Cost-benefit analysis of an enhanced recovery protocol for pancreaticoduodenectomy

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Background: Enhanced recovery after surgery (ERAS) programmes have been shown to decrease complications and hospital stay. The cost-effectiveness of such programmes has been demonstrated for colorectal surgery. This study aimed to assess the economic outcomes of a standard ERAS programme for pancreaticoduodenectomy.

Methods: ERAS for pancreaticoduodenectomy was implemented in October 2012. All consecutive patients who underwent pancreaticoduodenectomy until October 2014 were recorded. This group was compared in terms of costs with a cohort of consecutive patients who underwent pancreaticoduodenectomy between January 2010 and October 2012, before ERAS implementation. Preoperative, intraoperative and postoperative real costs were collected for each patient via the hospital administration. A bootstrap independent t test was used for comparison. ERAS-specific costs were integrated into the model.

Results: The groups were well matched in terms of demographic and surgical details. The overall complication rate was 68 per cent (50 of 74 patients) and 82 per cent (71 of 87 patients) in the ERAS and pre-ERAS groups respectively (P = 0.046). Median hospital stay was lower in the ERAS group (15 *versus* 19 days; P = 0.029). ERAS-specific costs were €922 per patient. Mean total costs were €56 083 per patient in the ERAS group and €63 821 per patient in the pre-ERAS group (P = 0.273). The mean intensive care unit (ICU) and intermediate care costs were €9139 and €13 793 per patient for the ERAS and pre-ERAS groups respectively (P = 0.151).

Conclusion: ERAS implementation for pancreaticoduodenectomy did not increase the costs in this cohort. Savings were noted in anaesthesia/operating room, medication and laboratory costs. Fewer patients in the ERAS group required an ICU stay.

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Introduction

Pancreatic surgery, in particular pancreatic head resection for cancer, remains associated with high morbidity rates and poor long-term survival¹. As multimodal therapies are nowadays considered the most promising to improve outcomes, a postoperative course with the fewest possible complications is key for a timely start of adjuvant therapies². From this point of view, pancreatic surgery represents an ideal target for a clinical approach considering enhanced recovery after surgery (ERAS) principles.

ERAS protocols consist of multimodal perioperative management that aims to improve postoperative recovery³. Reduction of perioperative morbidity is the main goal, and

a shortened length of hospital stay is just one of the effects. ERAS protocols encompass the interval before operation until the day of discharge. In recent years, ERAS protocols have been implemented gradually for various types of surgery with important clinical benefits^{4–9}, for example in colorectal surgery.

Following the publication of dedicated ERAS guidelines¹⁰ for pancreaticoduodenectomy (PD) by the ERAS[®] Society, enhanced recovery protocols have been developed for major pancreatic surgery. Initial studies have shown the feasibility and safety of ERAS for pancreatic surgery^{11–13}, including reduced hospital stay without increased readmission or mortality rates^{14–16} and fewer complications¹⁷. Although clinical benefit to the patient

remains the primary aim, cost saving is of increasing importance as cost containment represents a serious issue in most national healthcare systems. So far, ERAS protocols have been showed to be beneficial in terms of costs for colorectal surgery¹⁸, but data for pancreatic surgery are lacking. The primary aim of this study was to evaluate the cost–benefit ratio of an ERAS protocol for PD. Secondary aims were to assess complication rates and length of hospital stay.

Methods

An ERAS pathway for pancreatic surgery based on the recommendations of the ERAS[®] Society¹⁰ was implemented in the Department of Visceral Surgery, University Hospital of Lausanne, CHUV, Lausanne, Switzerland, in October 2012 (*Table 1*). ERAS for colorectal surgery had been implemented in this department in June 2011, so the dedicated ERAS team (composed of surgeons, anaesthetists, nurses and nutritionists) as well as the medical and nursing staff were already familiar with ERAS protocols and their related patient care. The department is certified as a centre of excellence by the ERAS[®] Society (www.erassociety.org) and contributed actively to the establishment of the ERAS pancreatic surgery guidelines.

