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ORIGINAL ARTICLE

The impact of smoking on postoperative complications following elective off-pump CABG in an ERAS setting

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Abstract

Purpose This study investigates the impact of smoking on major postoperative complications following elective off-pump coronary artery bypass graft (CABG) surgery within an enhanced recovery after surgery (ERAS) program.

Methods A total of 3168 patients who underwent elective off-pump and minimally invasive direct CABG under ERAS between January 1, 2017, and December 31, 2020, were enrolled. Propensity score matching was applied to minimize potential confounders when comparing postoperative outcomes between smokers and non-smokers.

Results Multivariate logistic regression analyses showed no significant difference in 30-day postoperative mortality between smokers and non-smokers (adjusted odds ratio [aOR]: 1.06, 95% confidence interval [CI]: 0.40–1.56). However, smokers had a higher risk of 30-day major complications, including postoperative acute myocardial infarction (AMI) (aOR: 1.43, 95% CI: 1.02–1.99) and overall postoperative complications (aOR: 1.18, 95% CI: 1.04–1.48). Similarly, for the 31–90-day period, smokers had no significantly higher risk of mortality (aOR: 1.06, 95% CI: 0.49–1.19), but experienced higher rates of major complications, including postoperative AMI (aOR: 1.73, 95% CI: 1.17–2.55) and overall postoperative complications (aOR: 1.48, 95% CI: 1.13–1.92).

Conclusions The ERAS program benefits patients undergoing CABG surgery, including smokers, by providing similar major postoperative outcomes to non-smokers, except for increased risks of postoperative AMI and overall complications.

Keywords ERAS · CABG · Smokers · Non-smokers · Adverse outcomes

Abbreviations

OR	Odds ratio
CABG	Coronary artery bypass graft
ERAS	Enhanced recovery after surgery
aOR	Adjusted odds ratio
AMI	Acute myocardial infarction

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CI	Confidence interval
NHIRD	National health insurance research database
ICU	Intensive care units
PSM	Propensity score-matched
ICD-9-CM	International Classification of Diseases: Ninth Revision: Clinical Modification
ASA	American society of anesthesiologists
ICD-10-CM	International classification of diseases: tenth revision: clinical modification
SD	Standard deviation
IQR	Interquartile range
y	Years-old
CCI	Charlson comorbidity index

Introduction

Coronary artery bypass graft surgery (CABG) is a recommended treatment for obstructive coronary artery disease, and for patients with angina refractory to medical therapy where percutaneous coronary intervention is not an option [1, 2]. The procedure involves constructing one or more grafts between the arterial and coronary circulations [3]. Traditionally, CABG has been associated with a slow recovery process and prolonged hospital stay [3]. However, the implementation of enhanced recovery after surgery (ERAS) protocols, a multidisciplinary approach involving evidence-based interventions in the preoperative, intraoperative, and postoperative periods, has significantly reduced recovery time and hospital stay [4, 5]. ERAS has been widely implemented in Taiwan since 2017 and has been shown to improve patient outcomes following surgery [6].

ERAS has been widely implemented in the perioperative care of patients undergoing CABG surgery [7–10]. However, the effect of ERAS on postoperative complications in smokers undergoing CABG has not been fully evaluated. Smoking is a known risk factor for adverse outcomes following CABG, including wound infections, pulmonary complications, and cardiovascular events [11]. Smoking has also been shown to increase the inflammatory response and impair wound healing, which can lead to delayed recovery and increased length of stay [11–20]. Therefore, it is important to investigate whether the benefits of ERAS protocols can extend to smokers undergoing CABG surgery. The impact of ERAS on the postoperative complications in smokers undergoing CABG surgery warrants further investigation.

The purpose of this study is to examine the impact of smoking on major postoperative complications following elective off-pump CABG surgery under an ERAS program. Our primary objective is to compare the occurrence of wound infections, pulmonary complications, and cardiovascular events between smokers and non-smokers who undergo CABG surgery within the context of an ERAS program.

