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ASSOCIATION BETWEEN INTRAOPERATIVE ELECTROLYTE AND ACID–BASE DISTURBANCE WITH ACUTE POSTOPERATIVE MYOCARDIAL INJURY IN LUNG CANCER RESECTION UNDER ONE-LUNG VENTILATION

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Abstract

Background Postoperative myocardial injury and its correlation with intraoperative electrolytic and acid-base disorder are not clear. This study sought to determine postoperative myocardial injury incidence and its potential link with intraoperative electrolytic and acid-base disorder for patients without cardiovascular and renal diseases scheduled for lung cancer resection.
Purpose The present study sought to determine the incidence of acute postoperative myocardial injury and associated–risk factors, and assess its potential relationship with intraoperative electrolytes and acid–base disorders in patients without known cardiovascular and renal diseases who underwent elected lung cancer resection.
Methods This retrospective observational study received approval from the Medical Ethics committee of NanFang Hospital of Southern Medical University, and adheres to the STROBE principles. This study enrolled every patient scheduled for lung cancer resection. The exclusion criteria included patients with cardiovascular and renal diseases, preoperative hs–cTnT and NT–proBNP levels ≥ 0. 14 ng/ml and ≥ 125 pg/mL, respectively, and an eGFR< 45 ml/min. Statistics were handled via 25 IBM SPSS software packages, and the chi–square test was used to compare categorical variables. A P–value less than 0.05 was considered statistically significant.
Results Among the 1175 clients, acute postoperative myocardial injury occurred in 79 (6.7%) clients. Electrolytic imbalance, sex, type of resection, intraoperative transfusion, one–lung ventilation and surgery durations, and estimated blood loss were identified as factors for postoperative myocardial injury. Among the 79 patients who experienced postoperative myocardial injury, 78(98.7%) patients had experienced intraoperative electrolyte disorder, and electrolytic disorder was therefore associated with postoperative myocardial injury [P<0.001, OR95%CI: 22.1(3.06~159.71)].
Conclusions In this study, the incidence of postoperative myocardial injury was 6.7%, and electrolytic disorders were a relevant associated-risk factor. Even patients without known cardiovascular and renal diseases prior to surgery may experience acute postoperative myocardial injury. Systematic cardiac biomarkers screening before and after lung cancer surgery may help to prevent or reduce its incidence.

Keywords: lung, cancer, resection, electrolytic, disorder, myocardial, injury.

I. INTRODUCTION

Anesthesia for lung resection due to early–stage non–small–cell lung cancer (NSCLC) is common worldwide. Lung cancer resection is included in more than 300 million of noncardiac surgeries(NCSs) performed worldwide each year[1–4]. Nearly 20% may experience postoperative major adverse cardiovascular events (MACEs)[4–7]. One–lung ventilation (OLV) is an anesthesia technique widely applied in lung cancer resection. OLV is known to cause electrolytes and acid–base disorders(EADs) via the hypoxemia induced by frequent ventilation-to-perfusion (V/Q) mismatch[8,9]. OLV may, then, exacerbate the EADs which are already at a high prevalence until 64%[10] in lung cancer patients. Unlike in the USA, the incidence of lung cancer, which is dominated by NSCLC, is still steadily increasing in China[8–10]. Surgery, at an early stage, is a treatment of choice with encouraging outcomes[11–15]. Although number of intraoperative deaths associated with surgery and anesthesia has dramatically decreased during recent decades, postoperative mortality due to postoperative myocardial injury (MI) remains a very large concern. It accounts for 1–2 % of surgery-related deaths [2,16] and represents 7.7% of all deaths[3]. MI pathophysiology involves a cardiomyocyte oxygen supply–demand mismatch as a primary culprit[7,17]. MI can evolve towards atrial fibrillation (AF), defined as new–onset AF after surgery without a previous history of AF[21] which can trigger of stroke[22]. Moreover, AF can induce thromboembolism, myocardial infarction and congestive heart failure (CHF)[23]. A secondary analysis of randomized control trials (RCTs) revealed that many NCSs components, comprising abdominal, orthopedic, heart and neurosurgical or NCS components, in general, with related–postoperative MI complications, have been sufficiently addressed[21–24]. However, lung cancer resection–associated postoperative MI, has not yet been fully assessed[25,26]. The scarce evidence reported in the literature concerned only very high–risk patients (65 years older and above or 45 years older and above with known chronic diseases). The highest postoperative incidence usually occurs within two (2) days after NCS[30]. The perioperative prevention of acute postoperative MI still equivocal[28–30]. Actually, much attention is focused on same ongoing RCTs: a perioperative cardioprotection via the perioperative ischemic evaluation (POISE)-3 study and the STOP–or–NOT trial (NCT03374449), an ongoing open–label RCT undertaken to evaluate tranexamic acid for POISE and the impact of stopping or continuing ACE/ARB medication 2 days prior to NCS[27]. The third is a triple–blind, international, multicenter, randomized, placebo-controlled, parallel group randomized trial called the "Funny" RCT[34], which sought to investigate potential properties of ivabradine 2.5–7.5 mg TID vs a placebo for MI prevention. Ivabradine is known as a hyperpolarization-activated cyclic nucleotide–gated–4 (Funny) channel blocker and is a relatively novel medicine used to control heart rate at sinus rhythm (≥70 beats/min) for the symptomatic management of stable angina pectoralis, and HF from dilated cardiomyopathy in adult patients. In contrast to beta–blockers and nondihydropyridine calcium channel blockers, which have undesirable side effects due to their negative inotropic effects; ivabradine that selectively inhibits the "funny"(If) channel pacemaker current in the sinoatrial node in a dose-dependent manner, was designed as a pure HR–lowering drug without negative impact on autonomic control, heart contractility, or blood pressure[34]. Thus, MI management continues to elude consensus, which, ipso facto, keeps NCS an area of extensive research[27] until complete understanding and addendum to current existing guidelines are gained[5]. Hs–cTnT and NT–ProBNP are reliable cardiac biomarkers for detecting this silent complication, which can be triggered by anesthesia and surgical procedure–induced stress[5,6,35–40]. To date, very few studies have investigated the incidence of intraoperative EADs and their impact on postoperative outcomes in lung resection. It is also unclear whether relatively young and healthy patients are exempt from acute postoperative MI. Research has recommended studies including thoracic surgery with a population not at high–risk, for better management of postoperative MI[41]. We hypothesized that intraoperative EADs may predict postoperative MI during lung cancer resection.

