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Estimation of mortality and morbidity risk of radical cystectomy using POSSUM and the Portsmouth predictor equation

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Introduction The Physiological and Operative Severity Score for the enumeration of Mortality and Morbidity (POSSUM) and the Portsmouth predictor equation (P-POSSUM) are simple scoring systems used to estimate the risk of complications and death postoperatively. We investigated the use of these scores to predict the postoperative risk in patients undergoing radical cystectomy (RC).

Material and methods In this retrospective study, we enrolled 280 patients who underwent RC for invasive bladder cancer between January 2003 and December 2011. Morbidity and mortality were predicted using the POSSUM and P-POSSUM equations. We further assessed the ability of the POSSUM and P-POSSUM to predict the mortality and morbidity risk in RC patients with a Clavien–Dindo classification of surgical complications of grade II or higher.

Results The observed morbidity and mortality rates were 58.9% (165 patients) and 1.8% (5 patients), respectively. Predicted morbidity using POSSUM was 49.2% (138 patients) compared to the 58.9% (165 patients) observed (P <0.0001). Compared to the observed death rate of 1.8% (5 patients), predicted mortality using POSSUM and P-POSSUM was 12.1% (34 patients) and 3.9% (11 patients), respectively (P <0.0001 and P = 0.205). The mortality risk estimated by P-POSSUM was not significantly different from the observed mortality rate.

Conclusions The results of this study supported the efficacy of POSSUM combined with P-POSSUM to predict morbidity and mortality in patients undergoing RC. Further prospective studies are needed to better determine the usefulness of POSSUM and P-POSSUM for a comparative audit in urological patients undergoing RC.

Key Words: POSSUM ‹› P-POSSUM ‹› morbidity ‹› invasive bladder cancer ‹› radical cystectomy

INTRODUCTION

Bladder cancer is the second most common urologic malignancy, of which urothelial carcinoma (UC) accounts for almost 90% of all primary bladder tumors [1]. With advances in medicine and technology, the population of the United States has progressively aged as life expectancy has increased [2]. In Japan, the average age of patients with bladder cancer is currently 69.8 years old. The age adjusted death rate from bladder cancer in 2012 was 7.2. Males were affected about 4 times more than females. This is expected to increase along with the increasing mean age of the general population. Among the

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general population, bladder cancer is the 11th leading cause of cancer related death. UC of the bladder generally affects older patients, with a peak incidence in the seventh decade of life [3]. Therefore, with an aging population, the management of UC in the elderly has become increasingly important. Most patients with UC present with non–muscle-invasive disease, but 20–40% either present with or develop muscle-invasive disease. Radical cystectomy (RC) is the standard treatment for localized muscle-invasive bladder cancer and is also a viable treatment option for patients with high grade, non-muscle invasive disease. However, RC is associated with relatively high perioperative morbidity and mortality, despite improvements in surgical techniques and perioperative patient care [4, 5, 6]. The impact of the quality of surgery and postoperative care in patients who undergo RC remains unclear due to large variability.

The Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity (POSSUM) provides a useful tool for risk adjustment and comparative audit. POSSUM was developed by Copeland et al. [7] using cohorts of general surgical patients. The system uses commonly recorded preoperative data to determine a physiological score and an operative severity score from which the expected morbidity and mortality rates are calculated using logistic regression equations. POSSUM was revised to the Portsmouth predictor equation (P-POSSUM) by Whiteley et al. [8] who reported that POSSUM overpredicted postoperative mortality in general surgical patients, especially in low-risk patients. P-POSSUM uses the same set of variables as POSSUM, but uses a different logistic regression equation [8]. There has been limited evaluation of the POSSUM and P-POSSUM scoring systems for urological surgery patients [9, 10]. In this study, we retrospectively evaluated postoperative morbidity and mortality in patients who underwent RC.

MATERIAL AND METHODS

The institutional review board approved this retrospective analysis of 280 patients who underwent RC for bladder cancer between January 2003 and December 2011. In our study, lymphadenectomy was not considered because of the lack of a definite rule regarding the range of lymphadenectomy. The POSSUM was determined for all patients by review of their medical records. Physiological scores were determined by review of preoperative anesthesia records, while the operative severity scores were determined by review of the operative reports (Appendix 1).

