

## Correlation of Pre-Operative Co-Morbidity Indices with Peri-Operative and Post-Operative Metrics in Urological Patients Undergoing Major Open Procedures

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### Abstract

**Background:** Individual surgeon and institutional performance are usually assessed by morbidity and mortality rates, which can be calculated using peri-operative metrics, such as POSSUM (Physiological and Operative Severity Score for the enUmeration of mortality and morbidity). Post-operative risk can be estimated using the surgical Apgar outcome score. However, pre-operative co-morbidity may contribute to case risk diversity and affect immediate peri-operative metrics and short- and long-term morbidity and mortality. We estimated the correlation between pre-operative co-morbidity or risk assessment indices and peri-operative metrics in urological patients.

**Material and Methods:** The study included 100 consecutive patients (80.8% males, mean age  $\pm$  SD 66.3  $\pm$  10.7 years, range 30 - 88 years) undergoing major open urological procedures (39 nephrectomies, 43 radical prostatectomies, 18 radical cystectomies). Pre-operative co-morbidity was assessed using Charlson Comorbidity Index (CCI), age-adjusted CCI (AA-CCI), Cumulative Illness Rating Scale (CIRS), and Index of Co-Existent Diseases (ICED). Pre-operative risk was assessed with the American Society of Anesthesiologists index (ASA). Functional status was quantified based on estimation of the metabolic equivalent (MET). Peri-operative metrics included POSSUM and surgical Apgar scores.

**Results:** All pre-operative indices significantly correlated with POSSUM, but none correlated with the surgical Apgar score.

**Conclusions:** In patients undergoing major open urological procedures, risk stratification in the post-operative setting using the surgical Apgar score is independent of pre-operative co-morbidity status. In contrast, pre-operative co-morbidity and risk assessment correlated with peri-operative metrics used to calculate morbidity and mortality risk. Reports of death and complication rates do not take into account case diversity and, therefore, should be adjusted for co-morbidity status.

### Introduction

Quality evaluation of health care services utilizes several parameters: structural, describing the characteristics of the system's organization; procedural, describing the protocols followed; and outcome measurements. In surgery, data correlating to the outcome (post-operative morbidity/complication and mortality) are broadly used, as the service provided depends on a predictable, unique event (the operation) that has an expected and measurable result<sup>[1]</sup>. Given the effortlessness of relevant data collection, post-operative morbidity and mortality rates are used to compare surgeon and institution performance, with an improvement of provided service quality being the main objective<sup>[2,3]</sup>. These parameters have two basic disadvantages: the usual number of events is insufficient for statistical analysis<sup>[4]</sup>, and they directly correlate with the highly varying severity of cases handled in several institutions and by individual surgeons<sup>[5]</sup>. Their utilization, especially mortality as a measure of healthcare service quality, is strongly criticized<sup>[6,7]</sup>.

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Apart from the specific pathology and type of surgery, the severity of surgical cases is determined mainly by the co-morbidity, which is defined as the “diseases or disorders that coexist with a disease of interest” [8]. Comorbidity may increase the possibility of hospitalization and delay diagnosis, affect curative decisions, correlate with complications, alter survival, require greater skill from care providers, increase the cost of care services, and constitute a confounding factor in data analysis [8,9].

Predicting post-operative morbidity and mortality is important in most suitable curative decision-making and in organizing provided services. Therefore, indices of pre-operative morbidity and peri-operative and intra-operative morbidity have been used. The objective of the present study was to assess the correlation between pre-operative co-morbidity indices and peri-operative and post-operative metrics in urological patients undergoing major open procedures.

