



Impact of an oral nutrition protocol in patients treated with elective radical cystectomy: a long term follow-up

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Abstract

Background After radical cystectomy, delayed return of bowel function is relatively common. Although studies investigating on the best modality for delivering nutritional support to this patient group are limited, parenteral nutrition was standard of care in those patients at the urological ward of the University Hospitals Leuven. In 2015, we published the findings from our study conducted in patients undergoing elective regular radical cystectomy at the urological ward of the University Hospitals Leuven comparing the length of hospital stay in patients with early postoperative parenteral nutrition (n=48) versus an immediate oral nutrition protocol (n=46). It was demonstrated that the implementation of an oral nutrition protocol was associated with a significant reduced length of hospital stay (median [IQR] of 18 [15–22] to 14 [13–18] days ($p < 0.001$)). The sample size was however too small to investigate the impact of the oral nutrition protocol on the incidence of catheter-related bloodstream infection, a common parenteral nutrition related complication. **Objective** To investigate the long term impact of an oral nutrition protocol on the incidence of catheter-related bloodstream infection, duration of catheterization and the length of hospital stay. **Method** Retrospectively, before (parenteral nutrition group) and after the implementation of the oral nutrition protocol (since March 10th 2010), two cohorts of 549 patients who underwent an elective regular radical cystectomy were included. The incidence of a catheter-related bloodstream infection and the length of stay were compared. A central venous catheter was present in every patient, which is standard of care. **Results** Catheter-related bloodstream infection was reduced from 22 (4%) to 10 (1.8%) ($p = 0.031$). The median duration of catheterization was 10 [7–13] days for the parenteral nutrition versus 7 [7–7] days for the oral nutrition group ($p < 0.001$). The median length of stay between both groups, 20 [17–25] before versus 17 [14–21] days after the implementation of the oral nutrition protocol, also differed significantly ($p < 0.001$). Implementing the oral nutrition protocol resulted in a parenteral nutrition associated cost saving of €470 per patient. **Conclusion** This large follow-up study showed that the oral nutrition protocol is associated with a reduction in catheter-related bloodstream infection. Besides, postponing parenteral nutrition in favour of oral nutrition enhances recovery.

Keywords Belgium · Catheter-related bloodstream infection · Costs · Length of stay · Oral nutrition protocol · Parenteral nutrition · Radical cystectomy

Impacts on Practice

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- As surgery is foremost uncomplicated in the majority of cases in regular elective radical cystectomy, systematic postoperative parenteral nutrition should not remain the standard of care in those patients.
- An oral nutrition protocol is a valid and safe alternative for systematic use of parenteral nutrition after elective regular radical cystectomy.
- For the patients, an oral nutrition protocol results in fewer catheter-related bloodstream infections and earlier hospital discharge.

- The avoidance of parenteral nutrition by the implementation of an oral nutrition protocol leads to important cost savings.

Background

Bladder cancer and neurogenic bladder problems can be treated by radical cystectomy (RC) and immediate urinary reconstruction. After RC, delayed return of bowel function is relatively common and parenteral nutrition (PN) is often used to deliver nutritional support [1–7]. However, the European Society for Parenteral and Enteral Nutrition supports the idea of early oral or enteral nutrition in uretero-ileal and ileo-ileal anastomosis, both carried out after RC [8]. To the best of our knowledge, studies investigating the impact of postoperative oral nutrition compared to parenteral nutrition on clinical outcomes in this patient group are limited.

In this specific setting, Roth et al. conducted a prospective, randomised, single-centre study comparing 74 RC patients with postoperative PN with 83 patients receiving oral nutrition. In this study, postoperative oral nutrition was associated with a lower incidence of infections and costs. However, length of hospital stay did not differ between the two groups [6].

Other studies investigating postoperative complications and length of stay (LOS) in RC patients often dealt with Enhanced Recovery After Surgery (ERAS) regimen implementation [9–13]. ERAS regimens are multimodal care pathways, including enhanced postoperative oral nutrition support. The implementation of ERAS regimens led to fewer postoperative complications and shorter LOS in most studies [9–13]. Infection rates were not assessed in those studies. Since postoperative oral nutrition support was only one of many altered aspects in ERAS regimen implementation, it is consequently difficult to draw conclusions about the impact of this specific aspect in these patients.

