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Ultrasound Measurement for Abdominal Aortic Aneurysm Screening: A Direct Comparison of the Three Leading Methods

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WHAT THIS PAPER ADDS

This study examines which is the best method for measuring the abdominal aorta in ultrasound. Currently, there are three leading methods: outer edge-to-outer edge (OTO), leading edge-to-leading edge (LTL), and inner edge-to-inner edge (ITI). We found that all three methods have good repeatability and reproducibility regardless of the size of the aorta or the grade of the assessor. However, ultrasound underestimates the size of the aorta when compared with CT, with the ITI method the most significant by up to 5 mm. This finding has profound ramifications on the current NHS AAA screening programme where the ITI is used.

Objectives: Ultrasound (US) is non-invasive and cost-effective for screening abdominal aortic aneurysms (AAAs) but there is no universally accepted method to measure the aortic diameter. This study evaluates the accuracy, reproducibility, and repeatability of three methods: inner-to-inner (ITI), leading-to-leading edge (LTL), and outer-to-outer (OTO). The secondary objective of this study was to determine whether aneurysm size or grade of operator had any effect on either intra- or inter-observer variability.

Methods: Fifty static US images were measured by six assessors (2 vascular radiologists, 2 interventional radiology trainees, and 2 sonographers) on two separate occasions 6 weeks apart. Repeatability and reproducibility were calculated and compared with computed tomography (CT) as the gold standard.

Results: All three methods have high repeatability and reproducibility when static images are used. The interobserver reproducibility coefficients between assessors were 0.48 cm, 0.35 cm, and 0.34 cm for ITI, LTL and OTO, respectively. The intra-observer repeatability coefficients between assessors were 0.30 cm, 0.20 cm, and 0.19 cm for ITI, LTL and OTO, respectively. The mean difference between CT and OTO, LTL, and ITI was 1 mm, 3 mm, and 5 mm, respectively (all underestimations) (p < .0001).

Conclusions: US consistently underestimates aortic size when compared with CT, with ITI demonstrating the greatest underestimation (on average 5 mm). In the UK, this underestimation by the NHS Abdominal Aortic Aneurysm screening programme reduces the sensitivity of the screening test and may impact on the way in which vascular specialists interpret the findings of the screening programme.

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INTRODUCTION

Ultrasound (US) is the imaging modality of choice for screening abdominal aortic aneurysms (AAA). It is a reliable, non-invasive, and cost-effective method for assessing aortic size, the best clinical predictor of rupture.^{1–3} However, there is no universally accepted method for aortic size measurement.⁴ The three main methods utilised on US to measure the abdominal aorta (AA) are inner-to-inner

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edge (ITI), leading-to-leading edge (LTL), and outer-to-outer edge (OTO).

The argument for use of the ITI method is based on better resolution of the posterior aortic inner wall. Proponents of this method suggest that the adventitia of the aorta blends into surrounding connective tissue, which results in weak reflective boundaries of the outer wall, hence poorer resolution. In contrast, the interphase between intima and blood has a high acoustic impedance mismatch (from high to low acoustic impedance) which results in better resolution.⁵ In comparison, proponents of the OTO method state that the anterior external aortic wall is easier to identify than the inner wall because US reflection is strongest when it travels from a poor to a stronger reflector (low to high acoustic impedance) and weakest from a strong to a lesser reflector (high to low impedance). As blood is a

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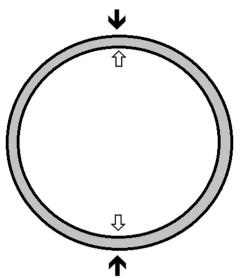


Figure 1. Schematic transverse image of the abdominal aorta. The inner circle represents the tunica intima, the grey area tunica media and the outer circle tunica adventitia. The three main methods of measuring aortic diameter are inner-to-inner edge (hollow arrows), leading-to-leading ledge (downward solid arrow to downward hollow arrow and out-to-outer edge (solid arrows).

lesser reflector than soft tissue, the resolution for the inner wall is inferior to that of the external wall.⁵ As for the LTL method, it attempts to measure aortic size by using the two best interphases: the anterior external wall and the posterior internal wall.

