ASSESSMENT OF THE RISK OF CARDIOVASCULAR COMPLICATIONS IN CANCER SURGERY

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ABSTRACT

Cardiac complications of non-cardiac surgeries are an actual and unresolved interdisciplinary problem of clinical medicine today. The incidence of cardiovascular events after non-cardiac surgery is higher than in the general population and does not tend to decrease. The risk of cardiac complications in cancer surgery is the highest. Evidence-based approaches to risk assessment and prevention of cardiovascular events in surgical patients with malignant neoplasms have not been developed. In current clinical guidelines on the prevention, prognosis and treatment of cardiac complications of non-cardiac surgeries, the aspects of this problem in surgical oncology are not considered separately.

The aim of this review *was to analyze the current sources of literature on the prediction of cardiovascular complications in surgical treatment of cancer patients. The distinctive features of cancer surgery and additional factors causing an increased risk of adverse cardiac outcomes in patients with malignant neoplasms are described. The article presents the results of large cohort studies on the search for reliable predictors of cardiac complications in non-cardiac surgery and on the development of stratification scales and algorithms for preoperative risk assessment. Particular attention is paid to the possibilities and prospects of using these predictive tools in the surgical treatment of cancer. The surgical risks of interventions for malignant neoplasms are described, as well as methods for calculating cardiac risk and functional status assessment that have been validated in oncological patients cohorts. The data of recent studies on the role of serum biomarkers of myocardial damage and increased cardiovascular risk (cardiac troponins and brain natriuretic peptide) in predicting postoperative cardiac events in non-cardiac surgery are presented. Further prospects for the inclusion of biomarkers in risk stratification systems in patients with malignant neoplasms are discussed.*

Key words: *neoplasms, surgical oncology, myocardial infarction, postoperative complications, risk assessment, natriuretic peptides, troponin*

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ОЦЕНКА РИСКА СЕРДЕЧНО-СОСУДИСТЫХ ОСЛОЖНЕНИЙ В ОНКОХИРУРГИИ

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РЕЗЮМЕ

Кардиальные осложнения внесердечных операций – актуальная и нерешённая на сегодняшний день междисциплинарная проблема клинической медицины. Частота развития сердечно-сосудистых событий после внесердечных хирургических вмешательств выше, чем в общей популяции, и не имеет тенденции к снижению. К наиболее высокому относится риск кардиальных осложнений в онкохирургии. Научно обоснованные подходы к оценке риска и профилактике кардиоваскулярных событий у хирургических пациентов со злокачественными новообразованиями не разработаны. В актуальных клинических руководствах по профилактике, прогнозированию и лечению кардиальных осложнений внесердечных операций аспекты данной проблемы в хирургической онкологии отдельно не рассматриваются.

Целью данного обзора *явился анализ современной литературы по теме прогнозирования сердечно-сосудистых осложнений хирургического лечения онкологических больных. Описаны отличительные особенности онкохирургических вмешательств и дополнительные факторы, обусловливающие повышение риска неблагоприятных кардиальных исходов у больных злокачественными новообразованиями. В работе приведены результаты крупных когортных исследований по поиску надёжных предикторов кардиальных осложнений во внесердечной хирургии, разработке шкал стратификации и алгоритмов предоперационной оценки риска. Особое внимание уделено возможностям и перспективам использования данных инструментов прогнозирования при хирургическом лечении рака. Описаны хирургические риски вмешательств по поводу злокачественных новообразований, валидированные в когортах онкологических пациентов методы расчёта кардиального риска и оценки функционального статуса. Представлены данные работ последних лет о роли сывороточных биомаркеров повреждения миокарда и повышенного сердечно-сосудистого риска (прежде всего сердечных тропонинов и мозгового натрийуретического пептида) в прогнозировании послеоперационных кардиальных событий во внесердечной хирургии. Обсуждаются дальнейшие перспективы включения биомаркеров в системы стратификации риска у пациентов со злокачественными новообразованиями.*

Ключевые слова: *злокачественные новообразования, онкохирургия, инфаркт миокарда, послеоперационные осложнения, оценка риска, натрийуретические пептиды, тропонин*

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The incidence of cardiovascular complications (CVD) of non-cardiac surgery reaches 5 % [1, 2]. Of the 300 million major non-cardiac surgeries performed annually worldwide, more than one million are complicated by postoperative myocardial infarction (MI), and 750,000 are fatal from cardiac causes within one month of the intervention [3, 4].

Malignant neoplasms significantly increase the risk of perioperative CVD. For example, in surgical treatment of lung cancer, the incidence of all events in high-risk groups reaches 11.9 % [5], and the incidence of MI reaches 9.8 % [6]. In a large cohort of 280,000 cancer patients, any arterial thrombosis developed in lung, gastric, and pancreatic cancer patients – 8.3 %, 6.5 %, and 5.9 % of cases, respectively – over 6 months of follow-up. The relative risk of events was 2.2 times higher than in patients without malignant neoplasms [7]. This is due to a variety of factors: large surgical volume, low functional status of patients due to predominantly elderly age, "frailty", cancer cachexia, sarcopenia, nutritional status disorders and anemia; comorbidity with cardiovascular diseases and chronic obstructive pulmonary disease (COPD); combination with other high cardiovascular risk factors (arterial hypertension, smoking, diabetes mellitus, dyslipidemia); increased thrombogenic risk and systemic pro-inflammatory response characteristic for malignant neoplasms; exposure to neoadjuvant radiation and drug anticancer therapy [8–11]. In advanced cancer stages, the risks of cardiovascular events increase significantly, from 2.3 % for stage 0 to 7.7 % for stage IV [7]. In this regard, disseminated cancer is one of the criteria for the ACS NSQIP (American College of Surgeons' National Surgical Quality Improvement Program) perioperative risk assessment [12].

Implementation of clinical guidelines and algorithms, risk stratification systems in clinical practice allows to improve the quality of medical care, including in non-cardiac surgery [13, 14]. Current guidelines on the prevention, prognosis, and treatment of CVD of non-cardiac surgery lack recommendations with class and level of evidence for cardiovascular risk assessment in oncosurgery [15–17]. Despite the growing interest in this topic, the scale of the problem of cardiac complications and their prognosis is still underestimated by clinicians.

THE AIM OF THIS REVIEW

To analyze the data of current literature on prediction of cardiovascular complications during surgical treatment of cancer patients.

The review was performed using the Russian Science Citation Index, PubMed, and ClinicalTrials databases for the period from 2007 to 2022. The search was performed using the following keywords: neoplasms; surgical oncology; myocardial infarction; heart diseases; postoperative complications; risk assessment; biomarkers; natriuretic peptides; troponin.

