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Intracoronary ECG monitoring during provocative acetylcholine test in chest pain patients with non-obstructive coronary artery disease — results from AChPOL Registry

Short title: icECG in non-obstructive coronary artery disease

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Introduction

Even 30%–50% of subjects undergoing coronary angiography due to chest pain have no significant lesions in coronary arteries [1]. The problem of patients with ischemia with non-obstructive coronary arteries is still rising. These patients characterize not only recurrent hospitalizations but also the impaired quality of life and, what is the most vital, poor prognosis [2]. In recent years, considerable progress in the invasive assessment of coronary microcirculation has been made, enabling during one procedure to assess the function of epicardial and microcirculation vessels [3]. But it is interesting whether patients with microcirculation dysfunction also have baseline ischemia. The intracoronary electrocardiogram (icECG) is an established method for monitoring ischemia during percutaneous coronary intervention. It provides an opportunity to detect ischemia in its early stages when changes on surface electrocardiogram or angina are not yet prominent [4, 5].

This study aimed to assess if baseline ischemia can be detected with icECG in patients with microcirculation spasm confirmed in a provocative test with acetylcholine (AChT).

Methods

AChPOL Registry was a prospective observational study described earlier [6]. We included patients undergoing AChT with suspicion of angina evoked by epicardial coronary spasm or coronary microcirculation dysfunction according to Coronary Vasomotion Disorders International Study Group criteria [7]. The institutional review board approved the registry protocol, and all patients provided written informed consent before enrollment to the AChPOL Registry. All patients underwent AChT according to a standardized protocol. We administered increasing acetylcholine (ACh) doses over 3 min into the coronary arteries via a diagnostic catheter (25, 50, and 100 μg for the left coronary artery, 25, 50, and 75 μg for the right coronary artery) [7–9]. Epicardial coronary spasm was defined as focal or diffuse reduction of epicardial coronary diameter ≥ 90% compared to baseline and accompanied by patient's symptoms and ischemic electrocardiographic changes (standard superficial leads). Microcirculation spasm was diagnosed in patients with ischemic ST-segment changes (in standard superficial leads) and angina symptoms, but with epicardial spasm <90% in diameter decrease. Diameter artery changes were measured with quantitative coronary angiography [7, 10, 11].

The recording and analysis of icECG were also described previously [12]. Briefly, to obtain the icECG signal, we applied a standard coronary guidewire (BMW Universal II, Abbott Vascular, Plymouth, MN, US). The proximal end of the guidewire was connected to a unipolar lead, used for recording V1–V6 on surface ECG. The guidewire was placed in distal segments of each coronary artery. The absolute ST-segment shift in icECG lead and surface leads I, II, and aVF, was determined before AChT, during the test, and at the end of the procedure. The recorded intracoronary and surface ECG leads, with simultaneously recorded aortic blood pressure curves, were printed and analyzed consecutively. The paper speed was 50 mm/s, and ECG amplitude was calibrated as 10 mm/mV. The points of the beginning of QRS-complex, end of QRS complex, and end of T-wave were connected and constituted the isoelectric line. If some hallmark points were not distinct, the definition of the isoelectric line was based on 2 hallmark points; the ST-segment shift was calculated as the distance of the corresponding point from the isoelectric line in a perpendicular direction (Figure 1A). icECG recordings were analyzed by two independent researchers who were not aware of the AChT results.

Patients were followed up for 60 months during telephone and/or at clinical visits.

We present the data as means (standard deviation [SD]) or percentage. We used the χ^2 or Fisher's exact test in all categorical variables, while one-way analysis of variance was used for all continuous variables. Post hoc analyses using 2-tailed Tukey's honestly significant difference test were conducted to verify the differences between the groups. No corrections for multiple comparisons were applied. The level of statistical significance was set as 0.05. Two-sided tests were used. We performed statistical analyses with R 3.0.2 for OS (R Foundation, Vienna, Austria).

Results and Discussion

We performed 54 AChT with the simultaneous icECG recording. The epicardial spasm was observed in 35 patients (64.8%), microcirculation spasm – in 13 (24.1%) patients, and in 6 (11.1%) patients the AChT was negative. The baseline characteristics are presented in Supplementary material, *Table S1*. There were more women in the microcirculation spasm group than in the other two groups (48.6% vs. 76.9% vs. 33.3%; $P = 0.01$). Also, there were no major periprocedural complications with no episodes of atrial fibrillation, allergic reactions, coronary artery injury or myocardial infarction, or death.

When analyzing baseline icECG recordings, we observed more pronounced ST depression in the microcirculation spasm group than in the epicardial spasm ($P < 0.01$) or AChT(-) groups ($P < 0.01$). During ACh test (just after completing ACh administration), there was no difference between the epicardial and microcirculation spasm groups regarding ST-elevation in icECG. Moreover, after the procedure (also after administering the nitroglycerin) in the group microcirculation group again, ST depression was more pronounced compared with two other groups (*P* <0.01) (Figure 1B).

