European Journal of Radiology 99 (2018) 34–39

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Strain of ascending aorta on cardiac magnetic resonance in 1027 patients: Relation with age, gender, and cardiovascular disease

Marco Scarabello[a], Marina Codari[b], Francesco Secchi[b,*], Paola M. Cannaò[b], Marco Alì[c], Giovanni Di Leo[b], Francesco Sardanelli[b,d]

[a] Postgraduate School in Radiodiagnostics, Università degli Studi di Milano, Via Festa del Perdono 7, 20122, Milan, Italy
[b] Unit of Radiology, IRCCS Policlinico San Donato, Via Morandi 30, San Donato Milanese, 20097, Milan, Italy
[c] PhD Course in Integrative Biomedical Research, Department of Biomedical Sciences for Health, Università degli Studi di Milano, Via Mangiagalli, 31, 20133, Milano, Italy
[d] Department of Biomedical Sciences for Health, Università degli Studi di Milano, Via Morandi 30, 20097, San Donato Milanese, Italy

A R T I C L E I N F O

Keywords:
Magnetic resonance imaging
Ascending aorta
Tetralogy of Fallot
Ischemic heart disease
Aging

A B S T R A C T

Objectives: To evaluate ascending aortic strain (AAS) with cardiac magnetic resonance (CMR) in a large consecutive series of patients with different types of cardiovascular disease (CVD).

Methods: Two-dimensional phase-contrast gradient-echo sequences of the ascending aorta were retrospectively reviewed in 1027 patients (726 males, 301 females). Aortic lumen area was segmented using a semi-automatic approach to calculate AAS values. Subgroup analysis was performed for patients with normal CMR, tetralogy of Fallot (ToF), and ischemic heart disease (IHD). Multivariate and post-hoc analyses were performed to evaluate the effect of age, gender, and CVD on AAS values. Shapiro-Wilk, three- and two-way ANOVA, Mann-Whitney *U*, and Spearman correlation statistics were used.

Results: Multivariate analysis showed significant differences in AAS among decades of age ($p < 0.001$), genders ($p = 0.006$) and CVD subgroups ($p < 0.001$) without interaction among these factors. A gender-related difference (higher AAS in females) was significant in ToF ($p = 0.008$), while an AAS reduction during aging was observed in all CVD subgroups. Post-hoc analysis showed a significantly lower AAS in ToF and IHD patients compared to subjects with normal CMR ($p < 0.001$).

Conclusion: Differences in age, gender, and CVD independently affect AAS. The lower AAS observed in ToF fosters its assessment during follow-up in adulthood. Future studies on causes and clinical implications of a higher AAS in females affected by ToF are warranted.

1. Introduction

Arterial stiffness is one of the earliest manifestations of adverse structural and functional changes within the vessel wall. When the aorta is considered, stiffness is a main determinant of age-related systolic and pulse pressure increase, a major predictor of stroke and myocardial infarction, and has been associated with heart failure [1–3]. Pulse wave velocity measured by applanation tonometry is a well-known functional method to non-invasively quantify aortic stiffness providing an average measure of stiffness over a certain vessel length. Conversely, strain, compliance, and distensibility are local markers of arterial elasticity, which can be measured using magnetic resonance (MR) imaging, allowing the detection of more subtle changes in regional stiffness [4].

The use of MR imaging has several advantages over ultrasound imaging including three-dimensional visualization that allows to place the imaging plane perpendicular to the vessel with a high reproducibility. Thus, aortic distensibility can be measured as a change in two-dimensional vessel perimeter or area instead of one-dimensional vessel diameter [4]. Previous authors showed that ascending aortic strain (AAS) measured with cardiac MR (CMR) is markedly decreased before the fifth decade of life and that can be considered as an early manifestation of vascular aging [5]; AAS was also shown to be independently correlated with coronary atherosclerosis and coronary calcium content [6] as well as to be an independent predictor of progression toward hypertension in non-hypertensive subjects [7].

