

Aorto-esophageal Fistula After Thoracic Aortic Stent-Graft Placement

A Rare but Catastrophic Complication of a Novel Emerging Technique

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Objectives Our goal was to report characteristics and outcomes of 6 patients with aorto-esophageal fistula (AEF) after thoracic endovascular aortic repair (TEVAR).

Background Neurologic events are severe complications of TEVAR. With growing experience of TEVAR, other yet unexpected devastating complications have emerged.

Methods Between July 1999 and August 2008, 268 patients underwent TEVAR for various thoracic aortic diseases at our institution.

Results Six of 268 patients (age 49 to 77 years, 50% female patients) developed AEF (incidence 1.9%) within 1 to 16 months after the procedure. Indications for TEVAR were acute aortic dissection (n = 3), chronic aortic dissection (n = 1), and thoracic aortic aneurysm (n = 2). Four patients presented with sudden massive hematemesis whereas 2 patients were readmitted for new-onset fever and elevated markers of inflammation that preceded hematemesis. Esophago-gastro-duodenoscopy identified deep esophageal ulcerations at the level of the implanted aortic stent-graft in 4 patients, but only mild erosive lesions within the proximal esophagus without signs of active bleeding in the remaining 2 patients. Surgical repair was performed in only 1 patient and declined in the remaining because of comorbidities and multiorgan system failure. Despite this, all patients died due to fatal rebleeding (n = 4) or mediastinitis (n = 2).

Conclusions AEF is a rare and unusual complication of TEVAR that occurs relatively early after the procedure and is almost invariably fatal. New-onset fever with elevated inflammatory markers or hematemesis should heighten clinical suspicion of AEF in TEVAR patients and prompt computed tomography or esophago-gastro-duodenoscopy in the hope of detecting, triaging, and treating this early to improve the otherwise dismal outcomes of these patients. (J Am Coll Cardiol Intv 2009;2: 570–6) © 2009 by the American College of Cardiology Foundation

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Thoracic endovascular aortic repair (TEVAR) is increasingly applied in clinical practice as a novel, less invasive treatment for patients with aortic aneurysms and dissections, particularly in patients deemed at high-risk for conventional surgical repair (1,2). Observational nonrandomized data suggest that the risk of acute complications of TEVAR, most notably paraplegia and stroke, appears to compare favorably with open surgery (3-5). Mid-term and long-term complications remain less well defined, and—as with any new technology—TEVAR bears the risk of unusual, previously unanticipated complications, which are only detected by a high level of clinical suspicion and surveillance as experience and use of this technology increases (6). In our early experience, we have reported 3 patients who developed sudden massive hematemesis due to aorto-esophageal fistula (AEF) formation secondary to TEVAR (7). While TEVAR continues to be increasingly embraced, many patients treated with this technique will be cared for by physicians in the community at large. Both interventionalists and general physicians are generally unaware of AEF as an important but rather rare differential diagnosis of hematemesis or other symptoms among other more common etiologies in patients with prior TEVAR. Increasing awareness of this complication may facilitate rapid diagnosis and/or triage and treatment. Accordingly, the goal of the current report is to summarize our experience with the presentation, diagnostic approach, management, and outcomes of this unusual, but catastrophic, complication of TEVAR and to increase its familiarity within the interventional community.

Methods

Patients. Between July 30, 1999, and August 25, 2008, a total of 213 patients (70% men, median age 67.5 years, range 22 to 87 years) underwent retrograde transfemoral/transiliac TEVAR at our institution. Additionally, 55 patients (71% men, median age 60 years, range 34 to 78 years) underwent antegrade stent-grafting of the descending thoracic aorta (DTA) during open ascending aortic or arch surgery. After TEVAR, all patients were subjected to a strict follow-up protocol, including clinical assessment and imaging of the aorta before discharge, as well as at 3, 6, or 12 months, and then annually after the procedure. Follow-up information was available for all but 2 patients (99%) who underwent TEVAR with a median follow-up of 13.0 (interquartile range 2.6 to 41.8) months.

