

# Evaluation of Aortic Flow Alterations using MRI: Associations with Left Ventricular Remodeling

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## Abstract

**Aims:** Evaluate ascending aorta (AA) flow alterations from MRI velocity data and their associations with age and LV remodeling, defined as LV-mass (LVM) divided by end-diastolic volume (EDV), in comparison with tonometric stiffness indices (pulse wave velocity (PWV) and reflection index (AIx)). **Methods:** For 70 healthy volunteers (46±15 years; 40 males), MRI LV cine data and through-plane AA velocity were used to assess LVM and EDV as well as late systolic morphological flow and velocity curves changes, such as a) time-interval required for deceleration to reach half of systolic peak, normalized by systolic deceleration time-interval (DT), b) decelerating slopes calculated using these timings and c) decrease in magnitude during half of DT, expressed in percentage of systolic peak. **Results:** While slopes were independent correlates of age ( $r>0.35$ ,  $p<0.002$ ) and AIx ( $r>0.40$ ,  $p<0.001$ ), magnitude ( $r>0.35$ ,  $p<0.002$ ) and timing ( $r>-0.39$ ,  $p<0.002$ ) indices were independently associated with LVM/EDV, after adjustment for age, gender, weight, height, heart-rate and systolic blood pressures. PWV was significantly associated with LVM/EDV ( $r=0.25$ ,  $p<0.04$ ) but did not remain significant after adjustment. **Conclusion:** Local indices of AA flow alterations are stronger correlates of LV remodeling than conventional indices of arterial stiffness.

## 1. Introduction

Arterial stiffness caused by physiological (aging) and is compounded by pathological causes (cardiovascular and metabolic disorders), is a well-established factor in cardiovascular diseases [1] and is considered as an independent predictor of cardiovascular events and mortality [2]. Proximal aorta which plays an immediate

role in buffering the flow originating from the heart is central in the process of left ventricular (LV)-aortic coupling in the pathways of normal aging. Accordingly, several studies focused on the characterization of aortic hemodynamics and their changes with age and pathology. Most of these studies were focused on pressure waveforms. Indeed, Murgu et al. [3] classified central pressure waveforms using as reflections timing and amplitude resulting in earlier occurrence of second systolic peak with aging. This qualitative observation resulted in quantitative indices of arterial stiffness and wave reflection such as augmentation index (AIx), which is defined as the ratio of the difference between central first and second pressure peaks and pulse pressure (PP).

Regarding flow waves, although their physiological usefulness in the evaluation of arterial system pulsatile characteristics was previously investigated throughout impedance estimation [4], the mechanisms of their variation with aging, arterial stiffness, and LV remodeling have not been fully investigated. This is because flow waves have been mainly estimated using invasive measurements or Doppler echocardiography measurements, which are based on the estimation of the flow envelope (highest particle flow), while ignoring the backward component. Previous works [5] explained flow changes in the ascending aorta (AA) using invasive data and more recently some non-invasive works in carotid artery, using Doppler Echocardiography, characterized velocity patterns [6, 7].

Accordingly, the purpose of this work was to focus on the AA local flow variations, which can be measured non-invasively and with high accuracy by velocity-encoded MRI along with an appropriate segmentation. Thus our aims were: 1) to quantify individual changes in AA velocity and flow waveforms, using MRI velocity data, 2) to investigate associations between these changes and age, reflections as well as LV remodeling.

## 2. Materials and methods

### 2.1. Population

We studied 70 healthy volunteers without history of cardiovascular disease ( $42.1 \pm 15.2$  years, 40 males) who underwent MRI and applanation tonometry exams on the same day. The study protocol was approved by the institutional review board and subjects signed an informed consent. Table 1 provides subjects' characteristics.

Table 1. Subject characteristics, central pressure measurements, LV-remodeling index

Subject Characteristics	
Age (years)	$42.1 \pm 15.2$
Weight (kg)	$68.7 \pm 10.8$
Height (cm)	$171.6 \pm 8.3$
Heart rate (beats/min)	$65.4 \pm 10.3$
Central Pressure	
Systolic pressure (mmHg)	$104.2 \pm 13.7$
Diastolic pressure (mmHg)	$68.3 \pm 10.3$
Stiffness Indices	
PWV ( $m \cdot s^{-1}$ )	$7.1 \pm 1.9$
LV parameter	
LVM/EDV ( $g \cdot ml^{-1}$ )	$0.9 \pm 0.2$

