DE GRUYTER
OPEN

Role of Duke treadmill score in the diagnosis of ischemic heart disease in women

ALEXANDRA DĂDÂRLAT[1], D. ZDRENGHEA[1,2], DANA POP[1,2]

[1]University of Medicine and Pharmacy, Cluj-Napoca, 4 Pasteur street, Romania
[2]Rehabilitation Hospital, Cluj-Napoca, 46-50 Viilor street, zip code 400437 Romania

Ischemic heart disease is underdiagnosed in women due to atypical symptomatology as well as to the lower specificity of several paraclinical tests, such as exercise stress testing. The aim of the study was to ascertain whether the Duke treadmill score (DTS) could be an efficient parameter in the diagnosis of ischemic heart disease in women.

Material and method. 105 patients were enrolled in the study, 45.71% women with average age ranged between 20 and 70 years, investigated in the Rehabilitation Hospital, Cardiology-Departament, Cluj-Napoca, Romania. All the patients were clinically assessed as concerns the presence of cardiovascular risk factors, and they underwent electrocardiographic, echocardiographic and treadmill stress tests. DST was calculated according to the formula: exercise time – 5 x (ST deviation expressed in mm–4 x Angina Index).

Results. DTS was lower in women as compared to men: 2.54±5.36 *vs*. 6±4.69, p=0.0006. 54.28% of the patients were ranged with a low DTS risk category, whereas 45.71% belonged to a moderate and high risk category. DTS was significantly lower in women than in men with high blood pressure (2.03±4.8 *vs*. 5.8±4.28), hypercholesterolemia (1.14±4.51 *vs*. 6.24±4.13), diabetes mellitus (1.83 ± 3.73 *vs*. 6.13±4.8), and obesity (2.42±5.35 *vs*. 5.81±4.64). By analyzing the presence of cardiovascular risk factors only in women, we noticed that only those with high blood pressure (2.03±4.89 *vs*. 8.13 ±7.85) and hypercholesterolemia (2.31±4.76 *vs*. 3.89±5.95) had a statistically significant low DTS (p<0.05). In conclusion, our research, which showed differences in DTS between women and men, raises concerns about the early diagnosis of ischemic heart disease in women.

Key words: women, Duke score, ischemic heart disease.

INTRODUCTION

Cardiovascular diseases are responsible for most deaths in women worldwide. Cardiovascular disease represents among Europe the leading cause of death in women. About 55% of deaths in women are due to these diseases, especially coronary heart disease and stroke [1-8].

According to AHA – Heart Disease and Stroke 2013 Statistical Update, published in the early 2013, the first three places in the world in terms of mortality from ischemic heart disease and stroke are occupied by the Russian Federation, Bulgaria and Romania [9].

Although the last years have brought an upswing in the diagnosis and clinical management of women with different cardiovascular diseases, their risk of developing ischemic heart disease is still underestimated. This might be related with the perception that premenopausal women are protected by their hormones. The prevalence of cardiovascular pathology strongly climbs in post-menopausal women, catching up or even surpassing men. Unfortunately, ischemic heart disease is underdiagnosed and undertreated in women due to atypical symptomatology as well as to the lower specificity of several paraclinical tests, such as exercise stress testing [10]. The Duke treadmill score is a composite index which is used in the evaluation of symptomatic patients to predict the presence of coronary artery disease and their prognosis. So, investigating the relation between different cardiovascular (CV) conditions and the DTS may contribute to an early diagnosis and proper therapy of coronary artery disease (CAD) and also may advance the knowledge on this topic.

The goals of this study are to present the relationship of different cardiovascular conditions in women and DTS and the gender-related differences.

MATERIALS AND METHODS

We conducted an analytical transversal study of 105 cardiovascular consecutive patients admitted in the Cardiology Department of the Rehabilitation Hospital, Cluj-Napoca, Romania. Inclusion criteria

DOI: 10.1515/rjim-2015-0020

were the presence of the chest pain. The selected patients were informed about the study protocol and gave their signed informed consent. The lot was compressed of 48 (45.71%) women and 57 (54.29%) men. All patients were assessed for the presence of cardiovascular risk factors: obesity, blood pressure, smoking status, lipid profile (total cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol), fasting plasma glucose.

