



# ANGINA PECTORIS AND PHYSIOLOGICAL CORONAROGRAPHIC FINDINGS

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## ABSTRACT

Angina pectoris may be associated with normal coronary arteries. Normal coronary arteries status is defined as absence of visible disease or the irregularity of lumen (less than 50%) as assessed visually on the interventional cardiologists. In our retrospective study among 1130 patients we have identified 181 patients with normal angiographic findings with various risk factors, as male sex, body mass index (BMI), lipid disorders, smoking, hypertension, diabetes mellitus type 2. The analysis results suggest that 56.3% patients of 181 verified normal coronary findings involve female patients with high BMI, unregulated hypertension and lipid disorders. In order to find real causes of chest pain, patients with normal coronary status need careful examination and treatment. The reduction of risk factors and adequate medications are important preconditions for the good quality of life in these patients.

KEY WORDS: angina pectoris, normal coronarographic findings, risk factors

## INTRODUCTION

Angina pectoris may be related to coronary arteries that appear normal. Normal coronary arteries status is defined as absence of visible disease or the irregularity of lumen (less than 50%) as assessed visually in heart coronagraphy (1). Earlier studies reveal that 20-30% patients with angina pectoris and similar symptoms referred to coronary angiography have unobstructed coronary arteries (2). Normal coronary angiogram is five times more frequent in female than in male patients with chest pain (4). There may be various causes of chest pain in women with normal coronarographic findings. In women with chest pain and normal coronarographic findings, pathophysiology is not homogenous. Certain patients experience chest pain that is not of cardiac origin (3). Other patients suffer from heart related non-ischemic pain. The third group suffers from pain caused by myocardial ischemia connected with atherosclerotic coronary vascular abnormalities, which is mainly related to diffuse illness without focal obstruction (3). The studies emphasize this last group of patients as the one with an increased risk of myocardial infarction and sudden cardiac death (4). Bugiardini et al. underline that the prognosis for the patients with chest pain and normal or near-normal coronary angiogram is not as favourable as previously believed (3). In our retrospective study aim was to identify the group of patients with normal coronary status, define their characteristics and risk factors and suggest appropriate therapy.

## MATERIAL AND METHODS

In a retrospective study, we analysed the medical histories of 1130 patients referred to Heart Center Sarajevo for coronary angiography with the suspicion of CAD due to typical chest pain or ischemic findings on treadmill exercise test or myocardial scintigraphy. The patients have been examined over period January 1st – December 31st, 2008. The total number of patients with normal coronary status was 181. The medical histories of patients included anamnesis, family anamnesis, 12-lead electrocardiography, parameters as age, sex, BMI, smoking, lipid status, diabetes mellitus, hypertension and the therapies administered to patients prior to coronary angiography. The patients with valve disease and normal coronary status were excluded from the analysis.

### *Statistic analysis*

Data are presented as absolute and relative numbers and were analyzed the data using standard

methods of descriptive statistics. In the analysis we used the statistical package Arcus Quickstat.

## RESULTS

We analysed the histories of 1130 patients examined over one year period and extracted those with established normal coronary status. We analyzed demographic data, risk factors and the therapy received prior to coronary angiography. The data is given in tabular form (Table 1. and Table 2.).

Patients	Number	Percentage
<b>The total number of patients</b>	1130	100%
Male	787	69,6%
Female	343	30,4%
<b>Number of normal coronarographic findings</b>	181	100%
Male	79	43,7%
Female	102	56,3%

TABLE 1. Demographic data on the patients referred to coronary angiography

Characteristics	Male	Female
Sex	79 (43,6%)	102 (56,3%)
Age	55±10,8	61±9,6
BMI (kg/m <sup>2</sup> )	26,8	29,1
Smoking	33	17
Dyslipidaemia	25	29
Hypertension	58	64
Diabetes Type 2	4	8

TABLE 2. Characteristics of patients with normal coronary status

The therapy that patients with normal coronary status received prior to coronary angiography is given in Table 3.

Medication	Number of patients receiving the medication (n)	Female
NTG	55 (62,5%)	102 (56,3%)
Ca-antagonist	17 (19,5%)	61±9,6
Beta-blocker	32 (36,7%)	29,1
ACE inhibitor	37 (42,5%)	17
Aspirin	85 (96,5%)	29
Diuretic	9 (19,3%)	64
Statins	28 (32,1%)	8

TABLE 3. Therapy received prior to coronary angiography

## DISCUSSION

Similarly to the earlier studies (1), our study established dominance of female individuals among patients with chest pain that were submitted to coronary angiography (Table 1). Our female patients generally have excessive BMI, unregulated blood pressure and they are 61±9,6 years old. There were 79 male patients with normal

