Detection and Hemodynamic Evaluation of Flap Fenestrations in Type B Aortic Dissection with 4D Flow MRI: Comparison with Conventional MRI and CTA.

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Abstract

Purpose: The purpose of this study was to compare dissection flap fenestration visualization between 4D flow MRI, clinical MRI/MRA, and clinical CTA studies and describe the presence of hemodynamically active fenestration flow using 4D flow.

Materials and Methods: Nineteen patients with type B dissection (age: 57±5 years) who had undergone standard of-care MRI/MRA of the chest including 4D flow MRI were retrospectively identified. Fourteen of the 19 patients also had CTA performed within 2 years of the MRI/MRA study with no interval surgery. Image review was performed independently by two radiologists. The number of fenestrations (including entry and exit tears), location, and flow directionality were recorded. Differences in the rate of detection between techniques was assessed using a Wilcoxon signed rank test.

Results: 4D flow detected more fenestrations relative to MRI/MRA [rev 1: +3 (10%), rev 2: +5 (20%)]. There were similar numbers of fenestrations detected by 4D flow relative to CTA [rev 1: +1 (4%), rev 2: −3 (−12%)]. MRI/MRA detected fewer fenestration relative to CTA in this cohort [rev 1: −6 (−24%), rev 2: −5 (−19%)]. No differences were significant. Combining 4D flow and MRI/MRA resulted in additional fenestration detection. Most fenestrations demonstrated biphasic flow over the cardiac cycle (flow entering false lumen in systole and exiting during diastole, rev 1:18/33, rev 2: 16/30).
Conclusions: 4D flow MRI can detect small flap fenestration in type B dissection patients while providing additional information about flow through fenestrations throughout the cardiac cycle relative to CTA and conventional MRI.

Summary Statement:
4D flow MRI detects small type B aortic dissection flap fenestrations and provides additional hemodynamic characterization of flow between true and false lumens at fenestration sites relative to CTA and conventional MRI.

Keywords
MR Angiography; Hemodynamics; Aorta; Dissection; Vascular

Introduction
Treatment approaches for Type B aortic dissections (TBAD) can range from medical therapy with imaging surveillance to thoracic endovascular aortic repair (TEVAR) and less frequently open surgical repair. Identifying patients at increased risk of dissection progression (i.e., flap propagation or aneurysm formation) or rupture is important in therapy selection. (1) While multiple, primarily anatomic imaging characteristics have been described for use in patient risk-stratification (2), hemodynamic characterization of the dissection may further improve risk assessment. (1) Previous work from the International Registry of Acute Aortic Dissection (IRAD) has shown that descending aortic size, false lumen patency/thrombosis, as well as the size of entry tears are important predictors of adverse events in TBAD patients. (3)

TEVAR can be used in the treatment of TBAD with the aim of decreasing flow and pressure in the false lumen. (4) Small fenestrations within the native flap are often “hemodynamically active” (i.e., flow entering or exiting the false lumen) and have been shown in computational fluid dynamics (CFD) studies to substantially impact false lumen hemodynamics. (5) Thus, these small fenestrations may change the likelihood of false lumen thrombosis after endograft placement, alter the risk of dissection progression or rupture, and impact downstream perfusion, although are often difficult to detect by standard clinical imaging techniques. (6) Small fenestrations can be identified with high-resolution, ECG-gated CT angiography (CTA), however, the dissection flap is often mobile and fenestrations may be obscured by motion artifact. Additionally, the relatively low spatial resolution of MRI and MR angiography (MRA) can limit identification of small fenestrations. More than just visualization, a better understanding of the hemodynamic behavior of small fenestrations could alter risk profiles of patients, and impact surgical planning and endograft positioning.

Three-dimensional, time-resolved, phase contrast MRI with 3-directional flow encoding (4D flow MRI) is an established technique for evaluating 3D blood flow dynamics in the aorta and has been previously used to evaluate hemodynamics in patients with dissection of the thoracic aorta. 4D Flow derived hemodynamic parameters such as false lumen stroke volume and velocity, distal dominant entry tears, and helical flow in the false lumen have been shown to correlate with the rate of aortic expansion. (7–11) Furthermore, due to pressure...
gradients across the dissection flap, small fenestrations can produce comparatively larger flow jets that can be detected by 4D flow MRI. In this study, we hypothesized that 4D flow MRI will allow for superior dissection flap fenestration identification relative to standard MRI/MR angiography (MRA) approaches and provide similar fenestration counts to CTA. Moreover, the presence of forward and retrograde flow through fenestrations was assessed as a potential indicator of local hemodynamic properties at the sites of fenestration.

