Evidence for contrast-enhanced ultrasound in fenestrated EVAR surveillance

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Endovascular aneurysm repair (EVAR) has been reported as an effective alternative to open surgical repair.[1,2] Since its first introduction into clinical practice in the early 1990s, endovascular stent-grafting has progressed rapidly, following an improved understanding of the strengths and limitations of various devices and treated patient populations.[3-6] Endovascular technology has evolved to produce fenestrated stent-grafts which are designed to deal with patients with short-necked and juxtarenal aneurysms.[7-18] Fenestrated stent-grafts have concerns similar to those that apply to conventional endovascular repair, i.e., structural durability, endoleak, renal dysfunction, and migration. Moreover, there is the potential loss of the target vessel resulting from the fenestrated technique. Two published systematic reviews confirm the potential lower perioperative mortality of the fenestrated technique in comparison with open repair, based on short to midterm data.[19, 20] Fenestrated stent-grafts have become commercially available and provide an alternative to open surgery, especially in patients who are unfit for open repair or standard endovascular repair.

Although fenestrated repair of abdominal aortic aneurysms (AAA) has been shown to reduce perioperative mortality compared to open repair, it is associated with a higher rate of subsequent re-intervention.[19] Thus, postoperative surveillance is considered mandatory to identify graft-related complications such as visceral vessel stenosis and to direct re-intervention and avoid later morbidity and mortality.[21, 22] Imaging techniques play an important role in the detection of any abnormalities associated with fenestrated endovascular repair. Helical computed tomographic angiography (CTA) is the routine technique used to assess the patency of the fenestration vessels and target vessel stents in relation to the arterial branches.[20]

The diagnostic value of CTA in EVAR has been enhanced with development of multislice CT technology and use of a series of 2-dimensional (2D) or 3D reconstructed visualizations

which are generated to improve the understanding of stent-grafts in relation to the aortic branches.[23-29] CTA is currently the gold standard for EVAR surveillance, however, it is associated with radiation exposure. This raises increasing concerns about the cumulative radiation dose of CTA, since patients treated with EVAR including fenestrated repair undergo regular surveillance imaging (serial CT scans) to monitor the integrity of the endovascular repair and to enable secondary intervention to prevent rupture should CT imaging reveal a problem. It has been reported that the cumulative dose from a series of CT scans following EVAR could be as high as 205 mSv over five years. [30] This equates to a lifetime attributable risk of cancer of 0.60% (1 in 170). In addition, CTA contributes to the decline in renal function after EVAR due to contrast-induced nephropathy.[31] Therefore, duplex ultrasound, an alternative to CTA in the follow-up of EVAR, has been investigated as the potential method of imaging modality.

In the current issue of the *JEVT*, Perini et al [32] evaluated the accuracy of contrast-enhanced ultrasound (CEUS) as an effective alternative to CTA in the endoleak detection, aneurysm sac diameter measurement and target vessel patency during follow-up after fenestrated EVAR. The authors studied 62 patients (mean age 72 years) who underwent fenestrated EVAR with a maximum of 3 fenestrations. Both CEUS and CTA examinations were performed in all patients for comparative analysis. Maximum aneurysm sac diameters were measured with both imaging modalities. Detection of endoleaks was evaluated and differences in endoleak detection were assessed between the two modalities. Target vessel patency following fenestrated EVAR was analyzed, and the agreement between two modalities was compared. The authors demonstrated the good to excellent agreement between the two modalities in the follow-up performance based on the first postoperative images. The mean difference in aneurysm sac diameter was –1.13±3.19 mm (95% CI –0.34 to –1.92), with CTA measurements tending to be slightly larger. Both CEUS and CTA

showed the same diagnostic accuracy with excellent agreement in the endoleak detection. A complete agreement was reached between CEUS and CTA in the assessment of fenestrated vessels, with 144 (98.6%) vessel being patent, 1 having significant stenosis and another being thrombosed. The study by Perini et al therefore concluded that CEUS is as accurate as CTA in monitoring endoleaks, aneurysm sac diameters, and target vessel patency in patients treated with fenestrated stent grafts. CEUS is not recommended as the sole imaging modality for fenestrated EVAR surveillance, however, it could be used as an effective alternative to CTA due to its advantage of reducing lifetime exposure to ionizing radiation associated with the CTA scans.

