ORIGINAL ARTICLE

Which risk score better predicts in-hospital mortality in radical nephrectomies with cavo-atrial thrombectomy

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Abstract: Objectives – Radical nephrectomy with cavo-atrial thrombectomy is a combination of abdominal and cardiac surgery in a patient with oncological problems. This work aims to identify which of the most commonly used risk scores in cardiac (EuroSCORE, Logistic EuroSCORE, EuroSCORE II) and non-cardiac (Lee Revised Cardiac Risk Index, National Surgical Quality Improvement Program-NSQIP) surgery better predicted the in-hospital mortality. **Methods –** The retrospective study included patients diagnosed with kidney tumour with venous extension at the supra-diaphragmatic inferior vena cava level and/or at the atrial level, undergoing complex surgery, radical nephrectomy with extraction of the venous thrombus using extracorporeal circulation, performed at Prof C.C. Iliescu Cardiovascular Diseases Emergency Institute between 2004 and 2018 by mixed teams composed by urologists, cardiac surgeons, anaesthetists, and perfusionists. The risk scores (EuroSCORE, Logistic EuroSCORE, EuroSCORE II, Lee Revised Cardiac Risk Index, NSQIP) were calculated according to the clinical records. Comparison between scores was performed by calculating the area under the ROC curve (AUC). The retrospective study received the approval of the ethical committee of the Institute. **Results –** There were included in the study 30 consecutive patients. There were recorded 6 (20%) in-hospital. The additive EuroSCORE and logistic EuroSCORE showed a high predictive power in the case of in-hospital death (AUC = 0.816 and AUC = 0.830, respectively). EuroSCORE II, NSQIP-mortality and Lee Revised Cardiac Risk Index failed to predict in-hospital mortality. **Conclusions –** Additive EuroSCORE and logistic EuroSCORE were the risk scores that better predicted in-hospital mortality in our retrospective study.
Keywords: complex surgery, extracorporeal circulation, mortality, risk scores.

Rezumat: Obiective – Nefrectomia radicală cu trombectomie cavo-atrială reprezintă o combinație între o intervenție chirurgicală abdominală și una cardiacă, la un pacient cu probleme oncologice. Lucrarea de față își propune să identifice care dintre scorurile cele mai utilizate în practică, în cadrul chirurgiei cardiace (EuroSCORE, EuroSCORE logistic, EuroSCORE II) și non-cardiace, (Scorul Lee Revizuit, NSQIP) a previzionat cel mai bine mortalitatea intraspitalicească. **Metode –** Studiul retrospectiv a inclus toți pacienții diagnosticați cu tumoră renală cu extensie venoasă la nivelul venei cave inferioare supradiafragmatice sau/și la nivel atrial, supuși intervenției chirurgicale complexe, nefrectomie radicală cu extragerea trombului venos sub circulație extracorporeală, în cadrul Institutului de Urgență pentru Boli Cardiovasculare „Prof. C.C. Iliescu" în perioada 2004-2018, în echipă mixtă: urologi, chirurgi cardiaci, anestezişti, perfuzioniști. Scorurile de risc (EuroSCORE, EuroSCORE logistic, EuroSCORE II, Scorul Lee Revizuit, NSQIP) au fost calculate conform datelor din foile de observație. Comparația între scoruri s-a efectuat calculând aria de sub curba ROC (AUC). Studiul retrospectiv a primit aprobarea comisiei de etică a institutului. **Rezultate –** Au fost incluși în studiu 30 de pacienți consecutivi. Au fost înregistrate 6 (20%) decese în cadrul aceleiași internări. EuroSCORE aditiv și EuroSCORE logistic au prezentat o mare putere de predicție în cazul decesului intraspitalicesc (AUC=0.816, respectiv AUC=0.830). EuroSCORE II, NSQIP-mortalitate and Scorul Lee Revizuit nu au reușit acest lucru. **Concluzii –** EuroSCORE aditiv și logistic au fost scorurile care au prezis mai bine decesul intraspitalicesc, în cadrul studiului nostru retrospectiv.
Cuvinte cheie: chirurgie complexă, circulație extracorporeală, scoruri de risc, mortalitate.