SURGICAL RISK ASSESSMENT

The risk magnitude of cardiovascular complications in non-cardiac surgery is determined by three interrelated groups of factors: 1) factors related to the type and volume of surgical intervention (surgical risk); 2) predictors of cardiovascular risk (concomitant heart disease, cardiovascular risk factors, biomarkers); 3) functional status of the patient (Fig. 1).

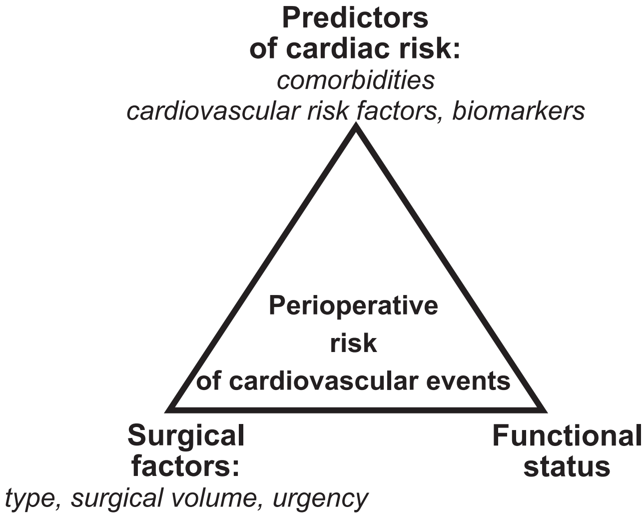

FIG. 1.

Risk factors for perioperative cardiovascular complications of non-cardiac surgery

This is the stepwise approach to perioperative cardiovascular risk assessment proposed in the current clinical guidelines. According to the 2014 ACC/AHA (American College of Cardiology/American Heart Association) Guideline on Perioperative Cardiovascular Evaluation and Management of Patients Undergoing Non-cardiac Surgery, the diagnostic and therapeutic management of a patient is determined by the following sequentially assessed factors: urgency of surgery; presence of signs of acute coronary syndrome; estimated risk of serious adverse cardiovascular events calculated using risk scales/calculators; and functional capacity of the body. The highest risk of CVD is predicted when the calculated risk of serious adverse cardiovascular events and low functional status are elevated, which requires an in-depth cardiologic examination and/or a change in surgical approach [16].

The above-mentioned algorithm is designed to assess the cardiac risk of any non-cardiac surgery. Due to the lack of specialized algorithms validated on cohorts of cancer patients, this approach has been applied in oncosurgery.

When assessing surgical factors in patients with malignant neoplasms, it should be borne in mind that interventions for the most common tumors are classified as high surgical risk due to their extensiveness and are associated with a maximum probability of 30-day cardiovascular mortality or myocardial infarction (MI) (> 5 %) regardless of cardiovascular factors and functional status of the patient. These include open esophageal and gastric surgeries, pneumonectomies, pancreatoduodenal resections, liver resections, cystectomies, and adrenalectomies [17]. In the 2018 GRICS II (The Goal-Directed Resuscitation in Cancer Surgery) randomized clinical trial to optimize postoperative management of cancer patients, additional criteria for high surgical risk were duration of intervention > 90 min and patient's postoperative stay in the intensive care unit [18]. Medium surgical risk (1–5 %) is associated with interventions on the head and neck, pelvic organs, and minor thoracic surgeries. In such interventions, the outcome of surgery depends largely on the circulatory system and comorbid conditions. Low risk (< 1 %) is associated with surgeries, including oncosurgeries, on skin and subcutaneous tissue, breast, thyroid, minor gynecologic, and urologic (transurethral resection of the prostate).

Surgical risk will increase when the scope of surgery is expanded, such as total resection of the affected organ, anastomosis, and lymph node dissection [19]. In patients with lung cancer, right-sided pneumonectomy had a threefold higher risk of CVD than left-sided pneumonectomy (odds ratio (OR) of developing MI or acute myocardial ischemia was 3.2 with 95 % confidence interval (95% CI): 1.6–6.3) [20]. Conversely, the use of minimally invasive approaches in oncosurgery, such as video-assisted thoracoscopic surgery or robot-assisted surgery, can reduce the incidence of postoperative complications without worsening oncologic outcomes [21, 22].

Surgical risk factors, such as the specific type of surgery and urgency of intervention, are included in modern integral perioperative risk assessment systems, such as the ACS NSQIP Calculator [12]. The presence of high surgical risk procedure is also considered in the calculation of the Revised Cardiac Risk Index (RCRI) [23].

CARDIOVASCULAR RISK ASSESSMENT

Specific scales for assessing the risk of perioperative cardiovascular complications in oncosurgery have not been developed. At the same time, the prognostic significance of previously known risk stratification systems was studied in cohorts of cancer patients. In general non-cardiac surgery, the most widely used index today is the RCRI or "Lee index", which is a revised and simplified version of the first CRI (Cardiac Risk Index) or L. Goldman index created for this purpose. The RCRI index was developed from a single-center cohort study (4,315 patients, 92 events) and determines the risk of MI, pulmonary edema, ventricular fibrillation, cardiac arrest or complete atrioventricular block, and mortality within 30 days after non-cardiac interventions. It includes 6 predictors: high-risk surgery (for abdominal aortic aneurysm, on peripheral vessels, thoracotomy, major abdominal surgery); congestive heart failure; coronary heart disease (CHD); pre-existing acute cerebrovascular accident (CVA); insulin-dependent diabetes mellitus; chronic kidney disease (serum creatinine > 2.0 mg/dL (177 µmol/L) or glomerular filtration rate < 50 ml/min/1.73 m^2), – each of which is assigned one point. With a total score of 0 points, the risk corresponds to 0.4 %, 1 point to 0.9 %, 2 points to 7 %, and 3 points or more to 11 % [23].

However, the prognostic accuracy of the RCRI scale in oncosurgery has proven to be insufficient. In a study by R. Wotton et al. (2013), the RCRI index was calculated in 703 patients (including 640 patients with lung cancer) who underwent lung resection. Cardiac complications in the form of MI, pulmonary edema, cardiac arrest and atrial fibrillation within 30 days after surgery were detected in 34 (4.8 %) patients. According to the results of ROC analysis, the ability of RCRI to correctly predict postoperative cardiac complications was low (area under ROC curve (AUC, area under curve) – 0.59) [24]. In a retrospective case-control study including 163 patients with non-small cell lung cancer (NSCLC) (of whom 33 had postoperative MI, 130 without cardiac complications), RCRI index was not associated with the development of postoperative MI (OR = 1.0 with 95% CI: 0.5–2.2) [25]. In a prospective observational study of 82 patients undergoing pneumonectomy for lung cancer, the associations of RCRI with 6-month overall postoperative mortality were examined. According to univariate regression analysis, the relative risk of mortality increased 2.8-fold with a 95% CI [1.2–6.4] for each point increase in RCRI. However, in multivariate regression, this relationship became statistically insignificant [26].

