# Normal Local Pulse Wave Velocity Predicts Absence of Local Aorta Diameter Growth in Marfan Syndrome: A Comprehensive MRI-Approach

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**Introduction:** The leading cause of premature death in patients with Marfan syndrome (MFS) is aortic dissection and subsequent wall rupture after progressive dilatation. Yearly growth in aortic diameter – determined from aortic contrast-enhanced MR angiography (MRA) – is typically increased in MFS, and used as a prognostic marker for prediction of dissection. The underlying reason for this abnormal growth is thought to be the abundance of microfibrillar proteins in the aortic media leading to degeneration of the elastin laminae, which results in stiffening of the aortic wall. Increased wall stiffness − expressed by global aortic pulse wave velocity (PWV, i.e. the propagation speed of systolic flow velocity wave front through the aorta) assessed with multi-site one-directional velocity-encoded MRI [1] − has proven prognostic value for prediction of aortic dilatation [2]. In a recent publication it has been shown that PWV can be obtained accurately on a local level in the aorta (i.e. at 200 sample points along the centerline) with two-directional velocity-encoded MRI [3].

**Purpose:** To test whether local PWV assessed with MRI at baseline can predict local aorta dilatation at 2-year follow up in MFS.

**Methods:** The local ethics committee approved this study and all patients gave informed consent. Ten MFS patients (mean age 36±11 years, 4 male) with no previous aortic surgery were examined at baseline and at 24-month follow up. MRI was performed on a 1.5T Gyroscan ACS/NT15 MRI (Philips, Best, The Netherlands). The body coil was used for RF transmission and signal reception.
MRA: A contrast-enhanced MRA of the whole aorta was obtained by imaging the arterial first-pass of a 30mL contrast bolus Dotarem (0.5 mmol/mL) (Guerbet, Gorinchem, the Netherlands), intravenously infused at 2mL/s. A three-dimensional (3D) T1-weighted gradient-echo was performed (volume of 500×200×180mm$^3$, acquisition voxels of 1.25×2.46×3mm$^3$, echo time/repetition time (TE/TR) =1.5/4.9, flip angle 40º, centric k-space filling). Image analysis was performed using the in-house developed LKEB Automated Vessel Analysis (LAVA) software package [4]. Based on a user-defined proximal point at the aortic root and a distal point above the iliac bifurcation, a centerline is automatically detected through the aorta using LevelSet methods [4]. A 3D deformable model is positioned around that centerline and fitted to the image [5]. From this, aortic diameters can be determined at 200 equidistant sample points along the centerline of the aorta.
PWV: Local PWV was obtained at the same 200 sample points, from the propagation speed of the systolic flow velocity wave front along this centerline [3]. The complete aorta was acquired with two-directional velocity-encoded MRI in a stack of three consecutive double-oblique sagittal slices with slice thickness 10mm, FOV 450×270mm$^2$, acquisition voxel size 3.5×2.1×10mm$^3$, TE/TR=2.4/4.3, flip angle 10º, velocity sensitivity $V_{enc}$ 150 cm/s in anterior-posterior and feet-head direction, and maximal number of reconstructed phases (temporal resolution 5-10 ms). The transit-time of the systolic flow velocity wave front between sample points is determined and in combination with the distance between sample points, this defines the local PWV. The 200 sample points along the centerline in the PWV-assessment are matched with those of the MRA-assessment at baseline and follow up. For ten patients, all sample points along the aorta centerline were evaluated on diameter growth from baseline to follow up and local PWV at baseline. A change in diameter ≥1.5mm was considered significant growth. In addition, for each patient, local PWV at baseline was compared with the global PWV averaged over the whole aorta. In case local PWV was in the upper tertile of all PWV-values, the local PWV at this point was considered high.