This study aimed to determine the incidence of acute postoperative MI and associated-risk factors.

The secondary objectives were to (1) determine the incidence of intraoperative EAD and identify associated risk-factors, (2) investigate whether intraoperative EAD is associated with postoperative MI during lung cancer resection in patients without cardiovascular and renal diseases, and (3) explore the interactive effects of anesthesia -related factors with EAD for postoperative MI prevention.

II.MATERIALS AND METHODS

Study design, setting and ethics: The present study is a retrospective observational cohort study conducted at a teaching and tertiary hospital named NanFang Hospital located in Guangzhou, southern China. Procedure complied with the 2020 checklist of STROBE principles and is carried out in the spirit of the declaration of Helsinki 2013. Ethical clearance was gotten via Medical Ethics committee of NanFang Hospital of Southern Medical University, before data collection. Written informed consent was waived by the same Medical Ethics committee of NanFang Hospital of Southern Medical University, as it is feasible for retrospective studies.

Study population: This study included both female and male patients of all ages who underwent elective lung cancer resection under OLV. After ethical clearance (Approval letter N°. NFEC-2023-466), variables were collected. The exclusion criteria included an ASA physical status greater than III, pregnancy, organ transplantation and cardiovascular insults, a high HR (above120 beats/minute), an eGFR <15 ml/min, hs-cTnT ≥14 ng/mL and NT–proBNP ≥125 pg/mL before surgery, coronary artery disease, and stroke prior to surgery. Patients whose postoperative hs–cTnT and NT–proBNP levels within two days after surgery, scr levels, HR and LVEF were not reported were also excluded. The exclusion criteria also included secondary causes of cTn elevation, such as direct myocardial trauma, pericarditis, sepsis, pulmonary embolism and severe renal failure[3, 42].

Outcome screening, definition and variable collection The primary endpoint of the present study is acute postoperative MI confirmed by, at least, one positive measurement within one week after surgery. An hs–cTnT concentration of ≥14 ng/mL[43], as used in the BASEL–PMI study and other researchers[3,20,42,44], and/or a NT–ProBNP of ≥300 pg/mL [5,45,46], as adopted by Nanfang Hospital, were considered positive. This study analyzed the three most important electrolytes[47] usually recorded in blood gas analysis (BGA), which are serum sodium, potassium and calcium. With respect to the habits of NanFang Hospital on clinical anesthesia conduct, electrolytes imbalances were accepted with values out of follow normal range of 135–135 mmol/L, 3–5.5 mmol/L and 1.2–2.5 mmol/L for sodium, potassium and calcium, respectively. Acid–base disorder assessed by pH, BE and HCO_3^- values out of follow normal range of 7.35–7.45, -3–3mlEq/L, and 22–26mmol/L, respectively[48].

Sociodemographic data included age, sex, patient BMI, baseline systolic blood pressure (SBP), serum sCr, hs–cTnT, NT–proBNP, smoking status, surgery type, and OLV and surgery duration. The collection of intraoperative variables concerned the latest invasive Mean arterial pressure (MAP) and SBP, highest HR, urine output, postoperative pain control technique, type of resection, fluid intake, access balance, and estimated blood loss. Sodium, calcium, potassium, bicarbonate, potential hydrogen (pH), BE (B), latest blood glucose, and hemoglobin (HB) levels were collected. Postoperative data included hs–cTnT and NT–pro BNP, HR, LVEF and sCr values at one week. Data were collected at Nanfang Hospital from October 2023 until January 2024.

Statistical analysis: Variables were coded and recoded into IBM SPSS version 25. We expressed baseline sociodemographic data as the mean, median, standard deviation (SD), minimum, maximum or number (%) as indicated in the descriptive statistics table. Categorical data are presented as counts (numbers) and percentages (%). Univariate regression analysis, along with the odds ratio (OR) and 95CI, was performed via the Pearson chi–square test. All covariates were entered into a multivariate regression analysis model to identify relevant outcome risk- factors. A P–value less than 0.05 was considered statistically significant. The final results are displayed in tables and figures.

III. RESULTS

Among 3348 patients who underwent noncardiac thoracic surgery between 2019 and 2022, 659 patients were not undergoing lung surgery and were excluded early. One thousand three hundred four (1304) patients were excluded for data incompleteness and inconsistency, whereas 87 patients were found not to have NSCLC and were subsequently excluded. The remaining patients (n=1385) were carefully checked. One hundred thirty-nine (139) patients were pregnant, had chronic cardiovascular and renal diseases; had undergone organ transplantation; had elevated preoperative cTnT and NT–proBNP; had a postoperative hospital stay of less than 2 days; and had CHF with a LVEF of less than 35%. This study ultimately included a cohort of 1175 patients, as shown in Figure1 below.