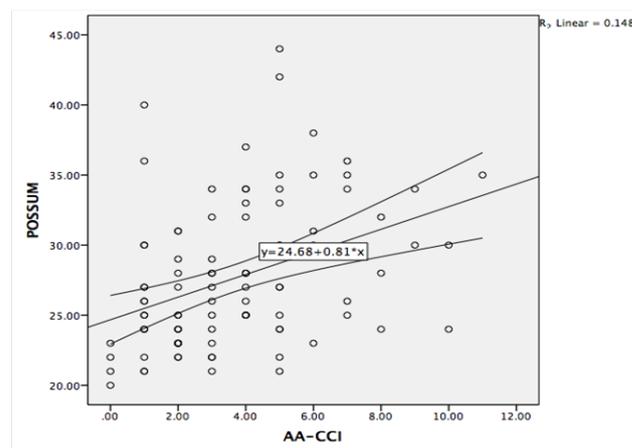
**Material and Methods**

The study included 100 consecutive patients (80.8% males) undergoing major open urological procedures (39 nephrectomies, 43 radical prostatectomies, 18 radical cystectomies). Patient age ranged from 30 to 88 years (mean ± SD: 66.3 ± 10.7 years). Pre-operative co-morbidity was assessed using a series of indices: Charlson Comorbidity Index (CCI) [10], age-adjusted CCI (AA-CCI) [11], Cumulative Illness Rating Scale (CIRS) [12], and Index of Co-Existent Diseases (ICED) [13]. Pre-operative risk was assessed with the American Society of Anesthesiologists index (ASA) [14]. Functional pre-operative status was quantified based on estimation of the metabolic equivalent (MET) [15]. Peri- and intra-operative metrics included POSSUM (Physiological and Operative Severity Score for the enUmeration of mortality and morbidity) [16] and surgical Apgar scores [17].

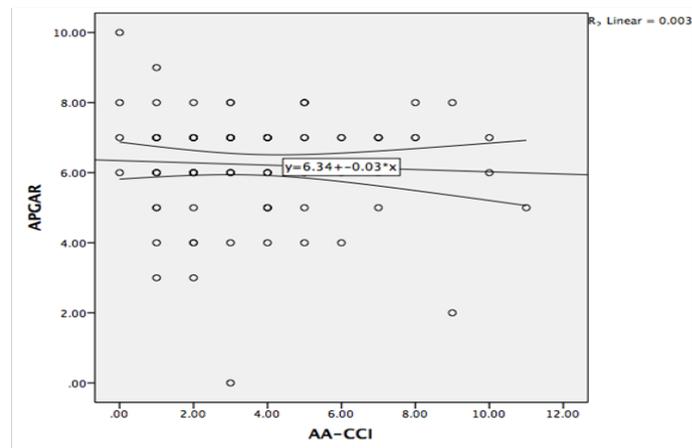
Statistical analysis was performed using IBM SPSS Statistics v. 21.0 software. Continuous variables are described by their minimum, maximum, and mean ± standard deviation (SD) values. Differences in mean values among groups were estimated using analysis of variance. The quantitative measure of correlation was depicted by calculating Pearson’s correlation coefficient.

**Results**

The scores of the different indices are depicted in Table 1. All pre-operative indices significantly correlated with POSSUM, but no significant correlation with the surgical Apgar score was noted (Table 2). Similar results were observed in different groups of patients according to the procedure performed. Example representations of the correlation of AA-CCI with POSSUM and the surgical Apgar score are depicted graphically in Figures 1 and 2.



**Figure 1:** Significant correlation between AA-CCI and POSSUM



**Figure 2:** No significant correlation between AA-CCI and APGAR

**Table 1:** Pre-, peri-, and post-operative indices

	All patients	Nephrectomies	Cystectomies	Prostatectomies
<b>Pre-operative co-morbidity</b>				
CCI	0-8; 1.5 ± 1.8	0-8; 1.7 ± 2.2	0-5; 1.3 ± 1.4	0-7; 1.1 ± 1.7
AA-CCI	0-11; 3.7 ± 2.4	0-11; 3.5 ± 2.9	1-7; 3.5 ± 1.8	1-8; 3.4 ± 1.9
CIRS	0-8; 3.0 ± 2.1	0-8; 3.0 ± 2.1	0-8; 3.9 ± 2.1	0-7; 3.0 ± 2.2
ICED	0-16; 4.7 ± 3.9	0-14; 5.0 ± 4.3	2-16; 6.7 ± 3.8	0-14; 4.8 ± 4.5
<b>Operative risk assessment</b>				
ASA	0-4; 2.2 ± 0.7	1-4; 2.1 ± 0.8	1-3; 2.2 ± 0.6	0-4; 2.1 ± 0.8
<b>Functional status</b>				
MET	2-6; 3.8 ± 0.9	2-6; 3.7 ± 0.9	2-5; 3.6 ± 0.8	2-6; 4.1 ± 1.0
<b>Peri-operative metrics</b>				
POSSUM	20-44; 27.6 ± 5.1	20-42; 27.3 ± 5.2	24-40; 30.7 ± 4.4	21-38; 26.7 ± 4.7
SAS	0-10; 6.2 ± 1.4	2-10; 6.4 ± 1.4	0-7; 5.3 ± 1.9	3-8; 6.2 ± 1.2