Patient groups

A prospective ERAS cohort was compared with a retrospective control group (pre-ERAS). The ERAS group comprised consecutive patients who underwent PD in the first 2 years after implementation of ERAS for pancreatic surgery, from October 2012 to October 2014. The pre-ERAS group (control group) included consecutive patients who underwent PD between January 2010 and September 2012. There were no exclusion criteria. The nutritional status of the patients was assessed by means of nutritional risk screening, taking into account the malnutrition state and severity of disease¹⁹.

Postoperative outcomes and discharge criteria

Complications were graded according to the Dindo–Clavien classification²⁰. Minor complications were defined as grade I–II and major as grade III–IV. Postoperative mortality (grade V) was defined as death during the first 30 days after the index operation or during the hospital stay. Delayed gastric emptying, pancreatic fistula and haemorrhage were defined according to the International Study Group of Pancreatic Surgery^{21–23}. Intra-abdominal abscess was defined as organ or space

surgical-site infection as described by the Centres for Disease Control and Prevention²⁴. Bile leak was defined by the presence of bile in the drains. Wound infection was defined as a superficial or deep incisional surgical-site infection²⁴. Length of hospital stay was calculated as the interval between day of operation and discharge from hospital. Patients were discharged when pain was controlled by oral medication, when they were autonomous (in terms of ambulation, showering, eating, getting out of bed), and when oral diet was well tolerated.

Cost analysis

Detailed costs for each patient were retrieved via the administration service of the hospital accounting database. Costs were divided into intraoperative and preoperative/postoperative costs. They were real costs and not estimated values.

The intraoperative costs included the cost of disposable materials used in the operating room (OR), as well as anaesthesia and OR costs. Anaesthesia costs included the costs of the anaesthetist (counted per minute and based on the duration of anaesthesia), anaesthesia nurse (counted per minute and based on the duration of anaesthesia), drugs and materials used for anaesthesia. OR costs were based on the duration of OR occupation.

Preoperative and postoperative expenditure included the following costs: intensive care unit (ICU) and intermediate care unit (cost per day), medical care, nursing care, physiotherapy, drugs, blood transfusion and testing, laboratory tests, radiology, pathology, housing, administration and other (social work, priest and occupational therapy). Medical care included surgeon costs, medical costs (internal consultations, doctors' clinical activities) and the costs of other non-operative procedures (for example drainage and endoscopy). Nursing care costs were those of the standard ward, not comprising ICU and intermediate care costs, and were based on a list of 249 actions of care that determine the duration of nursing required for each patient (Project Research in Nursing)²⁵. Housing costs (hosting costs) were counted per day in hospital, whereas administrative costs were accounted per admission.

Cost-minimization analysis

A cost-minimization analysis was performed from a healthcare provider point of view in order to assess the hospital cost savings per patient. It corresponded to the mean difference in costs per patient between ERAS and pre-ERAS minus the ERAS-specific costs per patient. ERAS-specific costs included costs of the ERAS database and the full-time

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discharge	Glycaemic control	Insulin protocol in the event of hyperglycaemia	Not used routinely
Mobilization Out of bed for at least 2 b on day of surgery; at least 8 b No protocol	Laxatives	, , , , , , , , , , , , , , , , , , ,	Not used routinely
out of bed from day 1	Mobilization	Out of bed for at least 2 h on day of surgery; at least 8 h out of bed from day 1	No protocol
Systematic audit Audit meeting every 2 months None	Systematic audit	Audit meeting every 2 months	None

Table 1	Perioperative	procedures used	before and afte	r introduction	of the enhance	d recovery after surger	y protocol
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Adapted from reference 10. ERAS, enhanced recovery after surgery; LMW, low molecular weight; IPC, intermittent pneumatic compression; PONV, postoperative nausea and vomiting; POD, postoperative day.

ERAS-dedicated nurse (fixed costs), ERAS team meetings (fixed costs), carbohydrate drinks and patient logbooks.

Costs were obtained primarily in Swiss Francs (CHF) and were then converted to euros. The official exchange rate was CHF1 = €0.83 (current on 1 December 2014).

