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Are Patients at Nutritional Risk More Prone to Complications after Major Urological Surgery?

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Purpose: The nutritional risk score is a recommended screening tool for malnutrition. While a nutritional risk score of 3 or greater predicts adverse outcomes after digestive surgery, to our knowledge its predictive value for morbidity after urological interventions is unknown. We determined whether urological patients at nutritional risk are at higher risk for complications after major surgery than patients not at nutritional risk.

Materials and Methods: We performed a prospective observational study in consecutive patients undergoing major surgery. A priori sample calculation resulted in a study cohort of 220 patients. Interim analysis was planned after 110 patients. The nutritional risk score was assessed preoperatively by a specialized study nurse. Nutritional care was standardized in all patients. Postoperative complications were defined previously using the standardized Dindo-Clavien classification. The primary end point was 30-day morbidity. Univariate and multivariate analysis was performed to identify predictors of complications.

Results: The study was discontinued due to significant results after interim analysis. A total of 125 patients were included in analysis from June 2011 to June 2012 and 15 were excluded because of incomplete data. Of 51 patients at nutritional risk 38 (74%) presented with at least 1 complication compared to 28 of 59 controls (47%). Patients at nutritional risk were at threefold risk for compli-cations on univariate and multivariate analysis (OR 3.3, 95% CI 1.3−8.0). Cys-tectomy was the only other predictor of morbidity (OR 10, 95% CI 2−48).

Conclusions: Patients at nutritional risk are more prone to complications after major urological procedures. Whether this increased morbidity can be reversed by perioperative nutritional support should be studied.

Key Words: urology, surgery, malnutrition, complications, risk

Abbreviations and Acronyms

BMI = body mass index NRS = nutritional risk score

Malnutrition affects about 40% of hospitalized patients[1] and is asso-ciated with increased mortality, morbidity and hospital stay after digestive surgery.[2] Since malnutrition represents the most important modi-fiable risk factor, efforts have been made to develop clinical screening tools.[3] The European Society for Parenteral and Enteral Nutrition (ESPEN), and American Society for Parenteral and Enteral Nutrition (ASPEN) recommend using the pro-spectively validated NRS (fig. 1).[1,4] The score is composed of 3 compo-nents, including nutritional status, disease/intervention severity and pa-tient age. By attributing points to low BMI, decreased oral food intake or weight loss (0 to 3 points), increased

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	Nutritional Status	Disease/Surgery Severity	Age	
0	Normal	Normal	< 70 yr	
1	Weight loss > 5%/3 mo OR Food intake < 75%	Chronic disease, hip fracture, cancer, minor surgery, …	≥ 70 yr	
2	Weight loss > 5%/2 mo OR Food intake < 50% OR BMI 18.5-20.5	Major surgery, myocardial infarction, pneumonia, lymphoma, leukemia, …		
3	Weight loss > 5%/1 mo (or >15%/3 mo) OR Food intake < 25% OR BMI <18.5	Head trauma, transplantation, intensive care patients, …		**NRS**
	+	**+**		**=**

Figure 1. NRS is calculated by adding highest value from each column with range of 0 to 7. Patients with NRS 3 or greater are considered at risk for malnutrition. Weight loss is estimated as percent of total body mass. Food intake is evaluated by asking patient, "Within last week, were you able to eat whole meal/three-quarters of your meal/half of your meal/quarter of your meal?" BMI is shown in kg/m^2. *mo,* months. *yr,* years.

surgical stress (0 to 3 points) and age greater than 70 years (1 point) the NRS allows for the identification of patients at risk for malnutrition (NRS 3 or greater).[1]

While the risk of malnutrition has been largely studied for digestive surgery,[2,5,6] little is known about its impact on postoperative morbidity in urology. Karl et al recently reported that up to 33% of urological patients who underwent open surgery at a urology department in Germany were at risk for malnutrition (NRS 3 or greater).[7] In addition, recently 2 groups from the United States retrospectively evaluated the effect of preoperative nutritional deficiency on perioperative mortality and overall survival in patients undergoing oncological radical cystectomy or nephrectomy.[8,9] Nutrition deficiency was a strong independent factor for mortality in each study. Unfortunately, no data were available on morbidity.

Because urological surgery differs from digestive surgery in many points, the results of the latter cannot be extrapolated by implication. There is an urgent need to clarify the role of malnutrition in urology to properly use this information for preoperative counseling and risk stratifying, and also investigate whether perioperative nutritional intervention could positively affect the outcome, as shown for digestive surgery.[10,11] To our knowledge no group has prospectively evaluated the impact of nutritional risk on morbidity after urological surgery. This study aims to fill this gap.

