

Do we diagnose and treat coronary heart disease differently in men and women?

J. George Fodor¹, Rayka Tzurovska¹, Thomas Dorner² and Anita Rieder²

¹Prevention and Rehabilitation Centre, The University of Ottawa Heart Institute, Ottawa, Ontario, Canada

²Institut für Sozialmedizin, Medizinische Universität Wien, Vienna, Austria

Wird die koronare Herzkrankheit bei Männern und Frauen unterschiedlich diagnostiziert und behandelt?

Zusammenfassung. Es gibt geschlechtsspezifische Unterschiede bezüglich der Bedeutung kardiovaskulärer Risikofaktoren sowie bei Symptomen und bei der diagnostischen Abklärung kardiovaskulärer Ereignisse. In der täglichen Praxis basiert der unterschiedliche Zugang bei beiden Geschlechtern auf geschlechtsspezifischen Assessment der Risikofaktoren. Ein umfassendes Risikoassessment sollte bei Männern > 40 Jahren und bei Frauen > 50 Jahren oder in der Postmenopause vorgenommen werden. Diabetes und Hypertriglyceridämie erfordern eine aggressive Therapie, besonders bei Frauen. Abhängig vom Risikolevel sollte eine angemessene Therapie etabliert werden: Lebensstilberatung (Rauchen!), eine Therapie der Dyslipidämien, antihypertensive Therapie und Diabeteskontrolle. Symptome einer Herzattacke werden von Männern häufiger „klassisch“ beschrieben, während Frauen häufig unspezifische Symptome bieten, die eine angemessene medizinische Versorgung verzögern können. Eine entsprechende Aufklärung der PatientInnen, besonders junger Frauen ist erforderlich, um unnötigen Zeitverlust bei der Intervention akuter koronarer Syndrome zu vermeiden. Bezuglich der Diagnostik gibt es geschlechtspezifische Unterschiede in der Spezifität und der Sensitivität einiger nicht invasiver diagnostischer Tests, welche berücksichtigt werden müssen.

Schlüsselwörter: Geschlechtsunterschiede, Behandlung, Diagnostik, Risikofaktoren, Koronare Herzkrankheit.

Summary. There are gender-specific differences in the significance of cardiovascular risk factors, as well as in the symptoms and in the diagnostic approach of cardiovascular events. From the point of view of everyday clinical

practice, the differential approach toward both genders is based on gender-specific risk assessment. A global risk assessment should be carried out in males > 40 years of age and in females > 50 years or those who are postmenopausal. Diabetes and hypertriglyceridemia require aggressive therapy particularly in women. Depending on level of risk appropriate therapy should be instituted: life style counseling (smoking!), therapy of dyslipidemias, antihypertensive therapy and diabetes control. Symptoms of coronary attack are experienced by men more often “classically”, whilst women commonly present with unspecific symptoms, which may delay proper medical care. Appropriate patient education is needed particularly in younger women to avoid unnecessary delay of intervention in acute coronary syndromes. Regarding diagnostics, there are gender differences in the specificity and sensitivity of some noninvasive diagnostic tests, which should be taken into account.

Key words: Gender difference, treatment, diagnostic, risk factors, coronary heart disease.

Introduction

Millions people die from coronary heart disease (CHD) in the world every year. It is the leading cause of mortality in the developed countries. CHD affects both men and women and the total CHD mortality is equally prevalent in both genders. In general, risk factors for development of CHD, diagnostics and treatment of CHD are similar in men and women. However, biologically determined sex-related differences certainly exist and they should be taken into account with respect to prevention, diagnostic evaluation, management, and secondary prevention of this deadly disease in both men and women.

The high prevalence and incidence of coronary heart disease (CHD) in men was always well known to cardiologists and family physicians alike.

However, up until the 80s of the last century, there was a widely held belief among the medical profession that young and middle-aged women rarely suffer from CHD. Thus, in general, there was a low level of alertness for signs and symptoms indicating presence of coronary heart disease in women. This situation was, and is aggra-

Correspondence: Prof. J. George Fodor, Prevention and Rehabilitation Centre, The University of Ottawa Heart Institute, 40 Ruskin Street, Ottawa, Ontario, Canada K1Y 4W7.

Fax: ++1/613/761-5323

E-mail: gfodor@ottawaheart.ca

vated by the fact that women themselves tend to underestimate the risk of CHD. A survey of female Stanford University graduates with median age 50 years showed that 73 % of respondents placed their risk at less than 1 % by age of 70 years [1].

In the early 90s attention started to focus on issues of women and heart disease. It was noticed that women were less likely to be referred for diagnostic and therapeutic procedures [2, 3]. It was also ascertained that younger women have higher rates of death during hospitalization after acute myocardial infarction (MI) compared to men of the same age [4]. This could be a consequence of the well documented fact that female sex is an independent predictor of late arrival in the emergency room for symptoms compatible with MI [5].

