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ORIGINAL ARTICLE

Coronary computed tomography angiography to predict myocardial injury in patients undergoing high-risk cancer surgery

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ABSTRACT

BACKGROUND: Myocardial injury is one of the most common complications after surgery and is associated with increased mortality in high-risk patients. The aim of this study was to evaluate whether preoperative coronary computed tomography angiography can predict the occurrence of myocardial injury in cancer patients undergoing high-risk surgery.
METHODS: Patients diagnosed with solid tumors who possessed at least two cardiovascular risk factors and were scheduled for high-risk surgeries between August 2017 and July 2021 were included. All subjects underwent preoperative coronary computed tomography angiography, and troponin levels were measured immediately after surgery and daily within the first three days after surgery. The primary outcome was the occurrence of myocardial injury within 72 hours, defined as high-sensitivity troponin T values ≥0.014 ng/mL.
RESULTS: A total of 184 patients were included. The median age was 66 years (IQR: 60; 73 years). Myocardial injury occurred in 87 patients (48%). The logistic regression identified the following as myocardial injury predictors: bladder tumor (odds ratio [OR] 10.40 [95% confidence interval 95% CI] 2.51; 43.20, P=0.001), esophageal tumor (OR 7.39 [95% CI 2.27; 24.08], P=0.001), longer anesthesia time (OR 1.24 [95% CI 1.09; 1.43], P=0.002), calcium score of 401-1000 (OR 5.92 [95% CI 1.29; 27.08, P=0.022]), and calcium score >1000 (OR 4.62 [95% CI 1.18; 18.04, P=0.028]).
CONCLUSIONS: In cancer patients undergoing high-risk surgery, high calcium score on coronary computed tomography angiography identified patients who developed postoperative myocardial injury. Coronary computed tomography angiography might be considered in the surgical risk stratification of this population.

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KEY WORDS: Myocardial reperfusion injury; Computed tomography angiography; Surgical oncology; Postoperative complications.

Every year, over 300 million major surgical procedures are undertaken worldwide.[1] Approximately 10-20% of patients undergoing surgery fall into the high-risk category for complications, representing 80% of postoperative mortality and leading to a substantial decline in functional capacity.[2] The European Surgical Outcomes Study (EuSOS) revealed that postoperative mortality was independently associated with metastatic disease, advanced age and surgical procedure complexity. For these patients, it is imperative to implement strategies aimed at enhancing outcomes.[3]

In recent years, significant progress has been made in the care of cancer patients, who now live longer and are exposed to multiple therapies, including surgeries, chemotherapy, targeted therapies, immunotherapy, and radiotherapy.[4] Major oncologic surgeries are typically performed with curative intent and are often accompanied by endothelial injury and intense inflammation, resulting in vasodilation, hypercoagulability and clinical complications, such as acute renal failure, septic shock and cardiovascular complications.[5, 6] The association of multiple risk factors, such as advanced age, surgeries with anticipated fluid and blood loss, and cancer, significantly increases the risk of acute organ injury in cancer patients. This can result in both short-term and long-term complications, ultimately impacting 15-year mortality rates.[7]

Furthermore, a subset of patients may have prior exposure to cardiotoxic chemotherapy or thoracic radiotherapy.[8] Myocardial injury after noncardiac surgery (MINS) has been strongly associated with adverse cardiovascular outcomes, including increased risk of myocardial infarction, heart failure, and cardiovascular death in both the immediate postoperative period and over the long term. The occurrence of MINS is thought to reflect underlying coronary artery disease and myocardial vulnerability to surgical stressors such as hypotension, tachycardia, and inflammation. These factors not only contribute to acute myocardial injury but also exacerbate existing atherosclerosis, accelerating the progression of cardiovascular disease over time. Studies have shown that patients who experience MINS are at a significantly higher risk for future cardiovascular events, including fatal ones, and these risks can persist and accumulate over years. The long-term effects of MINS can lead to progressive heart failure, recurrent ischemic events, and chronic cardiovascular instability, which together contribute to increased mortality rates extending far beyond the perioperative period. Thus, MINS serves as both a marker and a driver of long-term cardiovascular morbidity and mortality, underlining the importance of identifying at-risk patients before surgery and implementing strategies to mitigate this risk in both the short and long term.[9, 10]

The most commonly employed preoperative scoring systems have typically excluded cancer patients, and their primary focus has been on major cardiovascular complications. Moreover, the utility of imaging methods in accurately estimating risk within this specific context remains inconclusive.[9, 10] The aim of this study was to evaluate whether preoperative coronary computed tomography angiography (CCTA) can predict the occurrence of postoperative myocardial injury in cancer patients undergoing high-risk noncardiac surgery.

