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ORIGINAL ARTICLE
Coronary artery disease

Ischaemic and bleeding risk after ST-elevation myocardial infarction in patients with active cancer: a nationwide study

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Aims

Treatment of patients with cancer presenting with ST-elevation myocardial infarction (STEMI) is complex given the increased risk of both thrombotic and major bleeding complications.

Methods and results

A nationally linked cohort of STEMI patients between January 2005 and March 2019 was obtained from the UK Myocardial Infarction National Audit Project and the UK National Hospital Episode Statistics Admitted Patient Care registries. The primary outcomes were major bleeding and re-infarction at 1 year following admission with STEMI. Major bleeding was defined as bleeding events that require hospital admission. Re-infarction was defined as acute MI according to the fourth Universal Definition of Myocardial Infarction. A total of 322 776 STEMI-indexed admissions were identified between January 2005 and March 2019. Of those, 7050 (2.2%) patients were diagnosed with active cancer. Cancer patients were older with more cardiovascular comorbidities. Cancer patients received invasive coronary angiography (62.2% vs. 72.7%, $P < 0.001$) and percutaneous coronary intervention (58.4% vs. 69.5%, $P < 0.001$) less often compared with patients without cancer and were less likely to be prescribed dual antiplatelet therapy (85% vs. 95.4%, $P < 0.001$). The incidence of major bleeding (6.5% vs. 3.5%, $P < 0.001$) and re-infarction (cancer 5.7%, no cancer 5.1%, $P = 0.01$) was higher in cancer patients at 1 year. After adjustment for differences in baseline covariates, a similar risk of re-infarction (sub-hazard ratios (SHR) 1.10, 95% CI 0.94–1.27) and a 50% increased risk of major bleeding (SHR 1.49, 95% CI 1.30–1.71) were observed in cancer patients.

Conclusion

Compared with non-cancer patients, cancer patients have a higher risk of major bleeding but not of re-infarction. Mitigating bleeding risk in STEMI patients with cancer is of paramount importance to improve outcomes.

Lay summary

- Little is known about the long-term risk of bleeding and re-infarction in acute myocardial infarction patients with active cancer.
- Compared with non-cancer patients, cancer patients have a higher risk of major bleeding but not of re-infarction.
- Mitigating bleeding risk in STEMI patients with cancer is of paramount importance to improve outcomes.

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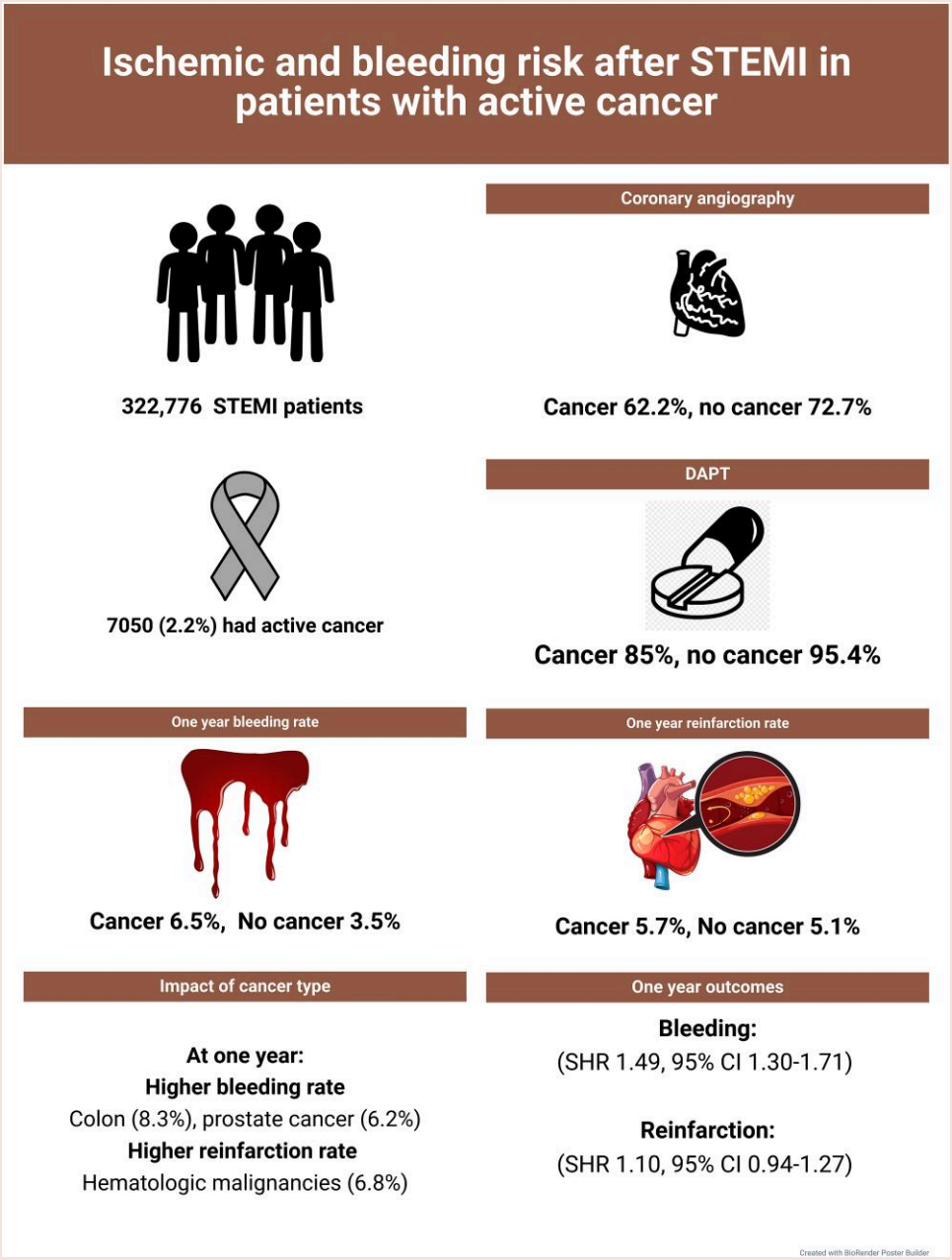
Graphical Abstract



