

Evolution of Standardized Clinical Pathways: Refining Multidisciplinary Care and Process to Improve Outcomes of the Surgical Treatment of Esophageal Cancer

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Abstract

Background The aim of this study is to determine the effect of the implementation and evolution of a multidisciplinary esophagectomy care pathway on postoperative outcomes over a 20-year experience.

Study Design All patients undergoing esophagectomy for cancer between 1991 and 2012 were included. Patients were divided into four groups (Gp1 1991–1996, Gp2 1997–2002, Gp3 2003–2007, and Gp4 2008–2012).

Results Five hundred and ninety-five patients were included (Gp1 92, Gp2 159, Gp3 161, and Gp4 183). Age remained consistent over time; however, a progressive significant increase was observed in BMI and Charlson comorbidity index. Increases were also noted in patients with clinical stage III cancers, in the use of neoadjuvant chemoradiotherapy, in salvage esophagectomy and in the utilization of pretreatment jejunostomy. We observed a significant reduction in estimated blood loss (EBL) and operative room IV fluid administration (ORFA) during the study period. Median ICU stay and length of hospital stay (LOS) (10 (5–50) to 8 (5–115) days) decreased over time. In-hospital mortality (0.3 %) and postoperative complications remained consistent over time. cumulative sum (CUSUM) analysis showed that EBL, ORFA, and LOS all declined during the study period, reaching mean values at case 120, 310, and 175, respectively.

Conclusions The results of this study show that process improvement within the pathway is likely more significant than the level of comorbidities, application of neoadjuvant chemoradiation, or technical approach in patients undergoing esophagectomy.

Keywords Esophageal cancer · Esophagectomy · Enhanced recovery

Introduction

In an era when cancer incidence is decreasing, the incidence of esophageal cancer, especially adenocarcinoma, continues to increase in the Western world and affects more than 450,000

people worldwide per annum.^{1,2} From 1975 to 2004, age-adjusted incidence in white men increased from 5.76 to 8.34 per 100,000 person-years. This is due to an estimated increase in adenocarcinoma of the esophagus in the order of 463 %.³ Esophageal carcinoma is now the eighth most common cancer worldwide but the sixth leading cause of cancer-related mortality.⁴

Despite improvements in adjuvant and neoadjuvant therapies, the overall 5-year survival remains poor and ranges from 20 to 30 %.^{5,6} Within the multimodality approach, esophagectomy remains an important component of the treatment for loco-regional esophageal cancer.⁷ However, esophagectomy remains one of the most demanding oncologic surgical procedures and is associated with significant morbidity and mortality. Categorized as a high-risk surgery by the Leapfrog Group, recent studies reported in-hospital mortality as high as 7 % for esophagectomy in the general population and as high as 8.9 % in

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Medicare patients as recently as 2008.^{8–10} The mortality associated with esophagectomy is 30 % higher than any other oncologic operation.⁹

There is significant heterogeneity in the technical approach to esophagectomy, and the choice of surgical technique depends on tumor location, patient comorbidities, and surgeon's preference or experience. Meta-analyses have shown no significant difference in the short-term outcomes or in long-term survival between different technical approaches.^{11–13} The more recent reduction of mortality and morbidity and improvement in survival is likely to be more a reflection of the progressive centralization of cancer services to high-volume centers, especially those with standardized pathways as a central component to enhanced recovery programs. In addition to a greater surgical experience, high-quality perioperative management requires the involvement of the entire multidisciplinary team.^{14–18} Nevertheless, there is still substantial morbidity, even among high-volume centers, with prolonged recovery and delayed hospital discharge.^{8,19,20}

Formal clinical care pathways have been successfully introduced in oncologic colorectal surgery to provide a targeted goal-directed patient recovery, which has translated into a reduction both in morbidity and in length of hospital stay.^{21–23} The use of these standardized pathways facilitates a system-wide approach to the perioperative management of these patients, and studies have clearly demonstrated improved postoperative outcomes and reduced costs.^{24,25} There are initial reports regarding clinical pathways in the setting of esophagectomy that have shown promising results, improving efficiency, and quality in perioperative care and operative outcomes.^{26,27}

In 1991, a standardized esophagectomy care pathway (ECP) was first introduced at the Virginia Mason Medical Center, Seattle, WA, USA. This pathway was designed to involve every component of the multidisciplinary team including anesthesia, critical care, hospital nursing, dietary, physical therapy, and trainees. This process has resulted in all members of the care team being focused on achieving specific goals within the pathway aimed at optimizing every aspect of the patient's treatment and postoperative recovery. The pathway is initiated at the time of the patient's referral and gives a goal-directed approach to the physiological work-up, staging, treatment, and recovery. This ECP has undergone five revisions up to 2012; the current perioperative standardized pathway is shown in Fig. 1. The evolution of the ECP has involved all services and subspecialties involved in the multidisciplinary treatment at our institution. It is important for surgeons to move their focus away from small modifications of the operation to improving all aspects of process and multidisciplinary care. The hypothesis under investigation is whether the implementation and evolution of an esophagectomy care pathway will result in the long-term and sustained

improvement in postoperative outcomes. The further aim of this study is to characterize important modifications within the esophagectomy care pathway that may have been responsible in part for any improvements observed in postoperative outcomes over the 20-year study period.

