

BOERHAAVE SYNDROME: SPONTANEOUS RUPTURE OF THE OESOPHAGUS SYSTEMATIC LITERATURE REVIEW AND TREATMENT ALGORITHM

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Abstract

Background: To compare different management modalities of spontaneous oesophageal perforation in the published literature and generate a treatment algorithm. **Materials and Methods:** A systematic search of published literature was undertaken between 1st and 20th November 2020 in two databases-PubMed and Science Direct, following the electronic search strategy and study selection methods according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement. **Result:** In 24 selected articles, the patients showed male predominance and range of patient's age spanned between 21-88 years. Common symptoms included nausea, vomiting, pain, and fever. The perforations were mostly in the lower/distal oesophagus, with a left-sided predominance. Computer tomography was the preferred diagnostic tool. The treatments included endoscopic procedures, minimally invasive surgeries, and open surgical methods. The maximum patient collective was in the surgical group. The range of hospital stay (2-11days) was shortest in the conservative group. There was no common complication across all modalities. The percentage of patients undergoing additional interventions(33.33%) and the percentage of additional interventions performed(39.32%) were highest in the endoscopic group. The open surgical grouped required the least far additional interventions. The highest proportion of mortality was found in management with conservative modalities (12.8%). **Conclusion:** The length of hospital stay was the shortest in the conservative group, here there was lack of true representation, whereas the range of stay was maximum in minimal invasive group. In our study atrial fibrillation and atelectasis were rare complications seen in minimal invasive- and open surgical group respectively. The requirement of additional interventions in conservatively managed group was the lowest, but due to lack of true representation of events, this data could be unreliable. Among other groups, the open surgical grouped required the least additional interventions. In terms of mortality, minimal invasive procedures were better than any modalities, but also had the lowest patient collective. With almost comparable patient collective between conservative and minimal invasive group, the latter showed clearly upper hand in terms of mortality and lack of fistula formation.

INTRODUCTION

Boerhaave Syndrome was first described by Herman Boerhaave in 1724 following the sudden death of Baron Jan Gerrit van Wassernaer.^[1,2] The classic Mackler triad: vomiting, thoracic pain, and subcutaneous emphysema was present in 50% of the cases,^[3,4] but could be infrequent.^[5] The most common symptoms were vomiting, thoracic pain, abdominal pain, and dyspnoea, occurring solely or in

conjunction.^[6] The rupture was usually post-emetic.^[7] The patients mostly had history of alcohol consumption.^[5] The true pathophysiology of Boerhaave syndrome is ambiguous.^[8] A prompt rise in intra-oesophageal pressure along with failure of cricopharyngeal relaxation resulted in oesophageal rupture by an acute barotrauma. The predominance of distal 1/3rd left sided oesophageal rupture could be due to insufficient nearby connective tissues support, the anterior angulation of oesophagus at the left

diaphragmatic crus, the anatomical discontinuity due insertion of clasp- and sling fibres at distal oesophagus, traction of diaphragm and the pressure exerted by vomitus.^[9,10] In Boerhaave syndrome, mortality and morbidity could rise above 50%, and more than half of the patients were misdiagnosed.^[11] Standardized treatment guidelines have not been established due to the inconsistent clinical presentation.^[12] Early diagnosis was crucial for the good prognosis of the patients.^[13,14] The order of prevalence for differential- and misdiagnosis were perforated gastric- or duodenal ulcers, myocardial infarction, pulmonary embolism, dissection of aortic aneurysm, and pancreatitis.^[13,15] Although computer tomography (CT) is superior in terms of ease of availability, greater precision, and delivery of additional information, contrast-enhanced oesophagography with gastrografin or barium remains theoretically the imaging technique of choice, due to its high sensitivity, even for small defects.^[4,16] An additional endoscopy could reaffirm the diagnosis, identify the exact location and extent of the tear, and even facilitate treatment.^[17,18]

