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Management Strategies in Iatrogenic Tracheal Injuries: A Literature Review and Case Series

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Abstract

Introduction: Iatrogenic injury to the tracheobronchial tree during intubation is a rare but life-threatening event. Since 1995 there have been isolated case reports of the use of Extracorporeal Membrane Oxygenation Therapy (ECMO) as an adjunct in the treatment of tracheal injuries.

Objective: Here we present a literature review of the management strategies employed in iatrogenic tracheal injury and the first case series using ECMO as an adjunct in its management.

Methods: We searched MEDLINE and EMBASE databases using the Healthcare Databases Advanced Search (HDAS) through the National Institute for Health and Care Excellence (NICE). We limited our search to articles after 1995, when ECMO was first introduced as an adjunct, and to articles written in the English language. We also searched the same databases separately for articles evidencing the use of ECMO in the treatment of iatrogenic tracheal injury.

Results: More recently conservative approach has been favoured over operative intervention unless the injury is observed intraoperatively and repaired primarily. Evidence for stenting is limited and of poor quality. No studies have investigated the use of prophylactic antibiotics. Numerous prevention strategies have resulted in a reduction in the incidence of iatrogenic tracheal injury. ECMO has been utilised successfully in the last 4 years in numerous institutions.

Conclusions: We have demonstrated in our case reports and the others reviewed that ECMO can be useful in patients with ventilatory difficulty either caused by concurrent respiratory pathology, direct sequelae relating to the injury or in the immediate post-operative phase.

Keywords: Extracorporeal Membrane Oxygenation Therapy (ECMO); Iatrogenic Injury

Introduction

Iatrogenic injury to the tracheobronchial tree during intubation is a rare but life threatening event. The incidence is estimated to be in the region of 0.00013% to 0.01% [1] and seems to occur most commonly in females between the ages of 45 and 75 [2]. Orotracheal intubation in the emergency situation is the most common mechanism of injury; caused by the endotracheal tube or adjunct lacerating the airway on insertion and by over inflation of the cuff [2,3]. In addition it can also occur during both surgical and Seldinger tracheostomy techniques. The injury is classically longitudinal, in the posterior membranous part of the trachea. Usually it located centrally or laterally and within 2.5 cm of the carina in the lower two thirds of the trachea [4]. On occasion they can extend down to right main bronchus [3,5,6].

The management options following injury are broadly categorised in to either conservative or surgical options. Evidence regarding which strategy is more efficacious with a given injury's extent or location is limited. Iatrogenic injuries to the tracheobronchial tree are associated with a high mortality of around 17% [7]. There is a consensus that these patients should be promptly transferred to a specialist Thoracic Surgery Department for definitive management [1]. Since 1995 there have been isolated case reports of the use of Extracorporeal Membrane Oxygenation Therapy (ECMO) as an adjunct in the treatment of tracheal injuries [2].

ECMO supplies temporary circulatory support for patients with pulmonary or cardiac failure [7]. Venous blood is drained through a cannula and oxygenated via an artificial lung before being returned to the patient [8]. There are two main types [8,9]:

1. **Veno-Arterial (VA):** Used in cardiac failure and after heart transplantation. Blood is returned to the circulation after the heart i.e. aorta. (ECMO is used as both mechanical pump and oxygenator)
2. **Veno-Venous (VV):** Used in respiratory failure. Blood is returned before entry in to the right side of the heart. (Native heart is mechanical pump and ECMO only used to oxygenate blood).

When using ECMO in tracheal injury the choice between the type employed depends on the patients cardiac function or if there is any concurrent cardiac pathology.

The decision to intervene surgically or treat iatrogenic tracheal injury conservatively is not clear cut. There are other approaches such as stenting that can and have been employed. Prophylactic antibiotics are considered central to management the evidence for this practice is lacking.

Here we present a literature review of the management strategies employed in iatrogenic tracheal injury and the first case series using ECMO as an adjunct in its management.