Materials and Methods

Information was prospectively collected on all patients undergoing esophagectomy between 1991 and 2012 and retained in an institutional review board (IRB)-approved database. Data points collected included preoperative demographics, clinical stage (AJCC 7th edition), treatment approach, and postoperative outcomes. Approach to clinical staging did vary during the study period. From 1991 to 2000, computerized tomography (CT) and endoscopic ultrasound (EUS) formed the mainstay of clinical staging and these modalities were applied to all patients through the study period. Positron emission tomography (PET) scanning became a routine part of clinical staging from 2000. From 2007, patients with gastro-esophageal junctional tumors that had a greater than 50 % gastric component also underwent a diagnostic laparoscopy and peritoneal lavage as part of their clinical staging investigations. Chemoradiotherapeutic regimes did vary as the majority of patients received their neoadjuvant therapy at their referring institution (81 % of patients since 2000); however, the most commonly utilized regime was 5-fluorouracil and cisplatin with the most common concurrent radiation dose being 50.4Gy.

Patients were divided into four groups based upon the year of esophagectomy (Gp1 1991–1996, Gp2 1997–2002, Gp3 2003–2007, and Gp4 2008–2012). The groups were compared with respect to preoperative comorbidities, clinical staging, neoadjuvant therapy use, operative outcomes, postoperative complications including maximum Accordion Severity Grading System score (ASGS), and mortality (in-hospital, 30, and 90 days). Statistical analysis to assign significance was utilized to compare outcomes from Gp1 (1991–1996) and Gp4 (2008–2012), in order to demonstrate changes in management and outcomes over time. Perioperative management and multidisciplinary coordination was directed by the ECP, which helped to standardize goals. The ECP also provided targeted and measurable goals involving extubation, hemodynamics, mobilization, nutrition, and discharge (see Fig. 1). Goals of the current pathway include immediate extubation, mobilization on the day of surgery with independent mobility achieved by postoperative day 4–5, initiation of enteric feeding via the jejunostomy on postoperative day 1 with an increasing rate to achieve nutritional goals by postoperative day 2–3, and a discharge goal of postoperative day 6–7.

Dichotomous data were analyzed by the chi-square or Fisher exact tests, and continuous variables were analyzed

