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Invasive cardiology — recent trials presented at ESC Congress in 2018

Kardiologia inwazyjna — najnowsze doniesienia naukowe z Kongresu ESC 2018

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The European Society of Cardiology Congress 2018 offered many interesting presentations of the results of large clinical trials. Doctors as well as nurses and medical technicians had the opportunity to become acquainted with many reports that will affect daily clinical practice and treatment of patients. In this paper, we offer you a subjective review of the most interesting and valuable reports in the field of invasive cardiology.

The results of one-year follow-up of patients included in the CULPRIT-SHOCK trial are of great practical importance. This trial evaluated clinical outcomes in patients with acute myocardial infarction and cardiogenic shock qualified for immediate multivessel percutaneous coronary intervention (PCI) compared with culprit-lesion-only PCI [1]. The inclusion criteria were: myocardial infarction, cardiogenic shock and hemodynamically significant lesions in at least two coronary arteries. A significant lesion was defined as a stenosis greater than 70% in a vessel with a diameter of more than 2 mm. Exclusion criteria included: resuscitation longer than 30 minutes, symptoms of the central nervous system (CNS) injury, shock occurrence earlier than 12 hours prior to admission, severe renal failure (glomerular filtration rate [GFR] < 30 mL/min). Patients were randomly assigned to one of two equal groups: a culprit-only PCI group and an immediate multivessel PCI group (in which complete revascularization of all significant lesions was performed). The primary endpoint included death from any cause or severe renal failure leading to renal replacement therapy at 30 days, while the secondary endpoint included death from any cause, renal replacement therapy, recurrent myocardial infarction, repeat revascularization and hospitalization for heart failure in one-year follow-up. The results of the trial showed that at 30 days the mortality rate in the culprit-lesion-only PCI group was 45.9%, while in patients who underwent multivessel revascularization it was 55.4% (a significant difference in favor of the culprit-vessel-only strategy, p = 0.01). In the 12-month follow-up the risk of death was not significantly different between groups, although death from any cause occurred 12% less frequently – in 50% of patients who underwent culprit-vessel-only PCI and in 56.9% of patients who underwent multivessel revascularization (relative risk [RR] 0.88; 95% confidence interval [CI] 0.76–1.01). Recurrent myocardial infarction occurred in 1.7% of patients in the culprit-lesion-only PCI group and in 2.1% of patients who underwent complete revascularization — there was no significant difference between groups (RR 0.85; 95% CI 0.29–2.5). As predicted, the need for repeat revascularization was observed significantly more common in the culprit-lesion-only PCI group than in the immediate multivessel revascularization group (32.3 vs 9.4%; RR 3.44; 95% CI 2.39–4,95) as well as rehospitalization due to heart failure (5.2 vs 1.2%; RR 4.46; 95% CI 1.53–13.04). The study confirmed that in patients with myocardial infarction and cardiogenic shock the risk of death or renal replacement therapy was lower with culprit-lesion-only PCI compared to multivessel revascularization, and in one-year follow-up there was no significant differences in mortality rate between the two groups. The CULPRIT-SCHOCK trial therefore confirms

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that mortality is still very high in patients with myocardial infarction and cardiogenic shock, but revascularization limited to the culprit vessel seems to be more favorable.

The Canadian Spontaneous Coronary Artery Dissection (SCAD) Cohort Study explored a poorly understood but clinically significant problem of spontaneous dissection of coronary arteries [2]. This mechanism is responsible for up to 24% of myocardial infarctions, mainly in women before the age of 50. The Canadian multicenter register is the largest in the world to date. The main aim of the study was to improve understanding of SCAD, and the secondary aim was to assess treatment strategies. The study included 804 patients. Mean age was 52 years, and women accounted for 88.5% of the study group, of which 55% were in the postmenopausal age. ST-segment elevation myocardial infarction (STEMI) was diagnosed in 29.7% of patients, non-ST-segment elevation myocardial infarction (NSTEMI) — in 69.9%. Lesions responsible for acute coronary syndrome (ACS) occurred mainly in left anterior descending (60%) and circumflex artery (38%). In 60% of patients, SCAD appeared as diffuse and smooth stenosis. Physical effort was a triggering factor in 29% of patients, and severe stress in as many as 50% of patients. The SCAD study confirmed that in 31.1% of patient a predisposing factor was fibro-muscular dysplasia (FMD), a non-inflammatory vascular disease that not only affects renal and cervical vessels, but also is a significant problem in the aspect of spontaneous coronary dissection.

In the SCAD study population, PCI was performed only in 12% of patients, of which as many as 30% of cases were unsuccessful and 41% — suboptimal. However, the 30-day mortality rate was only 0.1%. The mean follow-up period was 3.1 years and during this time, the risk of death was 1.2%, recurrent myocardial-infarction occurred in 4.8% of patients and 1.5% required unplanned repeat revascularization.

A special group of patients were women from the third trimester of pregnancy to one year after delivery. In this group of patients, the risk of adverse events was twice as high as in the general population and amounted to 20.6%, being also an important prognostic factor for 30-day adverse events (odds ratio [OR] 2.9). The Canadian SCAD study confirmed that SCAD is very important and often under--diagnosed condition, especially among young women. It seems that the conservative treatment strategy may be a better therapeutic option in this group of patients. Especially in young women diagnosed with myocardial infarction, spontaneous coronary dissection should be taken into account as the cause of myocardial infarction, which may affect the treatment strategy.

