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Title

Feasibility of Shear Wave Sonoelastography to Detect Endoleak and Evaluate Thrombus Organization after Endovascular Repair of Abdominal Aortic Aneurysm.

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Key points

1. Dynamic elastography with shear wave sonoelastography (SWS) detected 100% of endoleaks in abdominal aortic aneurysm (AAA) follow-up that were identified by a combination of CT angiography (CTA) and color Doppler ultrasound (CDUS).
2. Based on elasticity maps, SWS differentiated endoleaks from thrombi within the aneurysm sac ($P < 0.001$).
3. After 3 year follow-up, no new endoleaks were observed in SWS negative examinations.

Abbreviations

AAA: abdominal aortic aneurysm

CDUS: color Doppler ultrasound

CEUS: contrast enhanced ultrasound

CT: computed tomography

CTA: computed tomography angiography

EVAR: endovascular aortic aneurysm repair

kPa: kiloPascal

MRI: magnetic resonance imaging

PPV: positive predictive value

ROI: region of interest

SWS: shear wave sonoelastography

Abstract

Purpose

To investigate the feasibility of shear wave sonoelastography (SWS) for endoleak detection and thrombus characterization of abdominal aortic aneurysm (AAA) after endovascular repair (EVAR).

Materials and Methods

Participants who underwent EVAR were prospectively recruited between November 2014 and March 2016 and followed until March 2019. Elasticity maps of AAA were computed using SWS and compared to computed tomography angiography (CTA) and color Doppler ultrasound (CDUS). Two readers, blinded to the CTA and CDUS results, reviewed elasticity maps and B-mode images to detect endoleaks. Three or more CTAs per participant were analyzed: pre-EVAR, baseline post-EVAR and follow-ups. Primary endpoint was endoleak detection. Secondary endpoints included correlation between total thrombus elasticity, proportion of fresh thrombus and aneurysm growth between baseline and reference CTAs. Three-year follow-up was made to detect missed endoleak, EVAR complication and mortality. Data analyses included Cohen's kappa; sensitivity, specificity and positive predictive value (PPV); Pearson coefficient and Student's t-tests.

Results

Seven endoleaks in 28 participants were detected by the two SWS readers (k=0.858). Sensitivity of endoleak detection with SWS was 100%, specificity and PPV averaged 67% and 50%. CDUS sensitivity was estimated at 43%. Aneurysm growth was significantly greater in the endoleak group compared to sealed AAAs. No correlation between growth and thrombus

elasticity or proportion of fresh thrombus in AAAs was found. No new endoleaks were observed in participants with SWS negative studies.

Conclusion

SWS has the potential to detect endoleaks in AAA after EVAR with comparable sensitivity to CTA and superior sensitivity to CDUS.

Introduction

Due to lower perioperative complication rate, endovascular aneurysm repair (EVAR) of abdominal aortic aneurysm (AAA) represents the most common method of AAA repair in North-America [1-3]. Although EVAR has a lower perioperative complication rate and a long-term survival comparable to open surgical repair, it has a higher rate of reintervention mainly due to endoleaks [4]. An endoleak represents an increased risk of rupture if not properly detected [5]. Endotension [6] that represents aneurysm growth without evidence of endoleak on imaging [7; 8] can also lead to AAA rupture. Therefore, life-long imaging surveillance is required after EVAR [4; 9]. Current guidelines recommend surveillance with CTA during the first year and then with color Doppler ultrasound (CDUS) if there is no documented endoleak or sac growth [10]. However, most teams are still using CTA as a primary modality for long-term surveillance [11]. This follow-up increases costs of EVAR and exposes patients to ionizing radiation and contrast-induced nephrotoxicity [4; 12].

CDUS has a lower sensitivity and reproducibility than CTA to detect endoleak [13]. Conversely, contrast-enhanced ultrasound (CEUS) has shown comparable sensitivity to CTA [13; 14]. This dynamic examination is more time consuming and requires patient preparation. As CEUS hardly competes with CTA in terms of reproducibility, efficiency and productivity, its use in North America is still low [15].

After endovascular exclusion of an AAA with a stent-graft, its diameter tend to decrease unless there is a persistent flow or pressure in the aneurysm sac [16; 17]. Presence of fresh unorganized thrombus has been described in patients with endoleaks on MRI [16]. Little attention has been given to the temporal evolution of the thrombus organization and aneurysm regression after EVAR.

Shear wave sonoelastography (SWS) measures tissue elasticity [18; 19]. This approach has never been tested for EVAR surveillance in patients. Compression elastography has been attempted to detect and classify endoleaks but did not provide additional advantages compared to CEUS [20]. The potential of SWS to detect endoleaks and characterize thrombus was previously reported in a canine model after EVAR, where fresh thrombi reported lower elasticity values than organized thrombi [21].

The primary purpose of this study was to compare the endoleak detection rate of SWS to that of CTA and CDUS. The secondary purpose was to characterize thrombus organization in the aneurysm sac by correlating AAA growth and thrombus elasticity after EVAR.

Materials and Methods

Design and Subjects

This single-center prospective study at [blinded] was approved by the institutional review board and written informed consent was obtained from all participants. Participants were included if (Figure 1): 1) they underwent EVAR and had CTA follow-up imaging between November 2014 and March 2016, 2) this follow-up was performed more than one year after EVAR, and 3) within 8 months of the combined CDUS-SWS evaluation. Patients were then followed for three years to detect occurrence of endoleak or endotension. Participants were excluded if: 1) no pre-EVAR CT was available or 2) reference standard CT was performed without contrast injection.

