The influence of the 'golden 24-h rule' on the prognosis of oesophageal perforation in the modern era

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Abstract

Objectives: Rupture of the oesophagus is a surgical emergency with significant morbidity and mortality. We present our experience in managing such patients in a tertiary care cardiothoracic unit.

Methods: We conducted a retrospective clinical review of patients who were admitted following rupture of the oesophagus over a period of 6 years (2002–2008).

Results: In our unit, there were 27 admissions following isolated rupture of the oesophagus, of which 18 were males and nine were females. The median age was 65 years (range 22–87). Twenty-four (89%) presented with spontaneous perforations (Boerhaave’s syndrome) and three (11%) were iatrogenic. Primary surgical repair was done in 21 (77%) patients, a two-stage repair in 8% and conservative management in 16.6%. The mean hospital stay was 31 days (range 13–80 days). Overall, in-hospital mortality was five out of 27 patients (18.5%).

Conclusions: Our review confirms that an early diagnosis and management ('golden 24 h') are crucial for successful outcome in patients with rupture of the oesophagus. We reiterate the importance of critical care support, particularly in the early stages of management. For early detection, the primary and secondary care sectors need to be better educated.

Keywords: Rupture of the oesophagus; Golden 24 h

1. Introduction

Perforation of the oesophagus is a serious condition, which is associated with significantly high morbidity and mortality despite advances in diagnostics, surgery and critical care [1].

The aetiology of oesophageal perforations is commonly of two types: iatrogenic and spontaneous perforation (Boerhaave’s syndrome). Other less common causes include perforations secondary to malignancy or trauma [1].

Perforations of any cause are uncommon, making early diagnosis difficult, particularly in spontaneous perforations, which mimic more common serious intrathoracic conditions such as myocardial infarction. Outcome is also compounded by the fact that diagnosis of perforations commonly takes place at centres away from the ones they will be managed in which results in further delays in referral and initiation of appropriate management. This is important as several studies have found that late diagnosis (commonly >24 h) of oesophageal perforation is the main factor associated with poor outcome [2,3]. Despite a large number of studies, controversy still exists about many aspects of the management of oesophageal perforations, including the role of conservative management, primary repair, defunctioning of the oesophagus and methods of managing patients with delayed presentation, many of whom present critically ill, secondary to intrathoracic sepsis.

In recent times, the policy at our institution has been to favour primary surgical repair in all appropriate patients leaving conservative treatment for small contained leaks in systemically well patients or those unfit or too moribund for surgery. Clearly, however, each patient is assessed on a case-by-case basis. Here, we outline our experience over a 6-year period of the management of all confirmed oesophageal perforations referred to our institution.
2. Patients and methods

A retrospective review was conducted for all patients who were admitted to our institution with oesophageal perforation over a 6-year period between January 2002 and January 2008. Patients with oesophageal tears secondary to oesophageal or thoracic surgery were excluded. The hospital and theatre database as well as clinical notes were reviewed for information concerning clinical presentation, initial management, clinical course and mortality. Data gathered included aetiology, method and time to diagnosis, co-morbidities, patients’ clinical condition on admission and type of initial management (operative or non-operative). Data were also collected on critical care and management, postoperative progress and resumption of oral intake, postoperative imaging, inpatient complications, inpatient mortality and long-term outcome.

Early diagnosis was defined as confirmation of oesophageal perforation <24 h since presumed onset of symptoms. Late diagnosis was any time after 24 h. Major co-morbidities were defined as ischaemic heart disease, valvular heart disease, atrial fibrillation, diabetes, chronic obstructive pulmonary disease (COPD), renal failure or underlying malignancy. Gastro-oesophageal co-morbidity included oesophagitis, gastro-oesophageal reflux disease, peptic ulcer disease or a gastro-oesophageal malignancy. Surgical management consisted of primary repair or oesophagectomy and diversion.

Fisher’s exact test was used for all statistical analyses. Statistical analyses were conducted using MedCalc, MedCalc Software, Belgium.

3. Results

3.1. Patient demographics

A total of 27 patients with oesophageal perforation were identified from our database. There were 18 males and nine females with a median age of 65 (range 22—87) years. Seven patients had major co-morbidities (mainly cardiovascular), seven patients had gastro-oesophageal co-morbidities while two patients had both (Table 1). Three patients had a history of heavy alcohol use during their perforation (all spontaneous).

