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Gender aspects in cardiac imaging

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Summary

This article reviews existing gender differences in cardiac imaging in terms of extra-cardiac anatomy, cardiac anatomy, myocardium remodelling and cardiac response to injury. It underlines the need for "gender medicine", where gender differences and female patients' representation are taken into account in cardiovascular research and clinical trials, as a first step toward tailored therapies and health care.

Keywords: *gender differences, cardiac anatomy, cardiac remodelling*

Introduction

During the last decades, gender differences have become evident in cardiology, in terms of risk factors, prognosis, medical and interventional treatments, and enrolment in major studies. Noninvasive cardiac imaging, such as cardiac echography, cardiac magnetic resonance (CMR), cardiac computed tomography (CT), cardiac positron emission tomography (PET) or myocardial single-photon emission computed tomography (SPECT), plays a major role in the assessment, diagnosis and management of cardiovascular diseases. Little is known of gender aspects in cardiac imaging. The aim of this review is to underline existing gender differences in cardiac imaging and their repercussions in our daily practice.

Gender of the physician doing and/or reading the examination

Studies have revealed the influence of the gender of the treating physician in terms of guideline-recommended treatment heart failure [1] and, more recently, on hospital mortality and readmissions [2]. These articles underline differences in practice patterns between male and female physicians treating male or female patients, which may have important clinical implications for patient outcomes. In terms of cardiac imaging, differences in image acquisition and interpretation between male and female physicians probably exist, but may not have any important clinical impact. To my knowledge, such differences have not been studied yet.

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Gender of the patient

Extra-cardiac anatomy

Breast implant

Quality control and durability of medical devices in general have been recently questioned in the "Implant files" [3]. The safety and long-term outcomes of silicon- and saline-containing breast implants have been studied in large cohorts [4], but publications regarding their impact on cardiac follow-up are scarce. There is indeed little awareness in the medical community (other than cardiologists) and in the concerned female population that breast implants significantly impair echographic cardiac follow-up [5, 6]. This may have major clinical implications for women who need periodic echographic follow-up, such as those with congenital heart disease or who have received chemotherapy. Therefore, the medical community and women considering a breast implant should be informed that echocardiographic image quality might be considerably reduced. Attenuation artefacts caused by breast tissue are known to lead to decreased specificity of gated SPECT imaging. It appears that silicon- and saline-containing breast implants also impair detection of coronary artery disease with SPECT imaging [7].

Pregnancy

Cardiac imaging during pregnancy is challenging and recommendations have recently been published [8]. Transthoracic echocardiography is safe, reproducible, widely available and relatively cheap, and is therefore the preferred imaging method during pregnancy. Transoesophageal echography may be useful when transthoracic echogenicity is limited and when evaluation of the cardiac structures is absolutely needed, such as before cardioversion, when endocarditis is suspected or in the case of bioprosthetic valve thrombosis. However, the risk of vomiting and aspiration with a sudden increase in abdominal pressure must be evaluated, and fetal monitoring programmed if the mother is sedated. Fetal ionising radiation exposure caries a risk of growth restriction, intellectual disability, malignancies and neurological effects. Therefore, if ionising radiation is needed, risks and benefits must be discussed with the parents, and doses must be kept as low as possible. MRI seems to be safe, especially after the first trimester. However, the pregnant patient must lie on her back, which might not be well tolerated in the third trimester when the gravid uterus

may compress the inferior vena cava. Use of gadolinium is controversial and many questions can be answered without its use. It should therefore be avoided in pregnancy. Cardiac catheterisation is rarely used for diagnosis purpose during pregnancy. However, it may be needed to guide percutaneous interventions. Coronary angiography might be used in cases of acute coronary syndrome.

Cardiac anatomy

Six gender-differences have been described in terms of cardiac anatomy, remodelling and response to injuries such as ischaemic heart disease and Chagas disease.

Aorta and coronary arteries

Aortic stiffness is a major predictor of stroke and myocardial infarction [9, 10], and has been associated with heart failure [11]. Ascending aorta strain, assessed with cardiac magnetic resonance (CMR) is an early manifestation of vascular aging, correlates with coronary atherosclerosis and coronary calcium content, and is a predictor of hypertension. Very interestingly, ascending aorta strain assessed in patients with normal CMR, tetralogy of Fallot and ischaemic heart disease was independently affected by age, gender and cardiovascular disease [12], male patients having decreased aortic strain and therefore increased aortic stiffness. Animal studies have shown gender differences in genes and proteins that contribute to the age-related increase in vascular stiffness [13]. Qualitative and quantitative regulation of collagen differs between male and female monkeys, and may play a role in gender differences in aortic stiffness. Further studies are clearly needed to better assess and understand gender differences in aortic stiffness and their clinical implications.

Gender differences in cardiovascular risks factors, clinical presentation and treatment of coronary disease have been studied and described. Gender difference in mortality after acute myocardial infarction persists even when adjusted for age and co-morbidities [14]. Smaller coronary artery calibre may play a role, but the existence of a gender difference in coronary artery size is controversial. Nevertheless, in a population without cardiac disease, women had smaller coronary artery calibre normalised for left ventricular mass [15].