Materials and Methods:

Study Cohort

This study was approved by the local Institutional Review Board. Patients with TBAD were retrospectively identified from a cohort of patients who had undergone MRI/MR angiography (MRA) of the chest which included 4D flow MRI as part of their clinical evaluation from January 2012 – August 2017 at a single center. All patients with dissection of the descending thoracic aorta were considered eligible for inclusion including patients with previous surgical repair of Type A or Type B dissection with segments of residual dissection. Among eligible patients, CT angiography (CTA) of the chest was included for analysis when available, if the imaging was performed within 2 years of the MR study without interval surgery.

Imaging

MRI/MRA: All MR images were acquired on a 1.5 T system (Aera or Avanto, Siemens Healthcare, Erlangen, Germany). Standard cardiothoracic MRI for aorta evaluation at our institution includes axial and coronal T2 weighted images (Half-Fourier Acquisition Single-Shot Turbo Spin Echo, HASTE), axial and coronal pre- and post-contrast T1 fat-saturated images (Volumetric Interpolated Breath-Hold Examination, VIBE) or axial and coronal steady state free precession images (True Fast Imaging with Steady State Precession, TrueFISP) all covering the entire chest. Dedicated aorta imaging includes contrast-enhanced time-resolved MRA in the left anterior oblique (LAO) orientation (spatial resolution = 1.3×0.9×8.0mm³ and temporal resolution = 2.4 sec), LAO contrast-enhanced MRA or LAO TrueFISP MRA (spatial resolution: 1.1 × 1.1 × 1.4 mm³).

4D flow MRI: 4D flow images were acquired using prospective ECG and respiratory navigator gating with an imaging volume covering the entire thoracic aorta in the left anterior oblique orientation. Pulse sequence parameters were: spatial resolution = 2.1–2.9×2.2–4.0×2.5–5.0 mm³, temporal resolution = 36–39 ms, velocity sensitivity = 150–270 cm/s.

CT Angiography: ECG-gated, contrast enhanced CTA studies were acquired on a 64 slice, third generation CT (SOMATOM Definition, Siemens Healthcare, Erlangen, Germany) reconstructed in axial, coronal, and sagittal orientations (spatial resolution: 0.4 × 0.4 × 0.75 mm³, contrast: 70 mL of Iovue 370 injected at 5 mL/sec, bolus tracking trigger with region of interest in the ascending aorta, pitch: 3.2, prospective ECG flash gating).
Data analysis

4D flow images were post-processed by a single reviewer using dedicated software (cvi42, Circle Cardiovascular Imaging, Inc, Calgary, Canada). Post-processing included noise and eddy current correction, semi-automated aorta centerline generation, and semi-automated aorta segmentation. All image sets were evaluated by two cardiovascular radiologists with >4 years of experience in interpreting MRA and CTA studies. To minimize the potential for recall bias, images were grouped by modality (4D flow, MRI/MRA, and CTA) and reviewed in a random patient order with at least two days between each modality review.

4D flow image analysis included the display of the data as 3D velocity maximum intensity projection (MIP) images as shown in figure 1. 3D velocity MIPs were qualitatively evaluated in the dedicated post-processing software to provide the ability to pan, zoom, and rotate images as required. The evaluator was also able to change the velocity color scale to optimize visualization. Images were evaluated qualitatively for the number and location (proximal, mid, or distal descending aorta) of dissection flap fenestrations and the presence of antegrade flow (from true to false lumen) and retrograde flow (from false to true lumen) through the visualized fenestrations. Entry and exit tears were counted as fenestrations.

Standard MRI/MRA and CTA images were reviewed on the clinical picture archiving and communication system (PACS) with reviewers instructed to analyze the case using their standard clinical protocol with any additional zoom, window/leveling, sequence, or order of review necessary to optimize fenestration identification. For both MRI/MRA and CTA, the number of fenestrations and location (proximal, mid, or distal descending aorta) were reported. Entry and exit tears were counted as fenestrations.