Data are given as range; mean ± SD

**Table 2:** Correlation of pre-operative co-morbidity and operative risk assessment indices with peri-operative metrics

	POSSUM		SAS	
	<i>r</i>	P-value	<i>r</i>	P-value
CCI	0.382	< 0.01	-0.076	N.S
AA-CCI	0.385	< 0.01	-0.054	N.S
CIRS	0.437	< 0.01	-0.133	N.S
ICED	0.510	< 0.01	-0.057	N.S
ASA	0.368	< 0.01	-0.088	N.S
MET	-0.248	< 0.05	0.079	N.S

POSSUM: Physiological and Operative Severity Score for the enUmeration of mortality and morbidity; SAS: Surgical Apgar Score; N.S.: not significant

## Discussion

In contrast to clinical practice, in which age and co-morbidity impact assessment play an important role, its impact as a confounding factor in clinical research has been ignored until recently<sup>[18]</sup>. Efforts to quantify co-morbidity have resulted in the creation of a series of indices<sup>[19,20]</sup>. A co-morbidity index condenses all coexisting illnesses (and, occasionally, their severity) into one sum, providing the ability to compare it to the corresponding sums of other patients<sup>[8]</sup>. Co-morbidity should not be confused with multi-morbidity, which is defined as the coexistence of more than two illnesses in the same patient without recognizing the illness under study<sup>[19]</sup>. Moreover, co-morbidity does not constitute assessment of the impact of all illnesses on the overall health of a patient. This is assessed by performance scales, such as Karnofsky and Eastern Co-operative Oncology Group (ECOG), or functionality scales, such as Activities of Daily Living (ADL). These scales incorporate the reference illness and, therefore, have the same sum in each patient, regardless of the illness under study<sup>[8]</sup>. The relationship between morbidity and postoperative mortality has begun to be studied in oncological urology patients.

CCI<sup>[10]</sup> was designed and scaled to predict mortality by taking into account only the presence rather than the severity of 19 different diseases (myocardial infarction, congestive heart failure, peripheral vascular disease, cerebral vascular disease, dementia, chronic pulmonary disease, connective tissue disorders, ulcer disease, mild liver disease, diabetes, hemiplegia, moderate or severe kidney disease, diabetes with end organ damage, any type of tumor, leukemia, lymphoma, moderate or severe liver disease, metastatic solid tumor, and AIDS). AA-CCI<sup>[11]</sup> also includes an age-correlated score. In renal cell carcinoma, the attendant morbidity should be taken into account when indicating the outcome of therapeutic interventions<sup>[21]</sup>; CCI is associated with complications after nephrectomy<sup>[22]</sup> and the overall survival of patients with no metastatic renal cancer undergoing partial or radical nephrectomy<sup>[23,24]</sup>. CCI is also predictive of peri-operative death and 5-year all cause mortality after radical cystectomy<sup>[25-28]</sup>, whereas AA-CCI can predict early death in patients with localized or locally advanced prostate cancer<sup>[29]</sup>.

CIRS<sup>[12]</sup> grades the severity of dysfunction in 14 organs on a scale of 0 (no dysfunction) to 4 (extremely severe dysfunction), without taking into account the system under study. It has

been highly recommended for the pre-treatment evaluation of older patients with prostate cancer<sup>[30]</sup>.

