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Comorbidity and nutritional indices as predictors of morbidity after transurethral procedures: A prospective cohort study

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Abstract

Introduction: Preoperative scores are widely used predictors of complications after major surgery. These scores, however, are not widely used in transurethral procedures. The aim of this study was to assess the value of the Charlson Comorbidity Index (CCI), the age-adjusted CCI, the American Society of Anesthesiologist score (ASA) and the Nutritional Risk Score (NRS) in predicting early mor-bidity after transurethral urological procedures.

Methods: Consecutive patients undergoing transurethral resection of the bladder or the prostate were prospectively enrolled. The scores were calculated preoperatively; 30-day complications were prospectively recorded according to the Dindo-Clavien classifica-tion. Univariate logistic regression was performed to investigate the value of each score and of other factors (i.e., age, sex, body mass index, anemia, smoking habit, type of operation and anaesthesia) as predictors of complications. A multivariate model was then calculated using these predictors.

Results: Overall, 197 patients were included. The mean age was 72 (standard deviation ± 10). In total, 26.9% patients had at least 1 complication. Using univariate analysis, we found that each score significantly predicted complications. In multivariate analysis, only the ASA (odds ration [OR] 2.11; 95% confidence interval [CI] 1.01-4.43) and the NRS (OR 2.42; 95% CI 1.56-3.74) remained independent predictors. The best model incorporated ASA, NRS and gender, and predicted morbidity with an area under the curve of 76%. Our study's main limitations are population heterogeneity and limited sample size.

Conclusion: The ASA and the NRS are important and independent determinants of early morbidity after transurethral procedures. The use of these indices may assist clinicians in the decision-making process to balance the possible benefits of transurethral procedures with the potential risks.

Introduction

Transurethral resection of the bladder (TURB) and of the prostate (TURP) are key operations in the management of bladder tumours and benign prostatic hyperplasia (BPH), respectively. TURB is the cornerstone for initial diagnosis and risk stratification of suspicious bladder lesions, and is the first-line treatment for non-muscle invasive urothelial cancer.[1] TURP is the gold standard for men with moderate-to-severe bladder outlet obstruction due to BPH, and for patients with milder symptoms who do not respond to oral treatment.[2] The increased life expectancy in developed countries and the subsequent increase in incidence of both diseases have contributed to increased frequency of TURB and TURP. However, a parallel process with aging is the increased prevalence of severe comorbidity.

In an attempt to improve patient's selection, taking into account benefits and risks, various preoperative indices have been developed. The most common scores are the Charlson Comorbidity Index (CCI), the age-adjusted CCI and the American Society of Anesthesiologist score (ASA). Their value has been tested in some urological procedures with moderate to high perioperative risk.[3-5] The significance of their association, not only with the perioperative morbidity but also with survival, has led to the integration of these scores in nomograms to predict mortality after certain procedures.[6] Another preoperative score, the Nutritional Risk Score (NRS), has been associated with perioperative risk in gastrointestinal surgery, and might be also useful in urological surgery.[7,8]

Despite the theoretical usefulness of these scores in patients undergoing surgery, their use is very limited in urological procedures with expected low postoperative morbidity, like transurethral resections. Particularly, the additional value of the NRS in this population has never been tested.

The aim of this study was to assess the impact of the CCI, the ACCI, the ASA and the NRS on early postoperative morbidity after TURB and TURP.

Methods

Overview

This prospective study was approved by the local Ethics Committee (Protocol number 34/11); the results are reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement on observational studies.[9] This study was conducted at our tertiary university hospital from June 2011 to June 2012. Consecutive patients undergoing elective TURB or TURP were invited to participate. After signing a specific consent form, patients were included, unless the procedure had been anticipated or postponed due to an urgent reason. The procedures were performed by last-year trainees or by consultants. The normal perioperative course at our hospital for transurethral resections consists of an overall hospital stay of 4 days, including admission day, procedure day followed by 24-hour continuous bladder washing, trial without catheter and discharge.

Comorbidity, anesthesiology and nutritional scores

The 4 scores tested in this study were: the CCI, the age-adjusted CCI, the ASA and the NRS. The CCI was calculated by the operating urologist; the age-adjusted CCI was derived from the CCI by age-adjustment; the ASA was assessed by the anesthesiologist responsible for patient perioperative care; and the NRS was calculated by a clinical research nurse with specific training in malnutrition assessment (Table 1).

