Intracoronary ECG monitoring during provocation acetylcholine test in chest pain patients with non-obstructive coronary artery disease: Results from the AChPOL Registry

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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 growing. These patients are characterized not only by recurrent hospitalizations but also by impaired quality of life and, what is important, poor prognosis [2]. In recent years, considerable progress in the invasive assessment of coronary microcirculation has been made, enabling assessment of the function of epicardial and microcirculation vessels during one procedure [3]. But it seemed 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 microvascular spasm confirmed in a provocation test with acetylcholine (AChT).

METHODS

The AChPOL Registry was a prospective observational study described earlier [6]. We included patients undergoing the AChT with suspicion of angina evoked by epicardial coronary spasm or coronary microcirculation dysfunction according to the Coronary Vasomotion Disorders International Study Group criteria [7]. The institutional review board approved the registry protocol, and all patients signed written informed consent before enrollment in the AChPOL Registry. All patients underwent the AChT according to a standardized protocol. We administered increasing acetylcholine (ACh) doses of over 3 minutes 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 a focal or diffuse reduction of epicardial coronary artery diameter of ≥90% compared to baseline and accompanied by the patient's symptoms and ischemic electrocardiographic changes (standard surface ECG leads). Microvascular spasm was diagnosed in patients with ischemic ST-segment changes (in the standard surface ECG leads) and angina symptoms, but with an epicardial spasm of <90% decrease

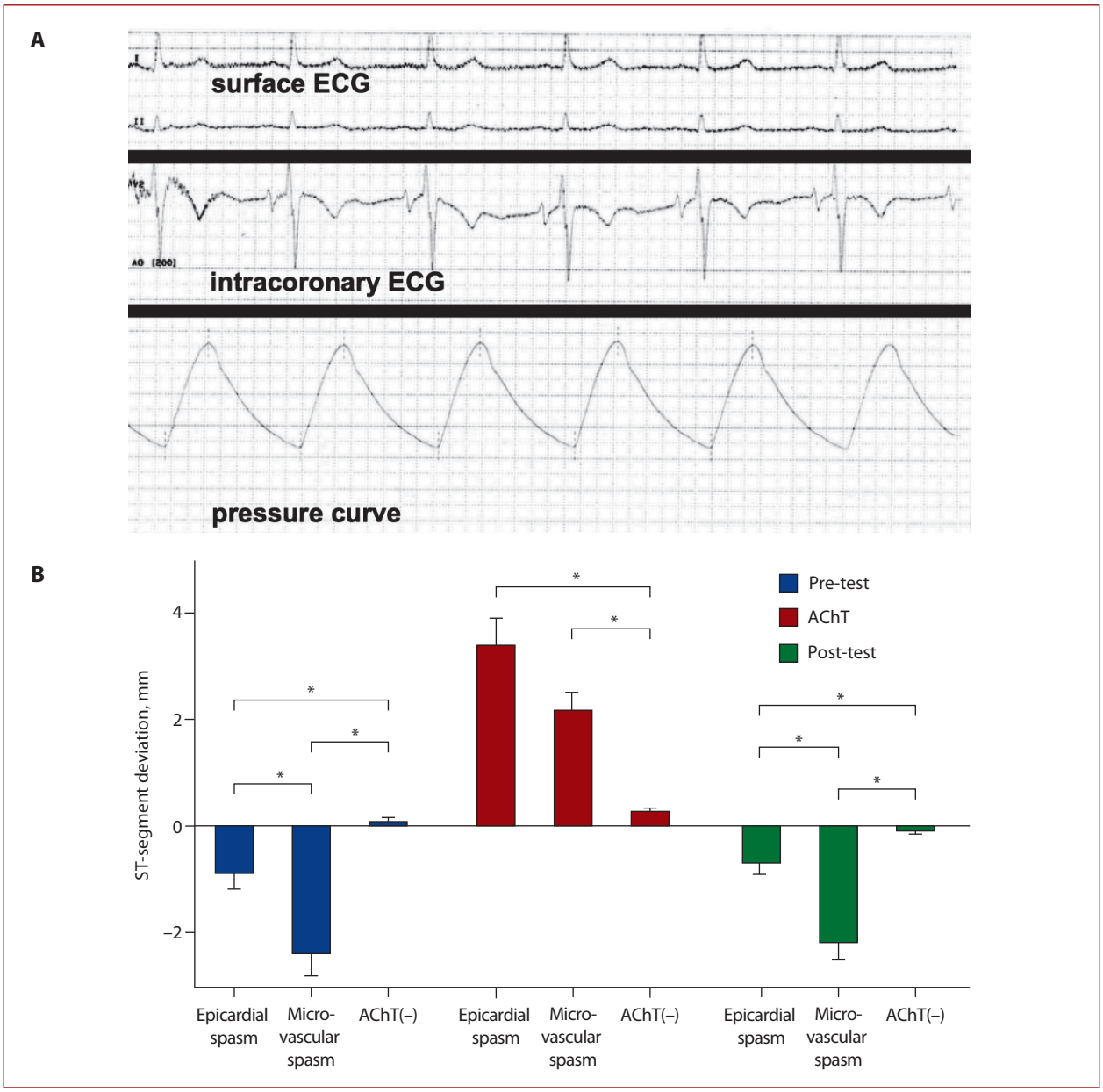

Figure 1. A. An example of intracoronary electrocardiogram (ECG) recordings. **B.** Change in ST-segment location during the provocation test with acetylcholine (ACh) in three groups. The first measurement was taken before ACh administration (pre-test), the second measurement was taken just after ACh 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, provocation test with acetylcholine

in diameter. 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 the icECG lead and surface leads I, II, and aVF was determined before the 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 at 10 mm/mV. The points of the beginning of the QRS complex, the end of the QRS complex, and the end of the 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 familiar with the AChT results.

Patients were followed up for 60 months with telephone calls and/or clinical visits.

We present the data as means (standard deviation [SD]) or percentages. We used the χ^2 or Fisher's exact tests in all categorical variables, while one-way analysis of variance was used for all continuous variables. Post hoc analyses using 2-tailed Tukey's honest 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 at 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 simultaneous icECG recording. The epicardial spasm was observed in 35 patients (64.8%), microvascular 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 microvascular 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, myocardial infarction, or death.

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

When observing these patients during a 5-year follow-up, we observed that in the microvascular spasm group, 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 the epicardial spasm, microvascular spasm, and AChT(-) groups, respectively (Supplementary material, *Table S2*). These findings might show that microvascular spasms were a rather stable or progressive state less susceptible pharmacotherapy, whereas epicardial spasms were a temporary state responding better to applied treatment. The microvascular spams can spark 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 explorative study assessed the application of icECG in detecting myocardial ischemia in patients undergoing the AChT icECG monitoring during AChT confirmed the presence of baseline ischemia in patients with microvascular spasm.

Supplementary material

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

Article information

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