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The impact of the acute respiratory distress syndrome on outcome after oesophagectomy†

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Abstract

Background: The Acute Respiratory Distress Syndrome (ARDS) is a serious complication of major surgery and consumes substantial healthcare resources. Oesophagectomy is associated with high rates of ARDS. The aim of this study was to characterize patients and identify risk factors for developing ARDS after oesophagectomy.

Methods: A secondary analysis of data from 331 patients gathered during the Beta Agonists Lung Injury Prevention Trial was undertaken. Characteristics and outcomes of patients with early (first 72 h postoperatively) and late (after 72 h) ARDS were determined. Linear and multivariate regression analysis was used to study the differences between early and late ARDS and identify risk factors.

Results: ARDS was associated with more non-respiratory organ failure (early 44.1%, late 75.0%, no ARDS 27.6% $P<0.001$), longer ICU stay (mean early 12.1, late 20.2, no ARDS 7.3 days $P<0.001$) and longer hospital stay (mean early 18.1, late 24.5, no ARDS 14.2 days $P<0.001$) but no difference in mortality or quality of life. Older patients (OR 1.06 (1.00 to 1.13), $P=0.045$) and those with mid-oesophageal tumours (OR 7.48 (1.62–34.5), $P=0.010$) had a higher risk for ARDS.

Conclusions: Early and late ARDS after oesophagectomy increases intensive care and hospital length of stay. Given the high incidence of ARDS, cohorts of patients undergoing oesophagectomy may be useful as models for studies investigating ARDS prevention and treatment. Further investigations aimed at reducing perioperative ARDS are warranted.

Key words: oesophageal neoplasms; oesophagectomy; one-lung ventilation; respiratory distress syndrome, adult

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Editor's key points

- Acute Respiratory distress syndrome (ARDS) has a high morbidity and mortality.
- In this secondary analysis, outcomes and risk factors in patients developing ARDS early (within three days) or late (four–28 days) after oesophagectomy were compared.
- ARDS was associated with higher morbidity, longer ICU and hospital stays but no increase in mortality.
- There was no difference in mortality or quality of life between early and late ARDS but the data may be underpowered to detect this.

The Acute Respiratory Distress Syndrome (ARDS) frequently complicates the recovery from major surgery.[1] It is associated with high mortality[2–4] and although this has improved with time,[5] it remains an important cause of death and morbidity. Management of patients with ARDS consumes substantial healthcare resources.[6] The definitions of ARDS were updated in 2013, with the removal of the term acute lung injury (ALI).[7] The term ARDS is used here to describe patients with ALI and ARDS.

The outcome of ARDS varies according to the underlying disease process responsible. In a recent study, where overall hospital mortality in ARDS was 41.1%, mortality was 43.6% in patients with ARDS caused by aspiration, 40.6% by pneumonia and 21.4% by severe trauma.[2] Major thoracoabdominal surgery, especially when combined with sepsis, is a common cause of ARDS with high associated mortality.[1]

Oesophagectomy carries a high risk for both mortality and morbidity, particularly pulmonary complications.[8] Tandon and colleagues[9] in 2001 reported rates of ARDS of 38.3%, with a mortality rate in patients developing severe ARDS of 50%. Another study comparing open oesophagectomy to hybrid procedures (laparoscopic abdominal and open thoracic resection), reported major pulmonary complications in 43% of the open group and 15% in the hybrid group, in whom the incidence of ARDS was also lower. Out of 280 patients, 21 cases of ARDS were reported and ARDS was diagnosed in six of the 12 patients who died.[10] Others have reported a respiratory complication rate of 27.4% and increased length of hospital stay, in patients who developed pulmonary complications after oesophagectomy.[11]

Despite a number of studies, no drugs that directly target the underlying pathophysiological mechanisms implicated in the development of ARDS have been identified.[12] In critical care, trials investigating the role of i.v. salbutamol,[13] simvastatin,[14] nitric oxide[15] and exogenous surfactant[16] in treating ARDS have all demonstrated no mortality benefit. The role of steroid administration remains unclear.[17] Reductions in mortality have been demonstrated by trials of lung protective ventilation[18] and neuromuscular blocking drugs.[19] Prone positioning is an effective measure in cohorts with severe ARDS.[20]

Given the limited treatments available, preventative strategies are attractive and could have substantial benefits if implemented in high risk groups, including patients undergoing oesophagectomy.[3] Valid clinical models are imperative for investigating preventative strategies.[21] Patients undergoing one-lung ventilation (OLV), such as occurs in patients undergoing oesophagectomy, provide a potentially useful model for investigating ARDS.

