Original Paper

The Impact of the Risk Factors in the Evolution of the Patients with Left Main Coronary Artery Stenosis Treated with PCI or CABG

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ABSTRACT: The aim of our study was to identify the cardiovascular risk factors present in patients with left main coronary artery disease (LMCAD), which influenced the progression of these patients in both percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG). We performed a clinical observational descriptive study in which, during three years, we followed the evolution of 81 patients who were diagnosed with left main coronary artery disease and who were treated either by interventional revascularization by stent implantation, by surgical revascularization by performing an aortic-coronary bypass. In our study the risk factors according to which the evolution of the patients was observed were represented by diabetes, smoking, age and gender. The primary endpoint was mortality from any cause and other clinical endpoints were the reduction of left ventricular ejection fraction, symptomatic ischemic heart disease manifested by angina pectoris, non-procedural myocardial infarction or need for repeated revascularization. In our study diabetes was the risk factor that negatively influenced the evolution of patients with LMCAD treated either by PCI or by CABG for the most part, followed by smoking, male gender and age over 65 years.

KEYWORDS: *Risk factors, left main coronary artery disease, PCI, CABG*

Introduction

The left main is part of the left coronary artery, being its first segment [1]. This segment originates from the mid portion of the left Valsalva sinus [2]. Typically, it contains three segments: the ostium (proximal to the origin of the aorta), the mid portion or shaft, and the distal segment [3].

Atherosclerotic obstructive lesion (defined as a stenosis greater than 50%) of the left main is found in approximately 4% of all patients evaluated by angiography for coronary artery disease and it occurs isolated in only 5-10% of these patients [1]. Patients with left main coronary artery disease (LMCAD) are at high risk because the obstruction of this coronary artery segment affects approximately 75% of the total blood flow of the left ventricle, leading to a poor prognosis due to the increased risk of massive infarction and of sudden cardiac death [2]. Therefore, the detection of such a lesion in coronary angiography needs revascularization regardless of the clinical context [1].

Revascularization methods are: percutaneous coronary intervention (PCI) and CABG (coronary artery bypass grafting). In the last ten years, several randomized clinical trials comparing PCI with CABG for LMCA disease [3-15] have been published. The differences between surgical and interventional revascularization are represented by the type of approach (thoracotomy in CABG and transluminal in PCI), the use of general anesthesia in CABG-treated patients and extracorporeal circulation (increased risk factors for myocardial infarction, infections or inflammatory reactions) or use of radiological contrast agents for patients treated with PCI [16]. Both methods have been progressing continuously, for example, in PCI-treated patients the use of pharmacologically active stents (DES) has become the standard treatment option, and in case of surgical revascularization, the grafting arteries (both internal and/or radial mammary arteries) [16].

With all these therapeutic improvements, these patients have a high risk of ischemic events over the medium and long term, therefore active secondary prevention is an essential element in their treatment [17].

The aim of our study was to identify the cardiovascular risk factors present in patients with left main coronary artery disease, which influenced the progression of these patients in both percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG).

Materials and Methods

We performed a clinical observational study in which, during three years, we followed the evolution of 81 patients who were diagnosed with left main coronary artery disease and who were treated either by interventional revascularization by stent implantation, by surgical revascularization by performing an aortic-coronary bypass. These patients were treated and/or monitored in three important centers from Romania: Cluj-Napoca, Timișoara and Craiova.

This study was carried out in accordance with all the indications given by the Declaration of Helsinki, Good Clinical Practice and other relevant regulations. The study was approved by the Ethics Committee of the University of Medicine and Pharmacy of Craiova, each patient included in the study signing both an informed and an acceptance consent.

The revascularization decisions were discussed in the Heart Team, the selection method for myocardial revascularization was determined by coronary anatomy and by the comorbidities of the patient.

In our study the risk factors according to which the evolution of the patients was observed were represented by diabetes, smoking, age and gender. Depending on these, we made four groups of patients. The primary endpoint was mortality from any cause and other clinical endpoints were the reduction of left ventricular ejection fraction, symptomatic ischemic heart disease manifested by angina pectoris, non-procedural myocardial infarction or need for repeated revascularization. Based on these, the patients were divided in five subgroups.

The follow-up was performed for three years, initially at one month, then at three and six months interval. For each patient included in the study the follow-up continued until death, withdrawal from the study or three years after randomization, all patients who were finally enrolled in the study were followed for at least one year.