### 2.2. MRI and tonometric data

MRI was performed using a 1.5T magnet (Signa HDx, GEMS, Waukesha, WI, USA) with cardiac phased-array coil and ECG-gated sequences. LV Steady-state free precession (SSFP) cine and proximal aorta through-plane phase-contrast (PC) acquisitions were acquired in an axial view at the level of the bifurcation of the pulmonary trunk, perpendicular to the ascending and descending aorta. LV cine SSFP sequences were acquired in short axis views during breath-hold to cover the whole ventricle using standard clinical protocol. LV SSFP data were analyzed using QMass 6® software (Medis, the Netherlands) while semi-automatically tracing endocardial and epicardial borders on all contiguous short axis slices, resulting in LV end-diastolic (EDV) volume and mass (LVM). The LVM to EDV ratio was used as a measure of LV concentric remodeling index [8, 9].

For aortic flow measurements, a PC slice was acquired during breath-hold using a velocity encoding gradient in the through-plane direction. The scan parameters were: repetition time = 7.4 ms, echo time = 3.0 ms, flip angle =  $20^\circ$ , views per segment = 2, rectangular field-of-view = 50%, acquisition matrix =  $256 \times 128$ , pixel size =  $1.64 \text{ mm} \times 1.64 \text{ mm}$ , slice thickness = 8 mm, and encoding velocity = 200 cm/s. View sharing was used resulting in an effective temporal resolution of 15 ms.

Immediately after MRI acquisitions, applanation tonometry of carotid and femoral arteries was performed with the Pulse Pen device (Diatecne, Milano, Italy). The carotid pressure curve resulted from the average of several cardiac cycles after rescaling tonometric measurements with those obtained at the brachial artery within the magnet. Rescaling was based on the assumption that mean and diastolic blood pressures remain unchanged throughout the arterial tree [10] and was performed to account for differences in blood pressures inside and outside the magnet.

Carotid femoral pulse wave velocity (PWV) was calculated as the difference between the suprasternal notch-femoral and the carotid-suprasternal notch distances measured by means of a tape ruler over the body surface, divided by the transit time measured as the foot-to-foot interval between carotid and femoral pressure curves. Augmentation index of pressure (AIx) is a well-known reflection and stiffness index and was calculated as the difference between late systolic peak and inflection pressure divided by carotid pulse pressure, which is defined as the difference between systolic and diastolic carotid pressures [10].

### 2.3. AA flow waveforms analysis

First, a reproducible and fast segmentation was performed on PC-MRI modulus images using the ART-FUN software (UPMC software protection agency) [11]. The resulting contours were superimposed on PC-MRI velocity images providing time-varying AA flow velocity and volume curves.

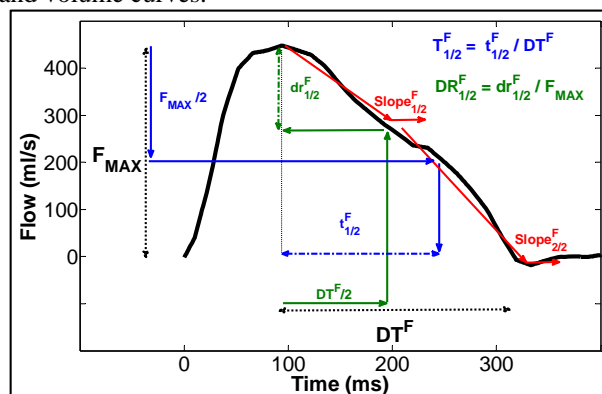


Figure 1. Systolic part of AA flow curve. Illustration of  $DR_{1/2}^F$ ,  $DT^F$ ,  $T_{1/2}^F$ ,  $Slope_{1/2}^F$  and  $Slope_{2/2}^F$  estimation. Velocity curve were analyzed similarly.

A software was designed and plugged on the ART-FUN software to analyze aortic velocity and flow waveforms and to derive indices reflecting their late systolic morphological changes (Figure 1). AA flow and velocity indices were: a) peak velocity ( $V_{MAX}$ ) and flow ( $F_{MAX}$ ), b) time-interval required for flow ( $T_{1/2}^F$ ) or velocity ( $T_{1/2}^V$ ) deceleration to reach half of systolic peak

amplitude, normalized by systolic deceleration time-interval ( $DT^F$  and  $DT^V$ ), and b) decrease in flow ( $DR^{F_{1/2}}$ ) or velocity ( $DR^{V_{1/2}}$ ) during half of systolic deceleration time-interval, expressed in percentage of systolic peak amplitude ( $F_{MAX}$  and  $V_{MAX}$ ) [7].

