IJC Heart & Vessels 3 (2014) 78–81

Contents lists available at ScienceDirect

IJC Heart & Vessels

journal homepage: http://www.journals.elsevier.com/ijc-heart-and-vessels

Echocardiographic elastic properties of ascending aorta and their relationship with exercise capacity in patients with non-ischemic dilated cardiomyopathy

Enrico Vizzardi *[,1], Giorgio Caretta [1], Ivano Bonadei [1], Riccardo Rovetta [1], Edoardo Sciatti [1], Natalia Pezzali [1], Carlo M. Lombardi [1], Filippo Quinzani [1], Francesca Salghetti [1], Antonio D'Aloia [1], Marco Metra [1]

Section of Cardiovascular Diseases, Department of Medical and Surgical Specialties, Radiological Sciences and Public Health, University of Study of Brescia, Italy

ARTICLE INFO

Article history:
Received 1 December 2013
Received in revised form 22 March 2014
Accepted 29 March 2014
Available online 18 April 2014

Keywords:
Heart failure
Aortic distensibility
Aortic stiffness
Dilated cardiomyopathy
Cardiopulmonary exercise test
Ventriculo-arterial coupling

ABSTRACT

Background: : Aortic stiffness, an independent predictor of mortality and cardiovascular events, is common among patients affected by non-ischemic dilated cardiomyopathy (NIDC) and heart failure (HF).
Methods: : A total of 55 patients with diagnosis of NIDC (aged 60 ± 11 years, mean ejection fraction (EF) 35.2% ± 7.7%) admitted consecutively to our department for mild to moderate HF (NYHA class II–III) underwent an echocardiographic study and cardiopulmonary exercise test (CPX). We evaluated elastic properties of ascending aorta, i.e. aortic stiffness and aortic distensibility (mm Hg^{-1}), derived from ascending aorta systolic and diastolic diameter (mm/m^2) measured 3 cm above the valvular plane through 2D-guided M-mode echocardiography.
Results: : Mean aortic stiffness was 15.63 ± 14.53 and aortic distensibility was 2.61 ± 2.39 mm Hg^{-1}. Collected parameters at CPX were peak oxygen consumption (pVO_2) (ml/kg/min), anaerobic threshold (AT) and the slope of the relation between minute ventilation (VE) and carbon dioxide production (VCO_2). Mean pVO_2 was 15.4 ± 3.9 ml/kg/min, VE/VCO_2 ratio at AT was 36.1 ± 6.1. Functional capacity measured through peak VO_2 was found to be directly correlated with aortic distensibility ($r = 0.47$, $p = -0.0002$) and negatively correlated to aortic stiffness index ($r = -0.51$, $p = -0.0001$). These results were the same at multivariate analysis, corrected by age, hypertension, diabetes mellitus and ejection fraction (respectively $r = 0.27$, $p = 0.008$ and $r = -1.75$, $p = 0.0002$).
Conclusions: : HF patients due to NIDC elastic properties of ascending aorta, evaluated by echocardiography, are correlated with a reduced functional capacity.

1. Introduction

The interaction between the heart and the peripheral vasculature is one of the major determinants of cardiovascular performance. The progression of myocardial systolic dysfunction in chronic heart failure (CHF) is characterized by a reduction of left ventricular end-systolic elastance (LVE) and increased arterial elastance (AE), or stiffness [1,2]. The relationship between AE and LVE represents the ventriculo-arterial coupling that is an important determinant of net cardiac performance and cardiac energetics [3]. Ventriculo-arterial coupling is known to progressively increase in CHF due to a reduction in LVE and a raise in AE [4,5]. The failing heart is so very linked to afterload conditions during exercise. Many studies showed a progressive alteration of large-artery function with the increasing severity of CHF [6]. Recent studies have shown that increased aortic stiffness leads to an increased afterload [7] and an impaired ventriculo-arterial coupling [8], thus reducing left ventricular systolic function and exercise capacity in patients with CHF [9,10].

The aim of our study was to demonstrate the possible relationship between elastic properties of ascending aorta, evaluated noninvasively by echocardiography, and clinical functional capacity evaluated by cardiopulmonary test in patients with NIDC.