The statistical tests used in our study were performed with GraphPad Software (version 6 or higher, GraphPad Software, La Jolla, CA, USA). All results were recorded as mean and standard deviation. We used the Kaplan-Meier curves with the Log-rank (Mantel-Cox) test to evaluate the primary and secondary endpoints in patients with LMCAD treated either by PCI or CABG depending on the risk factors. In all cases, the statistically significant difference was recorded if the value of P was less than 0.05. Moreover, Hazard ratio (HR) and 95% confidence intervals (CIs) for results of the primary end point and secondary end points were calculated.

Results

A number of 81 patients were enrolled in the study starting from 2012 until 2015 in 3 centers. Patients were followed for at least one year and follow-up was continued until 2018.

The average age (Fig.1) was 65.57 years in the female group and 63.75 in the male group (p=0.97).

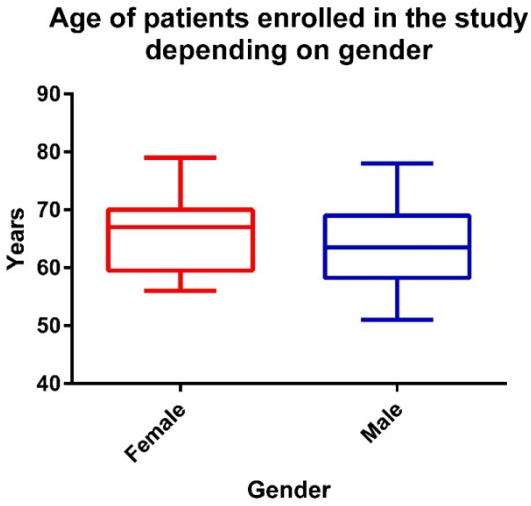

Fig.1. Age of patients enrolled in the study depending on gender

Left main coronary artery disease was classified into "ostial", "mid-shaft" or "distal" (Fig.2) based on the angiography findings.

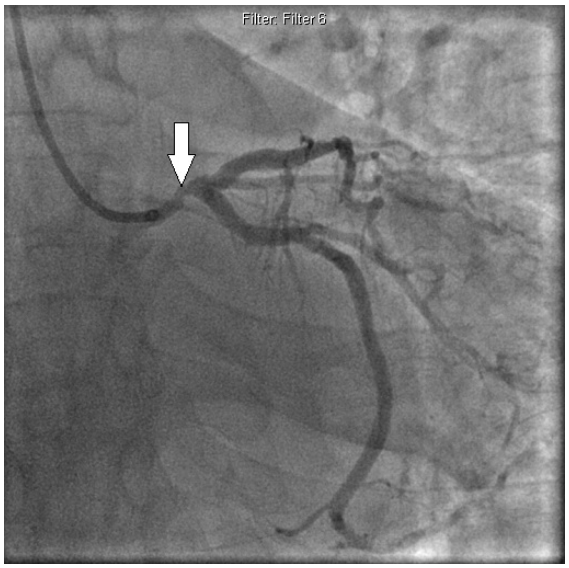

Fig.2. Examples of angiographic findings in patients with left main coronary lesions (the white arrow)

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Taking into account the evaluation of all mortality causes, depending on risk factors, in patients treated for left main coronary artery disease, we observed a higher mortality in the smoking group compared to the nonsmoking group (HR log=1.58, 95% CI ratio 0.4920 to 4.827 for active smoking, and HR log=0.6327, 95% CI ratio 0.2071 to 2.032 for nonsmoking, p=0.4682) as it can be seen in Fig.3A. Also, higher morality was recorded in the group of patients with diabetes mellitus compared to those without diabetes (HR logrank=7.833, 95% CI ratio 2.114 to 17.51 for patients with diabetes mellitus, and HR logrank=0.1277, 95% CI ratio 0.05712 to 0.4730 for patients without diabetes, p=0.0011) (Fig.3B), in the male group compared to the female group (HR log=8.289, 95% CI ratio 2.246 to 16.06 for the male group, and HR log=0.1206, 95% CI ratio 0.06228 to 0.4453 for the female group, p =0.0005) (Fig.3C), but also in 65 years old patients or older compared to the patients aged less than 65 years (HR logrank=2.419, 95% CI ratio 0.8086 to 7.123 for age≥65 years group, and HR log=0.4134, 95% CI ratio 0.1404 to 1.237 for age <65 years group, p=0.1218) (Fig.3D). Thus, with regard to the mortality assessment, statistically significant differences were recorded only depending on the presence of diabetes mellitus and gender.