B-Mode, CDUS and SWS Examinations

All CDUS and SWS examinations (SuperSonic Imagine, Aixplorer) were performed by a vascular technologist with 20 years of experience, with a 192-element curved array probe (Single Crystal SC6-1) at 6 MHz. Data acquisitions were performed in the following order: B-Mode, CDUS and SWS. Length of the aneurysm was measured in a longitudinal plane, diameters and areas were measured in three equidistant axial planes between the renal arteries and aortic bifurcation. Endoleak areas were detected on CDUS and delineated. The speed range scale was initially set at 10 cm/s, with a smoothing of 0 and low wall filter. SWS parameters were set as opacity of 50%, smoothing of 5 and acoustic power as low as reasonably achievable. SWS uses the same thermal and mechanical energy indices displayed in CDUS mode. Cine loops and static images were registered for each acquisition plane.

Brachial blood pressure was measured by sphygmomanometry before and after US procedures.

SWS Qualitative Image Analysis

On the acquired elasticity maps (elastograms), an endoleak area was defined as the absence of elasticity value (< 3KPa) within the aneurysm sac outside the stent-graft. As previously reported [21], areas without signal on the posterior wall of the aneurysm were deemed as non-diagnostic as shear wave transmission could be attenuated due to stent-graft interposition or limited penetration. A thrombus was defined as everything else but endoleak or stent-graft areas within the aneurysm sac. Elasticity was first measured on the entire thrombus (total thrombus). Then, based on a previous preclinical study, values ranging between 3 and 19 kPa on SWS elastograms were labeled as fresh thrombus, whereas organized thrombus had values above 19 kPa [21].

SWS elastograms were independently reviewed by 2 readers: an abdominal radiologist ([blinded], 10 years of experience) and a graduate student in medical physics under the supervision of a vascular radiologist ([blinded], 25 years of experience). They identified and delineated endoleak regions using three (proximal, mid and distal) static axial SWS elastograms and corresponding B-Mode images. They were blinded to the color map of CDUS and CTA examinations.

SWS Quantitative Image Analysis

Elastograms were manually segmented using ImageJ software to calculate elasticity of aneurysmal sac contents [22; 23] (Rasband, W.S., V.1.47b, Research Services Branch National Institute of Mental Health). Segmentation and region of interest (ROI) positioning were done by matching B-mode and SWS images. The aneurysms were divided in three ROIs namely: endoleak areas, fresh thrombus, and total thrombus (fresh + organized thrombus).

CT Examinations

At least three CTs per participants were analyzed in this study. The exams were performed on various CT scanners (Siemens Healthineers, Sensation 4, 16 and 64; Philips Healthcare, iCT 256 and Brillance 64; GE Healthcare, ProSpeed and LightSpeed Ultra) according to the clinical standard of care.

All 30 CTs performed before EVAR were contrast-enhanced. First post-EVAR CT (baseline) included 29/30 injected studies (1/30 without contrast) and were made on average 6.7 ± 9.5 months (0.1 to 45.1 months) post treatment.

Reference standard CTAs were performed on average within 4.1 ± 2.2 months (0.2 to 7.7 months) of the combined CDUS-SWS studies. Of these, 28/30 were injected and 2/30 were excluded because they had no contrast injection due to renal insufficiency. Reference CTAs were performed on average 39.5 ± 31.2 months after EVAR (8.5 to 157 months).

Clinical data and imaging were reviewed after 3 years to account for undiagnosed leaks, aneurysm growth, EVAR complication and mortality. A last follow-up examination was available in 18 participants including one non-contrast-enhanced and 17 contrast-enhanced CTs with a mean time period of 5.0 ± 3.5 years post baseline CT (1.4 to 15.1 years).

Contrast enhanced examinations were performed with intravenous contrast injection of 100-120 ml of Iohexol (Omnipaque 350 mgI/ml or Visipaque, GE Healthcare) at 4-5 mL/s. Scan parameters were a collimation of 0.5 to 1.0 mm and a pitch of 0.75 to 1.00. Parameters were set at 120-140 kVp and 280-724 mAs, depending on participant's weight.

Aneurysms were segmented to compute maximal diameters and volumes using dedicated software [24].

Endpoint Definition

Primary endpoint was the detection of endoleak type I, II, III or endotension with SWS by 2 readers blinded to CDUS and CTAs.

The reference standard was defined either by the presence of contrast in the aneurysm sac at reference CTA, the presence of flow in the aneurysm sac on the CDUS examination performed before the SWS examination or the presence of endotension. In case of negative CT and positive CDUS, the participant was classified as positive since the specificity of CDUS is in the high range (0.97 to 1.00) [13]. Endotension was defined as growth by a minimum of 5 mm in diameter between baseline and reference CTA. Matching between SWS and CT examinations to define true and false positive was based on the cranio-caudal level of acquisition, stent-graft position, aneurysm surface and diameter at each proximal, mid and distal regions on B-mode imaging.

Secondary endpoint was correlation of elasticity measurement with AAA growth. Relevant data to compute secondary endpoints included total thrombus elasticity (kPa), percentage of fresh thrombus relative to total thrombus area (%), aneurysm growth in diameter (mm) and volume (mL) and growth rate in diameter and volume (%).

Total thrombus elasticity measurements were obtained from color elasticity maps after stent-graft and endoleak area exclusion. Percentage of fresh thrombus was computed as follows: area of thrombus with an elasticity modulus between 3 and 19 kPa over total area of thrombus in each axial plane and averaged [21]. Growth was estimated as variation of maximum diameter and volume between baseline and reference CTA. Growth was assessed at year three when imaging was available.

