

Usefulness of contrast-enhanced transoesophageal echocardiography to guide thoracic endovascular aortic repair procedure

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| Aims | Thoracic endovascular aortic repair (TEVAR) is commonly considered as a valid alternative to surgery. Endoleaks occur- rence is one of the principal limitations of TEVAR. Transoesophageal echocardiography (TEE) is often adopted in adjunct to fluoroscopy and angiography (ANGIO) during stent-graft implantation. In the present study, we compare intraproce- dural ANGIO, TEE, and contrast-enhanced TEE (cTEE), and we also evaluate their accuracy in early endoleaks detection and characterization. |
|------------------------|--|
| Methods and results | Fifty-four patients with thoracic aortic disease suitable for TEVAR were prospectively enrolled in the study. After stent placement, the result of the procedure was assessed by ANGIO, TEE, and cTEE. The use of contrast (Sonovue, Bracco) significantly improved TEE quality ($P = 0.0001$). cTEE was superior in entry tears, false and true lumen and aneurysm thrombosis identification, and microtears and ulcer-like projections detection before stent deployment. After stent deployment, cTEE was more accurate than TEE and ANGIO in the detection of slow flow in the false lumen and in the aneurismal sac ($P = 0.0001$), and in the remaining flow identification ($P = 0.0001$). Notably, cTEE is more accurate in the endoleaks detection ($P = 0.0001$) and in the incomplete stent expansion diagnosis and need for a further balloon inflation ($P 0.002$), or a further stent implantation ($P 0.006$), compared with TEE and ANGIO. |
| Conclusion | TEVAR procedures are improved by the complimentary use of contrast fluoroscopy, multiplane TEE with Doppler flow interrogation, and cTEE. This triple imaging approach provides additional information in all phases of the procedure improving safety of stent-grafting and the procedural outcomes. |
| Keywords | aortic disease • transoesophageal echocardiography • contrast echocardiography • TEVAR |

Introduction

Thoracic endovascular aortic repair (TEVAR) has become widely accepted as an important option for treatment of acute and chronic thoracic aortic pathologies. $^{\rm 1-6}$

Imaging technologies play a crucial role for pre-procedural planning and for the intraprocedural and post-procedural results and complications assessment. Moreover, detailed and different imaging modalities are mandatory to assess the anatomic suitability of TEVAR and the proper patient's selection.^{5,7–11}

Transoesophageal echocardiography (TEE) offers definite advantages and diagnostic options as an adjunct to fluoroscopy and angiography (ANGIO) during TEVAR, mainly reducing radiation exposure and contrast load. TEE provides relevant information of morpho-functional characterization (i.e. aneurysm perfusion assessment, true and false lumen identification), leads the correct advancement and positioning of the stent-graft guidewires within the true lumen, and identifies the landing zone.^{12–16} Furthermore, TEE can confirm the technical success of stent-grafting achieved by the reduction of blood flow into the excluded aneurysmal sac or into the false lumen, and helps in the detection of new intimal tears distal or proximal to the stent-graft. In addition, TEE is useful to evaluate the presence of endoleaks and promptly recognizes early complications in adjacent aortic segments.^{13–16} Hence, endoleaks occurrence after

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TEVAR remains one of the principal limitations of this procedure, as mainly type I endoleak could increase the rupture rates of degenerative aneurysms and negatively impact on the long-term results of endovascular treatment of type B aortic dissections. $^{17-20}$ The intraoperative identification and treatment of endoleaks reduce the incidence of perioperative type I endoleaks.¹⁷⁻²⁴ Contrast-enhanced (cTEE) has been shown to be feasible and reliable in the diagnostic work up of acute aortic syndromes providing additional morphological and functional information compared with standard TEE.^{25,26} cTEE does not require ionizing radiation and has no side effects on renal function. Furthermore, published studies have already demonstrated that in patients undergone to endovascular abdominal aortic repair, contrast ultrasound has a higher sensitivity in endoleaks detection during follow-up than standard ultrasound and has similar diagnostic values of computed tomography angiography (CTA) and magnetic resonance. $^{27-30}$

In this prospective study, we aim to assess intraprocedural ANGIO, TEE, and cTEE capability to safely guide stent-graft placement and, in particular, we investigate their accuracy in the early detection and characterization of endoleaks during TEVAR procedures.