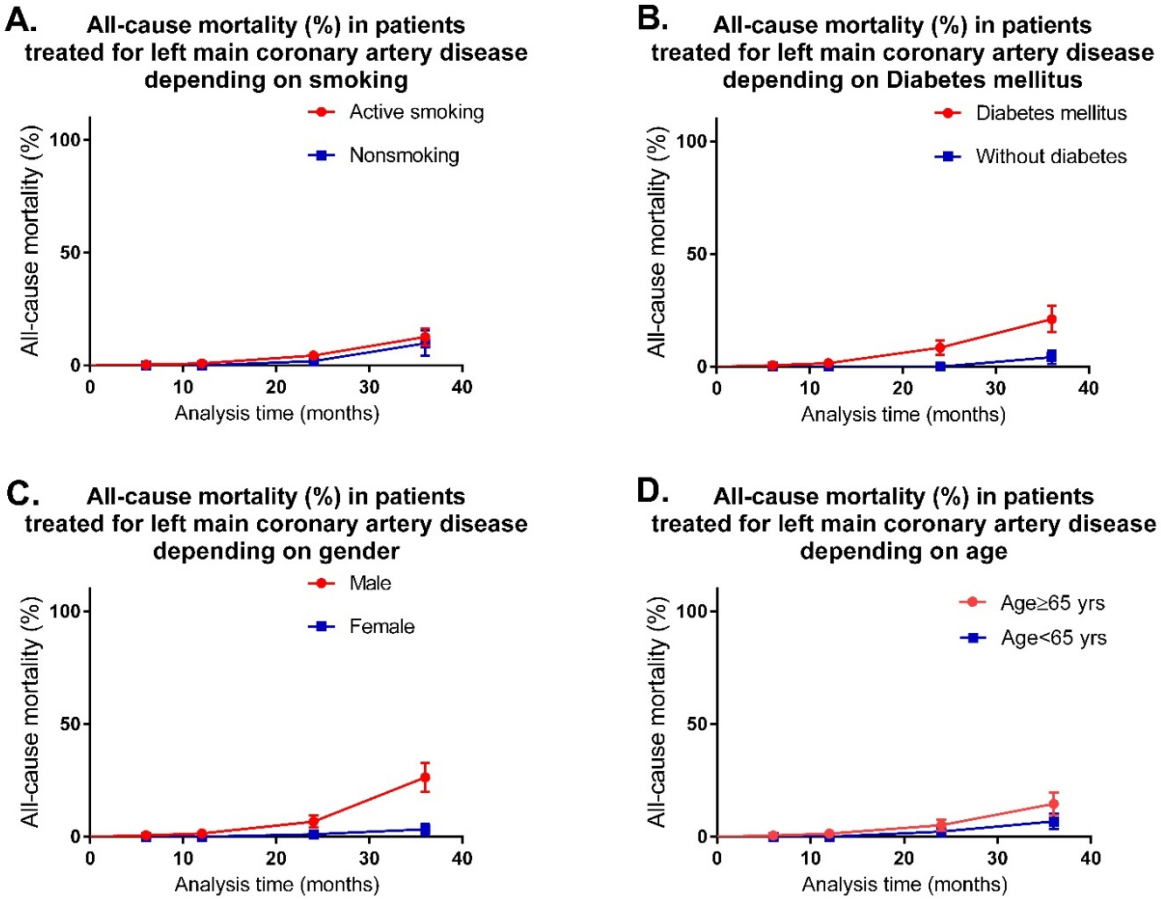

Fig.3. All-cause mortality (%) in patients treated for left main coronary artery disease depending on smoking (A), diabetes mellitus (B), gender (C) and age (D)

Analyzing the left ventricular ejection fraction (LVEF) for three years, in patients treated for left main coronary artery disease, we observed a decrease in LVEF in active smoking group compared to nonsmoking group (HR log=1.539, 95% CI ratio 0.7263 to 3.289 for active smoking, and HR log=0.6496, 95% CI ratio 0.3040 to 1.377 for nonsmoking, p=0.2838) as it can be seen in Fig.4A. Also, a significant decrease in LVEF was recorded in the group of patients with diabetes mellitus compared to the group without diabetes (HR logrank=9.139, 95% CI ratio 3.662 to 14.82 for patients with diabetes mellitus, and HR logrank=0.1094, 95% CI ratio 0.06745 to 0.2731 for patients without diabetes, p<0.0001) (Fig.4B), in the male group compared

to the female group (HR log=2.045, 95% CI ratio 1.058 to 4.448 for male group, and HR log=0.4889, 95% CI (Fig.4C), but also in the 65-year-old patient group compared to patients aged less than 65 years (HR logrank=1.737, 95% CI ratio 0.9394 to 3.607 for age≥65 years group, and HR log=0.5759, 95% CI ratio 0.2772 to 1.064 for age <65 years group, p=0.0933) (Fig.4D). Thus, in terms of left ventricular ejection fraction (LVEF), statistically significant differences were recorded only in relation to the presence of diabetes and gender.

