Estimation of Aortic Pulse Wave Transit Time in MRI using Complex Wavelet Cross-spectrum Analysis

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Abstract

Aortic pulse wave velocity (PWV) increases with arterial stiffness and aging and predicts cardiovascular mortality. It is commonly estimated using applanation tonometry at carotid and femoral arterial sites (cfPWV). Although cardiovascular MRI offers reliable segmental measurement of arterial length, accurate transit time (TT) determination between flow curves remains a challenge. We developed a wavelet-based method, which enables temporal localization of signal frequencies, to estimate TT by the weighted phase difference between ascending and descending aorta flow curves. We compared this approach in terms of linear correlations with age, cfPWV and effects of decreasing temporal resolution by factors of 2, 3 and 4, with previous methods which 1) restrict their analysis to systolic upslope (time domain upslopes-archPWV$_{TU}$) and 2) decompose into harmonics flow curves from the whole cardiac cycle (Fourier-based-archPWV$_F$-robust to low temporal resolution). We studied 71 healthy subjects (45±15 years, 29 females) who underwent MRI velocity acquisitions and cfPWV measurements. Wavelet method provided the highest linear correlations with age and cfPWV and was the most robust to low temporal resolutions. Wavelet method might help to overcome current limitations related to MRI low temporal resolution.

1. Introduction

Aortic stiffness through interplay between causal and aggravating factors is associated with cardiovascular mortality [1], as well as changes in aortic hemodynamics. Accordingly, the analysis of non-invasive carotid and femoral pressure curves has been proposed to estimate stiffness indices among which carotid-femoral pulse wave velocity (cfPWV), which was shown to increase substantially with aging and to predict cardiovascular events and mortality [2].

Recently, with the excellent MRI anatomical and functional aortic coverage, MRI aortic arch PWV (archPWV) can be calculated as the ratio between the length of an aortic segment and the transit time required by the flow wave to travel along this segment. A crucial advantage of MRI is its specific accuracy in the estimation of the arterial length travelled by the pulse wave. However, regarding transit time (TT) estimation, no consensual method has been chosen as the reference yet. This is mainly due to technical issues inherent to MRI, such as: 1) the relatively low temporal resolutions compared to tonometric techniques, 2) the time varying velocity-to-noise ratio caused by a fixed encoding velocity throughout the cardiac cycle, 3) the changes in late systolic flow waveform due to wave reflections [3] and to backward flow [3,4]. Consequently, many different TT estimation approaches from MRI flow have been proposed. These methods either analyze the whole cardiac cycle [5] or restrict their analysis only to the systolic upslope part [4]. Methods from the former category have been shown to be robust to relatively low temporal resolution, especially when TT is estimated by the phase difference between ascending (AA) and descending (DA) aortic harmonic components [5]. Methods from the latter category successfully avoid major effects of reflections and backward flow usually present in late systolic part of the flow curves. Accordingly, our aim was to develop a time-scale method, based on complex wavelet analysis, which enables temporal localization of phase difference between harmonics and thus, a proper restriction of the analysis to the systolic upslope. Then, using the same aortic length, archPWV resulting from the wavelet method was compared with the archPWV obtained using time domain upslope-to-upslope [4] and Fourier-based [5] methods, in terms of associations with: (i) age and (ii) tonometric cfPWV. Furthermore, the effect of temporal resolution on the three archPWV methods was evaluated using time under-sampled AA and DA flow curves.

2. Methods

2.1. Data acquisition

We studied 71 healthy volunteers (45 ± 15 years, 29 females) from two research centers using different CMR scanners (GE, 1.5T-36 individuals and Siemens, 3.0T-35 individuals). They underwent aortic MRI and carotid–femoral PWV as well as pressure measurements. The study protocols were approved by institutional review boards and all subjects gave written informed consent.