Methods

Patients and study design

We compared ANGIO, TEE, and cTEE before and after the implantation in 54 patients (26 women, 28 men, 67 \pm 11.6 years of age): 12 patients had type-B aortic dissection, 30 degenerative aneurysms, 5 penetrating aortic ulcers, 4 intramural haematoma, and 3 pseudoaneurysms. All of the patients fulfilled the criteria for surgical treatment of specific aortic disease, according to diagnosis and management of patients with thoracic aortic disease guidelines.¹⁹ All the patients underwent preoperative 64-row CTA scan with multiplanar aortic reformatting, 3D reconstruction, and vessel analysis using OsiriX software for planning and sizing purposes. The most appropriate graft was selected calculating a 10–15% oversize referring to the aortic outer–outer diameter. A minimum of 20 mm neck length was deemed adequate to safely implant the stent-graft. Diagnostic ANGIO and TEE were performed only at the time of the procedure.

All of the patients underwent intraprocedural triple imaging modalities.

The Institutional Review Board and Ethical Committee approved the study protocol. All the enrolled patients gave written informed consent to the study.

Aortic stent-graft implantation

The technique of stent-graft implantation has been described in detail elsewhere. ^{1,3,18–20,31,32} Briefly, in all the cases, the endovascular procedure was performed under general anaesthesia. The stent-graft was delivered through a surgical access: the common femoral artery at the level of the groin was used in all cases of this series. An adjunctive percutaneous access, femoral or brachial, was used for performing intraoperative angiogram through a pigtail catheter. The common femoral artery surgical exposed was cannulated with standard 'J' guidewire and then exchanged with a superstiff Lunderquist precurved guidewire (Cook, Inc., Bloomington, IN, USA). The stent-graft was carefully advanced over the stiff wire and deployed in the intended position. In all patients, endograft with Dacron fabric was adopted: Zenith Cook TX2 (William Cook Europe, Bjaerverskov, Denmark) in 27 patients, Bolton Relay Plus (Bolton Medical, Sunrise, FL, USA) in 19, and Jotec E-vita (Jotec, GmbH,

Hechingen, Germany) in 8. The average length of the stent-grafts was 187 mm based on postoperative CT scan measurements.

ANGIO

The procedure was performed using a portable digital C-arm image intensifier with road-mapping capabilities (Moonray Simad Medical Technology or Ziehm-Vision RFD Ziehm Imaging GmbH). Repeat contrast injections were performed during the endovascular intervention via the pigtail catheter placed in the upper thoracic aorta. After deployment of the endograft, a completion ANGIO was performed to ensure aneurysmal sac or false lumen exclusion, no evidence of endoleaks, and patency of all the supraortic and/or visceral vessels within the proximal or distal landing zones. Iopamidol (Solutrast 370, Bracco-Byk Gulden) was used as contrast agent.

Transoesophageal echocardiography

Echocardiographic studies were performed with IE33 Philips (Philips Medical System, Bothwell, WA, USA) using 2-7 Mhz Omni III probe. In all studies, standard TEE preceded cTEE. TEE with color and pulsed wave Doppler was performed using standard planes for the study of ascending aorta, arch, and descending aorta. After stent placement, TEE was used to check stent expansion and false lumen or aneurysmal sac exclusion. An initial 'smoke' phenomenon, indicative of initial thrombosis within the false lumen or aneurysm sac excluded by the stent-graft, was used as indirect evidence of closure of the primary entry tear or complete aneurysm exclusion and therefore as a marker of the good outcome of the procedure. Color Doppler TEE was also used to ascertain the absence of flow in the false lumen or aneurysmal sac excluded by the stent-graft. Sensitivity for slow blood flow was enhanced by reducing the color Doppler scale to 25 cm/s.¹⁴ In case of flow in the false lumen or aneurysm sac, color Doppler and pulsed Doppler were used to assess the direction of the flow to differentiate endoleaks from abdominal re-entry tears, to classify the endoleaks and identify the sites of origin (i.e. proximal vs. distal thoracic aorta).^{14,33,34} Furthermore, color Doppler was used to detect any new intimal tears, either proximal or distal to the stent.