There are three observations from Perini's study that bear discussions. First, the authors have validated CEUS in this study as an accurate modality for early follow-up of fenestrated EVAR. Color duplex ultrasound scanning has been considered a potentially attractive alternative to CTA in the follow-up of patients after standard EVAR, as it is less expensive and does not involve ionizing radiation or potentially nephrotoxic contrast. [33-36] Several studies have reported excellent results with color duplex ultrasound compared to CTA, while others have concluded that CTA is still the technique for surveillance after EVAR.[37-40] Several authors have pointed out the usefulness of CEUS because it seems to allow better identification and characterization of endoleaks.[41-45] In a study using CEUS, Napoli et al.[43] were able to differentiate a low-flow endoleak from endotension, which had been diagnosed on the basis of triple-phase contrast-enhanced CTA. Similarly, Henao et al [44] confirmed the efficacy of CEUS to detect endoleaks compared to CTA, as their results demonstrated that CEUS detected all of the nine endoleaks, while CTA failed to recognize three type II endoleaks observed by CEUS. CEUS may be used as a primary modality for the detection of endoleaks and characterization of the dynamic flow of endoleaks. Perini et al [45] in their recent study consisting of 395 patients who underwent both standard and fenestrated EVAR showed

the same efficacy by CEUS and CTA in post-EVAR follow-up. According to authors' experience, CEUS has been recommended to replace the 6-month and 24-month CTA examinations in the standard EVAR surveillance.

The second comment is related to some of the CEUS limitations which prevent it from being used as the sole imaging modality for fenestrated EVAR surveillance. In addition to the well documented operator dependency of ultrasound examinations and patient factors (e.g., large body mass index, bowel gas), the authors noted that CEUS has limitations in the reliable detection of other complications such as stent fracture, limb kinking, stent graft migration or component separation. In contrast, CTA provides superior information related to stent graft structure and integrity, and its diagnostic applications are augmented by 3D reconstructions which have been reported to provide valuable information for the assessment of stent graft migration, as well as its relationship with aortic branches.[23-29,46] Despite the advantages of CTA in the identification of stent graft details, the deleterious effect on renal function, radiation exposure, and significant cost of this surveillance procedure are considered problematic. As the authors recommended, 4-view abdominal radiographs should always be performed at the same time as ultrasound, [47] and their findings should be interpreted together. This significantly reduces the radiation dose as plain radiography produces radiation dose of less than 1 mSv, thus the radiation-induced risk of malignancy is negligible.

The third comment is related to the clinical applicability of these findings to patients treated with fenestrated stent-grafts. The authors highlighted the potential value of using CEUS as an alternative to CTA in the follow-up of fenestrated stent-grafts, however, their data was based on a single center experience and was restricted to the observation of the first postoperative investigation. Furthermore, the limited number of patients and the number of abnormalities in their first follow-up series represents another limitation of the study. The

authors indicated that further studies are necessary to better define the role of CEUS in surveillance of fenestrated EVAR. Many clinical centers initially undertook surveillance protocols from those outlines in the randomised controlled trials or early registries,[48] which used contrast-enhanced CT as the gold standard of surveillance. However, excessive dependence on CT is expensive and exposes the patients to nephrotoxic intravenous contrast and ionizing radiation.[49,50] Increasing the proportional use of non-nephrotoxic imaging modalities after EVAR has been advocated as an alternative approach to reduce surveillance-related morbidity.[51] Sternbergh et al [52] recommended a revised EVAR surveillance regimen according to their multicenter data from the US Zenith endovascular AAA trials. On the basis of these data and 5-year follow-up outcomes, they proposed a modified surveillance protocol to alter the intensity and frequency of postoperative imaging follow-up. In patients without early endoleaks, the 6-month surveillance is eliminated, and the yearly aortic ultrasound examination is recommended for long-term surveillance of more than 1 year. There is increasing evidence of a trend from using conventional CT follow-up to ultrasound monitoring,[52, 53] so there is a need for a contemporary evaluation of surveillance after EVAR. A recent survey which was administered to 41 clinical centers experienced in EVAR in the UK has shown there is significant heterogeneity in national practice for postoperative surveillance after EVAR.[54] Intensive use of CT was observed in some centers and this may lead to cumulative renal injury due to repeated administration of contrast agents and radiation exposure. The heterogeneity seen in this survey reflects the ongoing uncertainty about the surveillance protocol following EVAR. More evidence is needed to establish a consensus towards an optimal surveillance protocol that is clinically and economically effective.