Patients readmitted for AEF were identified from our institutional aortic stent-graft database. All patients' charts and records were thoroughly reviewed. Symptoms and laboratory status at readmission, clinical management, complications during further course, as well as date and cause of death were noted. All implantation angiographies and

computed tomography (CT) scans of the patients were reviewed in order to identify anatomic similarities among the patients potentially predisposing to AEF formation. From angiography, the proximal landing zone of the stent-graft was assessed dividing the aortic arch in 4 zones as previously described (8). All CTs were reviewed by experienced radiologists. The maximum diameter of the proximal aortic landing zone was measured. The DTA was evaluated qualitatively for the presence of significant elongation or pre-vertebral course. Elongation was present when the shape of the DTA was not round on the axial CT images, but significantly oval shaped, and the aorta took a deep left-lateral course in relation to the spine. The CT at readmission was evaluated for the presence of endoleakage.

Statistical analysis. Categorical data are presented as frequencies; continuous variables are expressed as median and range.

Results

Among 268 patients undergoing retrograde or antegrade TEVAR at our institution during the study period, AEF occurred in 5 (1.9%) (Table 1). One additional male patient (49 years) who underwent TEVAR at an external institution was admitted to our institution with AEF. Median age of these patients was 64.5 (range 49 to 77) years with one-half being men. Procedural data are given in Table 2. A 77-year-old female patient presented with ruptured thoracic aortic aneurysm (TAA) and penetration into the esophagus.

AEF occurred median 2.4 (1 to 16) months after TEVAR. Four of the 6 (67%) patients presented with sudden hematemesis. The remaining 2 patients were primarily readmitted for new-onset fever and elevated inflammatory laboratory parameters, but both developed massive hematemesis after 2 and 20 days, respectively.

CT angiography showed—similarly for all patients—new nonhomogenous masses between aorta and esophagus (Fig. 1). Air entrapment suggestive of esophageal perforation and mediastinitis was observed in 4 of 6 patients. Right-sided pleural effusion was present in one-half of the patients. Esophago-gastro-duodenoscopy (EGD) identified deep esophageal ulcerations at the level of the implanted aortic stent-graft in 4 patients (Fig. 2). In these patients, EGD showed large defects of the esophageal wall, allowing direct view of the aortic stent-graft (Fig. 3). In the remaining 2 patients, mild erosive lesions within the proximal esophagus without signs of active bleeding were observed. In both

Abbreviations and Acronyms

AEF = aorto-esophageal fistula

CT = computed tomography

DTA = descending thoracic aorta

EGD = esophago-gastro-duodenoscopy

TAA = thoracic aortic aneurysm

TEVAR = thoracic endovascular aortic repair

Table 1. Patient Data

Patient, Age, Gender	Aortic Disease	Date of TEVAR	Date of Readmission for AEF	Symptoms at Readmission	Laboratory Markers at Readmission*	Treatment	Complications During Hospital Course	Date of Death	Cause of Death
H.K., 62 yrs, male	AD	May 17, 2001	June 19, 2001	New-onset fever, back pain	Hemoglobin: 10.3 Leukocytes: 11.2 CRP: 25.1 Fibrinogen: 1,000 D-dimers: —	Antibiotics†	Hematemesis	September 7, 2001	Fatal rebleeding
I.L., 74 yrs, female	TAA	January 28, 2002	October 25, 2002	New-onset fever	Hemoglobin: 10.7 Leukocytes: 29.3 CRP: 20.5 Fibrinogen: 869 D-dimers: 489	PEG, antibiotics	Mediastinitis, hematemesis	August 11, 2002	Mediastinitis
H.P., 77 yrs, female	Ruptured TAA‡	April 24, 2002	July 6, 2002	Hematemesis, fever	Hemoglobin: 7.9 Leukocytes: 21.1 CRP: 24.5 Fibrinogen: 933 D-dimers: 340	Esophageal stent implantation, PEG, antibiotics	Mediastinitis, rebleeding	January 30, 2003	Fatal rebleeding
W.K., 67 yrs, female	AAD	October 24, 2005§	February 22, 2007	Hematemesis, fever	Hemoglobin: 8.9 Leukocytes: 10.9 CRP: 13.1 Fibrinogen: 749 D-dimers: —	Re-TEVAR, PEG, antibiotics	Mediastinitis, rebleeding	October 1, 2007	Mediastinitis
R.G., 49 yrs, male	AAD	February 23, 2006	April 24, 2006	Hematemesis	Hemoglobin: 6.8 Leukocytes: 16.5 CRP: 14.6 Fibrinogen: 686 D-dimers: 446	Surgical stent-graft explantation, redo surgery for mediastinitis, esophageal stent implantation, PEG, antibiotics	Mediastinitis	June 17, 2006	Fatal rebleeding
H.T., 52 yrs, male	AAD	May 30, 2007	October 8, 2007	Hematemesis	Hemoglobin: 8.7 Leukocytes: 18.3 CRP: 18.4 Fibrinogen: 412 D-dimers: 624	Esophageal stent implantation, PEG, antibiotics	Rebleeding	October 2, 2007	Fatal rebleeding

