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Early extubation after transthoracic oesophagectomy

經胸廓進行食管切除手術後的早期拔管

Objectives. To assess patient outcome following transthoracic (Ivor-Lewis) oesophagectomy and the effects of epidural analgesia and early extubation compared with overnight sedation and ventilation.
Design. Retrospective study.
Setting. University teaching hospital, Hong Kong.
Subjects and methods. A retrospective review of patients undergoing oesophagectomy during two periods, 1990 to 1994 (n=65) and 1995 to 1998 (n=83), was completed. In the latter period, factors associated with early extubation were also evaluated.
Results. Between 1990 and 1994, only three (4.6%) of 65 patients were extubated early compared with 34 (41.0%) of 83 patients between 1995 and 1998 (P<0.001). Comparing these two periods, there were no differences in respiratory complications or hospital mortality. In the period 1995 to 1998, more patients who were extubated early had received epidural analgesia (85% versus 41%, P<0.001). There were no differences between the early and late extubation groups in terms of respiratory complications and hospital mortality. Patients extubated early had shorter stays in the intensive care unit (1 versus 2 days, P=0.005). Epidural analgesia was an independent factor associated with early extubation (odds ratio=9.4; 95% confidence interval, 2.8-31.2).
Conclusion. After transthoracic oesophagectomy, early extubation is safe and can lead to a shorter stay in the intensive care unit. Epidural analgesia appears to facilitate early extubation.

目的：評估經胸廓進行食管切除手術後，即日拔掉喉管及硬腦膜止痛的效用，並比較其與通宵鎮靜及插喉呼吸的結果。
設計：回顧性研究。
安排：大學教學醫院，香港。
患者與方法：本研究回顧了兩段時期接受食管切除手術的患者，他們分別是：1990年至1994年的65名患者，以及1995年至1998年的83名患者。對於後段時期的患者，同時評估了與即日拔掉喉管相關的因素。
結果：在1990年至1994年期間接受手術的65名患者中，僅3名(4.6%)於手術當日拔掉喉管；而1995年至1998年期間，83名患者中有34名(41%)於手術當日拔掉喉管(P<0.001)。比較這兩段時期接受手術的患者，其呼吸系統併發症和住院死亡率均沒有差別。在後段時期，較多即日拔掉喉管的患者接受硬腦膜止痛(85% 比 41%，P<0.001)；而且於手術當日及翌日拔掉喉管的患者，其呼吸系統併發症和住院死亡率並沒有差別。即日拔掉喉管的患者在深切治療病房留醫的時間較短(1天比2天，P=0.005)。硬腦膜止痛是與即日拔掉喉管相關的獨立因素(機會比=9.4；95%置信間隔， 2.8-31.2)。
結論：經胸廓進行食管切除手術後，即日拔掉喉管是安全的做法，並有助縮短患者在深切治療病房留醫的時間。硬腦膜止痛相信對即日拔掉喉管有利。

Key words:
Analgesia, epidural;
Esophagectomy;
Mortality;
Postoperative complications;
Ventilation

關鍵詞：
硬腦膜止痛法；
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Introduction

After transthoracic (Ivor-Lewis) oesophagectomy, it has been customary to ventilate patients overnight.[1] This policy allows time for correction of physiological parameters enabling safe extubation the following morning. Prophylactic short-term ventilation can be associated with increased morbidity, however, including barotrauma, problems relating to endotracheal tube use, and nosocomial pneumonia. In addition, the need for sedation is associated with potential side-effects. For these reasons, as well as the cost of ventilating patients in the intensive care unit (ICU), early extubation is desirable. In 1993, Caldwell et al[2] reported the outcome of patients undergoing oesophagectomy following a change in protocol from overnight ventilation to early extubation. These data indicated that the change in protocol was associated with a decrease in cardiac complications, and shorter ICU and hospital stays, but did not increase respiratory complications. At the time of that report, some centres in the United Kingdom already had a policy of early extubation after oesophagectomy.[3]