Initial Contact	Initial Assessment /Staging	Pre-op Arrangement /Restaging	Surgery	POD 0 PPICU "step-down unit"	POD 1 Surgical ward	POD 2-3 Surgical ward	POD 4-5 Surgical ward	POD 6-7 Surgical ward / DC									
Phone interview Within 24 hr of referral -PMH -Current Symptoms -Assess Dysphagia and weight loss -Current Investigations -Travel Arrangements Ensure previous notes, investigations, films, pathology are available Preparation of tailored patient schedule ->physiologic and staging investigations completed in 48hr	Consultations Oncology -Radiation Oncology -Cardiology -Thoracic Surgery -Gastroenterology Investigations -CT -PET/CT -EGD, EGD-US -Path review -PFT -EGD + US -Tumor Board Nutritional Assessment Tailored according to -Tumor / Barrett characteristics -Patient Physiology -Previous Surgery -Conduit Availability Thoracic Tumor Board Within 7 days of consult Communicate results following day to patient and staging referring physician. Initiate neoadjuvant therapy Appropriate Patients with CT2-4, N1-4, Mx	Restaging 2-4 weeks following neoadjuvant therapy -CT -EGD, EGD-US -EGD + US -Tumor Board Surgical Approach Tailored according to -Tumor / Barrett characteristics -Patient Physiology -Previous Surgery -Conduit Availability On table epidurogram to verify correct epidural placement Immediate Post-op Anesthesia -PCA with pain service monitoring, no bolus Admit to PPICU (Step-down unit)	Thoracic epidural placed preoperatively Basal rate 3ml/hr Bupivacaine 0.05% Hydromorphone 10ug/ml Single dose 2nd Generation Cephalosporin Selective SQ Heparin Minimize blood loss / transfusion No routine central venous catheter Restrictive fluid administration intra-operatively Target 1.5-2l crystalloids Immediate Extubation	Medication <ul style="list-style-type: none"> Antiemetic Protocol Continue Beta Blockers, and ASA IV PPI – Monitor gastric pH 	Pain control <ul style="list-style-type: none"> PCA ± PCA Avoid bolus adjustment Consider -IV Acetaminophen 	Positioning and Mobilization <ul style="list-style-type: none"> Keep HOB>45° Compress Stocking Chair 4-6/hr postop 100ft walk 12-14/hr post-op 	Hemodynamics & Respiratory <ul style="list-style-type: none"> Avoid CPAP Maintain MAP>70mmHG Treat MAP>70mmHG Decrease epidural rate/no bolus Epinephrine drip Infuse up to 2l crystalloid 	Imaging <ul style="list-style-type: none"> Recovery room post-op CXR 	Drainage tube <ul style="list-style-type: none"> CD to 20 cm suction NGT – low cont. wall suction Foley Catheter 	Nutrition <ul style="list-style-type: none"> IV Fluid basal rate 70cc/hr D5/1/NS MAP>70 consider fluid bolus (max 2L) 	Consult <ul style="list-style-type: none"> Pain service PSY elderly patients Selective RT PT mobilization 	<ul style="list-style-type: none"> Continue Beta Blocker + ASA Selective start routine meds down J-tube IV PPI (esomeprazole) 	<ul style="list-style-type: none"> PCA ± PCA Consider Ketorolac 	<ul style="list-style-type: none"> Keep HOB>45° Compress Stocking In chair 2-3 hr/day 200ft walks 6-8/day 	<ul style="list-style-type: none"> Reinitialize CPAP if needed 	<ul style="list-style-type: none"> Consider Erythromycin if delayed gastric emptying Continue oral PPI Transition all meds to J-tube 	<ul style="list-style-type: none"> Oral PPI All routine meds and analgesics given liquid or crushed via J-tube
				1.Description Surgery & pathway	2.Description Surgery & pathway	3.Description Surgery & pathway	Critical measurable Goals	Immediate Extubation Maintain MAP >70mmHG Mobilize Day of Surgery	Transfer to Ward Initiate Enteric Feeding Mobilize 2-4 Walks	J-Tube Feeding to Goal Assess Gastric Emptying Remove NG and Chest Drain	Independent Mobility Start Oral Intake	Discharge Day 6-7					
				* oral protocol: Ward nurse direct advancement of liquid oral intake from 15cc/hr ≥ ½ Cup/hr				<small> PPM past medical history, CT computed tomography, PET/CT positronemissiontomography w CT, EGD gastroscopy, US ultrasound, PFT pulmonary function test, PPICU post procedural intensive care unit, PCA percutaneous epidural analgesia, PCA patient controlled analgesia, POD post-operative day, HOB head of the bed, MAP middle arterial pressure, CXR chest x ray, CD chest drain, NGT nasogastric tube, PSY psychiatric consult, RT respiratory therapy, IV intravenous, PPI proton pump inhibitor, J-tube jejunostomy, NSAID non steroidal anti-inflammatory drug, D/C discharge, J/D follow-up </small>				Routine post discharge goals -Represent at MTB (recommendations to referring and primary care MD's) -J-tube removed 4-12 weeks post discharge -Q.O.L and patient satisfaction assessment -Commit to 3 years follow-up					

Fig. 1 Virginia Mason Medical Center Esophagectomy Clinical Pathway

by Student’s *t* test or the Mann–Whitney *U* test and presented as median (range). All *P* values reported were two-tailed, and *P*<0.05 was considered statistically significant. Multi-variable linear regression analysis was performed for length of hospital stay as the dependent variable. Independent variables included in this analysis were year of surgery, age, body mass index, Charlson comorbidity index, American Society of Anesthesiology (ASA) score, surgical technique (left thoracoabdominal, Ivor Lewis, transhiatal, or retrosternal), use of neoadjuvant chemoradiotherapy, or definitive chemoradiotherapy (SPSS, version 18, Chicago, IL). The learning curve for and change over time in estimated blood loss, operating room fluid administration, and length of hospital stay were assessed using cumulative sum (CUSUM) analysis. CUSUM analysis is a well-established statistical methodology to assess the learning curve in the uptake of any new surgical process or procedure. It has previously been used to evaluate the learning curve associated with laparoscopic colorectal surgery, laparoscopic cholecystectomy, robotic Roux-en-Y gastric bypass, and laparoscopic paraesophageal hernia repair.^{28–31} The CUSUM is the running total of the differences between the individual data points and the mean for all the data points. The cases were ordered chronologically from the first case to the last case.