The aim of this study was to undertake a secondary analysis of the multi-centre Beta Agonist Lung Injury Prevention trial to characterize patients developing ARDS after elective oesophagectomy and identify risk factors for the syndrome.

Methods

Between April 2008 and June 2011, 362 adult patients undergoing elective oesophagectomy were enrolled into the BALTI-Prevention trial at 12 academic hospitals in the UK. The results have been published previously.[22] The North American-European Consensus Criteria were used to define ALI/ARDS: (ALI Pa_{O_2}:FI_{O_2}<40.0 kPa; ARDS Pa_{O_2}:FI_{O_2}<26.7 kPa) at the time and for the design of the study.[23]

Baseline characteristics, operative information and postoperative variables were recorded for all participants. Anaesthetists were instructed to follow a low tidal volume and fluid conservative strategy, but otherwise management was left to the individual clinician's discretion. Patients were defined as having ARDS in the presence of hypoxaemia (Pa_{O_2}:FI_{O_2} ratio less than 40.0 kPa), bilateral infiltrates on the chest x-ray and absence of clinical evidence of left atrial hypertension and categorized as having early (day 0–3), late (day 4–28) or no ARDS according to the timing of the first episode of ARDS. The categorization of ARDS was made *a priori* into 'Early' and 'Late', to separate 'primary ARDS' associated with the initial insult of surgery and anaesthesia from that acquired by later complications (secondary ARDS), such as anastomotic leak.

Study outcomes were ventilator free days, organ failure free days, 28 and 90 day mortality and health-related quality of life measured by Euroqol Health Outcome Questionnaire (EQ5D) at 28 and 90 days. Ventilator-free days were as previously defined.[22] Organ failure–free days were defined in a similar manner, with an organ failure–free day being a day without evidence of non-respiratory organ failure. Organ failure was defined by a Sequential Organ Failure Assessment score of four or more.[24] Postoperative pneumonia was recorded if diagnosed by the attending clinicians. As patients had undergone recent upper gastrointestinal surgery, non-invasive ventilation was not used as a standard measure, but was not strictly prohibited. Levels of care were determined according to United Kingdom Department of Health definitions.[25]

Linear regression of secondary outcomes comparing ARDS status was undertaken with and without adjustment for randomization. Linear regression models were then fitted for the secondary outcomes for ARDS status with an interaction term, to examine whether treatment difference depended on observed ARDS status.

Multivariate logistic regression was performed to establish a risk model for ARDS, examining all recorded potential risk factors. A forward stepwise regression model was produced using the specified baseline variables used in the univariate analysis, with P values of 0.05 and P value of 0.1 for subsequent removal from the model.

Multivariate analysis was then fitted for each stage of ARDS, to examine whether the response to different treatments was dependent on baseline characteristics. An unadjusted model was fitted, including terms for treatment allocation, baseline moderation and terms for treatment by moderator interaction. An adjusted model was also produced, containing terms for treatment, moderator and interaction with terms for age and hospital.

Safety outcomes were analysed according to ARDS status. These included respiratory, cardiovascular, surgical and other complications and sepsis. Adverse events were defined as