2. Methods

We evaluated 55 consecutive patients affected by mild to moderate CHF due to NIDC with reduced left ventricular ejection fraction (LVEF < 45%), admitted to Cardiology Department of Spedali Civili of Brescia, Italy. 30 patients (55%) were in NYHA class II and 25 (45%) in NYHA class III. They received standard therapy of CHF in accordance with the European Society of Cardiology guidelines for the treatment of

* Corresponding author. Tel.: +39 303995679; fax: +39 303996801.
E-mail address: enrico.vizzardi@tin.it (E. Vizzardi).
[1] The authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

http://dx.doi.org/10.1016/j.ijchv.2014.03.009

CHF [11]. NIDC was confirmed by coronary angiography. Every patient had a diagnosis of idiopathic cardiomyopathy.

The authors stated that written informed consent was obtained from each patient and that the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

All the patients underwent a complete echocardiography-Doppler examination (VIVID 7 echocardiograph General Electric Medical Systems, Horten, Norway). Left ventricle end-diastolic and end-systolic volumes, left ventricle end-diastolic and end-systolic diameters, ejection fraction and also left ventricular wall thicknesses at end diastole and end systole were measured in accordance with the guidelines [12]. The Doppler method was used to calculate trans-mitral early and late flow velocities (E- and A-wave components) and deceleration time. The ratio of early trans-mitral flow velocity to early mitral annular velocity (E/E′) was measured by tissue Doppler imaging [13]. LV diastolic dysfunction was classified as proposed by the Group on Diastolic Heart Failure [14]. Systolic blood pressure in pulmonary artery (sPAP) was estimated using Doppler echocardiography [15,16].

To evaluate aortic properties of ascending aorta we assessed aortic size at four levels: Valsalva sinuses (VS), sino-tubular junction (STJ), ascending aorta (AA), and aortic arch (AAr) at the end of diastole and systole. So, aortic elastic indexes, i.e. distensibility (AoDis) and stiffness (AoStif) were calculated from the echocardiographically derived thoracic aortic diameters (indexed by body surface area — mm/m^2) and assessed on the basis of a two-dimensional guided M-mode recording of systolic (AoS) and diastolic (AoD) aortic diameters, 3 cm above the aortic valve. AoD was obtained at the peak of the R wave at the simultaneously recorded ECG, and AoS was measured at the maximal anterior motion of the aortic wall; five measurements were averaged for each diameter. The following indexes of aortic elasticity were calculated: AoDis = [2 × (AoS − AoD) / AoD ∗ PP] ($mm\ Hg^{-1}$); (AoStif) = ln(SBP/DBP) / [(AoS − AoD) / AoD] (pure number) where SBP and DBP refer to brachial systolic and diastolic BP respectively, in mm Hg and pulse pressure (PP) was calculated as SBP − DBP [17].

All the patients underwent a cardiopulmonary exercise (CPX) test (Marquette Hellige). It was used as a constant ramp protocol where work rate was increased of 10 W/min. Gas exchange was monitored during the exercise test with a spirometer and a computer metabolic analysis (Medical Graphics). Collected parameters were peak oxygen consumption (pVO_2) expressed in ml/kg/min, anaerobic threshold (AT) expressed in ml/kg/min, the slope of the relation between minute ventilation (VE) and carbon dioxide production (VCO_2). Peak VO_2 was measured as the mean value during the last 30 s of exercise.

All data are given as mean ± standard deviation or number (percentage) of patients. Univariate and multivariate analyses were made to assess a correlation between pVO_2, age, LVEF, hypertension, diabetes and aortic stiffness. Statistical significance was established at a level of $p < 0.05$.

3. Results

Patients were 46 males (83%) and 9 females (17%). Mean age was 60 ± 11 years old. All patients were affected by CHF due to NIDC with mean EF of 35.2% ± 7.7% and were treated with optimized medical CHF-therapy according to current guidelines: ACE-I or ARB (96%), beta blocker (96%), aldosterone receptor antagonist (64%) and diuretics (70%).

All the other characteristics and all the echocardiographic parameters are summarized respectively in Tables 1 and in 2.

Peak VO_2 at CPX was 15.4 ± 3.9 ml/kg/min, VE/VCO_2 ratio at AT was 36.1 ± 6.1; mean respiratory exchange ratio (RER) was 1.1 ± 0.14 thus meaning that a maximum metabolic effort was performed. All the other parameters evaluated during CPX were summarized in Table 3.