Keywords Bleeding • Re-infarction • Cancer • Outcomes

Introduction

Cancer and cardiovascular diseases (CVDs) are the leading causes of hospitalization and mortality, with both being responsible for more than 65% of deaths in developed countries.[1,2] The concurrent diagnosis of cancer and coronary artery disease is on the rise, a trend driven by the increasing number of cancer survivors due to advancements in early detection and treatment of cancer.[3,4] Ischaemic heart disease accounts for 40–60% of cardiovascular fatalities in this group,[5,6] with CVDs overtaking cancer as the commonest cause of mortality in cancer survivors within 5–7 years.

Immediate coronary revascularization by percutaneous coronary intervention (PCI) followed by optimal medical therapy is considered the cornerstone of management of ST-elevation myocardial infarction (STEMI).[7] Nevertheless, in patients with active cancer, decisions around invasive interventions and antithrombotic therapies can be challenging due to the concurrent bleeding and thrombotic risks. Active cancer is one of the components of the academic research consortium definition

for high bleeding risk.[8,9] Coagulation and hematological abnormalities like anaemia, thrombocytopenia, and coagulopathies are common in cancer patients that increase the risk of major bleeding. Cancer can also induce a prothrombotic state through cytokines production, altered platelet activity, oxidative stress, and disruptions in coagulative and fibrinolytic activities[4,10] that increases the risk of ischaemic events, and many of the agents used to treat cancer can increase the risk of vascular thrombosis.[11] To date, only a few studies have explored the risk of re-infarction and bleeding in cancer patients after acute myocardial infarction (AMI)[12–15] and many of these have either only considered in-hospital risk, or have not studied whether risk varies by cancer type.

To better understand the balance between bleeding and ischaemic risk in AMI patients with cancer, we used multi-source linked national prospective clinical registries, including the UK Myocardial Infarction National Audit Project (MINAP) from the United Kingdom (UK) to study the ischaemic and bleeding risk after STEMI up to 1 year post-discharge in patients with active cancer.

Methods

Study design

We undertook a population-based linked health records cohort study on patients admitted with STEMI and active cancer in England and Wales between January 2005 and March 2019. Data were obtained by linking data from the National MINAP Registry (National Audit Project) with hospital admission data of the Hospital Episode Statistics (HES) registry and the national deaths registry at the Office for National Statistics (ONS).[16–18]