The NHS AAA Screening Programme (NAAASP) is currently rolling out in the UK and is based on the Multicentre Aneurysm Screening Study (MASS), the largest population-based AAA screening programme, which utilises measurements of the internal aortic diameter (ITI method).^{6,7} However, the threshold for AAA surveillance and treatment is based on the UK small aneurysm trial (UKSAT), which utilises external diameter measurements (OTO method).⁸ The LTL method, where measurements are taken from the anterior external wall to the posterior internal wall, is adopted by the Swedish AAA screening programme and is included in this study for comparison (Fig. 1).⁹

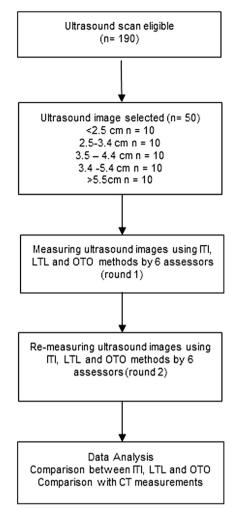


Figure 2. Study flowchart and selection criteria.

In the UK, the use of one method for screening and another for setting the treatment threshold can potentially impact significantly on clinical decision-making. The primary aim of this study was to investigate the differences between the three methods compared with multiplanar reformatted (MPR) computed tomography (CT) measurements as gold standard. The secondary aims were (a) to determine which method is the most reliable and reproducible, and (b) to

Table 1. Summary of studies comparing reproducibility of ultrasound measurements of abdominal aorta as identified in the systematic review by Beales et al.²³ On the basis of these studies, a convenient sample of 50 was chosen for this study.

Sample size	Number of observers	Plane of aortic measurements	Method of aortic measurements
10	2	AP and TS	ОТО
100	4	AP and TS	Unknown
33	3	AP and TS	Midpoint
35	2	AP	ITI
50	3	AP	ОТО
112	4	AP and TS	LTL
50	2	AP and TS	Unknown
50	2	AP	ITI and OTO
60	24	AP	ITI and OTO
50	6	AP	ITI, LTL, and OTO
	10 100 33 35 50 112 50 50 60	10 2 100 4 33 3 35 2 50 3 112 4 50 2 50 2 50 2 60 24	10 2 AP and TS 100 4 AP and TS 33 3 AP and TS 35 2 AP 50 3 AP and TS 50 3 AP 112 4 AP and TS 50 2 AP 50 2 AP 60 24 AP

Note. AP = anterior to posterior; ITI = inner edge-to-inner edge; LTL = leading edge-to-leading edge; OTO = outer edge-to-outer edge.

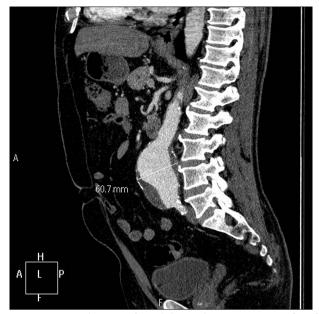


Figure 3. A sagittal image of an abdominal aortic aneurysm (AAA). *Note.* Measurements in CT scans were made at the level of maximal aneurysm diameter on the orthogonal slices after multiplanar reformats.

examine whether the size of AA measured or grade of assessor had any effect on repeatability and reproducibility.

METHODS

Six assessors, all working in Vascular Radiology Department at Hull and East Yorkshire NHS Trust were recruited for this prospective study. They consisted of two experienced sonographers, two interventional radiology (IR) fellows, and two consultant vascular IR radiologists. All six assessors have over 4 years' experience in US imaging and are trained in peripheral vascular imaging.

All three methods of measurement, ITI, LTL, and OTO, were agreed with the assessors prior to beginning the study. The protocol has been reviewed by the local Research and Development Department and formal ethical approval was deemed not necessary as no patient-identifiable data was used.

A convenient sample size of 50 was chosen based upon a thorough review of literature (Table 1). US assessments of the AA performed at Hull and East Yorkshire Hospitals NHS Trust between January 2010 to June 2012 were reviewed. All the images were acquired using either Philips HD9 scanners (Philips, Bothel, USA) with 3-5-MHz curvilinear probes or Toshiba Aplio 300 scanners (Toshiba Medical Systems, Crawley, UK) with 2-5-MHz curvilinear probes. Patients were included if a contrast-enhanced CT of the abdomen had been carried out within 3 months of the US. In total, 190 patients fulfilled these criteria. These patients were allocated into five groups depending on reported aortic diameters (group I–V): group I <2.5 cm (n = 42), group II 2.5–3.4 cm (n = 45), group III 3.5–4.4 cm (n = 25), group IV 4.5–5.4 cm (n = 32), and group V >5.4 cm (n = 45). Ten patients in each group were selected randomly to be included in the study. In each patient, a

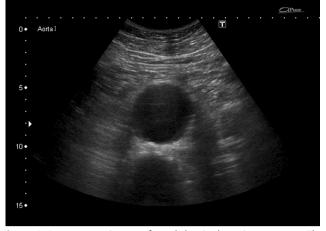


Figure 4. A transverse image of an abdominal aortic aneurysm. The aortic diameter is measured in the anterior—posterior axis.

static image in transverse was selected and anonymised (Fig. 2). The corresponding CT images were also anonymised and CT measurements of the aorta were performed by two experienced radiologists using the OTO anterior to posterior (AP) diameter at the level of maximum aneurysm diameter after multiplanar reformatting (MPR) and used as the gold standard (Fig. 3).