Prior to 1995, all patients at the Prince of Wales Hospital were routinely ventilated overnight after oesophagectomy. Patients whose condition was stable were extubated the following morning. All patients received intravenous opioids for pain control after discharge to the general surgical ward. Since 1995, some patients have been extubated earlier when clinically appropriate. This change of practice reflected an increasing body of literature showing that early extubation after oesophagectomy was safe.[2-6] This practice also coincided with the expansion of the epidural analgesia service to general surgical wards, allowing patients better pain control after discharge from the ICU. Between 1995 and 1998, the timing of extubation was left to the discretion and clinical judgement of the attending intensive care specialist or anaesthetist. Patients were extubated as soon as their physiological parameters were stable. Criteria for physiological stability and extubation were as follows:

(1) normothermia (36.5°C-37.5°C);
(2) stable haemodynamics—mean arterial pressure greater than 70 mm Hg and systolic blood pressure less than 180 mm Hg, and pulse 50 to 100 beats per minute;
(3) good oxygenation (SpO_2=95% on inspired oxygen concentration of 40%);
(4) stable respiratory parameters, with spontaneous breathing and a respiratory rate of 25 breaths per minute;
(5) normal arterial pH (pH 7.35-7.45); and
(6) satisfactory pain control.

This study was undertaken to determine the safety and efficacy of early extubation after oesophagectomy at the Prince of Wales Hospital. The outcome for patients who underwent a standard Ivor-Lewis oesophagectomy—laparotomy for gastric mobilisation, a right postero-lateral thoracotomy for oesophageal dissection, and en bloc lymphadenopathy and oesophagogastric anastomosis at the apex of the right lung—in the two periods of 1990 to 1994 and 1995 to 1998 was reviewed. In the former period, almost all patients were ventilated overnight, whereas in the latter period, some patients were extubated early. Factors associated with early extubation were also determined by comparing early and late extubation in the period 1995 to 1998.

Subjects and methods

The medical records of all patients who underwent standard transthoracic (Ivor-Lewis) oesophagectomy from January 1990 to October 1998 were reviewed. Data on patient characteristics and outcomes were retrieved from the oesophageal cancer registry. Early extubation was defined as extubation shortly after anaesthesia on the same day as surgery, and late extubation was defined as extubation on the day after surgery following overnight ventilation.

Postoperative analgesia protocols for oesophagectomy patients consisted of either patient-controlled intravenous morphine or thoracic epidural analgesia. Prior to 1995, patients who initially received epidural analgesia during the intra-operative period and the stay in the ICU were given intravenous morphine analgesia before returning to the general surgical ward. The practice of epidural analgesia was expanded and introduced to the general surgical wards after 1995. The choice of analgesia technique depended on the preference and expertise of the attending anaesthetist, patient preference, and the feasibility of epidural catheter insertion. For epidural analgesia, patients received a standard infusion of 5 to 10 mL of bupivacaine 1 mg/mL and fentanyl 2.5 µg/mL via epidural catheter. For patient-controlled analgesia, patients received morphine in a 1 to 2 mg bolus, with a lock-out interval of 5 to 8 minutes, and a 4-hour maximum dose of 0.4 mg/kg.

The following data were retrieved from the oesophageal cancer registry: age, sex, preoperative forced expiratory volume in 1 second (FEV_1), preoperative forced vital capacity (FVC), details of neo-adjuvant chemotherapy or radiotherapy, duration of surgery, intra-operative blood loss, and mode of analgesia. Primary outcomes recorded were respiratory complications, hospital mortality, and length of stay in the ICU. Respiratory complications included pneumonia, atelectasis, bronchospasm, and respiratory failure. Pneumonia was defined as new and persistent infiltrates on chest radiography, plus clinical evidence that the infiltrate was of an infectious origin, for example, fever (body temperature greater than 38.3°C), leukocytosis, or purulent sputum.[7] The rate of failed extubation in the period from 1995 to 1998 was documented. Failed extubation was defined as respiratory failure requiring reintubation within 24 hours after initial extubation.