In summary, Perini and colleagues have successfully shown the accuracy of CEUS in the surveillance of fenestrated stent-grafts. However, since the current study is based on a small number of patients and the first postoperative imaging session only, large-scale multicenter

studies are needed before generalizing conclusions regarding the use of CEUS in routine surveillance of fenestrated EVAR patients.

References

1. Greenhalgh RM, Brown LC, Kwong GP, et al. Comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: randomised controlled trial. *Lancet.* 2004;364:843-848.
2. Prinssen M, Verhoeven EL, Buth J, et al. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. *N Engl J Med*. 2004;351:1607-1618.
3. Parodi JC, Palmaz JC, Barone HD. Transfemoral intraluminal graft implantation for abdominal aortic aneurysms. *Ann Vasc Surg*. 1991;5:491-499.
4. Buth J, van Marrewijk CJ, Harris PL, et al. Outcome of endovascular abdominal aortic aneurysm repair in patients with conditions considered unfit for an open procedure: a report on the EUROSTAR experience. *J Vasc Surg*. 2002;35:211-221.
5. Lobato AC, Quick RC, Vaughn PL, et al. Transrenal fixation of aortic endografts: intermediate follow-up of a single-center experience. *J Endovasc Ther*. 2000;7:273-278.
6. Bove PG, Long GW, Zelenock GB, et al. Transrenal fixation of aortic stent-grafts for the treatment of infrarenal aortic aneurysmal disease. *J Vasc Surg*. 2000;32:697-703.
7. Browne TF, Hartley D, Purchas S, et al. A fenestrated covered suprarenal aortic stent. *Eur J Vasc Endovasc Surg.* 1999;18:445-449.
8. Stanley BM, Semmens JB, Lawrence-Brown MM, et al. Fenestration in endovascular grafts for aortic aneurysm repair: new horizons for preserving blood flow in branch vessels. *J Endovasc Ther*. 2001;8:16-24.

9. Muhs BE, Verhoeven EL, Zeebregts CJ, et al. Mid-term results of endovascular aneurysm repair with branched and fenestrated endografts. *J Vasc Surg*. 2006;44:9-15.

10. Verhoeven EL, Prins TR, Tielliu IF, et al. Treatment of short-necked infrarenal aortic aneurysms with fenestrated stent-grafts: short-term results. *Eur J Vasc Endovasc Surg*. 2004;27:477-483.

11. Greenberg RK, Haulon S, O'Neill S, et al. Primary endovascular repair of juxtarenal aneurysms with fenestrated endovascular grafting. *Eur J Vasc Endovasc Surg*. 2004;27:484-491.

12. Greenberg RK, Haulon S, Lyden SP, et al. Endovascular management of juxtarenal aneurysms with fenestrated endovascular grafting. *J Vasc Surg*. 2004;39:279-287.

13. Anderson JL, Berce M, Hartley D. Endoluminal aortic grafting with renal and superior mesenteric artery incorporation by graft fenestration. *J Endovasc Ther*. 2001;8:3-15.

14. Semmens JB, Lawrence-Brown MM, Hartley DE, et al. Outcomes of fenestrated endografts in the treatment of abdominal aortic aneurysm in Western Australia (1997-2004). *J Endovasc Ther*. 2006;13:320-329.

15. Halak M, Goodman MA, Baker SR. The fate of target visceral vessels after fenestrated endovascular aortic repair-general considerations and mid-term results. *Eur J Vasc Endovasc Surg*. 2006;32:124-128.