After 15 years of using the RCRI index in clinical practice, in 2014, European and American experts recommended a new risk stratification system developed by P.K. Gupta et al. (2011) [27]. The new scoring system, NSQIP MICA (The National Surgical Quality Improvement Program Myocardial Infarction & Cardiac Arrest), was created as part of the U.S. National Surgical Quality Improvement Program based on data analysis of more than 450,000 surgical patients from 250 centers and 2,772 events. Five major risk predictors were identified: type of surgery; functional status of the patient; blood creatinine level > 130 µmol/L; ASA (American Society of Anesthesiologists) class; and age. The risk of a predicted event – cardiac arrest or acute MI within 30 days after surgery – is expressed as %. If the index value is < 1 %, the risk is considered low; if the value is ≥ 1 %, the risk is considered elevated. Despite its widespread use in clinical practice, the NSQIP MICA Calculator has not been comprehensively tested outside of the NSQIP registry. No external validation was performed on cohorts of cancer patients.

The idea of creating a universal calculator to calculate the risk of any complications of non-cardiac surgery, including cardiac complications, was realized in 2013. A set of 21 predictors including all major components of perioperative risk was determined: characteristics of surgical intervention, cardiovascular and other clinical factors, and functional status of the patient. Thirteen adverse outcomes were predicted within 30 days of the intervention, including death from any cause and cardiac complications (cardiac arrest or MI) with a high degree of concordance between predicted and occurred events (c-statistic for cardiac outcomes 0.895) [12].

It should be noted that the ACS NSQIP Calculator includes disseminated cancer as one of the predictors for the first time, suggesting that the index can be used in cancer surgery. However, its external validation in several areas of oncosurgery has demonstrated mixed results. In particular, for gynecologic oncologic laparotomy, the scale predicted cardiac complications, deaths, and renal failure well, but failed to accurately predict most other complications [28]. After surgery for gastrointestinal neuroendocrine tumors (GI NETs), the calculator estimated the risks of cardiac complications, pneumonia, and urinary tract infection with acceptable accuracy (AUC > 0.70), but poorly predicted other complications, such as surgical site infection, reintervention, and hospitalization [29]. The ACS NSQIP index, in contrast to RCRI, was an independent predictor of postoperative MI in lung cancer patients undergoing thoracotomy. In this case-control study, 33 patients with MI and 130 patients without cardiac complications were included in the control group. Based on the results of univariate regression analysis, the OR for the development of MI for cardiac risk by ACS NSQIP was 2.2 [1.6–3.2] and for total risk by ACS NSQIP was 1.1 [1.06–1.2]. When the ACS NSQIP cardiac risk was included in multivariate regression, the predictive value of the odds ratio score increased to 3.86 [1.36–10.9] [25].

The Oncology NSQIP National Cancer Center Collaborative attempted to increase the predictive accuracy of the NSQIP ACS by adding oncology-related variables (prior surgery, XRT, or chemotherapy in the same area later and earlier than 90 from the time of index procedure). The sample size was 8,425, 3,166 (37.6 %) of whom underwent colon resection, 2,269 (26.9 %) underwent pancreatectomy, and 1,529 (18.2 %) underwent hepatectomy. The probability of developing a death or serious complication was calculated; cardiovascular outcomes were not counted separately. Univariate analysis showed a 34 % increase in the unadjusted odds ratio for the development of the endpoint in patients with more than 90 days of prior chemotherapy and a 44 % increase in patients with prior X-ray therapy. However, the added variables were not included in the predictive models in the multivariate regression analysis [30].

Attempts are being made to create specialized risk scales for specific tumor localizations, primarily lung cancer. The EuroLung1 and EuroLung2 scales and their simplified versions were developed to assess the risk of car-

TABLE 1

THE RISK ASSESSMENT OF CARDIAC COMPLICATIONS IN THORACIC SURGERY ACCORDING TO THE THRCRI SCALE

Criteria	Points
Prior CHD	1.5
Prior cerebrovascular disease	1.5
Serum creatinine > 2 mg/dL (177 μmol/L)	1
Pneumenectomy	1.5
Class A: 0 points. Risk of cardiac complications – 1.5 % (low)	
Class B: 1-1.5 points. Risk of cardiac complications – 5.8 % (moderate)	
Class C: 2-2.5 points. Risk of cardiac complications – 19 % (high)	
Class D: > 2.5 points. Risk of cardiac complications – 23 % (very high)	

diopulmonary complications (EuroLung1) and 30-day mortality (EuroLung2) after lung resections by analyzing the outcomes of 47,960 operations from the European Society of Thoracic Surgeons (ESTS) Database. They include spirometry, type and volume of surgical intervention, in addition to regular general cardiovascular risk factors (age, male gender, CHD and cerebrovascular disease, chronic kidney disease). Patients are stratified into 6 risk categories based on expected mortality or incidence of cardiopulmonary complications [31, 32]. However, external validation of the original and modified EuroLung2 scale on a sample of 6,600 patients did not confirm its ability to correctly predict 30- and 90-day mortality after lung resection [33]. No external validation of the EuroLung1 scale was performed.

The Thoracic Revised Cardiac Risk Index (ThRCRI) scale was developed based on the RCRI scale in a cohort of 1,629 patients with non-small cell lung cancer, 1,426 of whom underwent lobectomy and 270 of whom underwent pneumonectomy. This model has a reduced number of predictors compared to the RCRI scale. The scale ranks the risk of cardiac complications in thoracic patients from 1.5 % (at 0 points) to 23 % (at > 2.5 points) (Table 1) [34].

