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Letter by Zhu et al Regarding Article, "Aortic Wall Inflammation Predicts Abdominal Aortic Aneurysm Expansion, Rupture and Need for Surgical Repair"

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To the Editor

We read with great interest the article by The MA[3]RS Study Group regarding abdominal aortic aneurysms (AAAs) in the July issue of *Circulation*.[1] 342 patients with AAAs (average diameter ~ 5 cm) were studied using ultra-small superparamagnetic iron oxide particle (USPIO) enhanced MRI, and followed with ultrasound (US) for at least 2 years. While USPIO enhancement was associated with faster growth and AAA rupture or repair, it was not an independent predictor of clinical outcome. Nonetheless, we believe that molecular imaging with this novel MRI contrast agent has promise for better understanding AAA disease progression.

Although the US reproducibility (3.5%) reported in this study is much better than the measurement error of 5-10mm or greater than 10%, reported elsewhere.[2], high resolution CTA and volumetric MRI sequences offer even improved measurement accuracy and reproducibility (2.2-2.5%). Furthermore, those methods allow the assessment of maximal AAA diameter rather than the anterior-posterior diameter typically reported with US.[3] Over the relatively short two year time interval, the typically small changes in vessel size are better quantified if maximum diameter measurements can be aligned with the sometimes complex geometries of AAAs.

Several imaging approaches and contrast agents are available for characterizing AAA inflammation. These include ^{18}F-FDG positron emission tomography (PET), gadolinium enhanced MRI, and delayed MRI following USPIO administration. USPIO imaging is promising because it targets macrophages directly, whereas the other modalities target metabolism or vessel wall enhancement via the vasa vasorum, both indirect markers of inflammation. The authors characterized inflammation using binary categories on standard, two-dimensional T2* maps with 5mm slice thickness, 2.1 × 1.6 mm in plane resolution and a minimum echo time (TE) of 4.9 ms. Ultrashort TE (UTE) MRI sequences have substantially shorter TE values (minimum TE of 0.05 ms) and provide a linear relationship between signal intensity and USPIO concentration[4]. High resolution UTE (1.3mm isotropic)

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offers improvements in sensitivity and the ability to quantify USPIO uptake by macrophages and therefore has the potential to better assess vessel wall inflammation.

Inflammation imaging has three potential roles in the clinical management of patients with AAAs that should be explored in future studies targeting smaller AAAs with longer follow up durations. First, the majority of AAAs are small and undergo routine surveillance imaging. Surveillance intervals could be tailored to match the improved risk assessment of AAA progression that inflammation imaging affords. Second, intervention thresholds for AAAs could be adjusted to reflect the increased risk that inflammation imaging may reveal. This would reflect existing trends to intervene more aggressively (for example at 50 mm) in patients with family history of AAA, or female patients. Third, it can be used to evaluate the effect of novel therapies. Fish oil (Omega-3), for example, is one such therapy. It has been shown to alleviate the inflammatory component, reduce oxidative stress and elastin fragmentation, and slow down AAA progression in animal models.[5] Inflammation imaging with USPIO enhanced MRI may help to validate and optimize this therapy as it is applied in humans.

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