Mean AoDis was 2,61 ± 2.39 $mm\ Hg^{-1}$ and mean aortic stiffness 15,63 ± 14,53.

Table 1
Characteristics of the study population of mild- to moderate CHF (n = 55).

Age (years)	60 ± 11
Men/women	46 (83%)/9 (17%)
Body surface area (BSA) (m^2)	1,96 ± 0,2
Systolic blood pressure (mm Hg)	119 ± 15.2
Diastolic blood pressure (mm Hg)	74,9 ± 8,2
Heart rate (bpm)	68,4 ± 10,8
Arterial hypertension	8 (15%)
Chronic obstructive pulmonary disease (COPD)	6 (10%)
Diabetes mellitus	9 (18%)
Smokers	3 (5%)
Dyslipidemia	17 (30%)

Data are presented as the mean value ± SD, or number (percentage) of patients.

At univariate analysis only pVO_2 was found to be directly correlated with AoDis (r = 0.47, CI 0.25–0.66, p = 0.0002) and negatively correlated to AoStiff (r = −0.51, CI −0.68 to −0.20, p = 0.0001) [Figs. 1 and 2]. The correlations were also demonstrated at multivariate analysis, corrected by hypertension, diabetes, age and ejection fraction (respectively r = 0.27, p = 0.008 and r = −1.75, p = 0.0002). In Table 4 was shown the predictors of peak volume oxygen consumption.

4. Discussion

This study demonstrates that aortic stiffness (measured non-invasively using 2D guided M-mode echocardiography) is an independent predictor of exercise capacity in patients with CHF and NIDC.

Our results are consistent with other reports that showed a correlation between elastic properties of ascending aorta and functional capacity in CHF patients using different echocardiographic methods [9,10]. The echocardiographic method used to evaluate aortic stiffness in CHF patients is simple and easy to acquire and is not dependent on pulse wave Doppler echocardiography.

An impaired aortic compliance is frequent among CHF patients [18–20] and we showed that aortic stiffness is inversely related to peak VO_2, which is a major predictor of mortality among CHF patients [21]. Our study cannot establish a causal relation between aortic stiffness and decreased functional capacity. Actually, the elastic proximal aorta is the main region that is affected by aging, hypertension, diabetes or LV diastolic dysfunction. Therefore an increased aortic stiffness may represent a marker of more advanced disease in CHF patients. Despite that, several pathophysiological mechanisms suggest a possible causal

Table 2
Main echocardiographic parameters of the study population (n = 55).

End diastolic diameter (EDD) (cm)	6.66 ± 0.79
End systolic diameter (ESD) (cm)	5.32 ± 0.95
End diastolic volume (EDV) (ml)	183.27 ± 82.58
End systolic volume (ESV) (ml)	132.73 ± 94.38
End diastolic volume indexed (EDVi) (ml/m^2)	74.36 ± 49.23
Left ventricular ejection fraction (LVEF) (%)	35.2 ± 7.7
Posterior wall thickness (PWT) (cm)	0.95 ± 0.14
Interventricular septum thickness (IVT) (cm)	1.05 ± 0.18
Left ventricular mass (LV mass) (g)	
Valsalva sinuses (VS) (mm)	37.23 ± 6.37
Sino-tubular junction (STJ) (mm)	35.32 ± 2.56
Ascending aorta (AA) (mm)	42.93 ± 4.65
Aortic arch (Aar) (mm)	33.28 ± 2.96
Aorta in systole (AoS) (mm)	33.24 ± 5.03
Aorta in diastole (AoD) (mm)	34.95 ± 5.1
Aortic distensibility ($mm\ Hg^{-1}$)	2.61 ± 2.39
Aortic stiffness index	15.63 ± 14.53
E/A ratio	0.75 ± 0.20
Deceleration time (DT) (msec)	244.6 ± 80.4
E/e′ ratio	14.7 ± 6.26
Pulmonary artery systolic pressure (mm Hg)	30.5 ± 5.5
Left atrium diameter (cm)	4.63 ± 0.9
Left atrium area (cm^2)	25.01 ± 7.57

Data are presented as the mean value ± SD, or number (percentage) of patients.

Table 3
CPX parameters of the study population (n = 55).