Myocardium remodelling

Cardiac remodelling in response to volume or pressure overload is a well-known process. Gender differences in cardiac remodelling have been demonstrated in physiological and pathological circumstances, and may have clinical implications. In endurance athletes, for example, for the same amount of exercise, atrial and ventricular remodelling are more pronounced in males, and may participate in the increased risk of developing atrial fibrillation [16].

The prevalence of hypertension differs between different age and sex groups, with a higher prevalence in men between 45 and 54 years of age and in women older than 75 years [17]. Hypertension is one of the most important and prevalent risk factors for heart failure through the structural, functional and mechanical left ventricular changes it induces. Data regarding left ventricular hypertrophy, systolic and diastolic function, and mechanics in hypertensive male and female patients are somewhat contradictory with a slight tendency for a higher prevalence of left ventricular hypertrophy and diastolic impairment in hypertensive women, and a lower left ventricular ejection fraction (LVEF) and strain values in men [18]. Sex hormones are considered to be the most important mechanism explaining these differences. They probably also account for the gender differences in heart failure, women being more prone to develop heart failure with preserved ejection fraction (HFpEF) [19]. Gender differences in left ventricular response to hypertension and the resulting differences in heart failure underlines the needs for better representation of female patients in cardiovascular research and clinical trials enrolment [19].

In aortic stenosis, cardiac remodelling and reverse remodelling after aortic valve replacement significantly differ in male and female patients. In a very interesting paper recently published in the *Journal of the American College of Cardiology: Cardiovascular Imaging* [20], the authors demonstrated that, for the same amount of valve stenosis, there were major sex differences in CMR-assessed myocardial remodelling, fibrosis and resultant left ventricle function. Men predominantly had concentric or eccentric left ventricular hypertrophy, a lower LVEF and more fibrosis, whereas women exhibited a more favourable phenotype with less hypertrophy and fibrosis and a higher LVEF. These gender differences in remodelling patterns had been previously demonstrated [21], with a superior reverse remodelling in men 6 months after aortic valve replacement as a result of their more adverse remodelling at baseline. The causes of this gender dimorphism in myocardial response are incompletely understood but cellular, molecular and neurohormonal mechanisms have been proposed, including differences in profibrotic and inflammatory pathways, as well as differential expression of androgen and oestrogen receptors. Gender differences in the rennin-angiotensin system, nitric oxide activity and norepinephrine release may also contribute to remodelling differences [22]. These gender-related remodelling differences associated with aortic stenosis might raise the question of sex-specific threshold for aortic valve replacement.

Responses to damage

Like the gender differences in response to pressure and volume overload, men and women exhibit differences in myocardial damages to ischaemic and infectious assaults.

Gender-related early and late mortality after myocardial infarction has been prospectively studied [23, 24]. Very interestingly, it appears that female gender was not independently associated with worse outcomes, but that gender bias in management, as well as demographic and clinical characteristics, might account for the poorer prognosis in women. Noninvasive assessment of infarct size with CMR is an additional prognostic factor in risk stratification after acute myocardial infarction. Therefore, it has been postulated that infarct size and microvascular obstruction [25] might also play a role in gender differences in morbidity and mortality. Anyway, in a prospective study comparing scar characterisation between women and men with similar risk profiles, infarct size did not show significant gender differences [25]. Microvascular obstruction seemed to differ between men and women, with a lesser obstruction

in women, but whether this reflects better cardioprotective mechanisms needs to be further evaluated.

Chagas' disease, cause by *Trypanosoma cruzi*, affects millions of people worldwide and is a major cause of heart failure and death in Latin America and in nonendemic countries [26] such as the USA and European countries. The parasite may be responsible for acute perimyocarditis and chronic fibrosing myocarditis, resulting in increased risk of heart failure, cardiac arrhythmias, thromboembolism and cardiac death. Chagas' disease tends to affect relatively young patients, with a higher cardiovascular morbidity and mortality in men. Propensity for early myocardial fibrosis and scar formation might account for the increased mortality seen in Chagas' disease as compared with other nonischaemic cardiomyopathies. Therefore, it is very interesting to note that male gender was associated with a higher amount of myocardial fibrosis and ventricular remodelling on CMR, which may account for the worse clinical outcomes [27].

Key messages

- Gender differences definitely exist in cardiac imaging. These differences have to be recognised and taken into account when treating a patient.
- Obvious morphological gender differences, such as breast implants, may compromise imaging quality in women. Therefore, the medical community and patients have to be aware of this when considering breast implant surgery.
- Gender differences in cardiac fibrosis and remodelling have been demonstrated with CMR. This gender dimorphism might contribute to a better understanding of the cellular, molecular and neurohormonal physiopathological mechanisms behind adaptive and maladaptive mechanisms.
- Gender differences in response to hypertensive burden, ischaemic or infectious myocardial insults might explain gender differences in prognosis. This underlines the need for the development of a "gender medicine" with an improvement of female patient representation in cardiovascular research and enrolment in clinical trial as a first step toward tailored therapies and health care.

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