Our aim was to evaluate the AAS in a large consecutive series of patients who underwent CMR, comparing age classes, gender, and different types of cardiovascular diseases (CVD), also including subjects with normal CMR examinations.

Abbreviations: AAS, Ascending aortic strain; CMR, Cardiac magnetic resonance; CVDs, Cardiovascular diseases; ToF, Tetralogy of Fallot; IHD, Ischemic heart disease

* Corresponding author at: Unit of Radiology, IRCCS Policlinico San Donato, Via Morandi 30, San Donato Milanese, 20097, Milan, Italy.
E-mail address: francesco.secchi@grupposandonato.it (F. Secchi).

https://doi.org/10.1016/j.ejrad.2017.12.002
Received 20 July 2017; Received in revised form 16 November 2017; Accepted 5 December 2017

2. Materials and methods

2.1. Study design and population

The local Ethics Committee approved this retrospective study (Ethics Committee of the University Hospital San Raffaele; protocol code AS01; approved on April 7th, 2016) and informed consent was waived. Patients were selected from a database of CMR studies performed between September 2008 and August 2014 at the Radiology unit of the IRCCS Policlinico San Donato, San Donato Milanese, Italy. CMR examinations with an image quality that impairs AAS evaluation were excluded from analysis. Moreover, in the case of multiple CMR examinations in the same patient, only the first one was included.

2.2. Image acquisition

We retrospectively selected images acquired with two different 1.5 T machines. Magnetom Sonata Maestro Class (Siemens, Erlangen, Germany), was used to perform the studies from September 2008 to March 2014 (n = 1294); subsequent studies (n = 69) were performed using Magnetom Aera (Siemens, Erlangen, Germany). Retrospectively electrocardiographically (ECG)-gated breath-hold two-dimensional phase-contrast gradient recalled echo sequences with a through-plane velocity encoding gradient ranging from 150 to 350 cm/s were performed on a transverse plane above the aortic bulb. Sequence parameters were as follows: repetition time 49.75 ms, echo time 3.1 ms, flip angle 30° for Magnetom Sonata; 37.12 ms, 2.47 ms, 20° for Magnetom Aera. Parallel imaging with acceleration factor 2 and retrospective ECG-gating with 30 phases per cycle (with repetition time dependent on the R-R interval) were set on both machines.

2.3. Image analysis

Image post-processing was performed using Argus Flow software (Syngo Argus Flow, version 4.02, Siemens, Erlangen, Germany). Magnitude images were used to semi-automatically segment aortic contours in each cardiac phase. During the segmentation process, an expert cardiac radiologist with 2–7 years of experience in CMR selected the frame with the optimal contrast between aortic lumen and aortic wall. Then, the operator traced in the same frame the aortic contour, which was automatically propagated in all frames of the cardiac cycle and manually corrected when necessary.

The AAS was calculated as defined by Redheuil et al. [5], namely:

$$AAS = \frac{A_{max} - A_{min}}{A_{min}}$$

where A_{max} and A_{min} represent respectively the maximum and minimum aortic cross-sectional area measured during a single cardiac cycle.

2.4. Statistical analysis

The Shapiro-Wilk test was employed to assess normality of data distribution. Due to non-normal data distribution, descriptive statistics are provided as median and corresponding inter quartile range (IQR) values. To evaluate the influence of age, gender, and CVD on the AAS values, we performed a three-way ANOVA test. The log-transformation of the data was obtained to reach the condition of normal distribution needed to perform the tree-way ANOVA. Age was categorized into 7 age bins (0–9, 10–19, 20–29, 30–39, 40–49, 50–59 and ≥60 years). Moreover, post-hoc tests for CVD and age bin factors were performed.