Peak VO_2 (ml/kg/min)	15.4 ± 3.9
Peak VO_2 (ml/min)	1284.13 ± 369.2
Max theoretical VO_2 (ml/kg/min)	26.45 ± 5.02
Max theoretical VO_2 percentage reached (%)	58.56 ± 14.26
Anaerobic Threshold (AT) (ml/kg/min)	10.55 ± 3.59
VE/VCO_2 ratio at AT	36.1 ± 6.1
Respiratory Exchange Ratio (RER)	1.1 ± 0.14
Maximum workload (Watt)	102.4 ± 30.59

Data are presented as the mean value ± SD, or number (percentage) of pts.

relation between aortic stiffness and exercise tolerance and in our population a relation between aortic stiffness and functional capacity was maintained after correction for other variables.

The elastic properties of aorta are crucial for an optimal ventriculo-arterial coupling [7,22] and a stiffer aorta has a negative impact on cardiac function and functional capacity of CHF patients through different mechanisms. First, in a stiffer aorta the cushioning effect of its proximal tract is reduced, thus increasing LV afterload with further compromising the ability to generate an adequate cardiac output during exercise. This is particularly true in CHF patients because it is known that the function of the failing heart is very dependent on the increase of afterload. Kelly et al. have shown that a less compliant aorta may affect both LV systolic energetics and mechanics: when the aorta was experimentally stiffened, an increase in cardiac energetic cost for a given stroke volume (SV) was observed [23] and SV varied inversely with aortic stiffness [24]. The alterations of ventriculo-aortic coupling seem to further exacerbate during exercise due to increased heart rate and an earlier reflection of pulsed wave from the periphery back to the aortic root [4].

Secondly, combined ventricular–aortic stiffness could potentially reduce the cardiovascular reserve [25]. Therefore, the ability of the heart to accommodate the peripheral demands and the increased pre-load during exercise may be reduced, with an increase in left atrial pressure, and then in pulmonary capillary wedge pressure responsible of the appearance of shortness of breath eliminating the exercise capacity.

Thirdly, a stiffer aorta influences the exercise capacity by LV relaxation. The study of Patrianakos et al. shows a link between aortic stiffness and a more advanced grade of diastolic dysfunction [10]. This condition is associated with an increase of LV end-diastolic pressure at rest which increases more during exercise for an increase in heart rate and a reduction in diastolic period.

A study on a population of patients with CHF with preserved ejection fraction (HFPEF) observed that these subjects have a more stiffened

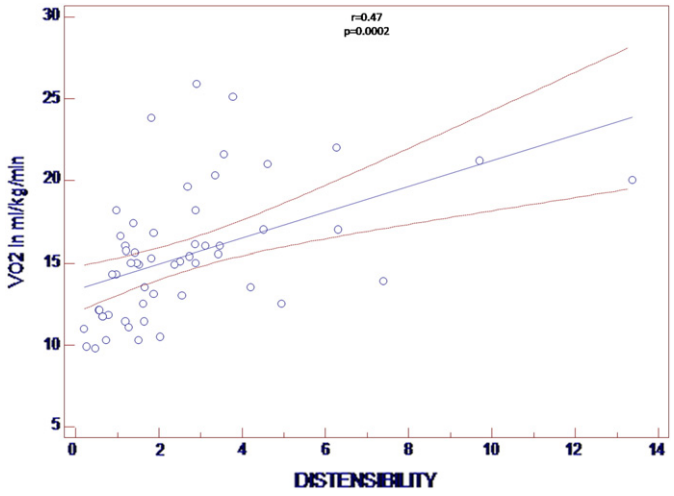

Fig. 1. Correlation between aortic distensibility and pVO_2 (dashed lines represent ±1 standard deviation interval).