Table 1 Patients' characteristics

	STEMI without cancer	STEMI with cancer	*P*-value
N	315 726	7050	
Age at admission, median (IQR)	64.7 (55.0, 75.1)	74.1 (66.4, 81.0)	<0.001
Women	88 885 (28.2%)	1756 (24.9%)	<0.001
Ethnicity			<0.001
White	250 345 (91.3%)	6114 (95.9%)	
BAME	23 821 (8.7%)	259 (4.1%)	
BMI, median (IQR)	26.8 (24.1, 30.1)	25.7 (22.9, 28.9)	<0.001
Cardiac arrest	24 685 (8.1%)	492 (7.2%)	0.005
Killip class			
Killip class I	115 896 (80.2%)	2688 (73.9%)	<0.001
Killip class II	11 563 (8.0%)	423 (11.6%)	
Killip class III	4535 (3.1%)	157 (4.3%)	
Killip class IV	12 443 (8.6%)	371 (10.2%)	
Left ventricular ejection fraction			
Preserved (EF > 50%)	74 926 (47.5%)	1483 (42.1%)	<0.001
Mildly reduced (EF 40–50%)	66 804 (42.4%)	1578 (44.8%)	
Reduced (EF <40%)	15 910 (10.1%)	465 (13.2%)	
Comorbidities:			
PMH of angina	38 296 (13.8%)	1140 (18.1%)	<0.001
Previous MI	39 883 (14.2%)	1173 (18.4%)	<0.001
DM	46 365 (15.6%)	1167 (17.4%)	<0.001
Hypertension	121 205 (43.1%)	2978 (47.0%)	<0.001
Hypercholestrolaemia	84 506 (30.8%)	1727 (27.9%)	<0.001
Peripheral vascular disease	7933 (2.9%)	241 (3.9%)	<0.001
Heart failure	8016 (2.2%)	207 (3.3%)	<0.001
Stroke/TIA	14 115 (5.1%)	465 (7.5%)	<0.001
FH of CAD	83 684 (35.1%)	1153 (22.4%)	<0.001
Smoking status			
Never smoked	98 261 (33.9%)	2349 (36.9%)	<0.001
Ex-smoker	80 152 (27.7%)	2640 (41.5%)	
Current smoker	111 453 (38.4%)	1378 (21.6%)	
Chronic kidney disease	6938 (2.5%)	348 (5.6%)	<0.001
Asthma/COPD	32 443 (11.8%)	962 (15.5%)	<0.001
Previous PCI	22 702 (8.2%)	590 (9.4%)	<0.001
Previous CABG	7550 (2.7%)	267 (4.3%)	<0.001
Metastatic cancer	NA	1445 (20.5%)	

BAME, Black, Asian, and Minority Ethnic; CABG, coronary artery bypass graft; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; EF, ejection fraction; FH, family history; IQR, Interquartile range; MI, myocardial infarction; PCI, percutaneous coronary intervention; TIA, transient ischemic attack.

Hospital Episode Statistics Admitted Patient Care (HES-APC) is a registry composed of data that are collected on all admissions to National Health Service hospitals in England.[17] MINAP is a national AMI audit registry that contains information on the presentation profile and clinical care of patients hospitalized with the diagnosis of AMI in England, Wales, and Northern Ireland.[19–21] The data collected are used for research and, audit the quality of care, and public reporting of patients with AMI.[16,20,22] The data routinely collected in the registry are patient demographics, admission time and method, cardiovascular comorbidities, clinical characteristics, relevant investigations, in-hospital pharmacological and interventional treatments, in-hospital outcomes and discharge treatments.[21,23–25] The ONS is the largest independent producer of official statistics in the UK. It is responsible for collecting and publishing statistics related to the economy, population, and society at national, regional, and local levels.[18]

Ethical approval

The study underwent formal ethical approval for the data linkages of MINAP, HES, and OSN registries. The ethical approval was provided by the Health Research Authority and the Health and Care Research Wales[26] and the Confidentiality Advisory Group, which is an independent body that provides expert advice on the use of confidential patient information.[27]

Study population

To identify STEMI patients with cancer, we used methods described in our previous publications.[6] For each patient who was admitted with a primary diagnosis of STEMI and survived to discharge, patients with diagnosis of active cancer were identified using the data from the HES-APC database using the International Classification of Diseases (ICD), 10th edition, clinical modification codes (ICD-10-CM). The ICD-10-CM was also used to identify readmissions with bleeding and re-infarction. The ICD-10 codes used in this study have been listed in Supplementary material online, *Table S1*. Active cancer was defined as any patient with ongoing cancer at time of admission with STEMI. The population-based studies from the national British registries showed the HES database to be a reliable source of information about cancer and myocardial infarction diagnosis.[28,29] For example, it was found that the ability of the HES database to detect cancer diagnosis like colorectal cancer at 1 year post-diagnosis was 94%.[29] HES is also used as a benchmark to validate the reliability of primary care registries in the detection of major bleeding.[30]

Quality indicators

We used the European Society of Cardiology (ESC) Association for Acute Cardiovascular Care quality indicators (QIs) that related to STEMI to evaluate the quality of care.[22,31] We specifically used the following indicators: Reperfusion within 12 h after presentation, door to balloon time (DTBT), revascularization (PCI/CABG), left ventricular ejection fraction (LVEF) evaluation prior to discharge, P2Y12 inhibitors at discharge, dual antiplatelet therapy (DAPT) received on discharge, high-intensity statin on discharge, angiotensin converting enzyme inhibitor or angiotensin receptor blockers (ACEI/ARB) on discharge for those with mildly reduced and reduced left ventricular systolic function, beta-blocker on discharge for those with mildly reduced and reduced left ventricular systolic function, and composite opportunity-based quality indicator (OBQI).[31] The OBQI reflects the number of care opportunities fulfilled in each hospital (numerator) divided by the number of care opportunities to provide care (denominator).[32] The score consisted of six evidence-based care processes: the prescription of aspirin, thienopyridine inhibitor, β-blocker, angiotensin converting enzyme inhibitor (ACEI/ARB), HMG CoA reductase enzyme inhibitor (statin), and enrolment onto a cardiac rehabilitation program at the time of discharge.[32] Excluded from both numerator and denominator were interventions that were contraindicated, not applicable, not indicated, or declined by individual patients.