MATERIALS AND METHODS

The current study was designed as a prospective, single center observational study. We tested the hypothesis that patients at nutritional risk (NRS 3 or greater) would be exposed to increased postoperative morbidity. The second aim was to identify other possible predictors of complications, namely the Charlson comorbidity index, American Society of Anesthesiologists (ASA) score, age, sex, BMI, previous abdominal surgery, smoking habits, oncological indication, anemia and hypoalbuminemia.

After receiving approval from the institutional board and local ethical committee (No. 34/11, April 27, 2011), consecutive patients treated with major elective surgery were prospectively included in analysis. Since no standard definition of major surgery exists, it was defined as any open surgery performed with the patient under general anesthesia that was planned to last more than 2 hours. Patients undergoing surgery for stone disease were excluded from study to avoid any potential infectious bias. Patients undergoing laparoscopic or robotic surgery were also excluded.

After providing written informed consent patients were enrolled in the study by the operating urologist about 3 weeks preoperatively. Notably, extended nutritional screening and treatment were not yet part of standard perioperative management in our department at the time of this study. Therefore, the few patients who received supplementation preoperatively were not included in this study to avoid possible bias related to preoperative nutritional support.

All patients were admitted to the hospital the day before surgery. Weight and height were measured, and a blood sample was obtained to determine hemoglobin and albumin. A specialized study nurse then determined the NRS and calculated the modified Charlson comorbidity index. Demographic information, including age, gender, BMI, etc, were recorded in a specifically designed Excel® 2007 spreadsheet. All complications were defined before the study began and previously reported.[12] Maximal length of stay was defined for each procedure. Postoperative nutritional support was standardized and all patients received 2 daily oral Ensure® Plus nutritional supplements in the first 3 days postoperatively, in addition to the standardized diet.

Complications were documented perioperatively by our specialized study nurse, who supervised resident

reporting of complications. All patients were discussed at our daily grand round and complications were noted. Moreover, the final report at hospital discharge was reread by the study nurse to ensure that no supplementary complications had been missed.

All patients attended an assessment visit 1 month after surgery. They were asked about any complications that could have developed at home. Those complications were reported on a standardized case report form and collected by the study nurse. The modified Dindo-Clavien classification was used to stratify complications (see Appendix).[13]

A sample size calculation was run on certain information. A 50% 30-day postoperative complication rate was assumed for patients at risk and a 25% rate was assumed for well nourished patients. A 40% prevalence of nutritional risk was expected in hospitalized patients treated with surgery. By adopting 90% power and a 5% 2-sided type I error, and considering interim analysis the calculated sample size was 220 patients. Interim analysis was planned for after half the sample total size was recruited. A stopping rule was defined for statistically significant benefit.

Descriptive statistics are reported as the median and IQR or the mean ± SD for continuous variables depending on the distribution, and the frequency and percent for categorical variables. To compare the 2 NRS groups we used the independent t-test or Mann-Whitney U test for continuous variables, and the Pearson chi-square test for categorical variables. To examine risk factors for complications we created univariate and multivariate logistic regression models to analyze the impact of age, gender, BMI, history of smoking or abdominal surgery, ASA score, anemia, albumin, surgical indication, Charlson comorbidity index and NRS variables. A stepwise selection procedure was used.[14] The OR on univariate analysis and the adjusted OR for multivariate analysis with the associated 95% CIs are reported for each explanatory variable. All analysis was done using Stata®, release 12 with significance considered at $\alpha = 5\%$.

RESULTS

A total of 125 patients were prospectively included in the study from June 2011 to June 2012 (fig. 2). After excluding 15 patients due to incomplete data, including 8 with NRS less than 3 and 7 with NRS 3 or greater, 110 (26 women) were included in final analysis since interim analysis revealed a significantly worse outcome in patients at nutritional risk ($p < 0.005$). A risk of malnutrition (NRS 3 or greater) was found in 51 patients (46%). Mean age ± SD was 63 ± 14 years. Mean BMI was 27 ± 4 kg/m^2 and 31 patients (28%) were obese (BMI greater than 30 kg/m^2). Of the patients 74% had an ASA score of 2. Previous abdominal surgery had been done in 32% cases. Only 26% of patients were smokers. Anemia and hypoalbuminemia were found preoperatively in 25% and 21% of the prospective cohort, respectively. The mean albumin level was 43 ± 6 gm/l. Of the patients 53% had a Charlson comorbidity index of 0.