After this global analysis, the statistical differences in AAS values were analysed in the larger subgroups, namely: subjects with normal CMR (i.e. unremarkable examination in subjects examined to exclude cardiac abnormalities), patients with Tetralogy of Fallot (ToF), and patients with ischemic heart disease (IHD). Taking into account only these types of CVD, the evaluation of AAS changes over all the selected age bins was not possible, due to the different age distribution of subjects affected by congenital (ToF) and age-related (IHD) CVD. Therefore, statistical inference on AAS trends over age was evaluated comparing ToF and IHD subjects only with normal CMR subjects. To this aim, the Mann-Whitney *U* tests was used for each age bin. On the other hand, to evaluate the influence of gender and CVD on AAS values, a two-way ANOVA was performed. Also in this case, log-transformation of the data was obtained to perform multivariate analysis. Finally, age was considered as a continuous variable and correlation between age and AAS values was estimated using Spearman correlation coefficient. Statistical significance level was set to $p < 0.050$ and the analysis was performed using SPSS (IBM Corporation, New York, NY, United States).

3. Results

A total of 1363 CMRs were retrieved; among them, 42 examinations were excluded due to an insufficient image quality. Moreover, in order to create homogenous CVD categories, we excluded disease subgroups composed of less than 10 subjects. For this reason, other 294 cases were excluded from the analysed sample.

The final number of analysed patients was 1027. Among them, 726 were men (median age 37 years, IQR18–60) and 301 were women (median age 34 years, IQR 16–54), with borderline significance between genders (p = 0.051). Fig. 1 shows age distribution between genders.

Taking into account all the analysed subjects, the median AAS value was 0.25 (IQR 0.17–0.38). Shapiro Wilks test showed that AAS data were not normally distributed ($p < 0.001$) The AAS resulted inversely correlated with age ($\rho = -0.51$, $p < 0.001$). Moreover, women showed a significantly (p = 0.006) higher AAS (median 0.28, IQR 0.20–0.41) compared to men (median 0.24, IQR 0.16–0.36). The results of the three-way ANOVA are shown in Table 1. Post-hoc analysis showed significant differences in AAS among all the age bins except for those between 30 and 49 years of age. Fig. 2 shows the AAS trend over decades of age, while results of post-hoc test for different CVD types and their corresponding descriptive statistics are presented in Table 2.

Of the total of 1027 cases, the major subgroups were represented by 192 subjects with normal CMR (128 men, 64 women; median age 36 years, IQR 18–51), 166 patients affected with IHD (132 men, 34 women, median age 64 years, IQR 58–71), and 92 patients affected with ToF (57 men, 35 women; median age 25 years, IQR 14–40). In all the three subgroups, there was no significant difference in terms of age between men and women (normal CMR, p = 0.997; IHD, p = 0.658, ToF: p = 0.361).

Multivariate analysis performed on the subsample composed by these three major subgroups showed significant differences in AAS values between genders (p = 0.002) and among CVD subgroups ($p < 0.001$), without interaction between CVD subgroups and genders (p = 0.119). In general, median AAS values were higher in women than in men, as can be seen in the boxplot represented in Fig. 3. However, post-hoc analysis showed a significant difference in AAS between men and women only for ToF patients (p = 0.008). Moreover, men with ToF showed a significantly lower AAS when compared with men with normal CMR (p = 0.005). In the other two subgroups, this difference appeared to be not significant within the analysed sample. No significant difference was found between genders in subjects with normal CMR (p = 0.728). In IHD patients, AAS was significantly lower compared to that of normal CMR subjects (men: $p < 0.001$, women: p = 0.016), without significant difference between genders (p = 0.732).

In subjects with normal CMR, the analysis of AAS trend over age showed an inverse correlation with age both in men ($\rho = -0.53$, $p < 0.001$) and women ($\rho = -0.54$, $p < 0.001$); AAS decreased with age also in IHD patients ($\rho = -0.16$, p = 0.039), this correlation remaining significant in women ($\rho = -0.40$, p = 0.021) but not in men ($\rho = -0.11$, p = 0.224). Evaluating AAS over decades of age, men