The ThRCRI is further validated on two external samples. The first consisted of 2,621 patients, 2,431 of whom underwent lobectomy and 190 underwent pneumonectomy. The incidence of major cardiac events was 0.9 %, 4.2 %, 8 %, and 18 % ($p < 0.0001$) in risk classes A, B, C, and D, respectively [35]. The second sample included 1,255 patients, 85 % of whom underwent lobectomy and 15 % of whom underwent pneumonectomy. The observed event rate was 2.4 % ($n = 30$). The calculated risk in both the test sample as a whole and in each of the risk categories was close to the observed [36]. Later, the ability of the ThRCRI scale to correctly predict not only the risk of perioperative cardiac complications, but also the long-term survival of patients, as well as mortality from cardiac causes [37] was proved. An algorithm for preoperative examination of patients with non-small cell lung cancer using this index has been developed [38]. According to the algorithm, it is necessary to calculate ThRCRI in the first step. If ThRCRI < 2, no further cardiovascular examination is required. A ThRCRI value ≥ 2 indicates increased risk and suggests examination by a cardiologist with additional non-invasive diagnostic tests according to the 2014 ACC/AHA general algorithm described above. [16]. All lung cancer patients scheduled for lung resection, irrespective of ThRCRI value, should have tests to assess external respiratory function and functional pulmonary reserve. Some attempts to validate the ThRCRI were unsuccessful: in a sample of 703 patients undergoing lung resection, the ThRCRI, as well as the RCRI, showed poor predictive efficacy as assessed by ROC analysis (AUC = 0.57) [24]. However, it is the only one of the cardiac risk stratification systems included in the current guidelines for perioperative risk assessment in lung cancer patients [39].

THE ROLE OF BIOMARKERS OF MYOCARDIAL INJURY IN RISK ASSESSMENT OF PERIOPERATIVE CARDIAC COMPLICATIONS

The biomarker concept of risk assessment is a promising and rapidly developing field in cardiology. In recent years, robust evidence has been obtained for the predictive value of preoperative levels of brain natriuretic peptide (BNP) or the N-terminal fragment of its precursor (NT-proBNP) and postoperative cardiac troponin levels in assessing the risk of overall mortality and cardiac complications in a general population of patients undergoing non-cardiac surgery [40, 41]. In a cohort of 4,632 cancer patients at long-term (up to 22 years) prospective follow-up, the biomarkers of myocardial injury troponin T and NT-proBNP were statistically significantly directly correlated with the incidence of cardiac events and mortality. Elevation of NT-proBNP > 900 pg/mL increased the relative risk (RR) of mortality by 2.95-fold (95% CI: 2.28–3.82; $p < 0.001$), and elevation of troponin T > 0.05 μg/L by 2.08-fold (95% CI: 1.83–2.34; $p < 0.001$) [42]. In the work of I.M. Shestopalova et al. (2008) an independent prognostic value of preoperative NT-proBNP in the development of fatal outcomes in cancer patients with different volumes of thoracoabdominal surgeries was revealed [43]. Among 82 patients with non-small cell lung cancer who underwent pneumonectomy, preoperative NT-proBNP level was an independent predictor of 6-month overall mortality after pneumonectomy (OR = 1.2 with 95% CI: 1.08–1.22 for every 100 pg/mL increase). Troponin I increment above the 99th percentile 24–48 hours after surgery was also associated with endpoint development in univariate regression (OR = 3.68 with 95% CI: 1.99–13.58), but lost its predictive value in multivariate regression analysis [26].

According to the 2017 Canadian Cardiovascular Society Guidelines on Perioperative Cardiac Risk Assessment and Management for Patients Who Undergo Noncardiac Surgery, it is recommended that BNP or NT-proBNP be measured before surgery in patients aged ≥ 65 or ≥ 45 years with cardiovascular disease or RCRI ≥ 1. When BNP ≥ 92 mg/L or NT-proBNP ≥ 300 mg/L, troponin levels should be measured daily for 48–72 hours postoperatively to screen for asymptomatic myocardial injury (strong recommendation, medium-quality evidence) [17]. The 2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery require that individuals with cardiovascular disease or its risk factors (including age of 65 years and older) or symptoms should have high-sensitivity troponin T or I measured in the blood before high- and intermediate-risk non-cardiac surgery and 24 and 48 hours afterward (I B). In addition, assessment of BNP or NT-proBNP levels before surgery is envisioned (Iia B) [15].

Thus, the determination of biomarkers of myocardial injury may be an independent criterion for cardiovascular risk assessment of non-cardiac surgery. According to a Cochrane meta-analysis of 51 studies, the inclusion of NT-proBNP, troponin and their combination in the RCRI scale as an additional predictor improved the prediction accuracy of cardiac complications of non-cardiac surgery (c-statistic increase of 0.08, 0.14 and 0.12, respectively) [44]. It remains unclear whether the inclusion of biomarkers in risk stratification systems for patients with malignant neoplasms improves prediction accuracy, which determines the need for specifically designed studies on this issue.

FUNCTIONAL STATUS ASSESSMENT

General approaches to assessing functional status in patients with malignant neoplasms do not differ from those in surgical patients without neoplasms. For this purpose, the Duke Activity Status Index (DASI) questionnaire is most commonly used in oncosurgery [19, 45]. After assessment of functional status expressed in metabolic equivalents (MET), further patient management is determined according to the ACC/AHA 2014 general algorithm. [16].

Cardiopulmonary exercise testing (CPET) provides the most accurate assessment of functional status. This technique allows to determine not only tolerance to physical exercise, but also a number of important additional parameters: peak oxygen consumption (VO_2max), anaerobic threshold, ventilatory equivalent for carbon dioxide (VE/VCO_2). A number of small-sample studies have confirmed the significance of these CPET parameters in predicting postoperative mortality and cardiac events in patients with gastroesophageal cancer [46], colorectal cancer [47], and liver and pancreatic cancer [48]. At the same time, a large multicenter cohort study evaluating the predictive value of various functional indices and biomarkers (n = 1,404, including 43 % of patients with malignant neoplasms) showed that neither VO_2max nor anaerobic threshold was associated with the development of postoperative MI, myocardial damage, or death [49]. Similar results were obtained in a large prospective study of 1,725 patients, including cancer patients, undergoing major thoracic and abdominal surgery [50]. An important factor limiting the use of CPET in real clinical practice is the high cost of the method and its unavailability in most Russian surgical and oncology clinics. The 2022 European Society of Cardiology (ESC) and 2017 Canadian Cardiovascular Society Guidelines on Cardiovascular Assessment and Management of Patients Undergoing Non-Cardiac Surgery do not include CPET for risk stratification of postoperative complications and mortality. According to the 2014 ACC/AHA guidelines, performing CPET may be considered (IIb B) in patients undergoing high surgical risk procedure in whom functional status is unknown [16].