In total, 50 static US images were used. The images were of standard digital imaging and communication in medicine (DICOM) format and measurements were made using a DICOM viewing programme (Agfa IMPAX client v6.2), which enabled assessors to measure the aortic sizes with an accuracy of \pm 0.01 cm. All three measurements (ITI, LTL, and OTO) were measured from the same images in the AP axis (Fig. 4).

The measurements were recorded onto a predetermined data sheet and assessors were blinded to previous measurements. Statistical analyses were performed using Graphpad Prism v5 (GraphPad Software, USA) and SPSS v19 (Chicago, IL, USA). Measurements using the ITI, LTL, and OTO methods were compared with CT measurements. Interclass correlation coefficient (ICC), inter-observer reproducibility, and intra-observer repeatability were calculated.¹⁰ Statistical comparisons of accuracy, repeatability, and reproducibility were also made between the different groups of aortic sizes and between the different grades of the assessors.

RESULTS

The CT and US scans had been performed within a median of 13 days (range 1–94 days). All six assessors routinely use the OTO method for measuring aortic diameters. A total of 1,800 measurements (50 measurements using 3 different methods measured twice by 6 different assessors) were performed.

Measuring aortic diameter using all three methods and CT

The mean aortic diameter measurement on CT MPR images was 4.22 cm (1.80–10.20 cm). The estimated inter-observer

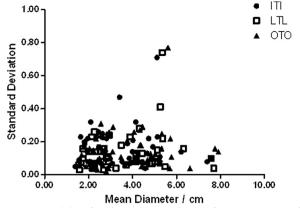


Figure 5. Variability for the three methods of measurements for the 50 images.

standard deviation was 0.12 cm and the corresponding reproducibility coefficient was 0.48 cm (95% CI 0.30-0.65).

On US, the mean aortic diameters (derived from all 6 assessors performing the measurements in each method twice) were 3.59 cm (1.39–10.84), 3.77 cm (1.55–11.16), and 3.99 cm (1.68–11.57) for the ITI, LTL, and OTO groups, respectively. There are significant mean differences of 0.17 cm (95% CI 0.14–0.20) between ITI and LTL measurements, 0.39 cm (95% CI 0.35–0.43) between ITI and OTO measurements, and 0.22 cm (95% CI 0.20–0.24) between LTL and OTO measurements (all p < .0001) (Fig. 5).

The mean aortic diameter of every image measured in all the ITI, LTL, and OTO groups were compared with CT measurements. Bland—Altman plots demonstrated underestimations of 0.50 cm (95% limits of agreement of -1.32 to -0.32) for ITI, 0.32 cm (-1.11 to 0.47) for LTL, and 0.10 cm (-0.93 to 0.73) for OTO measurements (Fig. 6).

Inter-observer variability

The ICCs for ITI, LTL, and OTO were all >0.99. The estimated inter-observer standard deviations were 0.17 cm for ITI, 0.12 cm for LTL, and 0.12 cm for OTO. The corresponding reproducibility coefficients were 0.48 cm (95% CI 0.30– 0.65) for ITI, 0.35 cm (0.22–0.47) for LTL, and 0.34 cm (0.21–0.46) for OTO. No statistical difference between the three methods was demonstrated (p = .12).

Intra-observer variability

All 50 images were again measured by the six assessors after 6 weeks. The ICCs in all three methods were all >0.99. The mean repeatability was 0.30 cm for ITI (95% CI 0.15–0.45), 0.20 cm for LTL (0.10–0.30), and 0.19 cm (0.09–0.29) for OTO. No statistical difference between the three methods was demonstrated (p = .52) (Table 2).

Size of aorta

The standard deviations of the six assessors in all five predetermined groups (i.e. different aortic sizes) in all three methods were compared and no statistical difference was identified (p = .79).

Types of assessors

The standard deviations between the three groups of assessors were compared in all three methods and again no statistical difference was found (p = .61 for ITI, 0.14 for LTL, and 0.55 for OTO) (Fig. 7).