Results were analysed using the Statistical Package for Social Sciences (Windows version 8.0; SPSS Inc., Chicago, United States). Categorical variables were compared using the Chi squared test and Fisher's exact test. Continuous and ordinal variables were compared using the Student's *t* test and Mann-Whitney *U* test, respectively. Multivariate logistic regression analysis was used to evaluate the contribution to early extubation of potential predictive factors. Factors assessed included age, preoperative FEV_1, FVC, neo-adjuvant chemotherapy or chemo-irradiation, duration of surgery, intra-operative blood loss, and mode of analgesia. Factors with $P<0.05$ on univariate analysis were entered into the model. A P value of less than 0.05 (2-sided) was considered significant.

Table 1. Characteristics of patients undergoing transthoracic oesophagectomy from 1990 to 1994 and from 1995 to 1998

Characteristic	1990-1994, n=65	1995-1998, n=83	P value*
Mean age (SD) [years]	63 (9)	62 (10)	NS†
Sex (M:F)	8:1	9.3:1	NS
No. (%) of preoperative neo-adjuvant therapy treatment	39 (60.0)	56 (67.5)	NS
Chemotherapy alone	39 (60.0)	37 (44.6)	<0.001‡
Chemo-irradiation	0	19 (22.9)	
No. (%) of early extubation	3 (4.6)	34 (41.0)	<0.001
Preoperative FEV_1§ (SD) [L]	1.9 (0.8)	2.1 (0.6)	NS
Preoperative FVC‖ (SD) [L]	2.6 (0.9)	2.8 (0.6)	NS
Duration of surgery (SD) [minutes]	251 (66)	298 (163)	0.025
Intra-operative blood loss (SD) [mL]	1452 (907)	1451 (1106)	NS

* P values for age, preoperative FEV_1, preoperative FVC, duration of surgery, and intra-operative blood loss were calculated using the Student's *t* test; P values for sex, neo-adjuvant therapy, and early extubation were calculated using the Chi squared test
† NS not significant
‡ This P value compares the three modes of treatment (surgery, surgery and chemotherapy, surgery and chemotherapy and irradiation) between the two periods 1990 to 1994 and 1995 to 1998
§ FEV_1 forced expiratory volume in 1 second
‖ FVC forced vital capacity

Table 2. Patient outcomes for the periods 1990 to 1994 and 1995 to 1998

Outcome	1990-1994, n=65 No.(%)	1995-1998, n=83 No.(%)	P value*
Complications			
Respiratory problems	19 (29.2)	22 (26.5)	NS†
Pneumonia	16 (24.6)	18 (21.7)	NS
Hospital mortality	6 (9.2)	6 (7.2)	NS
Intensive care unit stay (median no. of days)	2	1	NS

* P values for respiratory problems and hospital mortality were calculated using the Chi squared test; P value for intensive care unit stay was calculated using the Mann-Whitney *U* test
† NS not significant

Results

Between January 1990 and October 1998, a total of 148 transthoracic (Ivor-Lewis) oesophagectomies were recorded.

During 1990 to 1994, 65 patients underwent transthoracic oesophagectomy. All but three patients (95%) were ventilated overnight after their operations. In the second period, 1995 to 1998, eighty-three patients underwent oesophagectomy. Significantly more patients were extubated early (34/83, 41%; P<0.001). Table 1 shows the characteristics of patients undergoing oesophagectomy in the two periods. There were no differences in age, sex, preoperative lung function, and intra-operative blood loss between the two groups. In the first period, 39 (60.0%) patients received neo-adjuvant chemotherapy, while none received irradiation. In the latter period, 56 (67.5%) received neo-adjuvant treatment. Of these patients, 37 (44.6%) received neo-adjuvant chemotherapy alone, and 19 (22.9%) received combined chemo-irradiation. The mean operating time was significantly longer in the latter period (298 versus 251 minutes, P=0.025).

Table 2 shows the patient outcomes for the two periods. There were no significant differences seen in the rates of respiratory complications (26.5% versus 29.2%, P=0.713), pneumonia (21.7% versus 24.6%, P=0.674), hospital mortality (7.2% versus 9.2%, P=0.658), or length of ICU stay (median stay, 1 day versus 2 days; P=0.252).