3.2. Presentation and diagnosis

Of the 27 patients, 24 (89%) presented with spontaneous perforations (Boerhaave’s syndrome) and three (11%) were iatrogenic. Two of the iatrogenic perforations were secondary to gastroscopy and one was secondary to nasogastric tube (NG) insertion. All the perforations were situated in the thoracic oesophagus. Three of the patients with spontaneous perforations presented with chest pain and surgical emphysema. All except one patient had chest, back or epigastric pain and only two patients had no history of vomiting. Table 2 shows details of the different clinical presentations. Of the iatrogenic perforations secondary to gastroscopies, the first patient was diagnosed after he developed post-procedure chest pain, while the other patient developed thoracic back pain.
Developed sepsis following NG tube insertion – CT revealed perforation

Table 3
Reasons for delay in diagnosis.

Patient presented late 3
Initial misdiagnosis
- Pulmonary embolism 1
- Gastritis 1
- Upper GI bleed 1
- Pneumothorax 1
Equivocal findings on CT and contrast swallow 1
Developed sepsis following NG tube insertion – CT revealed perforation 1
Information not available 1

Time from onset of symptoms to diagnosis of oesophageal perforation was early (<24 h) in 17 (63%) patients and late (≥24 h) in the remaining 10 (37%) patients. The two most common reasons for a delay in diagnosis were initial misdiagnosis and late presentation of patients (see Table 3). The patient whose perforation was secondary to NG tube insertion (for management of another medical problem) was only diagnosed after the patient became septic and a search for the source of sepsis identified the perforation. Details of X-rays on presentation at the referral hospital were available for 20 of the patients. Most X-rays had more than one sign, the most common being a unilateral pleural effusion and/or a pneumothorax. Eight patients X-rays showed evidence of a pneumomediastinum and two patients had radiological surgical emphysema. Definitive diagnosis of oesophageal perforation was made with a computed tomography (CT) of the thorax, a soluble contrast swallow or both. Twenty patients had a CT scan; nine of these patients also required a contrast swallow to confirm the perforation. One patient required a gastroscopy to confirm the diagnosis because CT and contrast swallow results were equivocal. Seven perforations were diagnosed with contrast swallow alone; five of these showed signs of a pneumomediastinum on initial chest X-ray.

Twenty-two of the 27 perforations were located in the distal one-third of the oesophagus, 11 at or just above the gastro-oesophageal junction. The remaining five were in the middle third of the oesophagus. All three iatrogenic perforations were located on the right side, while 12 out of 24 (50%) of spontaneous perforations were on the left side.

3.3. Management on admission

On admission to our unit from their referring hospital, almost all the patients had intercostal drains in situ and were on broad-spectrum antibiotics on admission. Following initial resuscitation, further treatment consisted of placing patients nil-by-mouth, targeted antimicrobial therapy and drainage of any pleural collections.

3.4. Primary repair

Twenty-three patients were taken to theatre and assessed for suitability for primary repair of their perforation. Eighteen of the patients had a flexible oesophagoscopy under general anaesthesia to confirm which side the perforation was on prior to making the incision. If an oesophagoscopy was not done then the posterolateral thoracotomy approach was used on the side that the perforation was thought to be according to preoperative imaging. Thirteen patients were approached via a right thoracotomy, while 10 were approached from the left side. In 21 patients, a primary repair of the perforation was attempted. Repair of the perforation consisted of a two-layer interrupted suturing of the mucosal and muscularis layers, with absorbable sutures after debridement and excision of necrotic and inflamed tissue. Where possible, this was reinforced by a pedicled intercostal muscle flap sutured over the repaired defect.

3.5. Oesophagectomy and diversion

Primary repair was not attempted in two of the 23 surgical cases due to intrathoracic sepsis. In both cases, a subtotal oesophagectomy was performed removing the necrotic and severely inflamed tissue either side of the perforation along with a thorough washout. Once the patients were stable, they were offered a reconstruction of their oesophagus using a gastric interposition. One patient had this done as inpatient at day 53 and was discharged 20 days after the reconstruction, while the other had it at day 18 and was discharged 6 days later.

