## A Multimodal Perioperative Plan for Radical Cystectomy and Urinary Intestinal Diversion: Effects, Limits and Complications of Early Artificial Nutrition

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**Purpose:** We evaluated the effects of early parenteral and enteral postoperative nutritional support on the restoration of normal bowel function, on the protein depletion that follows cystectomy and on observed complications.

Materials and Methods: Immediate parenteral nutrition was initiated after surgery. It was progressively shifted to the enteral route through a needle catheter jejunostomy inserted at surgery.

**Results:** A total of 28 patients with a mean age of 74.2 years (range 55 to 82) were enrolled into the study. Disease was pathologically confined to the bladder in 22 patients, locally advanced in 3 and extravesical in 3. Urinary diversions included an ileocolonic pouch in 15 patients and an orthotopic ileal reservoir in 13. Of the 28 patients 15 (53.6%) completed the protocol, whereas 13 (46.4%) did not. Median time to peristalsis and spontaneous passage of flatus was postoperative day 2 (range 2 to 5) and median time to normal diet resumption was postoperative day 4 (range 3 to 8). No significant differences were observed between patients who completed the protocol and those who did not with regard to the restoration of normal bowel function, and total protein, serum albumin and lymphocyte count. Minor complications were observed in 9 patients and major complications developed in 4.

**Conclusions:** Early postoperative artificial nutrition did not affect the return of bowel function or postoperative protein depletion. Different strategies for more effective nutritional support will be explored in further studies.

Key Words: bladder, urinary diversion, bladder neoplasms, parenteral nutrition, enteral nutrition

n previous decades early postoperative provision of artificial nutrients has shown beneficial effects by decreasing septic morbidity, improving wound healing and preserving immunocompetence in patients undergoing major elective abdominal surgery or surgery for abdominal trauma. 1,2 Providing artificial nutrition initially focused on TPN, although EN has also gained wide acceptance. This is due to several factors, ie the avoidance of bacterial or fungal sepsis through the venous line, more physiological intake of nutrients in the digestive tract, which preserves mucosal integrity and normal gut flora, a protective effect against intestinal bacterial translocation, better glucose metabolism and lower costs.<sup>2-4</sup> A comparison of the 2 administration routes has been the subject of several randomized studies and meta-analyses, and yet no clear-cut superiority has been substantiated for either of the 2 methods.<sup>3–5</sup>

Although severe malnutrition is relatively rare in association with invasive bladder cancer, this population of patients is often elderly with coexisting multiple comorbidities and serum albumin is frequently in the low normal range. Any of these factors may be associated with the risk of complications. In addition, a period of fasting is expected due to preoperative bowel preparation, postoperative ileus,

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Study received internal Ethics Committee approval.

analgesic drugs, nausea and loss of appetite. Although the views on return of bowel function are changing, ie by the decrease or avoidance of nasogastric suction, this may require 5 to 7 days in elderly patients or those with complications. We investigated the impact of early postoperative nutrition using the parenteral route via a central venous line and the enteral route via needle catheter jejunostomy on the recovery of normal bowel function and on standard biochemical parameters in patients undergoing radical cystectomy and urinary intestinal diversion for invasive bladder cancer.

#### PATIENTS AND METHODS

Patients who were candidates for ablative and reconstructive surgery due to histologically proven muscle invasive bladder cancer were consecutively enrolled in a multimodal plan of perioperative management aimed at decreasing the morbidity associated with radical cystectomy and intestinal urinary diversion, as previously described. The plan included decreasing preoperative fasting time to 6 to 8 hours, administering combined general plus epidural anesthesia and postoperative pain control, and administering early postoperative parenteral plus enteral artificial nutrition, as previously described.

Inclusion criteria were histological evidence of intractable superficial or muscle infiltrating cancer (pT2 or higher), transitional cell carcinoma staged by transurethral resection and a life expectancy of at least 2 years. Previous abdominal or pelvic radiotherapy was a criterion for exclu-

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sion. All patients were asked to provide written informed consent, which included a description of the jejunostomy insertion. The study was approved by the internal Ethics Committee at our institution.

#### Surgical Jejunostomy

At the end of the surgical procedure the protocol included insertion of a needle catheter into the first tract of the small intestine, as described by Delany et al, 7 15 to 20 cm caudad to the Treitz ligament. An Intestofix® catheter was inserted into the bowel through a 16 gauge needle after developing a submucosal tunnel at least 10 cm long. The distal portion of the tube was manually milked through the bowel for an additional 20 cm. A purse-string suture was then sewn around the puncture site and additional stitches were oversewn on the intestinal wall. The catheter was secured to the inner abdominal wall and exteriorized.