Table 3. Characteristics of the patients in the early and late extubation groups, 1995 to 1998

Characteristic	Early extubation, n=34	Late extubation, n=49	P value*
Mean age (SD) [years]	61 (10.5)	63 (9.2)	NS†
Sex (M:F)	10:1	8.4:1	NS
No. (%) of preoperative neo-adjuvant therapy treatment	22 (64.7)	32 (65.3)	NS
Chemotherapy alone	15 (44.1)	21 (42.9)	NS‡
Chemo-irradiation	7 (20.6)	11 (22.4)	
Preoperative FEV_1§ (SD) [L]	2.30 (0.53)	2.02 (0.59)	0.031
Preoperative FVC‖ (SD) [L]	2.95 (0.55)	2.80 (0.69)	NS
Duration of surgery (SD) [minutes]	313 (191)	281 (140)	NS
Intra-operative blood loss (SD) [mL]	1218 (791)	1567 (1271)	NS
No. (%) of epidural analgesia	29 (85.3)	20 (40.8)	<0.001

* P values for age, preoperative FEV_1, preoperative FVC, duration of surgery, and intra-operative blood loss were calculated using the Student's *t* test; P values for neo-adjuvant therapy and epidural analgesia were calculated using the Chi squared test; P value for sex was calculated using the Fisher's exact test
† NS not significant
‡ This P value compares the three modes of treatment (surgery, surgery and chemotherapy, surgery and chemotherapy and irradiation) between the early and late extubation groups
§ FEV_1 forced expiratory volume in 1 second
‖ FVC forced vital capacity

Table 4. Patient outcomes for the early and late extubation groups, 1995 to 1998

	Early extubation, n=34 No. (%)	Late extubation, n=49 No. (%)	P value*
Complications			
Respiratory problems	9 (26.5)	13 (26.5)	NS†
Pneumonia	8 (23.5)	10 (20.4)	NS
Failed extubation‡	3 (8.8)	3 (6.1)	NS
Hospital mortality	2 (5.9)	4 (8.2)	NS
Intensive care unit stay (median no. of days)	1	2	0.005

* P value for respiratory problems was calculated using the Chi squared test;
P values for failed extubation and hospital mortality were calculated using the Fisher's exact test;
P value for intensive care unit stay was calculated using the Mann-Whitney *U* test

† NS not significant

‡ Failed extubation was defined as respiratory failure requiring re-intubation within 24 hours of initial extubation

In the second period 1995 to 1998, thirty-four of 83 patients were extubated early. Table 3 compares the characteristics of patients in the early and late extubation groups. There were no differences seen in age, sex, preoperative FVC, preoperative neo-adjuvant therapy, intraoperative blood loss, and duration of surgery. The early extubation group had a statistically higher preoperative FEV_1 than the late extubation group (2.30 versus 2.02 L, P=0.031). More patients in the early extubation group had received epidural analgesia (85.3% versus 40.8%, P<0.001). The outcomes for these patients are shown in Table 4. There were no significant differences in the rates of respiratory complications (26.5% versus 26.5%, P=0.995), pneumonia (23.5% versus 20.4%, P=0.734), and hospital mortality (5.9% versus 8.2%, P=0.693). There was also no difference seen in the rates of failed extubation (8.8% versus 6.1%, P=0.685). However, the early extubation group had a shorter length of ICU stay (median stay, 1 day versus 2 days; P=0.005).

Factors predictive of early extubation were evaluated in the second period 1995 to 1998. Early extubation was achieved in 34 (41%) patients. On univariate analysis, a higher FEV_1 and the use of epidural analgesia were factors shown to be associated with early extubation. On multivariate regression analysis, epidural analgesia was the only independent factor predicting early extubation (odds ratio= 9.4; 95% confidence interval, 2.8-31.2).