Materials and methods

Study design and setting

This was a prospective and observational study conducted between August 2017 and July 2021 at the Instituto do Coração InCor, Hospital das Clínicas HCFMUSP, Faculdade de Medicina, Universidade de São Paulo, São Paulo, Brazil. Consecutive high-risk surgical patients undergoing major cancer surgery were assessed for eligibility. The study was approved by the ethics committee of the Instituto do Coração InCor, Hospital das Clínicas HCFMUSP, Faculdade de Medicina, Universidade de São Paulo (Comissão de Ética para Análise de Projetos de Pesquisa, protocol number 4.082.786).

Funding was provided by the São Paulo Research Foundation (FAPESP, protocol number: 2015/22814-5). The initial version of the manuscript was drafted by the first and last authors, developed by the writing committee, and approved by all the members of the research. Ethical approval is available in the Supplementary Digital Material 1.

Participants

We enrolled patients who were aged 18 years or older, who had at least two cardiovascular risk factors (peripheral artery disease, cerebrovascular disease, diabetes, age >70 years, current or former smoker, dyslipidemia, and hypertension), and who were scheduled for major cancer thoracic or abdominal-pelvic surgery (the surgeries were planned to last at least two hours or with anticipated blood and fluid losses). We excluded patients with an allergy to iodine contrast, chronic renal failure (creatinine ≥2 mg/dL), a diagnosis of ischemic heart disease, current cardiovascular symptoms or who had a request for myocardial ischemia functional testing.

Procedures

Assessment of the eligibility criteria was performed on a weekly basis, and eligible patients were referred to an outpatient appointment. Then, informed consent was obtained. After study inclusion, patients were scheduled for CCTA and laboratory tests comprising a complete lipid profile, high-sensitivity T troponin, and N-terminal fragment of the B-type natriuretic peptide (NT-proBNP).

Clinical information on the risk factors for cardiovascular disease, medication use, functional capacity in metabolic equivalent (MET), Eastern Cooperative Oncology Group (ECOG), Karnofsky scale, oncological diagnosis, tumor staging, oncological treatments already performed (chemotherapy and radiotherapy), and planned surgery were collected. The revised cardiac risk index (RCRI) score was also calculated at baseline.[11] The definitions of MET and description of the score risks are provided in the Supplemental Digital Material 1.

CCTA

Coronary computed tomography was performed preoperatively in all patients. In patients with a heart rate greater than 60 beats per minute, 50 mg of metoprolol was prescribed. If necessary, supplemental doses of intravenous metoprolol were used for heart rate control, aiming to optimize image quality. The patients were also premedicated with isosorbide dinitrate 5 mg sublingually for coronary dilation. The examinations were performed on a Philips Brilliance iCT 256-channel computerized tomography scanner (Philips Healthcare, Andover, United States of America), preferably using prospective acquisition or retrospectively with dose modulation in patients with a heart rate >60 bpm even after using beta-blockers, with a tube voltage of 100 or 120 kV and current in milliamperes (mA), adjusted for the patient's body type.

Axial slices of the heart were obtained during the imaging procedure with a thickness of 0.67 mm, an increment of 0.3 mm, a standard cardiac filter, a tube rotation speed of 0.22 s, and a field of view adjusted to the cardiac area, and in percentile 75 of the cardiac cycle (diastole) and triggered by electrocardiogram, as well as in an interval of 100 ms, during the inspiratory pause according to the cardiac area (z-axis). After performing the image without contrast to acquire the calcium score, 50 to 80 mL of iodinated contrast was injected at a rate of 5 to 6 mL/second, depending on the patient's characteristics, for the acquisition of coronary angiography images.

The exams were reviewed by a cardiologist with experience in CCTA, and multiple analyses were performed: calculation of the calcium score of each artery, detection of plaques, and evaluation of the extent of the plaques and of the degree of calcification.

The quantification of luminal reduction was performed as recommended by the Society of Cardiovascular Computed Tomography as absent, minimal (<25%), mild (25% to 49%), moderate (50% to 69%), severe (70% to 99%) and occlusion (100%). Stenosis was also classified as obstructive (≥50%) and nonobstructive (<50%).

If CCTA identified high-risk coronary artery disease (stenosis ≥50% in the left main coronary artery, ≥50% in three coronary arteries, or ≥50% in two arteries, one of which was the anterior descending artery), the patient was reassessed by the cardiology team, and the computed tomography-derived fractional flow reserve (CTFFR) fraction was calculated using Syngo.via software (Siemens Healthineers, Forchheim, Germany). After selecting the images with the best technical quality, the coronary tree was evaluated using three-dimensional, multiplanar and curved reformatting (vessel probe), quantifying the degree of stenosis and the predominant composition of the plaque, if present (noncalcified, calcified and mixed). Postprocessing of CTFFR was performed in the same series as the visual anatomical analysis using the Frontier platform and the noncommercial prototype of the CTFFR software, version 3.0 (Siemens Healthineers, Forchheim, Germany).[12, 13]

If a coronary angiogram or functional ischemic testing was deemed appropriate by the cardiology team, the patient underwent the diagnostic pathway according to the institutional protocol.