Patients and methods

Data sources

We enrolled patients who underwent elective off-pump and minimally invasive direct CABG—between January 1, 2017, and December 31, 2020; their data were obtained from the Taiwan National Health Insurance Research Database (NHIRD). The NHIRD is a valuable resource for population-based research as it contains comprehensive medical claims data for all National Health Insurance beneficiaries in Taiwan, including diagnoses, surgical procedures, drug prescriptions, demographics, and enrollment profiles [21–27]. The data is encrypted using unique patient identifiers and is linked to the death registry, allowing for determination of vital status and cause of death for each included patient [21–27]. In addition, the Health Promotion Administration of the Ministry of Health and Welfare in Taiwan implemented a program for oral cancer screening in 2004, which enabled us to identify high-risk individuals for cancer through their smoking habits by linking the National Cancer Screening database with the NHIRD [28]. As a result, we were able to include active smokers from this linked NHIRD and the National Cancer Screening database in our study population, which represents over 99% of the Taiwanese population.

The study protocols were reviewed and approved by the Institutional Review Board of Tzu-Chi Medical Foundation (IRB109-015-B).

Inclusion and exclusion criteria

The inclusion criteria were as follow: patients who were aged ≥ 40 years, had no other cancer, and underwent first time elective off-pump and minimally invasive direct CABG in the Medical center. Patients were excluded if they had a history of cancers before the index date, had CABG in the non-Medical centers, had missing sex data, second or repeat receiving CABG, and had an unclear surgical types (unclear off-pump, on-pump, or traditional CABG). The hospital accreditation level (medical center or not) was also considered. According to the definition of the Taiwan Joint Commission on Hospital Accreditation, medical centers consist of 1000–2500 beds, conduct most staff training within the center, provide tertiary medical services, and have research facilities [29]. Since 2017, ERAS have been performed in the most medical cancers in Taiwan [6], especially in cardiovascular surgeries.

Patients undergoing elective off-pump CABG surgery under the ERAS program received standardized preoperative care. In our dataset, the average length of hospital stay before surgery was approximately 3 to 4 days. During this period, patients were encouraged to cease smoking as part of the preoperative preparation, consistent with standard clinical practices.

Smoking status classification

Smoking cessation guidance was not universally provided to all patients in this study, as it was specifically targeted toward patients in the smoker group. Non-smokers did not receive smoking cessation guidance because it was not applicable to them. For patients who quit smoking after the surgical decision was made as part of the ERAS program, they were still categorized as part of the smoker group. This classification aligns with our study's methodology, which defines smoking status based on any history of smoking, regardless of cessation timing. To clarify this distinction, we included patients in the smoker group if they had a record of ICD codes (ICD-9-CM: 305.1; ICD-10-CM: Z72.0, F17.200, F17.201, F17.210, F17.211) or if their smoking history was documented through smoking cessation clinic visits or cancer screenings.

Outcome measures

To evaluate the major postoperative major complications between smokers and non-smokers undergoing CABG in the ERAS era. Eight major postoperative complications were monitored: acute myocardial infarction, acute renal failure, pneumonia, deep-wound infection, postoperative bleeding, pulmonary embolism, septicemia, and stroke [21, 30]. These complications and subsequent overall in-hospital mortality within 30 days after the off-pump and minimally invasive direct CABG were the primary outcomes of the current study [21, 30]. Instead of 30-day mortality and postoperative major complications, the 90-day mortality and complications are a valid measure of surgical quality, especially in CABG [31].

PSM and covariates

To reduce the effects of potential confounders when comparing postoperative adverse outcomes between the smokers and non-smokers groups in the ERAS era, all patients were matched through propensity score-matched (PSM) using the following variables: age, sex, income, residence, ASA physical status, comorbidities, and Charlson comorbidity index (CCI) Scores (Table 1). We matched the cohorts at a ratio of 2:1 by using the greedy matching method, and covariates were matched with a propensity score within a caliper of 0.1 [32]. Comorbidities were determined according to *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) or ICD-10 and were defined as the main diagnosis in inpatient records or if the number of outpatient visits was ≥ 2 within 1 year. Comorbidities that presented 6 months before the index date were recorded. After adjustments for confounders, a multivariate logistic regression model was used to examine 30-day, and 90-day postoperative major complications from the index date (date of CABG performed) in patients with and without smoking.

In this study, continuous variables are presented as means $\pm$ standard deviations, where appropriate. A 1:2 PSM applied here for the smokers and non-smokers groups is a common technique used for selecting controls with identical background covariates as those of study participants to minimize differences among the study patients (that we deem necessary to be controlled based on the previous studies) [21, 30]. A multivariate logistic regression model was performed to analyze postoperative major complications and related variables in the smokers and non-smokers groups [33]. Multivariate logistic regression analysis was performed to calculate odd ratios (ORs) with 95% confidence intervals (CIs) for determining whether smokers was still the potential independent predictor for postoperative 30-day and 90-day major complications in the ERAS era.

