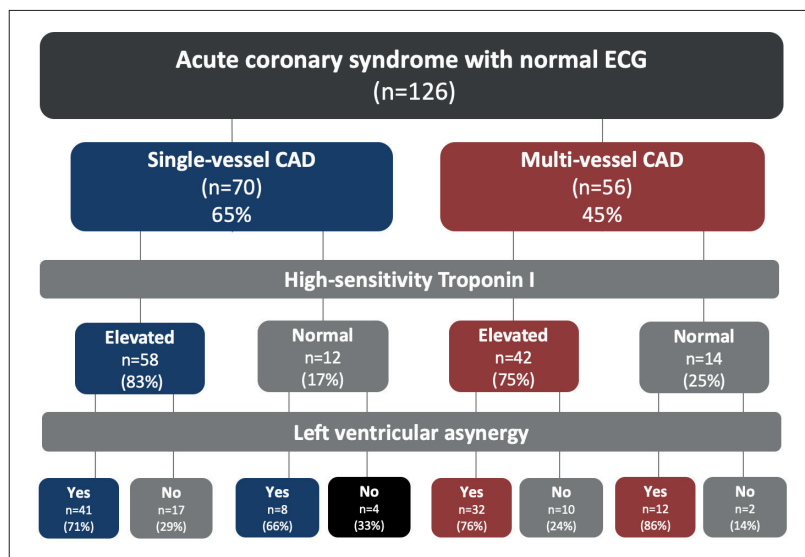**Table 2. The breakdown of coronary arteries' lesions**

Figure 1. Patient characteristics in relation to the extent of coronary artery disease (CAD), troponin values and the presence of left ventricular asynergy. ECG – electrocardiogram

centage had a normal ECG, normal high sensitivity, and normal regional LV systolic function.

It is estimated that approximately 2-5% of patients with ACS are discharged from the emergency department due to negative results of available diagnostic tests or an atypical clinical presentation (9), and that this is almost eight times more likely to occur in patients with a normal ECG (4). Although hospital mortality in patients with ACS who had a normal ECG on admission is lower than in patients with ECG abnormalities, it has been shown that patients with MI and normal ECG on admission do not always have a favorable hospital course and that hospital mortality is as high as 5.7% (10). In previous studies, patients with a normal ECG were younger, had a lower Killip class on admission and a higher LVEF, while there
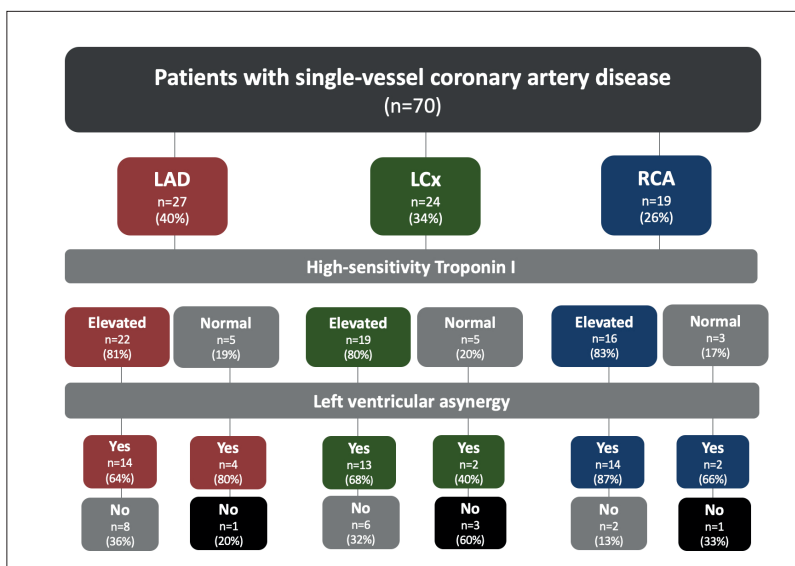
CAD and 2 patients (1.6%) with multi-vessel CAD had normal troponin levels and normal global and regional LV function in addition to a normal ECG (Figure 1).

Three patients with a lesion in the left circumflex (LCx), one with a lesion in the anterior descending artery (LAD) and one with a lesion in the right coronary artery (RCA) had normal ECG and normal troponin levels in the absence of LV asynergy. In patients with a normal ECG and a single-vessel CAD, there was no statistically significant difference in terms of the coronary artery involved (p>0.05 for the difference between the groups) (Figure 2).