3.6. Non-operative management

Non-operative management was used in four patients. Two were patients with small contained leaks, who showed no signs of a systemic inflammatory response or sepsis despite both presenting more than 48 h after the onset of their symptoms. One was a patient whose perforation was secondary to NG tube insertion in another institution. The patient was deemed to have a high anaesthetic risk and managed conservatively. The fourth patient was diagnosed early in the referring institution but was referred late after a trial of conservative management with parenteral nutrition. On arrival in our institution, the patient showed signs of sepsis and an abscess cavity was seen on repeat CT. It was considered that the patient would not benefit from an immediate operation given her state and was managed conservatively.

Fig. 1 shows the time to diagnosis and consequent mode of management.

Fig. 1. Time to diagnosis and mode of management.
3.7. Postoperative progress

The progress of perforations was monitored using repeated imaging, usually using water-soluble contrast swallows; however, some patients required CT scanning. In two cases, oesophageal patency was assessed using oral methylene blue dye, as the patient needed to stay in the intensive care unit. Intercostal and mediastinal drains were monitored for drainage of the dye, which would have suggested continued perforation. Where imaging showed no or minimal leakage at the perforation site, patients were allowed to drink and then eat if that was tolerated. Artificial feeding was stopped once the patient had tolerated a soft diet. Where imaging showed unsatisfactory healing of a perforation, patients remained nil-by-mouth and imaging was repeated at regular intervals until the perforation was sealed. The median time to first imaging was 8 days from the time of admission, being longer in patients who had a prolonged period of assisted ventilation. Thirteen patients had healed perforations at their first imaging. The rest (14 patients) required a median of two further swallows or scans to confirm the perforation had healed. The mean time from onset of perforation to commencement of food was 20 days on the primary repair group and 43 days in the patients managed conservatively.

Eight of the surviving patients developed non-fatal complications during their stay. Four patients developed chest infections with one patient progressing onto acute respiratory syndrome but surviving. Other complications included a pericardial effusion that required drainage, a gastric bleed, transient renal failure requiring dialysis and two wound infections.

Seven patients who underwent primary repair had persistent leaks on water-soluble contrast imaging, which required prolonged periods of parenteral or jejunal feeding. In one case, this progressed to form a loculated pleural collection and para-oesophageal abscess. Initial attempts at percutaneous drainage of the collection failed and this patient required a thoractomy to drain and debride the pleural and mediastinal collections without the need for oesophageal diversion.

3.8. Mortality

A total of five patients died during their hospital stay, making the overall in-hospital mortality 18.5%. Three patients died of multi-organ failure secondary to sepsis and two patients had cardiac arrests. One of the cardiac arrests was in a patient who was nearing discharge having recovered well from a primary repair 6 weeks prior to her death. The mean time to death was 39 days (29–62 days). In four out of the five non-survivors, there was a >24-h delay in diagnosis. The mortality rate among patients with a delayed diagnosis was 44% compared to 5.2% among those who were diagnosed in <24 h \( (p = 0.047) \). Patients presenting early (<24 h), who underwent surgical management, had the highest survival rate (88%), while survival in the conservative group was 75%. The number of patients with cardio-respiratory co-morbidities was lower in the patients who did not survive. Three out of the five patients who died did have a history of peptic ulcer or reflux disease compared to six out of 21 survivors, but this difference was not significant \( (p = 0.8) \).

3.9. Follow-up

Twenty patients were followed up for a median of 6 months following discharge. During follow-up, two patients complained of general fatigue and exertional dyspnoea, while two complained of gastro-oesophageal reflux, which was treated medically. Four patients complained of dysphagia, one of which required further treatment. Two of the 22 survivors died at 12 and 40 months post-discharge. The remaining 20 have remained alive a median of 36 months post-discharge (11–98 months).

4. Discussion

The optimal management of oesophageal perforation, in particular, spontaneous ones, remains a difficult challenge. To our knowledge, this series has the highest frequency of management of spontaneous perforations (more than four per year) of any recent study. Accurate diagnosis is made difficult as oesophageal perforation often presents with symptoms that mimic more serious conditions \[4\]. Thoracic oesophageal perforations (as all the ones in our series were) have always been the most difficult to manage and have poorer outcomes compared to cervical or intra-abdominal perforations due to the greater systemic complications resulting from mediastinal and pleural contamination \[1\].