Data analysis

We used the chi-square test to analyze the descriptive parameters for demographic status and coexisting medical conditions and compare postoperative major complications, and death rates between smokers and non-smokers undergo CABG under ERAS era. Continuous variables were analyzed using *t* tests to compare differences between the smokers and non-smokers groups. The propensity score adjustment for age, sex, income, residence, American Society of Anesthesiologists (ASA) physical status, comorbidities, and CCI Scores, and logistic regression models including postoperative outcomes and surgical outcomes, with propensity score adjustment for the same aforementioned variables. SAS v.9.4 (SAS Institute, Cary, NC, USA) was used for all statistical analyses; differences between groups were considered significant if two-sided p values were < 0.05.

Results

Study cohort

Our final cohort included 3,168 patients undergo off-pump and minimally invasive direct CABG under ERAS (708 and 2,460 in the smokers and non-smokers groups, respectively) who were eligible for further analysis; their characteristics

Table 1 The Characteristics of smokers and non-smokers undergoing off-pump coronary artery bypass graft in the enhanced recovery after surgery era

	Before propensity scores matching					After propensity scores matching				
	Non-smokers		Smokers		*p* value	Non-smokers		Smokers		*p* value
	N = 2460		*N* = 708			*N* = 1319		N = 703		
	N	%	*N*	%		*N*	%	*N*	%	
Age (mean ± SD)	61.55 ± 15.94		59.98 ± 12.23		0.0152	60.02 ± 15.13		59.98 ± 12.23		0.3852
Age, median (IQR), y	65.00 (55.00,72.00)		61.00 (52.00,69.00)		< .0001	61.00 (53.00,70.00)		61.00 (52.00,70.00)		0.3686
Age group, years										
40–55	655	26.6%	237	33.5%	< .0001	415	31.5%	234	33.3%	0.8121
56–65	641	26.1%	224	31.6%		415	31.5%	222	31.6%	
66–75	766	31.1%	189	26.7%		373	28.3%	189	26.9%	
> = 76	398	16.2%	58	8.2%		116	8.8%	58	8.3%	
Sex										
Female	879	35.7%	81	11.4%	< .0001	158	12.0%	80	11.4%	0.6906
Male	1581	64.3%	627	88.6%		1161	88.0%	623	88.6%	
Income (NTD)										
Low income	29	1.2%	7	1.0%	< .0001	10	0.8%	6	0.9%	0.1680
Financial dependent	824	33.5%	146	20.6%		313	23.7%	146	20.8%	
≤ 20 000	811	33.0%	235	33.2%		469	35.6%	234	33.3%	
20 001–30 000	484	19.7%	201	28.4%		307	23.3%	199	28.3%	
30.001–45 000	185	7.5%	76	10.7%		130	9.9%	75	10.7%	
> 45 000	127	5.2%	43	6.1%		90	6.8%	43	6.1%	
Residence										
Rural	638	25.9%	233	32.9%	0.0002	386	29.3%	230	32.7%	0.1082
Urban	1822	74.1%	475	67.1%		933	70.7%	473	67.3%	
ASA physical status										
1	124	5.0%	14	2.0%	0.0046	29	2.2%	14	2.0%	0.9013
2	122	5.0%	38	5.4%		62	4.7%	38	5.4%	
3	375	15.2%	103	14.6%		193	14.6%	101	14.4%	
4	1839	74.8%	553	78.1%		1,035	78.5%	550	78.2%	
Comorbidities										
Diabetes	937	38.1%	254	35.9%	0.2839	514	39.0%	253	36.0%	0.1884
Hypertension	1772	72.0%	507	71.6%	0.8256	953	72.3%	504	71.7%	0.7897
Hyperlipidaemia	1148	46.7%	398	56.2%	< .0001	711	53.9%	395	56.2%	0.3260
COPD	679	27.6%	227	32.1%	0.0206	383	29.0%	225	32.0%	0.1657
Alcohol-related diseases	32	1.3%	25	3.5%	< .0001	29	2.2%	24	3.4%	0.1033
Rheumatoid arthritis	77	3.1%	15	2.1%	0.1579	27	2.1%	15	2.1%	0.8964