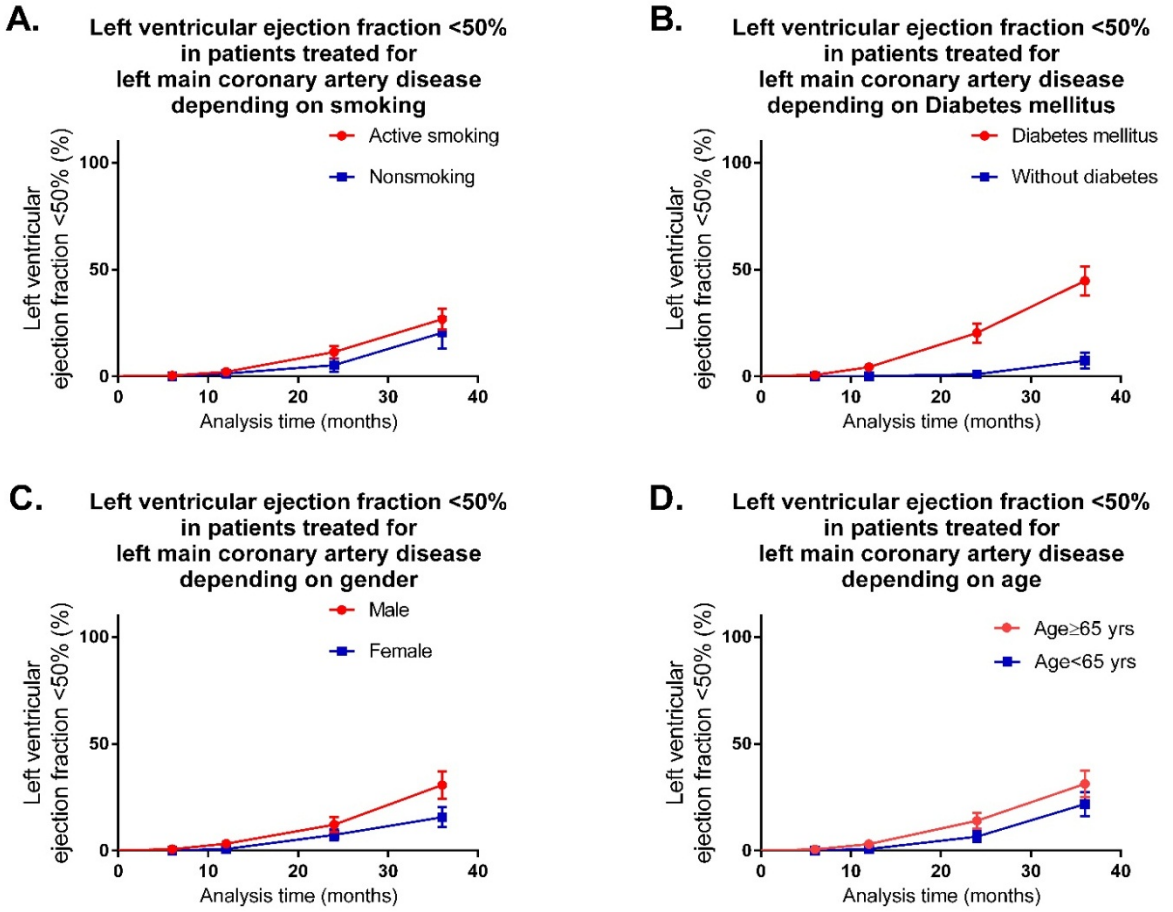

Fig.4. Left ventricular ejection fraction (LVEF) (%) in patients treated for left main coronary artery disease depending on smoking (A), diabetes mellitus (B), gender (C) and age (D)