Non-atherosclerotic ACS

A non-atherosclerotic etiology of ACS was found in 3 patients. In one patient, CT coronary angiography revealed a myocardial bridge across the LAD; in the second patient, invasive coronary angiography diagnosed a vasospasm of the RCA, while in the third patient, invasive and CT coronary angiography revealed coronary-pulmonary fistulas. In addition to a normal ECG, the first patient had a normal echocardiographic examination and normal troponin levels. On echocardiography, the second patient had LV asynergy in the irrigation zone of the RCA without elevated troponin levels, while the third patient had normal global and regional LV systolic function with elevated troponin levels.

5. DISCUSSION

Our study showed that a minority of patients (4%) hospitalized for NSTE ACS had a normal ECG, most of whom had single-vessel CAD. In addition, a small per-

Figure 2. Patients with single-vessel coronary disease in relation to the affected coronary arteries, elevated troponin values and the presence of left ventricular asynergy. LAD – left anterior descending coronary artery, LCx – left circumflex coronary artery, RCA – right coronary artery.

were no significant differences in risk factors for cardiovascular disease, family history of CAD and previous treatments (11). In our study, patients with normal ECG were on average 60 years old, and in >90% of cases had preserved LVEF, while diabetes mellitus was present in a quarter of cases, which corresponds to the prevalence of diabetes in patients with ACS (12). Although the measurement of high-sensitivity cardiac troponins is one of the most important tests for the early diagnosis of ACS, initially normal troponin levels should not be used as the only parameter to rule out MI, as 6-23% of acute myocardial infarctions may have initially normal levels (13). In the 2023 ESC guidelines for the treatment of ACS, the class I recommendation for the use of the ESC algorithm with serial cardiac troponin measurements (0 h/1 h or 0 h/2 h) to rule out NSTEMI was retained (5). The very

high safety and high efficacy of the 0 h/1 h ESC algorithm was recently confirmed in three studies, including a randomized controlled trial (14, 15, 16). However, even after excluding the diagnosis of acute MI, the need for invasive or non-invasive diagnosis of CAD should be considered, taking into account the clinical presentation and CAD risk assessment.

In our study, 21% of patients did not have elevated troponin levels throughout hospitalization, but they had significant CAD requiring revascularization. In previous studies, younger age, preserved renal function, and statin use were more commonly associated with normal troponin levels in ACS (17). In our study, 74% of patients had regional LV asynergy on echocardiographic examination. Regional LV asynergy on resting echocardiography may be a sign of myocardial ischemia, and the absence of these abnormalities has a high negative predictive value for ischemia but a low positive predictive value (18). Although a normal echocardiogram at rest, like a normal ECG, is an indicator of lower clinical risk, it may be insufficiently sensitive to detect subtle regional myocardial wall abnormalities that may indicate ischemia in patients with unstable angina who also have negative cardiac markers (19). In addition to the existing limitations of the ECG and the value of cardiac biomarkers in the diagnosis of ACS, LV asynergy may not be visible on 2D echocardiography if ischemia has affected less than one-fifth of the LV wall thickness, i.e. 1-6% of myocardial mass (20, 21), which may explain this finding. Previous studies have shown that the use of advanced echocardiographic techniques, such as myocardial strain, can improve the detection of LV myocardial dysfunction in a heterogeneous patient population with critical coronary stenoses compared with standard visual assessment of asynergy (22). However, echocardiography cannot distinguish between new or pre-existing regional myocardial dysfunction (19). Previous studies indicated the limited utility of ECG in detecting ischemia in the area of vascularization of the left circumflex coronary artery, i.e. the posterior wall of the LV, and in patients with previous MI (23). Patients with occlusion of the left circumflex coronary artery are at higher risk for delayed percutaneous coronary intervention and revascularization, partly due to the fact that it is more often associated with normal ECG findings on admission (24). For these reasons, the use of posterior leads is also recommended for diagnosis in patients with a clinical presentation of ACS and normal ECG findings in standard leads on admission (25). However, in our study, there was no statistically significant difference between the prevalence of arterial involvement in single-vessel CAD.

The current study is limited by its retrospective, observational, single centre design and small sample size. In addition, only patients with a normal ECG who were hospitalized for suspected ACS were included in the study, while the population of patients referred for outpatient investigations for suspected ACS was not considered.

6. CONCLUSION

Approximately 4% of hospitalized patients with NSTE-ACS have a normal ECG on admission, while neither elevated troponin levels nor LV asynergy are observed in about 5% of these patients.

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