The physiological score is a 12-factor 4-grade score including age, cardiac status, pulse rate, systolic blood pressure, respiratory status, Glasgow Coma Scale, serum urea, potassium, sodium, hemoglobin concentration, white cell count, and electrocardiography findings. A Glasgow Coma Scale of 15 was assumed in all patients unless specified preoperatively. The entire cohort underwent elective RC for UC with no evidence of metastasis on preoperative evaluation. Therefore, certain operative severity score components were assumed to be the same in all patients: operation category "Major", malignancy "Primary only", and operation timing "Elective".

Postoperative 30-day morbidity and mortality were determined by a retrospective chart review. Complications were stratified using the Clavien–Dindo classification. Major complications were defined as a Clavien socre ≥2, as patients of Clavien grade 1 did not require medical treatment. Predicted morbidity (POSSUM) and mortality (POSSUM and P-POSSUM) rates were calculated using previously validated equations. Morbidity was determined using the following equation:

$$\ln R/1 - R = -5.91 + (0.16 \times \text{physiological score}) + (0.19 \times \text{operative severity score}),$$

where R represents the morbidity risk.

Table 1. *Characteristics of the 280 radical cystectomy patients by the urinary diversion method*

	Ureterocutaneostomy (n=150)	ileal segmental urinary diversion (n=130)	p-value
Age (years), median (range)	74 ±8.31 (38-91)	67 ±7.84 (47-85)	0.075
Sex, n (%)			
Male	124 (82.7)	116 (89.2)	0.085
Female	26 (17.3)	14 (10.7)	0.095
Previous cardiac disease, n (%)	56 (37.3)	42 (32.3)	0.142
Previous pulmonary disease, n (%)	18 (12)	7 (5.4)	0.053
Estimated blood loss (ml)	1646 ±1838 (250-14970)	1541 ±838 (360-4480)	0.065
Form of urinary diversion, n (%)			
Ileal conduit	–	88 (67.7)	–
Neobladder	–	42 (33.1)	–

*median ±SD

Mortality was determined using the following equation:

$$\ln L/1 - L = -7.04 + (0.13 \times \text{physiological score}) + (0.16 \times \text{operative severity score}),$$

where L represents the mortality risk (Appendix 2).

The mean predicted risk for patients in each group was calculated and multiplied by the number of patients in the group to give the predicted number of patients.

Statistical analysis

To evaluate the use of the POSSUM equation to predict morbidity and mortality, observed and predicted outcomes were compared using the Hosmer and Lemeshow chi-square method (11). The predict-

Table 2. *Summary of complication type in the Clavien Dindo grading system over Grade II*

Ureterocutaneostomy (n=150)	Ureterocutaneostomy (n=47)	Ileal segmental urinary diversion (n=56)
Clavien grade, n	40	48
Ileus	16	26
UTI	17	12
FUO	1	
SSI	3	6
Pneumonia	2	2
Bowel leak		1
Hydronephrosis	1	1
Clavien grade, n	2	8
UTI	1	1
SSI		3
Bowel leak		2
Wound dehiscence	1	2
Clavien grade, n	5	0
Pneumonia	2	
Bleeding	2	
Pulmonary infarction	1	

In total, 165 patients suffered complications. Of these, 62 were Clavien–Dindo grade I and 103 were grade II or higher. No patients were classified as Grade IV.

Table 3. *Predicted vs. observed mortality and morbidity using POSSUM and P-POSSUM logistic regression equations*

Risk percentile	No. of patients	Mean risk	Total No. of Observed Events (No. of Clavein II/ No. of over clavien III or higher	No. of Predicted Events	Total Observed: predicted ratio
POSSUM morbidity:					
>0 ≤20	7	19.3	4 (3 / 0)	1	4
>20 ≤30	35	26.1	20 (13 / 1)	9	2.3
>30 ≤40	48	36.6	26 (15 / 5)	18	1.4
>40 ≤50	65	45.4	35 (19 / 3)	30	1.2
>50 ≤60	60	55.6	40 (17 / 4)	33	1.2
>60 ≤70	30	65.3	20 (13 / 1)	20	1
>70 ≤80	22	74.4	12 (6 / 1)	16	0.8
>80 ≤90	11	83.8	7 (5 / 0)	9	0.8
>90 ≤100	2	92.5	1 (1 / 0)	2	0.5
POSSUM mortality:					
>0 ≤10	155	7.5	1	12	0.08
>10 ≤20	92	13.9	3	13	0.23
>20 ≤30	26	23.5	1	6	0.17
>30 ≤40	5	35.8	0	2	0
>40 ≤50	1	43	0	0	0
>50 ≤60	1	52	0	1	0
P-POSSUM mortality:					
>0 ≤10	260	3	4	8	0.5
>10 ≤20	14	12.7	1	2	0.5
>20 ≤30	5	24.4	0	1	0
>30 ≤40	0	0	0	0	0
>40 ≤50	1	41	0	0	0

ability of the POSSUM was evaluated by receiver operating characteristics (ROC) curve analysis. We compared the POSSUM and P-POSSUM in RC patients with ureterocutaneostomy or ileal urinary diversion and a Clavien–Dindo classification of grade II or higher using the Mann–Whitney *U*-test. All statistical analyses were performed using SPSS version 8 (SPSS Inc.,) and the EMS package in R version 2.12.1 (http://www.r-project.org/). A P-value of <0.05 was considered to indicate statistical significance.