Table 1 lists the characteristics of patients at nutritional risk (NRS 3 or greater) vs those not at

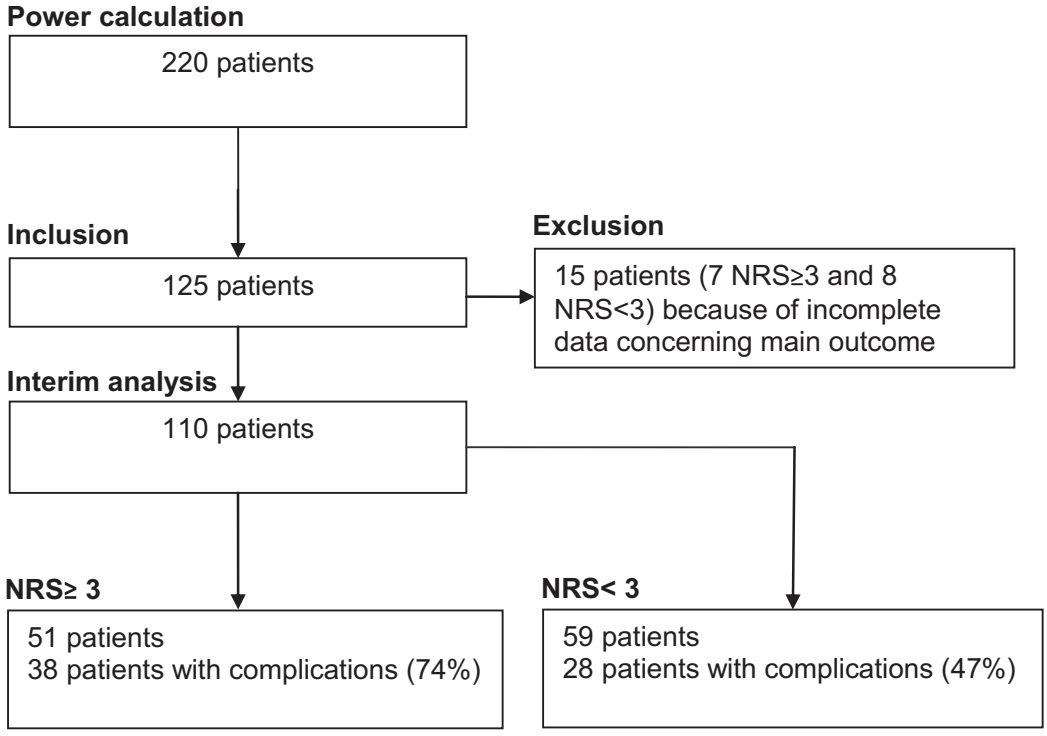

Table 1. *Patient characteristics*

	Overall	NRS 3 or Greater	NRS Less Than 3	p Value
No. pts	110	51	59	
Age:				
Mean ± SD	63 ± 14	71 ± 10	57 ± 14	<0.001
No. greater than 70 (%)	34 (31)	32 (63)	2 (3)	<0.001
Male	84 (76)	39 (76)	45 (76)	0.980
BMI (kg/m^2):				
Mean ± SD	27 ± 4	27 ± 4	27 ± 5	0.767
No. 30 or greater (%)	31 (28)	17 (33)	14 (24)	0.264
No. ASA score (%):				0.084
1	10 (9)	2 (4)	8 (14)	
2	81 (74)	37 (73)	44 (75)	
3	19 (17)	12 (24)	7 (12)	
No. previous abdominal surgery (%)	35 (32)	18 (35)	17 (29)	0.467
No. tobacco use (%)	29 (26)	12 (24)	17 (29)	0.530
No. preop anemia (%)*	27 (25)	16 (31)	11 (19)	0.122
No. preop hypoalbuminemia (%)†	23 (21)	8 (16)	15 (25)	0.210
No. Charlson comorbidity index (%):				0.014
0	58 (53)	23 (45)	35 (59)	
1–2	34 (31)	14 (27)	20 (34)	
Greater than 2	18 (16)	14 (27)	4 (7)	
No. cystectomy (%)	20 (18)	11 (22)	9 (15)	0.392

*Hematocrit less than 40% and less than 35% in male and female patients, respectively.
†Less than 35 gm/l albumin.

risk (NRS less than 3). Surgical interventions consisted of 46 prostatectomies, 41 retroperitoneal surgeries, 20 cystectomies and 3 functional operations.