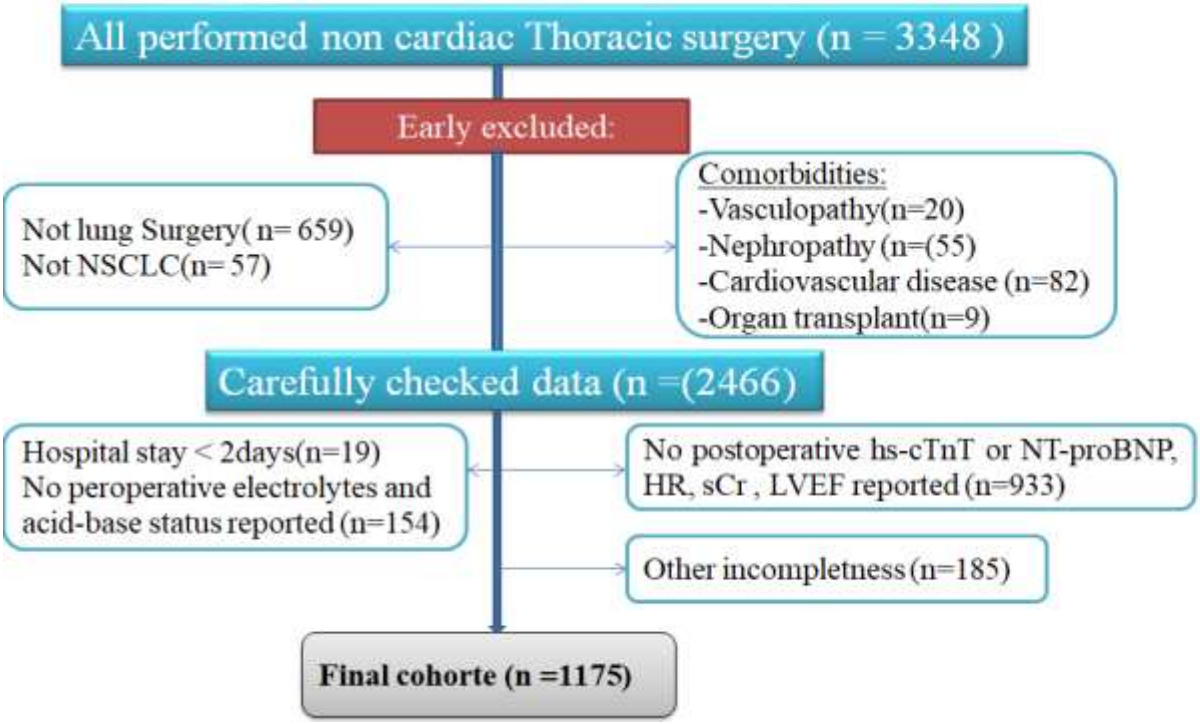


Fig.1 Study flow chart showing how we obtained our cohort

In this study, the mean age of the patients was 58.9 years, the median age was 59 years, with a minimum age of 13 years, and the maximum age was 86 years. Male sex represented 60%, and female sex represented 40%, with two types of resection: segmentectomy (seg) and lobectomy (lobe) with respective frequencies of 10.2% and 89.8%. The mean durations of surgery and OLV were 165 and 188 minutes, as displayed in Table 1.

Variable	Mean ±SD	Median (min, max)
Patient age (year)	58.9±10. 689	59(13,86)
BMI	23.15±3.20	23.01(14.53,36.51)
ASA-PS I/II/III/IV (%)	7.06 / 83.39	9.40 / 0.35
Baseline HR	77.21±5.74	7(53.57, 106.33)
Baseline SBP (mmHg)	123.99±11.175	123.5(88,176)
Baseline hs-cTnT	0.00795±0.0104	0.006(0.001, 0.134)
Baseline NT-proBNP	54.627±35,202	46.45(4.99,124.8)
Baseline sCr	74.08±20.688	71(24,254)
Duration of surgery(min)	165.35 ±63.58	155(31, 467)
Intraoperative HB (latest)	129.37±18.119	129(41,186)
Intraoperative MAP(latest)	54.68±13.733	57(21,96)
OLV duration(min)	187.71±64.223	178(38,492)
Total inflow fluid(mL)	1552.16±753.47	1000(20,3500)
Access balance(mL)	1044.81±532.47	1500(150,4400)
Estimated blood loss(mL)	94.41± 160.80	50(5,2000)
Sex: Female / Male (%)	40	60
Smoking: No+ Stopped / yes (%)	79.9	20.1
Resection type : Seg/Lob (%)	10.2	89.8