Results

Five hundred and ninety-five consecutive patients were included, and the number of esophageal resections in each group

increased over time (Gp1 92, Gp2 159, Gp3 161, and Gp4 183). Patient age and gender remained consistent; however, body mass index (BMI) increased over time (26 (18–38) [Gp1] to 27 (17–42) [Gp4]; *P*=0.03) (Table 1). Patients in later groups presented with a greater burden of medical comorbidities, including diabetes, hypertension, liver disease, and thromboembolic disease (DVT/PE). This was further reflected by an increase in Charlson comorbidity index (4 (0–7) [Gp1] to 5 (0–10) [Gp4]; *P*=0.02), despite no significant difference observed in mean American Society Anesthesiologists (ASA) grade.

The incidence of adenocarcinoma (72.8 % [Gp1] to 80.3 % [Gp4]; *P*=0.21) and squamous cell carcinoma (14.1 % [Gp1] to 12 % [Gp4]; *P*=0.76) remained consistent over time. The distribution of clinical stage also remained consistent, with the exception of an increase in clinical stage III patients undergoing esophagectomy (28.3 % [Gp1] to 44.3 % [Gp4]; *P*=0.01). There was an increase in the use of neoadjuvant treatments including an increase in neoadjuvant chemoradiotherapy (19.6 % [Gp1] to 60.7 % [Gp4]; *P*<0.0001), definitive chemoradiotherapy followed by salvage esophagectomy (0 % [Gp1] to 4.9 % [Gp4]; *P*=0.03), and endoscopic treatment followed by surgery (0 % [Gp1] to 14.8 % [Gp4]; *P*<0.0001) (Table 2). Nutritional assessment was assigned greater significance during the study period as reflected by an increased insertion of preneoadjuvant chemoradiation surgical jejunostomies (0 % [Gp1] to 21.3 % [Gp4]; *P*<0.0001). During the 20-year study period, there was a change in surgical approach with an increase in Ivor Lewis esophagectomy

Table 1 Evolution in patient demographics; age and medical comorbidities (1991–2012)

Variable	1991–1996 (group 1)	1997–2002 (group 2)	2003–2007 (group 3)	2008–2012 (group 4)	P value*
Case no.	92	159	161	183	
Patient age (range)	64 (16–90)	64 (15–89)	66 (32–89)	66 (37–90)	0.17
M-to-F ratio (%)	74 (80.4)	134 (84.3)	127 (78.9)	141 (77)	0.63
BMI (range)	26 (18–38)	25 (17–41)	26 (18–45)	27 (17–42)	0.03
Charlson (–age) (range)	2 (0–4)	2 (0–6)	2 (0–5)	2 (0–7)	0.005
Charlson (+age) (range)	4 (0–7)	4 (0–9)	5 (1–8)	5 (0–10)	0.02
ASA (range)	3 (1–4)	3 (2–4)	3 (2–4)	3 (1–5)	0.07
Arrhythmia (%)	9 (9.8)	11 (6.9)	14 (8.7)	21 (11.5)	0.83
IHD (%)	12 (13.0)	34 (21.4)	19 (11.8)	31 (16.9)	0.51
Diabetes (%)	2 (2.2)	2 (1.3)	3 (1.9)	29 (15.8)	0.0004
Hypertension (%)	11 (12.0)	29 (18.2)	39 (24.2)	90 (49.2)	<0.0001
Liver disease (%)	0 (0)	2 (1.3)	3 (1.9)	9 (4.9)	0.03
Renal insufficiency (%)	1 (1.1)	1 (0.6)	6 (3.7)	6 (3.3)	0.43
COPD (%)	7 (7.6)	11 (6.9)	4 (2.5)	19 (10.4)	0.60
DVT/PE (%)	0 (0)	0 (0)	0 (0)	11 (6)	0.02
PVD (%)	1 (1.1)	3 (1.9)	4 (2.5)	8 (4.4)	0.28

M-to-F ratio male-to-female ratio, *BMI* body mass index (kg/m²), *Charlson* median Charlson comorbidity index, *ASA* median American Society of Anesthesiology grade, *IHD* ischemic heart disease, *COPD* chronic obstructive pulmonary disease, *DVT/PE* deep vein thrombosis/pulmonary emboli, *PVD* peripheral vascular disease

(8.7 % [Gp1] to 39.9 % [Gp4]; *P*<0.0001), a reduction in cervical anastomosis (67.4 % [Gp1] to 45.9 % [Gp4]; *P*=0.001), and utilization of pyloric drainage procedures (9.8 % [Gp1] to 2.2 % [Gp4]; *P*=0.01).