A fenestration-by-fenestration analysis between modalities was also performed in patients with concurrent CTA. Fenestrations on CTA were identified by consensus between the two reviewers and used to guide the search for fenestrations on MRI/MRA and 4D flow images. The axial diameter of the fenestrations on CTA was recorded. The number of systolic and diastolic phases with visualized flow through fenestrations on 4D flow was also recorded as a qualitative estimate of pressure differences between true and false lumens.

Statistical Analysis

Data are reported as mean ± standard deviation. Due to the small number of patients available for analysis, fenestration counts for each reviewer were summated across all patients for statistical analysis of fenestration count. The numbers of fenestrations were compared pairwise between 4D flow, MRI/MRA, and CTA using a Wilcoxon signed rank test. Per patient differences in fenestration count were also compared between each technique. Interobserver variability was assessed for each modality using a weighted Kappa statistic. Fenestration by fenestration sizes were compared between modalities using analysis of variance (ANOVA). Spearman’s rank correlation coefficient was used for correlations analysis.
Results:

Study Cohort

A total of 19 patients were analyzed (age: 59±12 years, M/F: 11/8) including 7 patients with previous Type A dissection repair, 4 patients with ascending aorta repair, 1 patient with aortic valve replacement, and 2 with previous both Type A and B dissection repair. Five patients had no prior aortic surgical history. A total of 14 patients had CTA performed within two years of the MRI study without interval surgery (average length between studies: 5.5 ± 4.9 months) (Figure 2).

Fenestration Identification and Location

For individual observers, there was no statistically significant difference in the total number of fenestrations identified between any of the three techniques, however several trends were present in this small cohort. 4D flow detected more fenestrations relative to MRI/MRA (rev 1: 33 vs. 30 p = 0.64; rev 2: 30 vs. 25, p = 0.31). In the subgroup of patients with concurrent CTA, there were similar numbers of fenestrations detected by 4D flow relative to CTA (rev 1: 26 vs 25, p = 0.85; rev 2: 23 vs. 26, p = 0.68). MRI/MRA detected fewer fenestration relative to CTA in this cohort (rev 1: 19 vs. 25, p = 0.22; rev 2: 21 vs. 26, p = 0.30). (Table 1)

Given our sample size of n=14, the statistical power to detect differences between the three techniques was 27%. The average per patient differences in fenestration counts were similar between techniques (MRI – 4D flow: rev 1 = −0.2 ± 1.2, rev 2 = −0.3 ± 1.5; MRI – CT: rev 1 = −0.4 ± 1.3, rev 2 = −0.4 ± 1.2; CT – 4D flow: rev 1 = −0.1 ± 1.1, rev 2 = 0.2 ± 2.0; p = 0.59). There was excellent interobserver agreement for CTA (κ = 0.88), fair agreement for 4D flow (κ = 0.37), and poor agreement for MRI (κ = 0.04).

Regarding fenestration location, the majority of tears were identified proximally using all three modalities. CTA detected more mid descending aorta fenestrations (rev 1: 10, rev 2: 8) than both 4D flow (rev 1: 1, 90% difference, rev 2: 4, 50% difference) and MRI/MRA (rev 1: 4, 60% difference, rev 2: 3, 63% difference). (Table 1)

Fenestration-by-Fenestration Analysis

On consensus review of the 14 patients with CTA, CTA identified more fenestrations than 4D flow (28 vs. 20, p = 0.01) and MRI/MRA (28 vs. 17, p = 0.01), while there was no statistical difference between 4D flow and MRI/MRA (p = 0.46). The combination of 4D flow with MRI/MRA identified a total of 23 fenestrations with 4D flow visualizing 6 additional tears relative to MRI/MRA while MRI/MRA identified 3 tears not seen with 4D flow. The number of fenestrations identified with the combination of 4D flow and MRI/MRA was not statistically different from CTA (p = 0.06). There was no difference in the average size of fenestrations detected with any technique (CTA: 6 ± 4 mm, 4D flow: 7 ± 4 mm, MRI/MRA: 8 ± 5 mm, p = 0.46). The minimal size fenestration detected with CTA was 2 mm, while both 4D flow and MRI/MRA detected 3 mm fenestrations.