When observing these patients during a 5-year follow-up, we disclosed that in the microcirculation spasm, there was the lowest rate of entirely or nearly asymptomatic patients (after the introduction of proper medical treatment). These rates were 54.3%, 15.4%, and 66.7% in epicardial spasm, microcirculation spasm, and AChT(-) groups, respectively (Supplementary material, *Table S2*). These findings might show that microvascular spasm was a rather stable or progressive state less prone to pharmacotherapy, whereas epicardial spams was a temporary state responding better to applied treatment. The microvascular spams can spark the inflammation, and markers of increased inflammatory state which hamper the endothelial function as well as markers of procoagulant activity may predict ischemic events in coronary microcirculation [13].

This is the explorative study assessing the application of icECG in detecting myocardial ischemia in patients undergoing AChT. icECG monitoring during AChT proved the presence of baseline ischemia in patients with microcirculation spasm.

Supplementary material

Supplementary material is available at https://journals.viamedica.pl/kardiologia_polska.

Article information

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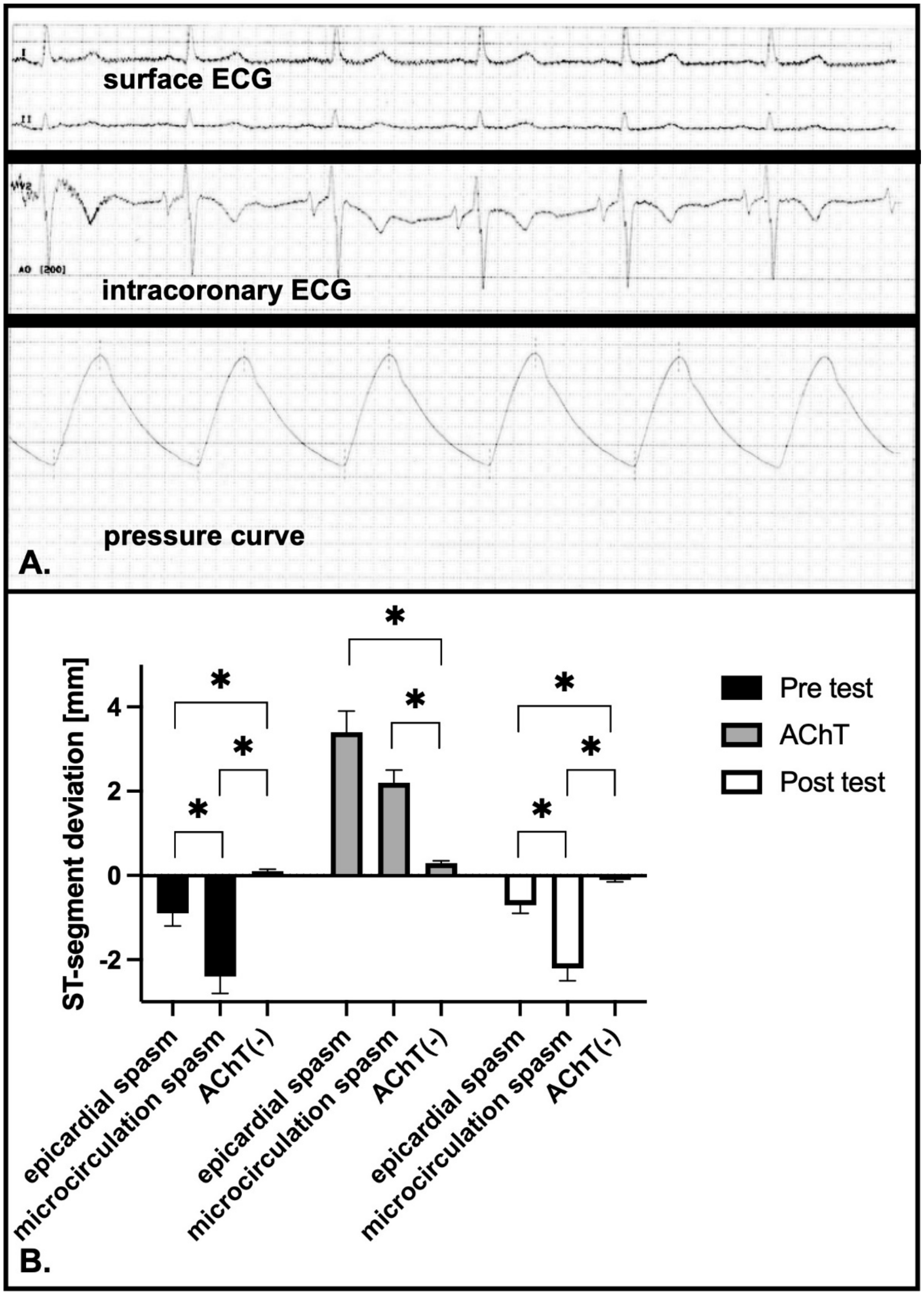

Figure 1. A. The example intracoronary electrocardiogram (ECG) recording. **B.** Change in ST-segment location during the provocative test with acetylcholine in three groups. First measurement was done before ACh administration (pre-test), the second measurement was done just after ACh

administration (AChT), and the third dose — at the end of the procedure just before removing the guidewire after nitroglycerine administration (post-test)

ST-segment deviation is presented as mean (SD). *P <0.05

Abbreviations: AChT, provocative test with acetylcholine