



Retrospective review of 65 atrioesophageal fistulas post atrial fibrillation ablation



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ABSTRACT

Background: Although a rare complication of catheter based ablation for atrial fibrillation (AF), atrioesophageal fistula (AEF) is a serious and fatal event [1–5]. Most reports of AEF are single cases or small case series.

Objective: The purpose of this study was to perform a comprehensive literature search of all published atrioesophageal fistula following catheter ablation for AF in order to identify the mortality rates associated with therapeutic modalities and suggest the most definitive management in reducing mortality.

Methods: A comprehensive literature review of reported observational cases of atrioesophageal fistula post catheter based ablation for atrial fibrillation was performed.

Results: Sixty-five cases of AEF post atrial fibrillation ablation were reviewed. The mean age was 55 years old. 73.8% (48/65) of the identified cases occurred in males ($p < 0.001$). Of the 65 cases, 13 underwent surgical radiofrequency ablation (RFA) and 52 underwent percutaneous RFA. Mortality resulted in 53.8% of those who underwent surgical RFA and in 55.8% of those who underwent percutaneous RFA ($p = .888$). The time range interval from procedure to onset of symptoms was 1–60 days. The most prevalent symptom, fever, occurred in 52 of the 65 cases, followed by neurological symptoms ($n = 44$). CT of the chest ($n = 37$), transthoracic echocardiogram ($n = 21$), and CT of the head ($n = 18$) were the preferred diagnostic modalities. Patients who underwent surgical correction with esophageal repair for treatment were more likely to survive, in comparison to patients who were treated with non-surgical interventions, such as antibiotic therapy, anticoagulation therapy or esophageal stenting. Of the total 34 patients who were treated surgically, 27 survived (79.4%). Of the total 31 patients who were treated non-surgically, only 2 survived (6.5%), reflecting significantly lower mortality with surgical versus non-surgical therapy ($p < 0.001$).

Conclusion: Atrioesophageal fistula is an uncommon but potentially fatal complication of atrial fibrillation ablation. Patients who underwent surgical repair were twelve times more likely to survive than those treated with stenting, antibiotic therapy or no intervention. Based on the observation that patients are 12 times more likely to survive an AEF with surgery than without, the authors believe that prompt surgical correction of AEF should be considered as standard of care when dealing with this dreaded complication.

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1. Introduction

Catheter based ablation is a common treatment option in

patients who either failed or declined medical therapy for atrial fibrillation (AF). With the incidence and prevalence of atrial fibrillation increasing worldwide, the frequency of catheter based ablations also continues to rise. Ablation of AF most commonly involves creating circumferential lesions around the pulmonary vein ostia or antra with or without the placement of additional ablation lesions within the left atrium [3]. The left atrium is anterior to the esophagus [3,4]. The close proximity of the esophagus to the

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Table 1

Case reports included.