#### **Artificial Nutrition**

Artificial nutrition consisted of 25 to 30 kcal/kg daily, that is 0.2 to 0.3 gm/kg, beginning with parenteral nutrition and followed by enteral nutrition. On the day of surgery parenteral nutrition was started at 8:00 p.m. The total amount of calories daily was constant and it was shifted progressively from the parenteral to the enteral route of administration to achieve a balanced infusion rate (50% and 50%, respectively).

#### **Enteral Solution and Feed Advancement**

Artificial nutrition consisted of the delivery of Impact® immunonutrients. It was started on postoperative day 1 at a rate of 21 ml per hour and the parenteral infusion rate was decreased to 63 ml per hour. On postoperative day 2 enteral feeding was advanced to a rate of 42 ml per hour and the parenteral infusion rate was decreased to 42 ml per hour. Such rates of administration were maintained until the return of spontaneous peristalsis and flatus. Patients were monitored hourly by staff members specifically trained in artificial nutrition. In the presence of abdominal bloating, discomfort or pain due to bowel distention certain measures were adopted sequentially and recorded in the patient charts, ie prokinetic agent administration, a 50% decrease in the enteral infusion rate or temporary discontinuation.

Clinical and biochemical parameters were the study end points. Clinical parameters were time to return of spontaneous peristalsis and flatus, the presence and duration of delayed gastric emptying, and time to resumption of a normal diet. Standard biochemical parameters were complete blood count with lymphocytes, total protein and albumin serum, which were assessed on postoperative days 1, 3 and 5, and on the day of hospital discharge.

#### **Complications**

Complications were prospectively recorded to monitor safety and feasibility. Minor complications were defined as complications that compromised successful completion of the enteral nutrition protocol and that resolved conservatively, whereas major complications were defined as events that led to re-laparotomy.

#### Study Design and Statistical Considerations

The study was designed as a 2-stage phase II trial. Sample size was calculated by the Simon minimax method. Stage 1 was considered completed if at least 17 of 34 patients successfully completed the protocol. Furthermore, a 30% complication rate was anticipated based on previous results in similar studies of jejunal feeding protocols with an overall complication rate of 3.5% to 69.1% (table 1). The study would have been discontinued if the complication rate exceeded 30%. If the observed complication rate was within 30% or if at least 17 consecutive patients completed the protocol, the study would proceed to stage 2.

#### **RESULTS**

Between September 2003 and November 2004, 39 consecutive patients underwent radical cystectomy for infiltrative bladder cancer. Advanced disease stage and/or poor general condition were the reasons for ureterocutaneostomy in 11 patients, while 28 with locally advanced disease who underwent surgery with curative intent also underwent urinary reconstruction with intestinal segments and were enrolled in the study. Mean patient age was 74.2 years (median 74, range 55 to 82). The cohort included 22 males and 6 females. Surgical risk graded according to ASA category was ASA 1 in 12 patients, ASA 2 in 8 and ASA 3 in 8. All patients underwent radical cystectomy, pelvic lymphadenectomy and urinary reconstruction with intestinal segments. A heterotopic ileocolonic pouch was constructed in 15 patients using the Indiana technique, while an orthotopic bladder replacement using the Studer technique<sup>10</sup> was created in 13.

Pathological stage was pT0 in 1 patient. Disease was pathologically confined within the bladder (stages pTis, pT1 G3 and pT2 G3) in 21 patients, while it was locally advanced (stages pT3 a and b) in 3 and extravesical (pT4 and N positive) in 3.

#### **Protocol Feasibility**

Eight of 28 patients (28.5%) experienced some degree of abdominal discomfort and nausea due to bowel distention concomitant with the infusion or advancement of the enteral solution infusion rate. They did not complete the protocol despite the concomitant administration of promotility agents and/or a decrease in the feeding rate.

#### **Effect on Postoperative Ileus**

In patients who completed the enteral nutrition protocol median time to peristalsis and spontaneous passage of flatus

Table 1. Complications due to needle catheter jejunostomy				
		No. Complications		
References	No. Pts	Major	Minor	Total No. (%)
Kudsk et al <sup>3</sup>	51	1	11	12 (23.5)
Heslin et al <sup>4</sup>	97	1	26	27 (27.8)
Pacelli et al <sup>5</sup>	119	8	26	34 (28.6)
Delany et al <sup>7</sup>	115	_	59	59 (51.3)
al-Shehri et al <sup>14</sup>	133	_	92	92 (69.1)
Sarr <sup>15</sup>	464	3	120	23(26.5)
De Gottardi et al <sup>16</sup>	100	2	44	46 (46)
Myers et al <sup>17</sup>	2,022	34	910	944 (47)
Smith-Choban and Max <sup>18</sup>	129	10	61	71 (55)

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