Overweight was defined as a body mass index (BMI) from 25 to 29 kg/(m)^2 and obesity as a BMI≥30 kg/(m)^2 [11]. Blood pressure was measured according to standard protocol as the mean of two readings after the participant was at rest for 5 min in a sitting position. According to current European Society of Cardiology guidelines, hypertension was classified as: mild hypertension (140/90 mmHg – 159/99 mmHg), moderate hypertension (160/100 mmHg – 179/109 mmHg) and severe hypertension (> 180/110 mmHg) [11]. Blood glucose was measured by the glucose oxidase method, and serum lipids, total cholesterol, triglycerides, high density cholesterol were measured using commercially available kits. Low density cholesterol was estimated using the Friedewald's formula. Using the criteria set out in the National Cholesterol Education Program Adult Treatment Panel III Approach to dyslipidemias total cholesterol levels over 200 mg/dL, LDL-cholesterol levels over 100 mg/dL, triglycerides plasma concentrations exceeding 150 mg/dL and HDL-cholesterol levels less than 46 mg/dL in women and 40 mg/dL in men were considered abnormal [12].

All patients underwent maximal symptom limited exercise treadmill testing (ETT) using the standard Bruce protocol [13]. Heart rate, blood pressure and 12-lead ECGs were recorded before exercise, at the end of each exercise stage and after the first minute of the recovery phase. Exercise testing was discontinued for abnormal blood pressure or rhythm, ST segment depression ≥ 3 mm or limiting symptoms (angina, dyspnea or fatigue). An abnormal exercise ST response was defined as ≥ 1 mm of horizontal or down sloping ST depression or ≥1 mm of ST-segment elevation in leads without pathological Q waves.

Duke Treadmill Score (DTS) was calculated using the following formula: DTS=exercise time – (5 x ST deviation) – (4 x angina score index) [13]. The exercise time was measured in minutes with Bruce's protocol and the angina was scored with 0 – meaning no angina, 1- non-limiting angina with exercise and 2- exercise- limiting angina. DTS ranges from – 25 to + 15. DTS divided the patients into three categories: low risk (DTS ≥ 5), moderate risk (DTS -11 to 5) and high risk (DTS ≤ -11), but because a DTS ≤ -11 was uncommon in those patients, the categories used were low risk (DTS ≥ 5) and moderate risk (DTS < 5).

Exercise capacity was measured in METs (metabolic equivalents of oxygen consumption = 1.4 watt/kg body weight). 1 MET is a unit of sitting/resting oxygen uptake (≈3.5 mL of O_2 per kilogram of body weight per minute [mL • kg−1 • min−1].

Statistical analysis was performed using SPSS for Windows (v 16.0; IBM Corporation, Armonk, NY, USA) and MedCalc (v 10.3.0.0; MedCalc Software, Ostend, Belgium) software programs. The analysis of the differences between qualitative variables was performed using the $\chi 2$ test. The Kolmogorov–Smirnov test was used to assess the normal distribution of continuous numerical variables. The DTS was modeled as a continuous variable. A value of P< 0.05 was considered statistically significant.

RESULTS

The baseline demographic and clinical characteristics of the patients are summarized in Table 1.

Table 2 shows exercise treadmill testing (ETT) data. The mean ETT time as per Bruce protocol was 7.82 ± 2.68 minutes in women and 9.85 ± 3.18 minutes in men (p< 0.001). Exercise was stopped in 11 (22.92%) female patients and 4 (7.02%) male patients due to limiting angina. Maximum ST- segment deviation was 3mm during exercise in men and 2 mm in women. The mean ST deviation in women was 0.38 mm.

Although the percentages of men with true-positive and nondiagnostic tests were similar to women (89.48%-51 men *vs*. 89.58% – 43 women), women were more likely to have moderate DTS risk (58.34% *vs*. 35.09%). Women with ST-segment depression ≥1 mm had a lower BMI (27.38 ± 2.44 *vs*. 31.99 ± 6.15; p=0.02) and a higher maximal heart rate (139.2 ± 17.19 *vs*. 123.34 ± 21.87, p=0.03) than those with a true- negative treadmill testing. We found no relation with ST-depression and age, systolic and diastolic blood pressure, plasma LDL-cholesterol or fasting plasma glucose – Table 3.