RESULTS

Table 1 shows the characteristics of the 280 patients enrolled in this study (240 males and 40 females). Ureterocutaneostomy was performed in 150 patients (53.5%) and ileal urinary diversion was performed in 130 patients (46.5%). A history of cardiac disease or pulmonary disease was reported in 98 patients (35%) and 25 patients (8.9%), respectively. Estimated blood loss was 1646 ±1838 ml with ureterocutaneostomy and 1541 ±838 ml with ileal urinary diversion.

All complications within 30 days of surgery were categorized into 10 specific categories and graded in accordance with the modified Clavien–Dindo classification system. In total, 165 patients (58.9%) suffered complications and 5 patients (1.8%) died. Of that, 103 patients had a Clavien–Dindo grade of II or higher, which needed some medical care (Table 2). All deaths were of patients belonging to the ureterocutaneostomy group. Two deaths were attributable to hemorrhage, two to pneumonia, and one to an acute pulmonary infarction.

The mean physiological and operative scores were 18.6 ±4.6 and 15.6 ±2.1, respectively. The mean morbidity and mortality risks predicted by the POSSUM equation were 49.2% (138 patients) and 12.1% (34 patients), respectively (Table 3). The mean mortality risk predicted by the P-POSSUM equation was 3.9% (11 patients). There was a significant lack for the POSSUM to predict morbidity ($\chi^2 = 51.5$, 7 df, $P < 0.0001$) and mortality ($\chi^2 = 29.3$, 4 df, $P < 0.0001$). In contrast, there was no significant difference between the mortality rate estimated by P-POSSUM and the observed mortality rate ($\chi^2 = 4.57$, 3 df, $P = 0.2054$).

Empirical ROCs to assess the prediction of morbidity and mortality by the POSSUM and mortality by the P-POSSUM are shown in Figure 1. The AUC was 0.514 (CI, 0.446–0.583), 0.514 (0.446–0.583), and 0.518 (0.451–0.586), respectively.