Methods

We searched MEDLINE and EMBASE databases using the Healthcare Databases Advanced Search (HDAS) through the National Institute for Health and Care Excellence (NICE). In EMBASE our search strategy used the medical subject headings; Trachea or "Respiratory System", Physical Disease by Etiology, Pathogenesis or Injury and Iatrogenic Disease and Respiratory Tract Intubation or Endotracheal Intubation. In MEDLINE we mirrored this with; Respiratory System or Trachea or Endotracheal Anaesthesia, Disease Attributes or Iatrogenic Disease and Airway Management or Endotracheal Intubation. We limited our search to articles after 1995, when ECMO was first introduced as an adjunct, and to articles written in the English language. This search found 94 relevant articles to our subject of interest. After excluding articles that were not concerned with the management of iatrogenic injuries we were left with 43 results.

We also searched the same databases separately for articles evidencing the use of ECMO in the treatment of iatrogenic tracheal injury. For Medline we used the terms; Extracorporeal Membrane Oxygenation or ECMO, Trachea and Wounds and Injuries. In EMBASE we used Extracorporeal Circulation or Extracorporeal Oxygenation, Trachea or Respiratory System and Wound.

Results

The different management strategies in these articles involved supportive treatment, stent insertion or surgical intervention.

Surgical vs conservative treatment

Lee., *et al*. presented a series of patients that they had treated with Iatrogenic Tracheobronchial Rupture over a 5 year period and concurrently compared mortality rates in the literature between surgical and conservative approaches. They found no difference in the mortality rates between each approach. They did not explain their search strategy in their methods for this meta-analysis, which is presented as an after-thought in their article, and as such it is difficult to validate their findings [5].

A team from Iran presented a series of 12 of their patients with iatrogenic tracheal membrane ruptures. They treated 8 conservatively and 4 surgically but do not explain the decision making in triaging patients in to each treatment strategy. This would have been useful as all of their patients survived until discharge [10].

There are authors however who have decided on a conservative or surgical option based on a number of factors. Romero-Legro., *et al.* treated their patient conservatively due to two factors relating to the injury; the location (posterior and 1 cm above carina) and the length (3-4 cm) [11]. Paksu., *et al*. treated a 14 year old boy and opted for conservative management as the injury was small and there was no haemodynamic compromise. Unfortunately they do not detail the size of this injury exactly [12]. Two much smaller children, one at birth and the other at 15 months old, were successfully treated for iatrogenic tracheal injury through conservative means by Cunningham., *et al.* Their decision was based on the presence of a number of significant comorbid conditions in the first child and conversely a lack of sequelae in the second. This would suggest that there is a middle ground where surgery would be more likely to be employed but they do no state this in their article [13].

In a case series presenting 12 tracheobronchial iatrogenic injuries a team led by Jougon in France created an algorithm for conservative or surgical intervention based on their own experiences. They advocate surgical intervention in all patients who are undergoing thoracic procedures where the tear is diagnosed immediately, where there are immediate symptoms, when the tear is greater than 4 cm in length and when the patient does not stabilise with conservative measures [14]. Carbognani., *et al.* advocate a reduced threshold and they repair injuries over 2 cm in length [15]. Since these studies there have been case reports of successful conservative treatment in patients with injuries greater than 4 cm in length. Fong., *et al*. treated two patients successfully with conservative measures one of which had a 5 cm tear [16].

In perhaps the largest prospective study of tracheobronchial rupture, Conti., *et al.* developed an algorithm to treat patients over a 12 year period. 30 patients entered the study and were treated conservatively if they were judged unfit for an operation or if they did not require mechanical ventilation they underwent bridging. Those who required mechanical ventilation and were fit for intervention were operated on. They note that the decision regarding fitness to surgery was multidisciplinary but they do not attempt to quantify where the boundaries lie. Only two of their 30 patients underwent surgery and both ultimately died. 4 of the 13 patients who underwent bridging unfortunately passed away but none of the conservative treatment arm, those off mechanical ventilation, all survived. There is an obvious bias here in that the patients undergoing surgery will have had a poorer baseline, in that they required mechanical ventilation, and as such will have a higher morbidity and mortality to the conservative group. The authors make an important conclusion that patients whose injury was sustained during emergency procedures have a much higher mortality rate compared to those who were injured during elective cases [6].