16. O'Neill S, Greenberg RK, Haddad F, et al. Prospective analysis of fenestrated endovascular grafting: intermediate-term outcomes. *Eur J Vasc Endovasc Surg*. 2006;32:115-123.

17. Anderson JL, Adam DJ, Berce M, et al. Repair of thoracoabdominal aortic aneurysms with fenestrated and branched endovascular stent grafts. *J Vasc Surg*. 2005;42:600-607.

18. Verhoeven EL, Vourliotakis G, Bos WT, et al. Fenestrated stent grafting for short-necked and juxtarenal abdominal aortic aneurysm: An 8-year single-centre experience. *Eur J Vasc Endovasc Surg*. 2010; 39: 529-535.

19. Nordon IM, Hinchliffe RJ, Holt PJ, et al. Modern treatment of juxtarenal abdominal aortic aneurysms with fenestrated endografting and open repair-a systematic review. *Eur J Vasc Endovasc Surg.* 2009; 38: 35-41.

20. Sun Z, Mwipatayi BP, Semmens JB, et al. Short to midterm outcomes of fenestrated endovascular grafts in the treatment of abdominal aortic aneurysms: a systematic review. *J Endovasc Ther*. 2006; 13: 747-753.

21. Nordon IM, Karthikesalingam A, Hinchliffe RJ, et al. Secondary interventions following endovascular aneurysm repair (EVAR) and the enduring value of graft surveillance. *Eur J Vasc Endovasc Surg*. 2010;39:547-554.

22. Troisi N, Donas KP, Austermann M, et al. Secondary procedures after aortic aneurysm repair with fenestrated and branched endografts. *J Endovasc Ther*. 2011;18:146-153.

23. Sun Z, Winder J, Kelly B, et al. CT virtual intravascular endoscopy of abdominal aortic aneurysms treated with suprarenal endovascular stent grafting. *Abdom Imaging*. 2003;28:580-587.

24. Sun Z, Winder RJ, Kelly BE, et al. Diagnostic value of CT virtual intravascular endoscopy in aortic stent-grafting. *J Endovasc Ther*. 2004;11:13-25.

25. Sun Z, O'Donnell M, Winder RJ, et al. Effect of suprarenal fixation of aortic stent-grafts on the renal artery ostia: assessment of morphological changes by virtual intravascular endoscopy. *J Endovasc Ther*. 2007; 14: 650-660.

26. Sun Z, Allen YB, Nadkarni S, et al. CT virtual intravascular endoscopy in the visualization of fenestrated stent-grafts. *J Endovasc Ther*. 2008;15:42-51.

27. Sun Z, Allen YB, Mwipatayi BP, et al. Multislice CT angiography in the follow-up of fenestrated endovascular grafts: effect of slice thickness on 2D and 3D visualization of the fenestration stents. *J Endovasc Ther*. 2008; 15: 417-426.

28. Sun Z, Mwipatayi BP, Allen YB, et al. Computed tomography virtual intravascular endoscopy in the evaluation of fenestrated stent graft repair of abdominal aortic aneurysms. *ANZ J Surg*. 2009; 79: 836-840.

29. O'Donnell M, Sun Z, Winder RJ, et al. Suprarenal fixation of endovascular aortic stent grafts: assessment of medium-term to long-term renal function by analysis of juxtarenal stent morphology. *J Vasc Surg*. 2007; 45: 694-700.

30. White HA, MacDonald S. Estimating risk associated with radiation exposure during follow-up after endovascular aortic repair (EVAR). *J Cardiovasc Surg*. 2010; 51: 95-104.

31. Walsh SR, Tang TY, Boyle JR. Renal consequences of endovascular abdominal aortic aneurysm repair. *J Endovasc Ther*. 2008; 15: 73-82.

32. Perini P, Sediri I, Midulla M, et al. Contrast-enhanced ultrasound vs. CT angiography in fenestrated EVAR surveillance: a single-center comparison. *J Endovasc Ther*. 2012 (in press).

33. Zannetti S, De Rango P, Parente B, et al. Role of duplex scan in endoleak detection after endoluminal abdominal aortic aneurysm repair. *Eur J Vasc Endovasc Surg*. 2000;19:531-535.