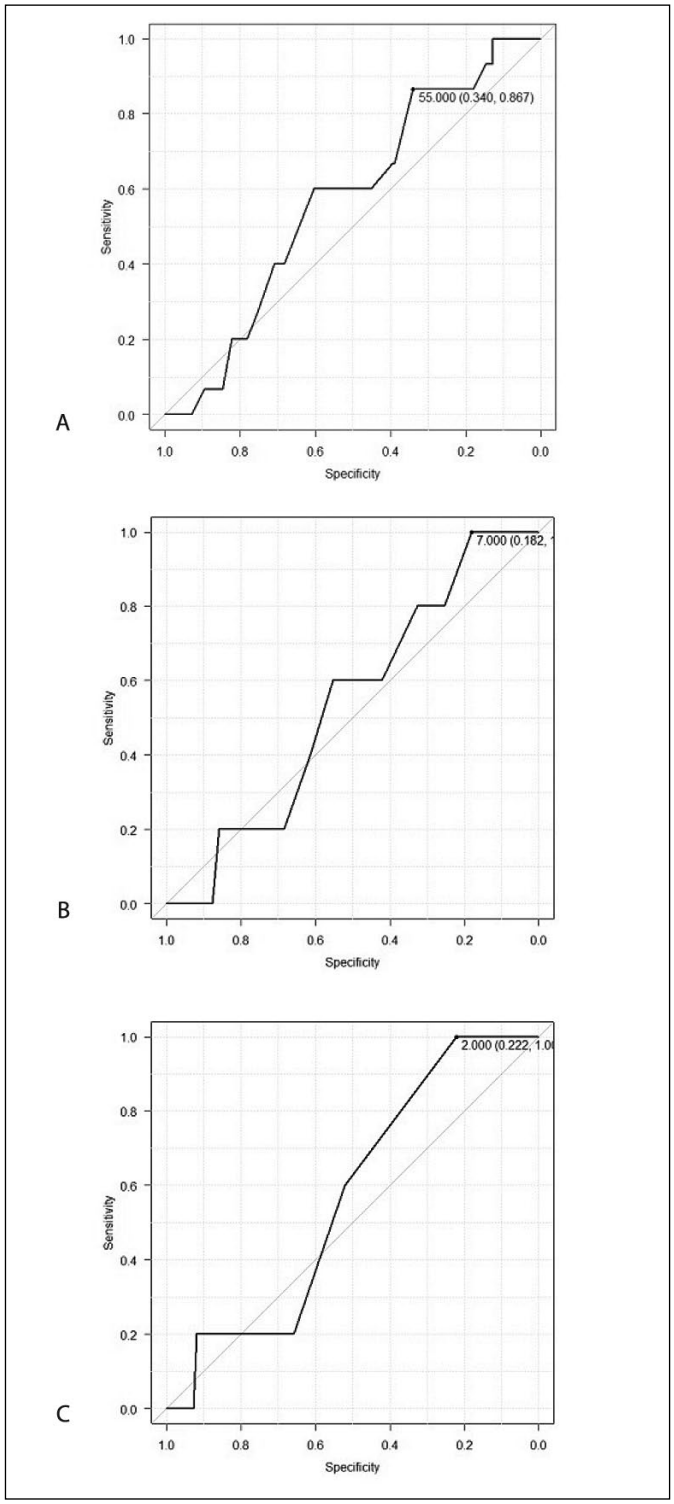

Figure 1. *Empirical receiver operating curves (ROCs) to assess the prediction of morbidity and mortality by the POSSUM, and the prediction of mortality by the P-POSSUM. The area under the curve (AUC) is used as a measure of overall diagnostic accuracy. A. The POSSUM morbidity does not accurately predict the observed morbidity. B. The POSSUM mortality does not accurately predict the observed mortality. C. The P-POSSUM mortality accurately predicts observed mortality.*

DISCUSSION

Invasive UC of the bladder is a potentially fatal disease that requires aggressive therapy. If untreated,

fewer than 15% of UC patients will survive 2 years [12]. The standard treatment for localized muscle-invasive bladder cancer is RC, and this surgery is also a viable treatment option for patients with high grade, non-muscle invasive disease. In a large series of patients with long-term follow-up, Stein et al. [1] demonstrated that RC could be performed safely and patients could expect excellent bladder control postoperatively. More than 69% of invasive bladder cancer patients survived 5 years without evidence of recurrent disease [1]. However, RC remains a highly complex procedure, associated with comparatively high perioperative morbidity and mortality, despite ongoing improvements in surgical techniques and perioperative patient care [4]. In our study, 150 patients underwent ureterocutaneostomy. The longer the operative time, the more complications occurred. Therefore, the tendency would be to say that ureterocutaneoustomy is preferred to save the total operative time.

A review of more than 100 RC patients conducted prior to 1990 reported a mortality rate of 2.4–15% and an early morbidity rate of 28–42% [13]. In the past decade, the mortality rate has been reduced to 0–3.9%, but the early morbidity rate remains high, at 11–68%. Among perioperative and postoperative complications, acute blood loss is common in RC, and predicting blood loss and transfusion requirements remains difficult. Most of the blood loss occurs during manipulation of the bladder vasculature and pedicles. Certainly, the anatomical understanding of RC has contributed to a reduction in blood loss. Careful patient selection and combined epidural and general anesthesia may help to further lower transfusion rates [14].

The POSSUM was developed for use in general surgery [7] and has been validated in more than 15,000 patients. The scoring system has become a well-established method to assess patients prior to vascular, gastrointestinal, pulmonary, and colorectal surgery [15]. It is easy to use, with the score determined in about 10 min. However, there are two important limitations to the use of the POSSUM equation system [9, 10]. First, the timing of data collection for the physiological and operative score components is critical. Therefore, standardized prospective data collection methods are required to avoid artificially altering the predicted outcomes [16]. Operative parameters used in the POSSUM equations do not account for different surgeons, operative times, and blood loss over 1000 ml, all of which are implicated in the outcomes after RC. A single scoring system may not be applicable to all surgical fields because of differing subspecialty procedures and patient populations. Second, some studies have found that the POSSUM overpredicted mortality in general surgical patients, especially in low-risk groups [10]. To the best of our knowledge, there have only been two previous studies of the use of the POSSUM for urological surgery. Our studies reached a different conclusion than the past studies. In the previous studies, considering all stratified risk groups together, the POSSUM tended to overpredict morbidity and mortality, especially in low-risk groups. In the present study, the POSSUM significantly underpredicted morbidity and mortality in low-risk patients undergoing RC. The discrepancy could be derived from two reasons. First, when we reviewed the data of Clavien grade III and higher, the POSSUM would overpredict. Therefore, it was dependent on the data we obtained. Second, the discrepancy could be due to low-volume hospitals and surgeons. Follow up after surgery depended on the surgeon. Concerning the background of 25 low-risk patients, their common factor waslong operational time. The patients with a high risk for morbidity, as determined by the POSSUM, tended to belong to the ureterocutaneostomy group and to have a Clavien–Dindo grade of II or higher. Two of the five deaths occurred in patients with a history of severe heart disease or pulmonary disease, but three had no significant past history. All of those factors were unexpectable to predict the death.