These and similar data led to the development of special guidelines for the prevention and treatment of coronary heart disease in women [6].

What is different and what action should be taken?

Age. Men are affected mostly in their middle age while women are more affected after the menopause. Therefore, every middle aged man and every postmenopausal woman should be assessed for existence of risk factors of CHD.

Men are at greater risk for developing CHD than women even in older age. Women are somewhat protected during their reproductive years, but they lose this protection after the menopause, no matter whether it be a natural or artificial one. Women with premature menopause are at higher risk. Hormonal replacement therapy (HRT) has no cardioprotective effect and may produce harm. HRT should not be recommended to reduce CHD risk [7].

Family history is particularly important in young individuals. Paternal history of early MI (before age of 60) is associated with a greater risk of coronary heart disease for both genders. Women with a maternal history of premature CHD are at even greater risk than those with a paternal history [8]. A family history of myocardial infarction in first order relatives e. g. parents, siblings occurring in men < 50 and women < 60 years of age is doubling the risk of CHD.

Hypertension is identified as a major risk factor for CHD. Contrary to earlier belief, women do not tolerate effects of hypertension on cardiovascular and renal system better than men. Men are less aware of their hypertension, less likely to receive antihypertensive medication, less compliant, and they have poorer control of their blood pressure. Therefore newly diagnosed hypertension in men, particularly in younger men requires appropriate education and encouragement to maintain the compliance with the therapy [9].

Increased level of *triglycerides* and low levels of HDL have a more ominous prognostic significance in women [6]. The rise in CHD risk with increasing triglycerides is much steeper in women than men [10]. Hypertriglyceridemia in women is often associated with diabetes or use of contraceptive pills. Women are less likely to be prescribed lipid-lowering medications including the

secondary prevention after a myocardial event. More attention needs to be paid to women with lipid abnormalities and lipid-lowering medication, preferably with statins, should be prescribed [6].

Diabetes is another co-morbid condition which is associated with a worse prognosis in women as compared with men [11].

There is also some indication that *cigarette smoking* may have a more deleterious impact in women [12].

The "apple" type *obesity*, in which the fat is distributed more on the upper body and around the waist, is characteristic more for men, while so called "pear" type with the fat distributed more around hips is characteristic for women. The "apple" type obesity is associated with a higher risk for cardiovascular disease than the "pear" type in both sexes. Subjects with high waist circumference and "apple" appearance should raise a suspicion and should be assessed for risk of metabolic syndrome and CVD [13].

Weight reduction and appropriate physical activity should be advised. Women usually tend to have a more sedentary lifestyle, so they should be encouraged to accumulate a minimum of 30 minutes of moderate physical activity, e. g. brisk walking, on most days of the week.

The SCORE risk tables should be used for the global CHD risk assessment by gender, age, systolic blood pressure, total cholesterol and smoking status. For Central Europe the "high risk" version of these tables should be used [14].

Clinical presentation. At the time of presentation, women are usually 10 years older than men and have more co-morbidities – diabetes, hypertension, dyslipidemia, heart failure, and unstable anginal patterns than their male counterparts, which makes the management of the problem more difficult.

Men experience more frequently the "classical" symptoms of coronary attack. Women very often present with a vague chest pain or discomfort in the neck, jaw, stomach and back, or nausea ("equivalent angina"), which may delay their seeking and receiving proper medical care [15]. The general attitude of men and women toward chest pain is different. Men are more likely to seek for help when they are symptomatic, women are more likely to wait (e. g. finish cooking first) before seeking help. Education of women about the nature of CHD and its symptoms may have a significant impact on timely, proper diagnostic and treatment, and better outcome of CHD.

Diagnostic tests and procedures. The misperception of lower CHD probability may result in a limited number of diagnostic tests and procedures in women. Women, who present to the emergency room with chest pain or equivalent symptoms, should undergo the necessary diagnostic procedures.

Diagnostic tests and procedures are generally the same for men and women. However, there are some differences in the specificity and sensitivity of some noninvasive tests, which should be taken into account. Stress ECG testing has a lower specificity and sensitivity in women than in men [16].

The accuracy of exercise thallium (Tl-201) in men is higher than in women. These minor differences do not

change the diagnostic and predictive value of currently used diagnostic tests and it is highly recommended that they be fully used in all clinically suspicious cases of CHD.

Thus, from the point of view of every-day clinical practice, the differential approach toward both genders is based, first of all on risk assessment, and this is clearly different in both genders. There is a need for high alertness in suspected coronary events, particularly in young women.

What is the “take home” message?