Discussion

This study demonstrates that early extubation after transthoracic oesophagectomy did not adversely affect patient outcome. Patients who were extubated early had a generally shorter ICU stay. This is of benefit from both the perspective of health care and health costs. This analysis indicated that epidural analgesia was independently associated with early extubation. These results are consistent with previous reports.[6,8-10]

The authors consider that thoracic epidural analgesia facilitates early extubation by providing good pain relief, allowing patients to cough effectively and to cooperate with manoeuvres designed to prevent atelectasis such as deep breathing exercises and incentive spirometry. Watson and Allen[6] showed that routine use of thoracic epidural analgesia for oesophagectomy allowed early extubation and also decreased the incidence of fatal and non-fatal respiratory complications. In another study, Tsui et al[8] showed that after the introduction of postoperative epidural analgesia, all oesophagectomy patients were extubated immediately after their operation. There was also a reduction in cardiopulmonary complications, hospital stay, and mortality rates compared with the rates prior to the standard use of epidural analgesia. Brodner et al[9] showed that with the introduction of a multimodal approach combining thoracic epidural anaesthesia, postoperative patient-controlled epidural analgesia, early extubation (within 6 hours), and forced mobilisation, the ICU stay after oesophageal resection was reduced. These authors stated that this approach may reduce the costs of this major surgery. Terai et al[10] showed that earlier extubation after oesophagectomy could be successfully performed with thoracic epidural bupivacaine combined with thoracic and lumbar epidural morphine.

In the univariate analysis in this study, a higher FEV_1 was associated with successful early extubation. The typical pattern of airflow obstruction was a reduced FEV_1/FVC ratio. The actual numerical value of this ratio is difficult to interpret, however. For example, after clinical improvement with bronchodilator treatment in a patient with emphysema, it is not uncommon to see a greater rise in FVC than in FEV_1, that is, a fall in the FEV_1/FVC ratio. Some authorities believe that in the assessment of the severity of airflow obstruction, FEV_1 is the best criterion for most patients.[11,12] The current study group consisted mostly of chronic smokers with some degree of chronic obstructive airways disease and, given this, FEV_1 may have been a more accurate reflection of lung function than FVC. This may explain why preoperative FEV_1 rather than FVC was a predictor of successful early extubation.

There are inherent limitations to this retrospective analysis, however. Firstly, comparing patients treated from 1990 to 1994 with those treated from 1995 to 1998 may not be entirely valid. For example, neo-adjuvant chemo-irradiation was introduced in the period after 1995 in place of neo-adjuvant chemotherapy alone. Due to the increased difficulty in operating on patients after chemo-irradiation, the operating times could be longer and these patients could also be at higher risk for respiratory complications. Despite longer operating times, however, the data in this study did not show a higher rate of respiratory complications for this group of patients. Secondly, the data in this study showed that epidural analgesia was an independent factor associated with early extubation. The study was not designed to demonstrate that epidural analgesia was responsible for early extubation, however. In fact, the enthusiasm of the attending intensive care specialist or anaesthetist for practising early extubation may be as strong a factor influencing the extubation strategy as the mode of analgesia.

A randomised study comparing routine early extubation or overnight ventilation in patients undergoing transthoracic oesophagectomy would require a large sample size. For example, 219 patients would be needed in each group to detect a 50% reduction (from 20% to 10%) in the rate of respiratory complications (α=0.05, 2-sided, 1-β=0.8). Such patient numbers would be difficult to recruit, even in major centres. In clinical practice, early extubation depends on many clinical factors that would also influence recruitment. For example, circulatory instability during the course of surgery would make a patient unsuitable for early extubation and such patients would thus have to be excluded from a prospective clinical trial.

A randomised controlled trial was reported in the German literature comparing early extubation (within 6 hours postoperatively) and prolonged ventilation (more than 24 hours) in 104 patients after oesophageal resection.[13] The early extubation group were noted to have a higher hospital mortality compared to the prolonged ventilation group, although this did not reach statistical significance (9.8% versus 1.9%, P=0.08).

Conclusion

This study and others have demonstrated the safety and potential cost-effectiveness of early extubation after transthoracic oesophagectomy. The use of epidural analgesia was associated with early extubation. Epidural analgesia and early extubation for patients in a stable condition should be the goal of good anaesthesia management for patients post-oesophagectomy.

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