coronary status. Also, they have excessive BMI and they are  $55 \pm 10,8$  years old (Table 2). There were fewer patients with hypertension in this group; however, the number of smokers was higher. There were the totals of 12 individuals with diabetes mellitus. Therapeutic administration of some form of nitro-preparation was found in 62,5% patients. Also, 36,7% patients used beta-blockers while only 19,5% used a Ca-antagonist (Table 3). Only 32,1% patients used statins. The number of patients using Aspirin (95,5%) was adequate. It is important to emphasize that the number of female individuals referred for coronarographic examination was three times lower than the number of males. However, the number of female patients with normal coronarographic findings was twice higher than the number of males, i.e. one third of all female patients had normal coronary status. Potential causes of chest pain in our patients may be of either coronary or non-coronary aetiology. Yang and Lerman underline that coronary aetiology of chest pain may be a consequence of either epicardial illness or microvascular dysfunction (5). Epicardial illness may be related to endothelial dysfunction, coronary spasm or coronary bridge. Recent research involving patients with chest pain and normal coronary status indicate that up to 30% patients with chest pain and severe endothelial dysfunction develop angiographically visible atherosclerotic changes over the next ten years (6). Myocardial bridge is defined as a systolic compression of coronary artery caused by the contraction of myocardial muscle bundle or bridge. Angiographic studies indicate incidence of 0,5-33% (9). Myocardial bridge and coronary arterial spasm in normal coronary status may be the causes of cardiac arrest and sudden cardiac death. Microvascular dysfunction is secondary consequence of hypertension, cardiomyopathy, infiltrative, valvular and other diseases. Precise mechanisms of the influence of hypertension on chest pain are not known, however it is be-

lieved that the causes may include increased myogenous tonus due to elevated diastolic pressure and/or compression of microcirculation due to hypertrophied myocardium (5). Infiltrative diseases, such as amyloidosis may also cause chest pain. Non-coronary causes of chest pain might be a consequence of various disorders of gastrointestinal, pulmonary or muscle-skeletal systems.

No specialized protocol for the treatment of patients with chest pain and normal coronary status has been developed to date (1,3). The treatment of patients with normal coronary status is focused on the elimination of symptoms and causes of chest pain. In the case of endothelial dysfunction necessary therapy needs to be administered according to the standing protocol. It is extremely important to advice the patient to alter the life-style (quit smoking and increase physical activity) (10). Also, good control of lipid status is necessary, with obligatory administration of statins (11). Aggressive therapy with statins and ACE-inhibitors is advised in the cases of patients with established cardiological risk factors and recorded atherosclerotic changes and endothelial dysfunction (3). When coronary spasm is the cause of the chest pain, Ca-channels blockers and long-acting nitrates are treatments of choice. Beta-blockers are the first line of defence in the cases of myocardial bridge (3). Should therapy fail to eliminate chest pain in these patients, it is possible to consider stent or myocardium revascularization. Good blood pressure control greatly benefits patients with chest pain caused by hypertension. The patients with non-coronary chest pain necessitate detailed diagnostic procedure for the purpose of cause identification. Further monitoring of patients with chest pain of coronary aetiology and normal coronary status should include exercise test and heart ultrasound at least once a year as minor endothelial dysfunctions may progress into severe atherosclerotic changes.

## CONCLUSION

Among our patients, the number of female individuals referred for coronarographic examination was three times lower than the number of males. In the group of patients with normal coronarographic findings the number of females was twice as high as the number of males, i.e. one third of all female patients had normal coronary status. Our female patients generally are characterized with the excessive BMI, unregulated blood pressure and lipid disorders. Careful examination and optimal treatment of causes of pain are needed in patients with normal coronary status. Also, changes in life-style such as quitting smoking, increasing physical activity and reducing BMI are important elements of treatment and improvement of the quality of life in those patients.

## REFERENCES

- (1) Bugiardini R., Badimon L., Collins P., et al. Angina, "Normal" Coronary angiography, and vascular dysfunction: risk assessment strategies. *PLoS Med.* 2007; 4(2):e12.
- (2) Kemp H.G.Jr., Vokonas P.S., Cohn P.F., Gorlin R. The anginal syndrome associated with normal coronary arteriograms. Report of six year experience. *Am. J. Med.* 1973; 54:735-742.
- (3) Bugiardini R., Bairey Merz C.N. Angina with "normal" coronary arteries: a changing philosophy. *JAMA.* 2005; 293(4):477-484.
- (4) Bugiardini R. Women, "non-specific" chest pain, and normal or near-normal coronary angiograms are not synonymous with favourable outcome. *Eur. Heart J.* 2006; 27(12):1387-1389.
- (5) Yang E.H., Lerman A. Angina pectoris with a normal coronary angiogram. *Herz.* 2005; 30(1):17-25.
- (6) Bugiardini R., Manfrini O., Pizzi C., Fontana F., Morgagni G. Endothelial function predicts future development of coronary artery disease: a study of women with chest pain and normal coronary angiograms. *Circulation.* 2004; 109(21):2518-2523.
- (7) Abelmann W.H., Loreli B.H. The challenge of cardiomyopathy. *J. AM. Coll. Cardiol.* 1989; 13(6):1219-1239.
- (8) Pasternac A., Noble J., Streulens Y., Elie R., Henschke C., Bourassa MG. Pathophysiology of chest pain in patients with cardiomyopathies and normal coronary arteries. *Circulation.* 1982;65(4):778-789.
- (9) Möhlenkamp S., Hort W., Ge J., Erbel R. Update on myocardial bridging. *Circulation.* 2002; 12:106(20):2616-2622.
- (10) Hambrecht R., Wolf A., Gielen S., Linke A., Hofer J., Erbs S., et al. Effect of exercise on coronary endothelial function in patients with coronary artery disease. *N. Engl. J. Med.* 2000; 17:342(7):454-460.
- (11) Manfrini O., Pizzi C., Morgagni G., Fontana F., Bugiardini R. Effect of pravastatin on myocardial perfusion after percutaneous transluminal coronary angioplasty. *Am. J. Cardiol.* 2004; 1:93(11):1391-1393.