

# Enhanced recovery in elderly patients undergoing pancreatic resection

## A retrospective monocentric study

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### Abstract

Enhanced recovery after surgery (ERAS) pathway for pancreas has demonstrated its value in clinical practice. However, there is a lack of specific evidence about its application in elderly patients. The aim of the present study was to assess the impact of age on compliance and postoperative outcomes. Patients  $\geq 70$  years old that underwent pancreatic resection within an ERAS pathway between 2012 and 2018 were included, and divided into three groups: 70–74, 75–79, and  $\geq 80$  years old. Compliance with ERAS items, length of stay, mortality, and complications were analyzed. 114 patients were included: 49, 37, and 28 patients aged 70–74, 75–79, and  $\geq 80$  years, respectively. Overall compliance to ERAS items between groups was not different (66%, 66%, and 62%,  $P = .201$ ). No significant difference was observed in terms of median length of stay (14, 17, and 17 days,  $P = .717$ ), overall complications (67%, 78%, and 71%,  $P = .529$ ), major complications (26%, 32%, and 39%,  $P = .507$ ), or mortality (0%, 3%, and 4%,  $P = .448$ ) with increasing age. Application of an ERAS pathway is feasible in elderly patients with pancreatic resection. Increasing age was neither associated with poorer compliance nor worse postoperative outcomes.

**Abbreviations:** ERAS = enhanced recovery after surgery, IQR = inter quartile range.

**Keywords:** enhanced recovery, elderly, outcomes, pancreas surgery

### 1. Introduction

The incidence of pancreatic cancer increases with advancing age, while 5-year relative survival decreases with advancing age, from around 20% in 15 to 44-year-old, to 2% to 4% in the elderly.<sup>[1]</sup> To date, surgery remains the only potentially curative option. However, pancreas resection remains a difficult and major surgical procedure with high postoperative morbidity, ranging from 40% to 60%.<sup>[2,3]</sup> In the last decades, enhanced recovery after surgery (ERAS) pathways have been increasingly implemented and contributed to reduce overall morbidity, length of hospital stay and costs, by implementing multimodal measures influencing the pre-, peri- and post-operative periods.<sup>[4–8]</sup>

Specific enhanced recovery guidelines for pancreatoduodenectomy were developed in 2012<sup>[9]</sup> and subsequently updated in 2020.<sup>[10]</sup> A recent multicenter study has shown the feasibility of enhanced recovery protocol for pancreatoduodenectomy, but with specific challenges.<sup>[11]</sup> Age itself has not been described as exclusion criteria for enhanced recovery, however, it could

represent an irrational barrier to implementation of ERAS protocol and lead to specific adaptations.<sup>[12]</sup> Few studies have investigated the feasibility of enhanced recovery in elderly patients in pancreatic surgery,<sup>[13,14]</sup> and specific data on the effect of age on compliance to the various ERAS items are lacking.

The aim of the present study was to assess the impact of age on ERAS compliance and postoperative outcomes in subgroups of elderly patients with pancreatic surgery.

### 2. Materials and methods

This study is a retrospective analysis based on a prospective database, including all consecutive patients  $\geq 70$  years old with elective pancreatic resection within an ERAS pathway in a tertiary referral center between October 2012 and August 2018. Documentation was performed by a dedicated enhanced recovery nurse using ERAS Interactive Audit System (www.erassociety.org, ENCARE, Krista, Sweden). The system analyzes

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The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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the database for patients' characteristics, treatment, compliance and outcomes. Patients were treated according to a previously published protocol, and follow-up was performed by a surgeon 4 to 6 weeks after discharge.<sup>[15]</sup> ERAS refers to a multimodal perioperative care pathway designed to reduce the patient's surgical stress response, optimize physiologic function, and facilitate recovery after surgery. Current updated ERAS recommendations for pancreatoduodenectomy are based on the best available evidence and processed by the Delphi method.<sup>[15]</sup> These recommendations include 27 pre-, intra-, and post-operative items covering various aspects, such as prehabilitation, biliary drainage, nutrition, antimicrobial prophylaxis, analgesia, fluid balance, and mobilization.

