Applying fast-track protocols in bladder cancer patients undergoing radical cystectomy with ileal urinary diversions-early results of a prospective randomized controlled single center study

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Abstract

Introduction and objectives. Fast-track protocols (FTP) have been used in colorectal surgery for more that two decades, resulting in better rehabilitation after surgery, shorter hospital stay, less morbidity and mortality, lower overall costs. Recent studies emphasize the importance and benefits of applying FTP also in urologic surgery. This study represents the initial experience and results of implementing FTP in radical cystectomy (RC) patients in our center.
Materials and methods. The study comprises 20 randomized patients divided into two groups: group A which includes 10 patients with RC and ileal urinary diversion (IUD) benefiting of classical perioperative approach and group B which also includes 10 patients with RC and IUD in whom we used the FTP. The FTP used is adapted from the guidelines for perioperative care after radical cystectomy for bladder cancer: Enhanced Recovery After Surgery (ERAS) Society recommendations and consist of pre-, intra- and postoperative measures. The parameters analyzed during this study were major complications (Clavien grade ≥III) and minor complications (Clavien 1 or 2), type of urinary diversions, age, gender, ASA Score, pathologic stage, operative time, time to first flatus, time to first stool, time to normal diet, intolerance to oral feeding, postoperative ileus, length of hospital stay, smoker/non-smoker, and also in the FTP group we recorded the implementation of each FTP element per patient in order to test the feasibility of applying all items of the protocol.
Results. We noticed a decrease in median time to first stool in the FTG of 2.5 days compared with the CSG and a lower median time to first stool - 6 days in the FTG compared with 7 days in the CSG. Moreover, the median time to a normal diet was lower for the FTP patients, resuming to a normal diet after 4.5 days compared to CSG patients who began oral feeding in 6 days. Intolerance to oral feeding was encountered in 2 patients in the FTG and in 4 patients in the CSG. In our opinion, the NGT plays a key-point issue. When analyzing complications we encountered complications in 4 patients from the FTG and in 6 patients from the CSG. Seven minor complications were found in the FTG and 17 in the CSG respectively and we encountered two cases of major complications in the CSG - bowel evisceration, while there was none in the FTG.
Conclusions. As a conclusion to our study, we can state that from these initial data, FTP applied in RC patients have promising results with a good overall implementation of protocol items, nearly 84%.

Keywords: fast-track, radical cystectomy, ileal urinary diversion, complication rate, hospital stay.

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Introduction and objectives

Radical cystectomy (RC) is the standard treatment in patients with muscle invasive bladder cancer (MIBC) or patients without muscle invasive disease, but at high risk of recurrence and progression [1-3].

Fast-track protocols (FTP) have been used in colorectal surgery for more that two decades. A large amount of studies have clearly underlined the importance and benefits of applying these protocols in colorectal patients resulting in a better rehabilitation after surgery, shorter hospital stay, less morbidity and mortality, lower overall costs [4].

Even today RC represents a challenging procedure not only for the surgeon, but also for the patient. Moreover, the vast majority of patients are smokers, of old age, associating more than one comorbidity. With that said, a recent large study found early complications rates (first 3 months) in 58% of patients who underwent RC [4].

Even though RC represents a different type of procedure when compared with colorectal surgery due to a longer operating time, small bowel anastomosis, larger dissection area, extended or supra-extended pelvic lymph node dissection (LND), greater blood loss, urine leak in the peritoneal and pelvic cavity, intra- and extraperitoneal access and dissection, some authors emphasize the importance and benefits of applying FTP in urologic surgery [6-9]

This study represents the initial experience and results of implementing FTP in RC patients in our center.

Materials and methods

Annually we perform in our clinic an average of almost 200 radical cystectomies.