In what the occurrence of ischemic heart disease symptomatology manifested by angina pectoris depending on risk factors in patients treated for left main coronary artery disease is concerned, we observed an increase in symptomatology in the smoking group compared to the nonsmoking group (HR logrank=1.94, 95% CI ratio 1.240 to 3.925 for active smoking, and HR log=0.5156, 95% CI ratio 0.2548 to 0.8063 for nonsmoking, p=0.0226) as it can be seen in Fig.5A. Also, an increased rate of symptomatic patients was recorded in the group of patients with diabetes mellitus compared to those without diabetes (HR logrank=2.684, 95% CI ratio 2.280 to 6.625 for patients with diabetes mellitus, and HR logrank=0.3726, 95% CI ratio 0.1509 to 0.4385 for patients without diabetes, p=<0.0001) (Fig.5B), in the male group compared to the female group (HR log=1.861, 95% CI ratio 1.390 to 4.055 for the male group, HR log=0.5374, 95 % CI ratio 0.2466 to 0.7195 for the female group,=0.0075) (Fig.5C), but also in patients older than or equal to 65 years of age compared to patients aged less than 65 years (HR logran=1.355, 95% CI ratio 0.8773 to 2.604 for age ≥65 years group, and HR log=0.7378, 95% CI ratio 0.3840 to 1.140 for age <65 years group, p=0.2021) (Fig.5D). Thus, with regard to the occurrence of ischemic heart disease symptomatology manifested by angina pectoris, statistically significant differences were recorded only for smoking, diabetes mellitus and gender.

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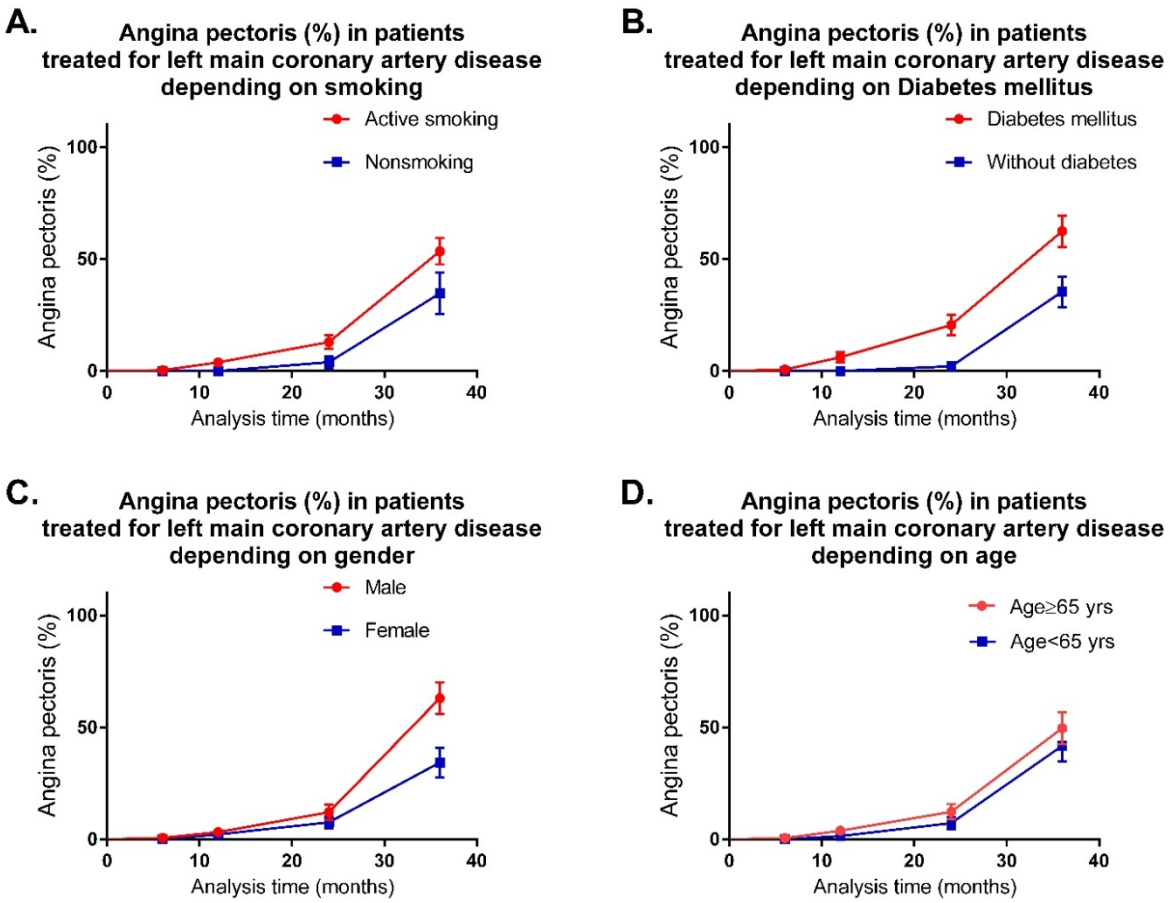