DISCUSSION

It is generally accepted that abdominal aortic measurements are taken from AP on a transverse plane due to its superior repeatability.^{11,12} However, there is no consensus on which part of the aortic wall (i.e. inner vs. outer wall) that measurements should be taken from. Our study showed that US underestimates aortic size when compared with CT, with ITI measurements demonstrating the largest underestimation of up to 5 mm. These results are similar to other published studies (mean differences of 0.1-9.4 mm between CT and US¹¹⁻¹⁷). The mean ITI and LTL measurements were 4 mm and 2 mm smaller, respectively, in comparison with OTO measurement. An explanation for the underestimation can be attributed to the intrinsic aortic wall thickness. Other investigators, using magnetic resonance angiography (MRA) and intravascular US, have demonstrated that the aortic wall is approximately 2 mm thick, suggesting an innate difference of 4 mm between ITI and OTO measurements and 2 mm between LTL and OTO measurements.18,19

The NAAASP, based on the MASS trial, utilises ITI measurements and has three major decision points: entry into the surveillance programme, continual surveillance, and referral to vascular services for potential treatment. For aortas less than 30 mm in size, patients are discharged from the screening programme. For aortic diameters over 55 mm, patients are referred to the vascular surgeons for consideration of aneurysm repair. In between these two groups, they are kept under surveillance.⁷ However, the 55 mm size threshold for AAA repair was based on OTO measurements of the UKSAT study.⁸ With a mean difference of 4 mm between the two methods, patients screened using the ITI method will only be eligible for treatment when their AAA reaches 59 mm on OTO diameter. At the other end of the screening programme spectrum, using an ITI approach, patients may not be enrolled into the surveillance programme until they reach 34 mm on OTO measurements or 35 mm on CT.

The underestimation of aortic size using the ITI method has potential medico-legal implications. This underestimation increases the number of false-negative (reduces sensitivity) and delays treatment. For a subgroup of small female patients in whom AAA rupture risk is higher at 5–5.5 cm, this can potentially delay life-saving treatment.²⁰ In other established screening programmes such as breast and cervical screening, one of the most common reasons for medical litigation is a delay in diagnosis. Previous cases of false-negative in cervical screening have resulted in significant patient compensation.^{21,22} One of the most important aspects of a good screening programme is to have a test that has a high sensitivity and specificity. The main rationale

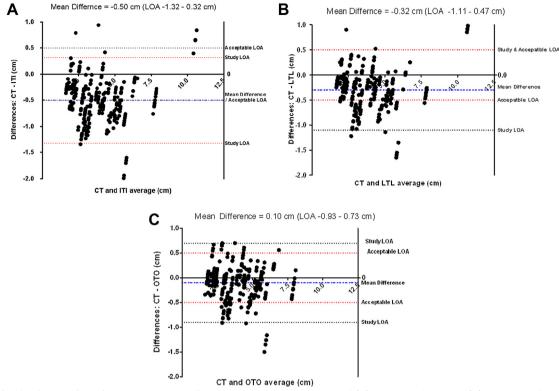


Figure 6. Bland—Altman plots showing agreement between CT measurements and (A) mean ITI diameter, (B) mean LTL diameter and (C) mean OTO diameter. Blue dashed line represents the mean difference, black dashed line the calculated 95% limits of agreement and reddashed line the acceptable 95% limits of agreement as defined by the NHS AAA Screening Programme. *Note.* ITI = inner edge-to-inner edge; LTL = leading edge-to-leading edge; OTO = outer edge-to-outer edge.

for using the ITI method was that it was deemed to have "superior" repeatability and reproducibility. However, we have shown that inter- and intra-observer variability in adequately trained operators are the same for all three methods. ITI underestimates aortic size and therefore has a lower sensitivity than the OTO method. If the ITI method continues to be the mainstay in measuring AAA in screening, there is an argument to reduce both the enrolment threshold into the surveillance programme and subsequent referral for repair to take into account of this underestimation. Surely, it is more logical to adopt OTO in the screening programme and therefore use the same yardstick for both screening and the treatment threshold.

Table 2. Inter-observer and intra-observer variability.

	Inter-observer Reproducibility coefficient (cm) (95% Cl)	ICC	Intra-observer Repeatability coefficient (cm) (95% Cl)	ICC
ITI	0.48 (0.30–0.65)	0.99	0.30 (0.15–0.45)	0.99
LTL	0.35 (0.22–0.47)	0.99	0.20 (0.10-0.30)	0.99
OTO	0.34 (0.21-0.46)	0.99	0.19 (0.09-0.29)	0.99

Note. Our results showed that all three methods have good interand intra-observer variability and within limits of acceptability as defined by the NAAASP to be 0.50 cm. The interclass correlation coefficient confirms the high correlation between and within all assessors in all three methods. ICC = interclass correlation; ITI = inner edge-to-inner edge; LTL = leading edge-to-leading edge; OTO = outer edge-to-outer edge.

