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ORIGINAL ARTICLE

Implementation and Evaluation of a Clinical Pathway for Pancreaticoduodenectomy Procedures: a Prospective Cohort Study

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Abstract

Introduction Medical and nursing protocols in perioperative care for pancreaticoduodenectomy are mainly mono-disciplinary, limiting their integration and transparency in a continuous health care system. The aims of this study were to evaluate adherence to a multidisciplinary clinical pathway for all pancreaticoduodenectomy patients during their entire hospital stay and to determine if the use of this clinical pathway is associated with beneficial effects on clinical end points.

Materials and Methods A prospective cohort study was conducted in 95 pancreaticoduodenectomy patients treated according to a clinical pathway, including a variance report, compared to a historical control group ($n = 52$) with a traditional treatment regime.

Results Process evaluation of the clinical pathway group revealed that protocol adherence throughout all units was above 80%. Major complications according to Clavien-Dindo classification grade ≥3 decreased from 27 to 13%; $p = 0.02$. Hospital length of stay was significantly shorter in the clinical pathway group, median 10 days [IQR 8–15], compared with the control group, median 13 days [IQR 10–18]; $p = 0.02$.

Conclusion The use of a clinical pathway in pancreaticoduodenectomy patients was associated with high protocol adherence, improved outcome and shorter hospital length of stay. Variance report analysis and protocol adherence with a Prepare-Act-Reflect Cycle are essential in surveillance of outcome.

Keywords Pancreaticoduodenectomy · Clinical pathway · Protocol adherence · Perioperative care

Introduction

Pancreaticoduodenectomy for pancreas tumours and periampullary tumours is considered high-risk surgery and is associated with high morbidity (30–70%) and a mortality of 1–5% in specialized centres.[1, 2] Centralization of pancreas surgery and advances in surgical techniques resulted in more patients being operated for advanced-staged tumours.[3, 4] Patients with more comorbidity receiving pre-operative chemotherapy and/or vascular reconstructions in advanced disease, need more complex perioperative care. Currently this is facilitated by multiple guidelines and medical and nursing protocols. This complexity demands an overall multidisciplinary approach and clear communication.

Different departments are involved in the treatment during the patients' journey through the surgical ward, operation theatre, post-anaesthesia care unit (PACU) and intensive care unit (ICU). However, large differences in the actual use of these protocols are present between the different units and medical and nursing staff members.[5, 6] Moreover, while multidisciplinary teamwork for these patients is essential, the development and implementation of a clinical pathway (CP) involve many aspects of the total patient care and should therefore be multidisciplinary by doctors and nurses as well.

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A CP may facilitate the care for this group of high-risk surgery patients by unifying different protocols into one multidisciplinary protocol for all units during the hospital stay of the patients. This may result in an increased protocol adherence, less morbidity and improved outcome. Key elements of a CP are guidelines, evidence-based clinical protocols and best practice rules, together with a coordinated sequence of activities of the multidisciplinary team.[7] Registration, monitoring and evaluation of adherences, variances and outcomes are part of a CP and can be part of a process-driven pathway.[8] A multidisciplinary CP has therefore many evaluation moments and scheduled actions. To keep the patient on the 'pathway', the CP mandates a registered response of the nurse or doctor if results are outside the range of the prescribed boundaries.

Many CPs have been developed for high volume with low-risk and with average-risk health care procedures in order to reduce complications.[9–12] The post-operative phase of the patient spent in the ICU or PACU, however, is a seldom part of a CP.[13] A CP including the PACU/ICU stay mandates an hour-to-hour care plan during the post-operative stay in the ICU/PACU.[14] Many standardized care plans related to a pancreaticoduodenectomy have been published, focussing on the use of an enhanced recovery program after surgery (ERAS) with elements like early mobilization, early enteral feeding, pain treatment and reduction of iv fluid administrations to shorten the length of hospital stay.[15–19] In these care plans, a reduction of hospital length of stay (LOS), morbidity or mortality was not always observed. Crucially, the ICU period of these patients was not integrated in these protocols.

The aim of this study was first to determine the feasibility to develop and implement a multidisciplinary CP including a variance report for all pancreaticoduodenectomy patients during their entire hospital stay and second to determine if the use of this CP is associated with an improvement of patient's morbidity and outcome.

Methods

Setting and Patients

The Radboud University Medical Center in Nijmegen is a 1000-bed university hospital, including a 32-bed closed-format ICU, a 5-bed PACU and a 30-bed gastrointestinal (GI) oncology surgical ward. An anaesthesiologist with a resident are supervising the PACU. The ICU is supervised by the intensivists, with intensivists-in-training and residents. They all work in close relation with the surgical team. On the surgical ward, nurses, physician assistants and young residents are caring for patients undergoing a pancreaticoduodenectomy, under daily supervision of the senior GI-oncology medical staff. Since the centralization in 2012 of pancreas surgery in the Netherlands, approximately 80 pancreas operations (60 malignant cases) are operated annually in the Radboudumc. As a result, the logistics and perioperative care of our pancreatic surgical program needed reflection and rescheduling.

Development of the CP

The development of the multidisciplinary CP for pancreaticoduodenectomy was a multistep procedure with the use of lessons learned from the development and implementation of the cardiac and oesophageal CPs, previously developed in Radboudumc, and started in 2013.

The first step was redefining and searching for evidence underneath the surgical, anaesthesiology and ICU protocols in the perioperative period. This was a multidisciplinary procedure, undertaken by the physician assistants, senior nurses, 'key' nurses and medical staff.[20–27] Instead of a traditional 'day-to-day-care' plan for the surgical ward, an 'hour-to-hour' care plan had to be developed, including the PACU and ICU care. It was important to identify potential barriers and facilitators in these settings, in order to tailor the implementation strategy.[28–31] An evidence-based implementation strategy according to Grol was used.[32] Second, a unique variance report ('Radboud variance report'; Appendix 1) had to be incorporated and developed together with the CP.[33] This Radboud model of variance report enables nurses, physician assistants and young residents to execute predefined actions in accordance with and within the preset boundaries of a variance protocol, without having to wait for approval of the responsible physician first (Dutch law and order for health care professionals BWBR0006251 chapter IV, article 35).