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INTRODUCTION

Among the solid neoplasms in adult people, renal carcinomas represent 5% of neoplasms in men and 3% of neoplasms in women[1]. Albeit it seems a rather small percentage, it should be noted that they only become symptomatic at an advanced stage of the disease, often being unnoticed, so that at the time of diagnosis they are often in the metastasis stage[2]. In addition, a feature of renal carcinomas is to tumour extension at the level of the renal vein, up to the level of the inferior vena cava and even at the atrial level. The only therapeutic option in these cases is the surgical removal of the kidney tumour and its venous extension, with or without extracorporeal circulation. However, patients with venous extensions have a better prognosis than those diagnosed with metastases[3]. 60% of them survive for 5 years after the surgery[4]. Risk stratification in these patients is very difficult to perform, as we are dealing with a combination between abdominal surgery and cardiac surgery in a patient with oncological problems. This work aims to identify which of the most commonly used scores in cardiac and non-cardiac surgery better predicted in-hospital mortality in case of these complex surgeries.

We used the most commonly used risk scores in cardiac surgery: EuroSCORE[5], Logistic EuroSCORE[5], EuroSCORE II[5]. From the risk scores used in non-cardiac surgery we chose Lee Revised Cardiac Risk Index[6] and National Surgical Quality Improvement Program-NSQIP[7].

PATIENTS AND METHODS

The retrospective study included all consecutive patients diagnosed with kidney tumour with venous extension at the supra-diaphragmatic inferior vena cava and/or at the atrial level, undergoing complex surgery, radical nephrectomy with extraction of the venous thrombus under extracorporeal circulation. Surgical interventions were performed at Prof C.C. Iliescu Emergency Institute for Cardiovascular Diseases between 2004 and 2018 by a mixed medical team composed by urologists, cardiac surgeons, anaesthetists, and specialists in PCI. Because our study is a retrospective one, we obtained the approval of the ethical committee of the institute. The medical data was collected from the medical records.

EuroSCORE[5], Logistic EuroSCORE[5], EuroSCORE II[5], Lee Revised Cardiac Risk Index[6] and NSQIP[7] have been calculated based on the medical records. For the NSQIP we used the prediction of mortality. In this study, in-hospital mortality refers to intraoperative and postoperative death in the same hospitalization.

STATISTICAL ANALYSIS

The statistical analysis was conducted by using the IBM SPSS Statistics 20 Program. Nominal (qualitative), ordinal and quantitative variables were used. The quantitative variables were presented as average, standard deviation, minimum and maximum values. After testing the normal distribution of data by using the Shapiro Wilk test, the *T* test or the Mann Whitney test were independently applied, as appropriate. Kendall's tau test was used to identify and quantify the statistical correlation between the variables. The ROC curves were generated as well for each risk scores versus the endpoint in- hospital death, with the calculation of the area under the curve, testing also its statistical significance. We identified a cut-off of them, targeting as

Table 1. Preoperative characteristics of patients included in the study

Preoperative characteristics		Number of patients (%)
Age (years old)	57.4+/-9.5	30 (100%)
Sex	-men	21 (70%)
	-women	9 (30%)
Kidney tumour	-right	20 (66.7%)
	-left	10 (33.3%)
Venous extension level	- supradiaphragmatic inferior vena cava	13 (43.3%)
	- right atrium	17 (56.7%)
Comorbidities	-diabetes mellitus	4 (13.3%)
	-hypertension	22 (73.3%)
	-obesity	4 (13.3%)
	-heart failure	15 (50%)
Preoperative creatinine clearance		
	> 85 ml/min	11 (36.7%)
	50-85 ml/min	14 (46.7%)
	<50 ml/min	5 (16.6%)

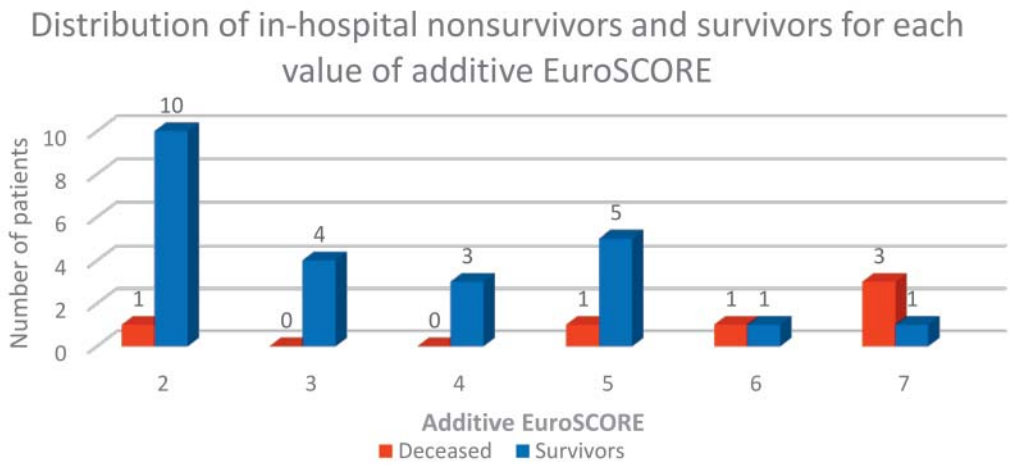

Figure 1. Distribution of in-hospital nonsurvivors and survivors for each EuroSCORE value.

much sensitivity as possible. The area under the ROC curve was the main element of risk score comparison within the risk scores for the endpoint. The threshold of statistical significance is 95% ($p<0.05$).