Table 1: Patient characteristics

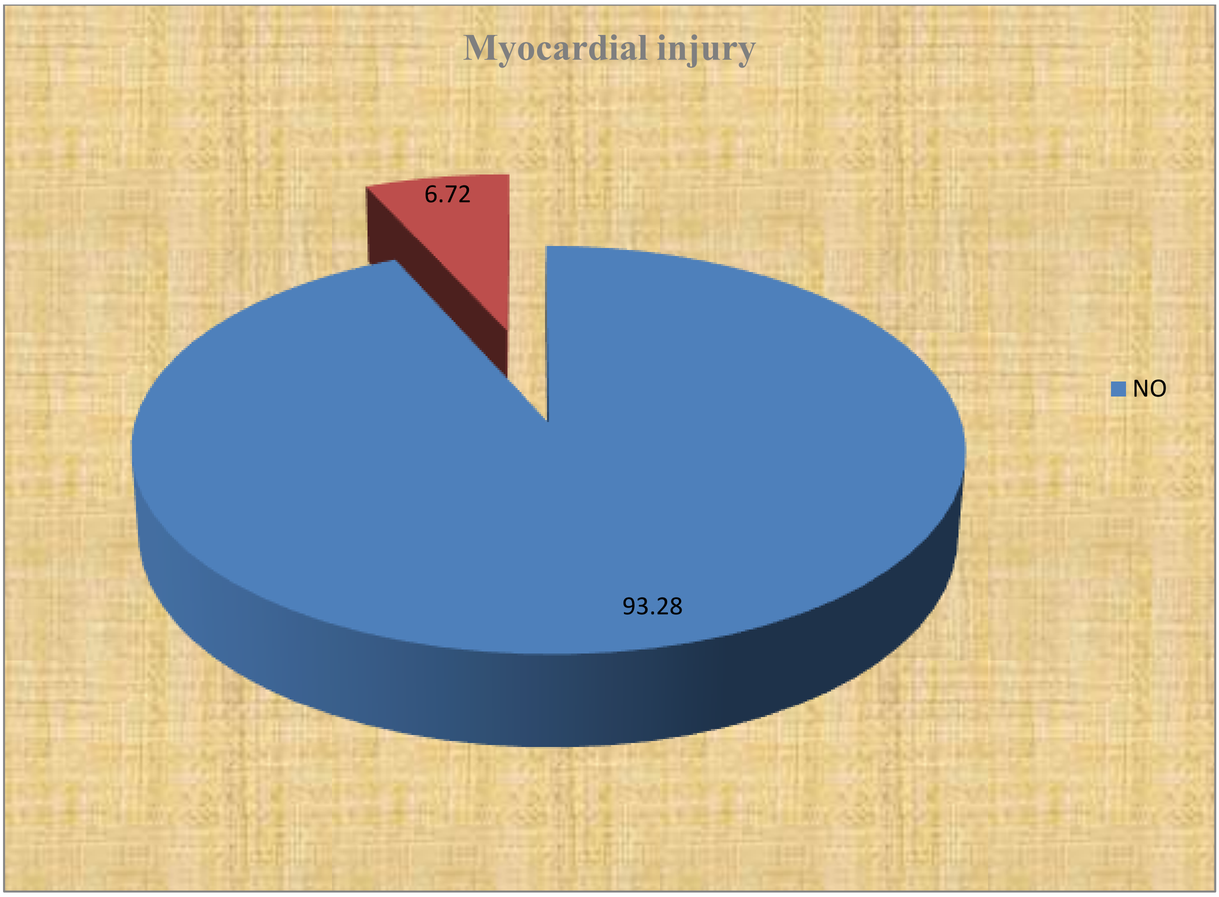


Fig. 2 Global incidence of myocardial injury among patients who underwent lung resection

0=No myocardial injury incidence (93.28%)

1= Yes myocardial injury incidence (**6.72%)**

After univariate analysis, the factors associated with MI were sex, electrolyte imbalance, type of surgery, intraoperative transfusion, invasive latest Hb, OLV duration, surgery duration and estimated blood loss, as shown in Table 2 below. These results were obtained before adjusting the OR, as shown in Table 4 above. Acid–base imbalance is likely to influence the occurrence of myocardial injury.

Variable	**Group**	**n**	**%**	MI occurrence:		**p Value**	COR95%CI
				Yes	No		
Age(years)	<45	235	20	24(10.2)	211(89.8)		1
	[45,69]	860	73.2	51(5.9)	809(94.1)	0.735	1.20 (0.42 ~
	≥70	80	6.8	3.40)			
Sex	Male	705	60	4(5)	76(95)	0.055	2.16 (0.73 ~
	Female	470	40	6.43)			
Vasopressors	No	271	23	59(8 .4)	649(91.6)		1
	Yes	904	77	20(4.3)	450(95.7)	**0.006**	0.49 (0.29 ~ 0.82)
Electrolytic	NO	243	20.7	13(4.8)	258(95.2)		1
imbalance	Yes	932	79.3	66(7.3)	838(92.7)	0.149	1.56 (0.85 ~ 2.88)
Acid–base	No	223	19	1(0.4)	242(99.6)		1
imbalance	yes	952	81	78(8.4)	853(91.6)	**<0.001**	22.1
	No	193	16.4	(3.06~159.71)			
PCIA use	Yes	982	83.6	9(4)	214(96)		1
Access balance(mL)	<1000	597	50.8	70(7.4)	882(92.6)	0.075	1.89 (0.93 ~ 3.84)
	≥1000	578	49.2	14(7.3)	179(179.7)		1
Intraoperative	<10	961	81.8	65(6.6)	717(93.4)	0.748	1.56 (0.85 ~
latest	≥10	214	18.2	2.88)			
blood glucose	Lob	1057	89.8	3(5.5)	564(94.5)		1
Type of resection	Seg	118	10.2	46(8)	532(92)	0.096	0.91 (0.50 ~ 1.65)
	No	1109	94.4	66(6.9)	895(93.1)		1
Intraoperative	Yes	66	5.6	13(6.1)	201(93.9)	0.675	0.88 (0.47 ~ 1.62)
transfusion	<25	860	73.2	63(6)	994(94)		1
BMI (kg/m2)	≥25	315	26.8	16(13.6)	102(86.4)	**0.002**	2.47 (1.38 ~
	No	939	79.9	4.44)			
Smoking status	Yes	236	20.1	64(5.8)	1041(94.2)		1
	<120	283	24	15(21.4)	55(78.6)	**<0.001**	4.80 (2.56 ~
Baseline SBP	≥120	670	76	9.00)			
(mmhg)	<90	849	72.2	64(7.4)	796(92.6)		1
	≤90	326	27.8	15(4.8)	300(95.2)	0.104	0.62 (0.35 ~ 1.11)
Invasive latest SBP	<70	1012	86.1	60(6.4)	879(93.6)		1
	≥70	163	13.9	19(8.1)	217(91.9)	0.362	1.28 (0.75 ~
Latest Invasive	<100	89	7.6	2.19)			
MAP	≥100	1086	92.4	18(6.4)	265(93.6)		1
(mmHg)	<188	628	53.4	40(6)	630(94)	0.818	0.61 (0.35 ~
Invasive latest Hb	≥188	547	46.6	1.05)			
(g/L)	<1500	462	39.3	57(6.7)	792(93.3)		1
OLV duration(min)	≥1500	713	60.7	22(6.7)	304(93.3)	0.983	1.01 (0.60 ~
	<165	641	54.5	1.67)			
Total inflow	≥165	534	45.5	71(7)	941(93)		1
fluid(ml)	<150	974	82.3	8(4.9)	155(95.1)	0.319	0.68 (0.32 ~
	≥150	201	17.7	1.45)			
Surgery				24(27)	65(73)		1
duration(min)				55(5.1)	1031(94.9)	**<0.001**	0.14 (0.08 ~
Estimated blood				0.23)			
loss				8(1.3)	620(98.7)		1
(mL)				71(13)	476(87)	**<0.001**	11.56
				(5.51~24.24)			
				24(5.2)	438(94.8)		1
				55(7.7)	658(92.3)	0.092	1.53 (0.93 ~
				2.50)			
				30(4.7)	611(95.3)		1
				49(9.2)	485(90.8)	**0.002**	2.07 (1.29 ~
				3.30)			
				59(6.1)	915(93.9)		1