Author	# of Cases	Gender	Age (years)	Procedure	Post-procedure Day	Clinical presentation	Imaging Findings	Diagnostic Procedure	Treatment	Outcome
Pappone et al. [4]	1	Male	59	CPVA	2	Chest pain, fever, weakness, rigors, grand mal seizures	TTE/TEE CT of the head	unremarkable	Autopsy	Nonsurgical, Antibiotics
Mohanty et al. [8]	9	Male	46	RFCA 8 = endocardial catheter based radiofrequency	21	Fever, leukocytosis, stroke/TIA, Bilateral arm weakness	Chest CT w/ contrast	AEF	Chest CT w/ contrast	Esophageal Stent Death IV antibiotics Anticoagulation
		Male	61	1 = hybrid endo- epicardial left atrial ablation	28	Fever, leukocytosis, stroke/TIA, hemiparesis, seizure	Chest CT w/ contrast	AEF	Chest CT w/ contrast	Esophageal Stent Death IV antibiotics Anticoagulation
		Male	45	7 = intraluminal temperature monitoring with esophageal probe	35	Fever, stroke TIA, leukocytosis, grand mal seizures, focal cortical signs	Chest CT w/ contrast	AEF	Chest CT w/ contrast	Esophageal Stent Death IV antibiotics Anticoagulation
		Male	58	4 = general anesthesia	28	Chest pain, stroke/TIA, leukocytosis, hemiparesis, confusion	Chest CT w/ contrast	AEF	Chest CT w/ contrast	Esophageal Stent Death IV antibiotics Anticoagulation
		Female	62	5 = conscious sedation	42	Stroke/TIA systemic embolism, chest pain, GI hemorrhage, leukocytosis, decreased reflexes, paresis	Chest CT w/ contrast	AEF	Chest CT w/ contrast	Esophageal Stent Death IV antibiotics Anticoagulation
		Male	51		28	Fever, chest pain, sepsis, stroke/TIA. Leukocytosis, AMS, hemiparesis	Chest CT w/ contrast	AEF	Chest CT w/ contrast	Surgery IV antibiotics Anticoagulation
		Male	59		14	Fever, rigor, chest pain, sepsis, GI bleed, stroke/TIA, sudden blindness weak leg	Chest CT w/ contrast	AEF	Chest CT w/ contrast	Surgery IV antibiotics Anticoagulation
		Male	42		21	Fever, rigor, chest pain, sepsis, stroke/TIA, sudden blindness weak leg	Chest CT w/ contrast	AEF	Chest CT w/ contrast	Surgery IV antibiotics Anticoagulation
		Male	56		28	Fever, chest pain, dysphagia, confusion, leukocytosis, postprandial TIA, multiple petechiae, weak arm	Chest CT w/ contrast	AEF	Chest CT w/ contrast	Surgery IV antibiotics Anticoagulation
Pappone et al. [9]	1	Male	36	Percutaneous CPVA	3	Fever, Pleuritic chest pain, seizures	CT of the head	Bilateral ischemia	CT of chest	Surgical
Pappone et al. [9]	1	Male	21	Percutaneous CPVA	1	Fever, Grand mal seizure	CT of the head	Unremarkable	TEE	Non-surgical
Aryana et al. [11]	1	Female	55	MAZE	21	Seizures, left hemiparesis, severe chest pain	Head CT	Cerebral pneumocephalus	Chest CTA	Non-surgical
Vassileva [12]	1	Female	72	Percutaneous radiofrequency isolation of the pulmonary veins	14	Shortness of breath, nonproductive cough, palpitations, elevated WBC, seizure	Head CT Chest CT	Air in the left atrium	Chest CT	Surgery
Sonmez et al. [13]	1	Female	58	Surgical: LRFA – melo technique	22	Fever, shivers, numbness right arm	TTE	LA thrombus	EGD	Thrombectomy, pericardial sutures
Doll et al. [14]	1	Male	42	Surgical: IRAAF	10	Fever, postprandial TIA	TTE	Normal	Exploratory thoracotomy	Surgical
Doll et al. [14]	1	Female	62	Surgical: IRAAF	6	Hematemesis,	EGD	NA	Pathology	None
Doll et al. [14]	1	Male	59	Surgical: IRAAF	12	Fever, neurological symptoms	CT of the chest	Contrast and free air in the mediastinum	Exploratory thoracotomy	Surgical
Doll et al. [14]	1	Male	36	Surgical: IRAAF	11	Chest pain	CT of the chest	Esophageal perforation	Exploratory thoracotomy	Surgical
Scanavacca et al. [15]	1	Male	72	Percutaneous RFA	22	Seizures, Hematemesis	NA	NA	EGD	None
Zirlik and Nordt [16]	1	Male	66	Surgical: MVR and MAZE procedure	14	Collapse	CT of the head	Multiple intracerebral air emboli and infarction	EGD	Non-surgical
Bunch et al. [17]	1	Male	48	Percutaneous RFA	14	Fever, chest pain, dysphagia	CT of the chest		EGD	Non-surgical

(continued on next page)

Table 1 (continued)

