Aortic reflection coefficients and their association with global indexes of wave reflection in healthy controls and patients with Marfan’s syndrome

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Early return of reflected pressure waves increases the load on central arteries and may increase the risk of aortic rupture in patients with Marfan’s syndrome (MFS). To assess whether wave reflection is elevated in MFS, we used ultrasound and MRI to measure central pressure and flow waveforms in 26 patients (13–54 yr of age) and 26 age- and gender-matched controls. Aortic systolic and diastolic cross-sectional areas were measured at the ascending and descending aorta (AA and DA), diaphragm (DIA), and lower abdominal aorta (AB). From these measurements, local characteristic impedance (Z0,local) and local reflection coefficients (Γx,y) were calculated. Calculated global wave reflection indexes were the augmentation index (AIx) and the ratio of backward to forward pressure wave (Pb/Pf). The aorta was wider in MFS patients at AA (P < 0.01) and DA (P < 0.01). Aortic pulse wave velocity was 42 cm/s higher in MFS patients (P < 0.05). Z0,local was not different between groups, except at DA, where it was lower in MFS patients. In controls, ΓAA-DA was 0.31 ± 0.08, ΓDA-DIA was 0.00 ± 0.11, and ΓDIA-AB was 0.31 ± 0.16. Mean values of Γx,y were not different between MFS patients and controls. In controls, aging diminished ΓAA-DA but increased ΓDIA-AB. Clear age-related patterns were absent in MFS patients. AIx or Pb/Pf was not higher in MFS patients than in controls. There were indications for enhanced wave reflection in young MFS patients. Our data demonstrated that the major determinants of AIx were pulse wave velocity and the effective length of the arterial system and, to a lesser degree, HR and Pf/Pf.

THE PROPAGATION AND REFLECTION of pressure and flow waves along the arterial tree have been the subject of early fundamental biofluid mechanical research, but it was only in the early 1980s that the pathophysiological effect of pressure wave reflection was most clearly demonstrated by Murgo et al. (13). Early return of reflected waves boosts systolic pressure and presents an extra load for the heart and central vessels (15, 22, 24).

In the past few years, the study of arterial wave reflection has reached the medical/clinical community, mainly because of the effort of Kelly and colleagues (9), who developed the “augmentation index” (AIx). This easy-to-use index can be derived from central pressure (or diameter) waveforms and formally quantifies the wave contour classification scheme of Murgo et al. (13) and O'Rourke and co-workers (16). Because AIx is a composite index, its interpretation is not always straightforward. It is dependent not only on the magnitude of wave reflection (the reflection coefficient), but also on the time delay between the forward and the reflected wave. As such, AIx is also determined by body stature, stiffness of the aorta (aortic pulse wave velocity (PWV)), and even heart rate (HR).

Early return of reflected pressure waves from the peripheral arteries, has been reported in MFS patients (4, 5, 8). MFS primarily affects the proximal part of the aorta (6) and may change the gradual proximal-to-distal evolution of the mechanical properties of the aorta and give rise to reflections originating from an “impedance mismatch” along the aorta. MFS patients are, in general, taller than the normal population (one of the visual landmarks of the disease), and their height affects the distance to reflection sites. It has been suggested that the global wave reflection coefficient may be elevated in MFS patients (25).

Local reflection coefficients along the aorta will be assessed through calculation of changes in characteristic impedance (Z0) along the vessel, with Z0 estimated from MRI recordings of the systolic and diastolic cross-sectional area at different levels along the aorta. Global reflection will be estimated via AIx and linear wave separation analysis. The ratio of the amplitude of the backward (Pb) to the forward (Pf) wave (Pb/Pf) will be used as an estimate of the global reflection coefficient (24). The in vivo data should thus provide local aortic reflection coefficients and have the potential to reveal a possible relation between local reflection along the aorta and the global wave reflection indexes, such as AIx and Pb/Pf.
WAVE REFLECTION IN MARFAN’S SYNDROME