For the purpose of the analyses and based on the literature, all indices were dichotomized as follows: CCI 0 versus ≥1; age-adjusted CCI 0 to 5 versus ≥6; ASA 1 to 2 versus 3 to 4; NRS 0 to 2 versus ≥3.[3,10,11] Similarly, potential confounders were dichotomized as follows: age (<70 vs. ≥70), gender, smoking (yes vs. no), type of resection (TURB vs. TURP), type of anesthesia (spinal vs. general), body mass index (BMI, <18.5 vs. ≥18.5), and anemia (cutoff heamatocrit value at 35% and 40% for women and men, respectively).

Table 1. Calculating the Nutritional Risk Score (NRS)

	Nutritional status	Disease/surgery severity	Age
0	Normal	Normal	<70
1	Weight loss >5%/3 months **or** Food intake <75%	Includes chronic disease, hip fracture, cancer, minor surgery	≥70
2	Weight loss >5%/2 months **or** Food intake <50% **or** BMI 18.5-20.5	Includes major surgery, myocardial infarction, pneumonia, lymphoma, leukemia	
3	Weight loss >5%/1 month (or >15%/3 months) **or** Food intake <25% **or** BMI <18.5	Includes head trauma, transplantation, intensive care patients	

BMI: body mass index. The Nutritional Risk Score (NRS) is calculated by adding 3 different components: nutritional status + disease/surgery severity + age. Only the more severe contribution to the overall score of each of these 3 elements is considered in the overall score.

Assessment of complications

Complications were classified by type, and graded using the Dindo-Clavien classification adjusted for transurethral procedures.[12] Based on the treatment undertaken to manage 1 complication, the Dindo-Clavien classification uses the severity of the complication.[13]

In the final analysis, if 1 patient had more than 1 complication, only the most severe complication was considered. In-hospital complications were recorded and graded by a dedicated research nurse under the supervision of the study team. Also, complications were recorded at the first follow-up visit at 30 days.

In all patients, source data verification of all data entered, including the calculation of the CCI and the age-adjusted CCI, was performed by a clinical research nurse to verify the completeness and validity of the case report form.

Statistical analysis

Continuous variables are reported by mean ± standard deviation (SD), or by median and interquartile range (IQR) according to their distribution. Categorical variables were given using frequencies and proportions. To examine the impact of preoperative indices and possible confounders on complications, we performed univariate logistic regression. Multivariate logistic regression was performed to determine the best model using the different indices alone, or combined with the other predictors. A stepwise selection procedure was used.[14] Odds ratio (OR) for univariate analysis and adjusted OR for multivariate analysis with their associated 95% confidence interval (95% CI) were reported for each explanatory variable. All statistical tests were analyzed by a statistician using Stata (Stata Statistical Software: Release 12, College Station, TX). P values less than 0.05 were considered statistically significant.

Results

In the study period, 55 patients were excluded, either because they did not meet the inclusion criteria (n = 36), because of incomplete preoperative data (n = 11) or because they did not attend the first postoperative visit at 1 month at our institution (n = 8). Overall, 197 patients were included in the final analysis (Table 2).

The mean patient age was 72 (SD ± 10); 158 (80.2%) patients were men. The CCI identified more patients with comorbidities as compared to the age-adjusted CCI and to the ASA score (68% vs. 36% vs. 30%, respectively). Using the NRS, 17.3% of the patients were considered at nutritional risk.

Within the study period, 53 patients (26.9%) had at least 1 complication (Table 3). Among these complications, 13 were classified as grade I, 32 as grade II, 4 as grade IIIb, 1 as grade IVa, 1 as grade IVb, and 2 patients died (grade V). Moreover, 8 of these patients had a secondary complication, and 1 had 2 additional complications. All secondary and tertiary complications were grade I (n = 3) or II (n = 7).

All the comorbidity and nutritional indices were significant predictors of complication on univariate analysis: NRS (OR 4.25), ASA (OR 3.20), CCI (OR 1.23) and age-adjusted CCI (OR 1.22). Further, men (OR 3.65), patients over 70 (OR 2.58) and with anemia (OR 3.81) were more prone to complications. In contrast, the type of operation and of anesthesia, the smoking status and the BMI did not affect postoperative morbidity (Table 4).

After multivariate analysis, the NRS and the ASA remained the only statistically significant predictors of postoperative complications, with an OR at 2.42 and 2.11, respectively (Table 5). Among the other factors, being male was the only substantial predictor of early postoperative morbidity in multivariate analysis (OR 4.37). The best predictive model combined the NRS, the ASA and gender, and had a sensitivity of 63%, a specificity of 79% and an area under the curve of 76%.