Author	# of Cases	Gender	Age (years)	Procedure	Post procedure Day	Clinical presentation	Imaging Findings	Diagnostic Procedure	Treatment	Outcome
3 mm esophageal perforation at the level of the atrium										
Schley et al. [18]	1	Male	37	Percutaneous: RFA	25	Fever, Grand mal seizure, status epilepticus	CT of the head	Ischemic lesions	CT of chest	Surgical
Cummings et al. [19]	9	Male = 4 Female = 5	NA	Percutaneous: PRFA	12.3 (10–16)	Sepsis (9), neurological symptoms (8), angina (2), GI bleed (3), occult bleed (5)	CT of the head (2)	Intravascular air	CT of chest (3/4); autopsy(6/9)	Surgical = 3 Death = 9
Dagres et al. [20]	5	Male = 4 Female = 1	51 (35–76)	Surgical: RFA (n = 4); Percutaneous: RFA (n = 1)	8–28	Fever (3) chest pain (2), hemiparesis (3), grand mal seizure (1), aphasia (1)	NA	Free air in mediastinum (3), pericardium (1), left atrium (1)	CT of chest	Surgery = 3 Attempted surgery = 2
Preis et al. [21]	1	Male	56	Percutaneous: PVI with RFA	38	Malaise, chills, bilateral arm weakness	TEE	No vegetations	CT of chest	Surgical
Malamis et al. [22]	1	Male	59	Percutaneous: RFA	35	Fever, altered mental status, petechiae	CT of the head	Negative	CT of chest	Surgical
D'Avila et al. [23]	1	Male	56	Percutaneous: RFA	28	Epigastric pain, dysphagia, tactile fever, focal weakness, anoma, acalculia, agraphia	MRI of the brain	Multiple subacute embolic events	CT of chest	Surgical
Borchert et al. [24]	1	Male	59	Percutaneous: PVI with HIFU ablation catheter	10	Chest discomfort and atypical atrial flutter; VF arrest	MRI of the brain	Cerebral and cerebellar ischemic lesions	CT of chest	Surgical
Ouchikhe et al. [25]	1	Male	58	Percutaneous: RFA	21	Fever, confusion, meningitis	CT of the head	Bilateral hyperdense lesions (frontal, occipital parietal and temporal)	TTE	Nonsurgical
Hazell et al. [26]	1	Male	72	Percutaneous: PVI roofline mitral isthmus line CFAE	16	Weakness, loss of consciousness, chest pain	CT of the head	Right parietal subcortical matter ischemic changes	CT of chest	Nonsurgical
Vijayaraman et al. [27]	1	Male	45	Percutaneous: RFA with 3D reconstruction	10	Chest pain, low grade fever, hypotension	CT of the chest	Fluid and air in pericardium and air in right superior mediastinum	Thoracotomy	Surgical
Baker et al. [28]	1	Female	67	Surgical: RFA	20	Substernal chest pain, nausea, vomiting, confusion, fever, seizures, hematemesis	MRI of the brain	Multiple acute emboli	EGD	Nonsurgical
Cazavet et al. [29]	1	Male	35	Percutaneous: RFA	38	Fever, chest pain, vomiting, left hemiplegia and seizures	CT of the head	Initially negative	CT of chest	Surgical
Gilcrease et al. [30]	1	Male	61	Percutaneous: RFA	10	Dysphagia, substernal chest pain, fever	CT of the chest	Ulcer at anterior portion esophagus adjacent to PV	CT of chest (after 2 months)	Surgical
Khandhar et al. [31]	1	Male	46	Percutaneous: RFA	27	Fever, pericarditis, followed by hemiparesis	CT of the chest	Normal	CT of chest	Surgical
Siegel et al. [32]	1	Male	41	Percutaneous: RFA	30	Fever, rigors near syncope; followed by right sided hemiparesis	MRI of the brain	Multifactorial infarcts	CT of chest	Surgical
Grubina et al. [33]	1	Male	72	Percutaneous: RFA	9	Pleuritic chest pain	CT of the chest PAD # 15	Pneumo-pericardium	EGD	Surgical
St Julien et al. [34]	1	Male	59	Percutaneous: transeptal LA ablation with ThermoCool catheter	42	Chest pain, diaphoresis, headache, fever, altered mental status	TTE	No vegetations	CT of chest	Surgical
Zellerhoff et al. [35]	1	Male	63	Percutaneous: RFA with 3D mapping	14	Muscle weakness, generalized fatigue followed by fever and left sided hemiparesis	CT of the head	Several large intracerebral lesions suspicious for air embolism	CT of chest	Nonsurgical
Purerfellner et al. [36]	1	Male	49	Percutaneous: RFA	29	Fever, chills, nausea, emesis, altered mental status, athetotic movements, skin changes, hematemesis	EGD	Unable to localize source of bleeding	EGD	Nonsurgical
Stockigt et al. [37]	1	Male	78	Percutaneous: cryoballoon PV isolation	28	Fever, shivers, cough for 10 days, followed by neurological symptoms	CT of the chest and abdomen	Negative	Cardiac CT	Nonsurgical