Measurement of NT-proBNP

NT-proBNP was analyzed as a preoperative marker of cardiac dysfunction. Plasma NT-proBNP levels were measured using the Cobas h232 assay (Roche, Basel, Switzerland) and classified as normal values below 125 pg/mL.

Intraoperative data

The following intraoperative data were obtained from the anesthetic database: duration of surgery and anesthesia, type of anesthesia, use of blood transfusion, use of vasoactive drugs, and volume of intravenous fluids administered.

Blood pressure (BP) measurements were recorded every five minutes in addition to heart rate and oxygen saturation by the multiparameter monitor of vital signs in the operating room (Dixtal-Philips Health Care, São Paulo, Brazil). Invasive BP measurements were obtained through an intra-arterial catheter, and noninvasive measurements were obtained through a sphygmomanometer. Hypotension was defined as a mean arterial pressure below 65 mmHg.

Measurement of troponin T

High-sensitivity troponin T (hs-cTnT) levels were obtained by an electrochemiluminescence immunoassay on the Elecsys 2010 immunoassay analyzer, Cobas 411, with a 99th percentile threshold (URL) of 0.014 ng/mL (Roche Diagnostics GmbH, Manheim, Germany). Measurements were performed in the immediate postoperative period and daily until the third postoperative day.

Postoperative data

High-sensitivity troponin T levels and electrocardiograms were obtained at admission and daily until the 3rd postoperative day. In addition, data on blood count, hematocrit, renal function, electrolytes, CRP (C-reactive protein), CPK (creatine phosphokinase), blood glucose, albumin, coagulation tests, and lactate were collected.

Outcomes

The primary outcome was myocardial injury as defined as an increase in serum troponin T to a value greater equal or higher than 0.014 ng/mL in the first hours after surgery. Secondary outcomes included a combined endpoint of acute renal failure, septic shock, cardiac arrhythmia, acute myocardial infarction, stroke, venous thromboembolism, cardiovascular death, and all-cause death at 30 days or until hospital discharge.

We also reported the 30-day hospital readmission rate, intensive care unit length of stay, hospital length of stay, and predictors of and myocardial injury within 72 hours post-surgery and predictors of postoperative complications in 30 days or until hospital discharge. The outcomes definitions are described in the Supplementary Digital Material 1.

Statistical analysis

We considered three possible predictor variables to calculate the sample size. The sample size consisted of ten events for each predictor variable; therefore, we calculated 30 events. The incidence of MINS described by Smilowitz *et al.* was 17.9%.[14] Thus, 184 patients would be needed, considering an estimated loss to follow-up of 10%.

Continuous variables are presented as the mean and standard deviation (SD) or median and interquartile range (IRQ). They were analyzed using Student's *t*-test or the Mann-Whitney U Test, and categorical variables were analyzed using the Chi-square Test, Fisher's Exact Test, or the likelihood ratio test.

Variables with a P value <0.10 were used to adjust the MINS in the multiple logistic regression model. The ROC curve (receiver operating characteristic) and respective cut-off values, selected by the highest sensitivity and specificity values, were used in the estimated logistic regression model.

The occurrence of the first event was evaluated by fitting the univariate and multivariate Cox proportional hazards model. Variables that presented a value of P<0.10 were selected for the adjustment of the multivariate model.

Values of P<0.05 were considered significant, and the IBM SPSS Statistics for Windows program, version 25.0 (IBM Corp., Armonk, NY, USA), was used for the calculations.

Results

A total of 1238 patients were evaluated for eligibility, and 1005 patients were excluded according to the prespecified criteria. Thus, 233 patients were included, of which 49 were excluded from the analysis (36 patients did not undergo surgery due to refusal, death, or progression of oncological disease, in 11 serum biomarkers were not obtained in the postoperative period and two patients had uninterpretable CCTA). In total, 184 patients were analyzed (Figure 1).