Statistical Analysis

SPSS Statistics 24.0 was used to perform statistical analyses. Sensitivity, specificity and positive predictive value (PPV) for endoleak detection with SWS were calculated for each reader and averaged. Agreement between the two readers for endoleak detection with SWS was assessed by Cohen's kappa. Analysis comparing total thrombus elasticity, proportion of fresh thrombus and growth between groups with and without endoleak was made using Student's t-tests assuming equal variance and setting statistical significance to $P < 0.05$. Mean percentage of fresh thrombus and total thrombus elasticity were correlated with diameter and volume growth with a Pearson coefficient.

Results

Three patients lacking appropriate CT reference imaging were excluded from the 41 potential participants recruited between November 2014 and March 2016. Out of 38 eligible participants, 28 underwent the study whereas others refused to participate or could not be reached (Figure 1).

A total of seven endoleaks were detected with the reference standard imaging (Table 2): one type Ib, five type II and one endotension. One was detected by CDUS alone, three by CTA alone, two both by CTA and CDUS (CDUS sensitivity of 43%). The endotension with a 7 mm increase in diameter was detected on CT.

Giving the small sample size, apart from age and mean diastolic pressure, risk factors and comorbidities were not statistically different between groups. Clinical and imaging characteristics of participants are summarized in Table 1.

As expected, mean variation in diameter and volume between baseline and reference studies were different in participants with and without endoleak ($P < 0.001$). A greater growth was observed in the endoleak group having a mean diameter and volume expansion of respectively 10.1 ± 14.5% and 39.0 ± 50.2%. Conversely, participants without endoleak demonstrated shrinkage with -16.3 ± 12.0% average variation in diameter and -25.9 ± 15.7% in volume.

Endoleak Detection

All seven participants with endoleaks detected by reference standard were also categorized as having endoleaks by the two blinded SWS elasticity map readers. This finding brings the sensitivity of SWS for endoleak detection to 100% in this study. As depicted in Table 3, 6 to 8 participants were incorrectly diagnosed with endoleaks lowering the SWS specificity to 62% for reader 1 and 71% for reader 2, an average of 67%. The PPV of SWS was 47% for reader 1 and 54% for reader 2, an average of 50%. Inter-observer Cohen's kappa was in the high range for agreement on endoleak diagnosis (k = 0.858).

Areas deemed non-analyzable on SWS due to absence of signal on the posterior wall were estimated to 5.1 % of the cumulated areas of SWS acquisitions. Examples of endoleak detection discrepancies with different imaging modalities are given in Figure 2 (endoleak missed on CDUS), Figure 3 (endoleak detected with all modalities), Figure 4 (false positive on SWS) and Figure 5 (no endoleak in sealed aneurysm confirmed with all modalities).

Thrombus elasticity and endoleak

In all participants, the ROIs labeled as endoleak with SWS had an elasticity modulus close to zero with an average of 0.053 ± 0.087 kPa. Significantly higher values of elasticity were found in the total thrombus averaging at 23.0 ± 11.6 kPa ($P < 0.001$).

However, total thrombus elasticity within aneurysm sac (after endoleak exclusion) was not statistically different between the endoleak group (26.9 ± 13.7 kPa) and the sealed aneurysm group (21.7 ± 10.8 kPa) with a *P*-value of 0.318.

Likewise, an average of 20.5 ± 6.3 % and 25.2 ± 8.7 % of area containing fresh thrombus were found in groups with and without endoleak, which was not significantly different (*P* = 0.203).

Elasticity modulus and aneurysm growth

No correlation was found between the thrombus elasticity and diameter (R = 0.278) or volume (R = 0.333) change over time.

A weak negative correlation was found between the proportion of fresh thrombus and growth in diameter and volume. The correlation was -0.453 between the amount of fresh thrombus and diameter growth and -0.386 between the amount of fresh thrombus and volume growth.

Long-term follow-up

By March 2019, 18/28 participants had had additional CT: 15 contrast-enhanced in arterial phase, one in portal phase and two unenhanced. No additional endoleak or significant increase in aneurysm sac size were detected. The remainder 12 participants either ceased to be followed by imaging with participant’s agreement (due to old age and comorbidities) or were lost to follow-up.

Out of the participants with type II endoleaks, one underwent an embolization while the four others were observed with a favorable outcome. A participant with endotension was eventually diagnosed with an infected prosthesis and was treated conservatively with antibiotics. A high mortality rate was noted with five deaths at three years, two of metastatic cancer, one of terminal liver failure and two of indeterminate cause. Out of the five deaths, three were in the endoleak group including the type Ib endoleak participant who died of indeterminate cause.

Discussion

This first clinical feasibility study showed that SWS is highly sensitive and fairly specific to detect endoleak and is reproducible. SWS provided mechanical information on the AAA sac contents that is complementary to B-mode and CDUS examinations. However, no correlation was found between overall sac elasticity measurement and presence of endoleak or AAA growth.

Endoleak detection

Because liquid does not support shear wave propagation, endoleak regions were mapped close to 0 kPa. SWS thus provides opportunities to depict low blood flow endoleaks that are difficult to find with other techniques [25; 26]. Unlike CDUS which provides a velocity-dependent and angle-dependent signal, shear wave sonoelastography permits detection of areas with minimal flow and even stagnant liquid. The high sensitivity of SWS in detecting areas of endoleak has been shown in this study where all seven endoleaks or endotension diagnosed by the reference standard were also detected by the two independent elastograms reviewers. Although the study was not designed to assess CDUS sensitivity, it is interesting to note that it only detected 3 endoleaks compared to 7 with SWS.