Contrast transoesophageal echocardiography

cTEE was obtained after administration of a second-generation contrast agent (SonoVue, Bracco, Milan, Italy). cTEE scans were acquired after the injection of a single bolus (2.0–2.5 mL) of contrast agent dissolved in 0.9% saline solution, followed by flushing with an injection of a 10 mL bolus of saline solution through a central line, placed in the jugular vein. Repeated boluses were injected to obtain complete information on the variables analysed in the different segments of the aorta using similar windows to conventional echocardiographic studies. During cTEE, pulsed inversion and power modulation harmonic imaging was applied, with a mechanical index ranging between 0.4 and 0.6. After few minutes of administration, when the contrast signal usually decreases, the color Doppler was superimposed to achieve strengthening of color Doppler signal. The same variables assessed with standard TEE were considered during cTEE examination. cTEE scanning was performed for at least 5 min after injection and assessed the presence of contrast enhancement within the aneurysm sac, false lumen, haematoma, or ulcer, with monitoring of the time of appearance (synchronous or delayed with respect to graft enhancement) and persistence (wash-out) to inflow and outflow vessels.

All standard TEE and cTEE exams were performed and read by a single operator, and TEE and cTEE results were analysed online, independently of angiographic results and findings.

For both standard TEE and cTEE, an evaluation of the image quality was established by the operator as poor, sufficient, good, and optimal.

Intraprocedural imaging-guided algorithm

After stent placement, the result of the procedure was assessed by triple imaging. When discordances among imaging methods were documented, the decision to further stent-graft ballooning (i.e. incomplete stent expansion) or an adjunctive stent-graft positioning (i.e. type I endoleak) was decided on the basis of cTEE results.

Outcome of procedure

CTA was used to assess the outcome of the procedure. Complete exclusion of the false lumen or aneurysm sac by the stent-graft, with false lumen or aneurysm sac thrombosis and exclusion of ulcer or intramural haematoma in the thoracic aorta with the absence of antegrade flow, was considered procedural success.

Statistical analysis

Data are expressed as mean \pm SD, percentage, or median (range). Continuous and categorical variables were compared using either the Student *t*-test or McNemar test when appropriate. For comparison of ANGIO, TEE, and cTEE, the ANOVA approach was chosen. Statistical significance was considered at a P < 0.05. The analysis was performed using SPSS for MAC version 20.0.

Results

The baseline characteristics of the study population are reported in *Table 1*. Seventy stents were implanted in 54 patients, mean per patient 1.29. Stent-graft implantation was performed with a mean duration of the procedure of 54 min. Patients were discharged after a median of 4 days. One death occurred during the hospital stay.

The results of the pre-procedural comparison among ANGIO, TEE, and cTEE are listed in the *Table 2*. While the proximal entry tear was identified in all patients with all the three imaging modalities, the number of all entries tears detected by cTEE was higher than with ANGIO and TEE alone. cTEE was also superior in the diagnosis of false and true lumen, although the values did not reach statistical significance. cTEE was superior to TEE in identifying aneurysm thrombosis. Furthermore, cTEE visualises the presence of microtears and islands of contrast in the intramural haematoma suggestive of ulcer-like projections better than TEE and ANGIO.

The TEE image quality was poor in 5.7%, sufficient in 26.4%, good in 52.8%, and optimal in 15.1% of patients, whereas with cTEE was good in 15% and optimal in 85% of patients (P = 0.0001 vs. TEE). No complications or side effects related to contrast administration were observed.

Table I Patient's main characteristics

| Sex | 44 (81) male |
|------------------------|--------------|
| Hypertensive | 38 (70) |
| Smoke history | 36 (66) |
| Diabetes | 24 (44) |
| Dyslipidaemia | 33 (61) |
| Prior vascular surgery | 29 (53) |
| | |

Evaluation after stent deployment

The results of the comparison among ANGIO, TEE, and cTEE in post stent deployment evaluation are listed in the *Table 3*. In two patients, TEE and cTEE were helpful for guidewire repositioning not possible with ANGIO and in one patient ANGIO failed to identify the proximal entry tear closure in aortic dissection. cTEE was also superior to both TEE and ANGIO alone in the assessment of slow flow in the false lumen/aneurysmal sac post stent-graft implantation and in detection of incomplete stent-graft apposition. cTEE demonstrated new intimal tears after stent-graft positioning in aortic dissection in four and three patients that were not visible at ANGIO and TEE, respectively (*Figure 1*).