Table 1 Clinical characteristics of patients summarized by ARDS status

	Early ARDS (*n*=59)	Late ARDS (*n*=24)	Total ARDS (*n*=83)	No ARDS (*n*=248)
Age (yr)				
Mean (range)	63.7 (42–85)	62.3 (49–79)	63.3 (42–85)	63.2 (25–85)
Gender				
Male	46 (78.0%)	18 (75.0%)	64 (77.1%)	199 (80.2%)
Ethnicity				
Caucasian	59 (100%)	24 (100%)	83 (100%)	247 (99.6%)
Missing	0	0	0	1 (0.4%)
Diagnosis				
Adenocarcinoma	47 (79.7%)	16 (66.7%)	63 (75.9%)	182 (75.2%)
Squamous cell	9 (15.3%)	6 (25.0%)	15 (18.1%)	43 (17.8%)
Other malignant (e.g. mixed)	0	0	0	4 (1.7%)
Barrett's Oesophagus	3 (5.1%)	2 (8.3%)	5 (6.0%)	13 (5.4%)
Missing	0	0	0	6
Preoperative chemotherapy				
Yes (%)	47 (79.7)	18 (75.0)	65 (78.3)	198 (80.2)
No (%)	12 (20.3)	6 (25.0)	18 (21.7)	49 (19.8)
Not applicable	0	0	0	1
Forced Vital Capacity (litres)				
Mean (SD)	4.1 (1.2)	4.3 (1.1)	4.2 (1.1)	3.9 (0.9)
Missing	22	3	25	73
Forced Expiratory Volume in One S (litres)				
Mean (SD)	2.8 (0.9)	2.9 (0.7)	2.8 (0.8)	2.8 (0.7)
Minimum	0.1–4.5	1.1–4	0.1–4.5	1.1–5.6
Missing	22	4	26	75
Staging T				
1 (%)	3 (5.4)	2 (8.7)	5 (6.3)	12 (5.0)
2 (%)	11 (19.6)	8 (34.8)	19 (24.1)	62 (25.9)
3 (%)	42 (75.0)	13 (56.5)	55 (69.9)	161 (67.4)
4 (%)	0	0	0	4 (1.7)
Missing	3	1	4	9
Staging N				
0 (%)	23 (41.8)	10 (43.5)	33 (42.3)	88 (37.1)
1 (%)	32 (58.2)	13 (56.5)	45 (57.7)	149 (62.9)
Missing	4	1	5	11
Tumour location				
Cervical (%)	1 (1.7)	1 (4.3)	2 (2.4)	3 (1.2)
Mid oesophagus (%)	12 (20.3)	7 (30.4)	19 (23.2)	69 (28.4)
Oesophageal/gastric junction (%)	46 (78.0)	15 (65.2)	61 (74.4)	171 (70.4)
Missing	0	1	1	5
Surgical approach				
Laparoscopic (%)	16 (27.1)	3 (12.5)	19 (22.9)	60 (24.4)
Open (%)	43 (72.9)	21 (87.5)	64 (77.1)	186 (75.6)
Missing	0	0	0	2
Open stage; If open surgical approach				
2 Stage (%)	34 (97.1)	13 (81.2)	47 (92.2)	138 (93.2)
3 Stage (%)	1 (2.9)	3 (18.8)	4 (7.8)	10 (6.8)
Missing	8	5	13	38
Thoracotomy; If open surgical approach				
Right (%)	28 (71.8)	16 (76.2)	44 (73.3)	146 (84.4)
Left (%)	11 (28.2)	5 (23.8)	16 (26.7)	26 (15.0)
Missing	4	0	4	13
N/A (%)	0	0	0	1 (0.6)
ASA grade				
I (%)	1 (1.9)	2 (8.7)	3 (3.9)	14 (5.9)
II (%)	37 (68.5)	19 (82.6)	56 (72.7)	164 (69.2)
III (%)	16 (29.6)	2 (8.7)	18 (23.4)	57 (24.1)
IV (%)	0	0	0	2 (0.8)
Missing	5	1	6	11

atrial fibrillation, ventricular bigeminy, hypokalaemia and sinus tachycardia. Serious adverse events included anastomotic leak, ARDS, arrhythmia, pleural effusion, pneumonia, chyle leak, respiratory failure, inoperable tumour, pneumothorax, sepsis, surgical complications and other. Data were analysed using STATA Version 11, (StataCorp LP, College Station, Texas, USA).

Results

Of the 362 patients in the BALTI-P trial, 331 patients were included in the analysis. Patients who did not undergo surgery (n=19) and who withdrew consent (n=2) were excluded, as were patients who did not have a defined ARDS status (n=10, 2.8%). Patient age, sex, height or body weight, diagnosis (adenocarcinoma, squamous cell carcinoma (SCC), Barrett's or other), staging, chemotherapy and lung function were all similar between groups (Table 1).