No death occurred during the study period. A total of 66 patients (60%) presented with at least 1 complication in the 30-day postoperative period. Major complications developed in 10 patients (table 2). Most complications were graded Dindo-Clavien I or II with bleeding usually requiring blood transfusion and ileus occurring most frequently (25 and 10 cases, respectively). The complication rate in patients at nutritional risk was 75% (38 of 51) vs 47% (28 of 59) in those not at risk (OR 3.24, 95% CI 1.44–7.28, p = 0.005).

Univariate analysis revealed that cystectomy (OR 10.4, 95% CI 2.14–50.83, p = 0.004) and a Charlson comorbidity index of greater than 0 (OR 2.47, 95% CI 1.12–5.44, p = 0.025) were also associated with postoperative complications. Other preoperative characteristics were not predictive, such as age, sex, BMI, previous abdominal surgery, smoking habits, ASA score, oncological indication, anemia and hypoalbuminemia.

On multivariate analysis only NRS 3 or greater (OR 3.27, 95% CI 1.33–8.02, p = 0.01) and cystectomy (OR 9.66, 95% CI 1.92–48.55, p = 0.006) were retained as significant independent predictors of complications.

DISCUSSION

The current study shows that patients at nutritional risk, as assessed by the NRS, are more prone to complications after major urological procedures. To our knowledge this is the first prospective study to link malnutrition with postoperative morbidity in urological patients undergoing major surgery.

Karl et al retrospectively correlated the risk of malnutrition to complications in a mixed (medical and surgical) urological population.[15] Of the 320 screened patients 68 (21%) were identified to be at nutritional risk (NRS 3 or greater). Unfortunately,

Table 2. *Major complications (Dindo-Clavien classification 3 or greater)*

Pt No.	Main Surgery	Oncological	Pt NRS	Complication	Treatment	Dindo-Clavien Classification
1	Transvesical prostatectomy	No	4	Bleeding	Reoperation, hemostatic suturing	3b
2	Nephrectomy	Yes	2	Pulmonary embolism	Catheter embolectomy	3a
3	Partial nephrectomy	Yes	2	Bleeding	Reoperation, clot evacuation	3b
4	Nephroureterectomy	Yes	2	Bleeding	Reoperation, packing, intensive care unit	4b
5	Transvesical prostatectomy	No	4	Bleeding	Reoperation, hemostatic suturing	3b
6	Radical prostatectomy	Yes	3	Bleeding	Embolization	3a
7	Cystectomy + Bricker	Yes	2	Wound infection	Abscess drainage using general anesthesia	3b
8	Radical prostatectomy	Yes	3	Lymphocele	Percutaneous drainage under computerized tomography guidance	3a
9	Cystectomy + Bricker	Yes	3	Anastomotic (ileo-ileal) leak	Reanastomosis	3b
10	Cystectomy + Studer	Yes	3	Anastomotic ureteral-neobladder stricture	Nephrostomy + antegrade balloon dilatation	3a

complications were not predefined and Karl et al did not stratify patients by other potential confounders such as comorbidity. They concluded that the complication rate was higher in malnourished patients (6 of 68 vs 16 of 252) but the study was hampered by several methodological flaws.

In our study 51 patients (46%) were at risk for malnutrition, greater than the 33% of urological patients treated with open surgery described by Karl et al.[7] In contrast, Roth et al from Bern reported their experience with postoperative parenteral nutritional support in 157 patients undergoing radical cystectomy and found that a risk of malnutrition, defined as NRS 3 or greater, was present in 84 (54%).[16] This shows the wide variation of malnutrition in hospitalized patients upon admission and preoperatively.[2,6,17] Factors such as decreased oral food intake, preexisting chronic disease, tumor cachexia and low socioeconomic status were identified as risk factors for malnutrition and contribute to the wide variation of its prevalence.[6]

At first glance the complication rate in our study seems higher than usually reported. We believe that this unusually high morbidity is related to the study design and the strict, standardized methodology of reporting complications. Our prospective study adheres to the criteria of Martin et al[18] and Donat[19] for reporting complications. Moreover, we used the Dindo-Clavien classification, which considers any deviation from the standard postoperative course as a complication. In the current study 20 patients (30%) had grade I complications, which might have been underreported in less strict studies. Our study nurse also had a key role in prospectively recording complications. When this task has been left to residents, 80% of complications are not recorded even after extensive audit and teaching.[20] This alarming statement reinforces the quality of our study and explains the high morbidity.