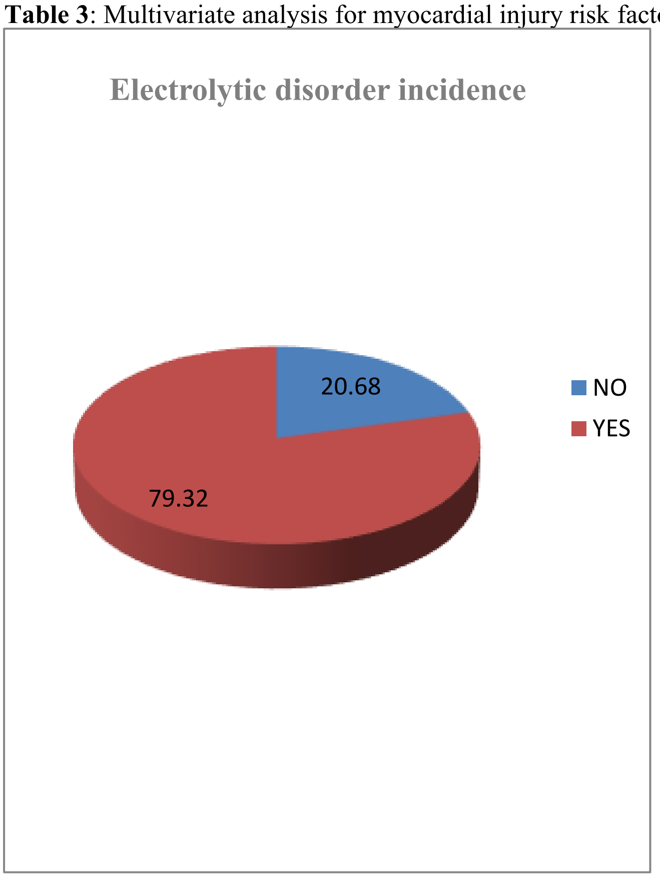
20(10) 1.48)	181(90)	**0.045**	0.35 (0.08 ~			

Table 2: Univariate regression analysis for MI factor identification

The multivariate regression analysis results in Table 5 show that electrolytic imbalance, intraoperative transfusion, invasive latest hemoglobin and OLV duration, modifiable and anesthesia- related factors, are strongly associated with postoperative myocardial injury.
After adjusting the odds ratios for age, sex, and other covariates, the relevant factors associated with the outcomes of the present study are displayed in Tables 3.

Variable	**Group**	**n**	**%**	**MI occurrence:** Yes	No	**p Value**	**AOR95%CI**
Sex	Male	705	60	59(8 .4)	649(91.6)		1
	Female	470	40	20(4.3)	450(95.7)	**0.039**	2.41 (1.05~ 5.55)
Smoking status	NO	939	79.9	60(6.4)	879(93.6)		
	Yes	236	20.1	19(8.1)	217(91.6)	**0.024**	2.99 (1.15~7.76)
Electrolytic	No	243	20.7	1(0.4)	242(99.6)		1
imbalance	Yes	932	79.3	78(8.4)	853(91.6)	**0.008**	0.04 (0.004~0.044)
Invasive latest Hb	<100	939	7.6	24(27)	65(73)		1
(g/L)	≥100	1086	92.4	55(5.1)	1031(94.9)	**<0.001**	7.62 (2.56~22.66)
OLV duration	<188	628	53.4	8(1.3)	620(98.7)		1
(min)	≥188	547	46.6	71(13)	476(87)	**<0.00**1	0.004 (0.001~0.02)
Surgery duration	<165	641	54.5	30(4.7)	611(95.3)		1
(min)	≥165	534	45.5	49(9.2)	485(90.8)	**<0.001**	42.57 (13.4~135.27)

Table 3: Multivariate analysis for myocardial injury risk factor detection



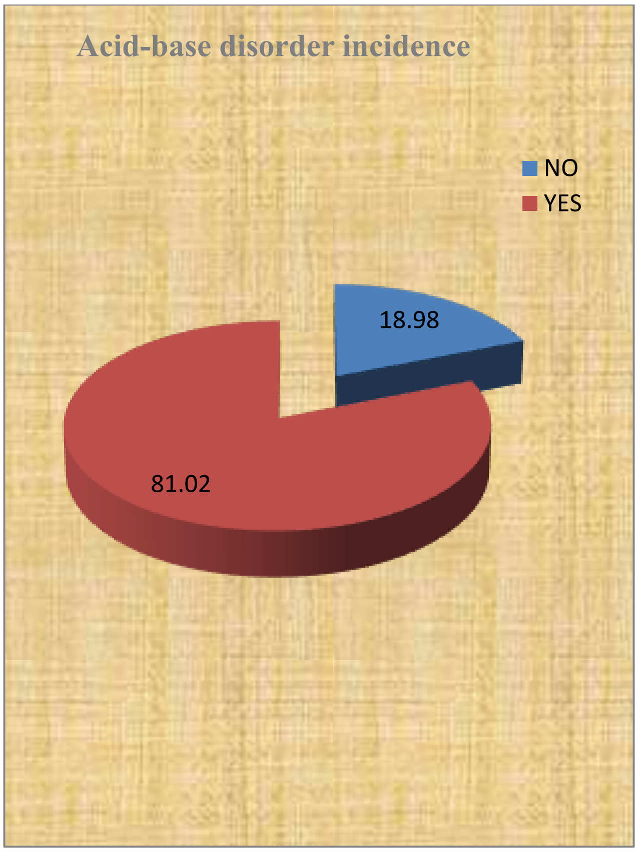


Fig. 3 Global incidence of electrolyte and

acid–base disorders among patients who underwent lung resection

Considering the analyzed electrolytes together, the global electrolyte disorder incidence was79.32%, and pH, BE and HCO_3^- resulted in an acid–base disorder incidence of 81.02%.