Table 1. Population characteristics and general hemodynamic data

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>MFS</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>M/F</td>
<td>12/14</td>
<td>12/14</td>
<td>1.00</td>
</tr>
<tr>
<td>Age, yr</td>
<td>35.5 ± 11.8 (14–60)</td>
<td>32.7 ± 11.5 (13–54)</td>
<td>0.37</td>
</tr>
<tr>
<td>Height, m</td>
<td>1.73 ± 0.11 (1.52–1.93)</td>
<td>1.83 ± 0.10 (1.72–2.10)</td>
<td>0.001</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>67.0 ± 13.0 (50–95)</td>
<td>75.4 ± 14.3 (47–105)</td>
<td>0.03</td>
</tr>
<tr>
<td>BSA, m²</td>
<td>1.80 ± 0.21 (1.53–2.16)</td>
<td>1.98 ± 0.20 (1.56–2.36)</td>
<td>0.003</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>62.6 ± 8.2 (48–80)</td>
<td>61.6 ± 8.6 (47–80)</td>
<td>0.68</td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>84.4 ± 9.4 (65.6–103.6)</td>
<td>84.8 ± 9.35 (68.8–107.5)</td>
<td>0.87</td>
</tr>
<tr>
<td>SBPca, mmHg</td>
<td>104.8 ± 11.8 (83.3–127.5)</td>
<td>106.4 ± 11.7 (87.8–142.8)</td>
<td>0.64</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>67.0 ± 10.0 (52.5–90.4)</td>
<td>61.8 ± 10.0 (41.2–78.9)</td>
<td>0.07</td>
</tr>
<tr>
<td>SV, ml</td>
<td>78.9 ± 22.4 (48.8–128.0)</td>
<td>82.0 ± 27.4 (33.3–149.9)</td>
<td>0.67</td>
</tr>
<tr>
<td>CO, l/min</td>
<td>5.2 ± 1.2 (3.0–7.4)</td>
<td>4.9 ± 1.4 (2.4–7.8)</td>
<td>0.51</td>
</tr>
</tbody>
</table>

Values are means ± SD, with range in parentheses; n = 26 in each group.

MFS, Marfan’s syndrome; M, male; F, female; BSA, body surface area; DBP, diastolic blood pressure; SBPca, carotid artery, systolic blood pressure; MAP, mean arterial pressure; HR, heart rate; SV, stroke volume; CO, cardiac output.

P values are results from t-test analysis of control vs. MFS patients.

MATERIALS AND METHODS

The study population consisted of 26 patients with confirmed MFS (13–54 yr of age) and 26 age- and gender-matched controls (Table 1). All MFS patients and controls underwent a 1-day measurement protocol, including MRI and echocardiography for the assessment of systolic and diastolic dimensions of the aorta at different levels, as well as central pressure and flow waveforms. This study was approved by the ethical committee of the Ghent University Hospital, and all subjects gave informed consent to participate in the study.

MRI: PWV, aortic dimensions, and local reflection coefficients. All MFS patients and controls were scanned on a 1.5-T magnetic resonance system (Magnetom Symphony, Siemens, Erlangen, Germany) with ECG gating. Aortic systolic and end-diastolic cross-sectional areas [A_s(x) and A_d(x)] were measured using trueFISP images (fast imaging with steady-state precession, temporal resolution of 25 ms, and spatial resolution of 1.33 mm/pixel in x and y direction) obtained at four levels (indicated by x) along the aorta:

- Ascending aorta (AA)
- Descending aorta (DA)
- Diaphragm (DIA)
- Lower abdominal aorta (AB)

Assessing central blood pressure waveforms. Central blood pressure waveforms were obtained via calibration of the common carotid artery diameter distension waveforms (Fig. 2) (17). With the subject in the supine position, a sequence of common carotid artery diameter distension traces typically containing three to five complexes was measured with a commercially available ultrasonographic system (Vivid 7, GE Vingmed Ultrasound, Horten, Norway) and a 12-MHz vascular probe (model 12L). The trace was averaged to obtain one representative waveform, which was subsequently transformed into a carotid artery pressure waveform (20), which was further used as a

Fig. 1. A: MRI of the aorta used to assess distance between the 4 aortic measuring locations: ascending aorta (AA), descending aorta (DA), diaphragm (DIA), and lower abdominal aorta (AB). B: measured normalized flows at AA, DA, DIA, and AB, with indication of the moment when half-peak flow is reached. AU, arbitrary units. C: plot of distance traveled by the propagating flow front as a function of this time; slope of regression line yields aortic pulse wave velocity (PWV, cm/s).
The aortic flow waveform is further indicated as $Q_{ao}$. Cardiac output was obtained as the product of SV and HR. It was verified that HR (5 beats/min) during MRI and ultrasound measurement was constant.