In total, 83 patients (24.6%) developed ARDS in the first 28 days after surgery, of whom 59 (71.0%) were classified as early and 24 (29.0%) late. Overall, reduced ICU and hospital length of stay was observed for those patients without ARDS, with a longer duration for those with late vs. early disease (Table 2). Specifically, there were fewer organ failure free days in the early and late ARDS groups, compared with those who did not develop ARDS.

Patients with late ARDS had fewer ventilator-free days (median 17, interquartile range (IQR) 11–24), compared with early ARDS (median 27, IQR 18–28) and no ARDS (median 28, IQR 27–28). The duration of intensive care stay was shortest in those without ARDS (mean 7.3 days, standard deviation (SD) 5.4), longer with early ARDS (mean 12.1 days, SD 9.0) and longer still with late disease (mean 20.2 days, SD 8.0). There were no observed

Table 2 Post-operative outcomes days 0–90 summarized by ARDS status. *Calculated using log-rank test. HR, hazard ratio; IQR, interquartile range; RR, relative risk

	Early ARDS (n=59)	Late ARDS (n=24)	No ARDS (n=248)	Statistics (95% CI) Early or late ARDS vs. no ARDS
Organ failure free days				
Mean (SD)	24.4 (6.2)	21 (6.8)	26.8 (3.2)	Early −2.40 (−3.60, −1.19) P<0.001, Late −5.77 (−7.55, −3.99) P<0.001
Missing	0	0	2	
Any ventilator support on day 0–28				
Yes (%)	33 (55.9)	21 (87.5)	72 (29.1)	RR=1.62 (1.23, 2.15)
Missing	0	0	1	
Ventilator free days				
Median (IQR)	27 (18–28)	17 (10.5–23.5)	28 (27–28)	Early −5.28 (−6.81, −3.76) P<0.001, Late −10.1 (−12.4, −7.89) P<0.001
Missing	0	0	1	
Duration of hospitalisation (days)				
Mean (SD)	18.1 (7.8)	24.5 (5.3)	14.2 (6.2)	Early 3.93 (2.09, 5.77) P<0.001, Late 10.3 (7.63, 13.1) P<0.001
Missing	0	0	3	
Duration of ITU stay (days)				
Mean (SD)	12.1 (9.0)	20.2 (8.0)	7.3 (5.4)	Early 4.82 (3.00, 6.65) P<0.001 Late 12.9 (10.2, 15.6) P<0.001
Duration of ITU stay excluding deaths (days)				
Mean (SD)	12.1 (9.2)	20.2 (8.0)	7.3 (5.4)	Early 4.78 (2.91, 6.64) P<0.001, Late 12.9 (10.2, 15.6) P<0.001
Missing	2	0	2	
Duration of level 0 or 1 care (days)				
Mean (SD)	8.4 (6.8)	7.8 (5.2)	10.2 (5.6)	Early −1.76 (−3.43, −0.10) P=0.04, Late 2.40 (−4.86, 0.06) P=0.06
Missing	0	0	1	
Duration of level 2 care (days)				
Mean (SD)	5.0 (3.4)	8.0 (4.2)	4.0 (3.0)	Early 0.98 (0.08, 1.88) P=0.033 Late 4.06 (2.73, 5.39) P<0.001
Missing	0	0	1	
Duration of level 3 care (days)				
Mean (SD)	5.3 (8.5)	9.5 (7.0)	0.8 (2.2)	Early 4.48 (3.21, 5.74) P<0.001 Late 8.76 (6.90, 10.6) P<0.001
Missing	0	0	1	
EQ-5D Day 28				
Mean (SD)	0.47 (0.31)	0.31 (0.42)	0.55 (0.29)	Early −0.08 (−0.18, 0.02) P=0.119 Late 0.24 (−0.39, −0.09) P=0.002
Missing	17	8	43	
EQ-5D VAS Day 28				
Mean (SD)	59.3 (18.5)	55.5 (24.1)	62.0 (16.5)	Early −2.76 (−8.60, 3.08) P=0.35, Late −6.56 (−15.70, 2.57) P=0.16
Missing	18	9	42	
EQ-5D Day 90				
Mean (SD)	0.64 (0.26)	0.54 (0.35)	0.66 (0.3)	Early −0.02 (−0.11, 0.06) P=0.63, Late −0.12 (−0.26, 0.01) P=0.07
Missing	14	8	49	
EQ-5D VAS Day 90				
Mean (SD)	65.4 (20.0)	60.3 (18.2)	68.2 (18.4)	Early −2.75 (−8.81, 3.30) P=0.37, Late −7.88 (−17.42, 1.65) P=0.11
Missing	14	8	48	
Mortality*				
Alive at 28 days (%)	56 (94.9)	24 (100)	243 (99.2)	HR=3.73 (0.74, 18.7); P-value=0.086*
Dead at 28 days (%)	3 (5.1)	0	2 (0.8)	
Missing	0	0	3	
Mortality*				
Alive at 90 days (%)	55 (93.2)	22 (91.7)	245 (99.2)	HR=3.36 (0.83, 13.6); P-value=0.072*
Dead at 90 days (%)	4 (6.8)	1 (4.3)	2 (0.8)	
Missing	0	1	1	