Table 1 (continued)

Author	# of Cases	Gender	Age (years)	Procedure	Post procedure Day	Clinical presentation	Imaging Findings	Diagnostic Procedure	Treatment	Outcome	
Tancevski et al. [38]	1	Male	45	Percutaneous transcatheter ablation	42	Fever, weakness, sensory loss of right limbs	CT of the chest and abdomen	CT of chest: AEF; CT of abdomen: multiple renal and splenic infarctions	CT surgery	Surgical	Survived
Haggerty et al. [39]	1	Male	27	Percutaneous PV RFA	22	Fever, chills, hypotension, hematemesis	CT of the chest	Pneumo-mediastinum adjacent to LA	CT surgery	Surgical	Survived
Kanth and Fang [40]	1	Female	69	Percutaneous RFA	60	Sepsis, ischemic stroke, melena	CT of the chest	AEF	EGD	Nonsurgical	Death
Ben-David et al. [41]	1	Female	73	Percutaneous RFA	9	Pneumo-mediastinum	UGI series	4 mm esophageal perforation at 6 cm from GEJ	EGD	Surgical	Survived
Hartman et al. [42]	1	Male	62	Percutaneous RFA	30	Odynophagia, fever, chills, rigors, syncope	Cardiac Cath	Negative	CT of chest	Surgical	Survived
Zini et al. [43]	1	Male	44	Percutaneous RFA	—	Altered mental status, stupor	CT of the head	Multifocal air emboli	EGD	Antibiotics, antithrombotics, fistula repair	Death
Rivera et al. [44]	1	Female	50	Percutaneous RFA	28	Minor hematemesis	CT of the chest	AEF and plural effusions	EGD	Surgical	Survived
Tan Coffey [45]	1	Female	67	Surgical: MVR and MAZE procedure	20	Nausea, fever, numbness of the left foot; unresponsive	CT of the head	CT of the head: air embolism RSFA	CT of chest	Nonsurgical	Death
Shim et al. [46]	1	Male	46	Percutaneous RFA	2	Fever, chills, cough, headache; confusion, generalized tonic-clonic seizures	TTE/TEE	No thrombus	CT of chest	Surgical	Survived
Neven et al. [47]	1	Male	69	Percutaneous HIFU	31	Fever, hematemesis, seizures, phrenic nerve palsy	CT of the head	Cerebral embolism	Autopsy	Nonsurgical	Death
Dixit et al. [48]	1	Female	NA	Percutaneous PV isolation	14	Fever, nausea, hematemesis	EGD	Possible Mallory-Weiss tear	CT of head	Nonsurgical	Death

AEF, atrioesophageal fistula; AMS, altered mental status; CFAE, complex fractionated atrial electrograms; CPVA, circumferential pulmonary vein ablation; EGD, esophagogoduodenoscopy; GEJ, gastroesophageal junction; GI, gastrointestinal; HIFU, high-intensity focused ultrasound; IRAAF, intra-operative radiofrequency ablation of atrial fibrillation; IV, intravenous; LA, left atrium; LRFA, linear radiofrequency ablation; MVR, mitral valve replacement; NA, not available; PAD, post-ablation day; PV, pulmonary veins; PVI, pulmonary vein isolation; RFA, radiofrequency ablation; RFCA, radiofrequency catheter ablation; RSFA, right superior frontal area; TEE, transesophageal echocardiogram; TIA, transient ischemic attack; TTE, transthoracic echocardiogram; UGI, upper gastrointestinal; VF, ventricular fibrillation; WBC, white blood cells.

left atrium makes it susceptible to potential injury during catheter based ablation of AF [7].

While the possible complication of atrioesophageal fistula is rare post catheter ablation of AF, it is, none-the-less a severe, life-threatening complication that is one of the most feared [1,3,6]. It is estimated to occur in 1 of 500–1000 cases [6]. The mortality rate associated with AEF has been reported to surpass 60%–80% [5,10].