34. d'Audiffret A, Desgranges P, Kobeiter DH, et al. Follow-up evaluation of endoluminally treated abdominal aortic aneurysms with duplex ultrasonography: validation with computed tomography. *J Vasc Surg*. 2001;33:42-50.

35. Pages S, Favre JP, Cerisier A, et al. Comparison of color duplex ultrasound and computed tomography scan for surveillance after aortic endografting. *Ann Vasc Surg*. 2001;15:155-162.

36. Sun Z. Diagnostic value of color duplex ultrasonography in the follow-up of endovascular repair of abdominal aortic aneurysm. *J Vasc Interv Radiol*. 2006;17:759-764.

37. Raman KG, Missig-Carroll N, Richardson T, et al. Color-flow duplex ultrasound scan versus computed tomographic scan in the surveillance of endovascular aneurysm repair. *J Vasc Surg*. 2003;38:645-651.

38. AbuRahma AF, Welch CA, Mullins BB, et al. Computed tomography versus color duplex ultrasound for surveillance of abdominal aortic stent-grafts. *J Endovasc Ther.* 2005;12:568-573.

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

40. Ashoke R, Brown LC, Rodway A, et al. Color duplex ultrasonography is insensitive for the detection of endoleak after aortic endografting: a systematic review. *J Endovasc Ther.* 2005;12:297-305.

41. Giannoni MF, Palombo G, Sbarigia E, et al. Contrast-enhanced ultrasound imaging for aortic stent-graft surveillance. *J Endovasc Ther.* 2003;10:208-217.

42. Bendick PJ, Bove PG, Long GW, et al. Efficacy of ultrasound scan contrast agents in the noninvasive follow-up of aortic stent grafts. *J Vasc Surg*. 2003;37:381-5.

43. Napoli V, Bargellini I, Sardella SG, et al. Abdominal aortic aneurysm: contrast-enhanced US for missed endoleaks after endoluminal repair. *Radiology*. 2004;233:217-225.

44. Henao EA, Hodge MD, Felkai DD, et al. Contrast-enhanced duplex surveillance after endovascular abdominal aortic aneurysm repair: improved efficacy using a continuous infusion technique. *J Vasc Surg*. 2006; 43: 259-264.

45. Perini P, Sediri I, Midulla M, et al. Single-centre prospective comparison between contrast-enhanced ultrasound and computed tomography angiography after EVAR. *Eur J Vasc Endovasc Surg.* 2011; 42: 797-802

46. Sun Z. Three-dimensional visualization of suprarenal aortic stent-grafts: evaluation of migration in midterm follow-up. *J Endovasc Ther.* 2006; 13: 85-93.

47. Sun Z. Transrenal fixation of aortic stent-grafts: current status and future directions. *J Endovasc The.* 2004; 11: 539-549.

48. EVAR Trial Participants. Endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR trial 1): randomised controlled trial. *Lancet.* 2005;365:2179-2186.

49. Michaels JA, Drury D, Thomas SM. Cost-effectiveness of endovascular abdominal aortic aneurysm repair. *Br J Surg*. 2005; 92(8):966-967.

50. Weerakkody RA, Walsh SR, Cousins C, et al. Radiation exposure during endovascular aneurysm repair. *Br J Surg*. 2008;95(6):699-702.

51. Boyle JR. Long-term outcome of endovascular abdominal aortic aneurysm repair. *Br J Surg*. 2009;96:447-448.

52. Sternbergh WC, Greenberg RK, Chuter TA, et al. Redefining postoperative surveillance after endovascular aneurysm repair: recommendations based on 5-yer follow-up in the US Zenith multicenter trial. *J Vasc Surg*. 2008; 48: 278-285.

53. Lawrence-Brown MMD, Sun Z, Semmens JB, et al. Type II endoleaks: when is intervention indicated and what is the index of suspicion for types I or III? *J Endovasc Ther*. 2009 (Suppl II); 16: I 106-118.

54. Karthikesalingam A, Page AA, Pettengell C, et al. Heterogeneity in surveillance after endovascular aneurysm repair in the UK. *Eur J Vasc Endovasc Surg*. 2011; 42: 585-590.