Our study has some limitations mostly inherent to its retrospective multicentric design and low volume hospitals and surgeons. We did not have the definite standard to choose the urinary diversion between centers. Absence of statistical difference did not mean equivalence. Finally, 5 patients died in the ureterocutaneostomy group only.

The POSSUM system could be useful to assess the operative risk before RC and to indicate operative skills, particularly relating to blood loss. However, to predict the risk of death after surgery was so complicated that the POSSUM system needs to be further improved.

CONCLUSIONS

In summary, the present study found that POSSUM underestimated postoperative morbidity and mortality in low-risk patients undergoing RC for invasive bladder cancer. On the other hand, the P-POSSUM equation accurately predicted postoperative mortality. Further prospective studies are needed to better determine the usefulness of POSSUM and P-POSSUM for a comparative audit in urological patients undergoing RC. If patients are predicted to be at high risk of mortality by P-POSSUM prior to RC, urologists should be aware of the potential need for intensive care after surgery.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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APPENDIX 1

Physiological and operative severity score for the enumeration of mortality and morbidity

	Score 1	Score 2	Score 4	Score 8
Phisiological				
Age	Less than 60	61-70	Greater than 71	
Cardiac signs	NormalCardiac drugs or steroids	Edema, warfarin, borderline cardiomegaly		Increased jugular venous pressure, cardiomegaly
Respiratory signs	Normal	Breath short on extension, mild chronicobstructive pulmonary disease	Breath short on stairs, moderate chronic obstructive pulmonary disease	Breath short at rest, any other
Systolic blood pressure(mmHg)	110-129	130-170 or 100-109	Greater than 170 or 90-99	Less than 90
Pulse rate (bpm)	50-80	81-100 or 40-49	101 – 120	Greater than 120 or ;ess than 40
Glasgow coma score	15	12~14	9~11	Less than 9
Serum urea (mmol/l)	Less than 7.5	7.5-10.0	10.1-15.0	Greater than 15.0
Serum sodium (mmol/l)	Greater than 136	131-135	126-130	Less than 126
Serum potassium (mmol/l)	3.5-5.0	3.1-3.4 or 5.1-5.3	2.9-3.1 or 5.4-5.9	Less than 2.9 or greater than 5.9
Hemoglobin (gm/l)	13.0-16.0	11.5-12.9 or 16.1-17.0	10.0-11.4 or 17.1-18.0	Less than 10.0 or greater than 18.0
White cell count (×109/l)	4.0-10.0	10.1-20.0 or 3.1-3.9	Greater than 20.0 or less than 3.1	
Electrocardiogram	Normal		Atrial fibrillation	Any other
Operative				
Operation category	Minor	Intermediate	Major	Major +
No. procedure	1	2	Greater than 2	
Total blood loss (ml)	Less than 100	101-500	501-999	1,000 or Greater
Peritoneal soiling	None	Less than 250 cc serous blood	Local pus	Any other
Malignancy	None	Primary only	Nodal metastasis	Distant metastasis
Operation timing	Elective		Urgent, within 2 hrs, resuscitation possible	Emergency, immediate, no resuscitation possible

APPENDIX 2

POSSUM and P-POSSUM morbidity and mortality predictor equations

POSSUM mortality equation, ln (R/1-R) = -7.04 + (0.13×PS) + (0.16×OS);
POSSUM morbidity equation, ln (R/1-R) = -5.19 + (0.16×PS) + (0.19×OS);
and P-POSSUM mortality equation, ln (R/1-R) = -9.065 + (0.1692×PS) + (0.1550×OS),where PS represents physiological severity, OS represents operative severity and R indicates probability of outcome.