Until 2012, a surgical pancreas matrix for (peri)operative care was used at the surgical ward. The historical control group was treated according to this matrix including the surgical medical and nursing protocols without the variance report. In the PACU and ICU, these patients were treated according to different PACU and ICU protocols. This pancreas matrix was used as backbone for further multidisciplinary development of the CP. As part of the development and implementation strategy, a small group of key nurses responsible for other CPs reflected on the concepts of the pancreas CP and variance report as part of a Prepare-Act-Reflect (PAR) Cycle.

The pancreas CP had to be a continuum from admission to discharge from the hospital. Essential elements included restrictive intra-operative fluid use, strict pain control, early mobilization, early drain and tube removal and early enteral feeding. Post-operatively, early warning scores (EWS) are measured at least once during every 8-h shift or more frequent, whenever indicated by the nurses, with strict directives for action by nurses according to the variance report.[34]

Patients with a malnutrition universal screening tool (MUST) score above 2 need an active feeding intervention according to the quality system of health care in the Netherlands. We decided that patients with a MUST above 2 should start with total parenteral nutrition (TPN) within 24 h after surgery. Publications on

calorie deficit and enteral feeding or TPN after surgery in ICU patients often do not take into account malnutrition and MUST score >2. Our protocol prescribes that if the gastric tube can be removed, the patients need to start with oral/enteral feeding, and TPN needs to stop as soon as the oral intake of the patients is above 1000 kcal.[22, 23, 35–37] TPN should be started on day 3 if patients had a MUST score of 1 and enteral feeding had not been started on day 3. All patients with a gastroparesis without signs of sepsis or ileus on day 7 will be given a naso-jejunal tube by the gastroenterologist through the gastrojejunostomy and start enteral feeding.[38] In contrast to ERAS-based protocols, deviations from the CP had to lead into prompt actions according to the variance report.

Implementation of the CP

After informative meetings for medical and nursing staffs, including reflections on the positive aspects of previous CPs, bedside training started on the surgical ward and PACU/ICU in 2014. Implementation of the pancreas CP would introduce an essential change in daily practice for most nurses, physician assistants and medical staff. The first step in teaching was getting acquainted to the CP vision that would result to one continuous multidisciplinary protocol.[32] In nursing and medical staff meetings, updates of the project were discussed, and feedback was welcomed by the CP developers. During this teaching period, especially new PACU-specific aspects arose for the pancreas CP, including new variance report criteria, and as an interactive process of PAR cycles, these criteria were incorporated in the pancreas CP during the development. In this try-out period, feedback was asked and given every 4 weeks during the multidisciplinary team meetings of the project. After 4 months of teaching and try-out period, it was concluded that it was feasible and safe to use the pancreas CP with the Radboud model variance report for patients during their entire clinical stay, including the PACU/ICU. With the completion of this implementation step, the pancreas CP was considered being implemented and our study on the use of the CP and variance report for all pancreaticoduodenectomy patients started on the first of September 2014, 18 months after the start of the development of the CP, including many PAR cycles. Patients treated for other pancreas procedures than pancreaticoduodenectomy were considered candidates to have the benefits of the pancreas CP during their stay in PACU/ICU and ward, but were not included in this study. Protocol adherence was measured per pathway action. We considered protocol adherence if a deviation from the CP resulted in the correct action, according to the CP, or if no action was needed and no action was started. No protocol adherence was defined as wrong actions or no actions if actions were needed. Deviations from the CP had to be described in the variance report or patient record.

Design

This is a pre-post design study. After the implementation of the pancreas CP, patients treated according to the CP were compared with a historical control group of patients treated with standard perioperative care for pancreaticoduodenectomy according to the original pancreas matrix and monodisciplinary protocols and operated on between 2009 and 2012.

End Points

Primary endpoint was to determine the feasibility and safety, including incidence of post-operative complications, according to Clavien-Dindo classification, of the use the CP. Secondary endpoints were in length of stay (LOS) in-hospital, post-operative fluid balance, gastroparesis, protocol adherence to mobilization, drain removal, radiologic and surgical re-interventions, ICU readmission, hospital readmission and mortality rate.

Statistics

Continuous variables were described as median and interquartile range [IQR] and tested with the Mann-Whitney *U* test. Differences in dichotomous variables were analyzed using the chi-squared test. Due to the exploratory nature of this study, and to increase the sensitivity to detect differences between groups, no correction for multiple testing was performed. With our convenience sample size of 95 patients in the CP group and 52 patients in the control group, our study had 80% power to demonstrate a 7% absolute reduction of post-operative complications. All statistical analyses were performed using SPSS version 20.01 for Windows (IBM, SPSS statistics, Chicago, IL, USA).

Results

Development Results of the CP

Nurses, physiotherapists, dieticians and medical staff specialized in pancreas surgery contributed to the development of the pancreas CP and the variance report. This resulted in a set-up of clear and safe boundaries in taking clinical treatment decisions and an upscaling system to consultation with a key nurse or senior staff members, if actions according to the variance report did not seem right.

First, the pancreas CP for medical and nursing decisions was written according to existing evidence-based protocols, best practices and guidelines. Finally, a multidisciplinary variance report was incorporated (Appendix Table 4: summary of the differences between CP and control surgery and Appendices 2 and 3: variance report).

For the analysis of the developmental process, we evaluated barriers and facilitators for protocol adherence. For this,

interviews and questionnaires were used, focussing on possible barriers and facilitators for protocol adherence to the new CP. An important facilitator was the motivation of nursing and medical staff to ask for guidance and training in the use of this protocol. The most important barrier was that using the protocols was experienced as a time consuming processes of getting acquainted with the system, resulting in feelings of loss of autonomy for doctors and nurses. Key nurses together with medical leadership were essential for awareness, feedback and motivation during development, implementation and the use of the CP.

Implementation Results of the CP

First, the medical aspects of the CP were implemented on the ward followed by the nursing aspects. Because of the lack of experience with CPs, the care providers working on the PACU received more time for training and bedside teaching and started later with implementation. Key nurses at the surgical ward gave guidance and were partner for the key nurses of the PACU.