Half of systolic deceleration time-interval allows the definition of two parts of the late systolic down-slope which are linearly fitted to calculate two deceleration slopes: 1) slope from systolic peak to half deceleration resulted in  $Slope^{V_{1/2}}$  for velocity and  $Slope^{F_{1/2}}$  for flow, 2) slope from half deceleration to end-systole resulted in  $Slope^{V_{2/2}}$  for velocity and  $Slope^{F_{2/2}}$  for flow.

### 3. Results

#### 3.1. Associations with age and LV remodeling

Table 2 summarizes univariate and multivariate analyses of associations of conventional stiffness indices, velocity as well as flow indices with age and LVM/EDV while adjusting for confounding variables (see Table 2).

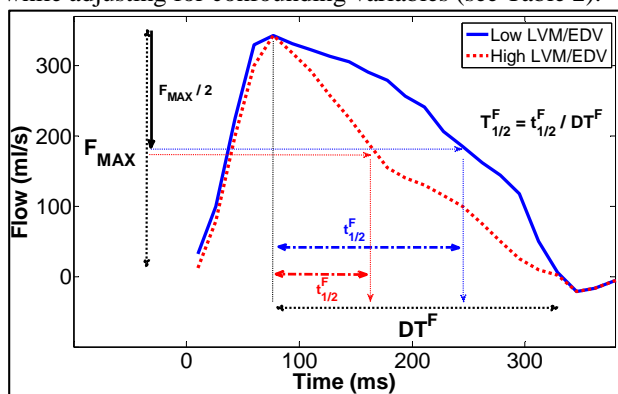


Figure 2. Systole part of flow curves from two subjects with low and high LVM/EDV ratio. Illustration of  $T_{1/2}^F$  decrease as LVM/EDV increases.

While conventional stiffness indices showed stronger independent associations with age compared with the newly proposed flow indices they were not independent correlates of LV remodeling. Indeed PWV was the only conventional stiffness index which was associated with LVM/EDV in univariate analysis but such association did not remain significant after adjustment. Interestingly, the majority of velocity and flow indices were independent correlates of LV remodeling index (Figure 2) with a slight superiority for flow-derived indices (Table 2).

#### 3.2. Associations with reflections

From the indices proposed by Miyashita [7] ( $T_{1/2}^V$ ,  $DR^{V_{1/2}}$ ,  $T_{1/2}^F$ ,  $DR^{F_{1/2}}$ ), only  $DR^{V_{1/2}}$  was associated with AIx ( $r=0.24$ ,  $p=0.04$ ) but this association did not remain

significant after adjustment for age. The newly proposed slopes were associated with AIx with a slight superiority for velocity-derived slopes ( $Slope^{V_{1/2}}$ :  $r=0.51$ ,  $Slope^{V_{2/2}}$ :  $r=0.64$ ,  $Slope^{F_{1/2}}$ :  $r=0.40$ ,  $Slope^{F_{2/2}}$ :  $r=0.56$ ,  $p<0.001$ ). These associations remained significant after adjustment for age, gender, height, weight and systolic blood pressures (SBP).

Table 2. Associations of stiffness indices, PC-MRI velocity and flow indices with age and LVM/EDV. Pearson correlation coefficients are provided. \*remained statistically significant after adjustment for gender, height, weight, systolic blood pressure (SBP) and heart rate. †remained significant after adjustment for the same parameters and age.

	<i>r</i>	Age	LVM/EDV
<b>Stiffness Indices</b>			
PWV		0.71*	0.25
AIx		0.64*	-
<b>Velocity</b>			
$DT^V$		0.30	-0.43†
$DR^{V_{1/2}}$		0.29*	0.35†
$T_{1/2}^V$		-	-0.39†
$Slope^{V_{1/2}}$		0.39*	-
$Slope^{V_{2/2}}$		0.58*	-
<b>Flow</b>			
$DT^F$		0.34	-0.41†
$DR^{F_{1/2}}$		-	0.44†
$T_{1/2}^F$		-	-0.46†
$Slope^{F_{1/2}}$		-	-0.25
$Slope^{F_{2/2}}$		0.35*	-