We have reviewed the clinical characteristics, discuss diagnostic modalities and determine the most definitive treatment options available, in order to recognize and promptly treat AEF, given its fatal outcome [1].

2. Methods

2.1. Search strategy

The purpose of this study was to collate cases of AEF post ablation for AF that were identified from published reports in the literature. PubMed is a searchable online database and service of the US National Library of Medicine that provides access to medical journal articles. A systemic search of the database PubMed from inception to June 2017 was performed. The search terms included “atrioesophageal fistula” or “atrio-esophageal fistula” or “esophagoatrial fistula” or “esophago-atrial fistula.” These terms were searched as free text in the title or the abstract [1]. In addition, Google Scholar, another searchable online database, was systematically searched with the same terms as above. Lastly, we reviewed reference lists of bibliographies of the listed articles.

2.2. Selection criteria

Case reports selected reported: (1) the primary diagnosis as AF for ablation procedure; (2) clinical presentation; (3) diagnostic imaging; (4) management and (5) outcome [1].

2.3. Statistical analysis

For this systemic review of case reports, we used the Preferred Reporting Items for Systemic Reviews and Meta-Analyses (PRISMA) statement protocol. Chi-squared analyses were used to determine differences in percentages between groups. Statistical significance was set at 0.05 [1].

3. Results

3.1. Demographics and clinical presentation

Sixty-five cases of AEF post atrial fibrillation ablation were reviewed and compiled into a table (Table 1). The mean age was 55 years old. 73.8% (48/65) of the identified cases occurred in males and 26.2% (17/65) occurred in females ($p < 0.001$) (Fig. 1). Of the 65 cases, 13 (20%) underwent surgical RFA and 52 (80%) underwent percutaneous RFA. Mortality resulted in 53.8% of those who underwent surgical RFA and in 55.8% of those who underwent percutaneous RFA ($p < 0.888$) (Fig. 2). Given these results, there is no clinical significance in mortality between those who underwent surgical versus percutaneous radiofrequency ablation. The range

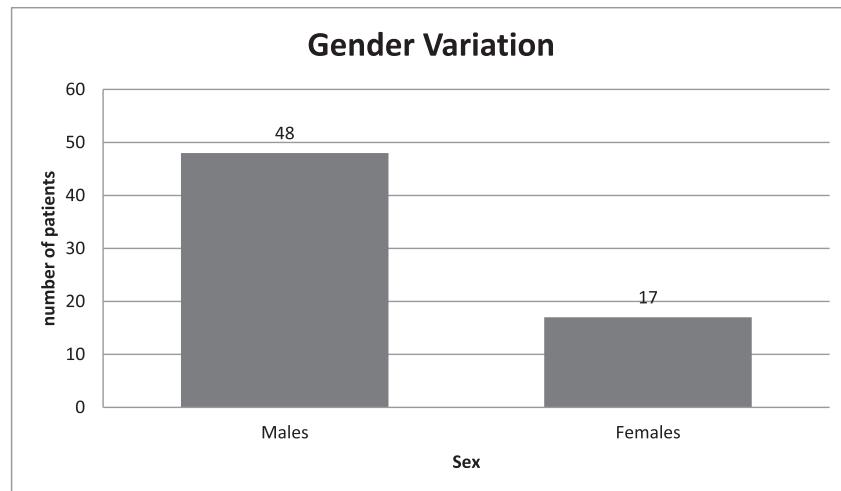


Fig. 1. The total number of males compared to females found to have atrioesophageal fistula post atrial fibrillation ablation. 73.8% (48/65) of the identified cases occurred in males and 26.2% (17/65) occurred in females ($p < 0.001$).