Evaluation after the implementation process was performed every 2 months during the first 6 months and after this period whenever needed. These evaluations resulted mostly in questions or new ideas for a change in the CP from the units or when less compliance was observed. The variance report was an important tool for evaluating compliance. When compliance of one of the CP domains was below 80%, feedback was given by the key nurse or surgeon through focussed teaching sessions for nurses and residents.

After a period of 18 months, the pancreas CP was implemented and evaluation of protocol adherence was 80% for PACU/ICU periods and 60% for the surgical ward. The latter was mainly influenced by a low compliance to drain removal (<50%). According to the pancreas CP, drain removal was allowed if amylase level in the drain was below 500 U/l and volume below 200 ml/day. Deviations turned out to be primarily a system problem of postponing drain removal during weekends. After recognition of this system problem, an active policy started and protocol adherence on this item improved to above 80%.

Following the implementation, in September 2014, the outcome study of the pancreas CP was started (Fig. 1 implementation flowchart).

Clinical Outcomes

Between September 2014 and September 2016, in total, 95 elective consecutive pancreaticoduodenectomy patients were treated within the pancreas CP. Semi-acute pancreaticoduodenectomies (for bleeding tumours) and other types of resections (e.g. total pancreatic resections or pancreaticoduodenectomies with resection of a secondary colorectal tumour) were no part of the study. A cohort of 52 consecutive elective pancreaticoduodenectomy patients treated before the CP implementation period between 2009 and 2012 was identified as historical control group. Their perioperative treatment had been according to the underlying matrix protocol that was used as base for the development of the CP. Three surgeons in the pre-CP period operated on the pancreaticoduodenectomy patients. Results between these surgeons did not differ, and perioperative care was regulated by protocols. These surgeons were also responsible for pancreas surgery in the CP period.

Baseline characteristics between the two groups were not significantly different, apart from a higher number of CP patients receiving portal vein resection or celiac trunk/superior mesenteric artery (SMA) vessel exploration (Table 1).

Intra-operative Data

The median intra-operative amount of fluids administered was 3900 ml [IQR 3000–4600] in the CP patients versus 5200 ml [IQR 4000–6000] in the control group ($p < 0.001$). Post-operative fluid balance and fluid balance on day 1 post-operative were also significantly lower in the CP group versus the control group ($p < 0.001$; Table 2). Although more portal vein resections and celiac trunk and explorations along the SMA were performed, blood loss was less in the CP patients: 755 ml [IQR 500–1100] versus 1303 ml [IQR 656–2402] ($p < 0.001$, Table 2).

Post-operative Data

Adherence of pain and hemodynamic interventions according to the variance report was 100% at the PACU/ICU, and a step-up approach regarding pain control was adequately used according to CP protocol. Hemodynamic interventions in accordance with the variance report were not needed and not started in 17% of the CP patients, and 57% of the CP patients needed an extra hemodynamic intervention which was subsequently started according to the CP protocol. In total, 26% of the patients were treated with vasopressors on arrival in the PACU/ICU, which could be reduced during their stay. Significantly more CP patients were swing mobilized within 24 h compared with the control group, respectively, 83 versus 19%, $p = 0.001$. Especially poor pain control and patients' feelings of weakness, early after the operation, were recorded as reasons not to start swing or mobilization at the surgical ward. Trigger for complications was the EWS; in 32% of the patients in the CP group, the EWS was above 3. Interventions on a high EWS were adequate and according to the variance report >95% of the patients.

Considering clinical outcome, major complications according to the Clavien-Dindo classification grade 3 or more occurred less frequently (13 vs 27%, $p = 0.02$) in the CP group, compared to the control group.[39] One patient had a Clavien-Dindo 4b complication as a result of pancreatic leakage complicated by sepsis with EWS >6 on day 7 and hemorrhagic bleeding on day 14 in the CP group. This complication was successfully treated by radiologic coiling of the gastroduodenal artery and splenic artery.