Increased use of CPET may be considered in patients with lung cancer when assessing the risk of cardiac events and mortality after lung resections or pneumonectomy. This is due to the fact that CPET indices reflect not only coronary but also pulmonary functional reserve and are associated with the prognosis of both cardiac and pulmonary postoperative complications [51]. There is now substantial evidence for the significance of VO_2max and VE/VCO_2 in the prognosis of cardiopulmonary complications of lung surgery. The prognostic value of CPET increases as pulmonary function deteriorates postoperatively [52, 53]. Therefore, the test appropriateness is established based on an assessment of the prognosis of pulmonary function after lung resection. The current American College of Chest Physicians guidelines "Physiologic evaluation of the patient with lung cancer being considered for resectional surgery" (2013) [39] recommend CPET with VO_2max determination for patients with lung cancer and predicted postoperative forced expiratory volume in 1 s (ppFEV1) < 30 % or predicted postoperative diffusing capacity of the lungs for carbon monoxide (DLCO) < 30 % (1 B).

Per the algorithm of M. Salati (2016) concerning preoperative examination of patients with non-small cell lung cancer, the indication for CPET is ppFEV1 < 60 % or predicted postoperative diffusing capacity of the lungs for carbon monoxide < 60 %. Next, VO_2max and VE/VCO_2 are estimated based on the CPET results. When VO_2max < 10 ml/kg/min or VE/VCO_2 > 35, the risk of cardiopulmonary complications after surgery and death is considered high, therefore minimally invasive surgery should be used or other therapies should be considered. If VO_2max is between 10-20 ml/kg/min, risk is assessed by VE/VCO_2. The risk is considered low when ppFEV1 > 60 % or VO_2max > 20 ml/kg/min [38].

"Low-tech" function tests (stair climbing test, 6-minute walk test (6-MWT), incremental shuttle walk test (ISWT)) can be used as a first screening test with exercise. In oncosurgery, their appropriateness is discussed primarily in lung cancer. In a stair climbing test in patients with impending lung resection, climbing less than 12 m (< 3 flights of stairs) was associated with a 2-fold and 13-fold increase in the incidence of postoperative complications and mortality, respectively, compared with climbing more than 22 m (< 1 % mortality) [54]. The 6-minute walk test is widely recognized, well reproducible, and the easiest to perform. The published data demonstrate the clear benefit of the test in perioperative risk stratification of lung resection. Preoperative 6-MWT distance ≥ 400 m was associated with a lower complication rate after lobectomy for lung cancer [55]. Conversely, 6-MWT distance < 525 m was associated with decreased overall patient survival [56]. The incremental shuttle walk test can also be used, especially in patients with concomitant chronic obstructive pulmonary disease. ISWT distance < 400 m correlates with VO_2max < 15 ml/kg/min and a 10% incidence of cardiopulmonary complications. Distance < 250 m in higher-risk patients was associated with a 2.5-fold increase in the rate of serious cardiopulmonary complications (44 % vs. 18 %; p = 0.04) [57]. Patients with ISWT distance < 250 m were 3 times more likely to develop complications after colorectal surgeries (specificity was 0.88, sensitivity – 0.58) [58]. According to a meta-analysis of 7 studies including 1,418 patients with colorectal cancer, walking distance < 250 m was associated with longer hospital stay after surgery, and no prognostic value could be identified [47]. According to the 2013 ACCP guidelines "Physiologic Evaluation of the Patient with Lung Cancer Being Considered for Resectional Surgery", patients with lung cancer are indicated to perform a stair climbing test or an incremental shuttle walk test when the PpFEV1 or predicted postoperative lung diffusing capacity for carbon monoxide (DLCO) is between 30 % and 60 % (1 C). If the test results show ISWT distance < 400 m or stair climbing height < 22 m, CPET is indicated [39]. Thus, "low-tech" functional tests can be used as an alternative to CPET in patients with a small decline in pulmonary function assessed previously by respiratory tests. Later published algorithms for perioperative evaluation of patients with lung cancer and other malignant neoplasms do not include these functional tests [45, 59].

CONCLUSION

Most cavitary surgeries for malignant neoplasms are categorized as high surgical risk with a probability of 30-day cardiovascular mortality or MI > 5 %.

No specialized guidelines have been developed to assess the risk of cardiac complications in oncosurgery. Preoperative evaluation of cancer patients follows step-by-step algorithms outlined in current guidelines for cardiac risk assessment of non-cardiac surgeries (e. g., the 2014 ACC/AHA Guidelines). The use of the universal ACS NSQIP Surgical Risk Calculator, which has been validated on cohorts of cancer patients, is preferred for quantifying the risk of CVD in patients with malignant neoplasms. In surgical treatment of lung cancer, the ThRCRI scale specifically designed for this category of patients should be used. ThRCRI values ≥ 2 indicate an increased cardiac risk and the need to expand the examination scope. The RCRI index in cancer patients has lower prognostic accuracy. The NSQIP MICA index has not been validated on cancer cohorts.

The significance of preoperative brain natriuretic peptide levels and postoperative cardiac troponins in predicting cardiac complications has been confirmed in cancer patients. If these biomarkers are increased (e. g., NT-proBNP > 300 mg/l preoperatively), careful postoperative screening for acute myocardial injury is required according to the CCS Heart Failure Comprehensive Guidelines (2017).

The Duke Activity Status Index (DASI) questionnaire is used to assess preoperative functional status in oncologic surgery. Low functional status (< 4 METs) suggests a pharmacological stress testing. In high-risk lung cancer patients (ThRCRI ≥ 2 or cardiovascular disease requiring drug therapy or newly diagnosed or inability to climb two flights of stairs), the use of cardiopulmonary exercise testing is being considered to determine functional status and further management. Values of ventilatory equivalent for carbon dioxide > 35 and/or peak oxygen consumption < 10 ml/kg/min indicate a high risk of cardiopulmonary complications, necessitating a change in treatment policy.

In asymptomatic patients with lung cancer with risk factors and a slight decrease in pulmonary function as a screening test, the diagnostic efficacy of "low-tech" functional tests (stair climbing test, 6-minute walk test, Incremental shuttle walk test) has been proved. A cardiopulmonary exercise testing is indicated if ISWT distance < 400 m or stair climbing height < 22 m.

Conflict of interest

The authors of this article declare the absence of a conflict of interest.