Moreover, cTEE was superior to both TEE and ANGIO in the detection of endoleaks (*Figures 2* and *3*). Of the seven endoleaks identified by ANGIO, six were of type I (2 type Ia and 4 type Ib) and one of type II (*Figure 4*). TEE classified the 16 endoleaks as 13 of type I (5 type Ia and 8 type Ib), 1 of type II, and 2 unclassificable. cTEE classified the 27 endoleaks as 26 of type I (9 type Ia and 17 type Ib) and 1 of type II. With respect to ANGIO, cTEE reclassified three type Ia instead of type Ib, and with respect to TEE reclassified the two unclassifiable endoleaks as type Ib and and 3 type Ia instead of Ib.

Accordingly, cTEE furnished significant decisive additional information to ANGIO and TEE determining changes in the intraoperative decision-making in terms of need for balloon inflation and additional stent implantation.

During intraoperative procedure, the TEE image quality was poor in 3.8%, sufficient in 26.4%, good 55.7%, and optimal in 15.1% of patients, whereas with cTEE was sufficient in 1.9%, good in 11.1%, and optimal in 87% of patients (P = 0.0001 vs. TEE).

Outcome of the procedure

The CTA to assess the outcome was performed at a median of 105 days (range 5–180) after the procedure. Fifty of 54 patients (92.5%) showed a complete thrombosis of the false lumen/aneurysmal sac or complete exclusion of ulcer or intramural haematoma in the thoracic aorta. Four patients presented an endoleak, three type I and one type II endoleak, and only partial thrombosis of the false lumen/aneurysm sac was present in three of them.

Table 2 Comparison of ANGIO, TEE, and cTEE for pre-operative findings

| | ANGIO | TEE | cTEE | P-value |
|--|-------|-----|------|------------|
| Entry tears, total no. | 11 | 15 | 22 | 0.001*,°,^ |
| True lumen false lumen identification | 9 | 11 | 12 | NS |
| False lumen thrombosis | _ | 11 | 12 | NS |
| Aneurysm sac thrombosis | _ | 23 | 30 | 0.016 |
| Ulcer-like projection (intramural haematoma) | - | 0 | 1 | NS |
| Microtears (intramural haematoma) | 0 | 0 | 1 | NS |

°TEE vs. ANGIO: P = 0.04.

*cTEE vs. ANGIO: P = 0.0001.

[^]cTEE vs. TEE: *P* = 0.009.

| • | | • | 0 | | |
|---|-------|-----|------|---------|---|
| | ANGIO | TEE | cTEE | P-value | |
| Correct guidewire position (AD) | 9 | 12 | 12 | NS | |
| Closure proximal entry tear (AD) | 10 | 11 | 12 | NS | |
| Slow flow false lumen/aneurysm sac post-stent | 44 | 36 | 29 | 0.0001 | TEE vs. ANGIO, <i>P</i> = 0.008 cTEE vs. ANGIO, <i>P</i> = 0.0001 cTEE vs. TEE, <i>P</i> = 0.01 |
| Endoleaks | 7 | 16 | 27 | 0.0001 | TEE vs. ANGIO, <i>P</i> = 0.03 cTEE vs. ANGIO, <i>P</i> = 0.0001 cTEE vs. TEE, <i>P</i> = 0.03 |
| Remaining flow post-stent | 4 | 12 | 25 | 0.0001 | TEE vs. ANGIO, <i>P</i> = 0.008 cTEE vs. ANGIO, <i>P</i> = 0.0001 cTEE vs. TEE, <i>P</i> = 0.0001 |
| New intimal tears no. (AD) | 0 | 1 | 4 | 0.05 | cTEE vs. ANGIO, $P = 0.03$ |
| Incomplete stent expansion | 5 | 18 | 20 | 0.002 | TEE vs. ANGIO, <i>P</i> = 0.0001 cTEE vs. ANGIO, <i>P</i> = 0.0001 |
| Need for balloon inflation | 5 | 16 | 20 | 0.002 | TEE vs. ANGIO, <i>P</i> = 0.001 cTEE vs. ANGIO, <i>P</i> = 0.0001 |
| Need for additional stent implantation | 4 | 10 | 16 | 0.006 | TEE vs. ANGIO, <i>P</i> = 0.03 cTEE vs. ANGIO, <i>P</i> = 0.0001 cTEE vs. TEE, <i>P</i> = 0.03 |