Table 3 Multivariate analyses of ARDS. OR: mean estimated odds ratio of the interaction term, CI: 95% confidence interval. Late ARDS estimates are missing because of insufficient numbers of patients in these groups for these to be calculated

	Early ARDS			Late ARDS			Total ARDS		
	OR (95% CI)	P	n	OR (95% CI)	P	n	OR (95% CI)	P	n
Age (yr)	1.06 (1.00, 1.13)	0.05	332	0.98 (0.90, 1.06)	0.57	331	1.04 (0.99, 1.10)	0.13	331
Gender	1.66 (0.41, 6.66)	0.46	332	0.71 (0.09, 5.35)	0.74	331	1.25 (0.37, 4.14)	0.72	331
Preoperative chemotherapy	0.74 (0.17, 3.17)	0.68	332	7.76 (0.70, 86.42)	0.10	331	1.74 (0.51, 5.93)	0.38	331
Duration of one lung ventilation (min)	1.01 (0.99, 1.00)	0.25	297	1.00 (0.98, 1.01)	0.61	297	1.00 (0.99, 1.01)	0.48	297
Cumulative fluid balance at end of surgery (litres)	1.16 (0.80, 1.68)	0.45	316	1.20 (0.61, 2.35)	0.60	315	1.24 (0.88, 1.75)	0.23	315
Surgical approach	0.69 (0.19, 2.49)	0.57	329	0.21 (0.02, 2.85)	0.24	329	0.45 (0.14, 1.49)	0.19	329
Tumour: Mid oesophagus	7.48 (1.62, 34.5)	0.01	325	–	–	–	1.74 (0.54, 5.62)	0.36	325
Tumour: Gastro-oesophageal junction	0.21 (0.05, 0.85)	0.03	325	–	–	–	0.85 (0.27, 2.65)	0.77	325