REFERENCES

1. Botto F, Alonso-Coello P, Chan M, Villar J, Xavier D, Srinathan S, et al. Myocardial injury after noncardiac surgery: A large, international, prospective cohort study establishing diagnostic criteria, characteristics, predictors, and 30-day outcomes. *Anesthesiology*. 2014; 120(3): 564-578. doi: 10.1097/ALN.0000000000000113

2. Smilowitz N, Gupta N, Ramakrishna H, Guo Y, Berger J, Bangalore S. Perioperative major adverse cardiovascular and cerebrovascular events associated with noncardiac surgery. *JAMA Cardiol*. 2017; 2(2): 181-187. doi: 10.1001/jamacardio.2016.4792

3. Smilowitz N, Gupta N, Guo Y, Berger J, Bangalore S. Perioperative acute myocardial infarction associated with non-cardiac surgery. *Eur Heart J*. 2017; 38(31): 2409-2417. doi: 10.1093/eurheartj/ehx313

4. Devereaux P, Sessler D. Cardiac complications in patients undergoing major noncardiac surgery. *N Engl J Med*. 2015; 373: 2258-2269. doi: 10.1056/NEJMra1502824

5. Ferguson M, Saha-Chaudhuri P, Mitchell J, Varela G, Brunelli A. Prediction of major cardiovascular events after lung resection using a modified scoring system. *Ann Thorac Surg*. 2014; 97(4): 1135-1140. doi: 10.1016/j.athoracsur.2013.12.032

6. Davydov MI, Akchurin RS, Gerasimov SS, Brand IaB, Dolgov IM. The surgical treatment of patients with lung cancer and severe cardiovascular disorders. *Pirogov Russian Journal of Surgery*. 2012; (7): 18-26. (In Russ.). [Давыдов М.И., Акчурин Р.С., Герасимов С.С., Бранд Я.Б., Долгов И.М. Хирургическое лечение больных раком легкого с тяжелыми сопутствующими сердечно-сосудистыми заболеваниями. *Хирургия. Журнал им. Н.И. Пирогова*. 2012; (7): 18-26].

7. Navi B, Reiner A, Kamel H, Iadecola C, Okin P, Elkind M, et al. Risk of arterial thromboembolism in patients with cancer. *J Am Coll Cardiol*. 2017; 70(8): 926-938. doi: 10.1016/j.jacc.2017.06.047

8. Sarkar R, Hatamipour A, Panjwani N, Courtney P, Cherry D, Salans MA, et al. Impact of radiation on cardiovascular outcomes in older resectable esophageal cancer patients with medicare. *Am J Clin Oncol*. 2021; 44(6): 275-282. doi: 10.1097/COC.0000000000000815

9. Zhang W, Xie K, Fu S, Jiang H, Fang M, Lian Y, et al. Comparison of the incidence of perioperative cardiovascular risk events among patients with and without a history of neoadjuvant chemotherapy. *Minerva Anestesiol*. 2019; 85(8): 822-829. doi: 10.23736/S0375-9393.19.13388-3

10. Koene R, Prizment A, Blaes A, Konety S. Shared risk factors in cardiovascular disease and cancer. *Circulation*. 2016; 133(11): 1104-1114. doi: 10.1161/CIRCULATIONAHA.115.020406

11. Sumin AN, Starovojtova AV, Scheglova AV, Gorbunova EV. Role of preoperative cardiology consultation in patients undergoing cancer surgery. *Terapevticheskii arkhiv*. 2020; 92(1): 25-29. (In Russ.). [Сумин А.Н., Старовойтова А.В., Щеглова А.В., Горбунова Е.В. Роль консультации кардиолога в обследовании больных перед онкологическими операциями. *Терапевтический архив*. 2020; 92(1): 25-29]. doi: 10.26442/00403660.2020.01.000478

12. Bilimoria K, Liu Y, Paruch J, Zhou L, Kmiecik T, Ko C, et al. Development and evaluation of the universal ACS NSQIP surgical risk calculator: A decision aide and informed consent tool for patients and surgeons. *J Am Coll Surg*. 2013; 217(5): 833-842. doi: 10.1016/j.jamcollsurg.2013.07.385

13. Fischer F, Lange K, Klose K, Greiner W, Kraemer A. Barriers and strategies in guideline implementation – A scoping review. *Healthcare (Basel)*. 2016; 4(3): 36. doi: 10.3390/healthcare4030036

14. McIsaac D, Montroy J, Gagne S, Johnson C, Ernst J, Halman S, et al. Implementation of the Canadian Cardiovascular Society guidelines for perioperative risk assessment and management: An interrupted time series study. *Can J Anaesth*. 2021; 68(8): 1135-1145. doi: 10.1007/s12630-021-02026-x

15. Halvorsen S, Mehilli J, Cassese S, Hall TS, Abdelhamid M, Barbato E, et al. 2022 ESC Guidelines on cardiovascular assessment and management of patients undergoing non-cardiac surgery. *Eur Heart J*. 2022: ehac270. doi: 10.1093/eurheartj/ehac270

16. Fleisher L, Fleischmann K, Auerbach A, Barnason S, Beckman J, Bozkurt B, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: A report of the American College of Cardiology/American Heart Association task force on practice guidelines. *J Am Coll Cardiol*. 2014; 64(22): e77-e137. doi: 10.1016/j.jacc.2014.07.944

17. Duceppe E, Parlow J, MacDonald P, Lyons K, McMullen M, Srinathan S, et al. Canadian Cardiovascular Society guidelines on perioperative cardiac risk assessment and management for patients who undergo noncardiac surgery. *Can J Cardiol*. 2017; 33(1): 17-32. doi: 10.1016/j.cjca.2016.09.008

18. Gerent A, Almeida J, Fominskiy E, Landoni G, de Oliveira G, Rizk S, et al. Effect of postoperative goal-directed therapy in cancer patients undergoing high-risk surgery: A randomized clinical trial and meta-analysis. *Crit Care*. 2018; 22(1): 133. doi: 10.1186/s13054-018-2055-4

19. Papadopoulou A, Mathers E. Risk stratification of the cancer patient: A narrative review. *Dig Med Res*. 2020; 3: 27. doi: 10.21037/dmr-2

20. Bolshedvorskaya OA, Protasov KV, Batoroev YuK, Ulybin PS, Dvornichenko VV. Postoperative cardiac ischemic complications in lung cancer patients. *Acta biomedica scientifica*. 2019; 4(5): 91-97. (In Russ.). [Большедворская О.А., Протасов К.В., Батороев Ю.К., Улыбин П.С., Дворниченко В.В. Послеоперационные кардиальные ишемические осложнения у больных раком лёгкого. *Acta biomedica scientifica*. 2019; 4(5): 91-97]. doi: 10.29413/ABS.2019-4.5.15