Table 3 Comparison of ANGIO, TEE, and cTEE for intraprocedural findings

AD, aortic dissection.



Figure I New intimal tear after true lumen expansion. (A) Type B dissection with evidence of malperfusion. (B) 2D TEE: stent deployment and true lumen expansion. (C) TEE: no tears evidence on color flow mapping. (D) cTEE: contrast administration demonstrated the presence of a new tear, as bubbles are moving from the true lumen to the false (arrow). (E) ANGIO: stent deployment and true lumen expansion. (F) ANGIO. A further stent was deployed to cover the tear; (G) postoperative CT scan shows complete exclusion and thrombosis of the false lumen.







Figure 3 Periprosthetic leak after aneurysmal exclusion. (A) 2D TEE after stent deployment to exclude thoracic aneurysm. TEE Color flow mapping shows almost complete thrombosis of the aneurysmal sac. (B) Contrast injection shows residual flow in the aneurysmal sac due to peri-stent leak (arrow).



Figure 4 Type 1 endoleak. Color TEE (A) and ANGIO (B) do not clearly demonstrate any endoleak; (C) Contrast administration shows the presence of a leak, as microbubbles fill the aneurysmatic sac at the level of the stent proximal edge (arrow).

Discussion

This is the first study that performed a systematic comparison among ANGIO, TEE, and cTEE to guide stent-graft implantation. We interestingly demonstrate that cTEE provides additional contributions in distinct phases of the procedure, from the pre-operative diagnosis and characterization of the aortic pathology (identification of number and sites of tears and aneurysmal thrombosis) to the intra and immediately post-procedural assessment (slow flow and/or remaining flow in false lumen or aneurysmal sac, the presence of peri-stent leaks, and its classification and detection of new intimal tears distal or proximal to the stent-graft). As a final result, cTEE furnished significant additional key information in the intraoperative decision-making in terms of need for balloon inflation and additional stent implantation.

ANGIO, TEE, and cTEE were able to detect the main entry of the dissection, which is essential for stent-graft procedures. Technical success is achieved when stent-graft placement covers the primary entry tear and excludes the false lumen, producing complete thrombosis and consequent decrease in false lumen diameter. Aortic dissection usually includes multiple intimal tears, some of which are very small and difficult to detect. In this context, however, cTEE was able to detect significantly more secondary entries than TEE. Thus, cTEE results lead to an extension of aortic segments to be covered by implanting a second stent-graft in four patients, a finding often undetected by ANGIO and TEE alone. Furthermore, in one patient with intramural haematoma, a tiny passage of contrast from the lumen to the haematoma was found that was not identified with CTA. In this patient, cTEE finding leads to cover the aortic segment with stent-graft with evidence of complete resolution of the haematoma at 6 months of follow-up (Figures 5 and 6). Thus, despite the limited series of data, a potential role for cTEE in the identification of microtears seems promising. Avoidance of stent implantation in the false lumen is life-saving. ANGIO alone also has difficulties in the localization of the guidewire in either the true or false lumen. TEE has the unique capability to detect both guidewire advancement and the intimal flap, and is decisive for positioning of the guidewire.