This high sensitivity comes to the detriment of specificity and positive predictive value that were averaged respectively to 67% and 50%. Both are expected to be low in a screening examination but should be improved to have a greater clinical impact. The number of false positives could be explained by the study design where both readers only had access to selected static axial elasticity maps and B-mode images. A dynamic examination with real-time feedback of thrombus mechanical properties combined with concurrent CDUS evaluation would probably improve the specificity. On the other hand, there was no apparition of endoleak or endotension in SWS negative patients on long-term follow-up.

Thrombus elasticity

No difference in total thrombus elasticity values or proportion of fresh thrombus in the aneurysm sac could be found between groups with and without endoleak. In addition to the small sample size, the accuracy of kPa measurements in a vessel with anisotropic properties may have played a role. Other techniques, as quasi-static vascular ultrasound elastography measuring the strain of vascular structures induced by the cardiac pulsation seems to have a more direct correlation with elasticity relying on aortic thrombus displacement rather than shear wave speed propagation [27].

Although endoleak group had a significant higher growth in volume and diameter no correlation has been found with the thrombus elasticity. This can be explained by the elasticity thresholds defining fresh thrombus (3 to 19 kPa) based on a preclinical study where a 7.5 MHz linear probe was used. This clinical study uses a lower frequency (6 MHz) curvilinear probe to achieve deeper penetration but uses the same post-processing algorithm to compute the elasticity maps. Areas of null elasticity are most likely valid given the presence of signal in its surrounding. However, we cannot confidently say that areas of 3 to 19 kPa represent fresh thrombus histopathologically as it was in a canine model [21]. Further evaluation of data translation between the higher and lower frequency probes and studies of fresh thrombus thresholds should be made.

Limitations

The small sample size represents the main weakness. At a feasibility stage, we considered this small sample was sufficient to evaluate if SWS should gain further attention. Elastograms were analyzed to favor a high sensitivity over specificity for the diagnosis of endoleaks. A real-time multimodal approach combining B-mode, CDUS and SWS would likely result in more accurate diagnoses. In future clinical work-flow, we could reserve injection of contrast-enhanced ultrasound examination only in participants with positive SWS examination to improve the specificity.

Combined SWS-CDUS examinations where all performed after the reference CTA on average 4.1 ± 2.2 months (0.2 to 7.7 months) which constitutes a long latency period during which endoleak might have occurred. If such event has happened and went undetected, SWS sensitivity was overestimated. In an attempt to mitigate the risk of missing an endoleak, a three-year follow-up was performed. Moreover, CDUS was acquired concomitantly with SWS (after reference CTA) and had the potential to detect new endoleak occurring in this time interval. This might explain why in patient 3 no endoleak were detected in the CTA but one was diagnosed by both SWS and CDUS performed 4.93 months after.

Nearly 5% of SWS signal had to be considered non-diagnostic because of the absence of wave transmission to the posterior wall of the aneurysm (Figure 2d). Without signal on the posterior aspect of the aneurysmal sac, one cannot conclude if it represents an endoleak or if the region is not assessable by the focused ultrasound beam. Again, a faster post-processing with real-time feedback would permit multiple elastogram acquisitions in different angles and planes than the three axials (proximal, mid, distal) analyzed in this study. This could enable the analysis of the whole aneurysmal sac and increase SWS sensitivity and specificity for endoleak detection.

Conclusion

This first-in-man study demonstrates the potential of SWS to detect endoleaks in abdominal aortic aneurysm after endovascular repair with an excellent sensitivity. SWS has shown its potential to characterize aneurysmal sac contents based on elasticity maps. Optimization of SWS thresholds to discriminate area of soft and organized thrombus, and testing SWS on a larger sample size constitute the next crucial steps to developing this screening tool. Addition of SWS is conceivable particularly using a multimodal approach with B-Mode, CDUS and, if needed, contrast-enhanced ultrasound examination.

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References

1 Eliason JL, Upchurch GR, Jr. (2009) Endovascular treatment of aortic aneurysms: state of the art. Curr Treat Options Cardiovasc Med 11:136-145

2 Levin DC, Rao VM, Parker L, Frangos AJ, Sunshine JH (2009) Endovascular repair vs open surgical repair of abdominal aortic aneurysms: comparative utilization trends from 2001 to 2006. J Am Coll Radiol 6:506-509

3 Jetty P, Husereau D (2012) Trends in the utilization of endovascular therapy for elective and ruptured abdominal aortic aneurysm procedures in Canada. J Vasc Surg 56:1518-1526, 1526 e1511

4 Schermerhorn ML, Buck DB, O'Malley AJ et al (2015) Long-Term Outcomes of Abdominal Aortic Aneurysm in the Medicare Population. N Engl J Med 373:328-338

5 White GH, Yu W, May J, Chaufour X, Stephen MS (1997) Endoleak as a complication of endoluminal grafting of abdominal aortic aneurysms: classification, incidence, diagnosis, and management. J Endovasc Surg 4:152-168

6 Koole D, Moll FL, Buth J et al (2011) Annual rupture risk of abdominal aortic aneurysm enlargement without detectable endoleak after endovascular abdominal aortic repair. J Vasc Surg 54:1614-1622

7 White GH (2001) What are the causes of endotension? J Endovasc Ther 8:454-456

8 Kato N, Shimono T, Hirano T et al (2002) Aneurysm expansion after stent-graft placement in the absence of endoleak. J Vasc Interv Radiol 13:321-326