A high index of suspicion is required to avoid delays in diagnosing perforations, in particular, spontaneous ones. Clinical presentation of spontaneous perforations does vary, as can be seen by our patients, with the most common symptoms being pain and vomiting. As has been found in other studies \[6,7\], Mackler’s triad of chest pain, vomiting...
and surgical emphysema is only present in a minority of patients (three in our series) and thus should not be solely relied upon to suspect oesophageal perforation. Delay in diagnosis has been shown to be a major contributor in several series [2,3]. This may represent the fact that a longer period without treatment following a perforation means further mediastinal contamination, inflammation and the subsequent development of systemic sepsis. Some groups, however, have found no difference in outcomes based on the time to diagnosis or treatment. It has been suggested that this may reflect more aggressive disease presenting early and better tolerated/non-dispersed collections presenting late, thus producing a paradoxical selection bias [5,6]. In our series, we had both stable and critically ill patients in both the early and late group and the mortality rate in our series was considerably higher in the late diagnosis group; however, we must admit that the numbers are small.

This difference is despite our institution being one of the biggest cardiothoracic critical care units in Europe with 38 beds capable of continuous invasive ventilatory and circulatory support and monitoring. This capacity means all patients transferred to our care as emergencies can be cared for immediately on the critical unit with a low threshold for increasing organ support, particularly in conditions such as oesophageal perforation that have potential for dramatic deterioration.

The presentation in our group of patients was quite atypical as only 50% of tears in the spontaneous rupture group were left sided, where Boerhaave in 1724 describes tears to be typically left sided in more than 85% of cases. This is probably due to pre-existing oesophageal pathology in 6/24 (25%) of spontaneous rupture cases, which is different from the typical definition of Boerhaave described many years ago for oesophageal perforation occurring in an otherwise normal oesophagus. We hence preferred to title this group as spontaneous (rather than Boerhaave’s) oesophageal perforation.

Clearly, early diagnosis would be favourable in any emergency; however, we feel this should not determine the mode of management and decisions should be based on clinical and radiological findings rather than an arbitrary point in time. Despite moves towards a more selective and individualised approach to the management of thoracic oesophageal perforations, the mainstay of treatment for the majority of patients still remains surgical. This is particularly true for spontaneous perforations (which the majority of our patients were), where there is more likely to be mediastinal and/or pleural contamination with an element of necrosis and severe oesophageal inflammation. Where appropriate, we aim to operate with the intention of a reinforced primary repair.

In addition to allowing drainage of infection and debridement of necrotic and inflamed tissue, primary repair allows full exposure of the mucosal defect and approximation of the mucosal and submucosal edges, resulting in optimal conditions for adequate healing. Results from several series [5,6,8,9,10], focussing mainly on spontaneous perforations, have found that primary repair offers the best chance of survival, regardless of presentation time. It is considered to be the best treatment option for uncontained thoracic perforations of an otherwise healthy oesophagus with other treatment modalities being the exception and reserved for select cases.

Differing opinions exist on the optimal surgical management of the non-viable oesophagus and it is difficult to interpret much from the results of our two cases. Both our patients underwent an oesophagectomy and diversion with delayed reconstruction with good long-term results. A recent review has shown oesophagectomy to be superior with regard to survival rates for the management of an unsalvageable oesophagus compared to other methods such as exclusion and diversion or drainage [1].

Non-operative management of thoracic perforations should be restricted to two groups of patients; those contained within the mediastinum with minimal signs of clinical sepsis and those in patients who are too unstable to be operated on. Unfortunately, we have no experience in oesophageal stenting, which can be useful in the unstable group or those with small tears as found in iatrogenic perforations. We advocate that spontaneous rupture group should be managed surgically due to a higher risk of mediastinal contamination. In a study done by Teh and his colleagues, 33 out of 34 oesophageal perforations who presented to their hospital had some sort of surgical management regardless of the time of the presentation [11]. The few series that have favoured non-operative management have tended to have a greater proportion of iatrogenic or cervical perforations, which have better outcomes [12]. Where wider criteria have been used to justify non-operative management in spontaneous perforations, many patients have required subsequent surgical intervention with greater rates of complication and inpatient stay [6,13].

