External validation of the thoracic revised cardiac risk index in patients undergoing lung resection for non-small-cell lung cancer

Cardiac risk index in lung resections

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Abstract

Aim: The Thoracic Revised Cardiac Risk Index (ThRCRI) is a cardiac risk stratification tool specific to patients undergoing thoracic surgery. However, its usage is not accepted in routine practice yet. In this study, we aimed to validate the reliability of ThRCRI for predicting cardiac complications in an independent cohort undergoing lung resections for non-small-cell lung cancer (NSCLC). Material and Method: Data of 249 patients were analyzed according to ThRCRI scores and cardiovascular complication rate. ROC analyses were also carried out to evaluate the reliability of ThRCRI categories. Results: Higher ThRCRI risk scores were found to be associated with higher overall cardiac complication rates (p<0.0001) with a moderate-to-high reliability. Discussion: This study externally validated the discriminative ability of ThRCRI to differentiate high-risk patients for major cardiac complications following major lung resections. We advocate its use as a cardiac screening tool for patients who are candidates for lung resection.

Introduction

Use of cardiac risk scores is a critical component of the pre-operative risk assessment workup for patients who are surgical candidates. The Revised Cardiac Risk Index (RCRI) [1] is one of the most accepted and recommended tool to evaluate cardiac risk in patients undergoing noncardiac surgery [2, 3]. In order to consolidate the wide surgical population, Brunelli and colleagues recalibrated the RCRI and suggested The Thoracic Revised Cardiac Risk Index [4] as a tool for cardiac risk stratification specific to patients undergoing thoracic surgery [1]. Recently, usage of Thoracic Revised Cardiac Risk Index (ThRCRI) as an initial step in the functional workup of the lung resection candidate was also recommended by the American College of Chest Physicians evidence-based clinical practice guideline [5]. The aim of our study is an external validation of the ThRCRI in an independent cohort undergoing lung resections for non-small-cell lung cancer (NSCLC) focusing on its reliability in predicting all cardiac complications.

Material and Method

This study was approved by the ethical committee of Hacettepe University Medical Faculty. Data of 265 patients who underwent resection for primary NSCLC at our institution (Department of Thoracic Surgery, Hacettepe University Medical Faculty) between January 2002 and December 2012 were retrospectively analyzed. We excluded 16 patients without complete data leaving 249 patients for validation. Patients undergoing open lung resection (pneumonectomy, bilobectomy, lobectomy, and segmentectomy) for NSCLC were included.

Patients' data were collected including the following variables: sex, age, forced expiratory volume in 1 second (FEV_1), type of resection, pathologic tumor stage, history of ischemic heart disease, history of cerebrovascular disease, diabetes mellitus, hypertension, smoking history, chronic obstructive pulmonary disease (COPD), preoperative serum creatinine level and postoperative cardiovascular complications (myocardial infarction (MI), pulmonary edema, atrial and ventricular arrhythmias, cardiac failure, cardiac arrest, and cardiac-related death). The characteristics of the patients are shown in Table 1.

Postoperative major cardiac complications included pulmonary edema, MI, ventricular fibrillation (VF), complete heart block and cardiac-related death occurring within 30 days of operation. Other cardiac complications were supraventricular arrhythmias, atrial fibrillation (6) and cardiac failure. The ThRCRI was calculated as previously published (1). The score comprises 4 weighted preoperative factors: history of ischaemic heart disease (risk score = 1.5), history of cerebrovascular disease (risk score = 1.5), preoperative serum creatinine level greater than 2 mg/dL (risk score = 1) and pneumonectomy (risk score = 1.5). The patients are then stratified into 4 risk classes according to the calculated risk scores: A (risk score of 0), B (risk score of 1-1.5), C (risk score of 2-2.5), D (risk score > 2.5).

Descriptive statistics were presented as mean ± Standard Deviation and median (minimum-maximum) for quantitative data and frequency (percentages) for qualitative data. Chi-Square test (Yates' Chi-Square test or Fisher Exact tests) was used to compare difference between groups for categorical variables. The Kruskal-Wallis test was performed to compare the differ-

ences among groups. The Kruskal-Wallis test of multiple comparisons was employed to determine significant differences between groups. ROC analyses were carried out to evaluate the performance of ThRCRI category according to all and major cardiac complications. The ROC curve was plotted. The area under the ROC curve was calculated. A $p<0.05$ was accepted as statistically significant. All statistical analyses were performed by using IBM SPSS Statistics 23.0 software.