RESULTS

There were identified 30 consecutive patients that were included in our study. Their preoperative characteristics and intraoperative data are presented in Table 1 and Table 2. There were 2 (6.67%) intraoperative deaths: one due to intraoperative bleeding and one due to major pulmonary embolism. There were other 4 (13.33%) postoperative deaths: one patient with intestinal infarction, two patients with multiple organ dysfunction and one patient with major bleeding.

Patients included in the study presented an additive EuroSCORE of 3.87 +/- 1.83 (range 2-7). The additive EuroSCORE was higher in nonsurvivors (Table 3). Figure 1 shows that in the case of the patients with higher EuroSCORE in-hospital mortality predominantly occurred. Table 3 presents the results of statistic tests. Generation of the ROC curve (Figure 2) of additive EuroSCORE for the in-hospital mortality endpoint identifies an area of 0.816 under the curve, with statistical significance ($p=0.018$). The cut-off of EuroSCORE of 4.5 corresponds to a sensibility of 83.33% and a specificity of 70.8%.

In non-survivors patients, Logistic EuroSCORE was higher (5.38+/-2.17) than in surviving patients (2.68+/-1.41). Generation of the ROC curve (Figure 3) of Logistic EuroSCORE versus the endpoint: in-hospital mortality reveals an area of 0.830 under the curve with statistical significance $p=0.014$. The cut-off of 4.54 corresponds to a sensitivity of 83.33% and a specificity of 91.7%.

EuroSCORE II was higher in non-survivors patients (2.12+/- 1.04) than in surviving ones (1.25+/-0.8), but this is not statistically significant (Mann Whitney Test). Table 3 presents the results of statistic tests. Gene-

Table 2. Intraoperative data

Characteristics		
Extracorporeal circulation time (minutes)		79.3 ± 49.5
Ascending aortic cross-clamping	-number of patients (%) -time (minutes)	21 (70%) 44.5 ± 23.8
Intraoperative blood loss (liters)		5.9 ± 4.4
Number of units of packed red blood cells		6.6 ± 4.9
Number of units of frozen fresh plasma		6.3 ± 4.9
Cell saver - number of patients (%)		26 (86.7%)
Temperature management in extracorporeal circulation-number of patients (%)	-normothermia -moderate hypothermia	18 (60%) 12 (40%)

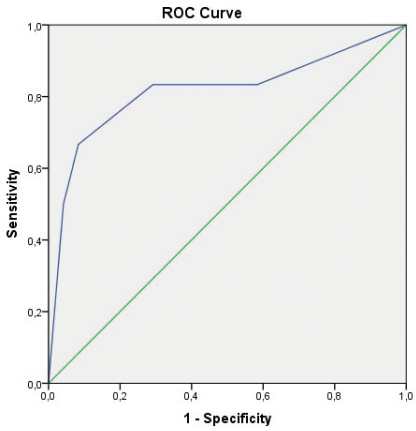

Figure 2. ROC of additive EuroSCORE versus in-hospital mortality.

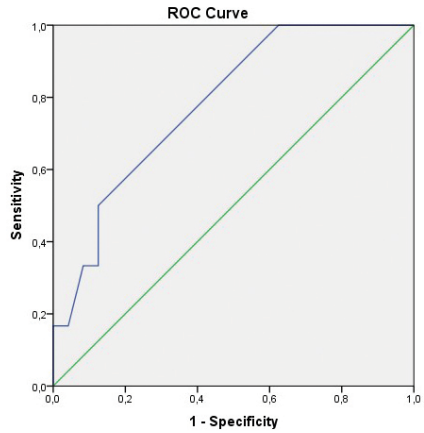

Figure 5. ROC of NSQIP-mortality versus in-hospital mortality versus in-hospital mortality.

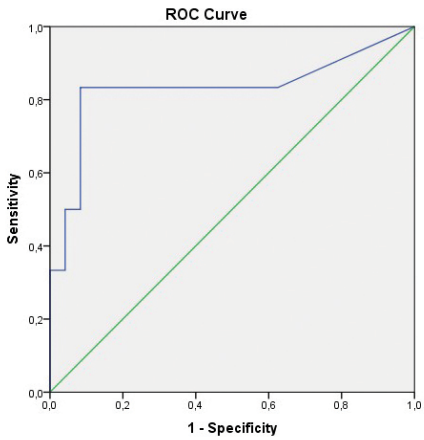

Figure 3. ROC of Logistic EuroSCORE versus in-hospital mortality.