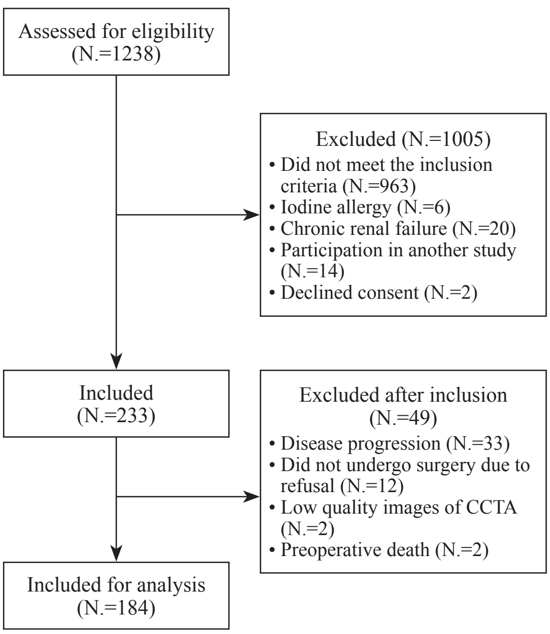


Figure 1.—Patient flow chart.
CCTA: computed coronary tomography angiography.

The median age of the patients was 66 years (IQR: 60; 73), and most of them were male (56.5%). Hypertension and dyslipidemia were the most frequent comorbidities. Performance measured through the ECOG and Karnosky Scales showed good functional ability of the patients. The baseline and demographic characteristics of the study patients and their data are shown in Table I. Most patients had colorectal tumors, nonmetastatic disease, and received chemotherapy with 5-fluorouracil. The preoperative hemoglobin and albumin levels were within the normal

Table I.—*Clinical and demographic characteristics of the patients.*

Variable	Total=184 N. (%)
Age (Years), median (IQR)	66 (60-73)
Sex (Male)	104 (56.5%)
Race	
White	119 (64.7%)
Black	15 (8.2%)
Multiracial	38 (20.7%)
Other	12 (6.5%)
Primary tumor	
Colorectal	95 (51.6%)
Esophagus	25 (13.5%)
Pancreas	20 (10.8%)
Stomach	17 (9.2%)
Bladder	15 (8.1%)
Lung	7 (3.8%)
Uterus	4 (2.1%)
Ovarian	1 (0.5%)
BMI (kg/m^2), median (IQR)	26 (23-30)
Smoking status	
Never	56 (30.6%)
Former	106 (57.9%)
Current	21 (11.5%)
Medical history	
Hypertension	151 (82.1%)
Dyslipidemia	79 (44.4%)
Diabetes mellitus	68 (37.6%)
Chronic obstructive pulmonary disease	13 (8.6%)
Stroke	9 (4.9%)
Medication	
ACEi/ARB	101 (55.2%)
Antidiabetic drugs	49 (27.1%)
Statin	48 (26.2%)
Diuretics	48 (26.2%)
Calcium-channel blockers	29 (16.0%)
Beta-blockers	29 (15.8%)
Aspirin	21 (11.5%)
Insulin	14 (7.7%)

Data are presented as median and interquartile range or absolute and relative frequencies. Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; BMI, body mass index; IQR, Interquartile range.

range. Proctosigmoidectomy was the most common procedure, followed by abdominal-perineal amputation. Most surgeries were gastrointestinal, the median duration was 300 minutes (IQR: 240; 420), and anesthesia lasted 450 minutes (IQR: 360; 563). Intraoperative hypotension was frequent, lasting 60 min (IQR: 25; 105). Norepinephrine was needed in 33% of patients. Data regarding neoplasm characteristics, treatment, performance status, preoperative laboratory variables, surgery type, and intraoperative characteristics are described in the supplemental material (Supplementary Table I, Supplementary Table II, Supplementary Table III). Table II shows data on the echocardiogram, CCTA and patient risk scores, preoperative cardiovascular assessment, and functional status. Most patients had a normal left ventricular ejection fraction (64% [IQR: 61; 68%]) without chamber dilation. The median Agatston's total score was 47 (IQR: 0; 187), and most patients had at least one obstructive vessel (70.7%), while 40 patients (21.7%) had at least one obstructive lesion classified as moderate (with an obstruction equal to or higher than 50%). The CTFFR assessment, conducted in moderate lesions, revealed ischemia in 35% of cases. These patients were re-evaluated by the cardiology team, and management decisions were made according to institutional protocols. When necessary, further diagnostic tests, such as coronary angiography, were performed to confirm the severity of coronary lesions. In cases where significant stenosis was confirmed, percutaneous coronary intervention (PCI) was performed when clinically indicated, although we prioritized avoiding delays in cancer treatment. We performed angiography in 12 patients, and five were submitted to PCI.

Most of the population exhibited favorable functional capacity, as defined by their metabolic requirements. The Revised Cardiac Index Risk classified most of the patients as having a high risk for cardiovascular complications, while the Destky risk classification identified patients as having a low risk for cardiovascular complications after surgery.