Analysis of perioperative outcomes revealed a consistent reduction in administration of intraoperative intravenous

fluids (5,000 mL (2,000–11,100) [Gp1] to 2,800 mL (1,200–7,900) [Gp4]; *P*<0.0001), and a reduction in estimated blood loss (300 mL (75–2,000) [Gp1] to 150 mL (50–500) [Gp4]; *P*<0.0001) (Table 3). Immediate extubation was performed in all but two patients during the study period (Table 3). Evolution of the standardized clinical pathway was associated with a

Table 2 Evolution in tumor stage and multimodality treatment of esophageal cancer (1991–2012)

Variable	1991–1996 (group 1)	1997–2002 (group 2)	2003–2007 (group 3)	2008–2012 (group 4)	P value*
Case no.	92	159	161	183	
Adenocarcinoma (%)	67 (72.8)	117 (73.6)	121 (75.2)	147 (80.3)	0.21
SCC (%)	13 (14.1)	25 (15.7)	21 (13)	22 (12)	0.76
Clinical stage I (%)	13 (14.1)	19 (11.9)	30 (18.6)	28 (15.3)	0.94
Clinical stage II (%)	36 (39.1)	58 (36.5)	59 (36.6)	56 (30.6)	0.21
Clinical stage III (%)	26 (28.3)	41 (25.8)	44 (27.3)	81 (44.3)	0.01
Neoadjuvant chemotherapy (%)	8 (8.7)	29 (18.2)	19 (11.8)	11 (6)	0.56
Neoadjuvant chemoradiotherapy (%)	18 (19.6)	40 (25.2)	53 (32.9)	111 (60.7)	<0.0001
Definitive chemoradiotherapy (%)	0 (0)	0 (0)	2 (1.2)	9 (4.9)	0.03
PreTx jejunostomy (%)	0 (0)	0 (0)	0 (0)	39 (21.3)	<0.0001
PreTx therapeutic endoscopy (%)	0 (0)	0 (0)	12 (7.5)	27 (14.8)	<0.0001
Left thoracoabdominal esophagectomy (%)	77 (83.7)	92 (57.9)	77 (47.8)	94 (51.4)	<0.0001
Ivor Lewis esophagectomy (%)	8 (8.7)	41 (25.8)	76 (47.2)	73 (39.9)	<0.0001
Transhiatal esophagectomy (%)	6 (6.5)	24 (15.1)	6 (3.7)	14 (7.7)	0.93
Cervical anastomosis (%)	62 (67.4)	98 (61.6)	76 (47.2)	84 (45.9)	0.001
Pyloric drainage (%)	9 (9.8)	7 (4.4)	2 (1.2)	4 (2.2)	0.01
Feeding jejunostomy (%)	46 (50)	150 (94.3)	147 (91.3)	144 (78.7)	<0.0001

SCC squamous cell carcinoma, *PreTx* pretreatment

Table 3 Evolution in clinical outcome following esophagectomy (1991–2012)

Variable	1991–1996 (group 1)	1997–2002 (group 2)	2003–2007 (group 3)	2008–2012 (group 4)	P value*
Case no.	92	159	161	183	
EBL (mL) (range)	300 (75–2,000)	175 (50–600)	150 (50–450)	150 (50–500)	<0.0001
OR fluids (mL) (range)	5,000 (2,000–11,100)	4,200 (1,900–8,100)	3,500 (900–8,000)	2,800 (1,200–7,900)	<0.0001
Immediate extubation (%)	92 (100)	157 (98.7)	161 (100)	183 (100)	
LOS (days) (range)	10 (5–50)	10 (6–33)	9 (6–35)	8 (5–115)	<0.0001
ICU stay (days) (range)	2 (1–30)	1 (1–12)	1 (1–19)	1 (0–22)	<0.0001
Lymph nodes resected (range)	11 (2–60)	15 (3–65)	16 (2–39)	21 (1–49)	<0.0001
Positive RM (%)	8 (8.7)	9 (5.7)	11 (6.8)	7 (3.8)	0.16
Anastomotic leak (%)	3 (3.3)	7 (4.4)	4 (2.5)	12 (6.6)	0.40
Re-operation (%)	5 (5.4)	4 (2.5)	6 (3.7)	3 (1.6)	0.12
AF (%)	12 (13.0)	14 (8.8)	32 (19.9)	44 (24)	0.03
Pneumonia (%)	4 (4.3)	12 (7.5)	13 (8.1)	28 (15.3)	0.009
Chyle leak (%)	4 (4.3)	7 (4.4)	4 (2.5)	5 (2.7)	0.49
Delirium (%)	3 (3.3)	16 (10.1)	22 (13.7)	15 (8.2)	0.19
In-hospital mortality (%)	0 (0)	1 (0.6)	0 (0)	1 (0.5)	>0.99
30-day mortality (%)	0	1 (0.6)	1 (0.6)	1 (0.5)	>0.99
90-day mortality (%)	0	1 (0.6)	1 (0.6)	2 (1.1)	>0.99
Max ASGS	2 (1–5)	2 (1–5)	2 (1–5)	2 (1–6)	0.50