We found that the inter- and intra-observer variability were high in all three US methods and not clinically significant. A recent systematic review identified nine studies that compared repeatability and reproducibility on US measurements.²³ In seven out of nine studies, only a single method was used. Interestingly, two studies comparing ITI with OTO methods produced conflicting results. In Thapar et al.'s²⁴ study, they found the inter-observer variability was greater using ITI measurements than the OTO method. The intra-observer variability was not examined. In Hartshorne et al.'s²⁵ study, there was a statistical difference in interobserver variability in favour of the ITI method amongst the technicians but no statistical difference for intraobserver variability. Our study is the first to compare all three methods directly and found that the repeatability and reproducibility coefficients were all less than 5 mm, which falls within the accepted limits of agreement required in the NAAASP.

Several investigators have examined the effects of increasing aortic diameter on inter-observer and intraobserver variability.^{11,13,24–28} Of the published studies, only two showed inter-observer standard deviation increases with aortic diameter.^{25,28} However, the disproportion in numbers in different group sizes may explain this "apparent" difference. In Singh et al.'s²⁸ study, there was only one AAA and in Hartshorne et al.'s²⁵ inter-observer variability comparison, only four out of 15 images were used where the aneurysms were over 5 cm in size. Despite

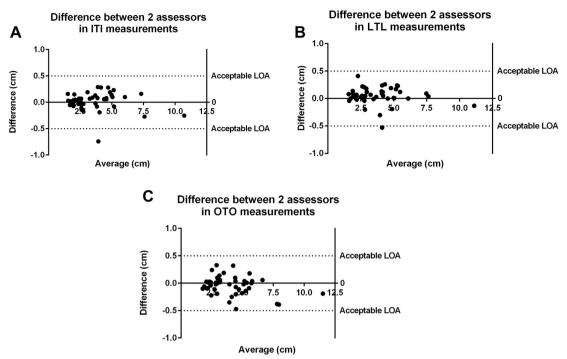


Figure 7. Representative Bland—Altman plots showing agreement between two assessors in (A) ITI measurements, (B) LTL measurements and (C) OTO measurements. *Note.* The figures demonstrate good agreement between assessors in all three methods. ITI = inner edge-to-inner edge; LTL = leading edge-to-leading edge; OTO = outer edge-to-outer edge.

using a larger cohort, we did not find any statistical correlation in measurements with increasing aortic size although the study was not powered to exclude the null hypothesis.

In most previous studies, limited number of observers were employed and they were usually from the same professional group or grade.²³ Only Hartshorne et al.'s²⁵ study examined whether there were any differences in measurements between two different observer groups. They have shown a statistical difference in the mean repeatability for OTO measurement between screening technicians and vascular sonographers (0.25 cm vs. 0.14 cm). This is not unexpected as the screening technicians did not have the same level of training in US compared with sonographers. They were only trained in measuring abdominal aortic sizes using the ITI method and this was reflected in their findings that no statistical difference was found on ITI measurements between the two groups. We did not find any statistical difference in inter- and intra-observer variability between the sonographers, fellows, or consultants for all three methods. Although the numbers were too few in our study to draw statistical conclusions, the ICCs in all three groups were high.

One of the major limitations of this study is that our study was underpowered, which increases the potential for a type 2 error (false negative). We accept that using static images from a third party inevitably underestimate the inter- and intra-observer variability when compared with "live" images. In "real-life" clinical practice, there will be additional confounding that affects measurements such as operator technique and their perceived level of the maximum aortic size. By using static images, we further ignore the effects of cardiac cycle on aortic size (which incidentally are not taken into account on CT measurements and there is no protocol that states they should be measured in either systole or diastole), which can vary up to 2 mm in AP diameter between systole and diastole.²⁹ This may affect the accuracy of the ultrasound images when compared with CT findings, but the primary aim of this study is to examine the perceived position of the vessel wall.

CONCLUSION

We have shown that when using static images, both ITI and OTO have similar inter- and intra-observer variability but the ITI measurement does not take into account the aortic wall thickness. Consequently, compared with OTO, ITI underestimates the aortic size by 4 mm. It seems illogical to measure the threshold for treatment using one method and to screen using another. Furthermore, to use a test that underestimates aortic size in a screening programme seems counterintuitive.

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CONFLICT OF INTEREST

None.

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