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**RESULTS**

The MFS patients were taller, with greater body weight and body surface area than controls (Table 1). There was no difference between MFS patients and controls for age, body mass index, brachial and central blood pressure, HR, SV, and cardiac output. General hemodynamic data and patient characteristics are summarized in Table 1. Mean ages were 22.7 ±...
higher in MFS patients than in controls (ascending aorta, the progression of dilatation with age was significantly higher in MFS patients and controls (Fig. 3). The evolution of aortic cross-sectional area progressively increased with age in controls and decreasing in MFS patients (Fig. 3). The difference was statistically significant in tertile 3 (P < 0.05).

Local reflection coefficients are displayed as a function of age in Fig. 3. In the control population, a positive reflection coefficient was found: $\Gamma_{AA-DA}$ was, on average, 0.31 ± 0.08. In the midaortic region, $\Gamma_{DA-DIA}$ was close to zero, whereas the most distal reflection coefficient, $\Gamma_{DIA-AB}$, was again positive (0.31 ± 0.16). When analyzed as a function of age, $\Gamma_{AA-DA}$ increased with age (P < 0.05), whereas $\Gamma_{DA-DIA}$ increased with age (P < 0.05). For the MFS patients, a similar global pattern was observed, with a positive proximal and distal reflection coefficient and no reflection in the midaortic region. In contrast with the control population, no correlation with age was found in any segment. By simple t-test analysis, it was determined that there were no differences in $\Gamma_{AA-DA}$ between controls and MFS patients. With use of ANOVA, a marginal difference between controls and MFS patients was found for $\Gamma_{AA-DA}$ (P = 0.049), with a lower reflection coefficient in the MFS patients.

Global reflection: AIX and distance to reflection site. AIX was, on average, virtually identical in controls and MFS patients: 102.1 ± 15.0 vs. 103.3 ± 10.6% (P = 0.75). When the data were displayed as a function of age (Fig. 4A), AIX tended to be higher in MFS patients than in controls in tertile 1 and lower in MFS patients than in controls in tertile 3, but the differences were not statistically significant. PWV was 486 ± 110 and 519 ± 100 cm/s in controls and MFS patients, respectively (P = 0.27 (not significant) by t-test). ANOVA, however, indicated a significant offset, estimated to be 42 cm/s, between both groups (P = 0.03; Fig. 4C). $\Delta T_f - b$ was not different between controls and MFS patients (0.165 ± 0.033 vs. 0.170 ± 0.039 s, P = 0.70). $\Delta x$, on the other hand, was shorter in controls than in MFS patients: 38.7 ± 6.0 vs. 43.4 ± 9.3 cm (P < 0.05). Data split per tertile of age is shown in Fig. 4D.

### Table 2. Aortic cross-sectional area in systole and diastole, local characteristic impedance along the aorta, and local reflection coefficients

<table>
<thead>
<tr>
<th></th>
<th>$A_{AS10}$, cm$^2$</th>
<th>$A_{ASD}$, cm$^2$</th>
<th>$Z_0$, mmHg·m$^{-1}$·s</th>
<th>$\Gamma_{xx-yy}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA</td>
<td>Control</td>
<td>MFS</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>6.34 ± 1.53</td>
<td>4.89 ± 1.32</td>
<td>0.065 ± 0.019</td>
<td>0.31 ± 0.08</td>
</tr>
<tr>
<td></td>
<td>DA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>MFS</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.44 ± 0.95</td>
<td>2.77 ± 0.85</td>
<td>0.127 ± 0.030</td>
<td>0.05 ± 0.08</td>
</tr>
<tr>
<td></td>
<td>AA-DA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>MFS</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.84 ± 0.91</td>
<td>1.43 ± 0.86</td>
<td>0.264 ± 0.111</td>
<td>0.31 ± 0.16</td>
</tr>
<tr>
<td></td>
<td>AA-DA</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SD. $A_{AS10}$ and $A_{ASD}$, cross-sectional area in systole and diastole; $Z_0$, local characteristic impedance; $\Gamma_{xx-yy}$, local reflection coefficient; AA and DA, ascending and descending aorta; DIA, thoracic abdominal aorta near the diaphragm; AB, lower abdominal aorta. *P < 0.05; †P < 0.01 vs. control.