MATERIALS AND METHODS

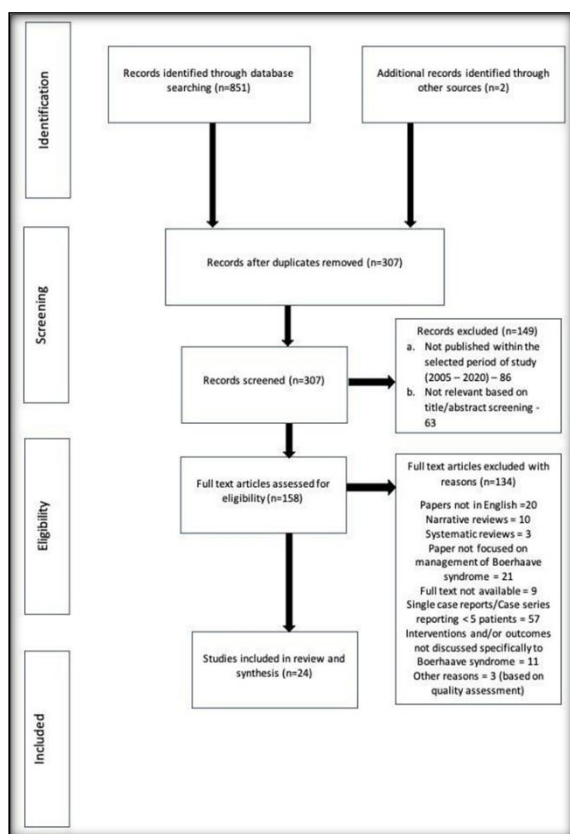


Figure 1: The electronic search strategy and study selection methods by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Checklist

A systematic search of published literature was undertaken between the 1st and 20th of November 2020 in two databases – PubMed and Science Direct. The electronic search strategy and study selection methods by the Preferred Reporting Items for

Systematic Reviews and Meta-Analyses (PRISMA) checklist were followed [Figure 1]. The articles were searched using the Medical Subject Headings (MeSH) terms “spontaneous oesophageal perforation”, “spontaneous oesophageal rupture” and “Boerhaave syndrome” separately, in combination with “management”, “intervention”, “treatment”, “conservative management”, “endoscopic (management/stenting/ligation/vacuum therapy)”, “endoscopy”, “minimally invasive management”, “minimally invasive surgery”, “minimally invasive procedure/procedures”, “surgery”, “open surgery”, “open surgical procedure/procedures”, “laparoscopic surgery”, “laparoscopic procedure/procedures” and “intercostal drainage”, using the Boolean operator AND. Original articles in English published between 2005 and 2020, that used one of the following three keywords in the title/abstract - “oesophageal perforation/tear/rupture”, “spontaneous oesophageal perforation/rupture/tear” or “Boerhaave syndrome” – were selected. Reviews, single case reports, case series reporting details of less than 5 patients, and those articles which had not discussed the management or outcomes specific to spontaneous oesophageal perforations have been excluded. The articles were independently reviewed by two reviewers at all stages of the review. The articles were subjected to quality assessment based on two criteria: description of aims and objectives and clear account of the management modalities/outcome. Eleven articles lacking this information were excluded to arrive at the final list.

RESULTS

In 24 selected articles, 20 dealt exclusively with the management and / or outcome of Boerhaave syndrome, along with 4 articles, which also dealt with oesophageal perforation of varying aetiology. All reviewed studies were hospital based, 21 articles utilized historical patient records, while 3 articles used accrual records. [Figure 2] shows a graphical representation of articles by year of publication. The findings are presented under the following subheadings: socio-demographic characteristics, clinical presentation, diagnosis, treatment modalities and outcome.

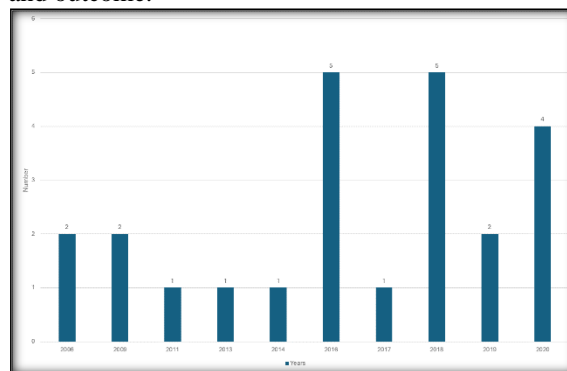


Figure 2: Graphical representation of articles by year of publication

Socio-demographic characteristics: Age composition was reported in all, except one article, whereas sex distribution was reported in 19 out of 24 articles, with a male predominance. The range of age spanned between 21 and 88 years. Mean/Median age ranged between 42.8 and 68 years.