Table II.—*Preoperative echocardiography, coronary computed tomography angiogram data and risk scores of patients.*

Variables	N.=184
Echocardiographic variables	
Left atrium (mm)	38 (34-41)
Septum (mm)	10 (9-11)
PP (mm)	9 (9-10)
LV diastolic diameter (mm)	47 (43-50)
LV systolic diameter (mm)	30 (27-32)
LVEF (%)	64 (61-68)
Variables obtained from coronary CT angiography	
Agatston's Total Score	47 (0-187)
Agatston's Total Score (Rank)	
0	51 (27.7%)
1-100	64 (34.8%)
101-400	42 (22.8%)
>400	27 (14.7%)
Number of vessels with obstruction	
No vessel	54 (29.3%)
One vessel	32 (17.4%)
Two vessels	40 (21.7%)
Three vessels or more	58 (31.5%)
Coronary obstruction ≥50%*	40 (21.7%)
CTFFR≤0.75	14 (35.0%)
Risk Score	
METS	
>7	79 (43.2%)
4-6	82 (44.8%)
<4	22 (12.0%)
Detsky risk classification**	
I (0-15 points)	181 (99.5%)
II (20-30 points)	1 (0.5%)
RCRI Score***	
Class I	2 (1.1%)
Class II	155 (84.2%)
Class III	27 (14.7%)

CT: computed tomography; CTFFR: computed tomography-derived fractional flow reserve; LV: left ventricle; LVEF: left ventricular ejection fraction; METS: metabolic equivalent score; PP: posterior wall.
Data are presented as N. (%) or median (IQR: interquartile range).
*At least one artery with an obstructive lesion ≥50%; **Detsky risk classification: Class I – low risk of cardiac complications (relative risk 0.48%), Class II – moderate risk (relative risk 3.38%). ***RCRI: Revised Cardiac Risk Index (Class I: 0 predictor, low risk (0,4%), Class II: 1 predictor, moderate risk (0,9%) Class III: 2 predictors, high risk 6,6% Class IV: 3 or more predictors (very high risk 11%).
Missing values were as follows: METS (0.5%), Detsky risk classification (1.1%).

Outcomes

The primary outcome, myocardial injury within 72 hours of surgery, occurred in 87 patients (47%). Combined events occurred in 70 patients (37.6%). The most frequent complications were acute renal failure in 55 patients (29.9%) and septic shock in 20 patients (10.9%). Cardiac arrhythmia was diagnosed in five patients (2.7%), thromboembolic events in three patients (1.6%), stroke in one patient (0.5%), and acute myocar-

Table III.—*Outcomes.*

Outcomes	Total=184 N. (%)
Primary outcome	
Myocardial injury	87 (47.3%)
Secondary outcomes (12 months)	
Combined events	70 (37.0%)
Renal Failure (AKIN≥1)	55 (29.9%)
AKIN Classification	
0	129 (70.1%)
1	39 (21.2%)
2	14 (7.6%)
3	2 (1.1%)
Septic shock	20 (10.9%)
Arrhythmia	5 (2.7%)
Stroke	1 (0.5%)
Thromboembolic events	3 (1.6%)
Acute myocardial infarction	1 (0.5%)
Cardiovascular death	1 (0.5%)
All-cause death	15 (8.2%)
Duration of anesthesia (min), median (IQR)	450 (360-563)
30-day hospital readmission	27 (14.7%)
ICU length of stay (days), median (IQR)	2 (1-4)
Hospital length of stay (days), median (IQR)	8 (6-12)

AKIN: Acute Kidney Injury Network; ICU: intensive care unit; IQR: Interquartile range.
Data are presented as median and interquartile range; absolute and relative frequencies.
Missing values were as follows: METS (0.5%), Detsky Risk Classification (1.1%), duration of anesthesia (0.5%).

dial infarction in one patient (0.5%). Cardiovascular death occurred in one patient, and death by all causes occurred in 15 patients (8.2%). The hospital readmission rate in 30 days was 14.7% (27 patients), the ICU stay median time was two days (IQR: 1; 4), and the hospital stay median time was eight days (IQR: 6; 12) (Table III).

The patients who developed myocardial injury were older (69 [IQR: 64; 74] years *versus* 64 [IQR: 59; 70] years, P=0.001) and had a higher prevalence of male sex (64.4% *vs.* 49.5%) (Supplementary Table IV). In addition, myocardial injuries occurred more frequently among patients with esophageal and bladder cancer (Supplementary Table V).

In patients with MINS, the following differences were observed compared to those who did not experience MINS: higher creatinine levels (0.91 mg/dL [IQR: 0.76; 1.13] *vs.* 0.8 mg/dL [IQR: 0.71; 0.96]), elevated NT-proBNP levels (112 pg/mL [IQR: 78; 223] *versus* 78 pg/mL [IQR: 32; 223]), and reduced albumin levels (4,0 [IQR: 3.9; 4.2] *versus* 4.2 [IQR: 3.9; 4.6]) (Supplementary Table VI).