Clinical outcomes

The primary clinical outcomes were readmission with myocardial infarction (re-infarction) or major bleeding. Major bleeding was defined as any bleeding

Table 2 In-hospital pharmacology and processes of care

	STEMI without cancer	STEMI with cancer	*P*-value
N	315 726	7050	
DTBT <60 min			
>60 min	60 091 (25.8%)	1185 (29.0%)	<0.001
<60 min	172 408 (74.2%)	2898 (71.0%)	
Admitted by a cardiologist	251 449 (81.9%)	5073 (74.4%)	<0.001
Coronary angiogram	211 498 (72.7%)	3835 (62.2%)	<0.001
PCI	201 300 (69.6%)	3569 (58.3%)	<0.001
CABG	3439 (1.2%)	51 (0.8%)	0.009
Coronary revascularization	204 206 (70.6%)	3611 (59.0%)	<0.001
Cardiac rehabilitation	258 571(90.8%)	5277(83.1%)	<0.001
Inpatient medications			
Glycoprotein IIb/IIIa inhibitors	43 340 (17.3%)	655 (11.5%)	<0.001
Warfarin	9253 (3.8%)	224 (4.0%)	0.38
Beta blockers	67 179 (32.3%)	1861 (39.0%)	<0.001
Loop diuretics	66 016 (24.9%)	1882 (31.1%)	<0.001
Medications on discharge:			
ACE inhibitors	251 909 (91.4%)	4937 (80.0%)	<0.001
Aldosterone antagonists	27 403 (14.2%)	605 (12.8%)	0.007
Aspirin	267 891 (97.2%)	5684 (92.7%)	<0.001
*DAPT	175 411 (93.7%)	3810 (85.5%)	<0.001
Statins	267 372 (84.9%)	5513 (78.2%)	<0.001

*Included DAPT data after 2010. Use of DAPT prior to 2010 was limited.
ACE, angiotensin converting enzyme; CABG, coronary artery bypass graft; DAPT, dual anti-platelets therapy; PCI, percutaneous coronary intervention.

event that require hospital admission or death due to a bleeding event after discharge. Re-infarction was defined as new ischaemic pain or other symptoms consistent with acute cardiac ischaemia (e.g. sweating, nausea, hypotension) that persists until relieved with analgesia or nitrates, accompanied by new ECG changes (new elevation of ST or changes in the depression or T wave in the territory of the initial event) and a new elevation of the acute marker of cardiac necrosis to more than the upper limit of normal or an increase to a value that is >50% of the last recorded value as per the fourth Universal Definition of Myocardial Infarction, or death due to AMI after discharge. Bleeding and re-infarction events requiring hospital admission were captured from the HES-APC database using ICD10 codes (see Supplementary material online, table *S1*). The deaths due to bleeding and re-infarction were captured from the ONS database using the ICD10 codes as well.

Statistical analysis

Continuous variables were expressed as mean and standard deviation, or as median and interquartile range between parentheses (IQR) if the data is skewed. Categorical variables were expressed using percentages. χ^2 test and the *t*-test were used to test for statistical significance between categorical and continuous variables, respectively. The Kruskal-Wallis test was used for skewed data. We used the Multiple Imputations with Chained Equations algorithm to impute the missing data. It was assumed that the missing data were missing at random, and 10 imputed data sets were generated and the subsequent analyses were performed on the imputed dataset.[33–35] We used competing-risks regression models based on Fine and Gray's proportional sub-hazards model to account for mortality as a competing risk factor