Fenestration hemodynamics

Given that flow velocity MIPS were used to visualize 4D flow data, only hemodynamically active fenestrations were identified using 4D flow. Qualitatively, both observers noted that
antegrade flow was most obvious in large fenestrations (Figures 1 and 3, videos 1 and 2), while retrograde flow from false to true lumen (diastolic flow) was often useful to identify smaller fenestrations (Figure 4). The majority of fenestrations demonstrated bi-directional flow [antegrade/retrograde] (reviewer 1:18/33, reviewer 2: 16/30). Reviewer 1 identified 15 isolated flow fenestrations (antegrade [systolic]: 14, retrograde [diastolic]: 1) and reviewer 2 identified 14 isolated flow fenestrations (antegrade [systolic]: 6, retrograde [diastolic]: 8). On consensus fenestration by fenestration assessment, there was no difference in the average number of phases of systolic flow and diastolic flow through fenestrations (4.1 ± 2.9 phases vs. 3.8 ± 1.5 phases, p = 0.56). There were positive correlations between fenestration size on CT and systolic flow phases (ρ = 0.52, p = 0.01) and diastolic flow phases (ρ = 0.50, p = 0.03).

**Longitudinal Follow-up**

Longitudinal clinical follow-up data was obtained in all patients and 5/19 patients (26%) had surgery to repair their TBAD following baseline imaging including two patients who required TEVAR, and three patients who underwent elephant trunk repairs. All patients who required surgery were in the CTA cohort. In this group, there was no difference between average fenestration count in patients who progressed to surgery from those who did not with CTA (2.0 ± 1.6 vs 2.0 ± 1.0, p = 1.00), 4D flow (1.2 ± 1.1 vs. 1.2 ± 1.1, p = 0.97), or MRI/MRA (1.5 ± 1.1 vs. 1.2 ± 0.5, p = 0.51). There was no correlation between fenestration count (ρ = 0.10, p = 0.73), fenestration size (ρ = −0.26, p = 0.19), systolic phases (ρ = 0.25, p = 0.29), or diastolic phases (ρ = 0.28, p = 0.24) and progression to surgery.

**Discussion:**

Our study demonstrates that hemodynamic assessment with 4D flow MRI is an effective way of visualizing and characterizing fenestrations in the dissection flap of patients with TBAD. While differences between numbers of fenestrations identified were generally not statistically significant, our results suggest 4D flow MRI may be additive in MRI/MRA assessment of type B dissection to evaluate flap fenestrations. Moreover, the ability to identify the hemodynamically active fenestrations may make 4D flow a complimentary study to CTA in terms of complete dissection characterization during planning for endovascular repair.

Better characterization and risk-stratification of patients with TBAD are important clinical needs. Complicated TBAD patients (presenting with rupture or evidence of end-organ malperfusion) are good candidates for TEVAR, but there is debate about appropriate management in uncomplicated cases. (12) Short term 30 day/in-hospital mortality outcomes favor medical management, but 5-year mortality is superior in patients who receive TEVAR. (1, 13, 14) Multiple studies have demonstrated increased false lumen and aortic remodeling in patients following TEVAR which are thought to be a primary drivers of improved outcomes in these patients.(15, 16) Lastly, while TEVAR does provide a long-term mortality benefit, the number needed to treat in uncomplicated TBAD patients to prevent one aorta-related mortality is 13 (17), suggesting there is a significant opportunity for advanced
imaging techniques such as 4D flow MRI to provide improved patient risk-assessment, reduce overtreatment and improve the cost-effectiveness of endovascular repair.

While the current study only qualitatively evaluates fenestration hemodynamics, quantification of flow, velocity, regurgitant fraction, and other hemodynamic markers are the next step in evaluation of TBAD with 4D flow. A recently described parameter such as regurgitant fraction at the site of fenestrations may provide insight into the pressure state of the false lumen.(18) Additionally, CFD studies in type B dissection show that complex flow geometry, velocity, wall pressure, and wall shear stress in the false lumen can result in progression, and the presence of exit tears can alter hemodynamics in the false lumen even after TEVAR. (5, 19) One of the challenges of CFD has been difficulty in modeling of realistic in-vivo boundary conditions as well as the impact of small fenestrations which, as our results demonstrate, are clearly hemodynamically active. (5) Computational modeling utilizing information obtained from 4D flow MRI may significantly improve modeling capabilities through empirical assignment of boundary conditions and validation of hemodynamic simulations.