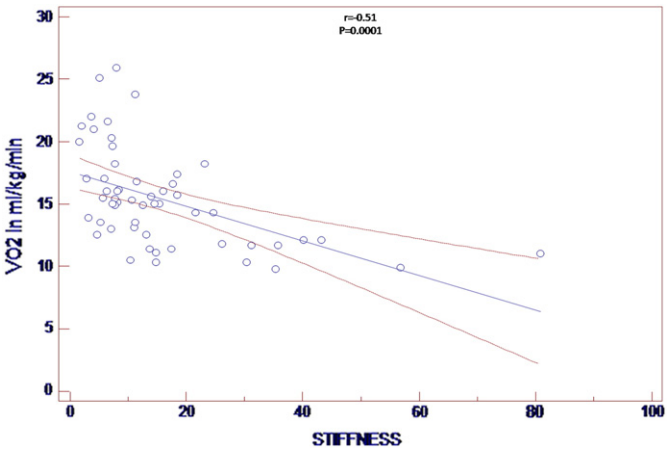

Fig. 2. Correlation between aortic stiffness and pVO_2 (dashed lines represent ±1 standard deviation interval).

aorta and this condition could determine the development of a more advanced diastolic dysfunction that consecutively could worsen the ventriculo-arterial coupling and contribute to the pathophysiology of HFPEF [26]. These data confirm the positive linkage between aortic stiffness and LV filling pressure. In these patients many comorbidities can explain the less aortic distensibility and the development of HFPEF such as elderly age [27], end-stage renal failure [28] and hypertension [29] that are known as causes of myocardial hypertrophy, the substrate at the basis of diastolic dysfunction.

There are several mechanisms that can affect aortic function. The ability of the aorta to buffer the pulsatile component of the LV afterload relies on a complex network of elastin, collagen and smooth muscle cells [30,31]. Changes in the relative proportion of these components alter the elastic properties of aorta: an increase in collagen, which is more stiffer, and a reduction of elastin, which is easily stretched, make the arterial wall less elastic [30]. This suggests that abnormalities in extracellular matrix turnover might involve the proximal elastic vasculature and can in part explain the progressive stiffening process of large artery in CHF [31].

The enhanced activation of renin–angiotensine–aldosterone system (RAAS) in patients with CHF and dilated cardiomyopathy is probably an important cause of aortic stiffness. Aortic stiffening involves vascular smooth muscle hypertrophy, inflammation, and collagen accumulation, mechanisms which have been reported to be induced by aldosterone [32]. Activation of RAAS leads to sodium and water accumulation in arterial walls and determinates wall edema, thus increasing vascular stiffness [33]. Sodium retention also promotes extracellular matrix (ECM) synthesis and deposition and changing smooth muscle cell phenotype, which impair vascular compliance [34]. Finally, vascular inflammation, which plays an important role in the progression of CHF, might be involved in the accelerated ECM turnover that contributes to both myocardial and arterial fibrosis [35], and a significant relation between high serum C-reactive protein levels and impaired aortic compliance has been described in patients with idiopathic dilated

Table 4
Predictors of peak volume oxygen consumption (VO_2).

Variable	Pearson's correlation coefficient	p
Age	−0.2640	0.0515
SAP	−0.1804	0.1876
DAP	−0.1777	0.1942
LVEF	0.1638	0.2322
LVMI	−0.1611	0.2400
Aortic distensibility	0.47	0.0002
Aortic stiffness index	−0.51	0.0001

cardiomyopathy [35]. Even in chronic inflammatory diseases like rheumatoid arthritis we have previously demonstrated a correlation between aortic stiffness and the progression of systolic and diastolic function with a possible explanation that altered ventriculo-arterial coupling could contribute to the pathophysiology of CHF [36].

There are potential limitations to the present study. First, we used a noninvasive brachial cuff pressure measurement instead of a direct assessment of the aortic pulse pressure by a catheter. It has been shown that pulse pressure may be lower using a noninvasive method; however, others have shown an excellent correlation ($r = 0.95$, $p < 0.001$) of the calculated aortic distensibility using invasive and noninvasive methods [37]. Second, most of our patients with systolic CHF received long-term medication with agents that might improve aortic distensibility (such as spironolactone) or decrease exercise tolerance (such as beta-blockers). Third, it is possible that impaired systolic performance could directly affect aortic distensibility in patients with systolic CHF; however, it is known that stroke volume and cardiac output are usually adequate in compensated patients with systolic CHF at rest. Moreover in our population no association was found between aortic stiffness and LVEF. Fourth, since 96% of our population was treated with beta-blockers we can hypothesize that these drugs may have influenced aortic elastic properties. To our knowledge, no studies have already evaluated the effects of beta-blockers on ascending aorta distensibility and stiffness.

In conclusion this study confirms that among HF patients with NIDC aortic stiffness is correlated with peak VO_2 and is an independent predictor of exercise capacity. These data suggest that decreased aortic distensibility may cause hemodynamic impairment. Aortic stiffness has a negative impact on cardiac function and functional capacity.