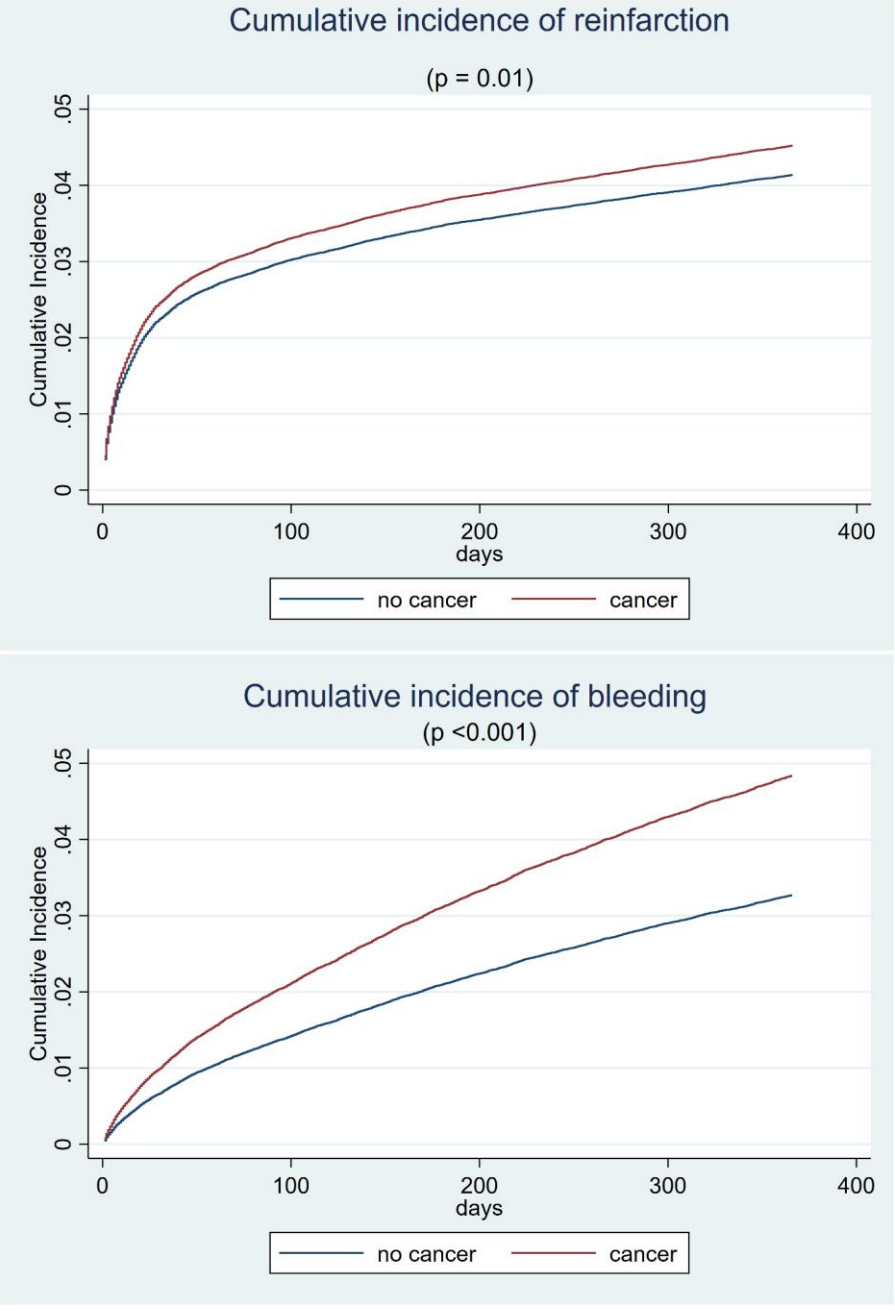


Figure 1 Cumulative incidence of re-infarction and major bleeding in STEMI patients with cancer.

for bleeding and re-infarction. The results were reported in form of the cumulative incidence function and the cumulative sub-hazard ratios (SHR). The variables we adjusted for in the models were age, sex, ethnicity, cardiac arrest, cardiogenic shock, LVEF, history of angina, previous MI, heart failure (HF), diabetes mellitus (DM), hypertension, hypercholesterolemia, peripheral vascular disease, stroke, family history (FH) of CAD, smoking, chronic kidney disease, asthma/COPD, previous PCI, previous CABG, composite quality indicator (OBQI), and DAPT. Model estimates were reported in the form of SHR and 95% confidence intervals (95% CI). The STATA version 16 software was used to complete the statistical analysis.

Results

Patients' characteristics

A total of 322 776 STEMI patients who survived to discharge were identified between January 2005 and March 2019. Of those, 7050 (2.2%) were diagnosed with active cancer. Cancer patients were older [median age (IQR) 74.1 (66.4, 81.0) vs. 64.7 (55.0, 75.1), $P < 0.001$] and were more likely to have a Killip Class II (11.6% vs. 8.0%, $P < 0.001$) and Killip Class III (4.2% vs. 3.1%, $P < 0.001$) at presentation. Cancer patients had higher frequency of cardiovascular comorbidities such as angina (18.1% vs. 13.8%, $P < 0.001$), previous MI (18.4 vs. 14.1, $P < 0.001$), DM (17.3% vs. 15.5%, $P < 0.001$), hypertension (47.0% vs. 43.1%, $P < 0.001$), peripheral vascular disease (3.9% vs. 2.9%, $P < 0.001$), chronic kidney disease (5.6% vs. 2.5%), and prior history of stroke (7.5% vs. 5.1%, $P < 0.001$). *Table 1* shows the baseline characteristics of patients with STEMI with and without active cancer. In patients with cancer, the most common cancer was prostate cancer (30.6%) and hematologic malignancies (15.2%). Supplementary material online, table *S2* shows the different types of cancer in the study population. Patients with cancer have higher rate of all-cause death at 1 year following STEMI (35.8% vs. 6.8%, $P < 0.001$). In patients without cancer, the rate of non-cardiac death was lower than cardiovascular death (2.0% vs. 4.8%). In contrast, in patients with cancer the rate of non-cardiac death was remarkably higher than cardiovascular death (28.1% vs. 7.8%). Supplementary material online, table *S3* shows the cause of death in patients with and without cancer.