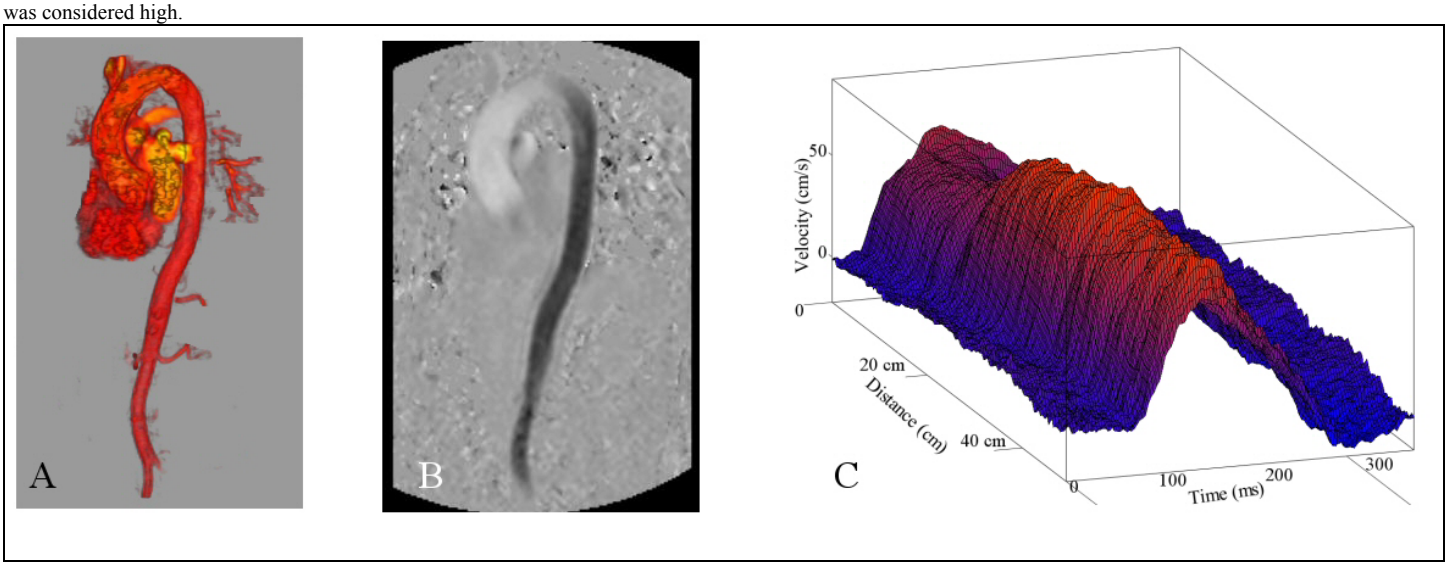


**Figure 1.** A: Volume rendering of MRA of the aorta, from which the aortic diameter is determined at 200 equidistant sample points along the centerline of the aorta. B: Velocity-encoded (feet-head direction) MRI of the aorta in same patient as in A. From this two-directional velocity-encoded MRI of the whole aorta, local PWV is assessed from the propagation of the flow velocity wave form, determined at the same 200 sample points along the aortic centerline (C).

**Results:** In ten MFS patients, a total of 1571 sample points along a total aorta trajectory of 337cm (mean aorta trajectory of 33.7±6.8cm) were evaluated on diameter growth and local PWV at baseline. The results are presented in Table 1. Sensitivity of this new method is 8% while specificity is 89%. These results imply that although increased local PWV may lead to a high count of false-positives in MFS patients, normal local PWV indicates in 89% of the cases no significant diameter growth. Increase of local PWV may be proceeding diameter growth in these patients

**Table 1.** Local PWV versus diameter growth

| High local PWV / Diameter growth | Yes | No |
|---|---|---|
| **Yes** | 84 | 59 |
| **No** | 955 | 473 |

**Conclusions:** Using a new comprehensive MRI-approach, normal local aortic pulse wave velocity assessed with two-directional velocity-encoded MRI predicts in 89% of the cases absence of aortic diameter growth in patients with Marfan syndrome after two years follow up.

**References**: [1] Grotenhuis, et al. JMRI 2009. [2] Nollen, et al. Eur Heart J 2004; [3] Westenberg, et al. JMRI 2010. [4] PJH de Koning et al., MRM 2003. [5] P. Makowski et al. LNCS 4072 2006.
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