In our case, two of the patients had presented 48 h after the onset of the symptoms and had localised perforations with no radiological evidence of pleural involvement and no evidence of sepsis. Non-operative management of this group of patients is advocated by most authors, including those who favour a more aggressive surgical approach. Only two patients with full-thickness perforations and mediastinal and pleural contamination were not taken to theatre. One patient was deemed unfit for surgery, while the other was initially managed conservatively at another institution before arriving at our hospital in a state of sepsis and with a large abscess on CT scan. The patient’s sepsis was treated aggressively with a possible view to operating if they did not improve; however, they did and were eventually discharged home. Recently, it has been argued that even this group of patients who present late should be managed by surgical intervention, which carries a lower mortality than conservative management [14].

The overall mortality rate in our group of patients was 18.5%, which falls to 17.4% when we only consider the surgically managed patients. This is comparable to most series, especially as more than 90% of this group had spontaneous perforations, which tend to have worse outcomes than iatrogenic tears. Four of the five who died were managed with primary repairs. One of the surgically managed patients presented early and three presented late, which reflects our policy of basing treatment solely on the clinical picture and not when the patient presents. Although we had a surprisingly high leak rate compared to other series [7,15]
following the primary repairs, most of these leaks were small and, apart from one case, did not require re-operation and had no bearing on mortality.

An initial chest X-ray, usually done in the emergency department, is an important tool in raising suspicion for oesophageal perforation, as most X-rays tend to be abnormal. Only one patient in our series had a normal X-ray on presentation.

Contrast oesopagography with water-soluble contrast is the investigation of choice to confirm perforations and has a sensitivity of around 90% in the thoracic oesophagus. However, because many patients present with symptoms that may mimic other intrathoracic or upper gastrointestinal pathologies, many patients undergo CT scans to evaluate the chest and upper abdomen. Seventy percent of our patients underwent CT scans as their initial investigation following presentation, with 50% of them going on to also have contrast oesophagographies. Only seven patients had contrast oesopagography alone, five of whom presented with classical symptoms and/or plain X-ray signs, suggesting there was a high suspicion of oesophageal perforation at the time. Interestingly, six of these seven patients were managed prior to 2003 when one could assume CT was slightly less readily available in emergency situations than in more recent times.

With increasing accessibility, CT scans may become the first-line investigation of patients who present with a history of a suspected perforation. CT also has the added advantage of being able to characterise any associated mediastinal or pleural contamination, which will help in management planning. As many patients require separate contrast oesophagographies to confirm and characterise oesophageal perforations, some groups have advocated a novel technique of simultaneous CT oesopagography in suspected perforations to speed up diagnosis and institute treatment in this group of patients. We have started using CT oesopagography in our institution in cases where we need confirmation of the site and extent of perforation. However, the use of this modality in a peripheral hospital would rely on there being a high suspicion of perforation in the first place.

Limited data are available on the long-term follow-up of patients who are successfully managed for oesophageal perforations. Two series followed a heterogeneous group of patients an average of 3.7 and 12.5 years with a late survival rate of 88% and 64%, respectively, which is comparable to our survival rate of 90% at 3 years. They found, as we have, that the most common follow-up problem was dysphagia, which in some cases required dilatation; however, long-term problems only affected around 10% of patients. Nevertheless, in a study by D’Journo and his colleagues, 85% of asymptomatic patients with repaired ruptured oesophagus followed up for a median period of 13 months had oesophageal motility disorders on manometry. Although it may be too early to conclude, the outlook for patients who survive the initial trauma of oesophageal perforation is generally positive.