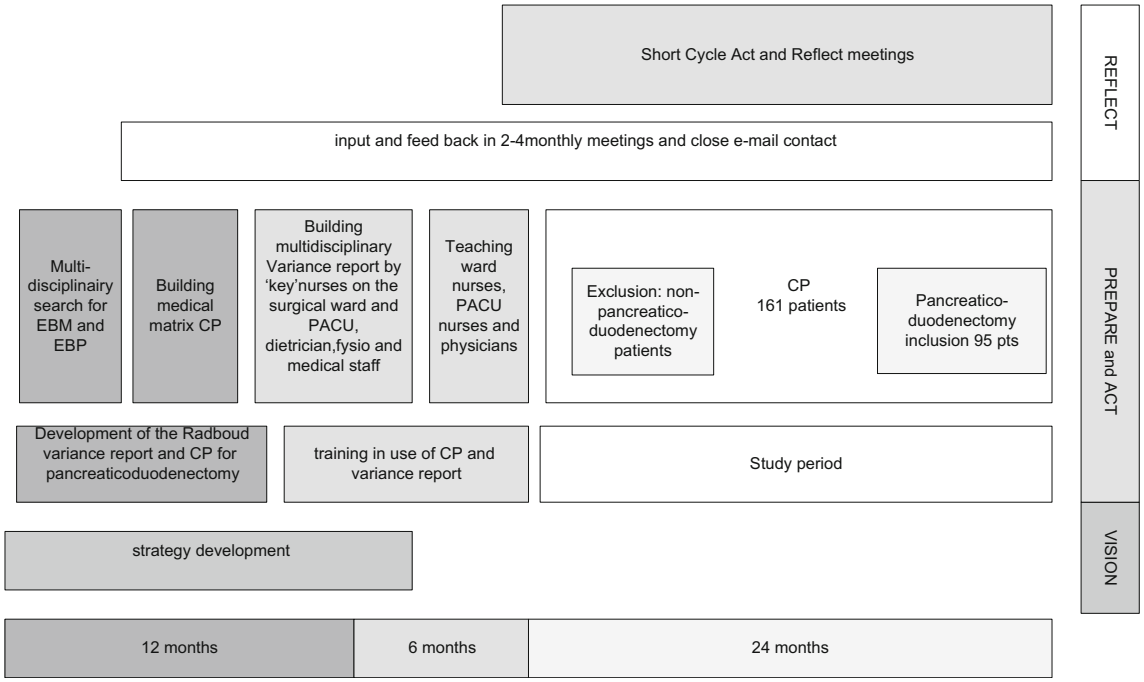

Fig. 1 Implementation of pancreas CP and study flowchart

Less patients suffered from gastroparesis grades B and C in the CP group compared to the control group, 9 versus 62%, $p < 0.001$, as were radiologic interventions: 11 versus 27%, $p = 0.04$. In the control group, the gastric tube was not removed when production was reduced but was left in place and blocked and could be removed if after measurement of retention after 8 and 16 h, it was less than 100 ml per 8 h. Pancreatic leakage and chylus leakage, readmission to ICU and readmission to hospital did not significantly differ between the CP group and control group. Median times to drain removal were also not influenced. The mortality rate was low and not different between groups (Table 3).

Discussion

This study illustrates that development of a CP for pancreaticoduodenectomy is an iterative multidisciplinary process, starting with a dynamic protocol with improvements through PAR cycle evaluation and change moments. Implementation of the pancreas CP in all units involved in the entire (peri-) operative process (OR, PACU/ICU/surgical ward) took 18 months. Process evaluation of the prospective CP group revealed that protocol adherence was successfully achieved in >80% for most of the criteria throughout the clinical stay. Comparison of both cohort groups on main clinical outcomes showed that major complications according to the Clavien-

Table 1 Baseline characteristics of pancreas CP and control groups of pancreaticoduodenectomy

	Clinical pathway, $N = 95$	Control, $N = 52$	P
Age, median (IQR)	66 (57–72)	66 (58–72)	0.98
Male, *n* (%)	56 (58.9)	35 (67.3)	0.26
Stent/(PTC) percutaneous drainage, *n* (%)	59 (61.5)	28 (53.8)	0.34
Pulmonary comorbidity, *n* (%)	13 (13.7)	4 (7.7)	0.52
Cardial comorbidity, *n* (%)	13 (13.7)	10 (19.2)	0.62
Vascular comorbidity, *n* (%)	29 (30.5)	16 (30.8)	0.80
Diabetes, *n* (%)	21 (22.1)	16 (31.4)	0.4
Preoperative chemotherapy, *n* (%)	4 (4.2)	0	
Portal vein resection, *n* (%)	20 (21.1)	1 (1.9)	<0.001
Celiac trunk/SMA exploration, *n* (%)	6 (6.3)	0	

IQR first and third interquartile range, *PTC* percutaneous transhepatic cholangiography, *SMA* superior mesenteric artery

Table 2 Intra-operative results of pancreas CP and control groups of pancreaticoduodenectomy

Fluid and vasopressor management	Clinical pathway, $N = 95$	Control, $N = 52$	P
Intra-operative fluids (ml), median (IQR)	3900 (3000–4600)	5200 (4000–6000)	<0.001
Fluid balance, at the end of the procedure, median (IQR)	405 (−107 to 833)	1926 (1253–2818)	<0.001
Intra-operative blood loss, median (IQR)	755 (500–1100)	1303 (656–2402)	<0.001
Intra-operative vasopressor use, *n* (%)	94 (99)	48 (92)	0.22

Dindo classification grade 3 or more and hospital LOS in the CP group were significantly lower compared to the control group. In addition, implementation of the CP was associated with a reduction of gastroparesis, an improved post-operative fluid balance, and patients in the CP group were more likely to receive early mobilization and adequate actions on EWS above 3. These data illustrate that implementation of a CP in this specific group of patients is feasible, safe and likely to be beneficial for the patient.

Analyzing reasons not to follow the variance report was part of this study. Human factors were often reasons for deviation from the report, for example, insecurity of young professionals on decisions leading to postponing gastric tube removal. The prevention of gastroparesis is part of a very active PAR cycle in the CP. Nurses, young doctors and patients want to prevent discomfort for the awake patient while repositioning the tube, even if early removal is according to protocol. The action was a team reflection on the discomfort of a needless gastric tube for too long and, as a result, delay in starting early oral nutrition and well-being.

Postponing early mobilization because of patients' pain or weakness did occur. In all situations, the iterative process of repeated and specific education was important to explain the reasons behind the CP and guidance.

Considering the diverse landscape of CPs and surgical care plans, it is difficult to compare the different studies. In studies, related to implementation of CPs, not all hospital wards involved in the clinical process (like PACU/ICU) were included, which negatively influences the continuous care process for the patient. Also different treatment regimes make reliable comparison and evaluation of different CPs difficult. Regarding the available studies, we found only studies not covering the whole clinical stay, excluding parts of the post-operative period. In these studies usually some specific aspects like ERAS, drain and gastric tube removal were addressed.[18] A standardized care plan for pancreaticoduodenectomy patients was retrospectively studied in another study focussing on predictors of LOS in-hospital.[15] Specific ERAS pathways, without PACU/ICU periods involved, focussed on in-hospital LOS, outcome mortality and morbidity. While these were unchanged, measurement of protocol adherence was not part of the study.[16] Braga et al. evaluated the compliance to the enhanced recovery protocol and concluded that patients with low compliance had a higher incidence of complications.[40]

Our results are in pursuance of previous studies that showed that a CP or standardized care plan for pancreaticoduodenectomy patients resulted in an earlier start of solid enteral feeding and a shorter hospital LOS and less readmissions. Importantly, protocol adherence to predefined targets has not been part of these studies as was analysis of the reasons not following the protocol and its association to outcome.