Using contrast medium, the true lumen has been identified in all the patients. Despite systolic expansion being a reputed hallmark of the true lumen identification, it is not always present since in some cases the intima remains fixed. Contrast administration unveiled the true lumen due to the early filling by the contrast agent with respect to false lumen.^{25,26} Another frequent problem is peri-stent leaks, which can cause late aortic dilation, usually calling for subsequent conversion to open surgery. It is therefore important to close any leaks present after stent implantation. In the present study, cTEE was significantly more sensitive than TEE and ANGIO in the identification of leaks. cTEE enabled detection of 27 peri-stent leaks, whereas only 16 and 7 of these leaks were visible at TEE and ANGIO, respectively. It is noteworthy that 11 cases of missed endoleaks at TEE were probably due to artefacts in 7 cases and in the remaining 4 cases because of the small extent of endoleak. cTEE allowed better classification of endoleaks compared with TEE and ANGIO. Regarding the classification of endoleaks, cTEE classified in five cases that were misdiagnosed by TEE as type I endoleak by the clear evidence of flow from proximal landing zone in three patients and distal landing zone in two patients. Moreover, cTEE has the advantage over TEE providing haemodynamic information on blood flow and direction in false lumen/aneurysmal sac in addition to the morphological evaluation, with the possibility of comparing in real time the baseline and contrastographic images.

It is also important to recognize new intimal tears that can be caused by the stent-graft procedure, because of the fragility of the aortic wall in the dissection. However, these 'new' intimal tears could be pre-existent thoracic re-entry sites that become detectable only after stent implantation, because of the increased pressure gradient between the true and the false lumen after closure of the primary entry tear.¹⁴ If the tears are in the thoracic aorta, it is important to close them, to avert any late expansion of the false lumen. In this context, cTEE was able to detect significantly more new intimal tears than TEE.

ANGIO is the method of choice to guide aortic stent-graft placement because of its ability to give the operator an immediate aortic overview, which is necessary for safe guidance. The exact anatomy



Figure 5 Intramural haematoma. (A) 2D TEE intramural haematoma. (B) Color Doppler do not identify any microtears. (C) Microtear was identified after contrast administration (arrow). After stent deployment, no endoleaks were documented on 2D TEE (D) and cTEE (E).



Figure 6 Evolution of intramural haematoma described in the *Figure 5*. (A) Pre-operative CT scan: intramural haematoma of the descending thoracic aorta. (B) Postoperative CT scan after endovascular treatment. (C) One-year follow-up CT scan: progressive shrinkage of the intramural haematoma.

of the aorta, including the site of the entry, is often difficult to identify on contrast ANGIO. Considering all phases of the procedure, cTEE furnished decisive additional information to ANGIO and TEE, determining changes within the procedure in 13 of 54 patients (24%). Intraoperative decision-making based on TEE and cTEE-guided algorithm determined a high positive success rate of procedure (92.5%) with assisted primary endoleak rate acceptably low as assessed at follow-up CTA.

Follow-up

Data regarding long-term follow-up were obtained after an average time of 6 months. Nine patients were lost at follow-up. One patient died the day after the procedure because of a haemorrhagic shock, another one after 3 months of the discharge because of a pneumonia. All the other patients performed a CT (average time from the operation 4 months). In 33 patients, the procedure was successful and no leaks were identified. Four patients had a residual type B aortic dissection distal to the stent, but without surgical indication. Ten patients had endoleak. Among them, those with a type one proximal endoleak (n = 3) underwent to a new TEVAR procedure. Three patients underwent to elective ascending aorta replacement, while one patient was operated in emergency because of a retrograde type A aortic dissection.

Limitations of the study

Pre-discharge TEE was not performed systematically. We did not use intravascular ultrasound, and therefore, a direct comparison between IVUS, TEE, and cTEE was not possible. A previous study showed good results with intravascular ultrasound in monitoring stent-graft implantation in aortic dissection.³⁵ Moreover, our study population was a mixed population including different aortic diseases; thus, we did not evaluate the additional diagnostic impact of cTEE in the single specific aortic disease.

Conclusions

Aortic stent-graft implantation is improved by complimentary use of contrast fluoroscopy, multiplane TEE with Doppler flow interrogation, and cTEE. This imaging approach implies no additional risk and provides decisive additional information in all phases of the procedure improving safety of stent-grafting and, thus, eventually the procedural outcomes.

Conflict of interest: None declared.

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