Table 1 (continued)

	Before propensity scores matching					After propensity scores matching				
	Non-smokers		Smokers		*p* value	Non-smokers		Smokers		*p* value
	N = 2460		*N* = 708			*N* = 1319		N = 703		
	N	%	*N*	%		*N*	%	*N*	%	
Renal dialysis	424	17.2%	97	13.7%	0.0253	188	14.3%	97	13.8%	0.7794
Acute renal failure	140	5.7%	16	2.3%	0.0002	31	2.4%	16	2.3%	0.9159
Osteoporosis	230	9.4%	41	5.8%	0.0029	75	5.7%	41	5.8%	0.8930
Peripheral vascular diseases	355	14.4%	83	11.7%	0.0659	164	12.4%	83	11.8%	0.6817
Stroke	610	24.8%	151	21.3%	0.0569	300	22.7%	150	21.3%	0.4687
Myocardial infarction	721	29.3%	209	29.5%	0.9136	401	30.4%	209	29.7%	0.7538
Congestive heart failure	1017	41.3%	279	39.4%	0.3562	523	39.7%	277	39.4%	0.9133
Hypothyroidism	33	1.3%	6	0.9%	0.2935	11	0.8%	6	0.9%	0.9635
Dysthymic disorder	104	4.2%	27	3.8%	0.6258	49	3.7%	27	3.8%	0.8874
Gout	552	22.4%	190	26.8%	0.0149	345	26.2%	188	26.7%	0.7756
Headache	498	20.2%	190	26.8%	0.0002	295	22.4%	186	26.5%	0.0396
Pressure ulcer	72	2.9%	11	1.6%	0.0438	22	1.7%	11	1.6%	0.8615
CCI Scores										
0	880	35.8%	234	33.1%	0.1814	466	35.3%	233	33.1%	0.3249
> = 1	1580	64.2%	474	67.0%		853	64.7%	470	66.9%	
CCI Scores										
Congestive heart failure	1058	43.0%	282	39.8%	0.1315	557	42.2%	281	40.0%	0.3264
Dementia	34	1.4%	8	1.1%	0.6052	12	0.9%	8	1.1%	0.6214
Chronic pulmonary disease	615	25.0%	201	28.4%	0.0691	342	25.9%	198	28.2%	0.2791
Rheumatic disease	36	1.5%	7	1.0%	0.3361	12	0.9%	7	1.0%	0.8487
Liver disease	275	11.2%	112	15.8%	0.0009	181	13.7%	111	15.8%	0.2079
DM with complications	315	12.8%	77	10.9%	0.1695	156	11.8%	76	10.8%	0.4947
Hemiplegia and paraplegia	0	0.0%	0	0.0%	0.9999	0	0.0%	0	0.0%	0.9999
Renal disease	330	13.4%	63	8.9%	0.0013	120	9.1%	63	9.0%	0.9341
AIDS	1	0.0%	0	0.0%	0.5916	1	0.1%	0	0.0%	0.4652

ASA American Society of Anesthesiologists, *SD* standard deviation, *IQR* interquartile range, *y* years-old, *CCI* Charlson comorbidity index, *NTD* New Taiwan Dollars

are listed in Table 1. Before PSM, there were more young age, male, higher income levels, rural residents, more elective CABG, higher ASA scores, more hyperlipidemia, more alcohol-liver diseases, more under renal dialysis, more gout, more headache, and more liver diseases in the smokers group. Furthermore, after PSM, the between-group differences in age, sex, income, residence, ASA physical status, all mentioned comorbidities, and CCI Scores. were not significant.

Outcomes: ICU, hospital stay days, and postoperative adverse outcomes

No significant differences were observed in the ICU stay and hospital stay between the smokers and non-smokers groups (mean 1.37 days vs. 1.43 days, p = 0.2472 and 18.36 days vs. 19.92 days, p = 0.4175, Table 2). There were no significant differences in the 30-day post-CABG mortality for smokers (5.3%) and non-smokers (3.2%) under ERAS (p = 0.0517). Moreover, there were no significantly different on the 30-day postoperative adverse outcomes between smokers and non-smokers undergo CABG under ERAS. During the 31–90-day, the postoperative mortality were 1.6% and 1.4% for non-smokers and smokers and the p value is 0.2501. However, there were significantly higher rate of acute myocardial infarction (AMI), pulmonary embolism, and all complications in the smokers undergo CABG during postoperative 31–90 days compared with non-smokers.