Comparing our study to these studies, a similar effect on reduction of complications, hospital LOS, readmissions, gastroparesis, time to enteral feeding and time to mobilization was found. Our present study also illustrates that it is feasible to implement a CP that covers the entire clinical admission, applying different targets of the various involved units (e.g. focus on hemodynamic and respiratory vital parameters at the PACU/ICU, versus focus on EWS and ERAS criteria at the

Table 3 Post-operative data of pancreas CP and control groups of pancreaticoduodenectomy

	Clinical pathway, $N = 95$	Control, $N = 52$	P
Post-operative PACU, *n* (%)	81 (85)	29 (55)	0.002
Mobilization swing, according to protocol (within 24 h) *n* (%)	78 (83)	10 (19)	0.02
Mobilization out of bed in days, median (IQR)	2 (1–2)	2 (2–3.3)	0.001
Gastroparesis (ISGPS): *n* (%)			
• Type A	20 (21)	15 (29)	<0.001
• Type B	7 (7)	18 (35)	
• Type C	2 (2)	14 (27)	
Pancreas leakage, *n* (%)	12 (13)	5 (10)	0.82
Drain in situ (days), median (IQR)	6 (4–10)	7 (5–12)	ns
Clavien-Dindo classification *n* (%)			
3a	9 (10)	9 (19)	0.02
3b	1 (1)	4 (8)	
4b	1 (1)	0	
5	1(1)	0	
Radiologic reintervention, *n* (%)	10 (11)	14 (27)	0.04
Relaparotomy, *n* (%)	3 (3)	4 (8)	0.01
Readmission ICU, *n* (%)	7 (7)	7 (14)	ns
Readmission hospital, *n* (%)	12 (13)	9 (18)	ns
LOS in-hospital (days), median (IQR)	10 (8–15)	13 (10–18)	0.02
30-day mortality, *n* (%)	1 (1)	0	ns
90-day mortality, *n* (%)	2 (2)	1 (2)	

surgical ward). Nurses were also able to start adequate therapy in accordance with the variance rapport when EWS deviated from the target. Moreover, new to the other studies is that this study, via the variance report method, exposed the barriers and facilitators of CP adherence. In addition, these two monthly formal meetings to evaluate variance report deviations and their barriers and facilitators enabled us to discriminate the difference of loss of compliance to a protocol due to complicated discourse of operations, versus loss of professional adherence to the CP protocol.

The current study has several limitations. Most importantly, this is a single-centre pre-post-intervention study. The intensity and duration to develop the CP, as well as the implementation process, limit the feasibility of using other study designs. In addition, the historical group was not formally matched, which, together with the fact that no randomization was carried out, induces a higher risk of confounding factors. No relevant differences in patient characteristics between the different study periods were observed. However, the case load per surgeon increased, which could be considered as a possible confounding factor. We considered the development of a CP as the most appropriate intervention to re-schedule the process. Prospective complication registration was part of the daily supervised perioperative care as well as the discharge procedure in both groups. Moreover the prospective database on outcome and complications of the control group (2009–2012) served as a document to identify barriers and facilitators for building the CP. Furthermore, no relevant changes in other procedures, staffing levels, technical infrastructure or other major changes that could influence patient management occurred, and during the whole study period, there were no changes in interventions that are known to influence morbidity or mortality in the ICU such as strict glucose regulation, early goal-directed therapy, use of corticosteroids, prone positioning and low tidal volume ventilation. Second, no a priori power calculation was carried out, implying that the risk for a type 1 or 2 error has not been overcome. Using our convenience sample, we did calculate that our study has 80% power to demonstrate a 7% change in complication rate, while we observed that the complication rate halved. Nevertheless, the sample size of the study and the discussed design issues should make us aware of the possible overestimation of the outcome differences. In contrast, this does not necessarily apply for the process analysis part. As no comparison of the CP group was made to the control group, the conclusions of the process analysis merely indicate that CP development, implementation and high level of adherence to such a CP, throughout all units involved in the perioperative process, are feasible within a relative short period and up to a high standard.

Lessons Learned

This study shows us, in line with the implementation of our cardiac surgery CP and oesophageal surgery CP,[41] that it is feasible to develop and implement a CP for pancreaticoduodenectomy procedures for all involved units like the PACU/ICU and surgical ward through the entire clinical perioperative period. In all units, the CP targets need to be aligned and the use of a variance report discriminates complication-related to failure of professional adherence. Implementation is an iterative process that takes time to become comfortable in use for all involved units. Key nurses together with medical leadership were essential for awareness, feedback and motivation during development, implementation and the use of the CP.

Future Perspectives

In order to overcome the methodological drawbacks of this study and to validate the CP methods, a multicenter stepped-wedged cluster randomized controlled trial would be ideal. However, due to the complexity of the implementation and intervention with barrier and facilitator analysis in different hospitals and units, interpretation of the results will be difficult. Exploring the validity of similar CPs is in line with the need for quality assurance of standardized treatment regimes with high protocol adherences.

For the near future, continuous monitoring, wearables and electronic medical data recording with pop-up facilities warning medical and nursing staff for deviations from the CP will likely be of help in building more complex pathways. Possibly, patients with high comorbidity will be able to follow their personalized clinical pathway (pCP) with the help of dedicated staff.

Conclusion

The use of the CP was associated with a reduction of perioperative morbidity. Essential new tools include a variance report analysis, scheduled barrier and facilitator analyses and the iterative PAR cycle protocol development, performed by a multidisciplinary team. Development, implementation and use of a CP throughout the hospital stay for patients undergoing pancreaticoduodenectomy are a multistep procedure in which we showed that this is feasible and safe.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Appendix 1