Process of care and European Society of Cardiology quality indicator

The cancer group was less likely to be admitted under a cardiologist (74.4% vs. 81.9%, $P < 0.001$) and had lower rates of invasive coronary angiography (62.2% vs. 72.7%, $P < 0.001$), PCI (58.4% vs. 69.5%, $P < 0.001$), and CABG (0.8% vs. 1.2%, $P = 0.009$) (*Table 2*). The proportion of STEMI patients receiving PCI increased from 23% in 2005 to 87% in 2019 as shown in supplementary material online, *Figure S3*.

Cancer patients were less likely to be referred to cardiac rehabilitation services (83.0% vs. 90.8%, $P < 0.001$) at discharge. There was a significant gap in administration of guideline-indicated medications such as DAPT (85% vs. 95.4%, $P < 0.001$), ACE inhibitors (80.0% vs. 91.4%, $P < 0.001$), and statins (78.2% vs. 84.9%, $P < 0.001$) in cancer patients (*Table 2*).

Bleeding and re-infarction events

The incidence of major bleeding (cancer 1.8% vs. no cancer 0.7%, $P < 0.001$) and re-infarction (cancer 3.6% vs. no cancer 3.1%, $P = 0.03$) was higher in cancer patients at 30 days. Likewise, the incidence of major bleeding (6.5% vs. 3.5%, $P < 0.001$) and re-infarction (cancer 5.7%, no cancer 5.1%, $P = 0.01$) was higher in cancer patients at 1 year. *Figure 1* shows the cumulative incidence of bleeding and re-infarction.

After adjusting for patients' characteristics and comorbidities, the risk of re-infarction (SHR 1.10, 95% CI 0.94–1.27) in cancer patients was comparable to patients without cancer. However, the risk of bleeding was higher by almost 50% (SHR 1.49, 95% CI 1.30–1.71). We performed a sensitivity analysis on patients who underwent PCI, which was consistent with the overall analysis, cancer patients were at higher risk of major bleeding (SHR 1.53, 95% CI 1.30–1.79), but not re-infarction (SHR 1.12, 95% CI 0.93–1.35) (*Table 3*). *Figures 2* and *3* show the cumulative SHRs for bleeding and re-infarction.

Table 3 One year risk of re-infarction and major bleeding in STEMI patients with active cancer

	SHR (95% CI)
All patients	
Re-infarction at 1 year	1.10 (0.94–1.27)
Major bleeding at 1 year	1.49 (1.30–1.71)
Patients received PCI	
Re-infarction at 1 year after PCI	1.12 (0.93–1.35)
Major bleeding at 1 year after PCI	1.53 (1.30–1.79)

PCI, percutaneous coronary intervention; SHR, sub-hazard ratio.

Figure 4 shows the average daily incidence of bleeding and re-infarction in STEMI patients with cancer. The re-infarction rate peaks on the first day post-discharge and then tapers down from 1.7% on the first day post-discharge to 0.2% at 60 days. Similarly, the bleeding rate peaks on the second day post-discharge and declines gradually and plateaus after 60 days. This pattern is also notable in patients without cancer (see Supplementary material online, *Figure S1* and *S2*).

Bleeding and re-infarction events increase the risk of death at 1 year after the event by more than nine-fold (*Figure 5*). Patients readmitted for major bleeding (HR 9.5, 95% CI 9.1–9.9) have a relatively higher risk of death at 1 year after the event than patients readmitted with re-infarction (HR 8.1, 95% CI 7.8–8.5). The risk of death after bleeding events is much higher in cancer patients as shown in *Figure 5* (HR 15, 95% CI 12.05–17.97) compared with patients without active cancer (HR 9.06, 95% CI 7.71–10.64).

Bleeding and re-infarction by cancer type

Figure 6 shows the bleeding and re-infarction events at 1 year in the most common cancers in the UK. The rate of bleeding was higher than re-infarction in patients with colon cancer (bleeding 8.3% vs. re-infarction 6.6%) and prostate cancer (bleeding 6.2% vs. re-infarction 5.2%). The rate of re-infarction was higher than bleeding in patients with hematologic malignancies (bleeding 5.2% vs. re-infarction 6.8%). The rates of bleeding and re-infarction were relatively comparable in patients with breast (bleeding 4.0% vs. re-infarction 4.3%) and lung cancer (bleeding 6.8% vs. re-infarction 6.9%).