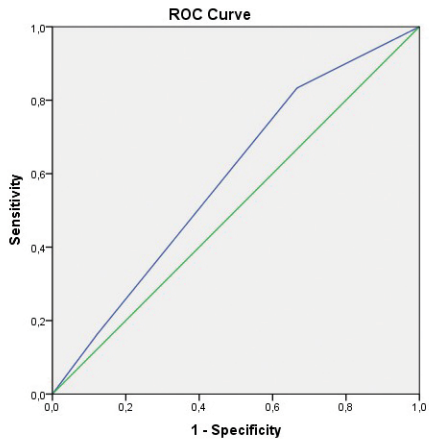

Figure 6. ROC Lee Revised Cardiac Risk Index versus in-hospital mortality.

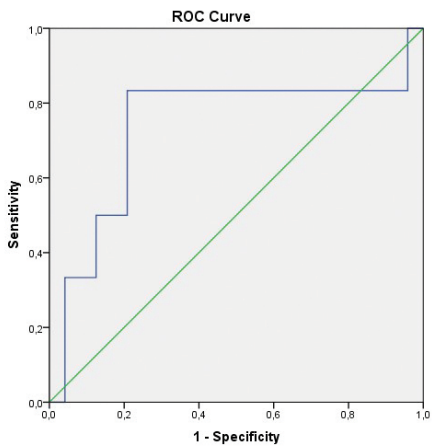

Figure 4. ROC of EuroSCORE II versus in-hospital mortality.

ration of the ROC curve of EuroSCORE II (Figure 4) versus the endpoint: in-hospital death reveals a 0.736 area under the curve with no statistical significance (p=0.078).

In the case of nonsurvivors patients, NSQIP-mortality (7.08+/-3.01) had higher values than in survivors (5.58+/-0.85). Table 3 presents the results of statistic tests. Generation of the ROC curve of NSQIP-mortality values versus the endpoint (Figure 5): the occurrence of in-hospital death shows an area of 0.740 under the curve, but with no statistical significance (p = 0.074).

The Lee Revised Cardiac Risk Index (range 1-3) had a ROC curve (Figure 6) of the score versus the endpoint: in-hospital mortality shows a 0.587 area under the curve, with no statistical significance (p = 0.527).

Table 3. Risk scores in survivors and non-survivors and the results of the statistic tests (Mann Whitney, Kendall tau correlation, ROC curve)

	Survivors (24 patients)	Non-survivors (6 patients)	Mann Whitney test (p value)	Kendall tau_b correlation coefficient (p value)	Aria under ROC curve (p value)
EuroSCORE	3.42+/-1.53	5.67+/-1.96	0.015	0.406 (p=0.015)	0.816 (p=0.018)
Logistic EuroSCORE	2.68+/-1.41	5.38+/-2.17	0.011	0.402 (p=0.012)	0.830 (p=0.014)
EuroSCORE II	1.25+/-0.80	2.12+/-1.04	0.082	0.274(p=0.078)	0.736 (p=0.078)
NSQIP mortality	5.58+/-0.85	7.08+/-3.01	0.033	0.305 (p=0.065)	0.740 (p=0.074)
Lee Revised Cardiac Risk Index	1.79+/-0.65	2+/-0.63	0.525	0.130(p=0.466)	0.587 (p=0.517)

DISCUSSIONS

This study shows that only EuroSCORE and Logistic EuroSCORE predicted in-hospital mortality. Logistic EuroSCORE, with the area under the ROC curve of 0.830, with statistical significance, best predicted the occurrence of in-hospital death. The additive EuroSCORE ranks second with a AUC of 0.816, also with statistical significance. The association between the Logistic EuroSCORE and additive EuroSCORE and in-hospital mortality is of medium intensity.

EuroSCORE II had no significant statistical correlation to the occurrence of in-hospital deaths. Even if the area under the ROC curve had a fairly good value, it is not significant. The correlation Kendall tau statistical method sustains this idea. Thus, EuroSCORE II could not accurately predict the occurrence of in-hospital death. Albeit NSQIP-mortality had different distributions in the two patients groups (Mann Whitney test), it was not correlated with the occurrence of in-hospital deaths (Kendall's tau test). In addition, its ROC curve shows an area under the curve of 0.740 which is not statistically significant. Lee Revised Cardiac Risk Index showed the lowest AUC of the ROC curve of the values versus the endpoint, with no statistical significance. In addition, it was not correlated with the occurrence of this event.