ICED<sup>[13]</sup> combines a measure of comorbid disease severity (14 organ systems) and a measure of functional impairment (10 functional areas) into an overall ordinal scale indicating no, mild, moderate, or severe co-morbidity. It is significantly correlated with health-related quality of life after prostate cancer treatment<sup>[31]</sup>.

ASA<sup>[14]</sup> is the oldest pre-operative risk assessment index, classifying patients into five categories (healthy, with mild systemic disease, with severe systemic disease, with severe systemic disease constituting a constant threat to life, and moribund-unable to survive without the procedure). It has been used as an index of mortality in major urological surgery<sup>[32]</sup>.

Functional condition is assessed by calculating functional equivalents<sup>[15]</sup>, with the functional equivalent corresponding to oxygen consumption by a man of 70 kilos at rest. The ability to conduct activity greater than 7 MET is considered outstanding functionality, whereas activity less than 4 MET is considered poor. Physical activity is adversely related to prostate cancer-specific mortality among men with prostate cancer<sup>[33,34]</sup>.

POSSUM<sup>[16]</sup> is the sum of the physiological and operative severity scores. The physiological score is a 12-factor 4-grade score including age, cardiac status, pulse rate, systolic blood pressure, respiratory status, Glasgow coma score, serum urea, sodium and potassium, hemoglobin concentration, white cell count, and electrocardiographic findings. The 6-factor 4-grade operative severity score includes type and number of procedures, total blood loss, peritoneal soiling or urinary tract infection, presence and extent of malignancy, and operative time. Each of these 18 variables for the physiological and operative severity scores is assessed using a 4-grade exponential score of 1, 2, 4, and 8. The POSSUM score is the sum of all variables, with a possible score of 18 to 140. The POSSUM score is rapid and easy to use and has been recommended for risk-adjusted urological audit and for comparing performance in different units<sup>[35]</sup>.

The surgical Apgar score<sup>[17]</sup> is based on three intra-operative parameters: lowest heart rate, estimated blood loss, and lowest blood pressure. Grading is expressed on a scale of 0-10, with 0 representing the highest risk of death. It can identify patients at higher risk of major complications and death after partial or radical nephrectomy<sup>[36]</sup>, radical cystectomy<sup>[37]</sup>, and radical prostatectomy<sup>[38]</sup>.

The various published indices were created based on different patient populations, and only CIRS and ICED seem to have the potential for generalized use compared to CCI, which is one of the most frequently used indices<sup>[8]</sup>. Another disadvantage of general indices is the inability to diagnose the particular impact of co-morbidity on the outcome of a specific illness, which has led to the development of illness-specific relevant indicators<sup>[9]</sup>. Despite the majority of indices not being developed to predict mortality, it is interesting to note that co-morbidity, even when estimated based on administrative data rather than medical records, seems to be related to the mortality of oncology patients<sup>[39]</sup>. Determining co-morbidity is vital to the development of systems that will assist with resource allocation and the provision of high quality health services<sup>[40]</sup>. Co-morbidity is also of particular interest for surgery and assessing the post-operative

mortality of oncology patients<sup>[41]</sup>, for which relevant computing systems have been developed<sup>[42]</sup>. These systems can also estimate the possibility of specific surgical complications<sup>[42]</sup>.

The assessment of intraoperative parameters for calculating the operative risk (surgical Apgar score) appears to have a strong relationship with both the probability and time of occurrence of postoperative mortality in urology patients<sup>[43]</sup> but has no additive value in the predictive value of pre-operative indicators of morbidity<sup>[44]</sup>. This finding confirms the “independence” of this indicator as highlighted by the findings of this study. This should stimulate new studies that will better define the intraoperative factors that determine postoperative morbidity and mortality and identify the high-risk patients who could benefit from properly allocated resources. In contrast, pre-operative morbidity indicators and surgical risk calculators are associated with peri-operative metrics used for prediction of post-operative morbidity and mortality risk. Reporting of crude morbidity and mortality does not take into account the severity of the individual cases and should be adjusted according to the pre-operative morbidity.

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