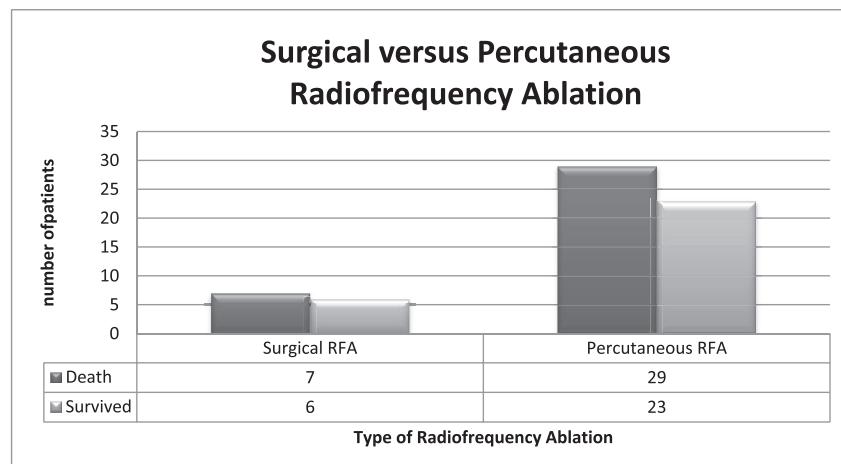


Fig. 2. Comparison of the number of patients with AEF who initially underwent surgical radiofrequency (RFA) versus percutaneous RFA for treatment of atrial fibrillation. Of the 65 cases, 13 (20%) underwent surgical RFA and 52 (80%) underwent percutaneous RFA. Mortality resulted in 53.8% (7/13) of those who underwent surgical RFA and in 55.8% (29/52) of those who underwent percutaneous RFA ($p < 0.888$). Thus, there is no difference in mortality between patients who underwent surgical RFA versus percutaneous RFA.

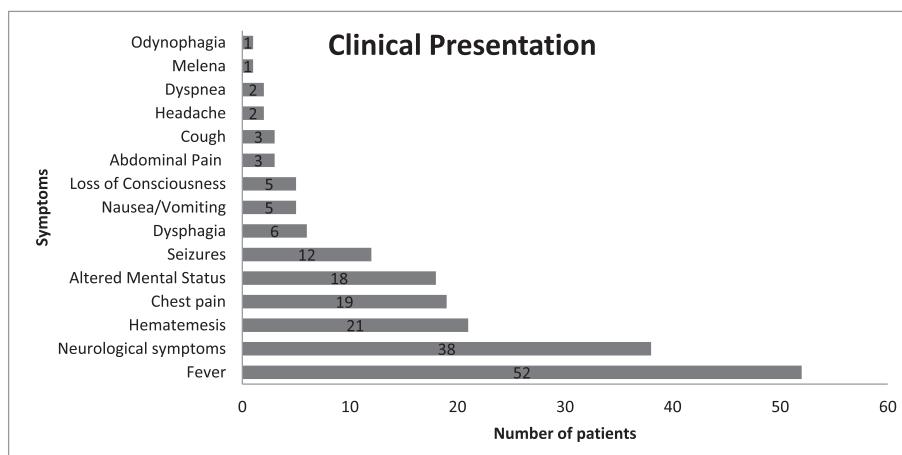


Fig. 3. The frequency of symptoms in patients with AEF post atrial fibrillation at the initial time of presentation. Symptoms will likely occur in a triad of fever, neurological deficits (such as hemiparesis) and/or hematemesis, all three of which make up the most frequent clinical presentations identified.

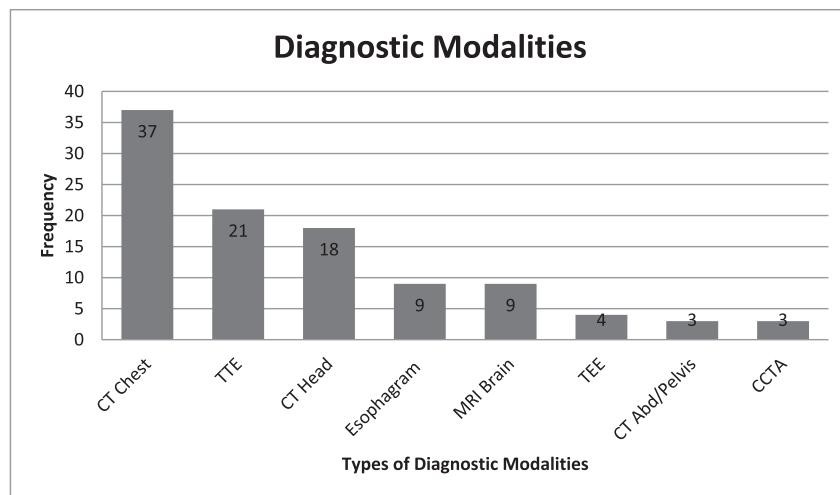


Fig. 4. Frequency of diagnostic modalities used to confirm AEF.