Table 2. Descriptive characteristics of the study population

Variable	Study population
Age	72 (±10)
Sex	
Male	158 (80.2%)
Female	39 (19.8%)
BMI	27 kg/m2 (24.3 - 29.4)
Anemia	
No	146 (74.1%)
Yes	51 (25.9%)
Smoking habit	
No	117 (59.4%)
Yes	80 (40.6%)
Anesthesia	
General	76 (38.6%)
Spinal	121 (71.4%)
Operation	
TURB	124 (72.9%)
TURP	73 (37.1%)
ASA	
I	12 (6%)
II	126 (64%)
III	59 (30%)
IV	0
CCI	
0	63 (32%)
≥1	134 (68%)
Age-adjusted CCI	
0–5	126 (64%)
≥6	71 (36%)
NRS	
1–2	163 (82.7%)
≥3	34 (17.3%)

BMI: body mass index; TURB: transurethral resection of the bladder; TURP: transurethral resection of the prostate; ASA: American Society of Anesthesiologists; CCI: Charlson Comorbidity Index; NRS: Nutritional Risk Score. Continuous variables are displayed by mean (± standard deviation), or by median (interquartile range); categorical variables are displayed by frequencies (proportions).

Discussion

This study shows that the NRS may be the best preoperative score to predict early morbidity after TURB and TURP. Based on this study, while the ASA has also a significant value in stratifying patients at risk, the CCI and the age-adjusted CCI did not add substantial value to the other indices. This is a surprising result as the ASA, the CCI and the age-adjusted CCI are widely used tools before surgical procedures across different specialties, whereas the NRS is poorly used in urology, and no study has previously assessed its predictive value in patients undergoing TURB or TURP.

The CCI has been validated in predicting mortality after TURP. In a large cohort of 7632 men, a nomogram, based on the CCI and age, was able to predict early mortality with an accuracy of 83% in the validation cohort.[15] In terms of morbidity, another study showed a significant association between complications after TURP and CCI.[16] While the association between survival and comorbidity status could

Table 3. The complications occurred in the study population are displayed per type

Type of complication	No. patients, %
Delayed length of hospital stay	18 (9.2%)
Hematuria	13 (6.6%)
Urinary tract infection	6 (3.1%)
Acute urinary retention	5 (2.5%)
Blood clot retention	3 (1.5%)
Organ perforation	3 (1.5%)
Deep vein thrombosis	1 (0.5%)
Renal failure	1 (0.5%)
Sepsis	1 (0.5%)
Myocardial infarction (Death)	1 (0.5%)
Pulmonary embolism (Death)	1 (0.5%)
Total	**53 (26.9%)**

Based on the outcome measure, which was the Dindo-Clavien classification, the same type of complication can be scored with different grades according to how it was managed.

Table 4. Univariate analysis of predictors of complications

Variable	OR (95% CI)	*p* value
Age	2.58 (1.26-5-27)	0.009
Sex	3.65 (1.22-10.86)	0.020
BMI	1.00 (0.93-1.08)	0.971
Anaemia	3.81 (1.84-7.91)	0.000
Smoking habit	0.80 (0.41-1.57)	0.521
Anesthesia	0.90 (0.46-1.76)	0.763
Type of operation	1.72 (0.89-3.33)	0.110
ASA	3.2 (1.62-6.33)	0.001
CCI	1.23 (1.07-1.42)	0.004
Age-adjusted CCI	1.22 (1.09-1.38)	0.001
NRS	4.25 (2.25-10.91)	0.000

OR: odds ratio; CI: confidence interval; BMI: body mass index; ASA: American Society of Anesthesiologists; CCI: Charlson Comorbidity Index; NRS: Nutritional Risk Score.

Table 5. Multivariate logistic regression using a stepwise selection to determine the best model to predict complications

Variable	OR (95% CI)	*p* value
Age	NS	
Sex	4.37 (1.27-10.08)	0.020
BMI	NS	
Anemia	NS	
Smoking Habit	NS	
Anaesthesia	NS	
Type of operation	NS	
ASA	2.11 (1.01-4.43)	0.048
CCI	NS	
Age-adjusted CCI	NS	
NRS	2.42 (1.56-3.74)	0.000
Area under the curve	76%	
Sensitivity	63%	
Specificity	79%	
Positive predictive value	51%	
Negative predictive value	86%	

NS: not significant; OR: odds ratio; CI: confidence interval; BMI: body mass index; ASA: American Society of Anesthesiologists; CCI: Charlson Comorbidity Index; NRS: Nutritional Risk Score.

not be evaluated in our study given the limited sample size and the short follow-up, the value of the CCI in predicting morbidity was verified only in the univariate analysis. Although this might also be related to a small number of patients, it is important to highlight that other preoperative indices, such as the ASA and the NRS, were significantly associated with postoperative morbidity.