Patients were allocated into three groups according to age: 70–74, 75–79, and  $\geq 80$  years old. Demographics, comorbidities, compliance to ERAS items, length of stay, mortality, readmission, overall complications, and major complications were assessed, and compared between groups. Overall compliance to ERAS pathway was calculated as the number of items fulfilled divided by 20 (total number of preoperative, intraoperative, and postoperative items). Individual item adherence was calculated as percentage of compliant patients divided by the total of patients. An item was considered with low compliance when it was  $\leq 70\%$ . Postoperative complications were graded according to Clavien classification.<sup>[16]</sup> Complications graded as III to V were considered as major. Specific complications after pancreatic surgery have been also described according to the International Study Group of Pancreatic Surgery: pancreatic fistula, delayed gastric emptying and hemorrhage.<sup>[17–20]</sup> Follow-up for postoperative outcomes was carried out for 30 days after hospital discharge. Hospital readmissions within 30 days after surgery or during same hospitalization were also recorded.

Descriptive statistics for categorical variables were reported as number and percentage, while continuous variables were reported as median and interquartile range or means and standard deviation as appropriate. Continuous variables were compared between groups with the one-way ANOVA for

normally distributed data or Kruskal–Wallis test for non-normally distributed data. Chi-square test was used for comparison of categorical variables. A  $P$  value  $\leq .05$  was considered statistically significant. All statistical analyses and graphics were two-sided and performed using GraphPad Prism version 8.3.0 (GraphPad Software, La Jolla, CA). Missing data was omitted based on the available case analysis (pairwise). The article was written according to the STROBE statement.<sup>[21]</sup>

This study was approved by the local Ethics Commission (CER-VD protocol 2016-01815) and has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All patients provided written consent before surgery.

### 3. Results

During the study period, a total of 337 patients underwent a pancreatic resection within an ERAS program. With a total of 114 elderly patients, 49 were aged 70 to 74 years (median 72, inter quartile range [IQR] 71–73), 37 were 75 to 79 years (median 76, IQR 75–77) and 28 were  $\geq 80$  years (median 82, IQR 80–84). Demographics and surgical details are summarized in Table 1. There was no difference in terms of comorbidities between groups. Eighty-seven had pancreatoduodenectomy (76%), 22 distal pancreatectomy (19%), 3 total pancreatectomy (3%), and 2 pancreatic enucleation (2%).

Overall ERAS compliance between groups was not different (66%, 66%, and 62%,  $P = .201$ , Fig. 1). There was also no difference in pre-operative (99% for all 3 groups,  $P = .816$ ), intra-operative (91%, 92%, and 88%,  $P = .570$ ) and post-operative items compliance (37%, 38%, and 30%,  $P = .330$ , Fig. 2). Items with low compliance ( $\leq 70\%$ ) are described in Figure 3.

Regarding outcomes, no significant difference was observed in terms of overall complications (67%, 78%, and 71%,  $P = .529$ ), major complications (67%, 78%, and 71%,  $P = .529$ ), mortality (0%, 3%, and 4%,  $P = .448$ ) or readmission (10%, 3%, and

**Table 1**  
Patients and surgical characteristics stratified by patients' age.

	70–74y (n = 49)	75–79y (n = 37)	$\geq 80y$ (n = 28)	<i>P</i>
Gender (m:f)	18:31	20:17	15:13	.193
ASA III/IV, n (%)	18 (36)	15 (41)	15 (54)	.345
BMI, kg/m <sup>2</sup> mean (SD)	26.6 (5)	25.2 (4)	24.7 (4)	.155
Smokers, n (%)	15 (31%)	7 (18%)	3 (11%)	.110
Type of surgery, n (%)				
Pancreatoduodenectomy	34 (69)	28 (76)	25 (89)	.141
Distal pancreatectomy	13 (27)	6 (16)	3 (11)	.202
Total pancreatectomy	2 (4)	1 (3)	0 (0)	.560
Other	0 (0)	2 (5)	0 (0)	.120
Open: laparoscopic	41:8	33:4	28:0	.080
Estimated blood loss, ml, median (IQR)	350 (175–600)	325 (200–500)	400 (200–688)	.593
Operation length, min, median (IQR)	324 (246–375)	306 (257–324)	330 (270–371)	.634
Pathology, n (%)				
Primary adenocarcinoma	35 (72)	32 (86)	25 (88)	.089
Other primary malignancy	2 (4)	1 (3)	0 (0)	.560
Metastasis or recurrence	1 (2)	0 (0)	1 (4)	.543
Benign tumor or disease	9 (18)	4 (11)	2 (7)	.349
Chronic pancreatitis	2 (4)	0 (0)	0 (0)	.259

ASA = American Society of Anesthesiologists, BMI = body mass index, IQR = inter quartile range, SD = standard deviation.