Axial and coronal SSFP MRI data were used for anatomical characterization of the aortic arch. Through-plane phase contrast (PC) images of the proximal aorta were acquired in a single axial view at the level of the bifurcation of the pulmonary trunk, perpendicular to both the AA and DA to simultaneously measure flow. For the GE scanner, scan parameters were: repetition time = 7.4 ms, echo time = 3.0 ms, flip angle = 20°, views per segment = 2, rectangular field-of-view = 50%, acquisition matrix = 256 × 128, pixel size = 1.64 × 1.64 mm², slice thickness = 8 mm, and encoding velocity = 200 cm/s. View sharing was used resulting in a temporal resolution of 15 ms. For the Siemens scanner, the scan parameters were: repetition time = 5.8 ms, echo time = 2.0 ms, flip angle = 30°, view per segment = 1, rectangular field-of-view = 75%, acquisition matrix = 192 × 192, pixel size = 1.5 × 1.5 mm², slice thickness = 5.5 mm, and encoding velocity = 150 cm/s, number of phases per cardiac cycle was fixed to 60 phases and average temporal resolution, 20 ms. Simultaneously to aortic MRI acquisitions, brachial pressures were measured using an oscillometric device (Vital Signs Monitor, Welch Allyn Inc, US).

Immediately after aortic MRI, pressure variations from right carotid and right femoral arteries were measured using applanation tonometry (for site 1: Pulse Pen device, Diatecne, Italy, for site 2: VP-2000, Colin Corp, Japan). cfPWV was assessed as the ratio of the difference between the suprasternal notch to femoral and the carotid to suprasternal notch distances measured by means of a tape ruler over the body surface, to the TT measured as the foot-to-foot interval between the carotid and femoral pressure waveforms [3]. Recorded carotid pressure curves were calibrated as previously proposed [3] using the brachial mean and diastolic blood pressures measured during MRI velocity acquisitions. Carotid systolic (SBP) and diastolic (DBP) blood pressure as well as the pulse pressure (PP) were recorded.

Aortic arch length was measured three-dimensionally from sagittal oblique SSFP or dark blood T1 acquisitions as described in [4]. The 3D approach was used to take into account possible tortuosity of the aortic arch [4].

AA and DA aortic lumen borders were automatically detected by a reproducible and fast segmentation on PC-MRI modulus images using the ART-FUN software (UPMC, Laboratoire d'Imagerie Biomédicale) [6]. The resulting contours were then superimposed on PC-MRI velocity images providing time-varying AA and DA flow curves.

2.2. Transit time (TT) estimation

Methods for transit time estimation between AA and DA flow curves were developed using Matlab software (Matlab 2013, The Mathworks, Natick, MA).

Time domain method: after automatic foot and systolic peak detections, previously proposed upslope method [4] estimates TT-TU as the time shift minimizing the error between normalized AA and DA systolic upslopes.

Fourier-based method: The Fourier-based group delay method [5] was used to estimate TT-F between AA and DA flow curves in the frequency domain by the harmonics' phase. TT-F was expressed as the weighted average of harmonics phase differences.

Wavelet-based method: This analysis enables temporal localization of harmonic components of AA and DA flow curves. While in Fourier-analysis signals are represented as sine wave components, in wavelet analysis, signals are represented as covariance with a set of functions derived from the scaled and shifted versions of an initial function named "mother wavelet" providing a time-scale distribution (Figure 1). In our case, complex Gaussian curve is used as a "mother wavelet". Scales corresponding to frequency components ≥ 10Hz were excluded in order to minimize the effect of noise lying in high frequencies [7]. Then, complex cross spectrum of AA and DA wavelet transforms was calculated and the derived time-scale map was restricted to the systolic upslope $\tau \in [\mathrm{Tfoot}, \mathrm{Tpeak}]$ (Figure 1). Systolic foot (Tfoot) and systolic peak (Tpeak) were automatically detected as in [4]. Then, similar to Fourier method, group delay was estimated by the weighted phase differences over harmonics ≤ 10 Hz, expressed in seconds.