Results

Cardiac and major cardiac complications occurred in 12.4% (31) and 4.0% (10) of all patients, respectively. In general, none of the variables were significantly associated with cardiac complications in univariate analysis. Table 2 demonstrates the analyzed variables and the incidence of cardiac complications. Overall, 58.6 % of patients were risk class A, 36.5% were risk class B, 2.0% were risk class C, and 2.8% were risk class D. The incidence of all cardiac complications within risk classes A, B, C, and D were 8.9%, 13.2%, 100.0%, and 14.3%, respectively ($p<0.0001$). The incidence of major cardiac complications within the same risk classes were 1.4%, 4.4%, 80.0% and 0%, respectively ($p<0.0001$) (Table 3). To sum up, higher ThRCRI risk scores were associated with higher cardiac complication rates.

Table 1. Patient Characteristics (n=265).

Variable	Mean (SD) (Minimum-maximum)
Preoperative	
Age (years)	60.5 (9.1) (33-81)
Male (%)	198 (74.7)
Diabetes (%)	24 (9.4)
Hypertension (%)	58 (21.8)
COPD (%)	18 (7.2)
Smoking history	192 (72.4)
FEV1 (l)	2.42 (0.5) (1.0-4.1)
History of ischemic heart disease (%)	40 (15.0)
History of cerebrovascular disease (%)	4 (1.5)
Serum creatinine level > 2 (mg/dl)	14 (5.2)
Operative	
Pneumonectomy (%)	68 (25.7)
Lobectomy (%)	191 (72.0)
Segmentectomy (%)	6 (2.3)
Postoperative	
Pathologic stage (%)	
IA	94 (35.5)
IB	55 (20.8)
IIA	55 (20.8)
IIB	25 (9.4)
IIIA	36 (13.5)
Myocardial infarction (%)	1 (0.4)
Pulmonary edema(%)	1 (0.4)
Ventricular fibrillation (%)	2 (0.8)
Cardiac related death (%)	6 (2.2)
Heart block (%)	0 (0)
Atrial fibrillation (%)	21 (7.9)
Cardiac failure (%)	2 (0.8)

COPD: Chronic obstructive pulmonary disease; FEV1: forced expiratory volume in 1 second.

Table 2. Patient Characteristics and Cardiovascular Complications

Patient Characteristic	Cardiovascular Complication		p
	Yes n (%)	No n (%)	
Age (mean ± SD)	63.55±9.1	60.43±9.1	0.07
Sex			0.406
Female	5(7.4)	62(92.6)	
Male	26(13.1)	172(86.9)	
FEV₁ (mean ± SD)	2.33±0.6	2.39±0.6	0.612
Pathologic Stage			0.425
IA	8(8.5)	86(91.5)	
IB	7(12.7)	48(87.3)	
IIA	6(10.9)	49(89.1)	
IIB	4(16.0)	21(84.0)	
IIIA	6(16.7)	30(83.3)	
History of ischemic heart disease (%)			0.470
Yes	5(12.5)	35(87.5)	
No	26(11.5)	199(88.5)	
History of cerebrovascular disease (%)			0.876
Yes	2(50)	2(50)	
No	29(13.0)	232(87.0)	

FEV_1: forced expiratory volume in 1 second.

Table 3. Distribution of Patients in Each Risk Class of THRCRI and Rate of Cardiac Complications

ThRCRI Score	Risk Class	n	Cardiac Complications	Major Cardiac Complications	p
0	A	154	12 (7.8%)	2 (1.2%)	
1-1.5	B	91	11 (12.1%)	3 (3.2%)	<0.0001
2-2.5	C	11	5 (45.4%)	4 (36.3%)	
>2.5	D	9	3 (34.7%)	1 (11.1%)	

ThRCRI: Thoracic Revised Cardiac Risk Index

In addition, ROC analysis demonstrated an area under the curve of 0.623 (95% confidence interval 0.51–0.73; P=0.027) and 0.640 (95% confidence interval 0.52–0.75; P=0.011) for identifying relative risk of all and major cardiovascular complications, respectively (Figure 1).
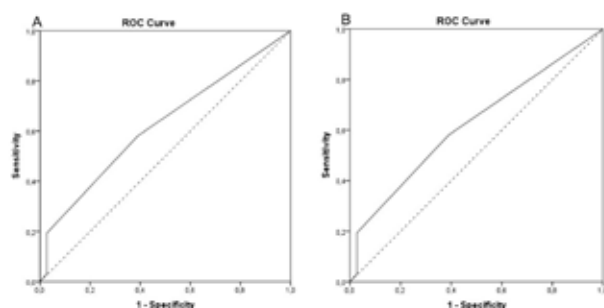

Figure 1. Receiver operating characteristic curve of ThRCRI for all cardiovascular (A) and major cardiovascular (B) complications.