*Units for laboratory markers: hemoglobin (g/dl); leukocytes (/nl); C-reactive protein (CRP) (mg/dl, normal <0.5); fibrinogen (mg/dl); D-dimers (µg/ml, normal <250); †performed at an external hospital for acute type B dissection with contained rupture; ‡definitive diagnosis was made only at necropsy; §with penetration into the esophagus; ||surgical antegrade stent-graft placement via the open arch during ascending aortic replacement for acute type A dissection.
 AAD = acute aortic dissection; AEF = aorto-esophageal fistula; PEG = percutaneous endoscopic gastrostomy; TAA = thoracic aortic aneurysm; TEVAR = thoracic endovascular aortic repair.

patients, the presence of AEF behind this mild erosive lesion was not recognized at first presentation and the first patient was even discharged after a few days. He developed fatal hematemesis within 14 days, and definitive diagnosis of AEF was made only at necropsy. In the other female patient

who underwent antegrade stent-grafting, hematemesis was suspected to be associated with endoleakage, and the patient underwent re-TEVAR. Three months later, the patient presented again with hematemesis and now large AEF became evident on EGD.

Table 2. Stent-Graft and CT Analysis Data

Patient, Age, Gender	Maximum Diameter of the Proximal Landing Zone	Stent-Graft Diameter (mm)	Number of Stent-Grafts Implanted	Proximal Aortic Landing Zone	Elongation of Descending Thoracic Aorta	Pre- or Right-Vertebral Course of the Descending Thoracic Aorta	Endoleak at the Time of AEF
H.K., 62 yrs, male	32	38	1	2	No	No	No
I.L., 74 yrs, female	36	42	3	2	Yes	Yes	Yes
H.P., 77 yrs, female	30	34	1	3	No	No	No
W.K., 67 yrs, female	24*	24	1	2	Yes	No	Yes
R.G., 49 yrs, male	35	38	2	2	No	No	No
H.T., 52 yrs, male	31	32	2	1	Yes	Yes	No

*Surgical ascending aortic replacement for acute type A dissection with 24-mm prosthesis.
 AEF = aorto-esophageal fistula; CT = computed tomography.