Having in mind the high morbidity rate, in an attempt to improve recovery and decrease morbidity, we started implementing FTP to RC patients undergoing ileal urinary diversion (IUD) for the past 90 days. This is a randomized controlled study, the main selection criteria being bladder cancer patients who undergo RC with IUD. The FTP used is adapted from the guidelines for perioperative care after radical cystectomy for bladder cancer*: Enhanced Recovery After Surgery (ERAS) Society* recommendations and consist of pre-, intra- and postoperative measures [6]. The preoperative measures are represented by counseling and education, no oral mechanical bowel preparation, preoperative optimization of medical conditions as good as possible (improving or balancing hypertension, anemia and diabetes, etc., start physical exercise, recommend smoking, drugs or alcohol cessation, preoperative carbohydrates loading (meals rich in carbohydrates 6-8h before surgery and 300 ml carbohydrates rich beverages 2-3 before surgery), prevention of deep vein thrombosis with compression stockings and low molecular weight heparin (LMWH) [6].

The intraoperative measures consist of thoracic epidural analgesia (in our study maintained usually for 48-72 hours), antimicrobial prophylaxis induced 1 hour before skin incision with only 1 dose of antibiotic, skin preparation with clorhexidine, use of perioperative balanced fluid management and maintaining a normal body temperature during surgery using electric thermal blankets [6].

The postoperative measures are represented by early removal of nasogastric tube (NGT) in first 24 hours after surgery, postoperative ileus prevention with chewing gum and oral magnesium chewing tablets, early mobilization (first day after surgery) and early feeding (first 48 h before surgery) [6].

The study comprises 20 randomized patients divided into two groups: group A which includes 10 patients with RC and IUD benefiting of classical perioperative approach and group B which also includes 10 patients with RC and IUD in whom we used the FTP mentioned above.

The parameters analyzed during this study were major complications (Clavien grade ≥III) and minor complications (Clavien 1 or 2), type of urinary diversions, age, gender, ASA Score, pathologic stage, operative time, time to first flatus, time to first stool, time to normal diet, intolerance to oral feeding, postoperative ileus, length of hospital stay, smoker/non-smoker, and in the FTP group we also recorded the implementation of each FTP element per patient in order to test the feasibility of applying all items of the protocol.

Major complications were represented by the presence or absence of evisceration, acute renal failure, cardiac ischemia, death, postoperative bleeding, pulmonary thromboembolism, and mechanical bowel obstruction.

Minor complications evaluated were postoperative ileus, nausea/vomiting, urinary tract infections (UTI), arrhythmias, atelectasis/desaturations, altered mental status, deep vein thrombosis, urine leak, Clostridium Difficile enterocolitis (CDE), pneumonia, wound dehiscence, fever of unknown origin.

Results

Regarding patient's characteristics, median age in the fast-track group (FTG) was 62.5 years, while in the classic surgery group (CSG) was 62 years, male to female ratio in both groups was 10/0, ASA score in FTG was ASA 1 in 9 patients and ASA 2 in 1 patient. In the CSG, ASA score was ASA 1 in 6 patients and ASA 2 in 4 patients. Clinical staging in the FTG was cT2N0M0 in 5 patients and cT4N0M0 in 5 patients. In the CSG we recorded 6 patients with cT2N0M0, 4 patients with cT3-4N0M0 and 1 patient with cT3-4anyNM0 (patient had lymph node metastasis in the common iliac lymph nodes N3-supraextended LND was performed).

Regarding the type of urinary diversion, in the FTG we performed 6 orthotopic neobladders (ON) and 4 Bricker ileal conduits (BIC), while in the CSG we had 5 patients with ON and 5 patients with BIC.

Median operative time was nearly equal in both groups: 350' in FTG and 354' in the CSG.

Median time to first flatus was 2.5 days in the FTG and 4 days in the CSG, with a median time to first stool was 6 days in the FTG and 7 days in the CSG.

Median time to normal diet was 4.5 days in FTG and 6 days in the CSG, 2 patients having intolerance to oral feeding in the FTG and 4 in the CSG.