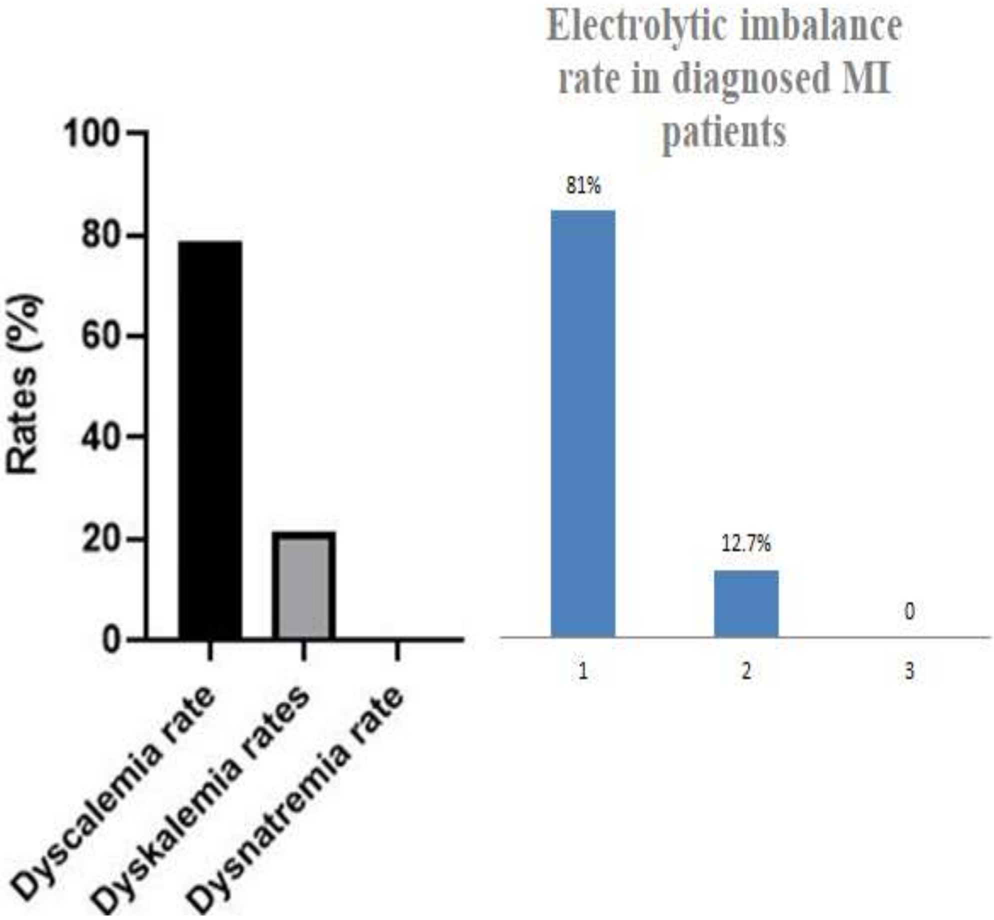


Figure4. The incidence of intraoperative electrolyte disturbance among patients who underwent lung surgery

Electrolytic imbalance among all patients   Electrolytic imbalance among MI patients
Dyscaelemia rate=79%
1.Dyscaelemia rate=81.94% Dyskalaemia rate= 21.5%
2. Dyskaelemia rate=12.7%   Dysnatraemia rate=0.5%
3. Dysnatraemia rate=0%

Among the79 patients who experienced postoperative MI, seventy–eight patients [78(98.7%)] experienced intraoperative electrolytic disturbance, which was dominated by hypocalcaemia.