For all TT estimates, archPWV was calculated as the ratio between aortic arch length and the estimated TT between AA and DA curves, resulting in $\mathrm{archPWV}_{TU}$, $\mathrm{archPWV}_{F}$, and $\mathrm{archPWV}_{WU}$ for the time (TU) and frequency (F) domain approaches as well as for the wavelet approach (WU), respectively. Of note, the same arch length was used for the three archPWV estimates and TT estimation was fully automated and thus reproducible for the three techniques.

To study the effect of temporal resolution, time points of AA and DA flow curves were averaged by blocks of 2, 3, or 4 as previously proposed [8]. Afterwards, the averaged flow curves were used to estimate $archPWV_{TU}$, $archPWV_F$ and $archPWV_{WU}$ after estimating TT as described on the original AA and DA flow curves.

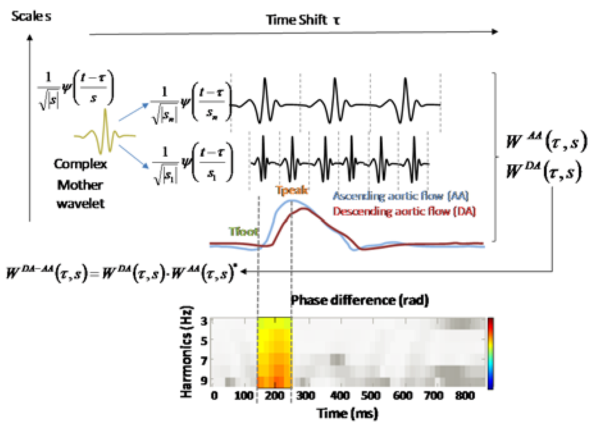

Figure 1. Complex wavelet decomposition of AA and DA flow curves, and estimation of phase difference through complex wavelet spectrum restricted to upslope.

Associations with age and the reference cfPWV were studied using linear regression and correlation coefficients were provided for archPWV estimated from original and averaged AA and DA curves. To further study the effect of temporal resolution, archPWV estimated from averaged curves was compared to archPWV estimated from original curves. Statistical analysis was performed using STATA/IC 12.0 software.

3. Results

Individuals' description including basic characteristics, central arterial hemodynamics, aortic arch length and cfPWV are summarized in Table 1.

Table 1.Individuals' characteristics.

	Total (n=71)
Age (years)	44.9 ± 14.8
BMI ($kg.m^{-2}$)	23.8 ± 3.9
Carotid SBP (mmHg)	108.8 ± 19.3
Carotid DBP (mmHg)	71.2 ± 12.2
Carotid PP (mmHg)	37.6 ± 11.3
Aortic length (cm)	11.9 ± 2.2
cfPWV ($m.s^{-1}$)	7.8 ± 2.4

Table 2 summarizes the average values of archPWV for all methods in individuals <50 years and individuals ≥50 years. As expected, archPWV provided by all methods were significantly higher in subjects ≥50 years ($p<0.001$). Moreover, values from upslope methods ($archPWV_{WU}$, $archPWV_{TU}$) were in the same range while $archPWV_F$ resulted in higher values for both age groups, with more pronounced difference for individuals ≥50 years. Interestingly, Fourier-based method ($archPWV_F$) resulted in more dispersed values among elderly individuals, sometimes even higher than cfPWV.

Table 2. archPWV from all methods for two age groups

Age	$archPWV_{WU}$	$archPWV_{TU}$	$archPWV_F$
<50 (n=44)	4.1±1.5m/s	4.4±1.2m/s	5.5±3.1m/s
≥50 (n=27)	7.8±2.2m/s	8.1±2.7m/s	11.7±6.2m/s

While all estimated archPWV values increased significantly with age, the wavelet-based PWV ($archPWV_{WU}$) resulted in the highest correlation with age ($r=0.84$, $p<0.001$), compared to both the time-based ($archPWV_{TU}$: $r=0.74$, $p<0.001$) and the Fourier-based methods ($archPWV_F$: $r=0.63$, $p<0.001$) (blue column in Figure 2A). Regarding associations with cfPWV, the highest correlations were found for the upslope techniques whether estimated using wavelets or in time domain ($r=0.58$, $p<0.001$ for both).