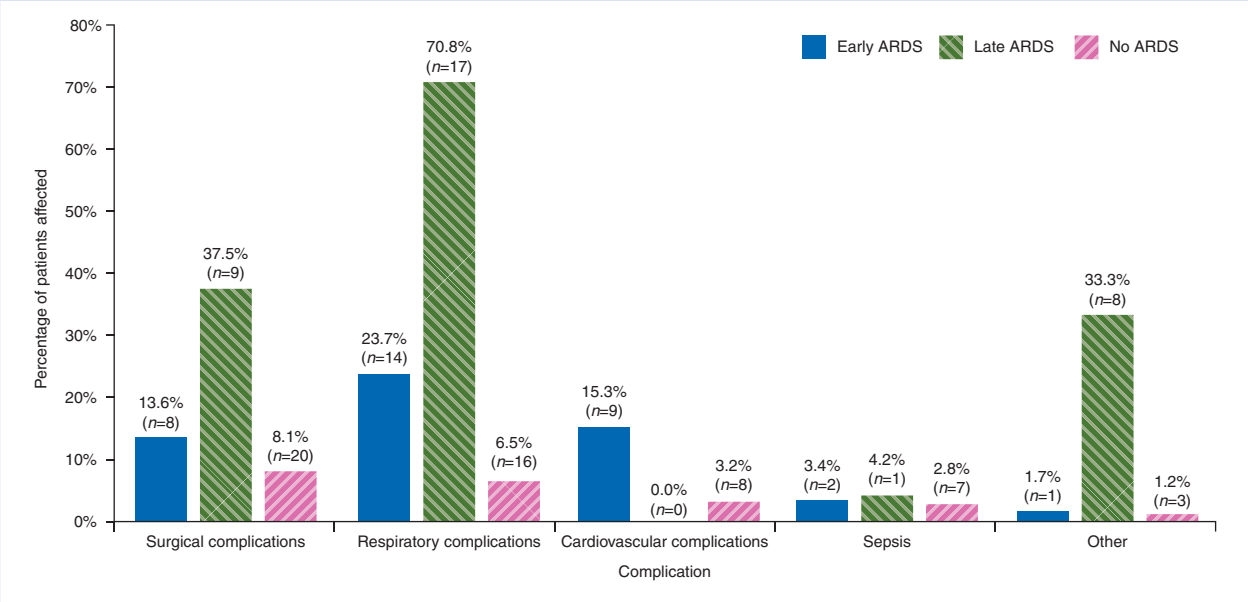

Fig 1 Safety outcomes according to onset of ARDS.

differences in mortality at 28 or 90 days. The findings were unchanged in the sensitivity analysis which adjusted for treatment allocation to salmeterol (Supplementary Table S1). Similarly, there were no differences in quality of life scores at 28 or 90 days (Supplementary Table S1).

Table 3 shows multivariate analysis grouped according to lung injury. Early ARDS was associated with increased age (OR 1.06 (1.00 to 1.13), P=0.05). There was an increased risk of ARDS in patients with mid-oesophageal tumours (OR 7.48 (1.62–34.5), P=0.01), whilst the risk was reduced with gastro-oesophageal tumours (OR 0.21 (0.05–0.85), P=0.03).

Analysis was undertaken adjusting for treatment allocation (salmeterol vs. placebo), but this made little difference (Supplementary Table S2).

Of those patients with late ARDS, 42% were also diagnosed with pneumonia, 25% with anastomotic leak and 13% with respiratory failure, whilst other surgical complications occurred in 12.5%. In those with early ARDS, 10.2% had pneumonia and surgical complications occurred in 8.5%. There were significantly more surgical, respiratory and 'other' complications (P<0.0001 for all), but no significant difference in sepsis between the groups. For surgical, respiratory and other non-cardiovascular complications, rates were higher in the late compared with the early ARDS groups (Fig. 1).

Discussion

These data demonstrate that ARDS was common after oesophagectomy surgery, with an incidence of almost 25%. We found no differences in mortality between patients with early and late ARDS at 28 or 90 days, nor to changes in their quality of life scores. This may be because of insufficient power, especially given the study was not designed to examine this outcome and because mortality after oesophagectomy has fallen with time.[26] However, both early and late ARDS are associated with more days of organ failure, spending more days ventilated and having longer ICU and hospital stays than patients who do not develop ARDS, a finding that has been observed elsewhere.[27]

Improvements in preoperative, intra-operative and post-operative care may all have contributed to apparent reduction

in harm associated with ARDS and the reduction in the frequency and severity of ARDS observed in older cohorts.[9] Another, more recent, study has shown that post-oesophagectomy respiratory failure and ARDS were independent risk factors for in-hospital death.[11] Overall, the rates of mortality and respiratory and cardiovascular complications were similar to contemporary studies of oesophagectomy outcomes elsewhere.[28]

Scoring systems, such as the Lung Injury Prediction Score (LIPS), have been developed to identify high incidence ARDS groups *a priori* for both clinical purposes and to provide groups with high ARDS incidences for preventative trials.[21] A cohort identified using the LIPS score had an incidence of ARDS of 7%.[29] The majority of ARDS detected in BALTI-P occurred in the first 72 h after surgery, with a similar pattern seen in the LIPS validation cohort, which identified only 25% of ARDS on or after day four.[29]

Oesophagectomy is attractive as a model of ARDS as the timing of the insult (surgery) is consistent and predictable. Patients can be identified, approached and consented in advance. Systemic and alveolar inflammatory changes are similar to those observed in ARDS[22] and include evidence of alveolar and endothelial damage, neutrophil infiltration and pulmonary vascular congestion.[4] One limitation to the model is that although the incidence of ARDS was high, the majority was classified as mild to moderate and this is partly reflected in the lower mortality detected in this study, compared with other studies in patients with more severe ARDS.[20] However, the increased organ failure, increased duration of ventilated and intensive care and hospital stay all demonstrate even early onset mild to moderate ARDS has adverse implications for both patients and healthcare resource utilization and it would therefore be beneficial to prevent it.