9 Zaiem F, Almasri J, Tello M, Prokop LJ, Chaikof EL, Murad MH (2018) A systematic review of surveillance after endovascular aortic repair. J Vasc Surg 67:320-331 e337

10 Chaikof EL, Dalman RL, Eskandari MK et al (2018) The Society for Vascular Surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. J Vasc Surg 67:2-77 e72

11 Mell MW, Garg T, Baker LC (2017) Under-Utilization of Routine Ultrasound Surveillance after Endovascular Aortic Aneurysm Repair. Ann Vasc Surg. 10.1016/j.avsg.2017.03.203

12 Brown LC, Brown EA, Greenhalgh RM, Powell JT, Thompson SG, Participants UET (2010) Renal function and abdominal aortic aneurysm (AAA): the impact of different management strategies on long-term renal function in the UK EndoVascular Aneurysm Repair (EVAR) Trials. Ann Surg 251:966-975

13 Karthikesalingam A, Al-Jundi W, Jackson D et al (2012) Systematic review and meta-analysis of duplex ultrasonography, contrast-enhanced ultrasonography or computed tomography for surveillance after endovascular aneurysm repair. Br J Surg 99:1514-1523

14 Bredahl KK, Taudorf M, Lonn L, Vogt KC, Sillesen H, Eiberg JP (2016) Contrast Enhanced Ultrasound can Replace Computed Tomography Angiography for Surveillance After Endovascular Aortic Aneurysm Repair. Eur J Vasc Endovasc Surg 52:729-734

15 Wilson SR, Greenbaum LD, Goldberg BB (2009) Contrast-enhanced ultrasound: what is the evidence and what are the obstacles? AJR Am J Roentgenol 193:55-60

16 Cornelissen SA, van der Laan MJ, Vincken KL et al (2011) Use of multispectral MRI to monitor aneurysm sac contents after endovascular abdominal aortic aneurysm repair. J Endovasc Ther 18:274-279

17 Farner MC, Carpenter JP, Baum RA, Fairman RM (2003) Early changes in abdominal aortic aneurysm diameter after endovascular repair. J Vasc Interv Radiol 14:205-210

18 Bercoff J, Tanter M, Fink M (2004) Supersonic shear imaging: a new technique for soft tissue elasticity mapping. IEEE Trans Ultrason Ferroelectr Freq Control 51:396-409

19 Sarvazyan AP, Rudenko OV, Swanson SD, Fowlkes JB, Emelianov SY (1998) Shear wave elasticity imaging: a new ultrasonic technology of medical diagnostics. Ultrasound Med Biol 24:1419-1435

20 Gurtler VM, Rjosk-Dendorfer D, Reiser M, Clevert DA (2014) Comparison of contrast-enhanced ultrasound and compression elastography in the follow-up after endovascular aortic aneurysm repair. Clin Hemorheol Microcirc 57:175-183

21 Bertrand-Grenier A, Lerouge S, Tang A et al (2017) Abdominal aortic aneurysm follow-up by shear wave elasticity imaging after endovascular repair in a canine model. Eur Radiol 27:2161-2169

22 Abramoff M MP, Ram S (2004) Image Processing with ImageJ. Biophotonics International 11:36-42

23 Schneider CA, Rasband WS, Eliceiri KW (2012) NIH Image to ImageJ: 25 years of image analysis. Nat Methods 9:671-675

24 Kauffmann C, Tang A, Therasse E et al (2012) Measurements and detection of abdominal aortic aneurysm growth: Accuracy and reproducibility of a segmentation software. Eur J Radiol 81:1688-1694

25 AbuRahma AF, Welch CA, Mullins BB, Dyer B (2005) Computed tomography versus color duplex ultrasound for surveillance of abdominal aortic stent-grafts. J Endovasc Ther 12:568-573

26 Elkouri S, Panneton JM, Andrews JC et al (2004) Computed tomography and ultrasound in follow-up of patients after endovascular repair of abdominal aortic aneurysm. Ann Vasc Surg 18:271-279

27 Salloum E, Bertrand-Grenier A, Lerouge S et al (2016) Endovascular Repair of Abdominal Aortic Aneurysm: Follow-up with Noninvasive Vascular Elastography in a Canine Model. Radiology 279:410-419

Figure Legends

Figure 1.

Study flow chart shows recruitment process. Sample size is 28. Seven endoleaks were detected by the defined reference standard.

Note.— CTA = computed tomography angiography, SWS = shear wave sonoelastography, EVAR = endovascular aneurysm repair, CDUS = color Doppler ultrasound.

Figure 2.

Endoleak detected with SWS and CT but missed with CDUS in participant 7. Axial B-mode **(a)** shows stent-graft (arrow). Axial CTA located slightly below the US acquisition **(b)** confirms a type II endoleak (arrow) from the median sacral artery. CDUS **(c)** shows no signal outside the stent-graft. SWS elasticity map **(d)** demonstrates absence of elasticity signal in the right posterolateral sac (arrowheads) compatible with endoleak. Note the absence of signal in the left posterior sac wall indicating a non-diagnostic region (arrow).

Figure 3.

Endoleak detected with SWS, CDUS and CT in participant 12. Axial B-mode **(a)** shows hypoechogenic posterior aneurysmal sac contents. Axial CTA **(b)** confirms a large contrast pooling (arrow) secondary to a type 1b endoleak. CDUS **(c)** shows signal in the stent-graft limbs and in the aneurysmal sac outside the stent-graft (arrow). SWS elasticity map **(d)** demonstrates absence of elasticity signal in the endoleak region (arrowheads).