4.6, 34.6 ± 4.7, and 49.5 ± 4.8 yr in tertiles 1, 2, and 3, respectively.

Aortic dimensions, $Z_0$, and local reflection coefficients. Population-averaged cross-sectional area measured at four levels along the aorta are given in Table 2. On average, the aorta was significantly wider in MFS patients than in controls at the two most proximal measuring locations: AA (P < 0.01) and DA (P < 0.01). To better appreciate the evolution of aortic size with age, data are also plotted as a function of age in Fig. 3. Aortic cross-sectional area progressively increased with age in MFS patients and controls (P < 0.01) at all levels. For the ascending aorta, the progression of dilatation with age was higher in MFS patients than in controls (P < 0.05), leading to a significantly higher aortic cross-sectional area in tertile 3 ($P < 0.05$).

$Z_0$ was similar at the ascending aorta and the two most distal locations and significantly lower in MFS patients for the descending aorta ($P < 0.05$; Table 2). For the lower abdominal aorta, the evolution of $Z_{AB}$ with age is significantly different between the two groups ($P < 0.01$), increasing with age in controls and decreasing in MFS patients (Fig. 3). The difference was statistically significant in tertile 3 ($P < 0.05$).

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Global reflection: linear wave separation ($P_b/P_f$). Input impedance derived from $P_{ao}$ and $Q_{ao}$ is plotted in Fig. 5. There were no differences between controls and MFS patients for any of the harmonics. $Z_0$ estimated from central pressure and flow was $0.091 \pm 0.051$ and $0.104 \pm 0.056$ mmHg·ml$^{-1}$·s in controls and MFS patients, respectively ($P = 0.39$ (not significant)]. There was no difference in $P_b/P_f$ between MFS patients and controls: $0.45 \pm 0.08$ vs. $0.47 \pm 0.09$ ($P = 0.44$; Fig. 4B).

Determinants of $AI_x$. To assess the relative importance of the major determinants of $AI_x$, multiple linear regression analysis (stepwise forward model) was performed with age, gender, central blood pressure (SBP, DBP, and MAP), SV, HR, height, patient or control, PWV, $P_t$, $P_s$, $P_b/P_f$, $\Delta x$, and the three local reflection coefficients as possible determining independent factors. The model obtained was as follows: $AI_x = 104.13 + 0.097PWV - 0.977\Delta x - 0.327HR + 24.00P_b/P_f$ ($r^2 = 0.80$, with PWV in cm/s, $\Delta x$ in cm, and HR in beats/min). The parameters are displayed in the order of their relative importance, PWV being the most important contributor. Table 3 displays the standardized $\beta$-coefficients and statistical significance of the different contributors and the increase in predictive value of the model ($r^2$) on additional inclusion of the parameter into the model. Local reflection coefficients did not contribute to the model.

DISCUSSION

The major findings of this study can be summarized as follows: 1) The morphological and functional changes in the (proximal part of the) aorta in MFS patients do not lead to a change in local aortic $Z_0$. 2) In controls, aging appears to diminish the local reflection coefficient in the proximal aorta,
controls, the age-related increase in lower abdominal aorta, opposite changes were observed. In 4) The major determinants of AIx are PWV and global wave reflection in young MFS patients. Nevertheless, there are indications for elevated wave reflection in young MFS patients. 4) The major determinants of AIx are PWV and Δx and, to a lesser degree, HR and Pb/Pf.

Consistent with common knowledge (4, 6, 8), we found that the aorta was widened in MFS patients at the ascending and descending levels only. In controls and MFS patients, aortic enlargement with age was observed at all levels (Fig. 4). Enlargement appeared to progress at the same rate, except at the ascending aorta, where aortic dilatation occurred at a higher pace in MFS patients. In this study focusing on wave reflection, it is Z0 and, more importantly, the changes in Z0 that deserve attention, inasmuch as these may locally provoke wave reflection. Vessel caliber and stiffness affect Z0 (see Eq. 2), and our data suggest that both effects counterbalance each other, with no net effect on Z0 for the most proximal part of the aorta. This observation also supports the findings of Yin et al. (25), who derived aortic Z0 from central pressure and flow and found Z0 within the normal range in MFS patients. In this study, Z0 was assessed from central pressure and flow as well as from changes in cross-sectional area along the aorta measured with MRI, which allowed us to study the aorta at different levels. It is generally accepted that, in the normal population, there is a gradual increase in impedance along the aorta [due to geometric and elastic taper (12, 14, 18)] but that impedance mismatch is most important in the periphery, where small arteries make the transition to arterioles and capillaries. For the descending aorta, the dilatation in the MFS patients seems to “overcompensate” for an increase in stiffness, with lower Z0 in the MFS patients.