(CCTA, computed cardiac tomographic angiograph; CT abd/pelvis, CT of the abdomen and pelvis with contrast; CT chest, CT of the chest with intravenous contrast; CT head, CT of the head without contrast; MRI brain, MRI of the brain; TEE, transesophageal echocardiogram; TTE, transthoracic echocardiogram).

interval from procedure to onset of symptoms was 1–60 days (Table 1) [1,3]. Fever occurred most commonly in 52 of the 65 cases, followed by neurological symptoms such as hemiparesis, stroke/TIA, motor and language impairment which occurred in 44 cases. Patients also presented with hematemesis ($n = 21$), chest pain ($n = 19$), altered mental status ($n = 18$), seizures ($n = 12$), dysphagia ($n = 6$), loss of consciousness ($n = 5$), nausea/vomiting ($n = 5$), abdominal pain ($n = 3$), cough ($n = 3$), dyspnea ($n = 2$), headache ($n = 2$), melena ($n = 1$), and odynophagia ($n = 1$) (Fig. 3).

3.2. Diagnostic modalities, treatment and outcome

Among the diagnostic modalities employed were CT of the chest ($n = 37$), transthoracic echocardiogram ($n = 21$), and CT of the head ($n = 18$) (Fig. 4). Air embolism was most commonly identified in 17 patients, followed by pneumomediastinum identified in 12 patients (Table 1).

Of the total 65 cases reviewed, 36 resulted in deaths, whether

surgically or non-surgically treated. Thus, the total mortality rate of all cases reviewed was 55.4%, making atrioesophageal fistula a rare, but grave outcome post atrial fibrillation ablation.

Patients who underwent surgical correction with esophageal repair for treatment were more likely to survive, in comparison to patients who were treated with non-surgical interventions, such as antibiotic therapy, anticoagulation therapy or esophageal stenting. Mortality rates were significantly reduced in those who underwent surgical intervention at 20.6% (7/34) versus a mortality rate of 93.5% (29/31) in patients who were not treated surgically ($p < 0.001$) (Fig. 5).

4. Discussion

Atrioesophageal fistula, an uncommon but adverse event of atrial fibrillation catheter based ablation, is associated with a high fatality rate. The mortality rate associated with surgical RFA was 53.8% (7 deaths in a total of 13 patients who underwent surgical

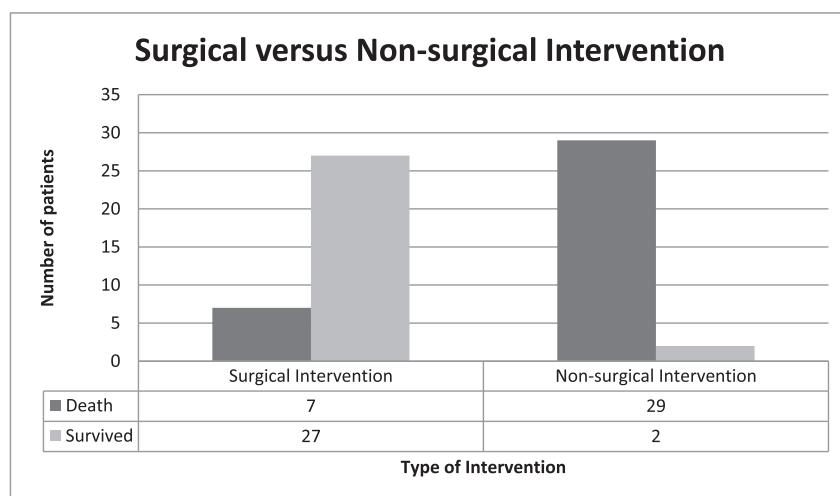


Fig. 5. Comparison of patients with AEF post AF ablation who underwent surgical correction with esophageal repair versus those who underwent non-surgical interventions, such as esophageal stenting, antibiotic therapy or no intervention at all. Overall, patients who underwent surgical correction had a higher survival rate at 79.4% (27/34) compared to those who were treated non-surgically ($p < 0.001$).