Table 1
The baseline demographic and clinical characteristics of the patients

VARIABLES	WOMEN (48 p)	MEN (57 p)
Age (years)	56.10 ± 8.69	57.59 ± 9.70
Smokers (%)	25% (12 patients)	33.33% (19 patients)
BMI (kg/m^2)	31.03 ± 5.67	29.57 ± 3.63
Glycemia (mg/dl)	116.22 ± 36.25	111.98 ± 29.4
Total Co (mg/dl)	208.54 ± 58.96	201.01 ± 39.12
LDL-Co (mg/dl)	131.6 ± 45.11	127.66 ± 31.47
HDL-Co (mg/dl)	43.41 ± 13.26	42.49 ± 10.03
TG (mg/dl)	164.85 ± 86.82	170.15 ± 81.19
Hypertension (%)*	91.66% (44 p)	87.71% (50 p)
Systolic blood pressure (mmHg)	191.97 ± 27.55	187.71 ± 30.09
Diastolic blood pressure (mmHg)	97.6 ± 11.34	92.19 ± 10.56
Diabetes (%) **	31.25% (15 p)	38.59% (22 p)
Valvulopathies (%)	40% (22 p)	60% (33 p)
Heart failure (%)	41.66% (20 p)	40.35% (23 p)
Mean ST deviation (mm)	0.38 ± 0.46	0.34 ± 0.59
Mean exercise capacity (METs)	4.95 ± 1.81	5.35 ± 1.35
WATTs	79.68 ± 26.62	100 ± 29.88

Table 2
Exercise treadmill testing (ETT) data

ETT	WOMEN (n=48) (45.71%)	MEN (n=57) (54.29%)
Duke's treadmill score (DTS) (mean ± SD)	2.54 ± 5.36	6 ± 4.69 $p < 0.001$
Duke score categories:		
Low DTS	20 (41.66%)	37 (64.91%)
Moderate DTS	28 (58.34%)	20 (35.09%)
High DTS	0	0
Angina index:		
0	20 (41.66%)	31(54.38%)
1	17 (35.41%)	22 (38.59%)
2	11 (22.92%)	4 (7.02%)
ETT results		
True- positive *	10 (20.83%)	15 (26.32%)
True- negative **	5 (10.42%)	6 (10.53%)
Nondiagnostic test ***	33(68.75%)	36 (63.16%)

ST segment depression induced during effort or in recovery of 1 mm or more.
** no ischaemic ST changes during the exercise test or immediately after effort, reaching or exceeding 85% of maximum predicted heart rate.
*** a negative test, but without achieving 85% of maximum predicted heart rate.

Table 3
Characteristics of women with ST – segment depression ≥ 1 mm
in comparison with those with a true-negative ETT

Patients characteristics	ST- segment depression ≥ 1 mm (n = 10)	ST- segment depression < 1 mm (n=38)	p Value
Age (mean ± SD) (yrs)	57.2 ± 8.23	54.13 ± 10.27	0.38
BMI (kg/m^2)	27.38 ± 2.44	31.99 ± 6.15	**0.02**
Systolic blood pressure (mmHg)	188.57 ± 20.95	194.63 ± 31.55	0.62
Diastolic blood pressure (mmHg)	94.28 ± 8.38	96.21 ± 11.97	0.68
Fasting plasma glucose (mg/dl)	120.3 ± 36.82	115.15 ± 36.53	0.69
Total-Co (mg/dl)	194 ± 39.66	207.65 ± 50.22	0.43
LDL-Co (mg/dl)	133 ± 44.95	123.86 ± 45.48	0.5
Triglycerides (mg/dl)	148.3 ± 61.04	162.15 ± 93.93	0.66
Angina Index Score	0.7 ± 0.67	0.84 ± 0.82	0.61
METs	4.92 ± 1.13	4.96 ± 1.97	0.94
Maximal heart rate	139.2 ± 17.19	123.34 ± 21.87	**0.03**

We found several statistically significant gender-differences regarding DTS, with lower scores among women than in men in the presence of the following CV diseases or CV risk factors: arterial hypertension (2.03±4.89 in females *vs*. 5.8±4.28 in males; p<0.001), history of ischemic heart disease (2.31±4.76 *vs*. 6.32±4.5; p< 0.001) valvular heart disease (3.12± 5.42 *vs*. 6.55±4.49; p=0.01) and chronic heart failure (2.07±3.73 *vs*. 6.39±4.92; p=0.002).