Clinical presentation: Location of perforation was reported in 13 articles,^[6,16,19-29] with the largest proportion in lower/distal part of oesophagus.^[16,19-23,25-29] Perforation location according to oesophageal segments was reported in 4 articles, 3 articles reported perforation in thoracic segments,^[22,24,27] while 1 article reported distribution in thoracic- and abdominal segment.^[26] Perforation side was reported in 4 articles,^[6,20,28,29] 3 articles showed left-sided predominance,^[6,20,29] whereas 1 article reported right dominated distribution.^[28] A mean length of 3 cm or more was reported in 6 articles.^[6,16,19,24,26,27] Symptoms such as nausea, emesis, pain (chest, abdominal, or epigastric), hematemesis, dyspnoea, and fever were reported in 16 articles.^[4,6,17,19-21,23,24,26,28-33] The clinical findings were pleural effusion, mediastinal inflammation, atelectasis, systemic inflammatory response syndrome, emphysema, empyema, and sepsis.^[17,18,26-28,32,33] Postprandial emesis was reported to be a trigger factor.^[28,32] The history of alcohol consumption was reported in 6 articles,^[21,28,30-32,34] and 3 of them reported that alcohol-induced vomiting preceded the presentation.^[28,30,31]

Diagnosis: The time from onset of symptoms to diagnosis was mentioned in 10 articles.^[6,18,23,24,26,27,29,31,32,33] In 9 of these articles, patients were categorized into groups based on the time elapsed: less than 24 hours and greater than 24 hours from onset of symptoms to diagnosis.^[6,18,23,24,26,27,29,31,32] Among these 10 articles, two reported the mean time as 27±12 hours^[23] and 3.6 days^[33], respectively.

The time from onset of symptoms to treatment was reported in 12 articles.^[4,8,16,17,20,22,25,28,30,31,32,34] In 3 of these 12 articles, patients were categorized into groups based on the time elapsed between onset of symptoms and treatment: less than 24 hours, 24-48 hours, and more than 72 hours.^[4,22,28] One article out of these 12 articles categorized patients into groups on time elapsed as less than 12 hours and greater than 12 hours from symptom onset to treatment.^[34] Another article reported the number of patients who received treatment after 48 hours from the onset of symptoms.^[17] Among the 12 articles, 5 reported the median time from symptom onset to treatment, which were 8 hours^[20], 36 hours^[8], 120 hours^[32], and 123 hours^[25] in the respective articles. One article out of these five articles reported the median time for two different groups of patients who underwent different treatments: 16 hours for the surgically managed group and 72 hours for the conservatively managed group.^[31] The mean time to treatment from symptom onset were reported in two of the 12 articles. One

article reported a mean of 22±33 hours^[30], while another article reported the mean for two different groups of patients undergoing different treatments: 13.7 hours and 17.2 hours for Group A and Group B, respectively.^[16] CT was the preferred diagnostic tool in majority of articles,^[4,6,16,17-19,26-30,32,33,35,36] along with contrast oesophagography,^[6,16,29,32,33,36] and endoscopy.^[6,17,33,35,36] Oesophagography,^[26,35] and endoscopy,^[27,29,35] were also used exclusively for the assessment. In 3 articles reaffirmation of CT diagnosis was done endoscopically.^[18,19,35]

Management modalities

[Table 1] depicts management modalities. Endoscopic procedures,^[17,22,25,30,32,33] minimal invasive surgeries,^[4,20,23] and open surgical methods,^[6,8,27-29] were solely used in these articles. A combination of treatment modalities, including conservative treatment, was observed in 10 articles.^[16,18,19,21,24,26,31,34-36] The use of conservative or surgical approach was discussed in 6 articles,^[21,26,31,34,36] endoscopic or open surgical approach in 2 articles,^[24,35] minimal invasive and open surgical approach in 1 article,^[16] conservative, endoscopic and open surgical approach in 2 articles.^[18,19] In 1 article, endoscopic treatment with the two-tube method was described, without a clear definition of control treatment.^[33] [Table 2] depicts the additional interventions performed after failure of primary treatment. These included endoscopic procedures like clipping and re-stenting; surgical interventions including revisions and even esophagectomy.