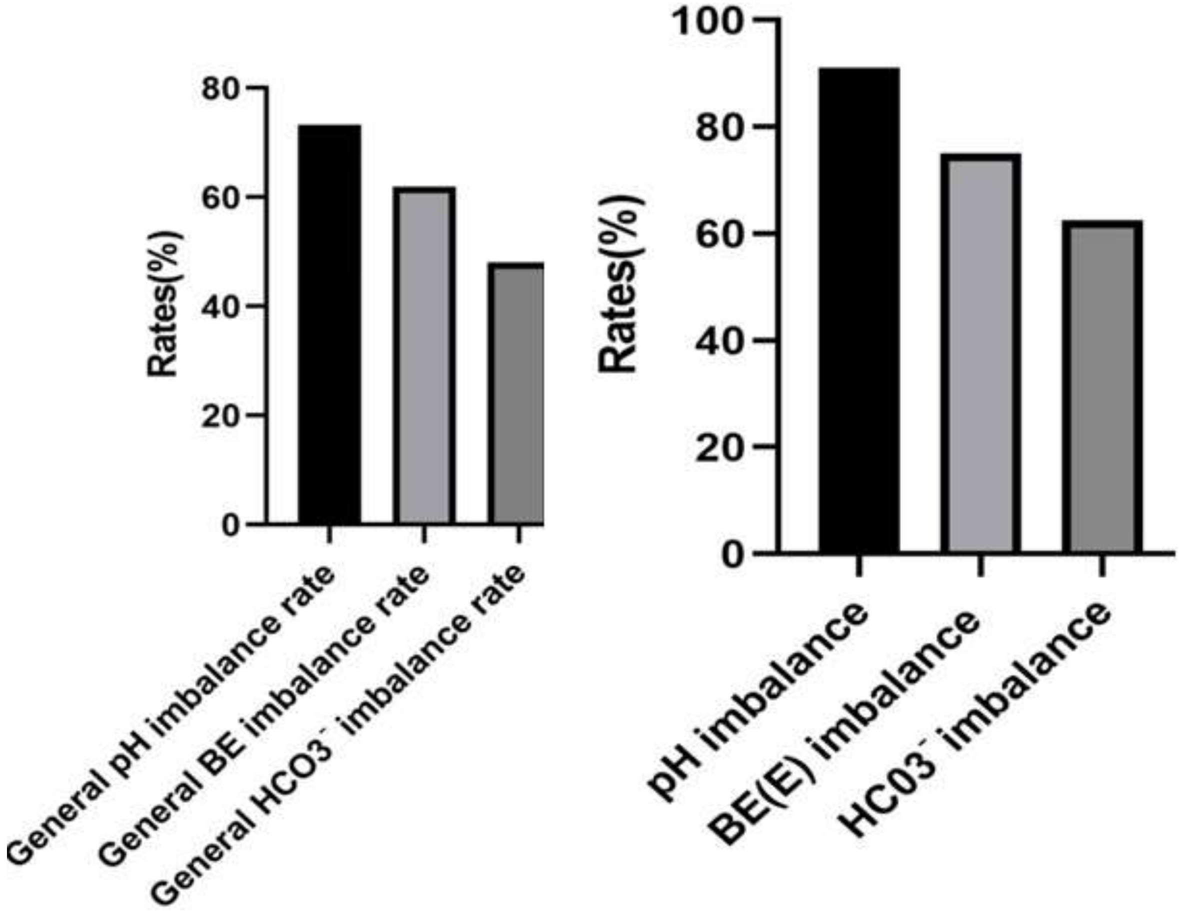


Figure 5. The incidence of intraoperative acid–base imbalance among patients who underwent lung surgery under one-lung ventilation

Acid–base imbalance among all patients **Acid–base imbalance among MI patients**

General pH imbalance rate= 73.3% Imbalanced pH rate= 91%
General BE imbalance rate= 61.9% Imbalanced BE (B) rate=75%
General $HCO3^{-}$imbalance rate= 48% Imbalanced $HCO3^{-}$rate= 62.5%

Seventy [70(88.6%)] out of the 79 patients who experienced postoperative MI had experienced intraoperative Acid–base disorders when the pH, BE (B), and $HCO3^{-}$ values from the BGA tests were considered.
After multiple binary logistic regression analysis of all covariates, the present study revealed that the covariates listed in Table 4 and 5 were relevant factors associated with EADs.
OLV and surgery duration, access balance and total inflow fluid volume are modifiable and anesthesia– related risk factors associated with EAD disorders.

Variable	Group	n	%	Electrolytic disorder: Yes	No	P-value	AOR95%CI
OLV duration	<188	628	53.4	495(78.8)	133(21.2)		1
(min)	≥188	547	46.6	437(79.9)	110(20.1)	**0.003**	0.24 (0.10~0.62)
Surgery duration	<165	641	45.5	516(80.5)	125(19.5)		1
(min)	≥165	534	82.3	416(77.9)	118(22.1)	**0.001**	4.68 (1.82~12.04)

Table 4: Multivariate analysis for the detection of electrolytic disorder risk-factors

Variable	Group	n	%	Acid–base disorder: Yes	No	P-value	AOR95%CI

Access balance	<1000	597	50.8	464(77.7)	133(22.3)		1
	≥1000	578	49.2	88(84.4)	90(15.8)	**0.049**	0.69 (0.48~1.00)
Type of surgery	Lob	1057	89.8	847(80.1)	210(19.9)		1
	Seg	118	10.2	105(89)	13(11)	**0.038**	0.53 (0.29~0.96)
BMI(kg/m2)	<25	860	73.2	685(79.7)	175(20.3)		1
	≥25	315	26.8	267(84.8)	48(15.2)	**0.047**	0.70 (0.49~0.99)
Total inflow	<1500	462	39.3	359(77.7)	103(22.3)		1
fluid(ml)	≥1500	713	60.7	593(83.2)	120(16.8)	**0.020**	1.15 (0.77~1.71)

Table 5: Multivariate analysis for acid–base disorder risk factor detection

IV DISCUSSIONS

In the present study, the incidence of acute postoperative MI, the primary endpoint, was 6.7%. Our findings are very close to the findings of previous studies[7,20] that reported MI incidence between 6.5 and 8 % [32] but for NCS in general. Cruz–Navaro et al. reported a MI incidence of 8%, but the cTnT threshold was 0.03 ng/ml, and patients were only aged above 45 years[49]. The latest VISION study findings for NCS among patients 45 years old and above with cardiovascular diseases or 65 years old and above, revealed a more substantial MI incidence of up to 23.9%[41]. MI incidence might then depend on the used immunoassay, the cohort nature and the thresholds of the biomarkers taken into account. A recent systematic review and meta-analysis[50] of observational studies reported a pooled MI between 10% and 41%, whereas the AHA scientific statement reported an acute postoperative MI prevalence between 17% and 34%[44]. This discrepancy was due to the fact that they included very high–risk patients that were excluded in our cohort, a situation described in previous research as an important study limitation[42]. Alparslan Turan and coworkers reported a MI incidence of 4.5% after NCS, with only cTn being used for MI screening[2]. Adding NT-proBNP monitoring in MI diagnosis might increase its incidence, as supported by previous researchers[44,46,51,52]. Furthermore, the application of the h-s assay in cardiac troponin screening increases the likelihood of MI detection[44]. Electrolytic imbalance was found to be a relevant postoperative MI risk–factor: p<0.001, OR95%CI: 22.1 (3.06~159.71). These findings are justified by cardiac electrophysiology. In fact, Ca^{++}, K^+ and Na^+ play crucial roles in cardiomyocyte contraction and relaxation. The imbalance interferes with normal heart function. Male sex was more strongly associated with MI occurrence than female sex was, p = 0.036, AOR95% CI: 2.41(1.05~5.55), findings similar to the results of previous studies[50,53]. Patients who still smoking before the day of the pre-anesthesia evaluation were more likely to experience MI than patients who never smoke or stopped smoking, with a P-value of 0.024 and AOR95% CI of 2.99 (1.15~7.76); this result is similar to the findings of previous researchers[41]. An invasive latest HB concentration of less than 100 g/L was strongly associated with MI incidence, with p<0.001, and 7.62 (2.56~22.66). The HB concentration is a very important component of cardiac myocyte function since MI in this setting is generally a matter of myocardial oxygen supply–demand mismatch, as assumed by previous studies [27,54]. An OLV duration above 188 min was associated with MI, p <0.001. A surgery duration above 165 minutes was also strongly associated with MI, (p<0.001, AOR95% of 42.57 (13.4~ 135.27)). The findings are similar to those of Christoph Ellenberger et al.[24].