### 4. Discussion

The aorta has an important role in regulating pulsatile flow originating from the heart, providing steady flow to the peripheral vascular system. The interplay between aortic stiffness and systolic blood pressure elevation, suggests an association between stiffness and LV concentric remodeling [8]. While several studies focused on pressure waveform analysis to characterize central aortic hemodynamics, only few studies considered flow and velocity waveforms, mainly because of the lack of non-invasive central flow measurements. Among these few studies, Miyashita et al. [7] proposed Doppler velocity waveform indices which were shown to be associated with age. Such late-systolic magnitude indices were also estimated from our MRI data and were shown to be related to age and wave reflection. Consistent with previous findings our aortic velocities decreased with age [6] along with aortic dilation [8]. Such phenomenon induced age-related conservation of flow. Importantly the newly proposed end-systolic decelerating slopes were better correlates of wave reflection reflecting its ability to characterize central pressure-flow interactions. Besides

another original feature of our study is the investigation of associations of our flow and velocity indices with LV remodeling (LVM/EDV), while comparing against conventional stiffness indices. Such analysis indicated a differential physiological meaning of our indices. Indeed while slopes were independently associated to age and wave reflection, magnitude and timing waveform indices were independent correlates of LV remodeling, with a slight superiority for flow indices. One potential explanation of this latter finding might be the effect of the aortic recoil function which is by definition taken into account in flow, through area variation, but not in velocity data. Regarding conventional stiffness indices, they were as expected highly associated with age however their association with LV remodeling, in our database, was not further significant after accounting for age and systolic blood pressure. This surprising finding might be due to the fact that only asymptomatic healthy subjects were included in our data. Still it reveals the complementary nature of our newly proposed flow and velocity waveform indices for a better characterization of aortic-LV coupling.

In conclusion, it seems that alterations of velocity and flow curves at the late systolic period carry information about both reflection and LV concentric remodeling providing complementary information for the interaction between LV and aortic alterations to the already well-established aortic stiffness indices. Further research on aortic hemodynamic properties might extract useful information about load-related cardiovascular diseases alterations such as hypertension.

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## References

[1] Mitchell GF. Arterial stiffness and wave reflection: Biomarkers of cardiovascular risk. *Artery Res* 2009;3(2):56–64.

- [2] Laurent S, Boutouyrie P, Asmar R, et al. Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. *Hypertens* 2001;37(5):1236–41.
- [3] Murgo JP, Westerhof N, Giolma JP, Altabelli SA. Aortic input impedance in normal man: relationship to pressure wave forms. *Circ* 1980;62(1):105–16.
- [4] Nichols WW, Denardo SJ, Wilkinson IB, McEniery CM, Cockcroft J, O'Rourke MF. Effects of arterial stiffness, pulse wave velocity, and wave reflections on the central aortic pressure waveform. *J Clin Hypertens* 2008;10(4):295–303.
- [5] O'Rourke MF, Avolio AP. Pulsatile flow and pressure in human systemic arteries. Studies in man and in a multibranched model of the human systemic arterial tree. *Circ Res* 1980;46(3):363–72.
- [6] Hirata K, Yaginuma T, O'Rourke MF, Kawakami M. Age-related changes in carotid artery flow and pressure pulses: possible implications for cerebral microvascular disease. *Stroke* 2006;37(10):2552–6.
- [7] Miyashita H, Ikeda U, Tsuruya Y, Sekiguchi H, Shimada K, Yaginuma T. Noninvasive evaluation of the influence of aortic wave reflection on left ventricular ejection during auxotonic contraction. *Heart Vessels* 1994;9(1):30–9.
- [8] Redheuil A, Yu W-C, Mousseaux E, et al. Age-related changes in aortic arch geometry: relationship with proximal aortic function and left ventricular mass and remodeling. *J Am Coll Cardiol* 2011;58(12):1262–70.
- [9] Cheng S, Fernandes VRS, Bluemke DA, McClelland RL, Kronmal RA, Lima JAC. Age-related left ventricular remodeling and associated risk for cardiovascular outcomes / CLINICAL PERSPECTIVE. *Circ Cardiovasc Imaging* 2009;2(3):191–8.
- [10] Laurent S, Cockcroft J, Van Bortel L, et al. Expert consensus document on arterial stiffness: methodological issues and clinical applications. *Eur Hear J* 2006;27(21):2588–605.
- [11] Herment A, Kachenoura N, Lefort M, et al. Automated segmentation of the aorta from phase contrast MR images: Validation against expert tracing in healthy volunteers and in patients with a dilated aorta. *J Magn Reson Imaging* 2010;31(4):881–8.

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