A similar algorithm was employed by Schneider., *et al.* and opted for surgery only when mechanical ventilation was not possible, subcutaneous or mediastinal lymphadenopathy was progressive and when there was an open perforation in to the pleural cavity. This resulted in 62% of their 29 cases being treated surgically and the rest conservatively. All the conservative group made a full recovery and there were 3 deaths in the surgical group from sepsis and progressive cerebral insult, these results are open to the same bias as discussed in the previous paragraph [4]. In a retrospective review of both traumatic and iatrogenic tracheal injuries Gomez-Caro., *et al.* deduce that conservative management is effective in membranous injuries but cartilaginous defects require surgical intervention. They also intervene if progressive emphysema or difficulty with mechanical ventilation is encountered [17].

The decision regarding the surgical approach for patients is discussed by Costa., *et al*. and Carbognani., *et al*. who advocate cervical incisions for upper and middle tracheal injuries and a right thoracotomy for distal lesions. Despite recommending these approaches Carbognani reported a vocal cord palsy rate of 33% in their thoracotomy group. Costa., et al. describe repairing middle third injuries through a cervical incision with a video assisted technique in a move to be minimally invasive in these critically ill patients. They do not comment however on the results of this technique in the two cases they present [15,18].

Welter., *et al.* describe an intra-luminal suture technique which they used with somewhat limited success. In one of their four patients they were unable to suture intraluminally and it was repaired via a thoracotomy, in another patient their repair ruptured after 12 days at which point it was treated conservatively [19]. In a published response to this article, Benhamed., *et al*. point to the effectiveness of their own preference of conservative treatment even in lacerations of up to 9 cm in length and question the need for suturing the defect at all [20].

Surgeons in Australia treated a wide iatrogenic tracheal injury with a bovine pericardial patch. They chose this novel method as the patient was unstable and they felt that prolonging the operative procedure with a muscular flap would not be to the patient's benefit. The patient had a protracted recovery due to associated medical issues but the repair succeeded [21]. Conversely, in an elective case, a 67 year old lady was successfully treated conservatively for a 4 cm long transmural rupture indicating that the size of the lesion should not necessarily mandate operative intervention [22].

Stenting

Stents provide another option for the management of iatrogenic injury to the Trachea. Tazi-²³(23) Mazalek., *et al.* published their experiences over a 10 year period of employing endotracheal stents to manage such pathology. Stents were placed in patients without a Tracheoesophageal Fistula, who required Mechanical Ventilation with an injury sited in the lower half of the trachea. In more proximal injuries a cuffed endotracheal tube was inserted distally and healing was monitored with surveillance bronchoscopy. Stents were removed when mechanical ventilation was no longer required. Just 7 of their patients had stents inserted and as a result it is difficult to come to any concrete conclusions despite this being the largest series on the topic. 5 of the 7 patients demonstrated complete healing within 4 weeks of presentation but 2 patients died (29%) [23].

A team from Virginia (USA) have also employed tracheal stents (polyurethane-covered nitonol) in the management of tracheal injury. Two of the four patients in their series experienced iatrogenic injuries. These patients were thought not fit to undergo surgical repair, due to the severity of their respiratory failure, and as such stents were placed under bronchoscopic guidance. After 6 weeks of supportive care the stents were removed to reveal a healed trachea in both cases [24].