Despite improved surgical technique and anesthetic protocols surgery still elicits central nervous system mediated release of stress hormones and inflammatory mediators.[21] This so-called surgical stress response[22] causes catabolism of glycogen, fat and proteins, resulting in systemic release of glucose, and free fatty and amino acids. The anabolic state required for optimal patient rehabilitation, immune response and wound healing is not attained.[3] Therefore, by placing the patient in a catabolic state before the surgical stress response occurs preoperative malnutrition might be an independent risk factor for increased morbidity and mortality after major urological surgery, as shown for digestive surgery.[23,24]

We used the NRS to assess the nutritional risk for several reasons. 1) It is the screening tool for malnutrition recommended by ESPEN and ASPEN.[1,4] 2) It is easily implemented in clinical practice since it does not require further biological or anthropological parameters. 3) It was internally and externally validated, and correlates with other biological screening tools.[25,26]

However, in the current study NRS did not correlate with a biological measure since hypoalbuminemia was found in only 21% of patients. This might be explained by the relatively acute (within 0 to 4 weeks) onset of malnutrition in some patients. Indeed, albumin levels usually reflect nutritional status in the last month in relatively stable patients. Moreover, albumin is influenced by inflammation, age, muscle mass, hepatic failure, etc and, therefore, it is suboptimal. In the current series albumin levels did not correlate with age. Although prealbumin is known to be more sensitive for detecting early malnutrition and might have been useful in this study, we decided not to sample it to keep costs low. This can be considered a study limitation.

Another potential limitation of this study is population heterogeneity since patients treated with different type of major surgery were included and analyzed as a whole. Although we believe that this prospective cohort of patients is representative of most centers with a mixed case load, it would have been relevant to stratify patients by surgical procedure, eg cystectomy, prostatectomy and retroperitoneal surgery. However, because of the limited number of patients undergoing each type of procedure, subgroup analysis was not feasible. While complications might be procedure specific, all of these surgical interventions induce a common stress in the patient. Since to our knowledge no definition of major surgery is available in the literature, we used a straightforward definition including 3 criteria, namely open surgery, general anesthesia and operative time of about 2 hours.

In addition, a possible limitation that may have affected our results is the early interruption of the study before recruiting the total number of patients. Such interim analysis might have led to potential overestimation of the effect. Nevertheless, the data monitoring committee believed that it would be unethical to pursue the study while knowing that nutritional supplements could have a favorable impact on patients at nutritional risk.

While we acknowledge these possible limitations, we believe that this study has a number of important clinical implications for the urological community that should reinforce the implementation of NRS screening in daily clinical practice. 1) The prevalence of patients deemed to be at risk for malnutrition is high, ranging from 30% to 50% in different studies. 2) The NRS was the only preoperative score that could predict early morbidity after stratifying patients by other possible confounders. Other

standardized and widely used tools, such as the Charlson comorbidity index and ASA score, were less useful than the NRS for predicting complications. 3) Nutritional status is at least partly a modifiable risk factor. To our knowledge whether preoperative nutritional support in patients at nutritional risk who are undergoing major urological surgery can improve postoperative outcomes remains unknown. However, preoperative oral nutritional supplementation, especially immunonutrition,[11] can decrease the postoperative morbidity, length of hospital stay and costs of major gastrointestinal surgery.[5,27,28] Well designed randomized, controlled trials specific to urological surgery might provide a definitive answer. Finally, the NRS is an easy, inexpensive tool to assess nutritional risk that can be effectively adopted by nurses after specific training, as in this study.

CONCLUSIONS

This series shows that the NRS is a strong independent predictor of early postoperative morbidity after major open urological surgery. Its usefulness seems more relevant than that of other tools routinely used for preoperative assessment, such as the Charlson comorbidity index and ASA score. Based on these findings assessing nutritional status should be encouraged to stratify perioperative risk. In addition, since malnutrition is a modifiable factor, future studies should investigate the hypothesis that immunonutrition or other forms of preoperative nutritional support can reverse malnutrition and decrease postoperative morbidity.

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APPENDIX

Dindo-Clavien Classification of Complications[13]

Grade	Definition
I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions. Allowed therapeutic regimens are drugs as antiemetics, antipyretics, analgetics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside.
II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included.
III:	Requiring surgical, endoscopic or radiological intervention:
IIIa	Intervention not under general anesthesia
IIIb	Intervention under general anesthesia
IV:	Life threatening complication (including central nervous system complications) requiring intensive care/intensive care unit management:
IVa	Single organ dysfunction (including dialysis)
IVb	Multiorgan dysfunction
V	Death of a patient

Example: in this therapy based classification a complication such as lymphocele is classified as grade IIIa if it is treated with computerized tomography guided drainage puncture, and as IIIb if it requires laparoscopic fenestration.

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