Fig.5. Angina pectoris (%) in patients treated for left main coronary artery disease depending on smoking (A), diabetes mellitus (B), gender (C) and age (D)

Looking at the incidence of the acute nonfatal myocardial infarction in patients with left ventricular coronary artery disease, we observed an increase in the rate of acute nonfatal myocardial infarction in the active smoking group compared to the nonsmoking group (HR log=1.832, 95% CI ratio 0.6961 to 4.492 for active smoking, and HR log=0.5459, 95% CI ratio 0.2226 to 1.437 for nonsmoking, p=0.2496) as it can be seen in Fig. 6A. Also, an increase in the rate of acute nonfatal myocardial infarction was recorded in the group of patients with diabetes mellitus compared to those without diabetes (HR logrank=7.833, 95% CI ratio 2.732 to 15.35 for patients with diabetes mellitus, and HR logrank=0.1277 , 95% CI ratio 0.06515 to 0.3660 for patients without diabetes, p <0.0001) (Fig.6B), in the male group compared to the female group (HR log=1.924, 95% CI ratio 0.8567 to 4.770 for male group and HR log=0.5197, 95% CI ratio 0.2097 to 1.167 for female group, p=0.1227) (Fig. 6C), but also in the group of patients aged 65 years or older compared with patients aged less than 65 (HR logrank=2.15, 95% CI ratio 0.9473 to 5.248 for age ≥65 years group, and HR log=0.4651, 95% CI ratio 0.1906 to 1.056 for age <65 years group, p=0.0778) (Fig.6D). Thus, with regard to the occurrence of acute nonfatal myocardial infarction, statistically significant differences were recorded only depending on the presence of diabetes mellitus.