EBL estimated blood loss, OR operating room, LOS length of hospital stay, ICU Intensive Care Unit, RM resection margin, AF atrial fibrillation, ASGS accordion severity grading system score

significant reduction in median length of hospital stay (10 (5–50) [Gp1] to 8 (5–115) [Gp4] days; $P<0.0001$) and in median length of intensive care unit stay (2 (1–30) [Gp1] to 1 (0–22) [Gp4] days; $P<0.0001$). Multivariate linear regression analysis demonstrated the only variable significantly associated with increased length of hospital stay was a Charlson comorbidity index score of 5 or greater (odds ratio=3.17; 95 % c.i.=0.13 to 17.54; $P=0.002$). The incidence of in-hospital and 30-day mortality remained under 1 % throughout the study period. Postoperative complications remained consistent over time, with the exception of increases in atrial fibrillation and pneumonia (Table 3). The average maximum ASGS for postoperative complications in each group also remained consistent over time. Analysis of postoperative pathology revealed no significant difference in the incidence of positive resection margins over time; however, there was a consistent increase in the number of lymph nodes harvested (11 (2–60) [Gp 1] to 21 (1–49) [Gp4]) (Table 3).

CUSUM analysis demonstrated that estimated blood loss (Fig. 2) reduced at a fast rate to reach the mean value for the dataset at approximately case 120 and has steadily declined at a slower rate since then. CUSUM analysis for operating room fluid administration (Fig. 3) showed that there was a steady decline over the 20-year study period, reaching the mean value at approximately case 310. CUSUM analysis also showed a steady reduction in length of hospital stay (Fig. 4) over the

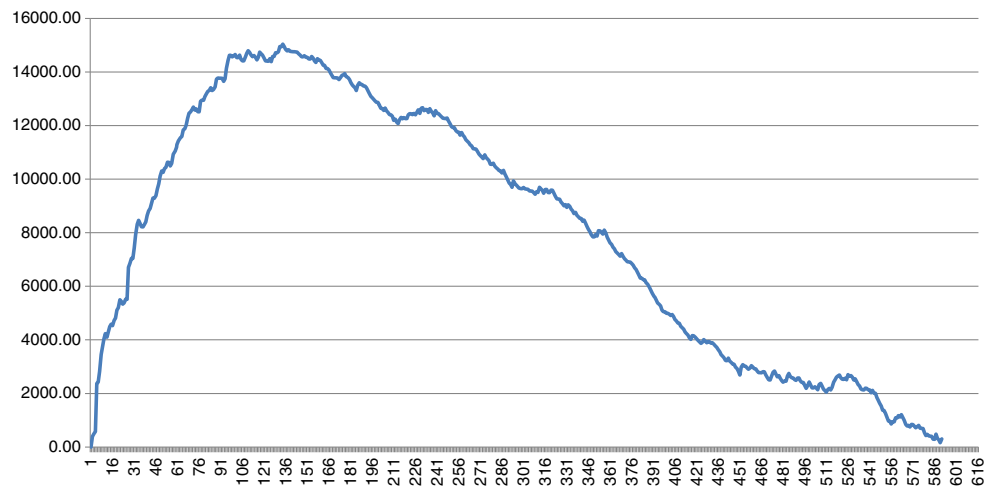
study period reaching a mean at approximately case 175 (one case was an extreme outlier in group 4 and was therefore excluded from the CUSUM analysis).

Discussion

The applications of standardized clinical pathways and enhanced recovery programs have been demonstrated to be associated with a reduction in postoperative mortality.³² Standardized clinical pathways provide a template for all medical personnel interacting with patients, and outline an individualized goal-directed recovery for each patient. As demonstrated by the current version of the ECP, they are often multifaceted, attempting to standardize all aspects of patient care including preoperative assessment and communication, procedural selection, intraoperative management, and postoperative care (Fig. 1). Previous studies have demonstrated that standardized clinical pathways can reduce length of stay and costs in the setting of esophagectomy^{33–35} as well as other oncologic and vascular surgeries.^{36–38} The hypothesis under investigation is that the implementation and evolution of an esophagectomy care pathway will result in the long-term and sustained improvement in postoperative outcomes.

Specific goals within the pathway that evolved during the period of study (see Fig. 1) included the following:

Fig. 2 CUSUM curve demonstrating progressive improvement in estimated blood loss



- Improving preoperative patient and family education regarding pathway targets.
- Adapting surgical approach according to individual presenting patient characteristics, i.e., in patients with preoperative cardiac disease, preferentially using a right thoracotomy so as to reduce cardiac manipulation and postoperative arrhythmias that are seen with a left thoracotomy or transhiatal approach in this patient cohort.
- Developing approaches to minimizing blood loss and perioperative fluid administration.
- Optimizing perioperative pain regimens to maintain targeted postoperative hemodynamics but facilitating postoperative mobilization goals to ultimately mobilize patients on the day of surgery, with independent mobility by postoperative day 4–5.
- Assessment and monitoring of nutrition prior to neoadjuvant therapy and esophagectomy.
- Earlier application of enteric feeding currently on postoperative day 1 and nasogastric tube removal on postoperative day 2–3.
- Modifying targeted discharge goals from 12 to 14 days in the early 1990s to 6–7 days in the current era.