Despite the absence of significant differences in mean values of many calculated parameters, there are trends in the data when they are studied as a function of age (Fig. 3). In the ascending-descending section, there is a more pronounced gradient in Z0 (increasing distally) in young controls than in older controls and MFS patients. The result is a positive reflection coefficient in the proximal aorta in young controls that decreases with age when the proximal aorta stiffens and the difference in Z0 with adjacent sections becomes less. In the lower abdominal aorta, opposite changes were observed. In controls, the age-related increase in Z0 results in an increase in local positive reflection coefficients in the distal aorta. Again, we did not observe any age-related changes in the MFS patients. We speculate that interpatient differences in severity of the disease complicate the detection of eventual age-related patterns in MFS patients.

The literature on the subject of local reflection coefficients in the aorta in the general population, and in MFS patients in particular, is scarce. Ting et al. (19), analyzing apparent phase velocity, reported that local wave reflection can differ markedly along different regions in the aorta, with pronounced reflections in the ascending aorta and from just proximal to the renal arteries to the aortoiliac bifurcation, but not in the mid thoracic region. This report (19) is consistent with data presented in Fig. 3, where IΔA-DIA is indeed much lower than reflection coefficients in the other sections. Also, more rapid mechanical aging near the aortic bifurcation has been reported by Gillessen et al. (2) and Greenwald et al. (3) studied the effect of aging on the local reflection coefficient of the aortic bifurcation. They concluded that the progressive increase of lower aortic Z0 (as also found in our study) decreases the impedance mismatch with the iliac arteries, decreasing the reflection coefficient from the bifurcation.

The following question remains: To what extent do local aortic properties and local reflection coefficients impact the global picture of arterial wave reflection, as quantified with indexes such as AIx? Our data seem to suggest that the effect, if any, is marginal. We found a (relatively weak) correlation between local and global indexes of wave reflection only between AIx and IΔA-DIA (r = 0.29, P < 0.05). However, none of the local reflection coefficients entered the model for AIx in multiple linear regression analysis. The impact of local reflection properties along the aorta thus seems to be negligible compared with the other coexisting sources of wave reflection. There is growing clinical interest in arterial wave reflection and AIx. Meijboom et al. (10) found elevated AIx in MFS patients, but in their MFS patients (n = 4) the aorta had been surgically repaired with a Dacron prosthesis, which may cause a drastic increase in PWV and compliance mismatch at the site of the anastomosis. Although it is recognized that AIx is a composite measure (14), no study has truly focused on dissecting the index into its determining factors. We could demonstrate that the main determinants of AIx were PWV and Δx and, to a lesser extent, reflection coefficient and HR (Table 3).

![Fig. 6. Association between body length and global wave reflection coefficient (Pb/Pf) in control subjects and patients with Marfan’s syndrome. Association was significant in control subjects only (dashed line; r = −0.64, P = 0.001).](http://ajpheart.physiology.org/)

Table 3: Contribution of PWV, Δx, HR, and Pb/Pf to augmentation index as assessed by linear regression analysis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>P</th>
<th>Standardized β-coeff</th>
<th>r²</th>
</tr>
</thead>
<tbody>
<tr>
<td>PWV, cm/s</td>
<td>0.000</td>
<td>0.791</td>
<td>0.373</td>
</tr>
<tr>
<td>Δx, cm</td>
<td>0.000</td>
<td>-0.635</td>
<td>0.694</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>0.001</td>
<td>-0.269</td>
<td>0.772</td>
</tr>
<tr>
<td>Pb/Pf</td>
<td>0.041</td>
<td>0.160</td>
<td>0.794</td>
</tr>
</tbody>
</table>