Sensitivity analysis

As some ERAS-specific costs are fixed and therefore independent of the number of patients, the ERAS-specific costs per patient will vary depending on the number of patients treated in the study. A sensitivity analysis was performed by varying the number of patients (\pm 50 per cent) in order to assess the effect of fluctuations in ERAS-specific costs per patient and to measure their impact on the cost-minimization analysis.

Statistical analysis

No power analysis was performed because it was estimated *a priori* that selecting a cohort of 70–80 consecutive patients treated according to an ERAS protocol would permit conclusions to be drawn. Approximately 40–50 PDs are performed per year at this institution, so it was decided that the study period after ERAS implementation would be 2 years. From previous studies, it is known that reimbursement changes often occur within a short time frame of 2-3 years, so comparability would be hampered.

Continuous variables were compared using Mann–Whitney U test or t test, depending on the data distribution and equality of variances. Discrete variables were compared by means of Fisher's exact test. The arithmetic mean was considered the most informative and explicit value from a decision-maker or pharmacoeconomic perspective,

 Table 2 Patient demographics and surgical characteristics

	ERAS group $(n = 74)$	Pre-ERAS group (n = 87)	P§
Age (years)*	67.5 (57-74)	67 (55–75)	0·861¶
Sex ratio (F:M)	39:35	31:56	0.082
Body mass index (kg/m ²)*	23.9 (22.1–26.7)	24.2 (22.1–27.3)	0.861¶
ASA grade			0.223
1–11	50 (68)	67 (77)	
III	24 (32)	20 (23)	
Active smoker	17 (23)	23 (26)	0.715
NRS score > 3	28 (38)	37 (43)	0.629
Procedure			0.102
Classical PD	71 (96)	87 (100)	
Pylorus-preserving PD	3 (4)	0 (0)	
Diagnosis			
Pancreatic ductal adenocarcinoma	45 (61)	53 (61)	0.998
Other cancer†	9 (12)	19 (22)	0.144
Benign lesion‡	20 (27)	15 (17)	0.183
TNM stage			0.970
1	3	3	
II	44	61	
III	4	5	
IV	2	2	
Unknown	1	1	
Neoadjuvant	1	1	1.000
treatment			

Values in parentheses are percentages unless indicated otherwise; *values are median (i.q.r.). †Duodenal adenocarcinoma, cholangiocarcinoma and malignant intraductal papillary mucinous neoplasm. ‡Chronic pancreatitis, cystadenoma, gastrointestinal stromal tumour, cystic dystrophy of duodenal wall in heterotopic pancreas, ampullary tumour and neuroendocrine tumour. ERAS, enhanced recovery after surgery; ASA, American Society of Anesthesiologists; NRS, nutritional risk screening26; PD, pancreaticoduodenectomy. §Fisher's exact test, except ¶Mann-Whitney U test.

and allowed resampling. The bootstrap method was used for resampling in the cost analysis. Different costs were compared using a bootstrap t test. P < 0.050 was considered statistically significant. Statistical calculations were performed using GraphPad Prism® version 5 for Mac OS X (GraphPad, San Diego, California, USA) and SPSS® version 19 for Mac (IBM, Armonk, New York, USA).

Results

The ERAS group included 74 patients and the pre-ERAS group 87 patients. The two groups were similar in terms of demographics and surgical characteristics (Table 2).

Perioperative outcomes

Median (i.q.r.) duration of operation was 326 (288-356) min for the ERAS group and 381 (319-462) min for

	ERAS group $(n = 74)$	Pre-ERAS group (n = 87)	P‡
Duration of operation (min)*	326 (288–356)	381 (319–462)	0.001§
Duration of anaesthesia (min)*	419 (374–458)	470 (410–539)	0·001§
Venous resection	16 (22)	29 (33)	0.115
Arterial resection	1 (1)	3 (3)	0.625
Concomitant procedure†	8 (11)	16 (18)	0.192
Delayed gastric emptying	20 (27)	29 (33)	0.397
Fistula	12 (16)	19 (22)	0.426
Complications	50 (68)	71 (82)	0.046
Minor (I–II)	18	30	0.171
Major (III–IV)	29	37	0.748
Death (V)	3	4	1.000
Length of hospital stay (days)*	15 (11–24)	19 (14–29)	0·029§
Length of ICU stay (days)*	0 (0-1)	1 (0-2)	0·002§
Length of intermediate care stay (days)*	5 (3–7)	5 (3-9)	0∙679§