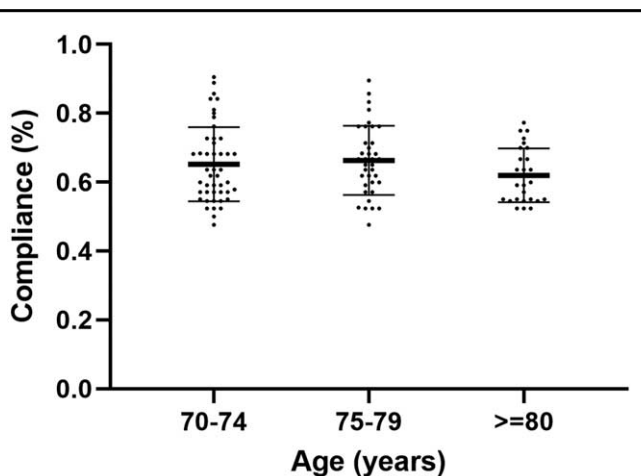


Figure 1. Overall compliance of enhanced recovery protocol stratified by patients' age.

10%,  $P=.361$ ). Specific complications according to International Study Group of Pancreatic Surgery are summarized in Table 2. Median length of stay was 14 days (IQR 8.75–22) for the 70 to 74 group, 18 days (IQR 5–26.25) for the 75 to 79 group and 16 days (IQR 7–30) for the  $\geq 80$  group, without any significant differences ( $P=.069$ ).

**4. Discussion**

In this study, increasing age was not associated with poorer ERAS compliance or postoperative outcomes for elderly patients with pancreatic resection. Implementing such a program in the elderly seemed consequently to be safe and feasible.

Some literature exists on pancreas surgery within an ERAS pathway, but too frequently the protocol applied is not clearly described and data on compliance for all items are lacking.<sup>[13,22]</sup> Moreover, all consecutive patients should be included in the pathway, in order to avoid selection bias as in the present study.

Pancreatic resection is a challenging surgery with high morbidity rate and some mortality. Experiences from single

high-volume institutions showed that age was not a predictor of perioperative morbidity and mortality.<sup>[23–25]</sup> Age alone seems no longer an absolute contraindication for pancreatic surgery, provided appropriate counselling of elderly patients about complications that leads to prolonged convalescence.<sup>[14,26]</sup> In reasonable risk elderly patients, the benefit of pancreatic resection does not decrease with age, moreover, once patients over 80 years have passed the 2-year survival mark without cancer recurrence, their survival is similar to their age-matched counterparts.<sup>[26]</sup> There is still a certain fear of operating on elderly patients, with fewer than 10% of patients over 80 years with loco-regional disease and no comorbidities being resected (versus 40% of patients 66–70 years).<sup>[26]</sup> Furthermore, increasing age may represent a limitation to the implementation of ERAS pathway and specific studies on its feasibility are lacking. One retrospective study performed a comparison with younger patients (<65 years) to better understand the role of age as a possible barrier for ERAS implementation, and no differences were found in terms of adherence between young and elderly patients.<sup>[13]</sup>

In the present study, all consecutive patients were included without any selection and calculation of compliance to ERAS items was thorough, using the ERAS Interactive Audit System, as previously described.<sup>[27,28]</sup> Overall compliance of elderly patients to ERAS items was more than 60%, which is slightly lower than reported by others (73%).<sup>[13]</sup> Compliance to pre-operative and intra-operative items was high (>90%), unlike compliance to post-operative items which was rather low (<40%), this is however known in pancreas surgery. Among these, mobilization, balanced intravenous fluid infusion and urinary catheter removal were associated with poor compliance. In another retrospective study of pancreas surgery in elderly patients (cut-off fixed at 75 years), the lowest adherence was observed for starting a solid food diet (32%) and early surgical drains removal (9%), while the highest adherence was observed for intra-operative glycemic control (95%), use of epidural analgesia (95%), mobilization (91%), and nasogastric tube removal (91%).<sup>[14]</sup> A Dutch group that also studied patients  $\geq 70$  years with pancreatoduodenectomies showed various compliance to ERAS items: 63% for solid food intake, 63% for mobilization, 51% for surgical drains removal and 60% for