There are published reports of stents being left in much longer. Yanamoto., *et al.* treated an 86 year old lady with a large tracheal tear with a Y-shaped Silicon stent which was left in situ for four months before removal. The decision for stenting was taken as the patient was deemed a poor surgical candidate due to their "compromised cardiopulmonary function" [25]. Marchese., *et al.* published a case where they left the tracheal stent in for 1 year before removal. In this case the patient was in a thoracic theatre when the iatrogenic injury occurred but the reasoning behind the decision for stent placement as opposed to conservative management or surgical repair is not discussed in the article [26].

Other adjuncts

In a letter to the editor of the Journal Minerva Anestesiologica, Umotoglu., *et al.* present a case where they employed an ET View Tracheoscopic Ventilation Tube (ET View TVT) as an adjunct in their management. This is a standard endotracheal (ET) tube which has been adapted to include a camera as well as a light source and irrigation port. In their presented case the ET tube could not be "rail-roaded" over a flexible endoscope and a ET View TVT was used to visualise tube placement and for confirmation of repair at the conclusion of the surgical procedure [27].

Antibiotics

Throughout case series and case reports there is often a mention that antibiotics were used as prophylaxis. This is based on opinion and no studies comment on successes or failures in cases where antibiotics are prescribed or not in the injury healing.

Prevention

Anaesthetists from Germany propose that the use of a balloon in the paediatric airway subjects the patient to a potential increased risk of tracheal injury. When there was a move to cuffed tubes from un-cuffed in the under 8 age group, around 1997 following im-

proved ventilation evidence, they witnessed the worst iatrogenic tracheal injuries of their series. They recommend careful "titration" of the ET tube to ensure the correct size is used and advise at least 3 sizes to be ready for use at intubation. Misjudgements can cause catastrophic injury [28].

Pratt., *et al*. instituted training in Endotracheal Intubation for pre-hospital Emergency Medical Technicians (EMT) in a rural setting on a North American island. This training involved a standardised approach to intubation with training in the classroom and in operating theatres. They assessed the course recipients to see if their teaching was successful. 94% of intubation attempts by these technicians were successful, which was defined as; an appropriately sized Endotracheal tube placed below the true vocal cords and above the carina [29]. Training programmes such as these are likely to prevent iatrogenic tracheal injury in the pre-hospital setting as a result.

Chada., *et al*. have developed a novel device which modulates cuff pressure via an automated system. They tested their device on 10 piglets; 5 of whom had a constant pressure endotracheal tube and the other 5 with a modulating device. After 4 hours of intubation the animals were killed and their tracheas assessed histologically. They found a significant reduction in tracheal damage with their modulating device compared with a constant pressure tube. Whilst this is a small sample and not conducted in human subjects, they postulate that modulation allows improved mucosal blood perfusion that could be translated in to a reduction in iatrogenic tracheal injury [30].

Extracorporeal membrane oxygenation (ECMO)

In the last 4 years case reports have emerged reporting the use of ECMO in iatrogenic tracheal injury. Ventilator support for patients with these injuries treated either conservatively or surgically can be complicated by underlying lung disease or respiratory failure. ECMO can be employed to support these patients specifically or in those where classical ventilator means are failing or predicted to be insufficient. The first case reports emerged in 2014 when Hussein., *et al.* and Son., *et al*. employed ECMO in cases where the injuries were complicated due to associated respiratory issues. In Hussein's case this was status asthmaticus and aspiration pneumonia in Son's it was related to massive endotracheal bleeding. Hussein., *et al.* opted for a Polyurethane Covered stent as an adjunct in their management and kept their patient on ECMO support for 48 hours following the insertion of this. In total Son., *et al*. kept their patient on ECMO for 28 days until the patient's lung had recovered, 40 days after injury bronchoscopy revealed the injury to have fully healed with conservative treatment and ECMO [24,31].

Similarly in a case of a 33 year old morbidly obese female, a team from Philidelphia, employed VV-ECMO to treat a patient who sustained an iatrogenic tracheal injury after presenting with acute respiratory distress syndrome (ARDS) secondary to H1N1 influenza. After being transferred to a tertiary centre and her respiratory requirements became unmanageable she was placed on urgent VV-ECMO. They monitored the injury daily with bronchoscopy and airway lavage. Ultimately after 20 days they weaned the patient off ECMO successfully [32].