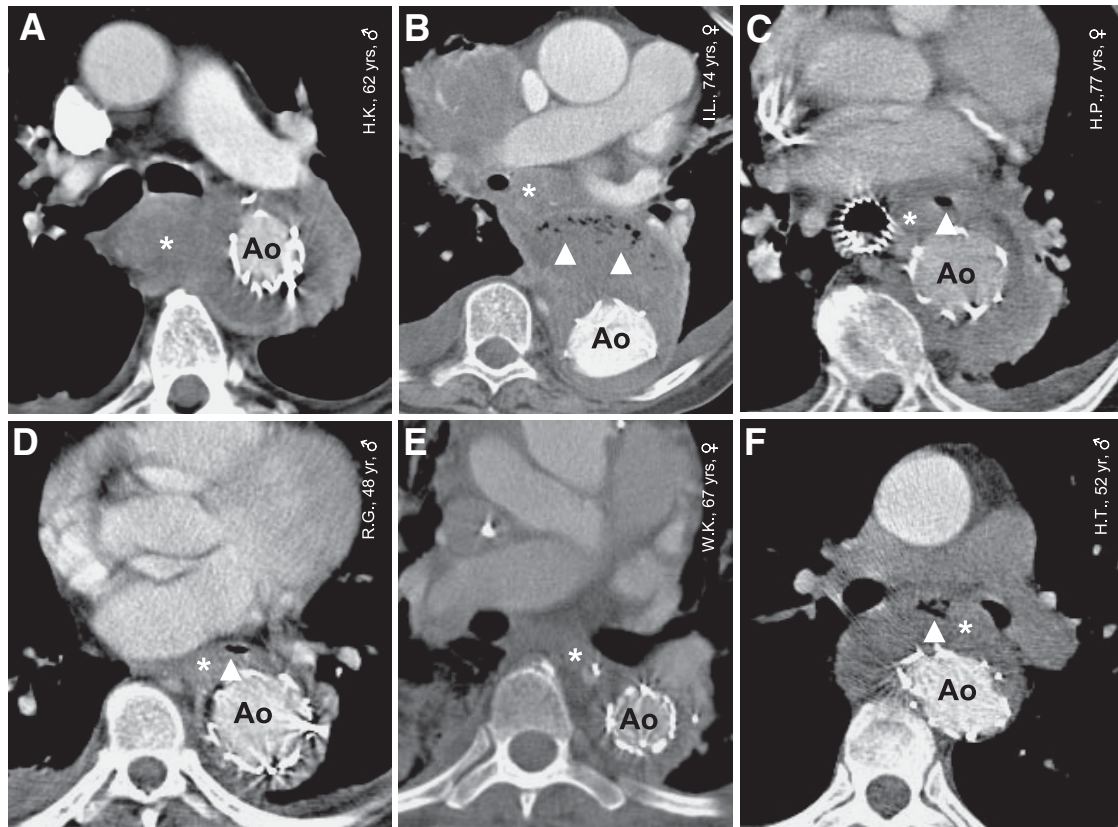


Figure 1. CT Images of Patients at Presentation

Contrast-enhanced computed tomography (CT) scans of the 6 patients (A to F) showing the characteristic appearance of an aortoesophageal fistula with evidence of new nonhomogenous masses between the aorta and esophagus (asterisks). Please note air entrapment within the thrombosed aneurysm/dissection in B to F (arrows). Ao = descending thoracic aorta.

In patients undergoing emergency EGD for massive hematemesis, placement of a Sengstaken-Blakemore tube (n = 1) or self-expanding esophageal stents (n = 2) was performed to control bleeding. Surgical repair was performed in a single patient, and was contemplated in another. In the remaining patients, surgery was refused due to their reduced general health condition. During surgery, the stent-graft was explanted and replaced by a Dacron graft. The post-operative course was complicated by mediastinitis requiring revision surgery. Conservative management was applied in the remaining 5 patients and included use of broad-spectrum antibiotics and proton pump inhibitor treatment, as well as percutaneous endoscopy-guided gastrostomy to unburden the esophageal lesion. Covered self-expanding metallic stents were implanted into the esophagus in 3 of 6 patients to prevent recurrent bleeding and promote healing of the ulcer site. However, healing of the ulcer was not observed in any of these patients, despite leaving the esophageal stent in place for up to 4 weeks. In the female patient who presented with a ruptured TAA, the

esophageal lesion did not show any signs of healing, but the ulcer had, in fact, progressed in size.

The in-hospital course was complicated by mediastinitis in 4 of 6 patients leading to fatal sepsis in 2 of them. Recurrent hematemesis occurred in the remaining 4 patients and was fatal in all of them (Fig. 1, Table 1). All patients died median 53 (20 to 221) days after readmission.