Patients with MINS had significantly longer surgical procedures (345 min [IQR: 245; 422] *vs.* 300 min [IQR: 236; 420], P=0.041) and an extended anesthesia duration (480 min [IQR: 390; 600] *vs.* 420 [IQR: 343; 540], P=0.007), a greater need for vasopressors. (44.7% *vs.* 22.8%, P=.007). *versus* the group without MINS 21 [22.8%], P=0.002) and a higher rate of blood transfusion (group MINS 18 [20.9%] *versus* 7 [7.2%], P=0.007) (Supplementary Table VII).

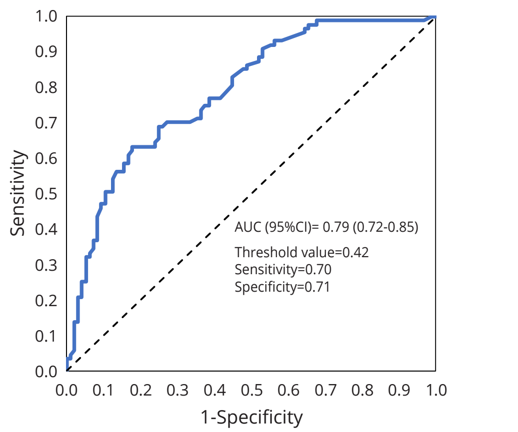
Patients with MINS exhibited a higher Agatston calcium score (97 [IQR: 1; 356] *vs.* 25 [IQR: 0; 120]), a greater prevalence of calcium score falling within the range of 401-1000 (11.5% *vs.* 3.1%), P=0.013, and an increased occurrence of obstructive disease as diagnosed through CCTA (Supplementary Table VIII).

A multivariate logistic regression analysis us-

Table IV.—*Multivariate logistic regression model for myocardial injury.*

Variables	Estimated parameter	Standard error	OR	95% CI		P
Primary location of the tumor Bladder	2.340	0.726	10.39	2.50	43.09	0.001
Primary location of the tumor Esophageal	2.013	0.600	7.48	2.31	24.25	0.001
Total Agatston coronary calcium score (classification)						0.012
0			Reference			
1-100	0.089	0.429	1.09	0.47	2.53	0.836
101-400	0.799	0.484	2.22	0.86	5.74	0.099
>400	1.640	0.565	5.16	1.71	15.59	0.004
Duration of anesthesia (min)	0.219	0.001	1.24	1.08	1.42	0.002
Constant	-2.652	0.682				

CI: confidence interval; OR: odds ratio.
Missing values were as follows: Duration of anesthesia (0.5%).



Probability of myocardial injury:

$$P_{\text{Myocardial injury}} = \frac{e^{2.340\ \text{Bladder} + 2.013\ \text{Esophageal+Agatston} + 0.219\ \text{Anesthesia duration} - 2.652}}{1 + e^{2.340\ \text{Bladder} + 2.013\ \text{Esophageal+Agatston} + 0.219\ \text{Anesthesia duration} - 2.652}}$$

where:
e = base of the natural logarithm
Bladder = 1 if the primary location of the tumor is the bladder, otherwise 0
Esophageal = 1 if the primary location of the tumor is esophageal, otherwise 0
Agatston:
1: if Agatston score is 0
2: if Agatston score is between 1 and 100
3: if Agatston score is between 101 and 400
4: if Agatston score is greater than 400
Anesthesia duration is measured in hours

Figure 2.—Receiving operator characteristic (ROC) curve for the multivariate logistic regression model for myocardial injury.
AUC: area under curve.

ing a stepwise procedure was performed to assess MINS predictors. The predictors were primary tumor in the bladder (OR 10.40 [CI 95% 2.51; 43.20], P=0.001) and esophagus (OR 7.39 [CI 95% 2.27; 24.08], P=0.001), a longer duration of anesthesia (OR 1.24 [CI 95% 1.09; 1.43], P=0.002), a calcium score of 401-1000 (OR 5.92 [CI 95% 1.29; 27.08], P=0.022) and a calcium score >1000 (OR 4.62 [CI 95%1.18-18.04], P=0.028) (Table IV).

Figure 2 represents the Receiving Operator Characteristic (ROC) curve for the multivariate logistic regression model for MINS. The diagnostic accuracy was 0.79 (CI 95% 0.72; 0.95, P<0.001).