21. Hanley C, Donahoe L, Slinger P. Fit for surgery? What's new in preoperative assessment of the high-risk patient undergoing pulmonary resection. *J Cardiothorac Vasc Anesth*. 2021; 35(12): 3760-3773. doi: 10.1053/j.jvca.2020.11.025

22. Straatman J, van der Wielen N, Cuesta M, Daams F, Roig Garcia J, Bonavina L, et al. Minimally invasive versus open esophageal resection: Three-year follow-up of the previously reported randomized controlled trial: The TIME trial. *Ann Surg*. 2017; 266(2): 232-236. doi: 10.1097/SLA.0000000000002171

23. Lee T, Marcantonio E, Mangione C, Thomas E, Polanczyk C, Cook E, et al. Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. *Circulation*. 1999; 100(10): 1043-1049. doi: 10.1161/01.cir.100.10.1043

24. Wotton R, Marshall A, Kerr A, Bishay E, Kalkat M, Rajesh P, et al. Does the revised cardiac risk index predict cardiac complications following elective lung resection? *J Cardiothorac Surg*. 2013; 8: 220. doi: 10.1186/1749-8090-8-220

25. Bolshedvorskaya OA, Protasov KV, Ulybin PS, Dvornichenko VV. Postoperative myocardial infarction in lung cancer patients with: incidence rate, clinical features, prognostic factors. *Russian Journal of Cardiology*. 2020; 25(11): 44-50. (In Russ.). [Большедворская О.А., Протасов К.В., Улыбин П.С., Дворниченко В.В. Послеоперационный инфаркт миокарда у больных раком легкого: частота выявления, клинические особенности, прогностические факторы. *Российский кардиологический журнал*. 2020; 25(11): 44-50]. doi: 10.15829/1560-4071-2020-3946

26. Bolshedvorskaya OA, Protasov KV, Batunova EV, Semenova EN. Biomarkers of myocardial injury in surgical treatment of lung cancer: perioperative dynamics and prognostic value. *Complex Issues of Cardiovascular Diseases*. 2022; 11(2): 27-38. (In Russ.). [Большедворская О.А., Протасов К.В., Батунова Е.В., Семенова Е.Н. Биомаркеры повреждения миокарда при хирургическом лечении рака легкого: периоперационная динамика и прогностическое значение. *Комплексные проблемы сердечно-сосудистых заболеваний*. 2022; 11(2): 27-38]. doi: 10.17802/2306-1278-2022-11-2-27-38

27. Gupta P, Gupta H, Sundaram A, Kaushik M, Fang X, Miller W, et al. Development and validation of a risk calculator for prediction of cardiac risk after surgery. *Circulation*. 2011; 124(4): 381-387. doi: 10.1161/CIRCULATIONAHA.110.015701

28. Rivard C, Nahum R, Slagle E, Duininck M, Isaksson Vogel R, Teoh D. Evaluation of he performance of the ACS NSQIP surgical risk calculator in gynecologic oncology patients undergoing laparotomy. *Gynecol Oncol*. 2016; 141: 281-286. doi: 10.1016/j.ygyno.2016.02.015

29. Armstrong E, Beal E, Lopez-Aguiar A, Poultsides G, Cannon J, Rocha F, et al. Evaluating the ACS-NSQIP risk calculator in primary GI neuroendocrine tumor: Results from the United States neuroendocrine Tumor Study Group. *Am Surg*. 2019; 85: 1334-1340.

30. Liu J, Weber S, Berian J, Chen S, Cohen M, Ko C, et al. Role of operative complexity variables in risk adjustment for patients with cancer. *JAMA Surg*. 2016; 151: 1084-1086. doi: 10.1001/jamasurg.2016.2253

31. Brunelli A, Salati M, Rocco G, Varela G, Van Raemdonck D, Decaluwe H, et al. European risk models for morbidity (EuroLung1) and mortality (EuroLung2) to predict outcome following anatomic lung resections: An analysis from the European Society of Thoracic Surgeons database. *Eur J Cardiothorac Surg*. 2017; 51(3): 490-497. doi: 10.1093/ejcts/ezw319

32. Brunelli A, Cicconi S, Decaluwe H, Szanto Z, Falcoz P. Parsimonious Eurolung risk models to predict cardiopulmonary

morbidity and mortality following anatomic lung resections: An updated analysis from the European Society of Thoracic Surgeons database. *Eur J Cardiothorac Surg*. 2020; 57(3): 455-461. doi: 10.1093/ejcts/ezz272

33. Taylor M, Szafron B, Martin G, Abah U, Smith M, Shackcloth M, et al. External validation of six existing multivariable clinical prediction models for short-term mortality in patients undergoing lung resection. *Eur J Cardiothorac Surg*. 2021; 59(5): 1030-1036. doi: 10.1093/ejcts/ezaa422

34. Brunelli A, Varela G, Salati M, Jimenez M, Pompili C, Novoa N, et al. Recalibration of the revised cardiac risk index in lung resection candidates. *Ann Thorac Surg*. 2010; 90(1): 199-203. doi: 10.1016/j.athoracsur.2010.03.042

35. Brunelli A, Cassivi S, Fibla J, Halgren L, Wigle D, Allen M, et al. External validation of the recalibrated thoracic revised cardiac risk index for predicting the risk of major cardiac complications after lung resection. *Ann Thorac Surg*. 2011; 92: 445-448. doi: 10.1016/j.athoracsur.2011.03.095

36. Ferguson M, Celauro A, Vigneswaran W. Validation of a modified scoring system for cardiovascular risk associated with major lung resection. *Eur J Cardiothorac Surg*. 2012; 41(3): 598-602. doi: 10.1093/ejcts/ezr081

37. Brunelli A, Ferguson M, Salati M, Vigneswaran W, Jimenez M, Varela G. Thoracic revised cardiac risk index is associated with prognosis after resection for stage I lung cancer. *Ann Thorac Surg*. 2015; 100(1): 195-200. doi: 10.1016/j.athoracsur.2015.03.103

38. Salati M, Brunelli A. Risk stratification in lung resection. *Curr Surg Rep*. 2016; 4(11): 37. doi: 10.1007/s40137-016-0158-x

39. Brunelli A, Kim A, Berger K, Addrizzo-Harris D. Physiologic evaluation of the patient with lung cancer being considered for resectional surgery: Diagnosis and management of lung cancer. American College of Chest Physicians evidence-based clinical practice guidelines; 3rd ed. *Chest*. 2013; 143(Suppl 5): e166S-e190S. doi: 10.1378/chest.12-2395