In 2015, we published a study [14] in patients undergoing elective RC comparing early postoperative PN in 48 patients with an immediate oral nutrition protocol (ONP) in 46 patients. We demonstrated that the implementation of an ONP was associated with a significant reduced LOS (median [IQR] of 18 [15–22] to 14 [13–18] days ($p < 0.001$)) and PN usage [median [IQR] of 8 [6–10] versus 0 [0–0] PN bags ($p < 0.001$)]. The direct PN-related cost saving was €500 per patient. Though postoperative ileus was present in 28% of patients in the ONP group, time to resumption of full diet was achieved by the fourth postoperative day, justifying the ONP approach. Based on these study results, the ONP became our hospital standard of care in elective RC.

Catheter-related bloodstream infections (CRBSI) is a common PN-related complication [15]. Although we found a numeric reduction from four CRBSI in the PN group to zero

in the ONP group in our previously published study [14], the sample size was too small to investigate the impact of the ONP on CRBSI incidence. Roth and colleagues showed that postoperative oral nutrition was associated with a lower incidence of infections, but they did not assess CRBSI in their study [6].

The primary objective in the current retrospective case-control study was to explore the impact of the introduction of an ONP on CRBSI incidence in a large elective RC patient group. Secondary endpoints were to evaluate if the proportion of patients needing PN, the number of administered PN infusion bags per patient, the LOS and PN associated costs sustained over time, as demonstrated in our previous study [14].

Ethics approval

This study was approved by the hospital's Ethics Committee (Ethical Committee for Research University Hospitals Leuven; S52942).

Methods

Patients

In this retrospective case-control study, adult patients admitted to the urological ward of the University Hospitals Leuven and treated with elective regular RC were eligible, based on the same criteria as stated in our previous study [14]. In brief, patients were included when admitted for one of the following reconstructions: an ileal conduit, an orthotopic neobladder (N-pouch) or a continent cutaneous urinary diversion. The surgical procedure was considered regular if the patient returned to the urological ward after the procedure and was not transferred to the intensive care unit (ICU). Exclusion criteria was transfer to the ICU.

A central venous catheter was inserted intraoperatively and left in place for at least seven postoperative days to ensure the possibility for postoperative PN therapy if needed. If the catheter was used for PN administration, the catheter was kept until two days after the cessation of PN.

Up to March 9th 2010, the standard of care was immediate PN after surgery until the patient was able to tolerate solid food. At the discretion of the treating physician, up to two l extra intravenous fluids per day were given as well. These patients were retrospectively assigned to the control group, further described as the PN group.

From March 10th 2010 onwards, an ONP was implemented (Table 1) [14]. These patients were retrospectively assigned to the case group, further described as the ONP group. Oral intake (oral fluids and easily digestible food)

Table 1 Oral nutrition protocol (ONP) implemented in the immediate postoperative setting after elective regular radical cystectomy in the case group

Post cystectomy	Breakfast	Lunch	Dinner
Day 1 IV FLUID MANAGEMENT: Up to two litres, depending on oral fluid intake	1 bottle of still water	1 cup of lime tea with sugar, honey and lemon (50 kcal) OR 1 glass of still water	1 cup of lime tea with sugar, honey and lemon (50 kcal) OR 1 glass of still water
Day 2 IV FLUID MANAGEMENT: Up to two litres, depending on oral fluid intake	Oral fluids at the discretion of the patient (same fluids as on Day 1)		
Day 3 IV FLUID MANAGEMENT: Up to two litres, depending on oral fluid intake	Yoghurt (60 kcal) + Oral energy sips (300 kcal)	Stock broth (20 kcal) + Oral energy sips (300 kcal)	Yoghurt (60 kcal) + Oral energy sips (300 kcal)
Day 4 IV FLUID MANAGEMENT: Up to two litres, depending on oral fluid intake	Toast with jam (105 kcal)	Poached fish + butter dressing + mashed potatoes (500 kcal)	Slices of white bread (150 kcal)
Day 5 IV FLUID MANAGEMENT: Up to two litres, depending on oral fluid intake	Slices of white bread (150 kcal)	Chicken + applesauce + mashed potatoes + pudding (550 kcal)	Slices of white bread (150 kcal)
Day 6 IV FLUID MANAGEMENT: Up to two litres, depending on oral fluid intake	Regular diet OR If the patient cannot meet energy requirements by mouth on the 6th day and has a CI for EN, start PN Energy requirements (kcal/day) = 30 kcal/kg ideal body weight* [14] ± 10% *Male BMI < 30 : $50 + 0.91 \times (\text{length (cm)} - 152.5)$ *Male BMI ≥ 30: $1.2 \times [50 + 0.91 \times (\text{length (cm)} - 152.5)]$ *Female BMI < 30: $45.5 + 0.91 \times (\text{length (cm)} - 152.5)$ *Female BMI ≥ 30: $1.2 \times [45.5 + 0.91 \times (\text{length (cm)} - 152.5)]$		

IV intravenous, CI contra-indication, EN enteral nutrition, PN parenteral nutrition, kcal kilocalories, BMI body mass index

was increased progressively, independent of bowel movements. At the discretion of the treating physician, up to 2 l extra intravenous fluids per day were given. Nurses verified daily whether the patient was able to tolerate the ONP. From the sixth day, the patient was allowed to eat at will. If oral intake remained insufficient after five days, according to the treating physician, PN could be initiated on the sixth day.