The probability of MINS was estimated considering tumor location, time of anesthesia, and classification by the Agatston calcium score. The cut-off value of P=0.43 observed in Supplemental Figure 1 represents the greatest sensitivity and specificity of the multivariate logistic regression model for myocardial injury. Patients diagnosed with bladder cancer had an elevated probability of MINS occurrence, regardless of the anesthesia duration and calcium score. Conversely, patients with esophageal cancer and calcium score >100 also demonstrated an increased probability of MINS, regardless of the anesthesia duration. In patients with a score of 0-100, the likelihood of MINS increases when the anesthesia duration exceeds 90 minutes. Among patients with other types of cancer, the probability of MINS rises when their score reaches 400, combined with an anesthesia duration exceeding 180 minutes.

Patients with MINS had a higher occurrence of combined events (59.8% *vs.* 18.6%, P<0.001). MINS was associated with a higher incidence of acute renal failure (45.9% *vs.* 15.5%, P<0.001), septic shock (19.5% *vs.* 3.1%, P<0.001), arrhythmia (5.7% *vs.* 0, P=0.022), all-cause death (16.1% *vs.* 1%, P<0.001) and a longer ICU length of stay [4(IQR: 2; 5) *vs.* 2(IQR: 0; 3), P<0.001] (Supplementary Table IX).

A Cox proportional hazards model for the combined endpoint was performed to assess predictors of postoperative complications. Predictors for combined events were CCTA with coronary lesions ≥3 vessels (HR 2.10 [CI 95% 1.11;3.96, P=0.022]), intraoperative hypotension (HR 1.02 [1.00; 1.04], P=0.019) and elevated preoperative creatinine (HR 4.71 [1.60; 13.88, P=0.005]) (Supplementary Table X).

Discussion

In cancer patients undergoing high-risk surgery, MINS was frequent (48%). In our investigation, the use of CCTA enabled the accurate identification of patients who developed myocardial injury and postoperative clinical complications. A multivariate logistic regression analysis identified bladder cancer, esophageal cancer, a prolonged duration of anesthesia, calcium score between 400 and 1000, and calcium score greater than 1000 as independent predictors of MINS.

To our knowledge, no previous study has evaluated the value of the calcium score and CCTA in cancer patients undergoing noncardiac major surgery. In a retrospective single center observational study, Yang *et al.* addressed the use of nongated computed tomography in intermediate-risk patients undergoing lung cancer surgery. In this setting, calcium score was associated with cardiovascular events and a prolonged hospital stay. Additionally, a greater calcium score was predictive of cardiovascular complications.[15] Nevertheless, CCTA was not performed in this investigation.

In a nononcologic setting, the largest study performed thus far was the VISION a prospective cohort evaluating 955 patients undergoing noncardiac surgery.[16] Preoperative CCTA findings improved the risk estimation of perioperative cardiovascular death or myocardial infarction.[17] A Korean study evaluated calcium score and the degree of coronary stenosis in the prediction of cardiovascular events in 239 patients undergoing intermediate-risk noncardiac surgery. They found that patients with multivessel coronary artery disease (2- and 3-vessel disease) had more events than patients with no stenosis or single-vessel disease. Moreover, calcium score was higher in patients who developed cardiac events, and the ROC curve analysis showed a reasonable performance of calcium score in the prediction of cardiac events.[18] Furthermore, a systematic review including 11 studies and 3,480 patients showed that the occurrence of perioperative major adverse cardiovascular events (MACE) increased with the severity of coronary artery disease on CCTA. Additionally, a greater calcium score was associated with higher perioperative risk, and a calcium score >1000 conferred an OR of 10.4, 95% CI 1.6; 69.7, $P<0.01$.[19] In a retrospective study conducted in 443 liver transplant recipients, a preoperative calcium score > 400 predicted cardiovascular complications developing within one month after surgery.[20] Finally, in a far greater at-risk population of 179 type-2 diabetes patients undergoing trans-femoral amputation, the greater the calcium score was, the lower the MACE-free survival rate, and likewise, a greater severity of coronary stenosis on CCTA was associated with lower MACE-free survival rates.[21]

In this study, we found that calcium scores were significant predictors of myocardial injury after high-risk noncardiac surgery in cancer patients. Notably, patients with an Agatston calcium score between 401-1000 had a higher risk of postoperative myocardial injury compared to those with scores >1000. This seemingly paradoxical finding may be explained by differences in plaque composition and stability. Patients with calcium scores in the range of 401-1000 are likely to have a mix of calcified and vulnerable plaques, which are more prone to rupture under the stress of surgery, leading to higher rates of myocardial injury. In contrast, very high calcium scores (>1000) often represent heavily calcified, more stable plaques, which, while indicating a greater overall atherosclerotic burden, may carry a lower risk of acute rupture. Additionally, patients with extremely high calcium scores may be more likely to have undergone aggressive cardiovascular management or monitoring, further reducing their risk of perioperative complications. The calcium score proved to be one of the five significant predictors of MINS, with a diagnostic accuracy of 0.79. This robustness in the final model indicates that the calcium score plays an important role in predicting MINS, possibly reflecting its ability to indicate the presence of underlying coronary artery disease that may affect the risk of myocardial injury. This highlights the value of coronary computed tomography in refining risk stratification and guiding clinical decisions in cancer patients undergoing major surgeries.