40. Duceppe E, Patel A, Chan M, Berwanger O, Ackland G, Kavsak P, et al. Preoperative N-terminal pro-B-type natriuretic peptide and cardiovascular events after noncardiac surgery: A cohort study. *Ann Intern Med*. 2020; 172: 96-104. doi: 10.7326/M19-2501

41. Smilowitz N, Redel-Traub G, Hausvater A, Armanious A, Nicholson J, Puelacher C, et al. Myocardial injury after non-cardiac surgery: A systematic review and meta-analysis. *Cardiol Rev*. 2019; 27(6): 267-273. doi: 10.1097/CRD.0000000000000254

42. Hou Y, Zhou Y, Hussain M, Budd G, Tang W, Abraham J, et al. Cardiac risk stratification in cancer patients: A longitudinal patient-patient network analysis. *PLoS Med*. 2021; 18(8): e1003736. doi: 10.1371/journal.pmed.1003736

43. Shestopalova IM, Gerasimov SS, Kadagidze ZG, Shelepova VM. Using NT-proBNP marker in monitoring of perioperative heart failure in cancer patients suffering from coronary heart disease. *Zhurnal Serdechnaya nedostatochnost'*. 2008; 4(48): 172-174. (In Russ.). [Шестопалова И.М., Герасимов С.С., Кадагидзе З.Г., Шелепова В.М. Применение маркера NT-proBNP в мониторинге периоперационной сердечной недостаточности у онкологических больных, страдающих ишемической болезнью сердца. *Журнал Сердечная недостаточность*. 2008; 4(48): 172-174].

44. Vernooij L, van Klei W, Moons K, Takada T, van Waes J, Damen J. The comparative and added prognostic value of biomarkers to the Revised Cardiac Risk Index for preoperative prediction of major adverse cardiac events and all-cause mortality in patients who undergo noncardiac surgery. *Cochrane Database Syst Rev*. 2021; 12(12): CD013139. doi: 10.1002/14651858.CD013139.pub2

45. Deana C, Vetrugno L, Bignami E, Bassi F. Peri-operative approach to esophagectomy: A narrative review from the anesthesiological standpoint. *J Thorac Dis*. 2021; 13(10): 6037-6051. doi: 10.21037/jtd-21-940

46. Patel N, Powell A, Wheat J, Brown C, Appadurai I, Davies R, et al. Cardiopulmonary fitness predicts postoperative major morbidity after esophagectomy for patients with cancer. *Physiol Rep*. 2019; 7: e14174. doi: 10.14814/phy2.14174

47. Lee C, Kong J, Ismail H, Riedel B, Heriot A. Systematic review and meta-analysis of objective assessment of physical fitness in patients undergoing colorectal cancer surgery. *Dis Colon Rectum*. 2018; 61(3): 400-409. doi: 10.1097/DCR.0000000000001017

48. Kumar R, Garcea G. Cardiopulmonary exercise testing in hepato-biliary & pancreas cancer surgery – A systematic review: Are we any further than walking up a flight of stairs? *Int J Surg*. 2018; 52: 201-207. doi: 10.1016/j.ijsu.2018.02.019

49. Wijeysundera D, Pearse R, Shulman M, Abbott T, Torres E, Ambosta A, et al. Assessment of functional capacity before major non-cardiac surgery: An international, prospective cohort study. *Lancet*. 2018; 391: 2631-2640. doi: 10.1016/S0140-6736(18)31131-0

50. Colson M, Baglin J, Bolsin S, Grocott M. Cardiopulmonary exercise testing predicts 5 yr survival after major surgery. *Br J Anaesth*. 2012; 109: 735-741. doi: 10.1093/bja/aes263

51. Brunelli A, Belardinelli R, Pompili C, Xiumé F, Refai M, Salati M, et al. Minute ventilation-to-carbon dioxide output (VE/VCO2) slope is the strongest predictor of respiratory complications and death after pulmonary resection. *Ann Thorac Surg*. 2012; 93: 1802-1806. doi: 10.1016/j.athoracsur.2012.03.022

52. Brunelli A, Pompili C, Salati M, Refai M, Berardi R, Mazzanti P, et al. Preoperative maximum oxygen consumption is associated with prognosis after pulmonary resection in stage I non-small cell lung cancer. *Ann Thorac Surg*. 2014; 98(1): 238-242. doi: 10.1016/j.athoracsur.2014.04.029

53. Teh E, Sinha S, Joshi N, Kamalanathan K, Molyneux M, Rasburn N, et al. Cardiopulmonary exercise testing (CPET) and the prediction of perioperative events in patients undergoing lung resection in the modern era: A comparison of clinical, CPET and combined assessment. *J Clin Anesth*. 2020; 62: 109749. doi: 10.1016/j.jclinane.2020.109749

54. Brunelli A, Refai M, Xiume F, Salati M, Sciarra V, Socci L, et al. Performance at symptom-limited stair-climbing test is associated with increased cardiopulmonary complications, mortality, and costs after major lung resection. *Ann Thorac Surg*. 2008; 86(1): 240-247. doi: 10.1016/j.athoracsur.2008.03.025

55. Wesolowski S, Orlowski T, Kram M. The 6-min walk test in the functional evaluation of patients with lung cancer qualified for lobectomy. *Interact Cardiovasc Thorac Surg*. 2020; 30(4): 559-564. doi: 10.1093/icvts/ivz313

56. Marjanski T, Badocha M, Wnuk D, Dziedzic R, Ostrowski M, Sawicka W, et al. Result of the 6-min walk test is an independent prognostic factor of surgically treated non-small-cell lung cancer. *Interact Cardiovasc Thorac Surg*. 2019; 28: 368-374. doi: 10.1093/icvts/ivy258

57. Fennelly J, Potter L, Pompili C, Brunelli A. Performance in the shuttle walk test is associated with cardiopulmonary com-

plications after lung resections. *J Thorac Dis*. 2017; 9(3): 789-795. doi: 10.21037/jtd.2017.03.22

58. Nutt C, Russell J. Use of the pre-operative shuttle walk test to predict morbidity and mortality after elective major colorectal surgery. *Anaesthesia*. 2012; 67(8): 839-849. doi: 10.1111/j.1365-2044.2012.07194.x

59. Liu D, Wen H, He J, Gao S, Li S, Liu L, et al. Society for Translational Medicine Expert Consensus on the preoperative assessment of circulatory and cardiac functions and criteria for the assessment of risk factors in patients with lung cancer. *J Thorac Dis*. 2018; 10(9): 5545-5549. doi: 10.21037/jtd.2018.08.91

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