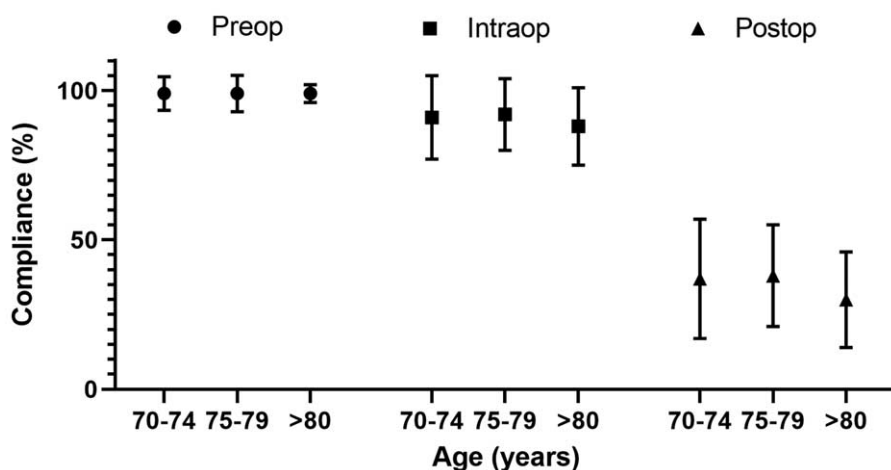


Figure 2. Mean compliance for pre-, intra-, and post-operative period with standard deviation errors bars.

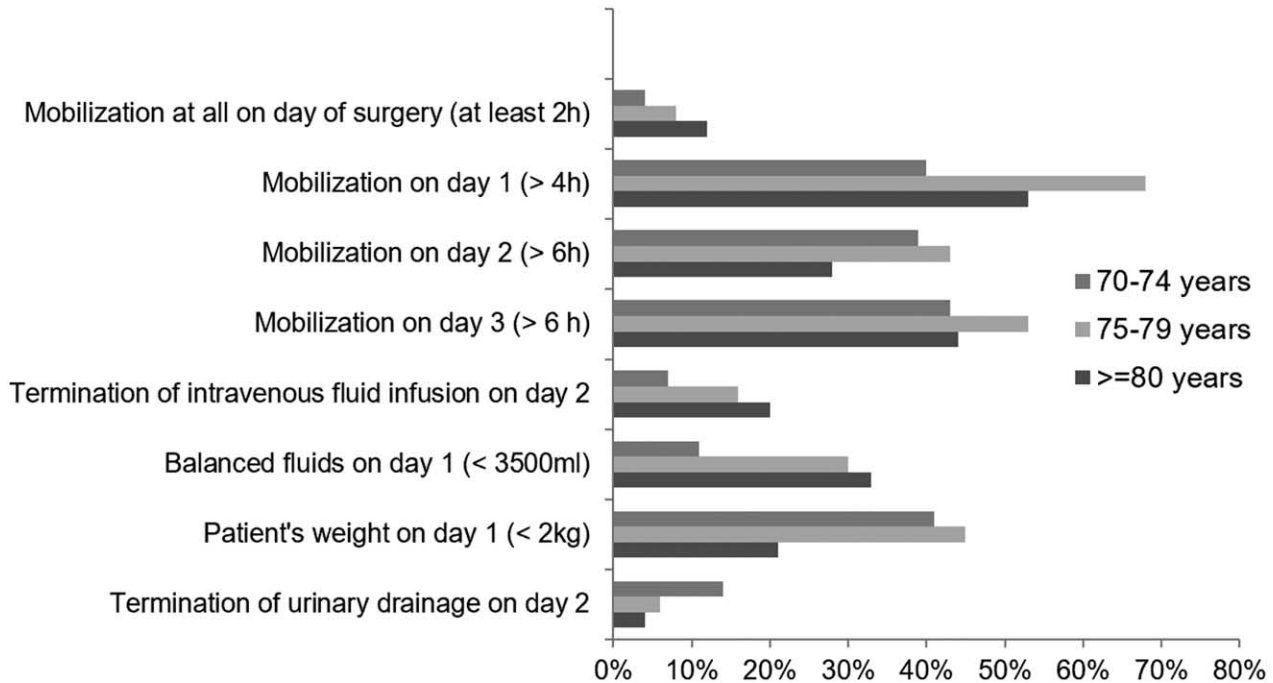


Figure 3. Difficult enhanced recovery items with mean compliance (%) less than 70% stratified by age.

urinary catheter removal.<sup>[13]</sup> Other studies in colorectal surgery have shown that preoperative and intraoperative adherence to ERAS items remained equal over time, while postoperative adherence generally decreases.<sup>[27,29]</sup> Still in colorectal surgery, previous retrospective reports showed that elderly patients did not present a worse compliance to ERAS when compared to younger.<sup>[30,31]</sup> In this present study, all three age groups (70–74, 75–79, and ≥ 80) showed a critical drop of postoperative compliance, however without affecting outcomes. One hypothesis is that elderly patients did not wish to perform the proposed postoperative tasks or accomplished them partially, due to their physical limitations linked to their age. Postoperative elements, such as the cessation of intravenous fluids, early mobilization, and early resumption of solid foods have also been described as the most difficult to implement.<sup>[32]</sup> However, it is still unclear which individual ERAS components are most important contributors to an improved outcome, the main point being to have the highest possible number of ERAS items fulfilled.<sup>[27,33]</sup>