Discussion

This nationwide study of more than 320 000 patients reports risks of bleeding and re-infarction after STEMI in patients with active cancer, providing important novel insights on the optimal management of this complex population. The study shows that the most common adverse event after STEMI at 1 year in cancer patients is major bleeding rather than re-infarction, highlighting the high bleeding risk characteristics of this population. After adjusting for patients' characteristics and comorbidities, cancer remains an independent risk factor for bleeding, but not for re-infarction. The risk of both re-infarction and bleeding in STEMI patients with cancer peaks on the first days post-discharge and tapers gradually until it plateaus after 60 days. Major bleeding is associated with a significant increase in all-cause death, which is larger in

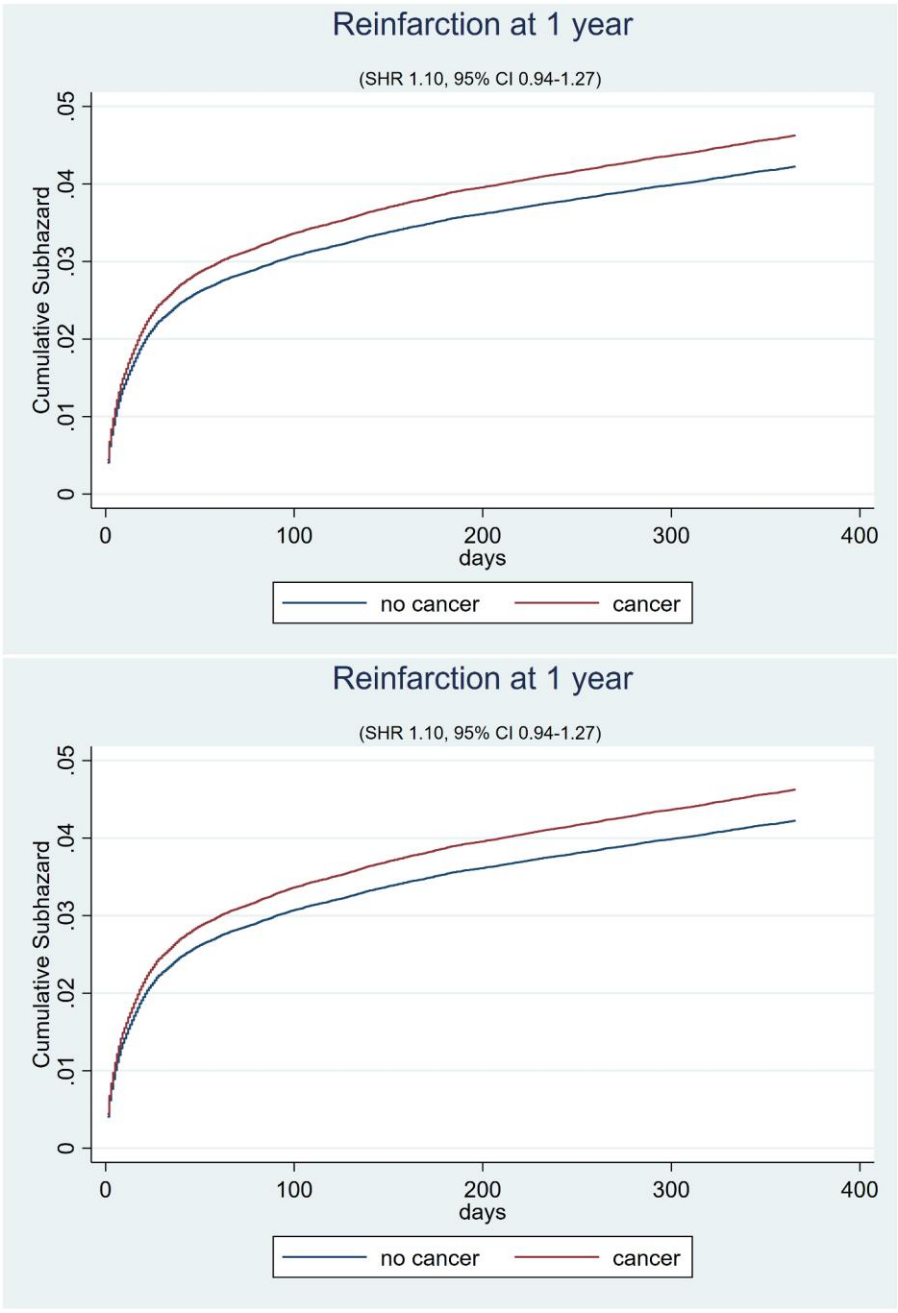


Figure 2 Competing risk models for re-infarction and bleeding events in STEMI patients with cancer.

magnitude compared with that associated with re-infarction. The balance between major bleeding and re-infarction risk changes based on cancer type, with major bleeding being dominant in colon and prostate cancer, whereas re-infarction is more common than bleeding in haematological malignancies. The risk of death after bleeding events is higher in cancer patients than patients without active cancer.