Outcome: Length of hospital stay, post operative complications, number of additional interventions and morality (in hospital and 30 day) were considered. All the articles reported mortality and complications. However, only 20 articles reported the length of hospital stay. While 18 articles reported at least a single mortality, 21 articles reported at least one postoperative complication. The range of hospital stay was 2-11 days, 1-114 days and 3-224 days in the conservative, endoscopic, and minimal invasive groups respectively. In surgical group, the mean hospital stay was between 6 and 91 days. There was no common complication across all modalities. [Table 3] depicts complications in each selected article. [Figure 3, 4] shows the complication and number of additional interventions with mortality respectively. The conservative treatment modalities include interventions like placement of drainage and administration of antibiotics. The number of complications, not the type was reported in 1 article pertaining to conservative management.^[36] In endoscopic group, 8 articles reported that patients managed endoscopically had postoperative complications. Pleural empyema, mediastinitis, or mediastinal abscess were present in 23%. Sepsis, suture dehiscence, stenosis and stent migration were present in 15.38%, 11.11%, 10.25% and 6.83% respectively. A total of 46 additional interventions (39.3%) were carried out in 39 patients (33.3%). The main additional intervention required were operative

repair or decortication, followed by re-stenting. A sub-analysis of this group showed 52.17% underwent surgical interventions and 36.95% required additional endoscopic interventions. The minimally invasive procedures mainly included primary suture and only one patient underwent esophagectomy. ARDS/Pneumonia was developed in 45.71% of patients. Pleural effusion in 20 %, whereas pleural empyema, mediastinitis, and mediastinal abscess were found in 17.14% of patients. In 9 patients (25.7%), 10 additional interventions (28.57%) were performed, out of which 72.72% was the placement

of a drain. In the surgical group, fistula formation was seen in 8.18% of patients. Additional interventions including 22 surgical interventions, 10 endoscopic procedures, and 33 drain placements were deemed necessary resulting in 17.25% of the patients underwent treatment. The sub-analysis showed that 33.84% and 15.38% of the interventions were surgical and endoscopic respectively. Besides, almost half of the additional interventions (50.76%) were the placement of a drain.

Table 1: Types of treatment across various modalities.

Treatment modalities	Total no: of Patients/Papers	Authors	Treatment type	Length of hospital stay			
				days	range(days)	mean (days)	median(days)
Conservative management	39/7	Tellechea et al	NPO+ AB+ IVF-1, CTD-1	-	-	-	-
		Harikrishnan et al	CON-1	-	-	-	-
		Li et al	NPO+AB+ED-22	-	-	-	-
		Villach et al	CON-1	2	-	-	-
		Schweigert et al	CON-2	OVD	OVD	OVD	OVD
		Pezzetta et al	AB+ED-1	-	-	-	-
Endoscopic management	117/10	Abbas et al	NPO+AB+IVF-10	11	-	-	-
		Lázár et al	EC-1	OVD	OVD	OVD	OVD
		Tellechea et al	STP-2	-	-	-	-
		Glatz et al	ECSES-16	-	15-114	-	35.5
		Freeman et al	STP-19	-	5-38	9 SD 12	-
		Fischer et al	STP-5	-	34-70	48.1	43
		Wu et al	ECSES-19	-	-	-	-
		Yu et al	TTM – 18	-	-	38.2 SD 5.6	-
		Schweigert et al	STP-13	OVD	OVD	OVD	OVD
		Hauge et al	STP+DT+TSY-5, STP+DT+TY-3, STP + ED -6, STP-1		1-80	-	20
Minimally invasive management	35/4	Dickinson et al	STP-6, OVC-1, EC-1		5-42	-	9
		Veltri et al	LSY+THSU+GV - 7		7-28	14.71	12
		Okamoto et al	TSPR, LD-6; TSEYSR-1; THSU+ TSY+ LD-5		10-224	46.58	22
		Elliott et al	TSPR-8; TSY+TTD-2		3-26	-	7
Open surgical management	342/15	Nakano et al	TSPR & ED- 6		17-75	32	-
		Lázár et al	PR-7, EYLR-4, TTD-3	OVD	OVD	OVD	OVD
		Yan et al	PR-16, PRRMF- 72	-	19-65	-	26
		Han et al	PR-18, ED+DT-3	-	12-66	-	-
		Velasco et al	SD-3, EE-4, EY-1, TTD-1, PD-1	-	17-62	36.6	-
		Tellechea et al	PR-3, EY & CR-1, ED-4, FPN & ED- 2	-	-	-	-
		Harikrishnan et al	THS-8, LY+RTTY-6, LY+LTYY-1	Average length of stay-18 days			
		Li et al	PR-51				
		D'Journo et al	TPR-15	-	-	-	-
		Villach et al	PR-4, EY- 2	-	6-91	57.83	76
		Nakano et al	LPR + ED-5	-	11-68	29	-
		Schweigert et al	PR-6, SUD-14, EY-3	OVD	OVD	OVD	OVD
		Sudarshan et al	PR-14, SD-1, EY-3	-	17-33	-	26
		Dickinson et al	PRRMF-6, ERWF-6, ERWOF-1, ED-1	-	7-80	-	26.5
		Pezzetta et al	PR+FPN-5, PRRMF-18, PDF-1	-	-	-	-
Abbas et al	PR-34	13 days-not mentioned if average/mean/median					