Values in parentheses are percentages unless indicated otherwise; *values are median (i.q.r.). †Colonic resection, adrenalectomy, small bowel resection, wedge hepatic resection and hernia repair. ERAS, enhanced recovery after surgery; ICU, intensive care unit. ‡Fisher's exact test, except §Mann-Whitney U test.

the pre-ERAS group (P = 0.001), whereas the duration of anaesthesia was 419 (374-458) and 470 (410-539) min respectively (P = 0.001) (*Table 3*). The overall complication rate was 68 per cent (50 of 74 patients) in the ERAS group compared with 82 per cent (71 of 87) in the pre-ERAS group (P = 0.046). Rates of minor and major complications did not differ significantly between the groups (Table 3). The numbers of surgical and medical complications were similar in both groups (Table S1, supporting information).

Median (i.q.r.) length of hospital stay was significantly lower in the ERAS group (15 (11-24) days versus 19 (14–29) days before the introduction of ERAS; P = 0.029). ICU stay was also shorter in the ERAS group (0 (0-1) versus 1 (0-2) day respectively; P = 0.002), whereas median stay in the intermediate care unit was 5 days in both groups (P=0.679). With implementation of the ERAS protocol, patients were scheduled mostly for intermediate care, as criteria for patient admission to the intermediate care unit were changed (acceptance of patients needing intravenous noradrenaline (norepinephrine) application). The rate of adherence to the ERAS protocol (compliance) was 70 per cent in the ERAS group.

Cost analysis

The mean costs for each administrative item are shown in Table 4. The mean(s.d.) intraoperative costs per patient

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Table 4	Mean	individual	costs	by	administ	rative	subdivision

	Cost per patient (€)						
	ERAS	group*	Pre-ER	AS group*	Differ	ence (ERAS – pre-ERAS)†	P§
Total intraoperative	13 322(6769)	(11 961, 14 825)	14 089(6942)	(12 768, 15 681)	-767	(-2866, 1265)	0.494
Disposable materials	3619(4447)	(2787, 4734)	2341(1994)	(1971, 2796)	1279	(309, 2507)	0.052
Anaesthesia and operating room	9703(3607)	(8915, 10 590)	11 748(6009)	(10 628, 13 132)	-2045	(-3680, -674)	0.012
Total preoperative and postoperative	42 761(28 193)	(36 331, 49 048)	49 732(47 347)	(40 862, 60 976)	-6971	(-19 782, 3417)	0.268
ICU/intermediate care	9139(11 655)	(6552, 12 015)	13 793(24 192)	(9523, 19 702)	-4653	(-10 790, 785)	0.151
Medical care	12 979(20 570)	(8837, 18 161)	12 339(11 701)	(9914, 15 228)	640	(-4709, 6264)	0.823
Nursing care	8891(8793)	(6940, 10 912)	9205(7933)	(7695, 10 931)	-314	(-2978, 2219)	0.805
Physiotherapy	727(797)	(551, 928)	1116(2084)	(753, 1582)	-390	(-897, 41)	0.174
Medication	670(929)	(486, 900)	2487 (2833)	(1943, 3126)	-1816	(-2492, -1205)	0.001
Blood	1022(1949)	(623, 1505)	1221 (1812)	(898, 1656)	-199	(-800, 422)	0.528
Laboratory	2048(2011)	(1609, 2545)	3115 (3142)	(2500, 3846)	-1067	(-1870, -313)	0.012
Radiology	1638(2048)	(1192, 2121)	1806 (1770)	(1442, 2179)	-168	(-784, 457)	0.595
Pathology	1963(957)	(1763, 2209)	1709 (628)	(1582, 1839)	254	(14, 533)	0.059
Housing	3155 (2330)	(2601, 3742)	2448 (1897)	(2095, 2923)	706	(29, 1374)	0.037
Administration	346(22)	(341, 351)	298(29)	(291, 304)	48	(40, 56)	0.001
Other‡	183(274)	(123, 247)	196(450)	(124, 302)	-13	(-129, 89)	0.819
Total	56 083(3468)	(48 908, 63 636)	63 821(5680)	(53 803, 77 105)	-7738	(–22 714, 5015)	0.273