The role of the other scores used in this study has been poorly assessed in patients undergoing transurethral resections. In our study, the same comments regarding the CCI might also be applied to the age-adjusted CCI since the 2 scores are closely related, the latter representing an adjustment of the CCI based on age. In contrast, the ASA confirmed its value in the present study. The paucity of the reports investigating this score after transurethral procedures may be because the ASA is already widely used in clinical practice by anesthesiologists.[17]

The most interesting finding of this study is the substantial utility of the NRS in predicting early morbidity after transurethral operations. Although the NRS is a composite score, including age and disease severity, the multivariate analysis suggests that nutritional status is the key feature of this score. Malnutrition is a strong predictor of morbidity and mortality after gastrointestinal surgery, and its prevalence among patients undergoing other procedures might be underestimated.[18] In fact, the consequences of malnutrition on the surgical outcome are related to the so-called "surgical stress," rather than the effects of specific procedures on the organism; therefore, malnutrition is likely to play an essential negative role in most of the surgical patients.[19]

In our study, only 17.3% of patients were considered at nutritional risk. This rate is significantly less than the rate of patients at risk of complications identified by the other scores, which ranged from 30% to 68%. This wide difference is possibly related to the outcome measure we used to identify patients at nutritional risk (the NRS). Indeed, while the CCI, the age-adjusted CCI and the ASA consider only the comorbidity status before treatment to determine the impact of coexisting diseases on surgical outcome, the NRS aims to identify patients at risk by combining 3 different components: nutritional status, severity of the surgery and age. In other words, in contrast to the other scores, the NRS is probably more selective since it considers a number of factors that seem to contribute to the "surgical stress."[11]

While this observational study has high internal validity and adheres to the STROBE guidelines for reporting observational studies, it has some limitations. The complications were evaluated only in the 30 days after the procedure. As a consequence, late complications after transurethral resections were not taken into account. In addition, it can be argued that including patients undergoing TURB for bladder cancer with men undergoing TURP for BPH can lead to heterogeneity bias. Although we agree that this bias is possible, we also believe that these procedures have many similarities regarding the endoscopic approach and the type of early complications; thus, the systematic error related to this heterogeneity should be minimal. This argument is also sustained by the fact that the operation type was not a predictor of morbidity either in the univariate or in the multivariate analysis. Moreover, all indices were dichotomized given the limited sample size that would have required a very large effect if each score was treated as a continuous or a categorical variable. This approach may have underestimated the predictive ability of indices with a wide range of possible values (namely the CCI and the age-adjusted CCI). Further, no power calculation was performed prior to the study. This was due to a lack of similar studies exploring the

value of these scores in this population. Finally, the predictive model was not validated, and should be additionally tested to demonstrate the results achieved in this study.

Despite these limitations, we believe that this study has worthy clinical implications and should guide future research. Based on our study, we feel that the use of NRS should be implemented in clinical practice since it was the single most significant predictor of complications. Considering the combined value of the nutritional status, the severity of surgery and age, the NRS appears to reflect at best the perioperative risk of surgical patients, even in minor surgery. Further, the NRS has attractive advantages over other indices. Indeed, it is validated and easily used by non-medical staff members, it correlates to biological measures of malnutrition, has no cost implications, and could be used to select patients who might benefit from nutritional support.[11] Finally, with a specificity of 79% and a negative predictive value of 86%, the best model to predict complications could assist clinicians to balance risk and benefit in the decision-making process. Still, this model has yet to be validated in external cohorts.

Conclusion

The importance of preoperative scores as predictors of early complications is applicable also to patients undergoing TURB or TURP. Particularly, the use of a simple nutritional score, the NRS, may be helpful to clinicians in the preoperative assessment.

Competing interests: Dr. Valerio, Dr. Cerantola, Dr. Fritschi, Dr. Hubner, Dr. Iglesias, Dr. Legris, Dr. Lucca, Dr. Vlamopoulos, Dr. Vaucher and Dr. Jichlinski all declare no competing financial or personal interests.

This paper has been peer-reviewed.

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