Adjusted ORs and 95% CIs for 30-day postoperative adverse outcomes

After adjustment for confounding factors shown in Table 1, multivariate logistic regression analyses revealed that the smoker group under ERAS had no significantly higher risk of 30-day postoperative mortality (aOR: 1.06, 95% CI: 0.40–1.56). The 30-day major complications, including postoperative AMI (aOR: 1.43, 95% CI: 1.02–1.99), and all

Table 2 30-day and 90-day adverse surgical outcomes in propensity scores matching smokers and non-smokers undergoing off-pump coronary artery bypass graft in the enhanced recovery after surgery era

	Non-smokers		Smokers		
	N = 1319	%	*N* = 703	%	*P* value
Hospital stay					
Mean (SD)	18.36 ± 11.97		19.92 ± 10.55		0.4175
Median (IQR, Q1-Q3)	16.00 (12.00,23.00)		16.00 (12.00,23.00)		0.7430
ICU stay					
Mean (SD)	1.37 ± 1.15		1.43 ± 0.74		0.2472
Median (IQR, Q1-Q3)	1.00 (1.00,2.00)		1.00 (1.00,2.00)		0.4052
30-day acute postoperative complication					
Postoperative mortality	42	3.2%	37	5.3%	0.0517
Acute myocardial infarction	253	19.2%	148	21.1%	0.3149
Acute renal failure	22	1.7%	8	1.1%	0.3479
Deep-wound infection	4	0.3%	4	0.6%	0.3647
Pneumonia	63	4.8%	38	5.4%	0.5363
Postoperative bleeding	47	3.6%	17	2.4%	0.1613
Pulmonary embolism	4	0.3%	3	0.4%	0.6526
Septicemia	89	6.8%	36	5.1%	0.1481
Stroke	114	8.6%	61	8.7%	0.9792
Any Complications	451	34.2%	281	40.0%	0.3199
31–90-day subacute postoperative complication					
Postoperative mortality	21	1.6%	10	1.4%	0.2501
Acute myocardial infarction	72	5.5%	59	8.4%	0.0107
Acute renal failure	5	0.4%	2	0.3%	0.7302
Deep-wound infection	2	0.2%	3	0.4%	0.2355
Pneumonia	21	1.6%	16	2.3%	0.2746
Postoperative bleeding	1	0.1%	0	0.0%	0.4652
Pulmonary embolism	0	0.0%	3	0.4%	0.0176
Septicemia	17	1.3%	6	0.9%	0.3793
Stroke	85	6.4%	48	6.8%	0.7404
Any complications	224	16.9%	147	20.9%	0.0088

ICU intensive care units, *SD* standard deviation, *IQR* interquartile range

postoperative complications (aOR: 1.18, 95% CI: 1.04–1.48) were still higher in the smokers under ERAS (Table 3).

Adjusted ORs and 95% CIs for 31–90-day subacute complications

The smokers undergo CABG under ERAS had no significantly higher risk of 31- 90-day mortality (aOR: 1.06, 95% CI: 0.49–1.19). The 31–90-day postoperative major complications, including postoperative AMI (aOR: 1.73, 95% CI: 1.17–2.55), and postoperative all complications (aOR: 1.48, 95% CI: 1.13–1.92) were higher in the smokers compared with non-smokers undergo CABG under ERAS (Table 4).

Discussion

Numerous reports have indicated that smokers who undergo CABG have longer ICU and hospital stays, as well as a higher incidence of adverse postoperative outcomes, compared to non-smokers [14, 34–36]. Furthermore, the medical complications arising from CABG are becoming increasingly common among smokers. [14, 34–36] However, it is important to note that the studies [14, 34–36] focus on patients who underwent on-pump CABG procedures, which differ significantly from the elective off-pump CABG procedures studied in this analysis. The implementation of the ERAS protocol has been associated with improved outcomes for CABG patients. [7–10] While previous studies demonstrated disparities in outcomes between smokers and non-smokers undergoing other types of CABG procedures, our study is the first to specifically evaluate these differences for elective off-pump CABG within an ERAS framework. We acknowledge the challenges of directly comparing outcomes with and without ERAS in similar populations. Given the routine implementation of ERAS protocols in recent years, such comparisons would inevitably involve cross-era differences, where advances in surgical techniques and perioperative care would independently influence postoperative outcomes. In addition, conducting a randomized controlled trial comparing ERAS with non-ERAS protocols may raise ethical concerns, as ERAS has consistently demonstrated safety and efficacy in improving patient outcomes.