VV-ECMO has also been employed in patients who were treated surgically. A 34 year old lady, suspected to have overdosed on Amitriptyline, had two failed intubation attempts in the community before being intubated in the emergency department. Difficulty in ventilation and associated surgical emphysema led to the diagnosis of a tracheal injury extending down the right main bronchus and she was placed on VV-ECMO. A Thoracotomy was performed and the 8 cm defect was repaired with autologuous pericardium which was sutured with 4.0 Polydioxanone sutures. After a recovery complicated by sepsis she was weaned off ECMO and discharged 50 days after admission [33].

Case Series

Case 1

A 68 year old lady was admitted electively under our thoracic team for a VATS/Thoractomy and upper lobectomy for biopsy proven left upper lobe non-small cell lung cancer (T1aN0M0). She had a past medical history of mild cognitive impairment and gastro-oesophageal reflux. An iatrogenic injury was caused during intubation for this elective resection. This was approximately 4-5 cm in length and was positioned 2 cm above the carina.

An immediate right thoracotomy and repair of the tracheal tear was undertaken with VV ECMO support due to difficulty in ventilation following the injury. The right jugular and right femoral veins were cannulated with a percutaneous technique under transthoracic echocardiographic guidance. The tear was repaired with interrupted figure-of-eight 5.0 prolene sutures. The repair site was covered with mediastinal pleura and pedicled intercostal muscle. We tested the repair site against a pressure of 25 cm H_2O and no leak was evident.

She was weaned from ECMO on the first post-operative day. Unfortunately she developed evidence of non-occlusive right jugular and right proximal subclavian vein mixed thrombus likely secondary to the ECMO treatment. She was started on Apixaban after discussion with our cardiology colleagues and discharged on the 7th post-operative day. She was admitted 1 month later for the lobectomy which was undertaken without complication.

Case 2

A 69 year old lady was transferred from a local district general where she was intubated in their Accident and Emergency department. She had a background of gall stone pancreatitis and was awaiting a cholecystectomy. She attended the emergency department as she was feeling generally unwell and she quickly deteriorated to a peri-arrest situation when the decision was made to

intubate. After she developed surgical emphysema and difficulty in ventilation an iatrogenic tracheal injury was diagnosed on bronchoscopy. She was transferred to our unit the following day. She initially required high levels of vasopressor support and the decision was taken to manage her conservatively until she improved, and required less inotropic input, which occurred after 3 days on our Intensive Care Unit.

She was placed on VV-ECMO the night before theatre to reduce ventilation requirements and facilitate the surgical repair. An extended right thoracotomy was used to delineate the full extent of the tear; it extended from the root of the right main bronchus for at least 6 cm along the right posterolateral border of the trachea. Interrupted 4.0 Prolene figure-of-eight sutures were inserted along the defect. An air leak test confirmed adequate repair. The 3rd intercostal muscle was raised as a pedicle and sutured on to the repair with 4.0 Prolene sutures.

She developed significant bleeding from her surgical chest drain overnight requiring 6 units of blood to be transfused. She was taken back to theatre where the right thoracotomy was reopened and a bleeding point in the 4th intercostal space was controlled with a stitch. She was weaned of ECMO after this procedure successfully. Similarly to Case1; a venous doppler identified deep vein thrombi in both her right and left internal jugular veins. Again this patient was started on a New Oral Anticoagulant (NOAC) and ultimately discharged after a full recovery.

Case 3

A 69 year old lady with a background of schizophrenia, vitamin B12 deficiency and ovarian cancer was admitted electively for Right Upper Lobectomy for squamous cell carcinoma. The histological diagnosis had been previously confirmed on CT guided biopsy. She was an ex-smoker and had presented to our respiratory colleagues with dyspnoea on exertion.