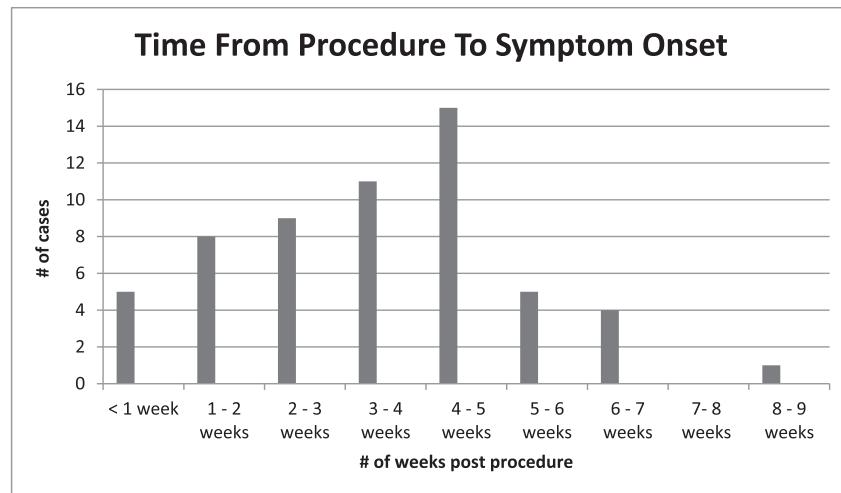


Fig. 6. Patients may present with non-specific symptoms, ranging from less than 1 week to 9 weeks after the ablation.

RFA) versus 55.8% with percutaneous RFA (29 deaths in a total of 52 patients who underwent percutaneous RFA) ($p < 0.001$). Thus, there is no difference in mortality between surgical RFA and percutaneous RFA.

Patients may present with non-specific symptoms, ranging from 1 to 60 days after the ablation (Fig. 6) [1,3]. Common symptoms may include a triad of fever, neurological deficits (such as hemiparesis) and/or hematemesis [1]. Other symptoms may include chest discomfort, altered mental status, seizures, abdominal pain, nausea, vomiting, dysphagia, odynophagia, melena, and dyspnea (Fig. 3). Given the high mortality rate, it is essential to hold a high index of clinical suspicion in patients who recently underwent ablation for AF and present with such non-specific symptoms [1,3,7].

The most common diagnostic modality for identifying AEF following AF ablation includes CT of the chest, TTE and CT of the head. Other methods of imaging used included esophogram, MRI of the brain, TEE, CT of the abdomen or pelvis, and Cardiac CTA (Fig. 4). Concern has been raised regarding the performance of esophagoscopy in the setting of potential AEF, in which air insufflation into the esophagus could push air or esophageal contents into the left atrium.

The total mortality rate of cases reviewed, with surgical and nonsurgical interventions, was 55.4% (36 total deaths out of 65 total cases). 79.4% of patients with AEF post AF ablation survived after undergoing surgical correction with esophageal repair, compared to 6.5% of patients who were treated with non-surgical interventions. Overall, patients who underwent surgical repair were twelve times more likely to survive than those treated with stenting, antibiotic therapy or no intervention at all [5]. With such a large survival advantage conferred by definitive surgical intervention, we advocate that definitive and prompt surgical intervention should be the standard of care for such a dreaded complication (Fig. 5).

5. Limitations

This is a retrospective review of published cases of AEF, and it is likely that many cases of AEF have not been published and so not available to include in this review. It is not possible from these data to assess or compare the incidence of AEF with catheter or surgical ablation. Additionally, there may be important differences between patients who underwent surgical versus non-surgical treatment for

AEF which might have impacted the mortality rates of these patients.

6. Conclusions

Atrioesophageal fistula is an uncommon but adverse event of atrial fibrillation catheter based ablation associated with increased fatality. Patients who underwent surgical repair were twelve times more likely to survive than those treated with stenting, antibiotic therapy or no intervention. Based on the observation that patients are 12 times more likely to survive an AEF with surgery than without, the authors believe that prompt surgical correction of AEF should be considered as standard of care when dealing with this dreaded complication.

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