Figure 4.

False positive endoleak on SWS in participant 16. Axial B-mode **(a)** shows an AAA deeply located 12 cm below probe AAA at the level of stent-graft limbs (arrowheads). Axial CTA **(b)** and CDUS **(c)** show no endoleak. Note the inferior vena cava signal (arrow in c) in the posterolateral right aspect of the AAA. SWS elasticity map **(d)** demonstrates low elasticity signal (arrowheads) in the left posterolateral sac without endoleak in the corresponding region of reference standard imaging. High elasticity modulus (>80kPa) in red indicates organised thrombus (arrow).

Figure 5.

Sealed aneurysm in participant 23. Axial B-mode **(a)**, CTA **(b)** and CDUS **(c)** show a small aneurysmal sac (arrowheads) without evidence of endoleak. SWS elasticity map **(d)** shows intermediate signal (20-40 kPa) surrounding the stent graft (arrowheads). Except for the lumen (arrow), no signal void suggesting endoleak is found on SWS map.

Table 1. Characteristics of participants and AAAs at baseline and reference CTAs

	Endoleak (*n* = 7)	**No Endoleak (*n* = 21)**	***P* Value**
Participants characteristics at last follow-up			
Men (%)	7 (100)	18 (86)	0.308
Women (%)	0 (0)	3 (14)	0.308
Age ± SD	83.3 ± 4.3	76.0 ± 7.5	0.022
Weight ± SD (kg)	73.9 ± 6.8	82.1 ± 16.1	0.213
Diabetes (%)	0 (0)	6 (29)	0.119
CVA (%)	3 (43)	2 (10)	0.048
Dyslipidemia (%)	6 (86)	17 (81)	0.786
Active smoking (%)	0 (0)	5 (24)	0.166
Past smoking (%)	2 (29)	10 (48)	0.397
Mean systolic mm Hg ± SD	141 ± 11	135 ± 19	0.424
Mean diastolic mm Hg ± SD	77 ± 10	68 ± 8	0.027
Abdominal aortic aneurysm characteristics at reference CTA			
Mean diameter ± SD (mm) [min ; max]	63.0 ± 5.8 [54.2 ; 72.1]	47.3 ± 11.5 [28.5 ; 76.0]	0.002
Mean volume ± SD (mL) [min ; max]	190 ± 107 [108 ; 416]	114 ± 56 [55 ; 287]	0.020
Mean total thrombus elasticity ± SD (kPa)	26.9 ± 13.7	21.7 ± 10.8	0.318

Mean fresh thrombus ± SD (%)	20.5 ± 6.3	25.2 ± 8.7	0.203
Aneurysm growth between baseline (post-EVAR) and reference standard CTAs*			
Diameter growth ± SD (%)	10.1 ± 14.5	-16.3 ± 11.9	< 0.001
Diameter growth ± SD (mm)	5.6 ± 7.8	-9.8 ± 7.8	< 0.001
[min ; max]	[-2.0 ; 21.0]	[-31.0 ; 0,2]	
Volume growth ± SD (%)	39.0 ± 50.2	-25.9 ± 15.7	< 0.001
Volume growth ± SD (mL)	57.7 ± 86.6	-48.4 ± 47.1	< 0.001
[min ; max]	[-0.7 ; 244.5]	[-196.2 ; 0.8]	

Note.— CVA = cerebrovascular accident. SD = standard deviation.

Mean fresh thrombus = proportion of 3 to 19 kPa thrombus over total thrombus

*A negative growth represents an aneurysm shrinkage

Table 2. Endoleak detection with various modalities

Participant	CDUS	CTA	Endotension	Reference Standard	Reader 1 SWS ‡	Reader 2 SWS ‡
1	-	-	-	-	-	-
2	-	-	-	-	1	1
3	1	-	-	Type II	1	1
4	-	-	-	-	-	-
5	-	-	-	-	-	-
6	-	-	-	-	1	1
7	-	1	-	Type II	1	1
8	-	-	-	-	-	-
9	1	1	-	Type II	1	1
10	-	-	-	-	-	-
11	-	-	-	-	1	1
12	1	1	-	Type Ib	1	1
13	-	-	-	-	-	-
14	-	-	-	-	-	-
15	-	-	-	-	-	-
16	-	-	-	-	1	1
17	-	-	-	-	1	1
18	-	-	-	-	-	-
19	-	-	1	Type V	1	1
20	-	-	-	-	-	-
21	-	-	-	-	-	-
22	-	-	-	-	1	1
23	-	-	-	-	-	-
24	-	1	-	Type II	1	1
25	-	1	-	Type II	1	1
26	-	-	-	-	1	-
27	-	-	-	-	1	-
28	-	-	-	-	-	-
Total	3	5	1	7	15	13

Note.— CDUS = color Doppler ultrasound, CTA = computed tomography angiography, SWS = shear wave imaging
‡ Inter-observer Cohen’s kappa = 0.858

Table 3. SWS imaging detection rate by two readers compared to reference standard

		Reference standard +		
		Endoleak	**No endoleak**	*Total*
SWS Reader 1	Endoleak	**7**	**8**	*15*
	No endoleak	**0**	**13**	*13*
	Total	*6*	*21*	*28*
SWS Reader 2	Endoleak	**7**	**6**	*13*
	No endoleak	**0**	**15**	*15*
	Total	*7*	*21*	*28*

+ Reference standard is defined as presence of contrast in the aneurysm sac in the reference CTA and/or CDUS signal in the aneurysm sac and/or endotension.

Note.— SWS = shear wave imaging.