This study has identified increased age and tumour site as risk factors for early ARDS. Finding no significant risk factors for late ARDS probably reflects the small numbers in this group. The magnitude of the increased risk of ARDS associated with mid-oesophageal tumours was unexpected.

Squamous cell carcinoma is the predominant histological subtype in cervical and mid-oesophageal tumours. A higher risk of pulmonary complications with more proximal tumours has been reported previously, with one study suggesting a relationship with increased surgical technical difficulty and recurrent laryngeal nerve injury.[30] In one small study, SCC histology was associated with more preoperative respiratory disease and alcohol use and with more severe postoperative complications and longer ICU stays.[31] Similar rates of COPD, cardiac disease, smoking and neoadjuvant chemoradiotherapy were seen for SCC and adenocarcinomas.[31] Preoperative radiotherapy, more commonly administered in the UK for SCC (and infrequently for adenocarcinoma), is associated with increased pulmonary complications,[32] and salvage oesophagectomy for SCC after definitive chemoradiotherapy, can be technically challenging with increased postoperative morbidity. These factors may explain the higher risk of ARDS observed with mid-oesophageal tumours.

It has been suggested that cumulative insults may aggregate to increase ARDS risk. McKevith and Pennefather[27] discussed the possibility that the combined 'hits' of multi-cavity surgery and OLV combine to give higher rates of ARDS when compared with other major surgery. An incidence of ARDS of 60% has been reported in patients who had undergone thoraco-abdominal surgery and developed sepsis, compared with 34.6% in those with sepsis without surgery, which suggests ARDS is more likely as pathological insults aggregate.[1] We believe that early ARDS in this dataset was driven by factors at the time of surgery such as OLV lung injury and/or inflammation induced by the surgical insult whereas ARDS in the late group was more frequently caused by complications after surgery.

A similar concept has been proposed elsewhere, with a study of ARDS after lung resection identifying what the authors termed 'primary ARDS' (i.e. as a result of surgery and OLV alone, without another identified cause) being observed shortly after surgery (median onset two days), whereas 'secondary ARDS' (where a causal factor other than the initial surgery, such as aspiration or sepsis, was identified) tended to occur later (median onset 5.5 days).[33] This again suggests that accumulated insults contribute to ARDS.

There are limitations in this study. This is a retrospective observational analysis, with the potential bias that confers. Furthermore, the ongoing changes in both the epidemiology of oesophageal cancer and its management render comparisons with other, especially older, cohorts less reliable. The total number of participants may have resulted in a lack of power to identify trends, particularly mortality but this is, nevertheless, to our knowledge, the largest cohort of patients undergoing oesophagectomy, who have been subject to systematic screening for ARDS. Potentially important information, such as tumour histology, use of radiotherapy, smoking status and alcohol consumption were not collected.

Both early and late ARDS are harmful for patients after oesophagectomy and increase ICU and hospital resource use. New preventative strategies to reduce the burden of perioperative ARDS would be valuable. Because of the high incidence of ARDS in patients undergoing oesophagectomy, it is a useful model for trialling such strategies and, compared with other methods for finding such cohorts, it has a number of favourable features.

Authors' contributions

Study design: G.P., D.T.
Study conduct: G.P., D.T., F.G., D.M., D.P., T.W., O.T.
Data analysis: C.K., P.H.
Writing paper: all authors
Revising paper: all authors

Supplementary material

Supplementary material is available at *British Journal of Anaesthesia* online.

Declaration of interest

G.P. and D.M. have both undertaken paid consultancy for GlaxoSmithKline. D.M. has also undertaken paid consultancy work for Peptinnovate, SOBI and Bayer and received funds from GlaxoSmithKline for undertaking bronchoscopy as part of a clinical trial with lipopolysaccharide challenge for a novel anti-inflammatory agent. T.W. has previously received funding from AstraZeneca and undertaken paid consultancy for Merck Sharp and Dohme and Smiths Medical Devices.

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