Our study emphasizes that it is the first to evaluate the impact of smoking on postoperative outcomes under an ERAS protocol for elective off-pump CABG. We also recommend that future studies explore innovative methodologies to isolate the effects of ERAS while acknowledging the inherent difficulties in such comparisons. To date, no studies have compared the ICU and hospital stays, postoperative mortality, and major surgical outcomes of smokers and non-smokers undergoing CABG under the ERAS protocol. The

Table 3 Adjusted ORs and 95% CIs for 30-day acute postoperative outcomes associated with propensity score-matched smokers and non-smokers undergoing off-pump coronary artery bypass graft in the enhanced recovery after surgery era

	Crude OR (95%CI)			p value	Adjusted OR (95%CI)			p value
30-day postoperative mortality								
Smokers (Ref. non-smokers)	1.02	0.38	1.01	0.0537	1.06	0.40	1.09	0.0993
Acute myocardial infarction								
Smoker (Ref. non-smokers)	1.12	0.90	1.41	0.3150	1.43	1.02	1.99	0.0365
Acute renal failure								
Smoker (Ref. non-smokers)	1.08	0.30	1.53	0.3508	1.11	0.13	1.95	0.3230
Deep-wound infection								
Smoker (Ref. non-smokers)	1.88	0.47	7.55	0.3725	1.87	0.39	9.08	0.4363
Pneumonia								
Smoker (Ref. non-smokers)	1.14	0.75	1.72	0.5366	1.17	0.76	1.80	0.4848
Postoperative bleeding								
Smoker (Ref. non-smokers)	1.07	0.38	1.18	0.1639	1.06	0.38	1.18	0.1598
Pulmonary embolism								
Smoker (Ref. non-smokers)	1.41	0.32	6.31	0.6539	1.40	0.22	8.85	0.7197
Septicemia								
Smoker (Ref. non-smokers)	1.05	0.50	1.11	0.1495	1.07	0.51	1.17	0.2142
Stroke								
Smoker (Ref. non-smokers)	1.00	0.73	1.39	0.9792	1.13	0.76	1.67	0.5402
Any Complications								
Smoker (Ref. non-smokers)	1.08	0.90	1.31	0.42	1.18	1.04	1.48	0.0166

OR odds ratio, *AMI* acute myocardial infarction, *CI* confidence interval, *Ref.* Reference Group

*Logistic regression for binary variables with propensity score adjustment of age, sex, income, residence, ASA physical status, comorbidities, and CCI Scores

Table 4 Adjusted ORs and 95% CIs for 31–90-day subacute postoperative outcomes associated with propensity score-matched smokers and non-smokers undergoing off-pump coronary artery bypass graft in the enhanced recovery after surgery era

	Crude OR (95%CI)			p value	Adjusted OR (95%CI)			p value
90-day postoperative mortality								
Smokers (Ref. non-smokers)	1.04	0.44	1.21	0.0513	1.06	0.49	1.19	0.0830
Acute myocardial infarction								
Smoker (Ref. non-smokers)	1.59	1.11	2.27	0.0113	1.73	1.17	2.55	0.0059
Acute renal failure								
Smoker (Ref. non-smokers)	1.05	0.15	3.88	0.7312	1.08	0.12	6.78	0.9057
Deep-wound infection								
Smoker (Ref. non-smokers)	2.82	0.47	16.93	0.2563	2.94	0.42	20.43	0.2755
Pneumonia								
Smoker (Ref. non-smokers)	1.44	0.75	2.78	0.2767	1.41	0.71	2.79	0.3279
Postoperative bleeding								
Smoker (Ref. non-smokers)	1.88	0.12	30.06	0.6562	4.12	0.10	34.09	0.9827
Pulmonary embolism								
Smoker (Ref. non-smokers)	0.94	0.09	10.36	0.9584	5.36	0.11	33.21	0.5424
Septicemia								
Smoker (Ref. non-smokers)	1.06	0.26	1.68	0.3827	1.11	0.23	1.63	0.3211
Stroke								
Smoker (Ref. non-smokers)	1.06	0.74	1.54	0.7404	1.19	0.80	1.78	0.3924
Any complications								
Smoker (Ref. non-smokers)	1.40	1.09	1.79	0.009	1.48	1.13	1.92	0.0041

OR odds ratio, *AMI* acute myocardial infarction, *CI* confidence interval, *Ref.* Reference Group

*Logistic regression for binary variables with propensity score adjustment of age, sex, income, residence, ASA physical status, comorbidities, and CCI Scores shown in Table 1

effect of the ERAS protocol on postoperative outcomes for smokers undergoing CABG remains unclear. Therefore, we propose a well-matched, PSM study to estimate the major surgical outcomes of smokers and non-smokers undergoing CABG under the ERAS protocol.