Data collection

Data were retrospectively collected. The identification codes of the patients treated with elective regular RC were provided by the Management Information and Reporting (MIR) group from the hospital. Since the ONP was implemented,

from March 10th 2010 until December 2017, 549 patients underwent an elective regular RC (ONP group). Via backward inclusion, an equal number of 549 elective RC patients (PN group) was selected (June 2000 to March 9th 2010).

Duration of catheterization—further described as the number of catheter days—, number of administered PN units and LOS were collected. PN consumption data were retrieved from the pharmacy data warehouse.

To identify patients with a CRBSI, information on positive blood cultures were extracted from the Laboratory Information System (LIS). For patients with positive blood cultures, the medical record was assessed in detail. CRBSI was defined as bacteraemia or fungemia when an intravascular device was present, with more than one positive blood

culture result obtained from both the catheter lumen and a peripheral vein, clinical manifestations of infection (e.g. fever, chills, and/or hypotension) and no apparent other source for bloodstream infection [15].

Endpoints

The primary endpoint was the comparison of the CRBSI incidence between both groups. Secondary endpoints were to compare for patients between both groups the number of catheter days, the proportion of patients in whom PN was initiated, the number of administered PN infusion bags, LOS and PN associated costs.

Evaluation of PN associated costs

The avoided cost associated with PN use in both groups was calculated in total and per patient. For both the PN and the ONP group, the total number of PN infusion bags per group was divided by the number of patients in that group and multiplied by € 60, which is the average actual cost in euros of one bag of Oliclinomel[®]/Olimel[®] supplied with micro-nutrients in Belgium at the time of the study. This resulted in a direct and comparable PN infusion bag related cost per patient per group.

Statistical analysis

Statistical analysis was performed using SPSS Statistics 25.0 for Windows. Chi-square was used to compare categorical and the Wilcoxon rank sum test was used for non-normal distributed continuous variables. The outcome measures were considered statistically significant if *p*-values were <0.05.

Results

In both the PN (June 2000–March 9th 2010) and the ONP (March 10th 2010–December 2017) group, an equal number of 549 patients were included.

The outcome measures are presented in Table 2. There was a significant decrease in CRBSI incidence from 22 (4%) in 549 PN patients to 10 (1.8%) in 549 ONP patients (*p*=0.031). From these 32 patients with a CRBSI, PN was administered in 27 (84%) of them.

The total number of catheter days was 6703 for the PN group and 4792 days for the ONP group. The median number of catheter days was 10 [7–13] days for the PN versus 7 [7–7] days for the ONP group (*p*<0.001).

In 465 (85%) from the 549 PN patients, PN was initiated with a total of 5173 administered PN infusion bags. A median of 8 [6–11] PN infusion bags were administered per patient. In 76 (14%) out of 549 ONP patients, PN was initiated with a total of 873 administered PN infusion bags. A median of 0 [0–0] PN infusion bags were administered per patient. None of these ONP patients started PN immediately after surgery. PN was only started, as stated in the ONP, in presence of postoperative ileus (manifested by vomiting or high nasogastric tube output), which is a contra-indication to start oral nutrition. The median number of administered PN infusion bags per patient between both groups differed significantly (8 [6–11] vs. 0 [0–0], (*p*<0.001)).

The median LOS between both groups was 20 [17–25] days in the PN group versus 17 [14–21] days in the ONP group (*p*<0.001).

Evaluation of direct PN associated costs

The direct PN cost for the PN group was 5173 PN infusion bags × €60 = €310.380 or an average cost of €565 per patient.