We also recorded lower Duke scores between women and men presenting different CV risk factors, such as: diabetes mellitus (1.83 ± 3.73 *vs*. 6.13 ± 4.8; p=0.006), obesity (2.42±5.35 *vs*. 5.81±4.64; p<0.001), high plasma levels of Total-Co (1.14±4.51 *vs*. 6.24±4.13, p<0.001) and LDL-Co (1.95±4.27 *vs*. 5.88±4.28, p<0.001). However, there were no sex –differences in scores between smokers (5.41± 5.03-women *vs*. 6.97 ± 3.99 – men, p=0.34) and also no lower scores were reported in smoker females in comparison to non-smoker ones (5.41±5.03 *vs* 1.86±5.18, p=0.07). Surprisingly, DTS was not significantly different in women previously diagnosed with valvular heart disease, chronic heart failure or ischemic heart disease in comparison to those without these diseases: 3.12± 5.4 *vs* 1.91±5.34 and 2.07±3.73 *vs* 2.07±3.73, respectively (p>0.05). But, there were differences in terms of DTS between hypertensive women compared to those without HTN (2.03±4.89 *vs*. 8.13 ±7.85; p=0.02). We found no relation between DTS and age either in women, or in men – Fig. 1.

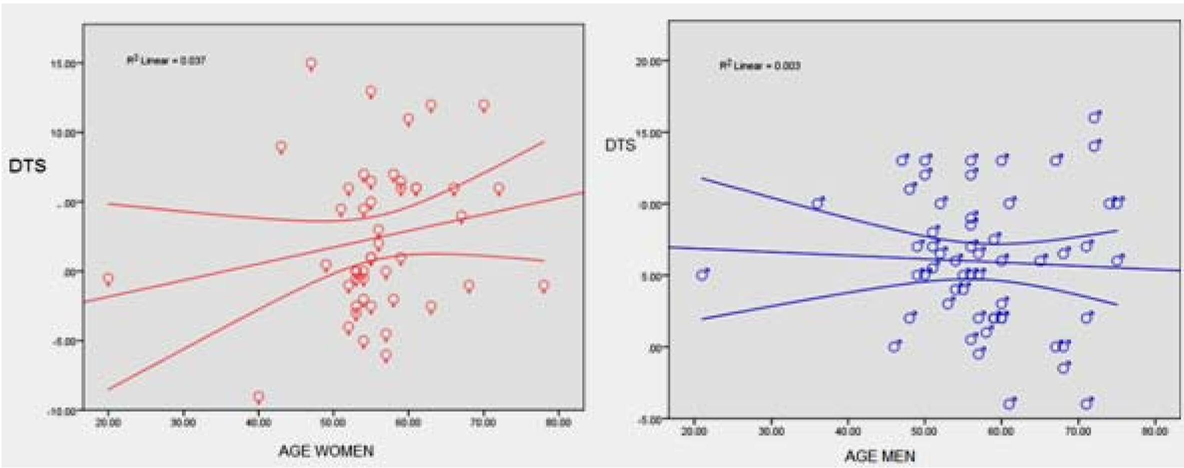

Fig. 1. Correlation between DTS and age.

DISCUSSION

Noninvasive diagnostic techniques, such as exercise treadmill testing or imaging methods, are indicated to symptomatic women with intermediate or high risk of cardiovascular disease [14]. Women suffering from angina pectoris are less likely than men to perform exercise treadmill tests or angiographies, despite the presence of CV symptoms and risk factors, which stratify them into high risk classes [15]. It is well known that exercise testing is less accurate in women, giving more false positive results [16]. However, only a quarter of women who have not performed an exercise test are referred to undergo other diagnostic investigations [16].

Men with pectoral angina are more often referred for additional investigations, such as echocardiography, stress echocardiography or angiography and also coronary revascularization procedures, than women, even compared to those with an already diagnosed cardiac disease [14,16].

Exercise treadmill testing is the oldest diagnostic tool, but also the most widely used assessment of coronary artery disease. The pre-test probability of coronary artery disease is influenced by various parameters, including age and nature of the chest pain. Among women, a high pre-test probability of coronary artery disease may be estimated in those over 60 years with typical chest pain and also in those who present cardiovascular risk factors (diabetes, metabolic syndrome) [16].

According to current guidelines, symptomatic, intermediate-risk women, able to maximal exercise with a normal baseline ECG, are referred for exercise testing [4,16].