References

[1] Khan Z, Millard RW, Gabel M, Walsh RA, Hoit BD. Effect of congestive heart failure on in vivo canine aortic elastic properties. J Am Coll Cardiol 1999;33(1):267–72.
[2] Arnold JM, Marchiori GE, Imrie JR, Burton GL, Pflugfelder PW, Kostuk WJ. Large artery function in patients with chronic heart failure. Studies of brachial artery diameter and hemodynamics. Circulation 1991;84(6):2418–25.
[3] Kass DA. Ventricular arterial stiffening: integrating the pathophysiology. Hypertension 2005;46(1):185–93.
[4] Hundley WG, Kitzman DW, Morgan TM, Hamilton CA, Darty SN, Stewart KP, et al. Cardiac cycle-dependent changes in aortic area and distensibility are reduced in older patients with isolated diastolic heart failure and correlate with exercise intolerance. J Am Coll Cardiol 2001;38(3):796–802.
[5] Suga H, Sagawa K, Shoukas AA. Load independence of the instantaneous pressure–volume ratio of the canine left ventricle and effects of epinephrine and heart rate on the ratio. Circ Res 1973;32(3):314–22.
[6] Elzinga G, Westerhof N. Pressure and flow generated by the left ventricle against different impedances. Circ Res 1973;32(2):178–86.
[7] Ooi H, Chung W, Biolo A. Arterial stiffness and vascular load in heart failure. Congest Heart Fail 2008;14(1):31–6.
[8] Antonini-Canterin F, Carerj S, Di Bello V, Di Salvo G, La Carrubba S, Vriz O, et al. Arterial stiffness and ventricular stiffness: a couple of diseases or a coupling disease? A review from the cardiologist's point of view. Eur J Echocardiogr 2009;10(1):36–43.
[9] Bonapace S, Rossi A, Cicoira M, Franceschini L, Golia G, Zanolla L, et al. Aortic distensibility independently affects exercise tolerance in patients with dilated cardiomyopathy. Circulation 2003;107(12):1603–8.
[10] Patrianakos AP, Parthenakis FI, Karakitsos D, Nyktari E, Vardas PE. Proximal aortic stiffness is related to left ventricular function and exercise capacity in patients with dilated cardiomyopathy. Eur J Echocardiogr 2009;10(3):425–32.
[11] McMurray JJ, Adamopoulos S, Anker SD, Auricchio A, Böhm M, Dickstein K, et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur Heart J 2012;33(14):1787–847.
[12] Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr 2005;18(12):1440–63.
[13] Oh JK, Appleton CP, Hatle LK, Nishimura RA, Seward JB, Tajik AJ. The noninvasive assessment of left ventricular diastolic function with two-dimensional and Doppler echocardiography. J Am Soc Echocardiogr 1997;10(3):246–70.
[14] Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. Eur J Echocardiogr 2009;10(2):165–93.
[15] Ommen SR, Nishimura RA, Hurrell DG, Klarich KW. Assessment of right atrial pressure with 2-dimensional and Doppler echocardiography: a simultaneous catheterization and echocardiographic study. Mayo Clin Proc 2000;75(1):24–9.
[16] Lam CS, Roger VL, Rodeheffer RJ, Borlaug BA, Enders FT, Redfield MM. Pulmonary hypertension in heart failure with preserved ejection fraction: a community-based study. J Am Coll Cardiol 2009;53(13):1119–26.
[17] Kawasaki T, Sasayama S, Yagi S, Asakawa T, Hirai T. Non-invasive assessment of the age related changes in stiffness of major branches of the human arteries. Cardiovasc Res 1987;21(9):678–87.
[18] Lage SG, Kopel L, Monachini MC, Medeiros CJ, Pileggi F, Polak JF, et al. Carotid arterial compliance in patients with congestive heart failure secondary to idiopathic dilated cardiomyopathy. Am J Cardiol 1994;74(7):691–5.
[19] Vaitkevicius PV, Fleg JL, Engel JH, O'Connor FC, Wright JG, Lakatta LE, et al. Effects of age and aerobic capacity on arterial stiffness in healthy adults. Circulation 1993;88(4 Pt 1):1456–62.