Table 2 Outcome measures and direct PN cost comparison

	PN group (n = 549)	ONP group (n = 549)	<i>p</i> value
Primary endpoint			
CRBSI incidence, n (%)	22 (4.0%)	10 (1.8%)	0.031
Secondary endpoints			
Number of catheterdays per patient, median [IQR]	10 [7-13]	7 [7-7]	<0.001
Number of patients in whom PN was initiated (%)	465 (85%)	76 (14%)	<0.001
Number of administered PN infusion bags per patient, median [IQR]	8 [6-11]	0 [0-0]	<0.001
LOS, median [IQR] days	20 [17-25]	17 [14-21]	<0.001
Direct PN cost per patient	€565	€95	n.a.

n number, *PN* parenteral nutrition, *ONP* oral nutrition protocol, *IQR* interquartile range, *CRBSI* catheter-related bloodstream infection, *LOS* length of stay, *n.a.* not applicable

In the ONP group, the direct PN cost was 873 PN infusion bags \times €60 = €52,380 or an average cost of €95 per patient.

Consequently, the direct PN associated cost savings after implementing an ONP when comparing both groups with an equal amount of patients, is 310,380 euro – 52,380 euro = 258,000 euro. Per patient, this means a cost saving of 470 euro.

Discussion

This long term follow-up case–control study in patients undergoing elective regular RC reinforces the findings from our previous study [14] that the implementation of an ONP, when compared to immediate postoperative PN, is associated with a reduction in LOS, PN usage and direct PN costs. Moreover, due to the larger patient number, it was also possible to demonstrate that the ONP was associated with a significant reduction in CRBSI incidence.

To our knowledge, this is the first report comparing the CRBSI incidence between two cohorts subjected to postoperative parenteral versus oral nutrition support, respectively. In a study conducted by Roth et al., comparing RC patients with postoperative PN versus oral nutrition, CRBSI was not assessed [6]. In studies implementing ERAS regimens, postoperative diet is only one of the many altered items and CRBSI incidence has not been reported either [9–13]. Hence, our CRBSI results cannot be compared to others.

Although CRBSI is believed to be a common PN-related complication [15], the data from a systematic literature review could not establish whether patients receiving PN are more at risk of developing a CRBSI than those who do not [16]. Our study does demonstrate a reduction in CRBSI. In our opinion, this reduction can be explained by the reduction in catheter days in the ONP group. The median number of catheter days per patient reduced from 10 [7–13] days in the PN group to 7 [7–7] days in the ONP group. ONP patients were less exposed to a catheter and thus to develop a CRBSI.

Besides the described impact on CRBSI incidence, the introduction of an ONP also significantly reduced LOS (a median reduction of 4 days) and PN usage (from a median of 8 to 0 PN infusion bags). These reductions were observed in the original study [14], and were sustained during this long term follow-up period. Our data concerning LOS corroborate data from literature. On the one hand, the median baseline LOS of 20 [17–25] days in the PN group, is in line with previously reported LOS in RC patients: i.e. 21 to 23 days, all expressed as mean LOS [17–19]. On the other hand, in our study population, implementation of the ONP was associated with a reduction in LOS to 17 days (IQR 14–21 days), which was also reported by research groups investigating enhanced recovery pathways in RC patients (mean of 18 days) [5–7].

Because of the presence of postoperative ileus on day six after RC in 76 (14%) out of the 549 ONP patients, oral nutrition was contra-indicated. Consequently, PN was initiated per protocol in this subgroup of patients at that moment. However, PN was not administered in the other 473 (86%) patients from the ONP group. This study reinforces the results from our previous study [14] that an ONP approach is justified and is associated with drastic reduction in PN use and shorter LOS after elective cystectomy.

Regarding the total PN associated cost saving, 258,000 euro was saved in 549 patients, corresponding to 470 euro per patient. This cost saving per patient corroborates with the cost saving of 512 euro as reported in our previous study [14].

This study has several potential limitations. Firstly, inherent to the retrospective design, the problem of missing data could be present. However, since this is a single institution study and since all data from both the blood cultures and the PN usage were extracted automatically from the electronic data file system, we have circumvented this issue. Secondly, the study was designed as a non-randomized before-after study. As such, it does not allow complete comparison for non-observed time-dependent differences between both groups. However, during the study period, the standard of care in elective regular RC patients did not change in our hospital. No change occurred in type of surgery, operation room capacity, number of urologists, catheter type and other care practices. Finally, patients with an irregular cystectomy course have been transferred to an ICU and subjected to an alternative nutrition protocol. Therefore, we cannot extrapolate our results to all RC patients. On the contrary, patients with an irregular cystectomy course would have been transferred to an ICU and subjected to an alternative nutrition protocol.

Conclusion

This study confirms that early oral nutrition should be standard of care in elective RC patients. For the patients, an oral nutrition protocol results in fewer catheter-related bloodstream infections and earlier hospital discharge.

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Conflicts of interest No authors have financial and personal relationships with other people or organizations that could inappropriately influence (bias) their work.

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