Sensitivity and specificity of exercise testing are lower in women (61%, respectively 70%) than in men (72%, respectively 77%) [4,14]. However, exercise stress testing shows a high negative predictive value in women with a low pretest probability of CAD [14].

ECG changes with exercise are less specific in women than in men (women are more likely than men to have baseline ST-segment changes and also low-voltage ECGs) [14]. ST-segment depression that occurs during exercise testing is less accurate in women than in men, so the results should be interpreted more carefully [15]. Although many clinicians usually rely only on ST segment changes, there are many other ETT variables that should be taken into account for major adverse cardiac events, prognosis, such as symptoms (unfortunately, without additional prognostic value in women), chronotropic and hemodynamic response, maximal exercise capacity, DTS, heart rate recovery (estimates long-term survival in women), maximal heart rate, ST / maximal heart rate ratio, QRS score [17].

As mentioned above, Duke score is a highly effective diagnostic tool in predicting the likelihood of CAD among women. Patients with a high DTS risk are 376 times more likely to have angiographically significant coronary artery stenosis than those with a low DTS risk [18]. A study which enrolled 976 symptomatic women, who performed both exercise testing and coronary angiography, shows that DTS is more accurate in women than in men for excluding CHD. Also, they reported that CHD is significantly correlated with DTS risk categories - 89.2% of high-risk DTS women had at least 1-vessel CHD with at least 75% stenosis [19]. In our study, more than half of women (58.34%) had moderate DTS risk. DTS also seems to be effective for predicting the risk of major adverse cardiac events, such as: cardiac death, myocardial infarction, revascularization procedures or survival in both sexes [20]. Thereby, a low-risk DTS is correlated with an annual mortality of approximately 25%, whereas in high-risk DTS patients these perecntages reach 25% [21]. The Women Take Heart Project, which included 5.636 asymptomatic women reported that those women with a moderate or high DTS risk had hazard ratios for death that were 2 times higher than those with a low-risk DTS [22]. Also, the same study showed that for each unit of DTS increase, there was a 9% reduction in mortality rate [22].

Previous studies assessed the diagnostic and prognostic value of the DTS, but few studies investigated the gender-related differences regarding the correlation between cardiovascular risk factors and reduced DTS. The results of the current report reveal that lower Duke scores were more likely to be recorded in women with cardiac diseases, such as chronic heart failure, valvular heart disease, or history of ischemic heart disease in comparison with men. Also, DTS was significantly lower in women with cardiac risk factors, including hypertension, diabetes mellitus, high plasma lipid fractions values, obesity, than in men.

A recent study published in Nigeria reported no differences in DTS between men and women diagnosed with diabetes mellitus [23]. There are studies demonstrating that DTS is also an important predictor of MACE in diabetic patients [24]. We found no data in the specialized literature regarding the possible correlations between DTS, other CV risk factors, besides diabetes mellitus and the risk of developing further cardiovascular events.

Nonetheless, among women lower scores were found only in hypertensive women in comparison with those without HTN. Although, these gender-differences regarding DTS are useful for understanding care delivery, it is important to determine whether the differences found demand a gender-based treatment disparity.

We found no relation between DTS and age in women. However, other studies propose that age should be added to the original DTS for a better diagnostic and prognostic value in women [25].

Several limitations of this study should be noted. First, our study included a relatively small number of patients. Also, due to the design of the study selection bias may have occurred.

Our study enrolled both women and men in an adequate number to record statistically significant results. The major advantage of the current study is the possibility of investigating the differences between the two sexes, in addition to a proper analysis of the data generated by women. Taking into account the recommendations posted by the European Society of Cardiology, we performed an analysis regarding the presence of cardiovascular risk factors and CV diseases for each of the two sexes in part, investigating the relation between them and the DTS. By this, we tried to bring more information in this area of knowledge not fully elucidated yet.

CONCLUSION

Overall, among this cohort of patients we identified lower DTS in women with cardiovascular risk factors and cardiac disease than in men. We believe that our research, which showed significant differences in DTS between women and men, raises concerns about the early diagnosis of ischemic heart disease in women. However, it remains unclear whether these differences are justified.