After artificial slight decrease in temporal resolution (averages by blocks of 2), archPWV from all methods remained unchanged in terms of associations with age and cfPWV. However, after more pronounced lowering of temporal resolution (averages by blocks of 3 and 4), while the time-based method was strongly affected, associations against age and cfPWV for archPWV based on wavelet and Fourier analysis remained fairly unchanged (Figure 2).

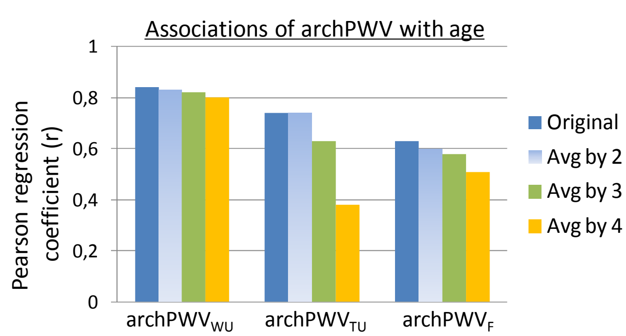

Figure 2. Associations of archPWV estimated from original and averaged curves with age.

Of note, no differences according to the MRI scanner or imaging center were found in our data.

4. Discussion-conclusion

In this study, a new method for arch TT estimation from AA and DA MRI flow curves (and thus for archPWV determination) was developed and tested in 71 individuals. This time-scale analysis allows identifying phase differences of low, medium and high harmonic components which occur during the systolic upslope, in order to avoid wave reflections effects. TT calculation was inspired by the idea of group delay previously presented by Meloni et al [5], which relies on the weighted average of phase differences. The proposed method was shown to be more robust than Fourier-based approach [5], as well as the time domain upslope method [4], in terms of associations with age and cfPWV. It is also less affected by low temporal resolution.

Pulse wave velocity measurements obtained by the wavelet-based technique were consistent with those previously reported using time domain methods ($archPWV_{TU}$) in terms of magnitude [4]. Regarding Fourier-based method, which takes into account the flow curves throughout the whole cardiac cycle, $archPWV_F$ showed significantly higher values that sometimes were higher than cfPWV, which is not consistent with physiological knowledge since PWV is expected to increase towards periphery. These erroneous estimates are more pronounced in elderly subjects probably due to the presence of wave reflections and late systolic backward flow which might significantly modify the time shift between AA and DA curves, as compared to the time-shift observed in early systole.

The time domain method failed to robustly estimate archPWV after significant reduction in temporal resolution (averaging by blocks of 3 or 4), because the number of available points characterizing the curve upslope decreases drastically and the estimation of time-shift optimizing curves overlap becomes more unstable and prone to sampling error. On the other hand, both decomposition methods (Fourier, wavelets) were highly robust to lower temporal resolution (Figure 2) corroborating the findings of Meloni et al [5]. Indeed, for both methods, even after averaging by blocks of 4, low frequencies which contain the majority of the flow curve energy are included in the TT measurement. Of note, when compared to Meloni et al [5] method, the advantage of the wavelet approach is its ability to focus the analysis on the upslope of the flow curve.

In conclusion, methods estimating TT from MRI aortic flow curves, focusing only on systolic upslopes, result in stronger correlations with age and cfPWV as compared to the Fourier-based approach which takes into account the entire cardiac cycle. In addition, while the effect of low temporal resolution was minor for methods based on the harmonic decomposition of AA and DA flow curves, it was more prominent for the time domain method. The method proposed in this study combines both advantages coming from harmonic decomposition and restriction to systolic upslope. Thanks to its robustness to low temporal resolution, the wavelet-based approach can be of major usefulness for the analysis of MRI derived 4D flow data in the aortic arch.

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