P, statistical significance of the parameter in the model; β, standardized coefficient, indicating relative importance of the parameter; r², predictive value of the model after additional inclusion of the parameter. PWV, pulse wave velocity; Δx, effective length of arterial tree; Pb/Pf, global reflection coefficient (i.e., ratio of backward to forward pressure wave).
This analysis also reveals why we could not demonstrate a (anticipated) difference in AIx between controls and MFS patients. The elevated PWV and the lower HR in the MFS patients are counterbalanced by the larger Δτ in MFS patients. This is not necessarily a pathophysiological consequence of the disease but, rather, probably a reflection of the difference in body length between both groups. The taller stature of the MFS patients thus seems to have a protective effect in terms of wave reflection, delaying the return of the reflected wave. These mechanistic determinants of AIx also apply to other diseases affecting the functional properties of the aorta, such as atherosclerosis, hypertension, and diabetes (1), where we speculate that the hemodynamic burden caused by early wave reflection may be higher, particularly in smaller subjects. Also, different classes of blood pressure-lowering drugs may induce alterations in HR (β-blockers) and in the location of reflection sites (vasoactive drugs) and, hence, differentially affect the impact of wave reflection independent of the level of blood pressure decrease (7).

In this study, input impedance was calculated as an intermediate step in the linear wave separation analysis. The data confirm that, when studied in a global manner, the arterial system in MFS patients is not drastically different from that in controls, an observation that confirms the findings of Yin et al. (25) that were based on invasive data. We also want to draw attention to a finding concerning P0/Pr. When P0/Pr is plotted as a function of body length (Fig. 6), it immediately becomes clear that this factor is not independent of body size, as one might expect of a true reflection coefficient (in the control population, there was a significant inverse association between P0/Pr and body length). We believe that the influence of length on P0/Pr is explained by the fact that, in taller subjects, P1 and P0 travel longer distances. So, on arrival at the reflection site, the amplitude of P0 is smaller because of damping. In addition, the reflected wave needs to travel a longer distance back up the aorta and is more damped as well. As a result, the taller the subject is, the smaller the amplitude of the reflected component P0 and, thus, P0/Pr.

In our opinion, one of the strong aspects of this study is its fully noninvasive character, which allows transfer of fundamental hemodynamic research from the experimental laboratory to the clinical setting. At the same time, it is acknowledged that this brings along methodological considerations and limitations that desire some attention and comments. 1) We scaled carotid diameter distension waveforms to assess carotid systolic pressure. Although the methodology of scaling diameter distension waveforms was found adequate (20), the relation between diameter and pressure is nonlinear (11), and we may have underestimated pulse pressure (and Z0.9xx), especially at the most distal locations (AB). The extent to which this assumption has affected our findings is an open question. For the controls, our findings on the variation of local reflection coefficients along the aorta are consistent with the data from Ting et al. (19) and Gillessen et al. (2) (see above), suggesting that the effect is not important enough to affect these general findings. Our data do not allow us to directly make a similar statement for the MFS patients. Nevertheless, using estimated regional PWV in the abdominal aorta segment and the relation between Z0.9xx cross-sectional area (A), and blood density (ρ; Z0.9xx = pPWV/A), the different evolution in Z0.9AB between MFS patients and controls in tertile 3 was confirmed (data not shown) using a method independent of blood pressure. 3) As evident from our data and the discussion above, body size is an important confounding factor in the analysis of wave reflection. Although the different stature allowed us to enlarge the range of physiological parameters affecting wave reflection, ill-matched populations, in terms of body size, may pose an important limitation in clinical studies. 4) By inclusion of older MFS patients, it cannot be excluded that the population is biased, in the sense that older patients would have a “milder” manifestation of the disease, inasmuch as they have reached a higher age without surgery, despite the presence of the disease. 5) For the wave separation analysis, we combined central flow with a surrogate for central pressure (and not the true central pressure). Although this methodology is quite commonly applied, it is acknowledged that this assumption may affect the accuracy of the wave separation and, hence, the value of P0/Pr.

In conclusion, we have demonstrated that stiffening and dilatation of the proximal aorta in MFS patients do not lead to an increase in local aortic Z0. Nevertheless, the different evolution in proximal aorta and virtually zero in the midaortic region. In healthy subjects, the proximal reflection coefficient diminishes with age but increases in the distal region. We could not demonstrate an association between local reflection coefficients along the aorta and AIx, which is primarily determined by PWV and Δτ.

GRANTS
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