Over the 20-year period studied, there were significant changes in the demographics of patients undergoing surgical resection for esophagectomy with an increase in average age, body mass index, and Charlson comorbidity index. Furthermore, a multimodal treatment approach was utilized more commonly, as reflected by significant increases seen in the use of neoadjuvant and definitive chemoradiotherapy and endoscopic therapy. Changes were also observed in the intraoperative management of these patients, which included altered procedural approach in addition to a reduction in intraoperative fluid administration and operative blood loss (Figs. 2 and 3). Technical evolution in this series did not include minimally invasive esophagectomy, although the outcomes are comparable to any contemporary minimally invasive series (see Table 3).^{39,40}

Significant improvements were noted in length of ICU (2 (1–30) to 1 (0–22) days) and hospital stay (10 (5–50) to 8 (5–115) days) (Fig. 4). However, the starting average period of ICU (2 days) and hospital stay (10 days) in the early 1990s was comparable to virtually any other series or national audit.^{41,42} This indicates a commitment to multidisciplinary care, even in the early years of the study, and patients in the

Fig. 3 CUSUM curve demonstrating progressive improvement in operating room intravenous fluid administration

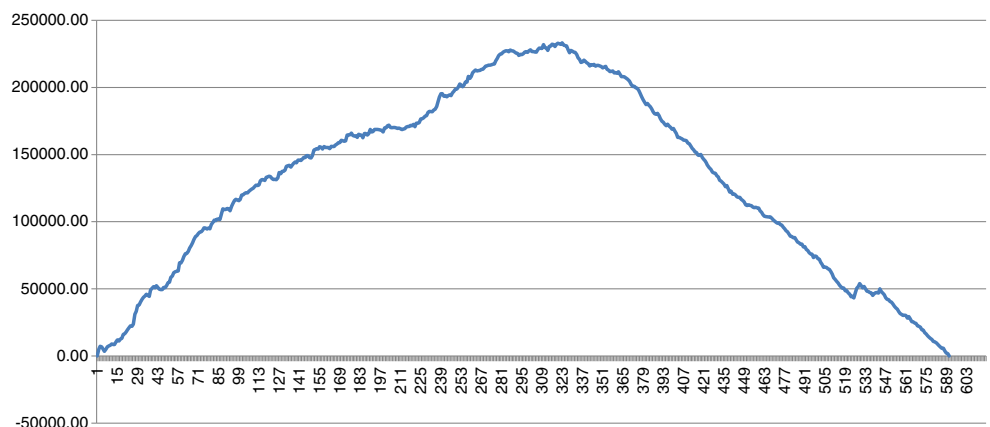
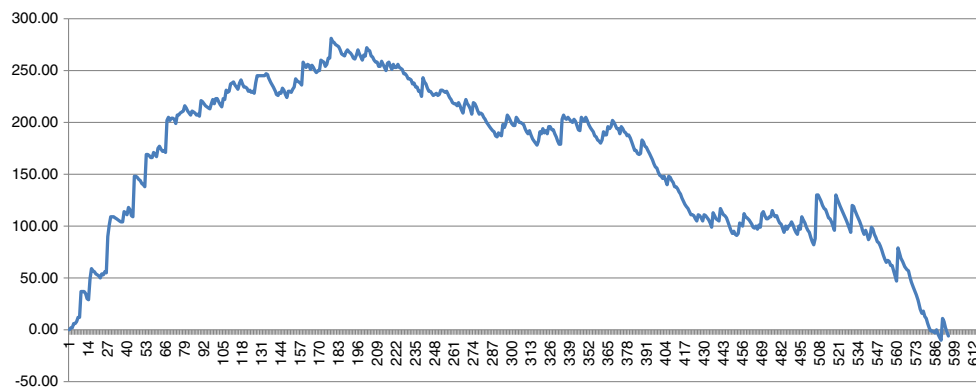