ERAS refers to evidence-based protocols that standardize care for elective procedures, with the goal of minimizing surgical stress responses, reducing complications, improving outcomes, and expediting recovery [37]. ERAS protocols for CABG aim to achieve early extubation, reduce hospital length of stay, and minimize postoperative complications through a multidisciplinary approach that includes minimizing stress responses, using multimodal analgesic strategies, and expediting recovery [37, 38]. Compared to conventional care, limited data suggest that implementation of ERAS is associated with faster postoperative extubation, reduced opioid administration, shorter stays in the ICU and hospital [39–43], and lower incidences of surgical and medical complications, improved analgesia, and decreased overall costs [39–43]. While some limited data show that implementation of ERAS may be associated with less adverse postoperative outcomes in patients receiving CABG [39–43], there are currently no reports of major postoperative outcomes for patients undergoing CABG under ERAS protocols in Taiwan. In addition, there have been no reports to demonstrate the association of ERAS with major postoperative outcomes between smokers and non-smokers receiving CABG. Our study aims to fill this gap by providing the first assessment of 30-day and 90-day major postoperative outcomes for active smokers and non-smokers undergoing CABG under ERAS protocols. If smokers who receive CABG under ERAS experience similar rates of major postoperative complications as non-smokers, this would suggest that implementation of ERAS is a valuable strategy for reducing complications and improving outcomes in CABG patients who smoke. These findings would provide important guidance for future randomized controlled trials in this area, as well as encourage the broader implementation of ERAS protocols for CABG patients who smoke.

Many patients who undergo CABG have a history of smoking or may currently smoke [11]. It is recommended that patients quit smoking at least four weeks prior to thoracic surgery [12, 44], as smoking cessation can reduce postoperative complications, especially in cases of pulmonary resection for lung cancer where lung tissue is lost and one lung ventilation is required. In addition, smoking cessation may also decrease long-term mortality [12, 13, 15]. The same reason can be the reproduced that smokers undergoing CABG may benefit from prehabilitation using an ERAS protocol to achieve optimal health before CABG, especially for smokers who need to quit smoking [16]. Our study found that implementation of an ERAS protocol may

lead to a decrease in-hospital stay, ICU stay, acute and subacute postoperative major complications, resulting in similar postoperative outcomes between smokers and non-smokers undergoing CABG (Table 2–4), with the exception of 30-day and 90-day AMI risk and cumulative overall postoperative complications. Smokers still have a significantly higher risk of posroperative 30-day and 90-day AMI compared to non-smokers due to long-term nicotine exposure leading to chronic stenosis, stiffness, and less elastic coronary arteries (Table 3–4) [17]. Although ERAS was performed, the long-term effects of nicotine exposure and unhealthy coronary arteries could not be overcome in the short-term (Table 3–4). Furthermore, smokers undergoing CABG had significantly higher 30-day and 90-day cumulative overall postoperative complications even with ERAS implementation.