Based on these results, we recommend to estimate the risk of in-hospital mortality in the case of radical nephrectomy with cavo-atrial thrombectomy using Logistic EuroSCORE and especially additive EuroSCORE, a risk score easy to perform without computational tools, despite the medical literature which favours EuroSCORE II. A value of the additive score of 5 must draw attention and taken in consideration, because its cut-off in predicting in-hospital mortality was 4.5 and the additive score is a natural number.

Additive EuroSCORE, has been proven to be a predictive tool for both mortality and morbidity after cardiac surgery since 1999[8,9]. Logistic EuroSCORE also starts from additive EuroSCORE, which is transformed according to the logistic regression equation. In 2003, Michel P et al. concluded that the logistic model is a better risk predictor, especially for high-risk patients, although it is more difficult to be performed in practice, requiring computational tools[10]. EuroSCORE II, first introduced in October 2011, seems to reduce risk overestimation by the first variant of the score[11]. The review conducted in 2012 by Siregar et al. analyses the performance of the additive EuroSCORE and Logistic EuroSCORE. Its conclusions were that, albeit the additive EuroSCORE overestimates mortality, however, in the case of high-risk patients their mortality is underestimated by this risk score[12]. Niv Ad et al. make a comparison in 2016 between the EuroSCORE additive and EuroSCORE II, demonstrating that the latter provides a better prediction of mortality than the first variant of the score, which overestimates this risk. This is why recently EuroSCORE II is proposed as a risk score in complex cardiac surgery[13]. Our study does not support this idea.

NSQIP is a decision-making support based on multi-institutional experience used to estimate the risk of most surgical interventions within the 30-day postoperative period[14]. Although urology has been among the surgical specialities introduced in this system ever since it was founded, some authors demonstrated the fact that there are some inadequacies in this field. In 2014, Frazier et al. drew attention to poor data regarding urology[15]. Some studies sustain the idea that NSQIP poorly predicted and discriminated among patients in urologic surgery, underestimating the occurrence of postoperative complications[16-18]. In 2018,

Blair et al. made a comparison between the predicted results and those observed 30 days after surgery in patients with partial nephrectomy for renal carcinoma, concluding that NSQIP underestimates postoperative complications[19] in line with our results.

It is known that NSQIP is based on 20 preoperative predictors, also taking into account the type of surgery[7]. The Surgical Operation Code was 50230. We selected a higher surgical risk in NSQIP because of the cardiac time which was not included in any surgical operation code. In our study, NSQIP did not predict the endpoint. Thus, we do not recommend NSQIP-mortality as a tool in risk assessment of in-hospital mortality in the surgery described, although it is recommended by the guidelines of cardiovascular assessment in non-cardiac surgery[20] and the guidelines of the *American Urology Association*. These recommend NSQIP as a good starting point in assessing preoperative risk in urology, but it is not recommended to be used alone, but together with other unspecified clinical information[21].

The Lee Revised Cardiac Risk Index makes a prediction of major cardiac events in adults undergoing non-cardiac surgery[6]. It takes into account elements of patient history, but also the magnitude of the surgery conducted. The score classifies the patient into a risk class, depending on which the risk of death, myocardial infarction, or cardiac arrest is assessed 30 days after surgery. However, in our study Lee Revised Cardiac Risk Index poorly predicted in-hospital death. Thus, we do not recommend to use this risk score in the surgery described.

In the international medical literature, radical nephrectomy with thrombectomy has been shown to be associated with major perioperative morbidity (up to 70%) and mortality (3-16%)[22]. The review of Gaudani et al. in 2016 finds surgical risk to be substantial in these cases, with in-hospital mortality up to 40%[23]. In our study there were recorded 6 (20%) in-hospital deaths. This is the reason why it is important to have a risk score to predict in-hospital mortality. Our study showed that additive EuroSCORE, and especially its logistic version predicts the endpoint, while EuroSCORE II, NSQIP and Lee Revised Cardiac Risk Index failed.

To our knowledge, none of this risk scores have been used before to predict mortality in the surgery described in this study, both in international and Romanian medical literature.

This study has his limits: it is a retrospective one, performed in a single centre, with a small number of patients due to the low incidence of the diagnostic. The results have to be tested in a large prospective multicentre study.

CONCLUSION

In conclusion, additive and logistic EuroSCORE were the only scores that predicted in-hospital mortality, while EuroSCORE II, NSQIP and Lee Revised Cardiac Risk Index failed to predict this endpoint in this study.

Conflict of interest: none declared.

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