In what concerns the oral feeding we started oral diet in all patients first with fluids and only after with solids in the first 48 h for the FTG in contrast with the CSG where oral diet was started after the passage of first flatus. We encountered postoperative ileus, defined as absence of bowel function 4 days after surgery in 2 patients in the FTG and in 4 patients in the CSG. Median length of hospital stay was 17.5 days in FTG and 20.5 in the CSG. We encountered complications in 4 patients from the FTG and in 6 patients from the CSG. Complications were divided into major (Clavien Grade ≥III) and minor complications (Clavien grade 1 or 2). Two patients (20%) from the CSG presented major complications like bowel evisceration, which was repaired in both cases using a polypropylene mesh applied under general anesthesia. Regarding minor complications in the FTG we found postoperative ileus in 2 patients, nausea and vomiting in 1 patient, urine leak in 1 patient (increased drainage on the lateral neobladder drain and also in the urethro-neobladder catheter - treated conservatively), CDE in 1 patient and wound dehiscence in 2 patients (supra-aponeurotic dehiscence treated conservatively). In the CSG we found 4 patients with postoperative ileus, 2 patients presented nausea and vomiting, 2 patients had UTI treated with antibiotics, 1 patients presented with arrhythmia-atrial fibrillation which was converted in the same day, 3 patients had CDE, 3 patients developed wound dehiscence and 3 patients had fever on unknown origin which was treated with broad spectrum antibiotics. Seven minor complications were found in the FTG and 17 in the CSG respectively. (see table No.1 and 2)

An important part of the study was represented by the possibility and the actual implementation of the protocol items. Not all protocol items have been fully implemented in all patients due to various reasons. We describe as follows the percentage of every protocol item.

Counseling and education was implemented in most of the patients (90%), a real problem encountered during the study being the preoperative optimization of medical conditions because most of our patients were smokers, reluctant to cease smoking. Another important issue was represented by cardiovascular illness, obesity and diabetes diagnosed but not treated due to patients lack of medical education and negligence, therefore obtaining an average of item implementation of 30%. No oral mechanical bowel preparation was applied in all of patients (100%), preoperative carbohydrates loading in 100% of cases, no preoperative fasting in all patients (100%), pre-anesthesia medication in 90% of patients.

One patient had increased anxiety and received medication.

Table No.1

Patient characteristics	Fast-track	Classic surgery
Median age	62.5	62.0
Male/Female	10/0	10/0
ASA score		
ASA 1	9	6
ASA 2	1	4
ASA 3	0	0
Pathological clinical stage		
T2N0M0	5	5
T3-T4N0M0	5	4
T4anyNM0	0	1
Type of diversion		
Orthotopic neobladder	6	5
Bricker diversion	4	5
Median operative time (min)	350	354
Median time to first flatus	2.5	4
Median time to first stool	6	7

Median time to normal diet	4.5	6
Intolerance to oral feeding (No. Patients)	2	4
Postoperative ileus (No. Patients)	2	4
Length of hospital stay (Median)	17.5	20.5
Complications (No. Patients)	4	6

Table No. 2

Major Complications	**Fast-Track**	**Classic surgery**
Eviscerating	0	2
Acute renal failure	0	0
Cardiac ischemia	0	0
Death	0	0
Postoperative bleeding	0	0
Pulmonary trombembolism	0	0
Mechanical bowel obstruction	0	0
TOTAL	0	2
Minor complications		
Postop Ileus	2	4
Nausea/Vomiting	1	2
UTI	0	2
Arrhythmias	0	1
Atelectasis/desaturations	0	0
Altered mental status	0	0
Deep vein thrombosis	0	0
Urine leak	1	0
Clostridium difficile enterocolitis	1	3
Pneumomia	0	0
Wound dehiscence	2	3
Fever of unknown origin	0	2
TOTAL	7	17

Epidural analgesia was applied in 90% of cases (9 patients), 1 patient being epileptic. Antimicrobial prophylaxis and skin preparation was achieved in 90% of patients, early removal of NGT in 90% of cases, prevention of deep vein thrombosis 100%, chewing gum and oral magnesium tablets in 80% of cases, 2 patients refusing it. Early mobilization was implemented in 60% of patients and in our opinion it represented a true impediment due to multiple drainage and catheters.