Table 4 Similarities and differences between clinical pathway and control period

	Clinical pathway	Control
Outpatient clinic	Tumour board treatment advice (PACON)	Tumour board treatment advice (PACON)
	Oral and written patient information	Oral patient information
	Dietician contact: MUST screening tool, nutrition advice and if needed supplemental feeding oral or enteral	Dietician contact if needed supplemental feeding oral or enteral
	Frailty screening tool	
	Medication verification	
	Training advice: home trainer use, 1-h walking per day	
Surgical ward	Use of ERAS protocol	Use of ERAS protocol
	Preoperative lanreotide®	Preoperative lanreotide®
	Thrombosis prophylaxis nadroparine® 5700 E	Thrombosis prophylaxis nadroparine® 2850 E
	6:00 day of operation: last preop or clear liquid intake, anti-thrombosis compression stockings.	
	Pain management and control according to protocol together with pain service team	Pain management together with pain service team
	Early warning score once per 8 h and whenever indicated together with actions by nurses	Early warning score once per 8 h and whenever indicated action by resident
	Patient communication between doctors, nurses and handover situations according to Reason, Story, Vital Signs and Plan (RSVP)	Patient communication between doctors, nurses and handover situations not specified
	Mobilization after surgery: swing and out of bed within 24 h	Mobilization after surgery: swing and out of bed within 24 h
	Gastric tube: if production <200 ml in 12 h, remove tube	Gastric tube: if production is reduced, start clamp tube and remove if retention is <100 ml in 8 h (after two consecutive periods of 8 h)
	Drain removal if production <200 ml and amylase <500 U/l per day	Drain removal if amylase <500 U/l per day and operating surgeon agrees
	Nutrition: MUST >2, start TPN on day 1 post-operative	Nutrition: enteral feeding will start on day 1 if the patient has a jejunostomy. Oral fluids according to ERAS
	MUST = 1: if gastric tube has not been removed on day 3, start TPN	If no enteral intake is possible on day 6, TPN has to start on day 7
	All patients: if the gastric tube cannot be removed because of gastroparesis on day 7 without signs of sepsis or ileus: placement of a jejunal tube through the gastrojejunostomy by the gastroenterologist and start enteral feeding	
	Glucose control	Glucose control
	Discharge criteria	Discharge criteria not specified
	Use of the variance report if actions are not according to protocol.	
Operating room	Use of ERAS protocol	Use of ERAS protocol
	Pain control by epidural catheter	Pain control by epidural catheter
	Central venous line in the vena jugularis, if indicated PiCCO	
	Antibiotic prophylaxis 15–60-min pre-incision. Cefazoline® and metronidazole®. If a stent or percutaneous transhepatic drain has been placed in the ductus choledochus, use piperacillin/tazobactam® as prophylaxis.	Antibiotic prophylaxis 15–60-min pre-incision. Cefazoline® and metronidazole®. Otherwise if indicated by the surgeon
	Target post-operative fluid balance between 0 and 500 ml	Post-operative fluid balance not specified but according to ERAS
	Handover to PACU team members by surgeon and anaesthesiologist according to RSVP	Handover to PACU team members by anaesthesiologist
PACU/ICU	Entrance in PACU: every 15 min: RR and heart rate control until stable, than every 30 min RR and pulse	Entrance in PACU: every 15 min: RR and pulse control until stable than every 30 min RR and pulse
	Continuation of antibiotics will be part of the sign-out procedure after surgery	Continuation of antibiotics at the decision of the surgeon
	Normothermia (>36.0 °C), Bair Hugger or heating system if necessary	Normothermia (>36.0 °C), Bair Hugger or heating system if necessary
	Every hour (1st until 24th hour):	Every hour (1st until 24th hour):
	Respiratory status after extubation: saturation, respiratory frequency, coughing and deep breathing exercises	Respiratory status after extubation: saturation, respiratory frequency, coughing and deep breathing exercises

Table 4 (continued)

Clinical pathway	Control
Hemodynamics: heart rhythm, heart frequency, RR, $ScvO_2$ (if indicated).	Hemodynamics: heart rhythm, heart frequency, RR, $ScvO_2$ (if indicated).
Excretions: urine, drain, gastric tube	Excretions: urine, drain, gastric tube
Temperature	Temperature
Pain and sedation: NRS pain score	Pain and sedation: NRS pain score
RASS and CAM ICU	RASS
Mean arterial pressure (MAP) between 70 and 100 mmHg and heart frequency between 60 and 90 per minute. Different targets than the CP prescribe possible after approval of the supervising anaesthesiologist .	Mean arterial pressure (MAP) targets need approval of the supervising anaesthesiologist.
MAP should be above 70 mmHg: if below, start norepinephrine.	
iv fluids: ERAS protocol Balance between 0 and +500 ml/24 h	
Urine production has to be above 0.5 ml/kg/h. Protocol 'oliguria PACU'	Urine production has to be above 0.5 ml/kg/h. Protocol 'oliguria PACU'
First choice of inotropics: dobutamine®	First choice of inotropics: supervising anaesthesiologist
Stress ulcer prophylaxis pantoprazole® 1 dd 40 mg iv/po	Stress ulcer prophylaxis pantoprazole® 1 dd 40 mg iv/po
Nausea and vomiting: 3/day 4 mg ondansetron® iv (maximum until 36 h after surgery) 3/day metoclopromide® 3/day 10 mg iv (3/day 5 mg iv when kidney function reduced) (cave QT time)	Nausea and vomiting: If indicated: 3/day 4 mg ondansetron® iv If indicated: 3/day metoclopromide® 3 day 10 mg iv (3/day 5 mg iv when kidney function reduced) (cave QT time)
Anti-thrombosis prophylaxis nadroparine® 5700IE	Anti-thrombosis prophylaxis nadroparine® 2850 IE
Mobilization according to protocol: starts within 24 h	
Gastric tube: see CP surgical ward	Gastric tube
Drain: 2 abdominal drains Drain production control every hour: aspect and volume, 100–200 ml/h. If production >200 ml/h or >400 ml/4 h, contact surgeon	Drain: 2 abdominal drains Drain production control every hour: aspect and volume, 100–200 ml/h. If production >200 ml/h or >400 ml/4 h, contact surgeon
Electrolyte control and interventions	Electrolyte control and interventions
Glucose regulation: normoglycaemia (glucose 5.0–10.0 mmol/l)	Glucose regulation: normoglycaemia (glucose 5.0–10.0 mmol/l)
Discharge criteria: handover procedure according to RSVP, vital signs accepted by the surgical ward. Use of the variance report if actions are not according to protocol.	Discharge criteria according to PACU

Appendix 2

Sticker patiënt	CP Pancreaticoduodenectomy (Whipple, total pancreasresection and if indicated for other pancreassurgery) DAy 1

Date day 1: .....