Values are *mean(s.d.) (95 per cent c.i.) and †mean (95 per cent c.i.). ‡Including social work, chaplain/priest and occupational therapy costs. ERAS, enhanced recovery after surgery; ICU, intensive care unit. §Bootstrap *t* test.

were €13 322(6769) and €14089(6942) in the ERAS and pre-ERAS groups respectively (P=0.494). Preoperative and postoperative costs per patient were €42 761(28 193) in the ERAS group and €49 732(47 347) in the pre-ERAS group (P=0.268). ERAS was associated with lower costs for some items (some not statistically significant), but not for disposable material used in the OR, medical care, pathology, housing or administrative costs.

Cost-minimization analysis

The total mean(s.d.) cost difference per patient between the two groups was \notin 7738(6655) in favour of the ERAS group (-12·1 per cent), but this was not statistically significant (*P*=0.273) (*Table 4*).

In ERAS-specific expenditure, fixed costs were the crude salary of the ERAS-dedicated nurse (€81 845 per year) and the costs of the quarterly ERAS pancreas meetings (€50 per meeting, including organization time and material). As the ERAS-dedicated nurse was also responsible for ERAS colorectal and liver programmes during the same interval, her salary was divided by three; it was then multiplied by two, as the study period for the ERAS pancreatic protocol was 2 years. Fixed ERAS costs per patient were therefore €743 (54 563/74 + 400/74). Variable ERAS costs were the costs of the ERAS database (€100 per patient), patient carbohydrate drinks (€75 per patient) and patient logbooks (€4 per patient). ERAS-specific costs were thus calculated to be €922 per patient.

The final total gain per patient was $\notin 6816 (-10.6 \text{ per cent})$ in favour of the ERAS group (*Table 5*).

Table 5 Cost-minimization analysis

	Cost per patient (€)						
	ERAS group	Pre-ERAS group	Difference (ERAS – pre-ERAS)				
ERAS-specific costs	922	0	922				
Intraoperative	13 322	14 089	-767				
costs	(11 961, 14 825)	(12 768, 15 681)	(-2866, 1265)				
Preoperative and	42 761	49 732	-6971				
postoperative costs	(36 331, 49 048)	(40 862, 60 976)	(–19 782, 3417)				
Total costs	57 005	63 821	-6816				

Values are mean (95 per cent c.i.). ERAS, enhanced recovery after surgery.

Sensitivity analysis

As some of the ERAS-specific costs were fixed and were divided by the number of patients, the effect of changing the number of patients was examined. If the number was decreased by 50 per cent (to 37 patients), the mean ERAS-specific cost per patient would be €1665, whereas if the number was increased by 50 per cent (to 111 patients) it would be €674. The total gain per patient would be €6073 and €7064 for 37 and 111 patients treated according to the ERAS protocol respectively.

Discussion

This study offers insight into the real costs of implementation of an ERAS protocol for PD. The mean total costs were similar for groups of patients treated before

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and after the introduction of the protocol at this institution. ERAS permitted cost savings per patient relating to anaesthesia and the OR, medication and laboratory testing compared with respective costs for patients following standard care.