[Table 1] Types of treatment across various modalities*- AB-Antibiotics, CON-Conservative, CR- Cardiac Resection, CTD-CT guided Drainage, DT-Debridement, EC-Endoscopic Clipping, ED- External drain, ECSES- Endoscopic covered self-expanding stents, EE- Esophageal Exclusion, ERWOF- Esophageal repair without flap, ERWF- Esophageal repair with flap ,EY- Esophagectomy, EYLR- Esophagectomy with late reconstruction, FPN-Fundoplication, GV-Gastric valve, IVF-Intravenous Fluids, LD-Lavage and Drainage, LPR-Laparotomic primary repair, LSY-Laparoscopy, LY-Laparotomy, NPO-Nil per oral, OVC-Ovesco Clip, OVD-Overlapping data, PD- Pleural drainage, PDF- Plasty with diaphragmatic flap, PRRMF- Primary repair with reinforced muscle flap, PR-Primary repair, RTTY- Right thoracotomy, SD- Suture & Drainage, STP-Stent placement, SUD- Surgical drainage, THS-Transhiatal Surgery, THSU- Transhiatal suture, TSEYSR- Thoracoscopic esophagectomy & secondary reconstruction, TSPR-Thoracoscopic primary suture, TSY- Thoracoscopy, TTD-T Tube Drainage, TTM- Two Tube Method (Trans-fistula drainage tube & 3-luminal jejunal feeding tube), TY- Thoracotomy. *All papers which have mentioned the additional interventions individually or in combination have been counted.

Table 2: Shows additional interventions required in each modality.

Primary treatment modalities*	Additional interventions required
Conservative management (1 Patient needed additional intervention)	Metallic stenting- 1 Patient ^[19] Not mentioned ^[31,36] 0 Patient ^[18,21,26,34]
Endoscopic management (39 patients needed additional interventions, total of 46 interventions) (24 Surgical interventions, 17 Endoscopic interventions, 5 Drainage)	Salvage intervention (VATS decortication & chest drain for empyema) & Re-Stenting- 1 Patient, Re- Stenting- 1 Patient: Total- 2 Patients ^[35] VATS with pleural debridement- 7 Patients, Open thoracotomy with decortication of the lungs- 2 Patients, Cervical mediastinotomy with insertion of mediastinal drainage-2 Patients: Total- 11 Patients ^[18] Re-stenting-5 Patients, Thoracotomy & debridement- 3 Patients, Thoracotomy with partial decortication of the lung- 1 Patient: Total- 9 Patients ^[22] Fundoplication & 2 nd CSES- 1 Patient, Muscular flap & 2 nd CSES- 1 Patient, Esophagectomy - 2 Patient, 2 nd CSES & Drainage-3 Patients, Drainage- 1 Patient: Total- 8 Patients ^[17] Transabdominal operative repair-2 Patients, Stent repositioning/replacement- 4 Patients: Total- 6 Patients ^[30] Bouginae- 1 Patient, Operation for wide drainage- 2 Patients: Total- 3 Patients ^[25]
Minimally invasive management (9 Patients needed additional interventions, total 10 interventions) (8 Drainage, 1 Dilatation, 2 Thoracocenteses)	Pleural drainage- 6 Patients, Stricture requiring dilatation- 1 Patient: Total- 7 Patients ^[23] Thoracocenteses with drainage- 1 Patient, Thoracocenteses-1 Patient: Total- 2 Patients ^[4]
Open surgical management (59 Patients needed additional interventions, total of 65 interventions) (22 Surgical interventions, 10 Endoscopic interventions, Drainage- 33)	Oversewing/primary suture after external drain-3 Patients, Endoscopic treatment-2 patients, 2 nd Fundoplication reinforcement, oversewing & endoscopy- 1 Patients: Total- 6 Patients ^[19] Salvage Therapy with endoscopic clipping & stenting- 1 Patient, stricture dilation- 1 Patient: Total- 2 Patients ^[35] Open thoracotomy with decortication of the lung- 6 patients: Total- 6 Patients ^[18] Oesophageal dilatation- 4 Patients: Total- 4 Patients ^[34] T- tube insertion & endoscopic stenting- 1 patient: Total- 1 Patient ^[24] Drainage- 29: Total- 29 Patients ^[6] Esophagectomy & jejunostomy- 1 Patient: Total- 1 Patient ^[21] Operative interventions- 9: Total-9 Patients ^[27] Surgical lavage and drainage-1 Patient: Total- 1 Patient ^[29]
[Table 2] Shows additional interventions required in each modality. *All papers which have mentioned the additional interventions individually or in combination have been counted. CSES- covered self-expanding stents, VATS- Video-assisted thoracic surgery	

Table 3: Shows complication across each modality.

