SYSTEMATIC REVIEW

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Early in-stent restenosis after revascularization in patients with ST-elevation myocardial infarction

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Abstract: *Background and aim: Obstructive coronary disease is one of the most important causes of death worldwide. Percutaneous coronary intervention is one of the most important treatments of this pathology. Using of coronary artery stents represented a major advance in interventional cardiology. While bare metal stents (BMS) set the reference point for improved safety over balloon-angioplasty, first-generation drug-eluting stents demonstrated significant improvements in efficacy, but not necessarily safety, and further technologic developments have focused on optimizing both.*
Methods: We studied 228 patients with STEMI in the last 6 months, divided in 2 groups – in the first group are 122 patients (53.5%) who developed in stent restenosis and the second group has 106 patients had no signs of restenosis (46.5%). The mean time of performing the angiographic reevaluation was 111 days for the first group and 154 days for the second group. The clinical signs that indicate the need of coronary reevaluation was stable angina (116, 50.87%), acute coronary syndrome (58, 25.4%) and asymptomatic patients (64, 28.9%). The cardiovascular risk factors correlate with high risk of restenosis was diabetes (24.3% in first group and 12.2% in the second one, p=0.004), active smoking (p=0.010) and metabolic syndrome (p=0.003). The stent's length >28mm, stent's diameter ≤ 2.5 mm and chronic occlusion correlate with high risk of in-stent restenosis in BMS.
Conclusion: Understanding the importance of risk factors control, will reduce the risk of restenosis, of other cardiovascular event, even sudden death.

Keywords: *stent, early restenosis, STEMI, revascularization*

INTRODUCTION

Cardiovascular disease represents the first cause of morbidity and mortality world-wide.

ST-elevated myocardial infarction (STEMI) represents a challenge for any cardiologist interventionist team who has to decide the best treatment option based on short, medium and long-time prognostic and possible complications.

The first successful percutaneous transluminal coronary angioplasty (PTCA) was performed using a balloon catheter.[1] Due to high rate of coronary occlusion during PTCA and of high rate of in-stent restenosis bare metal stent (BMS) was developed. First studies have shown that BMS are very effective in treating or preventing acute blood vessel obstruction, thus avoiding emergency surgical bypass interventions. Two randomized trials – the Benestend and STRESS (Stent Restenosis

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Study) have shown that stenting lesions de novo on native coronary have reduced angiographic restenosis by about 30% compared to conventional balloon angioplasty.[1,2,3]

Implanting stents leads to a luminal diameter larger than balloon angioplasty, both right after the surgery and in the follow up, thus to a lower restenosis rate.

Using BMS was compared with coronary artery bypass grafting (CABG) in the treatment of obstructive multi-coronary disease in ARTS trial (Arterial Revascularization Therapies Study). The 1 year follow up showed that the mortality, myocardial infarct and stroke rate was similar in the two groups. Survival rate without cardiovascular events was higher in CABG group (87.8% vs 73.8%). Also less surgery patients needed a second revascularization procedure (3.5% vs 16.8%).[4]

Stone et al, studying the safety and effectiveness of BMS and DES on 3006 patients with STEMI with immediate PCI noticed that in DES group the restenosis in stent and recurrent ischemia needing revascularization procedure in 1 year follow up was significant lower than in BMS group.[5] Although, mortality and in stent thrombosis rate were similar for the 2 groups.

Drug eluting stents are a newer coronary stent category, superior to BMS due to a significant reduction of in-stent restenosis, a significant decrease of major adverse cardiac events, as well as target lesion revascularization in those patients which benefited from DES at 6 month follow up.[6, 7] Results at 5 years have demonstrated a similar rate of in-stent thrombosis between the two groups, but a significant lower incidence of major adverse cardiac events in the DES group.[6]

The beneficial using DES is not absolute. DES are superior in reduction of in-stent restenosis incidence especially in high risk lesions. For low risk restenosis patients or for those with high risk of acute in-stent thrombosis due to need of early dual antiplatelet therapy abortion the using of BMS has an important indication.[8,9] Although, lot of research show that using BMS is an alternative for uncomplicated patients or for those with long term dual antiplatelet therapy contraindication, in high diameter vessels, in venous graft lesions or in patient with acute coronary syndrome – STEMI.[10-14]

Despite last decades progresses, in stent restenosis stays an unsolved problem. Revascularization needs in 1 year is 6.7% in DES using, and 11% in BMS, frequently due to restenosis.[15]

METHODS

This study is a unicentric, retrospective, non-randomized trial. The patient from this study were patients of "Academician Vasile Candea" Emergency Clinical Center of Cardiovascular Diseases of the Army Bucharest. We included in the study patients diagnosed with STEMI who underwent myocardial revascularization in less than 24 hours from the appearance of chest pain, who followed the medical treatment according to ESC Guideline, and who underwent angiographic reevaluation in the first 6 months after PTCA. The patients were divided in 2 groups: the study group who developed in-stent restenosis in less than 6 months from PTCA, and the control group who has no signs of restenosis. We evaluate local factors (type of stent, the length and the diameter of stent, the affected vessel and the type of restenosis – focal or diffuse restenosis) and general factors (genetic factors, demographic factors, smoke, and comorbidities – arterial hypertension, dyslipidemia, diabetes, metabolic syndrome, history of stoke, peripheral arterial disease).