The MITRA-FR study, which aroused a lot of controversy, evaluated transcutaneous treatment of mitral regurgitation with MitraClip in patients with heart failure [3]. The study included patients with secondary severe mitral regurgitation, decreased ejection fraction (15% < EF < 40%) and symptoms of heart failure. Severe secondary mitral regurgitation was defined as the effective regurgitant orifice (ERO) > 20 mm^2 and regurgitant volume > 30 mL. Patients were randomized in a 1:1 ratio to percutaneous mitral valve regurgitation repair (152 patients) or pharmacological treatment (152 patients). The composite endpoint included death from any cause or hospitalization due to heart failure at 12 months. In the group treated with MitraClip, the composite end-point occurred in 54.6% of patients, and in the group receiving conservative treatment — in 51.3% of patients (OR 1.16, 95% CI 0.73–1.84, p = 0.53). All-cause mortality rate was 24.3% in the invasively treated group and 22.4% in the conservatively treated group (OR 1.11, 95% CI 0.69–1.77). Similarly, there were no significant differences in unscheduled hospitalizations due to heart failure symptoms: 48.7% in the intervention group compared to 47.4% in the conservatively treated group. The presented results suggest the lack of benefits in terms of improved survival or decreased frequency of unplanned hospitalization for heart failure in patients with severe mitral regurgitation treated with MitraClip vs pharmacological treatment in the 12-month follow-up. Similarly, in the aspect of the New York Heart Association (NYHA) functional class, despite significant improvement in both groups at 12 months, there were no statistically significant differences between pharmacological vs invasive treatment with MitraClip device. These findings are in apparent contradiction with the results of the US COAPT, announced a few weeks later, which showed the excellent effectiveness of secondary mitral regurgitation repair with MitraClip device in a similar (though non-identical) patient population, including a reduction in overall mortality. A comparison of these trials provides instructive conclusions. The reasons for MITRA-FR failure may be a relatively low technical success rate of the procedure, its 3-fold lower durability and more frequent complications (14.6% vs 8.5% in the COAPT study). The limitation of the study was the lack of standardization of pharmacological treatment before the procedure — only COAPT assumed the maximum tolerated therapy in both therapeutic arms; drug therapy was also more stable during COAPT. Importantly, MITRA-FR patients had less severe mitral regurgitation (ERO = 31 ± 10 mm^2 vs 41 ± 15 mm^2 in COAPT) with more advanced heart failure--related remodeling (left ventricular end-diastolic volume [LVEDV] higher by 1/3). In the light of the unambiguous efficacy of MitraClip therapy demonstrated in COAPT, the MITRA-FR study rather provides information which errors in the qualification of patients should be avoided, with particular emphasis on the role of precise quantitative assessment of mitral regurgitation, which plays a key role in the clinical status of a qualified patient. The inconsistency between the results of the MITRA-FR and COAPT emphasize the need for further research aimed at optimally identify-

ing subgroups of patients who can benefit from MitraClip device implantation.

The GLOBAL LEADERS trial is another very interesting study that can have an impact on everyday clinical practice. The study compared the use of ticagrelor in combination with acetylsalicylic acid (ASA) for 1 month, followed by ticagrelor alone vs conventional antiplatelet therapy in patients after PCI. The study included 16,000 patients with acute coronary syndrome or stable coronary artery disease who had a biolimus-eluting stent implanted. Patients were randomly assigned to one of three groups:

— receiving ticagrelor and ASA for one month, followed by 90 mg ticagrelor twice daily for 23 months;
— receiving ASA and 75 mg clopidogrel once daily for 12 months, followed by ASA monotherapy for another 12 months (patients with stable coronary artery disease);
— or receiving ASA and ticagrelor for 12 months, followed by ASA monotherapy for another 12 months (patients with acute coronary syndromes).

The composite primary endpoint assessed at 2 years included all-cause mortality and new Q-wave myocardial infarction. Secondary endpoints included major bleeding (according to the Bleeding Academic Research Consortium criteria grade 3 or 5). At 2 years, 3.81% of patients receiving experimental therapy died or had myocardial infarction, compared with 4.37% of patients treated in accordance with the current standards of care (RR 0.87, 95% CI 0.75–1.01, p = 0.073). Analysis of the subgroups of acute coronary syndrome and stable coronary artery disease did not confirm significant differences in the occurrence of the primary endpoint depending on the treatment strategy. There were no statistically significant between-group differences in major bleeding (2.04% of patients receiving experimental therapy vs 2.12% of patients receiving standard therapy). Interestingly, 12-month results confirmed that in patients after MI or PCI treated with ticagrelor, discontinuation of ASA after 1 month did not increase the frequency of composite endpoint compared to dual antiplatelet therapy with clopidogrel and ASA. The study did not confirm improved prognosis in PCI patients treated with ticagrelor for 24 months compared to conventional 12-month therapy in combination with ASA. The lack of improvement may be caused by the fact that due to dyspnea, an adverse effect of ticagrelor therapy, and the frequent switching from ticagrelor to clopidogrel even in minor bleeding in the second year of observation, only 78% of patients took ticagrelor in the experimental group, while in the control group as many as 91.3% received clopidogrel. Further studies with a very thorough assessment of patients' compliance with the dosing protocol are needed to establish whether discontinuation of ASA after 1 month of follow-up and therapy with one antiplatelet agent in patient after PCI may be beneficial treatment strategy. Due to the above-mentioned limitations GLOBAL LEADERS did not provide a definitive answer, thereby being a negative research.

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