Fig. 4 CUSUM curve demonstrating progressive improvement in length of hospital stay



earliest component of the study period benefited from management under the pathway as it existed at that time. Most other reports of clinical pathways and enhanced recovery pathways have documented an improvement in mortality.^{25,26} Possibly the greatest expression of the success of the standardized pathway was the maintenance of an in-hospital mortality rate of under 1 % (see Table 3) throughout the 20 years of study, in spite of increasing levels of comorbidity and increasing application of neoadjuvant chemoradiation. Previous reports of enhanced recovery protocols have highlighted the challenges that elderly patients undergoing esophagectomy represent. Cerfolio et al.²⁶ demonstrated that 75 % of patients over 70 years of age failed their “fast track” protocol. However, we have previously published that selected patients over the age of 80 years can undergo surgical treatment for esophageal cancer within a standardized clinical pathway, and have a similar clinical outcome to younger patients.⁴³

All patients included in this study were presented at a multidisciplinary tumor board. Patient presentation at multidisciplinary tumor board included assessment of patient demographics including comorbidities, tumor characteristics, and more recently, nutritional status, to allow appropriate allocation of multimodality treatment. There was an increase in the utilization of pretreatment jejunostomy (0 to 21.3 %) during the study period; this is a highly important evolutionary aspect of the pathway to prevent malnutrition during neoadjuvant chemoradiotherapy, which may adversely impact surgical resection.

There were also significant changes in operative approach during the study period with an increase in two-stage Ivor Lewis technique. This reflects an emphasis in recent years on tailoring the surgical approach to tumor location as well as patient physiological status. In patients with preoperative cardiac arrhythmias, history of congestive heart failure, or ischemic heart disease, an Ivor Lewis approach was preferred so as to avoid the cardiac manipulation, which has been typically associated with intraoperative hypotension in other technical approaches.⁴⁴ There was also an increase in the utilization of perioperative jejunostomies (50 to 100 %), as patients are typically discharged on fluids only, by mouth and jejunal

feeding with a progressive return to a normal oral diet in the outpatient setting. This approach significantly improves the likelihood of achieving targeted discharge goals. During the study period, there was also a reduction in intravenous fluid administration⁴⁵ and operative blood loss. Avoiding blood loss and transfusions has clearly been associated with improved outcomes including complications, costs, and potentially survival.⁴⁶

It is important to acknowledge that during the 20-year study period, there have been significant advancements in anesthesia, pain service, and intensive care that may, in part, be responsible for some of the observed improvements in outcomes. However, utilization of a step-down unit, rather than the regular ICU, went from 0 to 100 % over the study period. In addition, ICU nursing and anesthesia staffs have both been involved in the evolution of the clinical pathways as part of the multidisciplinary approach to pathway revision. Furthermore, anesthesia has developed their own “standard work” for pre-, intra-, and post-operative care of the esophagectomy patient. There was also an early identification of the importance of immediate extubation, with only two patients during the study period not extubated in the operating room. Immediate extubation facilitates early mobilization, which initially began in 1991 with a goal of mobilization on postoperative day 2, and currently is aimed at mobilization on the day of surgery. Further targets have evolved during the study period, including discharge target that was set initially in 1991 at postoperative day 12–14, and now is set at postoperative day 6–7 (see Fig. 1), which has been achieved in 51 % of patients over the last year of study.

There are limitations associated with this study that must be acknowledged when interpreting the results presented here. Firstly, these are the results from a single surgeon practicing at a single institution, and therefore, it may be argued that they lack applicability to the widespread esophageal surgical community. However, we have previously documented accelerated improvement in short-term outcomes in other institutions and within other health systems by the translocation of the clinical pathway to a high-volume upper gastro-intestinal unit in the UK.⁴⁷ A further limitation is that the study has evaluated

outcomes over a long period of time, and there have been many transitions in other specialty areas that may, in part, be responsible for the improvement in outcomes seen; distinguishing these from one another is impossible given the study design. The clear strength of this study lies in the prospective data collection process that involved all stakeholders within this single institution that has allowed a comprehensive evaluation of clinical outcome over the period of study. The multidisciplinary involvement and regular assessment of measurable outcome goals facilitated identifying issues that were impeding achievement of pathway targets. It also allowed refining pathway goals to improve treatment quality and efficiency. This evolution has been aided by the fact that Virginia Mason Medical Center has been a leader in the introduction of “Lean Thinking” to medical delivery, which aids the initiation and acceptance of new and collaborative treatment protocols.⁴⁸ The continuous evaluation of outcomes and multidisciplinary approach to the implementation and revision of the standardized clinical pathway is of great importance to produce the continuing improvement in outcomes seen in this study.

Conclusion

The results of this study demonstrate the value to the implementation and revision of esophagectomy clinical pathways for the treatment of esophageal malignancy. These pathways must be multidisciplinary in nature and begin at the time of referral to ensure adequate assessment, optimization, and individualized selection of treatment approach. Ongoing assessment of outcomes following treatment remains important to identify areas for targeted improvement in order to continue to optimize clinical outcome following esophagectomy.

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