Premize. *Cardiopatia ischemică este subdiagnosticată la femei din cauza simptomatologiei atipice, dar şi a specificității mai scăzute a unor investigații paraclinice, printre care testarea de efort. Scopul studiului este de a evalua dacă scorul Duke poate fi un parametru eficient în diagnosticul ischemiei coronariene la femei.*

Material şi metodă. *S-au luat în studiu 105 pacienți, 45.71% femei, cu vârste cuprinse între 20 şi 70 de ani, evaluați în Clinca de Cardiologie-Recuperare Cluj. Toți pacienții au fost evaluați din punct de vedere clinc, al prezenței factorilor de risc cardiovascular, electrocardiografic, ecocardiografic şi au beneficiat de testare de efort pe cicloergometru. Scorul Duke a fost calculat după formula: timp de exercițiu-5x (deviația ST exprimată în mm – 4xindexul anginos. Statistica a fost efectuată utilizând programele SPSS 16.0 pentru Windows, Medcalc 10.3.0.0 (Demo Versions).*

Rezultate. *Scorul Duke a fost semnificativ mai scăzut la femei față de bărbați: 2.54±5.36 vs 6±4.69, p=0.0006. În funcție de valorile scorului Duke, 54.28% dintre pacienți (42% femei şi 65% bărbați) s-au încadrat într-o categorie cu risc mic şi doar 14.04% au avut test de efort pozitiv, iar 45.71% (58% femei şi 35% bărbați) într-o categorie cu risc moderat şi mare, 35.42% dintre aceştia fiind diagnosticați cu test de efort pozitiv. Scorul Duke a fost semnificativ mai scăzut (p<0.05) la femei față de bărbații cu hipertensiune arterială (2.03±4.8 vs 5.8±4.28), hipercolesterolemie (1.14±4.51 vs 6.24±4.13), valori patologice ale LDL (1.95±4.27 vs 5.88±4.28), diabet zaharat (1.83 ± 3.73 vs 6.13±4.8) şi obezitate (2.42±5.35 vs 5.81±4.64). Totodată analizând prezența sau nu a factorilor de risc cardiovascular doar la femei, s-a constatat că numai cele cu hipertensiune arterială (2.03±4.89 vs 8.13 ±7.85) şi hipercolesterolemie (2.31±4.76 vs 3.89±5.95) au avut un scor Duke scăzut semnificativ statistic (p<0.05). În concluzie, prezența factorilor de risc cardiovascular la femei contribuie la apariția unui scor Duke mai scăzut decât la bărbați, punându-se în discuție posibilul rol al acestuia în depistarea precoce a ischemiei miocardice la sexul feminin.*

Corresponding author: Zdrenghea Dumitru, Rehabilitation Hospital, Cardiology Department,
Cluj-Napoca, Viilor 46-50 str, zip code 400347, Phone: 0722159671
E-mail: dzdrenghea@yahoo.com

Conflicts of interest: none.

REFERENCES

1. NEWBY KL, DOUGLAS PS. *Cardiovascular disease in women*. In: Bonow RO, Mann DL, Zipes DP, Libby P. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 9th edition. Philadelphia: Elsevier Saunders, 2011;1757-1769.
2. MOSCA L, BENJAMIN EJ, BERRA K, BEZANSON JL, DOLOR RJ, LLOYD-JONES DM, *et al*. *Effectiveness-Based Guidelines for the Prevention of Cardiovascular Disease in Women – 2011 Update: a guideline from the American Heart Association.* Circulation 2011; **123**: 1243-1262.
3. ALFONSO F, BERMEJO J, SEGOVIA J. *Cardiovascular disease in women. Why now?* Rev Esp Cardiol 2006; **59**: 259-263.
4. STRAMBA-BADIALE M, FOX KM, PRIORI SG, COLLINS P, DALY C, GRAHAM I, *et al*. *Cardiovascular diseases in women: a statement from the policy conference of the European Society of Cardiology.* Eur Heart J 2006; **27**: 994-1005.
5. WENGER NK, SHAW LJ, VACCARINO V. *Coronary heart disease in women: update 2008.* Clin Pharmacol Ther. 2008; **83**: 37-51.
6. PILOTE L, DASGUPTA K, GURU V, HUMPHRIES KH, MCGRATH J, NORRIS C, *et al*. *A comprehensive view of sex-specific issues related to cardiovascular disease.* CMAJ 2007; **176**: S1-S41.