intra venous lines and drains									D	E	N	Nutrition		Variance observed		Intervention
☐	Peripheral infusion (NaCl 0,9%) (1): ..... ml/h	☐	Drains (1):	☐	Diabetes?Follow glucoseprotocol (Q portal). Beware of infusion protocol for patients without oral intake.				☐	☐	☐	Start oral intake: (500 ml/day clear fluids/day)	☐	gastric tube removed	☐	Start fluids and if possible 6-8x /day small light meals
☐	Peripheral infusion (NaCl 0,9% (2): ..... ml/h	☐	Drains (2):													
☐	Central venous cathetere(1):..... ml/h	☐	Bladdercatheter:						☐	☐	☐	MUST-score	☐	MUST 2	☐	Start TPN according to nutrition prot-ocol and judge refeeding chance
☐	Central venous cathetere(2):..... ml/h	☐	Gastri tube:						D	E	N	Woundcare		Variance observed		Intervention
☐	Epidural: ..... ml/h	☐	Oxygen: ..... ltr/min						☐	☐	☐	Control gastric tube:production and color	☐	No gastric tube	☐	Stop control
D	E	N	Vital Signs	Variance observed				Intervention	☐	☐	☐	care and control CVC and peripheral i.v. catheters	☐	surrounding red skin or infiltrate	☐	CVC sepsis or infusion protocol
☐	☐	☐	Control vitale signs acc. MEWS	☐	MEWS-Score>3	☐	Interventions acc. MEWS-protocol									
☐	☐	☐	Bloodpressure	☐	Syst < 90 and normal pulse	☐	1 x 250ml NaCl 0,9% in 15 min. If needed repeat 1x . No effect contact doctor		☐	☐	☐	Epidural introduction skin control	☐	swollen skin, red , infiltrate	☐	Contact painteam
☐	☐	☐	respiration/ saturation	☐	Sat 91-96 %	☐	More O_2 if needed up to 5 L O_2		☐			Wounddrain skin introductionL 1 x day dry bandage	☐	Leakage	☐	3x day care and bandage
						☐	No effect contact doctor									
				☐	Sat < 91 %	☐	Discuss with consultant if NRB-mask is needed and discuss MCU		☐			Abdominal wound care	☐	No leakage and no infection	☐	1x day woundcare
☐	☐	☐	Pulse	☐	Irr. pulse 1ste time	☐	call doctor and uptain an ECG						☐	Leakage and signs of infection	☐	Woundplan
				☐	Irr. pols (after the first time and high or lower RR than normal for the patient	☐	contact doctor		☐	☐	☐	Cô fixation drain en gastri tube	☐	not sufficient or traction drain or gastric tubeMH	☐	Fixation acc to protocol
☐	☐	☐	Temp	☐	Temp ≥ 39,0 ^{0}C and/or shiffering	☐	contact doctor and take bloodcultures		D	E	N	Other	Variance observed		Intervention	
D	E	N	Input/Output	Variance observed				Intervention	☐			Call PACU if patient will be transfered to the ward at 11 hours	☐	Patiënt stays at PACU or goes to IC/MC	☐	Bed is free for other patient
☐	☐	☐	fluidintake 24 h: max. 2,5 L (goal is 0-balance)	☐	Balance in 24 h > 1 liter positive or > 1 liter negative	☐	contact doctor and adjust iv infusion		☐			Venouspunction (PACU): KNK, Hb, Ht, ASAT, ALAT, AF, gamma GT, bili's total en direct, amylase	☐	Handover plan :labresults need interventions	☐	communicatie with doctor
				☐	Neg. Balance because of gastric tube production	☐	Contact doctor, uptain a plan									
☐	☐	☐	gastric tube production	☐	I< 200 ml in 12h	☐	remove gastric tube + start diet		☐			amylase in drain (PACU)	☐	drain has already been removed	☐	Stop control amylase
				☐	vomiting when Gastrictube is still in situ langs maagwand	☐	Reposition gastric tube		☐	☐		lumen CVC	☐	Not used lumina CVC	☐	Heparinisation of unused lumina CVC according to protocol
☐	☐	☐	Vomiting	☐	> 300 ml	☐	reposition gastric tube		☐	☐	☐	4x daily glucose daycurve	☐	3.6 <glucose > 10	☐	Glucose protocol
☐	☐	☐	fluidbalance	☐	Neg. Balance because of gastric tube production	☐	uptain a Fluid intake plan together with doctor for day and night		☐	☐	☐	Glucose day curve after initiation of TPN: 3 h after start TPN and 6 h after start TPN (Time see start of TPV)	☐	Glucose <5 en >15	☐	Contact physician
☐	☐	☐	Drainproduction	☐	No leakage of gal or amylase (<500U/L) production < 200 ml/day	☐	remove drain after consulting pancreassurgeon									
				☐	change of aspect or production > 200 ml in 3 h	☐	call doctor		☐	☐	☐	24 u/dag Comprinetstockings	☐	sufficient mobilisation(6-8 hours out of bed and walking)	☐	stop comprinet anti thrombose stockings
☐	☐	☐	Diuresis à 3 uur	☐	< ½ ml/kg/h during. 3 h	☐	Contact doctor		☐	☐	☐	consultation: dietician, painteam,physiotherapist, physician (if glucose is not in control according CP) Medical emergency team				
☐	☐	☐	TPN	☐	3.6 <glucose > 10	☐	according glucose protocol									
D	E	N	Wellbeing	Variance observed				Intervention								
☐	☐	☐	Painscore < 4	☐	NRS > 4	☐	Intervention acc painprotocol				☐	22.00 h Nadroparine 5700 EH	☐	check NTX, allergy	☐	contact doctor for alternative
☐	☐	☐	Orientation(time, place, person)	☐	Patiënt is desoriented	☐	Start DOS registration and Frail protocol risk for delirium									
☐	☐	☐	Welbeing according to the patient	☐	acceptable for the patiënt	☐	communicate with the patient		Rapportage							
☐	☐	☐	Abdominal pain	☐	pain, cramps, tense, ructus, bowelsounds	☐	contact doctor		Start of TPN: ..... Hour							
D	E	N	Mobilisation	Variance observed				Intervention								
	☐		2 x 15-30 min. Swing or transfer to chair	☐	Swing or transfer to chair not possiblen	☐	Reason has to be rapported in the patients medical file and further plan									
	☐		Breathing exercisies	☐	not sufficient because of pain	☐	contact painteam									
				☐	not sufficient but pain is not the reason	☐	contact doctor									