1. There are differences in symptoms, signs and significance of CHD risk factors between genders. Appropriate patient education is needed particularly in younger women to avoid unnecessary delay of intervention in acute coronary syndromes.
2. Diabetes and hypertriglyceridemia require aggressive therapy particularly in women.
3. A global CHD risk assessment should be done in males > 40 years of age and females > 50 or those who are postmenopausal. Depending on level of risk appropriate therapy should be instituted: life-style counseling (smoking!), therapy of dyslipidemias, antihypertensive therapy and diabetes control.
4. Aspirin 100 mg OD should be prescribed routinely in older males and females if there is no contraindication.
5. In those with existing CHD ACE inhibitors and beta-blockers should be an integral part of the therapeutic regimen in both sexes.

References

1. Pilote L, Hlatky MA (1995) Attitudes of women toward hormone therapy and prevention of heart disease. *Am Heart J* 129: 1237–1238
2. Tobin JN, Wassertheil-Smoller S, Wexler JP, Steingart RM, Budner N, Lense L, Wachspress J (1987) Sex bias in considering coronary bypass surgery. *Ann Intern Med* 107(1): 19–25
3. Ayanian JZ, Epstein AM (1991) Differences in the use of procedures between women and men hospitalized for coronary heart disease. *N Engl J Med* 325(4): 221–225
4. Vaccarino V, Parsons L, Every NR, Barron HV, Krumholz HM (1999) Sex-based differences in early mortality after myocardial infarction. National Registry of Myocardial Infarction 2 Participants. *N Engl J Med* 341(4): 217–225
5. Meischke H, Eisenberg MS, Larsen MP (1993) Prehospital delay interval for patients who use emergency medical services: the effect of heart-related medical conditions and demographic variables. *Ann Emerg Med* 22(10): 1597–1601
6. Expert Panel Writing Group. Mosca L, Appel LJ, Benjamin EJ, Berra K, Chandra-Strobos N, Fabunmi RP, Grady D, Haan CK, Hayes SN, Judelson DR, Keenan NL, McBride P, Oparil S, Ouyang P, Oz MC, Mendelsohn ME, Pasternak RC, Pinn VW, Robertson RM, Schenck-Gustafsson K, Sila CA, Smith SC Jr, Sopko G, Taylor AL, Walsh BW, Wenger NK, Williams CL; American Heart Association (2004) Evidence-based guidelines for cardiovascular disease prevention in women. *Circulation* 109:672–693
7. Writing Group for the Women's Health Initiative Randomized Controlled Trial (2002) Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA* 288: 321–333
8. Wenger NK (1996) Gender differences in coronary risk and risk factors. In: Manson JE et al (eds) *Prevention of myocardial infarction*. Oxford University Press, New York, pp 387–412
9. Joffres MR, Ghadirian P, Fodor JG, Petrasovits A, Chockalingam A, Hamet P (1997) Awareness, treatment, and control of hypertension in Canada. *Am J Hypertens* 10: 1097–1102
10. Assmann G, Schulte H (1992) Role of triglycerides in coronary artery disease: lessons from the Prospective Cardiovascular Munster Study. *Am J Cardiol* 8: 99–103
11. Kannel W, McGee D (1979) Diabetes and cardiovascular risk factors: the Framingham Study. *Circulation* 59(1): 8–13
12. Prescott E, Hippe M, Schnohr P, Hein HO, Vestbo J (1998) Smoking and the risk of myocardial infarction in women and men: longitudinal population study. *BMJ* 316: 1043–1047
13. Larsson B, Bengtsson C, Björntorp P, Lapidus L, Sjöström L, Svardsudd K, Tibblin G, Wedel H, Welin L, Wilhelmsen L (1992) Is abdominal body fat distribution a major explanation for the sex difference in the incidence of myocardial infarction? The study of men born in 1913 and the study of women, Göteborg, Sweden. *Am J Epidemiol* 135: 266–273
14. De Backer G, Ambrosioni E, Borch-Johnsen K, Brotons C, Cifkova R, Dallongeville J, Ebrahim S, Faergeman O, Graham I, Mancia G, Manger Cats V, Orth-Gomér K, Perk J, Pyorala K, Rodicio JL, Sans S, Sansoy V, Sechtem U, Silber S, Thomsen T, Wood D; Third Joint Task Force of European and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (2003) European guidelines on cardiovascular disease prevention in clinical practice. Third Joint Task Force of European and Other Societies on Cardiovascular Disease Prevention in Clinical Practice. *Eur Heart J* 24(17): 1601–1610
15. Milner KA, Funk M, Richards S (1999) Gender differences in symptom presentation associated with coronary heart disease. *Am J Cardiol* 84(4): 396–399
16. Arnold AL, Milner KA, Vaccarino V (2001) Sex and race differences in electrocardiogram use (The National Hospital Ambulatory Medical Care survey). *Am J Cardiol* 88: 1037