The main absolute difference in mean expenditure related to ICU and intermediate care costs (Table 4). This large absolute difference was nevertheless not statistically significant. This can be explained by a small relative difference, the small cohort size, or the statistical distribution of the variables. Only a few patients in the ERAS group were admitted to the ICU, whereas in the pre-ERAS era patients normally spent 1 day in intensive care. For patients who needed an ICU stay, the median duration was similar in the ERAS and pre-ERAS groups (3 versus 2 days respectively; P = 0.092). Moreover, there was no difference in median length of intermediate care stay between groups (5 days each), showing that shortening the ICU stay did not prolong intermediate care. This suggests that resources were probably being wasted before the introduction of ERAS. It should be noted that intermediate care criteria were changed when it was decided to implement ERAS, as standardization of criteria for admission was deemed necessary. The difference in ICU stay most likely reflects a change in institutional guidelines rather than ERAS implementation, but these changes were inspired by the standardization brought about by ERAS.

Anaesthesia and OR costs were responsible for the second main absolute gain in the ERAS group. Median duration of operation and anaesthesia were both reduced in the ERAS group. It is important to mention that the sequential design of the study could have had an impact on the anaesthesia and OR costs. As technical details of the operation were similar over the study interval, increased experience of the surgical and anaesthetic team, or a more favourable operating field and easier dissection of the tumour as a result of intraoperative fluid restriction, may have led to shorter operating and anaesthesia times in the ERAS group. This is very difficult to dissect out, but the use of a standard anaesthesia protocol and strict intravenous fluid balance implemented with ERAS could have contributed to the reduced costs. Moreover, standard perioperative pathways for PD have been shown to reduce the overall costs^{15,16}.

Another interesting finding was the reduction in medication costs in the ERAS group. Fewer postoperative medications were used, which may have been related to ERAS implementation, but it could also simply be a result of the use of standard clinical pathways (care maps). In contrast, more disposable materials were used during operations in the ERAS group. There is no clear explanation for this as the technical aspects of the operation did not vary during the study. All operations were performed by laparotomy and by the same three experienced surgeons over the 5 years.

Several articles including systematic reviews have showed the safety of an ERAS programme in pancreatic surgery^{12,13}. Coolsen and colleagues¹¹ even showed that ERAS was feasible and safe in patients aged over 70 years who underwent PD¹¹. A recently published French article by Faujour and colleagues²⁶ reported a simulation study of the costs of ERAS implementation in various surgical specialties. They calculated that implementation of an ERAS programme in digestive surgery (including colorectal, liver and pancreatic surgery), orthopaedics and urology would allow a total gain of €202000 per year across all surgical units in a single hospital once the programme had been implemented completely. A recent systematic review²⁷ of the general cost benefits of ERAS showed that an ERAS programme for pancreatic surgery was cost-effective. In 2000, Porter and co-workers14 had already shown that implementation of a standard clinical pathway for PD resulted a gain of US \$10888 per patient (€9702; exchange rate 10 September 2015)¹⁴; this was confirmed later by Vanounou and colleagues²⁸, who reported a gain of US \$5542 per patient (€4938). However, the present study included a detailed analysis of the real costs of patients undergoing PD in an ERAS pathway.

This study has several limitations. First, data collection for the pre-ERAS group was retrospective, and some data may have been missing for events not mentioned in the charts. Second, as the ERAS group had a shorter length of hospital stay, there could have been a transfer of costs to the general healthcare system (such as short-term rehabilitation unit costs, sick leave), which was not assessed here. It would be of particular interest to assess the costs of readmission and the longer-term expenditure associated with ERAS. A limitation related to the before-and-after study design is that the experience gained during the study could have had an impact on complications and length of hospital stay. Finally, it is very difficult to differentiate between the effects of implementation of an ERAS pathway and the sole effects of standardization.

An ERAS pathway for colorectal surgery was implemented in this department in June 2011. This might have influenced the care of patients undergoing PD and associated costs before implementation of the specific ERAS pathway for pancreatic surgery. The total mean costs for patients treated within the ERAS programme for PD were similar to those for patients who received standard management. It is possible that the economic gain from introduction of ERAS for pancreatic surgery could have been greater in a department that had previously been ERAS-free.

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Supporting information

Additional supporting information may be found in the online version of this article:

Table S1 Surgical and medical complications (Word document)