Discussion

Cardiovascular complications represent the most lethal complication type compared to the other complication types such as pulmonary, gastrointestinal and other systemic complications [7]. In addition, such complications are a significant cause of morbidity, hospital readmission, decreased long-term function, and survival [8]. Thus, cardiac risk assessment is considered valuable both for physicians and patients in terms of appropriate patient selection, predicting postoperative risks, obtaining informed consent and planning postoperative patient management.

Several risk assessment tools have been developed for this purpose, so far [9-11]. The first cardiac risk index was introduced by Goldman et al. in 1977. Lee et al. simplified Goldman's risk index and developed the revised Cardiac Risk Index (RCRI) which includes six independent predictors (high-risk surgery, ischemic heart disease, congestive heart failure, cerebral vascular accident, insulin therapy and creatinine >2 mg/dL) to predict postoperative cardiac complications [9, 12]. However, this index was developed in a cohort contained solely 12% of patients who underwent thoracic surgical procedures. Besides, RCRI demonstrated a moderate predictive ability for cardiovascular complications with a c-index of 0.62 [12]. Therefore, Brunelli et al. recalibrated the RCRI in a specific population who underwent thoracic surgical procedures and introduced the Thoracic Cardiac Risk Index (ThRCRI). They pointed out that only four out of six independent factors of the initial RCRI were associated with major cardiac complications and limited the scoring system with four factors. They also accomplished a better c-index of 0.72 for prediction of cardiovascular complications [1]. In this study, the area under the ROC curve for the ThRCRI score was 0.623 and 0.640 (all vs. major cardiovascular complications), which is lower than the previous studies in the literature.

ThRCRI was validated in a handful of studies with heterogeneous cohorts including reoperations and operations for benign diseases, in high-quality centers for thoracic surgery and procedures performed by highly experienced surgeons [4, 13, 14]. In all of these studies, the authors highlighted the importance of external validation of this index and recommended validation with a homogenous, specifically nationally representative, the population of patients in a wide variety of hospitals. Therefore, the objective of our study was to externally test the ThRCRI in a somewhat homogenous cohort of patients who underwent non-complex and open major lung resection for NSCLC. We clearly validate the discriminative role of ThRCRI for predicting major postoperative cardiac complications following major lung resections in our institution.

Brunelli et al. described the ThRCRI in their original study as a score to stratify the risk of major cardiac events and proposed evaluation of its application for predicting additional minor cardiac complications such as atrial fibrillation with further studies [4]. Based on their recommendation, we evaluated the role of ThRCRI for predicting both major and minor postoperative cardiac complications (supraventricular arrhythmias, atrial fibrillation, and cardiac failure) in this study and demonstrated its discriminative ability also for risk of all cardiac complications following lung resections.

In our series, major cardiovascular complications occurred in 4% of patients, which is in line with the recent ThRCRI studies (1.7% to 4.3%). Although in our series, the distribution of patients among risk classes is compatible with the literature, all cardiac and major cardiac complication rates in class C (100% and 80%) is higher than the reported studies [1, 4, 13, 15].

There is a conflicting distribution of cardiac complication rates among risk classes C and D (All cardiac and major cardiac complication rates are 100% and 80%, 14.3% and 0%, respectively). This imbalance is likely due to the small number of patients and events in class D, as comparatively small numbers of events may profoundly affect resulting incidences. The unequal distribution of patients and events in these two high-risk classes was also described in recent series. The authors suggest collapsing risk classes C and D into a single class which may simplify the scoring system and decrease the effect of unequal distribution [4, 13]. We also agree with their concept of combining high-risk classes very valuable for the upcoming ThRCRI studies.

Although this study was performed in a homogenous cohort of a single institution undergoing major pulmonary resections, the sample size was relatively small compared to the multicentre studies. In addition, this is a retrospective study which may entail inherent problems of selection bias. Prospective studies are needed to verify our results.

In sum, stratifying patients into cardiac risk classes before lung resection is considerably important. Firstly, estimating the potential risks helps both physicians and patients in accurate decision making. Secondly, low-risk class patients (A and B) may be fast-tracked postoperatively and discharged earlier. Finally, high-risk class patients (C and D) may be considered for additional preoperative evaluation and these patients may benefit from rigorous postoperative management strategies.

Our study validated that ThRCRI can differentiate high-risk patients for major cardiac complications following major lung resections. In addition, we demonstrated its moderate to high discriminative ability also for all cardiac complications and support its use as a cardiac screening tool for patients who are candidates for lung resection.

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