Our results showed that the incidences of EADs among our patients were 79.32% and 81.02%, for electrolytes and acid–base imbalances, respectively. In this study, incidence of hypocalcaemia or EADs in general is high compared to the that reported by Yang Li et al.[48]. The difference might be due to the anesthesia-induced stress, especially OLV drawbacks, behind the oncological disease its self [10]. Within the acute postoperative MI population in the present study, 98.7% and 88.6% of the patients experienced intraoperative electrolytes and acid–base disorders, respectively. Many risk factors associated with postoperative MI and intraoperative EADs, such as OLV duration, surgery duration, access balance and total inflow fluid volume, are anesthesia-related factors or modifiable factors, which are preventable. This highlights the interactive effect between perioperative anesthesia complications or anesthesia conduct and the incidence of acute postoperative MI. On the basis of the findings of the present study, anesthesia providers must be a cornerstone of postoperative MI prevention. Considering the high incidences (98.7% and 88.6%) of EADs among patients who experienced postoperative MI, these findings confirm a strong association of intraoperative electrolyte and acid–base disorders with acute postoperative MI, and may therefore predict it. Consequently, clinical anesthesiologists must be aware of these variables, specifically in pre-anesthesia evaluation and intraoperative anesthesia, to provide optimal safe anesthesia with the best outcomes, at least, in the short–and medium–term postoperative periods. This needs to be supported by updated new evidence–based guidelines and clinical practice protocols.

In contrast to previous studies that focused on MI incidence in very high-risk populations, such as cardiovascular patients for NCS generally, the present study included relatively healthy and young patients, excluded high–risk patients and searched exclusively for lung cancer resection. Yuan Chang and colleagues[50] reported in a recent study that more than 40% of cardiovascular patients experienced MI before NCS. This underpins the relatively low incidence of postoperative MI in our study, revealed at the same time that even clinically relatively healthy patients may experience postoperative MI after lung resection or NCS. Hereby we, not only provide additional support for the existing recommendations of expert societies[52,55], but also provide a new perspective to embed systematic cardiac biomarkers screening patients scheduled for lung cancer resection especially after each 4 hours in the postoperative setting, within the first 48 hours. This new insight is justified by many pathophysiological processes, including stimulation of the sympathetic nervous system by surgery and anesthesia- induced stress, which occurs in every patient undergoing surgery. Serum catecholamine are increased and trigger high HR, systemic inflammation, and hypertension; and create an oxygen supply–demand mismatch and subsequent MI[7,35]. Moreover, a recent study[50] questioned the definition of acute MI and assumed a lack of clear criteria for acute perioperative MI screening. It insinuates a plea of a revision of the Fourth Universal Definition of Myocardial Infarction or the initiation of new guidelines on perioperative MI management.

Strengths and limitations: Few studies have investigated acute postoperative MI with a cohort including young patients and excluding cardiovascular and renal disease patients. Moreover, the present study is among very scarce studies to investigate a relationship between intraoperative EADs and postoperative MI in patients with lung cancer resection.
The first limitation was the poor comparison of the findings of the present study with those of previous studies because of the paucity of literature on postoperative MI incidence when it was investigated among patients who underwent exclusively lung cancer resection, not NCS globally. Furthermore, evidence on the hs–cTnT assay used together with NT–pro BNP are scarce scattered[52]. The second limitation is the retrospective nature of this study and the fact that it is a single–center based that may sometimes be associated with a certain likelihood of hampering the accuracy of findings. Therefore, further prospective or RCT studies on lung cancer resection are encouraged. Whether the persistent occurrence of postoperative MI at relatively high rate despite the exclusion of high–risk factors was due to lung oncological disease or the OLV technique in this study population warrants further study.

In conclusion, the present study's findings revealed an acute postoperative MI incidence of 6.7%. Intraoperative electrolytic imbalance and OLV, among other factors, were strongly associated with acute postoperative MI ($p<0.001$, OR95%CI: 22.1 (3.06~159.71)). Calcium is the most important imbalanced electrolyte. On the basis of these study's findings, we plead for an embedding in the benchmark protocol and upcoming guidelines for anesthesia to conduct the perioperative systematic screening of both hs–cTnT and NT-proBNP for NCS, especially in lung cancer resection.

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Author contributions: For this study,

- all the authors participated in the study design and conception;
- all authors critically revised the manuscript for substantial intellectual content;
- all authors approved the final version to be submitted;

As authors of the present manuscript, we agree to be accountable for all aspects of this work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of interest: None

Statements: This work has not been published previously and is not under consideration for publication elsewhere. The current submission and publication were approved by all authors and by the responsible authorities of Nanfang Hospital. If accepted, it will not be published elsewhere in the same form, in English or in any other language, including electronically, without the written consent of the copyright holder.
Data availability : The raw data used for the current study are available from the corresponding author and may be provided upon reasonable request.
Declarations
Ethics approval and consent to participate:
This retrospective observational cohort study was conducted in accordance with the Declaration of Helsinki 2013. Procedure complied with the 2020 checklist of STROBE principles. It has been approved by the Medical Ethics committee of NanFang Hospital of Southern Medical University (Approval letter N°. NFEC-2023-466).
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