During the underwater check at the end of the operative procedure a significant air leak was discovered from a membranous tear in the lower part of the posterior trachea related to the endotracheal tube. This injury was secured with direct sutures and reinforced with a pedicled intercostal muscle flap.

Initially she had an uncomplicated recovery. After a 24 hour stay on our ICU she was transferred to ward level care. On the third post-operative day we were considering discharge but she suffered a cardiac arrest. Return of spontaneous circulation was achieved with cardiopulmonary resuscitation. After 7 weeks on ICU, with a long respiratory wean requiring tracheostomy, she survived to discharge after bronchoscopies had revealed good healing of the iatrogenic injury.

She was reviewed in clinic 6 weeks after discharge and was back to full normal activities.

Discussion

Iatrogenic tracheal injury, caused by endotracheal intubation, is an uncommon occurrence. When it occurs however it carries a high mortality and morbidity rate. Patients often require long stays on an level 3 intensive care unit setting which has an associated cost implication. A study in 2007 analysed the cost effectiveness of ICU and whilst it has a favourable Quality-adjusted life year for its success there is a daily cost of £1328 to the National Health Service [34]. As such it is important to avoid such injuries in the first instance. Ultimately education and rigorous training in intubation and tracheostomy will reduce these episodes from occurring. Certainly the results from Pratt., *et al.* training programme in a remote setting provides evidence that all those undertaking intubation, particularly in the emergency environment where these injuries most commonly occur, should be stringently trained and assessed [29]. In our institution we have instituted a policy in our theatres that all intubated patients will have cuff pressures checked before being moved from anaesthetic room to operating room. Chada., *et al*. modulating device may be an option for the future, once similar technology has been applied and validated in human subjects [30].

The choice regarding surgical or purely conservative management is unclear. Certainly in recent years there has been a move towards avoiding surgery and adopting a conservative approach where possible. Whilst numerous management algorithms have been produced these are based on expert opinion and therefore are of limited value. They often include criteria regarding the size of the injury but there is no evidence that this plays a role in the prognosis of these patients. When injuries as long as 9 cm have been treated conservatively deciding which approach based on this criteria should not be the first priority [20]. It seems sensible that if an injury is sustained during or before a thoracic surgery procedure then a surgical repair should be undertaken as trained operative staff are present and the injury is de novo. The difficulty arises when patients arrive from other hospitals or from the community where these injuries were sustained. This group of patients are more likely to have progressed and developed complications such as ARDS or pneumonia related to the injury which often has a period of delayed diagnosis.

Endotracheal Stents have been used on numerous occasions in iatrogenic tracheal injury but evidence for their use is limited when no intervention in patients treated conservatively has proven so widely effective. They will most likely play a role in injuries that are not healing with conservative treatment in patients who are deemed unfit to undergo operative intervention.

We have demonstrated in our case reports and the others reviewed that ECMO can be useful in patients with ventilatory difficulty either caused by concurrent respiratory pathology, direct sequelae relating to the injury or in the immediate post operative recovery phase. That said it does have iatrogenic issues associated

with it in itself as two of our patients developed Deep Vein Thrombosis requiring anticoagulation. The most common complication, reported in the literature, of ECMO is bleeding. These occur in 10-36 % of patients and intracranial haemorrhage is seen in up to 6% of patients(merged). ECMO can provide crucial support in patients with this injury but it is not without risks in itself.

Conclusion

In a pathology that is rare it is almost impossible to conduct a randomised trial between conservative and surgical intervention, even if it was international and multi-centre. As such we feel that meta-analysis, case series and expert opinion will guide management for the foreseeable future. Based on this review of the literature we recommend a conservative approach unless the injury is sustained whilst in a theatre where thoracic surgery support is immediate. If the injury does not heal promptly however then the decision regarding stenting or operative intervention should be guided by the patients physical condition. An expert meeting on the topic to produce a consensus statement or guidance on the topic would be welcomed.

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Conflict of Interest

No conflicts of interest are declared.

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