Smoking is associated with an increased risk of perioperative complications, including wound infections, pulmonary complications, and cardiovascular events such as myocardial infarction and stroke [11–20]. This increased risk may be due to the negative effects of smoking on the respiratory and cardiovascular systems, leading to impaired wound healing, thrombosis, and atherosclerosis [45]. Furthermore, smoking is linked to long-term complications after CABG surgery, such as graft failure, recurrent angina, and mortality [11]. The mechanisms behind this increased risk are complex, but may include accelerated atherosclerosis, oxidative stress, and inflammation [46]. Studies have consistently shown that quitting smoking prior to surgery can significantly reduce the risk of perioperative complications, improve long-term graft patency, and decrease the risk of recurrent angina and mortality [11–16, 18, 20, 45]. Therefore, it is strongly recommended that patients who smoke quit prior to undergoing CABG surgery, and smoking cessation is an integral part of the ERAS program for managing patients undergoing CABG surgery. In addition, patients who continue to smoke after surgery should be counseled on the importance of smoking cessation and offered appropriate support and resources to quit smoking. However, there is currently no comparative study evaluating the outcomes of smokers and non-smokers undergoing elective CABG after implementation of the ERAS program. Untill now, our study found that in the era of ERAS, the most 30-day and 90-day major postoperative complications were not significantly different for smokers and non-smokers undergoing elective off-pump CABG, except for 30-day and 90-day postoperative AMI and accumulative overall postoperative complications (Tables 2, 3, 4). Therefore, it is recommended that all smokers undergoing elective CABG should receive care under a well-designed ERAS program to decrease major postoperative complications and achieve outcomes comparable to those of non-smokers undergoing CABG. Given the persistent higher 30-day and 90-day AMI risk observed in smokers undergoing CABG even with an ERAS program, continued education on the importance of long-term smoking cessation remains crucial for patients at risk of undergoing CABG in future.

Our study has several notable strengths, including a large cohort of patients who underwent elective off-pump CABG under ERAS, allowing us to evaluate major postoperative outcomes in both smokers and non-smokers. The novelty of our study lies in the fact that, to our knowledge, no previous data has compared the differences in 30-day and 90-day major postoperative outcomes, such as ICU stay, hospital stay, mortality, AMI, acute renal failure, deep-wound infection, pneumonia, postoperative bleeding, pulmonary embolism, septicemia, and stroke, between smokers and non-smokers who underwent elective CABG during the era of ERAS. Our study represents the first investigation of an ERAS program's efficacy in achieving comparable major postoperative complications between smokers and non-smokers undergoing CABG (Table 2–4), with the exception of 30-day and 90-day AMI and accumulative overall postoperative complications. Given our findings, we strongly recommend the implementation of an ERAS program for patients undergoing CABG surgery, particularly smokers, as it can result in comparable outcomes to non-smokers. Furthermore, our results suggest that long-term education on smoking cessation is essential for patients at risk of receiving CABG in future, as smokers still face higher risks of AMI in the early postoperative period despite the use of ERAS.

While our study provides valuable insights into the efficacy of ERAS in improving outcomes for patients undergoing elective off-pump CABG, there are several limitations that should be taken into consideration when interpreting our findings. Firstly, our study only included patients from a single Asian population in Taiwan, and therefore, caution should be exercised when generalizing our results to other populations. Secondly, while we used PSM to balance known confounders, there is still a possibility of unknown or unmeasured confounders that could have affected the results [32]. Thirdly, important factors such as dietary habits and body mass index, which are known to be risk factors for perioperative or postoperative complications, were not included in our study. This may limit the generalizability of our results to other populations or settings where these factors may have a greater impact. Fourthly, the degree of compliance with the ERAS program was not specifically measured in our study, and therefore, the impact of adherence to the program on outcomes could not be assessed [40]. In addition, the ERAS program was not implemented under identical conditions in the smoker and non-smoker groups. While not all patients were able to quit smoking despite undergoing the ERAS program, these individuals were classified as part of the smoker group and not excluded from the analysis. This

reflects the real-world variability in adherence to program components but represents a limitation when comparing outcomes under "uniform" ERAS implementation. Unfortunately, our database did not capture detailed adherence metrics, such as the proportion of patients who successfully quit smoking before surgery, making it challenging to fully evaluate these differences. Lastly, our findings may be institution-specific as ERAS goals and outcomes are typically tailored to specific medical centers and surgical teams. Therefore, our results should be interpreted with caution when extrapolated to other hospitals or settings.

Conclusion

Our study highlights the novel finding that ERAS programs are effective in achieving similar postoperative outcomes for most major complications between smokers and non-smokers undergoing elective off-pump CABG surgery. However, smokers demonstrated higher rates of 30-day and 90-day postoperative AMI and cumulative overall complications, underscoring the persistent risks associated with smoking. This study contributes to the growing body of evidence supporting the implementation of ERAS programs in CABG surgery and emphasizes the importance of targeted strategies for smoking cessation as part of perioperative care.

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Data availability The datasets supporting the study conclusions are included within this manuscript and its additional files.

Declarations

Conflict of interests The authors have no potential conflicts of interest to declare. The datasets supporting the study conclusions are included within the manuscript.

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