This study is subject to several limitations, most notably the small sample size of patients with a full complement of imaging resulting in low power to detect differences between techniques (power = 27% for comparison between the three techniques). The low number of patients also limits comparisons of interobserver variability. Another important limitation is the retrospective nature of the study as well as the heterogeneity of the subjects in terms of chronicity of dissection and prior surgeries. Additionally, dissection flap motion is commonly encountered at CTA and it is unclear what impact this will have on fenestration detection with 4D flow. The flow jets identified in this study would be unlikely to result from bulk flap motion, but motion may alter the hemodynamic activity of fenestrations in such a way as to limit their detection with 4D flow. Finally, there is no true reference standard for validation of fenestration identification and hemodynamic assessment, therefore all results are based on the assumption that observed fenestrations are real.

In conclusions, our results suggest 4D flow MRI can detect and hemodynamically characterize small fenestrations in patients with type B aortic dissection. Given the complexity of hemodynamic-anatomic interactions in aortic dissection, the clinical utility of 4D for TBAD evaluation should be further explored.

**Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

**Abbreviations**

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<tr>
<td>MRI</td>
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<td>MRA</td>
<td>Magnetic Resonance Angiography</td>
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<td>CTA</td>
<td>Computed Tomography Angiography</td>
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4D flow MRI
Three-dimensional, time-resolved, phase contrast MRI with 3-directional flow encoding

TEVAR
Thoracic endovascular aortic repair

CFD
Computational Fluid Dynamics

MIP
Maximum Intensity Projection

References:


Radiol Cardiothorac Imaging. Author manuscript; available in PMC 2019 October 09.


Figure 1:
Visualization of 4D flow images in a patient with type B aortic dissection. A) Three-dimensional (3D) phase-contrast MR angiogram (3D PC-MRA) derived from 4D flow data demonstrates the anatomy of the pulmonary artery (PA), left ventricular outflow tract (LVOT), ascending aorta (AAo), true lumen (TL), and false lumen (FL). B) Late systolic phase 3D streamlines derived from time-resolved velocity data acquired with 4D flow MRI which are useful for visualization of complex flow patterns. C) 3D velocity maximum intensity projections (MIPS) at the same late systolic phase as B. These images are useful for detecting bulk flow or lower velocity/volume flow such as seen in diastole or small fenestration. D) Magnified 3D velocity MIPS at multiple phases through systole and early diastole demonstrate a high velocity flow jet through a large proximal descending aorta fenestration with associated jet impingement and helical flow in the FL followed by early diastolic retrograde flow into the TL.
Figure 2: CT angiogram (CTA) (A), 4D flow MRI velocity MIP overlaid on magnitude images in an oblique sagittal view (B), and contrast enhanced MR angiogram (CE MRA) (C). The CTA and MRA clearly demonstrate dissection anatomy (ascending aorta (AAo), aortic arch, and descending aorta (DAo), true lumen (yellow arrow), false lumen (FL)), however, both are often limited by blurring artifact related to pulsatile flap motion. The 4D flow velocity MIP reveals 4 discrete fenestrations from their associated flow jets into the false lumen during systole (white arrows).
Figure 3:
A) Time-resolved contrast enhanced MR angiogram (CEMRA) demonstrates anterograde filling of the false lumen. B) 4D flow MRI velocity MIP reveals this filling is occurring through a large fenestration with significant antegrade flow during systole (red arrow). A second smaller fenestration is also present in this location with a lower velocity systolic jet (yellow arrow).
Figure 4:
A) Contrast enhanced MR angiogram (CEMRA) demonstrating a complex type B dissection (ascending aorta (AAo), aortic arch, and descending aorta (DAo)). 4D flow MRI velocity MIPS during systole (B) reveals several large, relatively high velocity jets entering an aneurysmal segment of the false lumen (*) at the proximal DAo (white arrows) and impinging on the false lumen wall. In diastole (C), there is retrograde flow into the true lumen at these sites (white arrows), with an additional fenestration in the distal descending aorta seen only due to diastolic flow (red arrow). This fenestration was not seen on CT.
Table 1:
Fenestration count and hemodynamics in each modality by location. MRI/MRA – Magnetic Resonance Imaging/Angiography, CTA – Computed Tomography Angiography

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