Appendix 3

UMC St Radboud	**Variance CP POSTOPERATIve (day 0/1-2) Pancreaticoduodenectomy Date……**	sticker patiënt
variance respiratory status	**Action**	**Medical Plan, time, action**
Patient is not extubated < 6 hours because extubation goals are not achieved.	□ contact doctor	□
Variance respiratory status after extubation	**Action**	**Medical Plan, time, action**
SpO_2 < 96 % (in some patients a lower SpO2 is accepted, this should be part of the written treatment plan)	□ discuss possible reasons with the patient □ exclude pain and stress □ control oxygen supply/device □ O_2 use maxl 5ltr □ control leakage □ rest anasthetics? □ stimulate efficient coughing (small pillow) **If the result is not enough:** □ check SpO_2 at arrival in the hospital □contact doctor □ start non-rebreathing masker or aquapack 100 % after contact with doctor	reason: □ □ □ □ □ $SpO_{2\ \text{at arrival in the hospital}}$ > ……..…..% □ non-rebreathing mask/aquapack 100% □ re- intubation lower saturation can be accepted
breathing frequency > 30 / minute	□ SpO_2 < 96 %: see variancebij SpO_2 < 96% □ SpO_2 ≥ 96 %: ○ discuss possible reasons with the patient ○ exclude pain and stress ○ unknown ? contact doctor	□ □ ○ ○ ○ ○
breathing frequency < 10 / minute	□ observe and stimulate the patient □ reason? Medication? □ SpO_2 < 96 %: see variance SpO_2 < 96% □ contact doctor if apnoe and/or breathing frequency < 6 / minute	□ □ □ □
Variance hemodynamic stability	**Action**	**Medical Plan, time, action**
all combinations of hemodynamic changes including sinusrhythm > 90 / minute)	□ control situation physiology on arrival in the hospital, contact doctor	□
New rhythm and/ of disrhythmia	□ uptain ECG □ contact doctor	Rhyth analysis:
ABP MAP < 70 mm Hg	□contact doctor	□
ABP MAP > 100 mm Hg or systolic bloodpressure >150 mm Hg	□ contact doctor	□
ABP MAP 70 - 100 mm Hg:if PiCCO - CI > 3,0 l/min/m2 - ITBVi < 850 ml/m2 - EVLWi < 10 of > 10 ml/kg	□ If results are not sufficient after 2x 250 ml : contact doctor	□ 1stVolulyte® 250 ml ……..…time □ 2nd Volulyte® 250 ml……time □ result not sufficient:
ABP MAP 70 - 100 mm Hg:if PiCCO - CI > 3,0 l/min/m2 - ITBVi > 850 ml/m2 - EVLWi > 10 ml/kg	□ contact doctor	□

ABP MAP 70 - 100 mm Hg:if PiCCO - CI < 3,0 l/min/m2 - ITBVi < 850 ml/m2 - EVLWi < 10 of > 10 ml/kg	□ If results are not sufficient after 2x 250 ml : contact doctor	□ 1stVolulyte® 250 ml ……..….time □ 2nd Volulyte® 250 ml……..……time □ result not sufficient:
ABP MAP 70 - 100 mm Hg: if PiCCO - CI < 3,0 l/min/m^2 - ITBVi > 850 ml/m_2 - EVLWi < 10 of > 10 ml/kg	□ contact	□
$ScvO_2$ < 70%	□ contact doctor	□

UMC St Radboud	**Variance CP POSTOPERATIve(dag 0/1-2)pancreaticoduodenectomy Date……**	sticker patiënt

Variance Excretion	Action	Medical Plan, time, action
Diuresis < 0,5 ml/kg/hour	□ control function of bladder catheter □ contact doctor	□
Abdominal drain leakage	□ contact doctor if signs of infection □ contact doctor if bandage has to be renewed 2x per shift because of fluidloss	□ □
		Oorzaak : □
		□
Variance Temperature	**Action**	**Medical Plan, time, action**
< 35,0 ^{0}C	□ □ start Bair Hugger® / heating system □ breathing air has to be warm if the patient is still on the ventilator	□ □ □
< 36,0 ^{0}C	□ □ start Bair Hugger®/ heating system	□ □
> 38,0 ^{o}C	□ contact doctor	□ postoperative inflammatory response of infection related
Variance Pain en Sedation	**Action**	**Medical Plan, time, action**
sedated patient	□ continue sedation if temperature < 36,0 ^{0} C □ reduce sedation depending on blood results or stop sedation if temp > 36,0^0 C and the patient is hemodynamic and respiratory stable and no anesthesia (TOF)	□ Start of Sedation reduction ……..hour □ Sedatie stop ……..……...hour
NRS > 4 because of wound pain and the patient is on pain medication	□ control epidural block **60 minuten after start of extra pain medication (in contact with doctor):** □ New measure of NRS / CPOT □ communicate with doctor for extra pain medication □ contact doctor about the need of diagnostics and consultation	□ □ □ □ □
Variance general	**Action**	**Medical Plan, time, action**
patient lies in a position of 45^0	□ control □ if not than put in right position 45 degrees	□ □
subcutaneous emphysema	□ contact doctor	□
Patiënt has nausea	□ Ondansetron 4 mg i.v. □ insufficient result contact doctor	□ □
Patiënt has fear and stress	□ communicate fear and sress with the patient □ insufficient result contact doctor	□ □

Variance Labresults	Action	Medical Plan, time, action
Glucose < 6,0 mmol/l	□ glucose protocol	□
Glucose > 8,0 mmol/l	1st result at PACU/ICU entrance glucose > 8,0 mmol/l: □ control after 1 hour If second result or every other result after the first is > 8,0 mmol/l: □ glucose protocol PACU/ICU	□ □

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