[20] van den Broek SA, van Veldhuisen DJ, de Graeff PA, Landsman ML, Hillege H, Lie KI. Comparison between New York Heart Association classification and peak oxygen consumption in the assessment of functional status and prognosis in patients with mild to moderate chronic congestive heart failure secondary to either ischemic or idiopathic dilated cardiomyopathy. Am J Cardiol 1992;70(3):359–63.
[21] Mancini DM, Eisen H, Kussmaul W, Mull R, Edmunds Jr LH, Wilson JR. Value of peak exercise oxygen consumption for optimal timing of cardiac transplantation in ambulatory patients with heart failure. Circulation 1991;83(3):778–86.
[22] Cheriyan J, Wilkinson IB. Role of increased aortic stiffness in the pathogenesis of heart failure. Curr Heart Fail Rep 2007;4(3):121–6.
[23] Kelly RP, Tunin R, Kass DA. Effect of reduced aortic compliance on cardiac efficiency and contractile function of in situ canine left ventricle. Circ Res 1992;71(3):490–502.
[24] Urschel CW, Covell JW, Sonnenblick EH, Ross Jr J, Braunwald E. Effects of decreased aortic compliance on performance of the left ventricle. Am J Physiol 1968;214(2):298–304.
[25] Kitzman DW, Higginbotham MB, Cobb FR, Sheikh KH, Sullivan MJ. Exercise intolerance in patients with heart failure and preserved left ventricular systolic function: failure of the Frank–Starling mechanism. J Am Coll Cardiol 1991;17(5):1065–72.
[26] Desai AS, Mitchell GF, Fang JC, Creager MA. Central aortic stiffness is increased in patients with heart failure and preserved ejection fraction. J Card Fail 2009;15(8):658–64.
[27] Sutton-Tyrrell K, Najjar SS, Boudreau RM, Venkitachalam L, Kupelian V, Simonsick EM, et al. Elevated aortic pulse wave velocity, a marker of arterial stiffness, predicts cardiovascular events in well-functioning older adults. Circulation 2005;111(25):3384–90.
[28] Ford ML, Tomlinson LA, Chapman TP, Rajkumar C, Holt SG. Aortic stiffness is independently associated with rate of renal function decline in chronic kidney disease stages 3 and 4. Hypertension 2010;55(5):1110–5.
[29] Laurent S, Boutouyrie P, Asmar R, Gautier I, Laloux B, Guize L, et al. Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. Hypertension 2001;37(5):1236–41.
[30] Dobrin PB, Baker WH, Gley WC. Elastolytic and collagenolytic studies of arteries. Implications for the mechanical properties of aneurysms. Arch Surg 1984;119(4):405–9.
[31] Bonapace S, Rossi A, Cicoira M, Golia G, Zanolla L, Franceschini L, et al. Aortic stiffness correlates with an increased extracellular matrix turnover in patients with dilated cardiomyopathy. Am Heart J 2006;152(1):93 [e1-6].
[32] Cachofeiro V, Miana M, de Las Heras N, Martín-Fernández B, Ballesteros S, Fernández-Tresguerres J, et al. Aldosterone and the vascular system. J Steroid Biochem Mol Biol 2008;109(3–5):331–5.
[33] Zelis R, Delea CS, Coleman HN, Mason DT. Arterial sodium content in experimental congestive heart failure. Circulation 1970;41(2):213–6.
[34] Safar ME, Thuilliez C, Richard V, Benetos A. Pressure-independent contribution of sodium to large artery structure and function in hypertension. Cardiovasc Res 2000;46(2):269–76.
[35] Kosar F, Aksoy Y, Ozguntekin G, Yetkin E, Gunen H. C-reactive protein and aortic stiffness in patients with idiopathic dilated cardiomyopathy. Echocardiography 2007;24(1):1–8.
[36] Vizzardi E, Cavazzana I, Pezzali N, Ceribelli A, Bazzani C, Tincani A, et al. Elastic properties of the ascending aorta in patients with rheumatoid arthritis. Int J Cardiol 2011;150(3):368–9.
[37] Stefanadis C, Stratos C, Boudoulas H, Kourouklis C, Toutouzas P. Distensibility of the ascending aorta: comparison of invasive and non-invasive techniques in healthy men and in men with coronary artery disease. Eur Heart J 1990;11(11):990–6.