In agreement with the literature, MINS was a frequent phenomenon and was associated with relevant clinical complications.[10] Furthermore, our study was conducted in a large tertiary care referral center, which may account for the higher occurrence of MINS compared to previous studies.[22]

The use of CCTA has not been incorporated in recent perioperative care guidelines,[23] primarily due to the results of the last VISION study,[22] which reported an overestimated risk shown by CCTA in patients who did not develop a cardiac event. However, it is essential to recognize that such findings may not be directly applicable to cancer patients. Our population included individuals undergoing major surgery, compromised to a significant degree by the burden of their oncologic disease, as indicated by ECOG and Karnofsky scores, and the impact of cancer therapy, with the majority of patients receiving chemotherapy. These factors can significantly affect the individual physiologic reserve and increase their susceptibility to surgical stressors such as prolonged surgery and anesthesia, fluid loss and hypotension.

Intraoperative hypotension was observed frequently in our study, with a median duration of 60 minutes. Prolonged hypotension is concerning, as it has been associated with adverse outcomes, including myocardial injury after noncardiac surgery (MINS) and acute kidney injury (AKI). The high incidence of hypotension in our cohort may reflect the complexity and extended duration of the surgeries, along with significant fluid shifts and blood loss. Furthermore, the presence of multiple cardiovascular risk factors in our patient population predisposed them to hemodynamic instability, increasing their vulnerability to hypotensive episodes.

The use of anesthetic agents, such as propofol and inhalational agents, may have further contributed to systemic vasodilation. Additionally, vasopressor support was required in 33% of patients, reflecting the challenge of maintaining optimal BP during major oncologic procedures. Hypotension is a known contributor to MINS, with impaired myocardial perfusion and increased oxygen demand potentially precipitating myocardial injury. Similarly, sustained low BP can reduce renal perfusion, elevating the risk of AKI. Given these findings, our results underscore the need for meticulous intraoperative hemodynamic management. Strategies such as goal-directed fluid therapy, continuous invasive BP monitoring, and early vasopressor use should be considered in high-risk patients to mitigate the effects of hypotension. Preoperative cardiovascular risk stratification, including CCTA, may also help identify patients who could benefit from more intensive perioperative hemodynamic monitoring.

The currently available preoperative risk scoring systems often lack the specificity needed to address the unique aspects of different patient populations. Therefore, the use of a prognostic tool such as calcium score may prove valuable in identifying the highest risk patients and directing resources towards optimizing perioperative management in this specific context.

Limitations of the study

Our study has some limitations. First, the observational nature of the study limited our ability to entirely eliminate confounding variables. However, we employed additional methods to enhance our understanding of the causal relationship of calcium score on MINS, such as stratifying the calcium score estimation according to the primary location of the tumor. Second, the exclusion of patients with renal failure and a history of ischemic heart disease may have introduced selection bias to our findings. Nevertheless, our findings may still be relevant to patients who are unable to undergo preoperative cardiovascular stress testing. Finally, there is a potential for observer bias, as patients with more severe CCTA and calcium score may have received more extensive assessments. To address this limitation, the outcome assessors in our study were kept unaware of the CCTA and calcium score reports.

Conclusions

In cancer patients undergoing high-risk noncardiac surgery, CCTA was able to identify with high accuracy the subgroup of patients who developed myocardial injury and postoperative clinical complications. Factors such as bladder and esophageal tumors, extended anesthesia duration, and Agaston's calcium score exceeding 400 were identified as predictors for postoperative myocardial injury. This suggests that the incorporation of CCTA into risk assessment protocols may be valuable in evaluating high-risk surgical cancer patients.

What is known

- Over 300 million major surgeries occur annually, with 10-20% being high-risk, leading to 80% of postoperative mortality. Advances in cancer care have extended lifespans but increased surgical risks due to therapies and surgeries causing endothelial injury, inflammation, and related complications.
- Traditional preoperative scoring systems

often exclude cancer patients and mainly focus on major cardiovascular complications. The role of imaging methods in predicting risk for cancer patients undergoing high-risk surgeries remains unclear.

What is new

- CCTA effectively identifies cancer patients at risk for postoperative myocardial injury by highlighting high calcium scores.
- In high-risk surgical settings, cancer patients with elevated calcium scores on CCTA are more likely to experience postoperative myocardial injury.
- Utilizing CCTA to identify high calcium scores offers a valuable method for predicting and managing postoperative myocardial injury risk in cancer patients undergoing high-risk surgeries.

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Conflicts of interest
The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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