Our series included a surprisingly high proportion of spontaneous perforations despite iatrogenic perforations being the commonest aetiology in the UK. The hospitals to which we provide a tertiary thoracic service include a mixture of smaller hospitals and large teaching hospitals with busy oesophagogastric teams. Informal enquiries do suggest that the larger hospitals usually, but not always, manage their own perforations. Smaller hospitals, however, tend to refer all cases to larger hospitals including ours. It may be that iatrogenic perforations are more likely to be managed ‘in-house’ and other types of perforations referred on. This does highlight the potential need for streamlining the provision of an emergency oesophageal service. Although perforations will increase in number due to increased use of endoscopy, it is still a relatively uncommon condition. We feel, as others have, that providing a structured service in each region may be advisable to ensure that dedicated experienced thoracic and/or oesophagogastric teams are available to provide an optimum service that could potentially improve the outcomes further for this serious condition.

5. Conclusions

The ‘golden early 24-h rule’ for diagnosis still applies in the modern era as early diagnosis and management positively influences outcome. Our data support the use of operative intervention with the intention of primary repair as the mainstay of treatment for the management of oesophageal perforation with conservative management being the exception to the rule. We reiterate the importance of critical care support, particularly in the early stages of management. Further education in secondary care and a high index of suspicion is required to increase early detection.

References

Appendix A. Conference discussion

Dr T. Treasure (London, United Kingdom): Is the problem that these patients have all come to you late and the delays have been in the hands of others?

Dr Fontaine: In the referring hospital, yes.

Dr Treasure: I think you probably need to set the scene by explaining what proportion of patients with a ruptured oesophagus ever come to a thoracic surgeon, because you may be picking up worse end of the distribution and that the sickest patients are seen by thoracic surgeons and the usual management is in the hands of general surgeons in the UK who may be doing a perfectly good job. In terms of how you present this information, we need to know whether this is the standard of care or whether thoracic referral is the last resort for the sickest patients are seen by thoracic surgeons and the usual management is in the hands of general surgeons in the UK who may be doing a perfectly good job.

Dr Fontaine: There are other institutions in the region carrying out Upper GI surgery on an elective basis but not emergency work. So, all of these emergencies do actually come to our unit.

Dr Treasure: This has been a problem for all the time I have known — the neglected ruptured oesophagus. Do you think the problem is getting worse?

Dr Fontaine: It probably is getting worse. I think the delay in diagnosis may be a reflection of the way medical services are organised or a product of training issues.

Dr A. Lerut (Leuven, Belgium): There are a number of data in the literature that contradict the idea that it is the delay which is really causing the mortality and that perhaps mortality is more related to the comorbidity. I couldn’t find, in your slides or in the abstract, whether you made the correlation with the comorbidities of those patients who died. Did you make that correlation?

Dr Fontaine: The main factor that we found which was implicated in the death of patients who were diagnosed late was significant co-morbidity. The main factor that we found which was implicated in the death of patients who were diagnosed late was significant co-morbidity.

Dr Lerut: A number of those patients can be elderly patients and they have a lot of co-morbidities, and, in fact, you say that many of them are truly in sepsis.

Dr Fontaine: Yes.

Dr Lerut: As a matter of fact, for that particular reason there is an increasing tendency to treat those patients conservatively, because by doing the surgery, you only aggravate the immediate sepsis. Therefore in our own experience, we now rarely treat Boerhaave’s syndrome surgically. Most of them are treated conservatively.

Dr Fontaine: As you rightly say, the patients with significant co-morbidity are managed conservatively, and we have taken on more recently an aggressive conservative management at times which is not primary repair, but involves a VATS procedure to clean out the thoracic cavity, do perforations along the oesophagus, and put large drains along the oesophagus.

Dr Lerut: CT-guided.

Dr Fontaine: So aggressive conservative management as well.

Dr Lerut: Do you have any experience with placing stents?

Dr Fontaine: I know the Americans are quite big on using stents in ruptures, but we haven’t actually placed stents for acute perforations. We have on a couple of occasions in oesophageal cancer perforations, but not for Boerhaave’s syndrome.

Dr Li (Xian, China): I’m interested in your follow-up results. Did you find any cases of stenosis of the oesophagus after your repair?

Dr Fontaine: Well, 4 patients had dysphagia and they probably did have some partial stenosis, and one of those was significant enough to require another procedure.

Dr Li: Because you reported on the patients complaining of dysphagia after repair of the oesophagus.

Dr Fontaine: We did not study all of these patients endoscopically afterwards, so it would be difficult to tell.