Treatment modalities	Authors	Complications	Mortality
Conservative management	Tellechea et al	0	0
	Harikrishnan et al	0	0
	Li et al	FI-15	4
	Villach et al	PE-1	1
	Schweigert et al	0	0
	Pezzetta et al	0	0
	Abbas et al	US-5	0
Endoscopic management	Lázár et al	NM	0
	Tellechea et al	SM-3, PSS-1	1
	Glatz et al	SLD-8, PNE-1, MEA-1, PSS-7	2
	Freeman et al	SLD-2, SM-4, RF-1, ILS-1, DVT-2	0
	Fischer et al	PLE-4, SS-5, PSS-1	0
	Wu et al	FI-1, SS-5, CI-3	2
	Yu et al	NM	1
	Schweigert et al	SS-9, AKN-1, PLE-7, MEA-11	2
	Hauge et al	SLD-3, SM-1, PLE-4, BLE-2, PUEM-1, DIL-1, RF-1, PSS-3, SR-1	2
	Dickinson et al	FI-1	2
Minimally invasive management	Veltri et al	PE-2, FVR-1, CI-1	1
	Okamoto et al	ARDS+PNE-5, AF-1, PLE-3, SLD-2, MEA-2, WI-2	0
	Elliott et al	PLE-1, AF-5, PNE-5, ARDS-2, SLD-1, SuSTR-1, PE-5, MEI-1	1
	Nakano et al	PNE-3, ARDS-1, SLD-1	0
Open surgical management	Lázár et al	NM	1
	Yan et al	SLD-29	10
	Han et al	NM	0

study. ARDS/Pneumonia and pleural effusion were reported highest in the minimally invasive group. Atrial fibrillation, as a complication, was limited only to minimal invasive group patients, amounting to 17.14%. According to the literature, either anastomotic leakage,^[37] or iatrogenic pneumoperitoneum, resulting in sympathetic and parasympathetic imbalance, could cause a disturbance in cardiac autonomic function, leading to atrial fibrillation. Although the mortality was the lowest in this group in this study with 2 patients (5.7%), the patient collective (35 patients) in this group was the lowest. Atelectasis of one or both lungs in 1.75% as a post-operative complication was limited to open surgical group, this complication was mentioned in literature.^[39] The placement of a drain as a meticulous additional procedure was required in 4.27%, 9.6%, and 22.85% of patients in the endoscopic, surgical, and minimal invasive groups respectively.

The percentage of patients, who underwent additional surgical- and endoscopical procedures were higher in endoscopical group, when compared to open surgical group.

Based on the articles reviewed, time to treatment/diagnosis, the size of the lesion, and the results, we suggest a level 4 evidence-based treatment algorithm in [Figure 5].

CONCLUSION

A direct comparison was not possible in our study, because of the lack of literature comparing all the management modalities and unequal patient collective. The length of hospital stay was the shortest in the conservative group, here there was lack of true representation, whereas the range was maximum in minimal invasive group. If suture leakage was considered as direct evidence attributing to the success of the procedure, open surgical procedures had an upper hand over endoscopic procedures, followed by minimal invasive procedures. In our study atrial fibrillation and atelectasis were atypical complications seen in minimal invasive- and open surgical group respectively, they have been previously documented in the literature. The requirement of additional interventions in conservatively managed group was the lowest, but due to lack of true representation of events, this data could be unreliable. Among other groups, the open surgical grouped required the least far additional interventions. In terms of mortality, minimal invasive procedures were better than any modalities, but also had the lowest patient collective. With almost comparable patient collective between conservative and minimal invasive group, the latter showed clearly upper hand in terms of mortality and lack of fistula formation.

Limitation: The data reviewed were scarce and heterogenous. There were no prospective or retrospective study comparing all the above

modalities. There were a high probability of positive publication and selection bias, showing favourable results for chosen modalities. To overcome these issues, a prospective multicentric study involving all treatment modalities is recommended.

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