Discussion

We report the occurrence of AEF as an unusual, catastrophic complication of TEVAR, which is rare, occurring in 1.9% of TEVAR patients in our series and is thus probably not widely known within the medical community. These were encountered within 1 to 16 months after TEVAR, presenting either as hematemesis or new-onset sepsis. While presentation of AEF as hematemesis is intuitive, our experience suggests that AEF may also manifest as a new-onset fever accompanied by elevated markers of inflammation, and may herald the onset of eminent

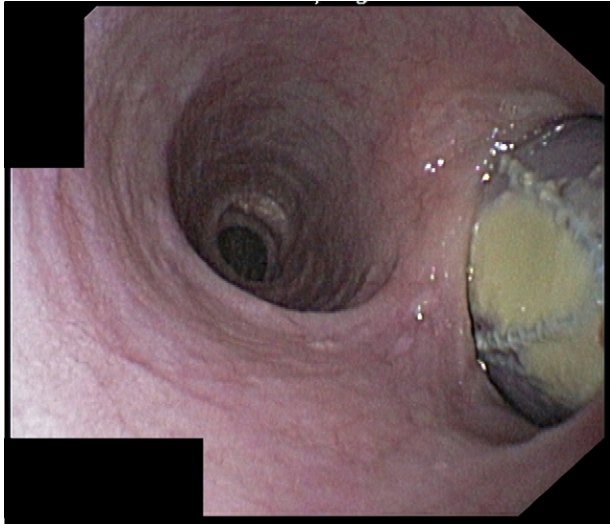


Figure 2. Aspect of Aorto-esophageal Fistula on Esophago-Gastro-Duodenoscopy

Esophago-gastro-duodenoscopy demonstrating large aorto-esophageal fistula with an apparent view onto the intact aortic stent-graft.

rupture of aorta into the esophagus. Thus, not only hematemesis but new-onset fever in patients with prior TEVAR should alert the physician to this potentially life-threatening complication of TEVAR.

AEF is a rare cause of upper gastrointestinal bleeding with etiologies including foreign body ingestion, malignancy, and post-operative trauma, but is often described in cardiovascular literature as being associated with penetrating or ruptured TAAs (9). Secondary AEF is well recognized as a complication of thoracic aortic surgery and has catastrophic consequences without treatment (10). It may also arise as aortoenteric fistula after open abdominal aortic surgery with an estimated incidence of 0.4% to 4% of patients (11,12). Few case reports, most with single cases, have also highlighted the risk of AEF after less invasive TEVAR procedures (11,13–15). The primary clinical presentation is uncontrolled hematemesis, usually resulting in exsanguination.

CT in our experience was particularly helpful in the patients as an initial modality, because evidence of a relatively characteristic new heterogeneous mass between the DTA and esophagus with or without air entrapment gave an early clue to the diagnosis. It is likely that in patients presenting with new-onset fever after TEVAR a CT performed early on with a finding of a new mass between the aorta and esophagus may provide an early clue that could then further be confirmed by prompt EGD. While AEF was directly visualized by EGD as large esophageal defects with a clear view onto the stent-graft in 4 patients, the findings of only mild erosive lesions in the other 2 precluded

early diagnosis in the other 2, 1 of whom was discharged home, only to present later with fatal hematemesis. Nonetheless, in retrospect when looking at all patients with this complication, it was clear that presence of new-onset fever or hematemesis together with findings of CT and EGD, when put together, would, in the context of previous TEVAR, have resulted in early diagnosis. Particularly, in the 2 patients who only had mild erosive lesions in their esophagus on EGD, recognition of this to be associated with AEF may have prompted early triage and/or surgical repair before development of ulcer and hematemesis, and may have had the potential for better outcomes. However, this theory needs to be proven in the future.

Published reports have confirmed that conservative management to control rebleeding and prevent mediastinitis is almost invariably a fatal outcome, potentially justifying a more aggressive surgical strategy involving esophageal resection, effective debridement, and aortic (homo)graft interposition (13,16). However, operative management of AEF carries significant mortality and is frequently complicated by mediastinitis, sepsis, and hemorrhage. It is important to recognize that the majority of our patients initially underwent TEVAR, because their general health status and comorbidities precluded open surgical repair. Therefore, the majority of our AEF patients were treated conservatively, because surgical repair was prohibitive due to their general health condition and frailty. Conservative management included the use of broad-spectrum antibiotics, proton pump inhibition, and enteral feeding via percutaneous