Regarding outcomes, no significant difference was observed in length of stay, complications, mortality, or readmission, which is interesting looking at octogenarians. Similarly, a retrospective

study including 110 patients showed that elderly patients ≥70 years treated according to ERAS had similar rates of postoperative complications, mortality, relaparotomy, and readmissions compared to patients treated with a standard protocol.<sup>[13]</sup> In the present study, overall morbidity (60.7%) for patients >80 years was higher compared to the morbidity reported in a case series involving 2698 patients undergoing pancreaticoduodenectomies (53%, 80–89 years) but mortality was similar (4% vs 4%).<sup>[23]</sup> Of note, our department records all complications based on the Clavien classification without any exception, even for marginal deviations.<sup>[16]</sup> In consequence, this increased morbidity could be due to the meticulous prospective complication registration. The rate of pancreatic fistula (14%) was however lower, compared to another elderly ERAS patients cohort, with rates of 23%, while post-pancreatectomy hemorrhage rates and delayed gastric emptying (7%) were comparable (respectively 7% and 7%, 46% and 39%).<sup>[13]</sup> The mortality and the readmission rate differed (respectively 11% and 13% vs 1% and 7% in present study).<sup>[13]</sup> In line with previous reports, the mortality recorded in patients ≥80 years (4%) in the present study was similar than in the younger group (70–79 years, 2%,  $P = .448$ ).<sup>[25,34,35]</sup> The length of stay of octogenarians in the

**Table 2**  
Postoperative complications stratified by patients' age.

	70–74y (n = 49)	75–79y (n = 37)	≥80y (n = 28)	P
Overall complications, n (%)	33 (67)	29 (78)	20 (71)	.529
Major complications (III–IV), n (%)	13 (26)	12 (32)	11 (39)	.507
Delayed gastric emptying, n (%)	17 (35)	22 (60)	12 (43)	.045
Pancreatic fistula (grade B-C), n (%)	5 (10)	7 (19)	4 (14)	.514
Postpancreatectomy hemorrhage, n (%)	5 (10)	2 (5)	2 (7)	.706
Mortality, n (%)	0 (0)	1 (3)	1 (4)	.448

present study (16 days) was comparable to another study assessing elderly ERAS patients (14 days).<sup>[13]</sup> These latest results show a marked reduction in length of stay compared to those reported with traditional care, varying from 13 to 25 days in the older population, and thus indicating a direct benefit of the ERAS program.<sup>[26,36,37]</sup>

Main limitations of this study were its retrospective and monocentric nature, as well as the limited sample size, which limits the interpretation of the results and their generalization, even if data was collected prospectively by a dedicated trained nurse. It is necessary to continue the prospective collection of data, and to plan multicenter projects to confirm these results in the elderly. It may also exist confounding effects of ERAS components, such as patients' comorbidities and kind of surgeries, which were not considered for compliance and outcome analyses. Furthermore, cognitive status, preoperative functional status and frailty were not assessed, while there are potential correlations. A strength of the study was that compliance with increasing age was assessed during a 6-year period and categorizing patients into 3 age groups. Compliance was defined precisely based on the ERAS pathway and no patient was excluded.

## 5. Conclusion

Application of an ERAS pathway was feasible in non-selected elderly patients with pancreatic resection, and increasing age was not associated with poorer compliance or altered postoperative outcomes.

## Author contributions

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**Investigation:** David Martin, Didier Roulin, Nermin Halkic, Nicolas Demartines, Susanna Scarsi.

**Methodology:** David Martin, Didier Roulin, Nermin Halkic, Nicolas Demartines, Susanna Scarsi.

**Project administration:** Nermin Halkic, Nicolas Demartines.

**Supervision:** David Martin, Didier Roulin, Nermin Halkic, Nicolas Demartines.

**Validation:** David Martin, Didier Roulin, Nermin Halkic, Nicolas Demartines, Susanna Scarsi.

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**Writing – original draft:** David Martin, Didier Roulin, Nicolas Demartines, Susanna Scarsi.

**Writing – review & editing:** David Martin, Didier Roulin, Nermin Halkic, Nicolas Demartines, Susanna Scarsi.

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