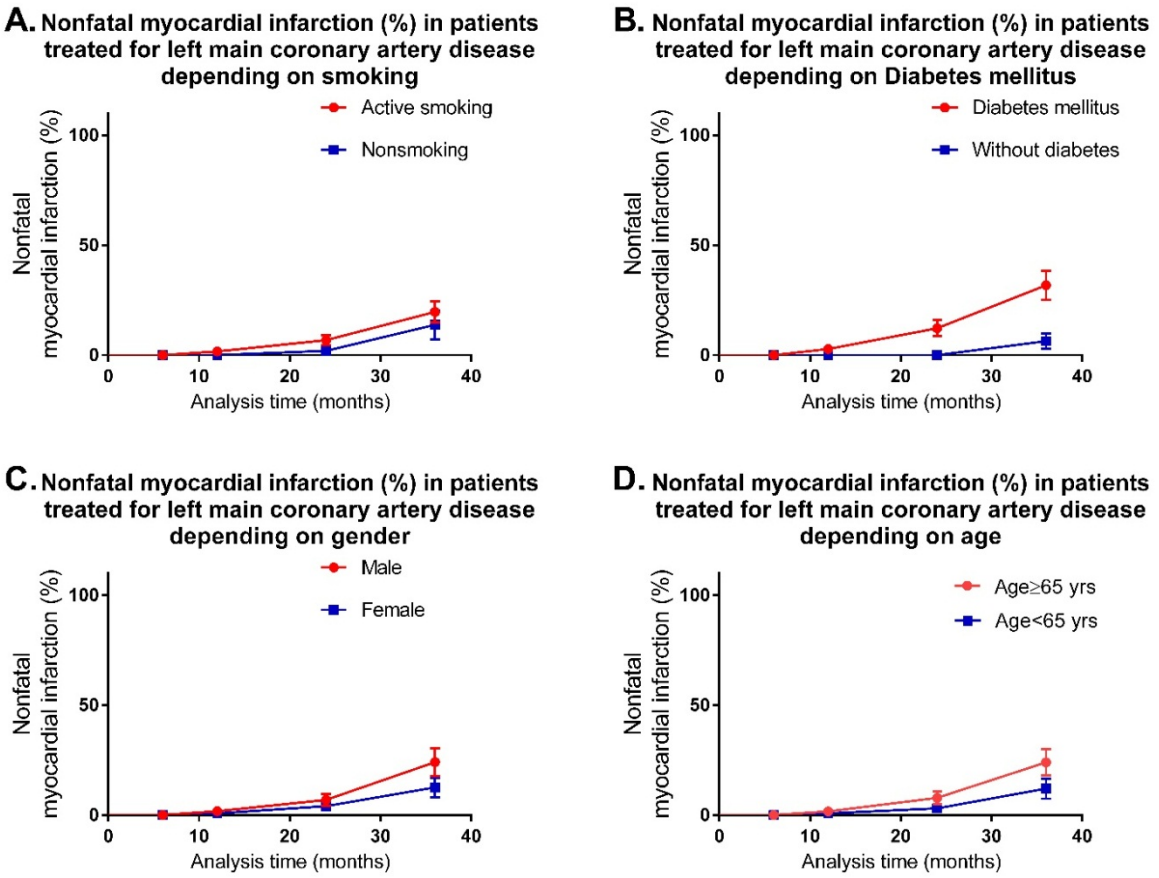

Fig.6. Nonfatal myocardial infarction (%) in patients treated for left main coronary artery disease depending on smoking (A), diabetes mellitus (B), gender (C) and age (D)

Regarding the need for revascularization after treatment (PCI vs. CABG) in patients with LMCAD depending on the risk factors, we noticed a higher need for revascularization in the smoking group compared to the nonsmoking group (HR logrank=2.155, 95% CI ratio 1.232 to 4.229 for active smoking, and HR logrank=0.464, 95% CI ratio 0.2365 to 0.8117 for nonsmoking, p=0.021) as it can be seen in Fig.7A. Also, a higher need for revascularization was recorded in the group of patients with diabetes mellitus compared to those without diabetes (HR logrank=3.808, 95% CI ratio 2.822 to 8.946 for patients with diabetes mellitus, and HR logrank=0.2626, 95% CI ratio of 0.1118 to 0.3544 for patients without diabetes, p <0.0001) (Fig. 7B), in the male group compared to the female group (HR log=1.842, 95% CI ratio 1.217 to 3.884 for male group, and HR log=0.5429, 95% CI ratio 0.2575 to 0.8214 for female groups, p=0.0202) (Fig.7C), but also in patients aged 65 years or older compared with patients aged less than 65 years (HR logrank=1.528, 95% CI ratio 0.9601 to 3.053 for age ≥65 years group, and HR log=0.6546, 95% CI ratio 0.3276 to 1.042 for age <65 years group, p=0.107) (Fig.7D). Thus, in what the need for revascularization is concerned statistically significant differences were recorded only depending on smoking, diabetes mellitus and gender.

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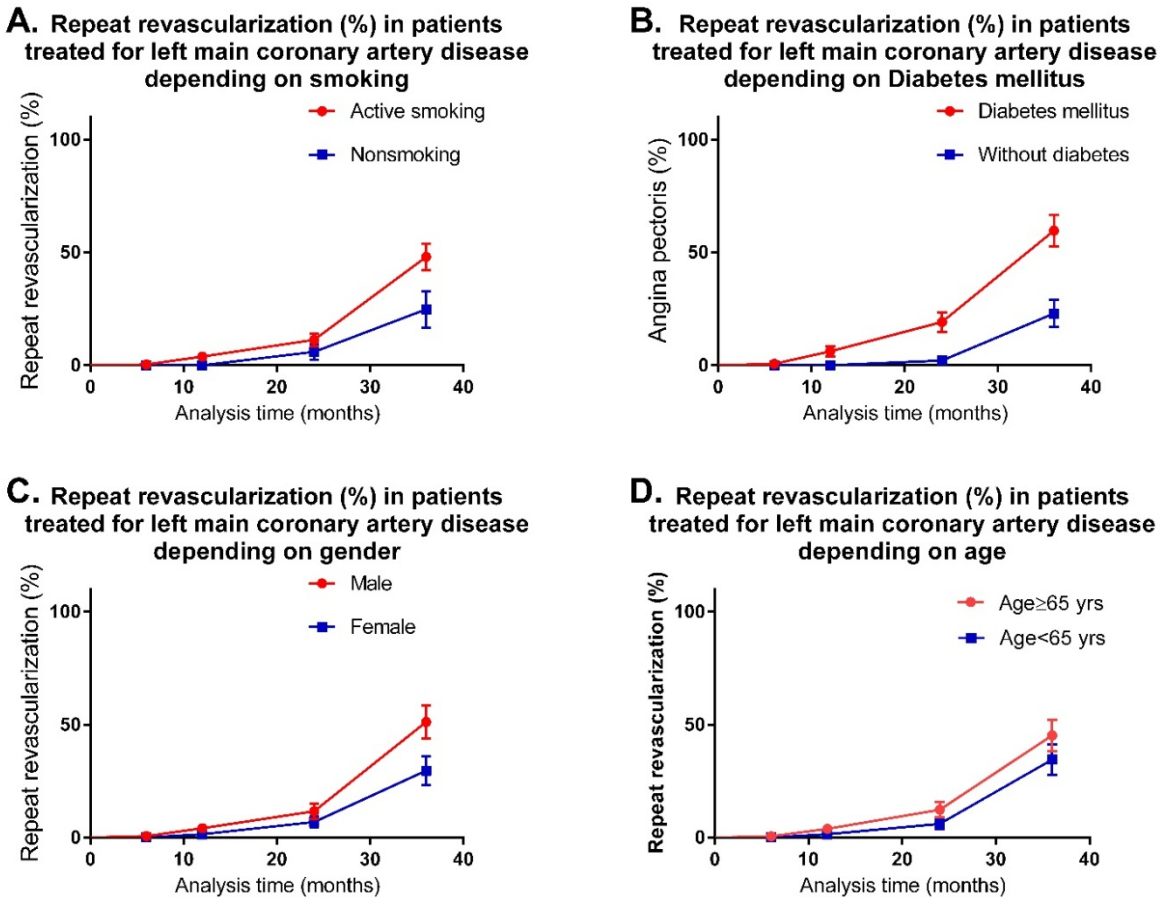