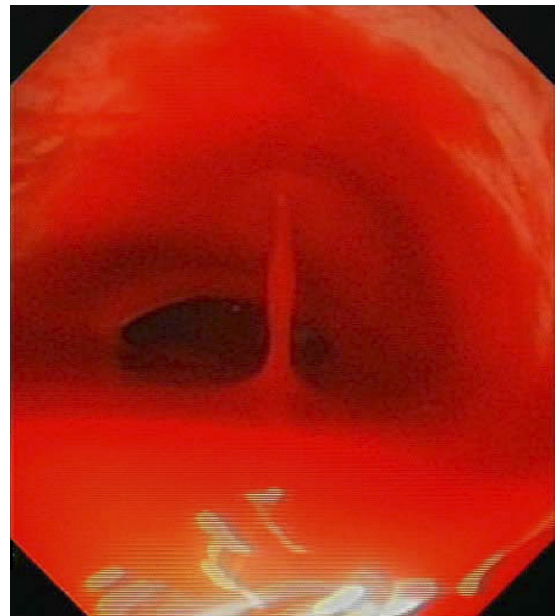


Figure 3. Fatal Bleeding of Aorto-esophageal Fistula

Esophago-gastro-duodenoscopy during fatal rebleeding in Patient #6 (H.T.).

endoscopic gastrostomy (PEG) to unburden the esophageal lesion. Although outcome was fatal in all patients, at least 2 patients could be stabilized by using these conservative measures for >6 months. In 3 patients, self-expanding esophageal stents were placed to promote healing and prevent rebleeding. However, in none of these patients healing of the esophageal fistula was ultimately observed on control EGD. In fact, all of these patients developed fatal rebleeding. Surgical repair was performed in a single case, but was complicated by mediastinitis and graft infection requiring revision surgery. A recent report suggested a surgical approach focused on the esophageal pathology and not on the potential infectious stent-graft in order to limit the extent of surgery in these ill patients (13). Recently, endovascular stent-graft placement also has been successfully used to treat secondary AEF after surgery (17,18). We also attempted re-TEVAR in a single patient, who later died. However, restent-grafting into a potentially contaminated or infected environment remains counterintuitive and debatable. So far, it is not completely understood whether the severe bleeding in AEF arises from esophageal vessels or aortic vasa vasorum or directly from the aorta. In all of our patients, the stent-graft itself was intact, rendering bleeding directly from the aorta somewhat unlikely. Therefore, it is questionable whether re-TEVAR will control the bleeding risk of AEF.

The exact pathophysiologic mechanisms of AEF formation secondary to TEVAR are unknown, so far. We were not able to identify anatomic or procedural similarities among our patients that may have predisposed to AEF. Hypotheses include: 1) direct erosion of the relatively rigid stent-graft through the aorta into the esophagus; 2) pressure necrosis of the esophageal wall due to the continuing forces of the self-expanding endoprosthesis; 3) ischemic esophageal necrosis due to stent-graft coverage of aortic side branches that feed the esophagus; and 4) infection of stent-graft prosthesis that eventually extends to the esophagus eroding its wall (11). The last 2 concepts may be supported by our observation that AEF did not show any healing tendency despite prolonged sealing by esophageal stents in 3 patients. Until further research in large number of patients will hopefully allow identification of patients at risk, close surveillance of all patients after TEVAR is mandatory. New-onset fever with elevated inflammatory markers and/or hematemesis with homogenous masses with or without air entrapment on CT should raise suspicion of AEF prompting immediate endoscopic evaluation.

Conclusions

In summary, our case series indicates that AEF after TEVAR is a rare unusual complications of TEVAR (incidence ~1.9%) that occurs relatively early after the procedure and is uniformly fatal. Additionally, these data indicate that

not only hematemesis, but fever and heightened inflammatory markers, should raise the clinical suspicion for AEF in patients with prior TEVAR. CT is an attractive initial tool particularly among those presenting with fever with upper gastrointestinal endoscopy, providing the eventual confirmation of the diagnosis. Most conservative strategies, including the use of broad-spectrum antibiotics, proton pump inhibitors, and enteral feeding, remain far from optimal for the management of this condition highlighting the need for further research in this area not only for identifying patients at risk, but also evaluating strategies for better management. Most importantly, as TEVAR use grows, physicians in the general community should be aware of AEF as one of the differential diagnoses in TEVAR patients presenting with commonly encountered symptoms of fever or hematemesis. This would allow prompt diagnosis and/or immediate triage for treatment.

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