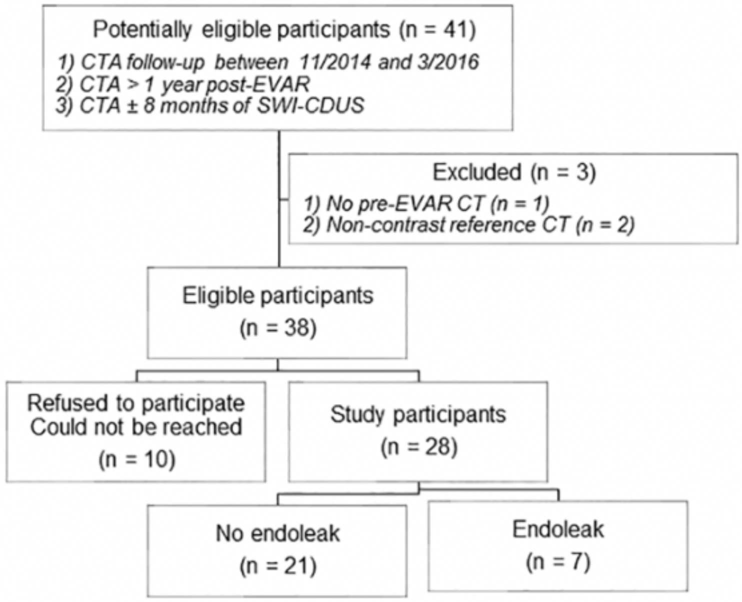

Figure 1 : Study flow chart shows recruitment process. Sample size is 28. Seven endoleaks were detected by the defined reference standard.

Note.— CTA = computed tomography angiography, SWS = shear wave sonoelastography, EVAR = endovascular aneurysm repair, CDUS = color Doppler ultrasound.

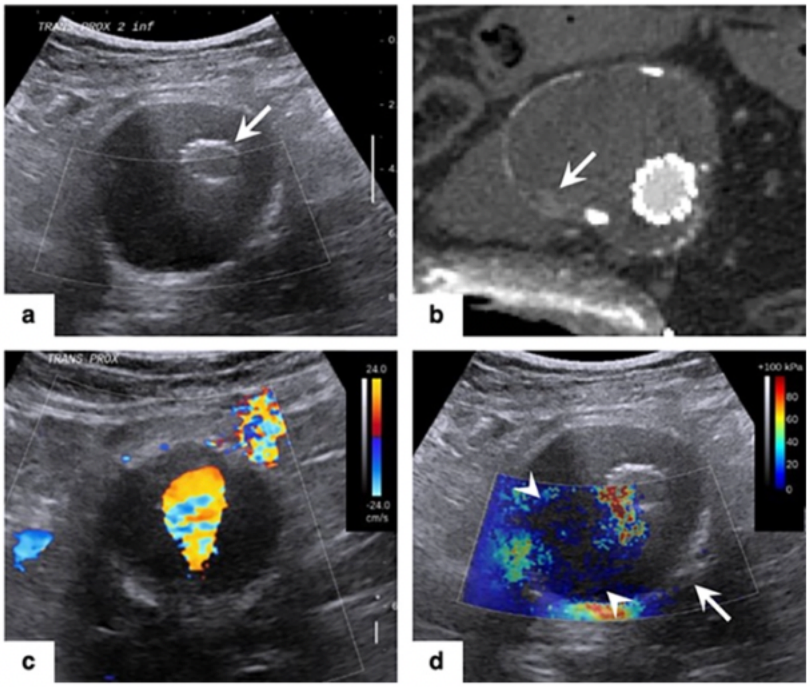

Figure 2 : Endoleak detected with SWS and CT but missed with CDUS in participant 7. Axial B-mode **(a)** shows stent-graft (arrow). Axial CTA located slightly below the US acquisition **(b)** confirms a type II endoleak (arrow) from the median sacral artery. CDUS **(c)** shows no signal outside the stent-graft. SWS elasticity map **(d)** demonstrates absence of elasticity signal in the right posterolateral sac (arrowheads) compatible with endoleak. Note the absence of signal in the left posterior sac wall indicating a non-diagnostic region (arrow).