Fig.7. Repeat revascularization (%) in patients treated for left main coronary artery disease depending on smoking (A), diabetes mellitus (B), gender (C) and age (D)

Discussions

The current European guidelines (2018) recommend both CABG and PCI for the treatment of LMCA stenosis in patients with overall low to intermediate complexity of coronary artery disease (CAD) [16].

We have previously published a study in which we highlighted the superiority of the treatment of left coronary artery disease through coronary artery bypass grafting compared to treatment of percutaneous coronary angioplasty [18]. Patients suffering from ischemic coronary artery disease are at higher risk for developing coronary events than the general population [17,19,20]. Thus, secondary prevention should include lifestyle changes, good control of risk factors, optimal medical treatment, and specific counseling with regard to these measures [17].

Regarding the factors influencing the evolution of the left main coronary artery disease patients treated either by PCI or CABG, until now there are no clinical trials or guides of medical practice that identify a total risk approach to risk assessment or risk management. According to clinical trials published so far, these factors are largely found in the profile of factors that increase the risk of atherosclerotic disease (coronary or peripheral) [3-17].

In our study diabetes was the risk factor that negatively influenced the evolution of patients with LMCAD treated either by PCI or by CABG for the most part, followed by smoking, male gender and age over 65 years.

Patients with diabetes have a higher incidence of coronary artery disease than patients without diabetes and CAD often manifest themselves early in their case [21]. Approximately 25-30% of patients admitted with acute coronary syndrome have diabetes mellitus and approximately 40% of patients undergoing coronary artery bypass grafting have diabetes [22]. The prognosis of the patients with coronary artery disease and also the response to revascularization will be clearly affected by the presence or absence of diabetes [17].

The results of our study were in accordance with the results of other published studies on

cardiovascular risk of over 65 years of age, male gender and smoking. It should be noted that over 83% of the population with ischemic coronary artery disease is over 65 years old, the incidence being lower in women than in men (especially before the age of 50) after menopause, the risk for ischemic heart disease is progressively increasing among women [17]. Also, smoking is a major risk factor for atherosclerotic disease, with cardiovascular risk declining rapidly for ex-smokers, at three years after withdrawal being similar to non-smokers [17].

If the risk factors that cannot be modified (age and gender) have to be considered in the management of the patients with left main coronary artery disease, the other risk factors that can be modified should be identified and treated intensively from first contact with the patient in order to have a lower cardiovascular events rate in the evolution of the patients treated for left main coronary artery disease.

Conclusion

In conclusion, we can say that most of the cardiovascular events that occurred in the evolution of the patients with left main coronary artery disease treated either interventional or surgically, recorded the highest prevalence in the group of patients with diabetes mellitus followed by smoker patients, male patients and elderly patients, these four factors representing negative prognostic factors for this category of patients.

Conflict of interest disclosure

The authors declare that there are no conflicts of interest to be disclosed for this article.

Author contribution

Silviu Paul Trașcă and Emilia Violeta Goanță equally contributed to the manuscript.

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