7. ANDREOTTI F, MARCHESE N. *Women and coronary heart disease*. Heart 2008; **94**: 108-116.
8. ANAND S, ISLAM S, ROSENGREN A, FRANZOSI MG, STEYN K, YUSUFALI AH, *et al*. Interheart Investigators. *Risk factors for myocardial infarction in women and men: insights from the INTERHEART study*. Eur Heart J. 2008; **29**: 932-940.
9. GO AS, MOZAFFARIAN D, ROGER VL, BENJAMIN EJ, BERRY JD, BORDEN WB, *et al.* American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Heart Disease and Stroke Statistics-2013 Update*: A Report From the American Heart Association. Circulation. 2013; **127**:e6-e245.
10. POP D, DĂDÂRLAT A, ZDRENGHEA D. *Novel cardiovascular risk markers in women with ischaemic heart disease.* Cardiovasc J Afr. 2014; **25**(3):137-4.
11. The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *2007 Guidelines for the management of arterial hypertension.* Eur Heart J. 2007; **28**:1462–1536.
12. Coordinating Committee of the National Cholesterol Education Program. *Implications of Recent Clinical Trials for the National Cholesterol Education Program Adult Treatment Panel III Guidelines.* Circulation. 2004; **110**: 227-239.
13. ZDRENGHEA D, POP D. *Testarea de efort în practica medicală.* Ed. Clusium, Cluj-Napoca. 2012.
14. MIERES JH, SHAW LJ, ARAI A, BUDOFF MJ, FLAMM SD, HUNDLEY WG, *et al*. Cardiac Imaging Committee, Council on Clinical Cardiology, and the Cardiovascular Imaging and Intervention Committee, Council on Cardiovascular Radiology and Intervention, American Heart Association. et al. *Role of noninvasive testing in the clinical evaluation of women with suspected coronary artery disease: Consensus statement from the Cardiac Imaging Committee, Council on Clinical Cardiology, and the Cardiovascular Imaging and Intervention Committee, Council on Cardiovascular Radiology and Intervention American Heart Association*. Circulation 2005; **111**: 682-696.
15. CRILLY M, BUNDRED P, HU X, LECKEY L, JOHNSTONE F. *Gender differences in the clinical management of patients with angina pectoris: a cross-sectional survey in primary care.* BMC Health Serv Res 2007; **7**: 142-150.
16. DALY C, CLEMENS F, LOPEZ SENDON JL, TAVAZZI L, BOERSMA E, DANCHIN N, *et al.* EURO HEART SURVEY INVESTIGATORS. *Gender differences in the management and clinical outcome of stable angina.* Circulation 2006; **113**: 490-498.
17. POP D, SITAR-TĂUT A, ZDRENGHEA D. *Cardiopatia ischemică.* In: Mitu F, Pop D, Zdrenghea D. *Particularităţi ale patologiei cardiovasculare la femei*. Editura Pim. Iaşi. 2012; 87-110.
18. KOHLI P, GULATI M. *Exercise stress testing in women: going back to the basics.* Circulation. 2010; **122**:2570-80.
19. ALEXANDER KP, SHAW LJ, SHAW LK, DELONG ER, MARK DB, PETERSON ED. *Value of exercise treadmill testing in women*. J Am Coll Cardiol. 1998; **32**:1657-64.
20. KLIGFIELD P, LAUER MS. *Exercise electrocardiogram testing: beyond the ST segment.* Circulation. 2006; **114**:2070–2082.
21. MARK DB, SHAW L, HARRELL FE JR, LEE KL, BENGTSON JR, MCCANTS CB, *et al. Prognostic value of a treadmill exercise score in outpatients with suspected coronary artery disease.* N Engl J Med. 1991; **325**:849–853.
22. GULATI M, ARNSDORF MF, SHAW LJ, PANDEY DK, THISTED RA, LAUDERDALE DS, *et al*. *Prognostic value of the duke treadmill score in asymptomatic women.* Am J Cardiol. 2005; **96**:369-75.
23. ADEKUNLE AE, AKINTOMIDE AO. *Gender differences in the variables of exercise treadmill test in type 2 diabetes mellitus.* Ann Afr Med. 2012; **11**:96-102.
24. LAKKIREDDY DR, BHAKKAD J, KORLAKUNTA HL, RYSCHON K, SHEN X, *et al*. *Prognostic value of the Duke Treadmill Score in diabetic patients.* Am Heart J. 2005; **150**:516-21.
25. RAFIE AH, DEWEY FE, MYERS J, FROELICHER VF. *Age-adjusted modification of the Duke Treadmill Score nomogram.* Am Heart J. 2008; **155**:1033-8.