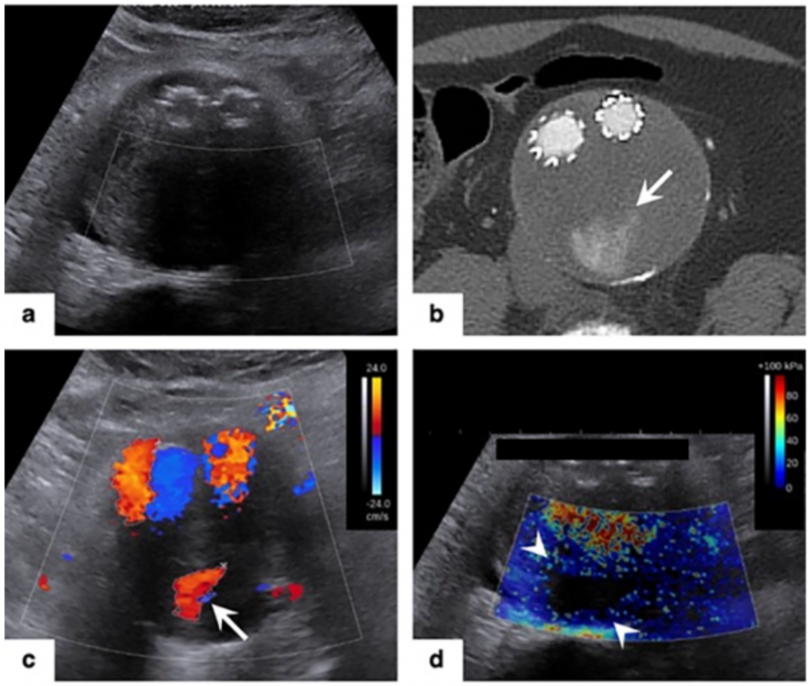

Figure 3 : Endoleak detected with SWS, CDUS and CT in participant 12. Axial B-mode **(a)** shows hypoechogenic posterior aneurysmal sac contents. Axial CTA **(b)** confirms a large contrast pooling (arrow) secondary to a type 1b endoleak. CDUS **(c)** shows signal in the stent-graft limbs and in the aneurysmal sac outside the stent-graft (arrow). SWS elasticity map **(d)** demonstrates absence of elasticity signal in the endoleak region (arrowheads).

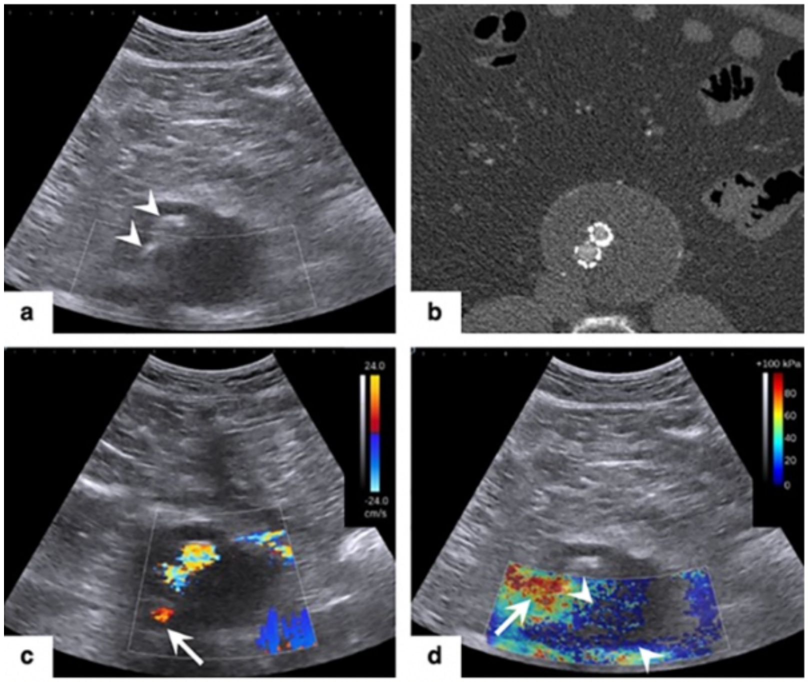

Figure 4 : False positive endoleak on SWS in participant 16. Axial B-mode **(a)** shows an AAA deeply located 12 cm below probe AAA at the level of stent-graft limbs (arrowheads). Axial CTA **(b)** and CDUS **(c)** show no endoleak. Note the inferior vena cava signal (arrow in c) in the posterolateral right aspect of the AAA. SWS elasticity map **(d)** demonstrates low elasticity signal (arrowheads) in the left posterolateral sac without endoleak in the corresponding region of reference standard imaging. High elasticity modulus (>80kPa) in red indicates organised thrombus (arrow).

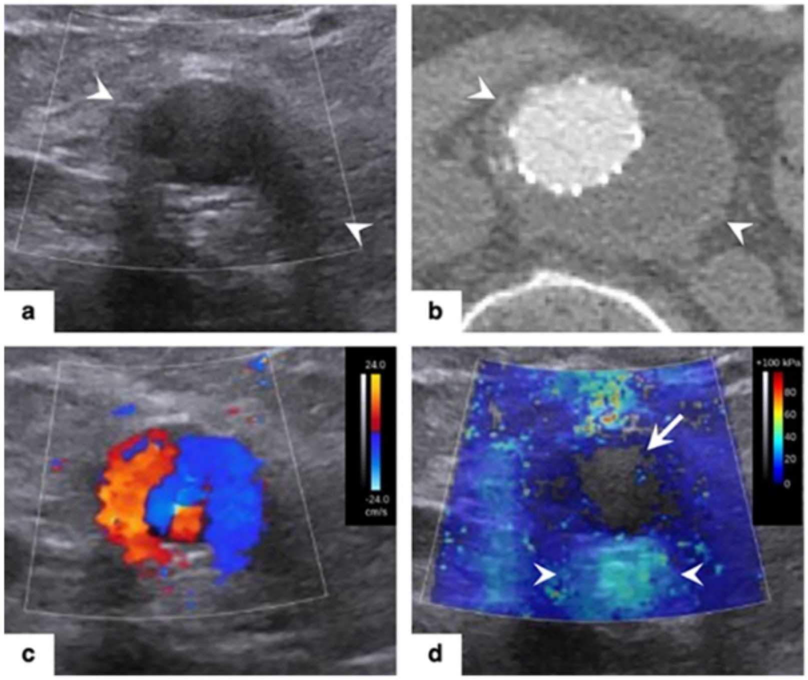

Figure 5 : Sealed aneurysm in participant 23. Axial B-mode (a), CTA (b) and CDUS (c) show a small aneurysmal sac (arrowheads) without evidence of endoleak. SWS elasticity map (d) shows intermediate signal (20-40 kPa) surrounding the stent graft (arrowheads). Except for the lumen (arrow), no signal void suggesting endoleak is found on SWS map.