RESULTS

We studied 228 patients with STEMI in the last 6 months, divided in 2 groups – in the first group are 122 patients (53.5%) who developed in stent restenosis, from minimal restenosis (24 patients, 20%) to occlusion (16 patients, 13.3%), and the second group has 106 patients which had no signs of restenosis (46.5%). The mean time of performing the angiographic reevaluation was 111 days for the first group and 154 days for the second group.

Most patients came from urban areas (67% for both groups – without significant differences between groups). In the study group the most patients are men (82 patients, 68.3%), while in the other group only 54%

were men (OR=2.476; CI 95% 1.465-3.780; p<0.003). The clinical signs that indicate the need of coronary reevaluation was stable angina (116, 50.87%), acute coronary syndrome (58, 25.4%) and asymptomatic patients (64, 28.9%).

The cardiovascular risk factors correlated with high risk of restenosis were diabetes (24.3% in first group and 12.2% in the second one, p=0.004), active smoking (p=0.010) and metabolic syndrome (p=0.003). The influence of arterial hypertension and dyslipidemia over the risk of in-stent restenosis is hard to appreciate. Prior PTCA, peripheral arterial disease, genetic impregnation also have little correlation with restenosis risk.

The most frequent location of stent implantation in left anterior descending artery (LAD), followed by right coronary artery and circumflex artery, but the stent location doesn't correlate this risk of restenosis.

If we talk about stent's characteristics which can interfere with evolution and prognosis of the patients, the stent's length >28mm (OR 2.77; CI 95% 1.45-4.44; p<0.001), stent's diameter ≤ 2.5 mm (OR 2.45; CI 95% 1.54-3.46; p<0.001), and chronic occlusion (OR 3.78; CI 95% 2.03-7.35; p<0.001) correlate with high risk of in-stent restenosis in BMS. Although, the stent's diameter ≥3.25 mm (OR 0.34; CI 95% 0.24-0.49; p <0.001), the length ≤15 mm (OR 0.58; CI 95% 0.42-0.81; p=0.001) correlate with further restenosis.

DISCUSSION

Our results shows that diabetes mellitus, metabolic syndrome, prior interventional myocardial revascularization, longer stent length and smaller stent diameter are important factors that correlate with risk of in-stent restenosis. Prior PTCA, peripheral arterial disease and genetic factors correlate with restenosis risk. Our research was design to study the risk factors for early in-stent restenosis. Thus, we compared our result with many available researches that studied risk of long term and very long term in-stent restenosis, and results are similar. [16-19] It is known that diabetes, history of myocardial infarction and/or PTCA, different stent and lesion factors correlate with risk of long term and very long term in-stent restenosis, even on BMS or DES.[20-22] Despite rigorous risk factors control and correct medical treatment some patients develop in-stent restenosis, many factors could be incriminated in this phenomenon according with clinical trials. The factors incriminated in in-stent restenosis development, in both BMS and DES, are biological factors (drug resistance, hypersensitivity), mechanical factors and technical factors.[23]

The drugs in DES have a cytostatic (Sirolimus and its analogs) or a cytotoxic effect (Paclitaxel). Statistic data indicate that patients genetic mutations can develop resistance to Sirolimus or Paclitaxel.[24, 25]

Other biological factor is hypersensitivity of compound element in stents. For BMS, release of nickel and molybdenum, and for DES, cobalt releasing, are potential triggers for in-stent restenosis due to local allergic reaction, which can accelerate the atherogenic process.[26, 27]

The mechanical factor responsible of in-stent restenosis are stent underexpansion during the procedure, which is undetectable angiographically, nonuniform drug distribution due to local blood flow alterations, damage of the polymer, stent fracture resulting an important decrease in local drug delivery.[28-31]

Technical factors potentially responsible for increased risk of restenosis include barotrauma outside the stent, randomized clinical trials indicate that restenosis occurred at the proximal margin of stent and uncovered residual plaque, which correlate with increased risk of myocardial infarction at 1 year.[32-33]

Clinical presentation of patient with in-stent restenosis was represented by stable angina in more than half of patients and a quarter of patients were completely asymptomatic. Also, almost ¼ of patients presented acute coronary syndrome, in which smoking and prior myocardial infarction are clinical predictor factors.

Thus, is very important for our patients to understand the importance of risk factors control, reducing the risk of restenosis, of other cardiovascular event and

sudden death. Also, there are some biological factors which are difficult to evaluate and some mechanical and technical issues that should be consider in patients with in stent restenosis. Further, we could study the impact of subclinical factors which could interfere with evolution and prognostic, early identifying technics and ways for prevention complications for increase the quality of live and decrease the costs of long term managing of patients.

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