Moreover, the epidural catheter also restrains the patient who is usually afraid to move. In addition an issue to be addressed is the lack of specialized personnel needed to mobilize these patients in the intensive care unit. Early feeding had a 70% implementation rate. The average rate of implementing the FTP in our patients was 84%. (See table No.3)

Table No. 3

FTP ITEMS	**Protocol implementation procent**
Counseling and education	90%
Preoperative optimization of medical conditions	30%
NO oral mechanical bowel preparation	100%
Preoperative carbohydrates loading	100%
NO Preoperative fasting	100%
Preanasthesia medication	90%
Epidural analgesia	90%
Antimicrobial prophylaxis and skin preparation	90%
Early removal of nasogastric tube	90%
Prevention of deep veen thrombosis	100%
Chewing gum and oral magnesium tablets	80%
Early mobilization	60%
Early feeding	70%
Average implementation percent of FTP items	84%

Discussions

Radical cystectomy remains a debilitating procedure with elevated complication rates. Most of the patients with MIBC are in their 7th decade and have high numbers of associated co-morbidities. In our center we perform a wide number of radical cystectomies and we are daily confronted with high complication rates and complex cases. In an effort to decrease early and late morbidity we started applying FTP to radical cystectomy patients undergoing IUD. When overviewing patients' characteristics, they were similar in the two groups: median age was 62.5 vs 62 years, ASA 2 was observed more in the CSG, pathological clinical stage was similar and also the type of urinary diversions performed.

We noticed a decrease in median time to first stool in the FTG, representing 2.5 days compared with the CSG and a lower median time to first stool - 6 days in the FTG compared with 7 days in the CSG. Moreover, the median time to a normal diet was lower for the FTP patients, resuming to a normal diet after 4.5 days compared to CSG patients who began oral feeding in 6 days.

Intolerance to oral feeding was encountered in 2 patients in the FTG and in 4 patients in the CSG. In our opinion, the NGT plays a key-point issue. An important meta-analysis by Nelson R. et al that analyzed 33 studies encompassing 5240 patients showed that although patients can and may develop abdominal distension or vomiting without NGT, it does not increase complications or hospital stay [10]. Not using a NGT results in earlier return to bowel function, decrease in pulmonary complications and shorter hospital stay. The author found no increased risk of anastomotic leak (no difference between the two groups), also vomiting proved to be more common for patients with routine tube use. In conclusion, nasogastric decompression does not accomplish any of its intended goals and should be abandoned in favor of selective tubing [10].

Eight patients in the FTG regained their bowel function normally (80% of the cases), only 2 patients (20%) having postoperative ileus compared to 4 patients in the CSG (40%).

Another important thing that we want to highlight here is the early start in oral feeding. In the FTG, patients benefited from this possibility due to early removal of NGT. This is of paramount importance in reducing inflammatory and catabolic responses after surgery as other authors concluded [11-13].

When analyzing complications, we encountered two cases of major complications in the CSG - bowel evisceration, while there was none in the FTG. Seven minor complications were reported in FTG patients, the most common being postoperative ileus and wound dehiscence.

CSG patients had a higher number of minor complications summing up to seventeen. The most encountered minor complications in the CSG were ileus, wound dehiscence and CDE. CSG have been treated postoperatively with antibiotics for prophylactic reasons, this could explain the incidence of CDC. Interestingly, although in the CSG patients received antibiotics we observed cases of fever of unknown origin and urinary tract infections.

However our cohort of patients is too small to draw any conclusions or to be statistically significant regarding these issues. More patients have to be enrolled in order to clarify these facts. Despite of the reduced group of patients the median length of hospital stay was clearly shorter for the FTG - 17.5 days compared with 20.5 days for the CSG. As a conclusion to our study, we can state that from these initial data, FTP applied in RC patients have promising results with a good overall implementation of protocol items, nearly 84%.

Conclusions

In our experience there are still impediments in the preoperative optimization of medical conditions due to the great number of high-morbidity patients with low medical education, slow onset of early mobilization due to multiple catheter and drainage, representing a challenge hard to accommodate with for the personnel. Nevertheless this new concept has still to gain favor because of its different approach compared to classic perioperative care.

Giving the early data of the study we consider proper to continue enrolling patients in order to best clarify the optimal perioperative care in RC patients in an attempt to reduce morbidity rates in this type of major surgery.

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