Clinicians increasingly face dilemmas when it comes to decisions related to invasive coronary therapy and prescription of antiplatelet/antithrombotic agents both in terms of type and duration in cancer patients due to the conflicting pathophysiologic effects of cancer. Cancer can induce a pro-inflammatory and prothrombotic state by interacting with coagulation pathways and inducing endothelial dysfunction.[36] Cancer treatments can also pre-dispose to myocardial infarction by accelerating atherosclerosis and plaque rupture, induce coronary vasospasm, or trigger coronary thrombosis.[37] On the other hand, bleeding is also a frequent challenge in cancer and can be triggered by local tumour invasion, tumours angiogenesis, or interaction with chemotherapeutic agents such as bevacizumab.[38] These challenges are compounded by the lack of robust evidence related to STEMI management in cancer patients due to exclusion of cancer patients from majority of concurrent clinical trials.[39]

Few studies explored the association between cancer and re-infarction in STEMI patients. Earlier studies reported a trend of higher risk of re-infarction in cancer patients. For example, data from the nationwide Japanese registry of all cardiac and vascular diseases and the

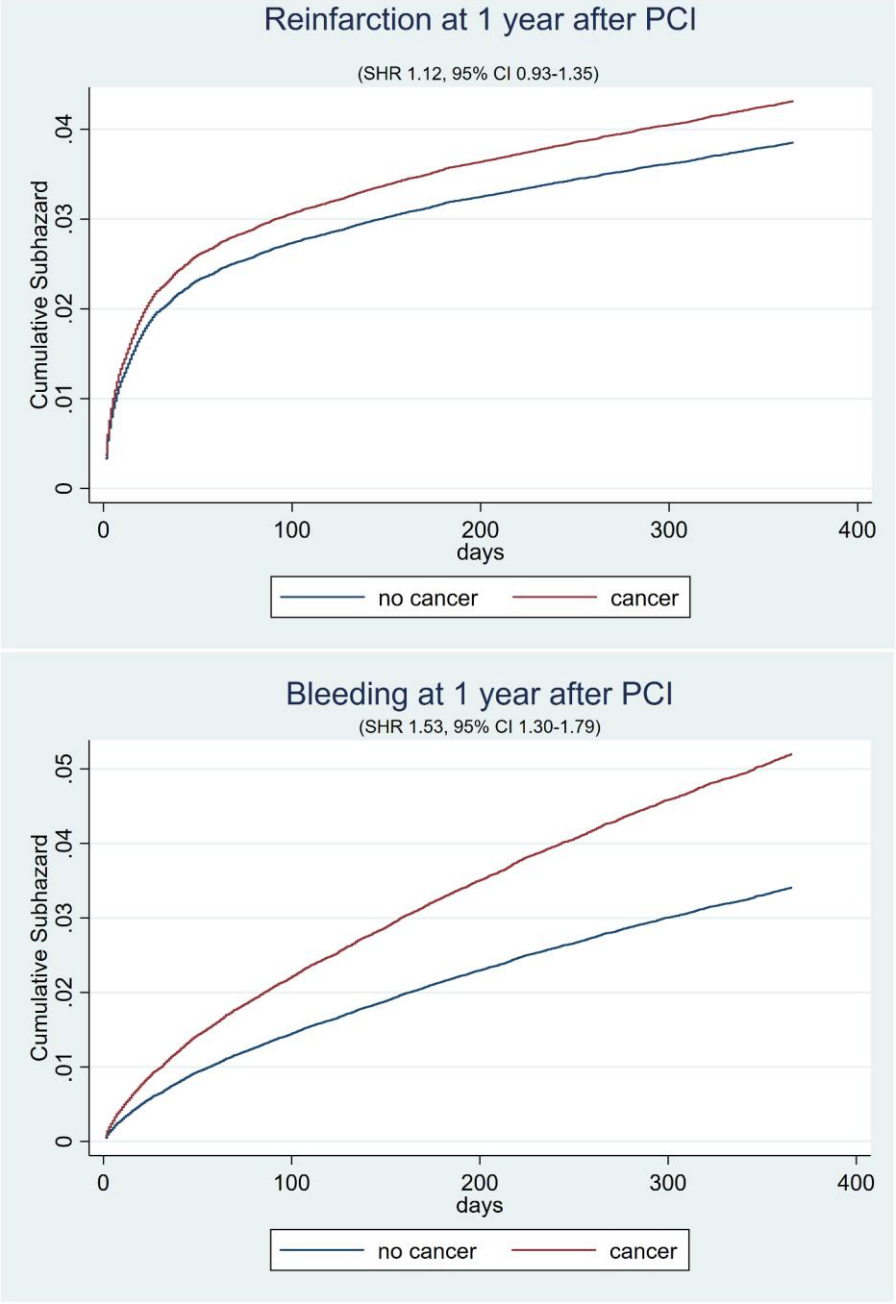
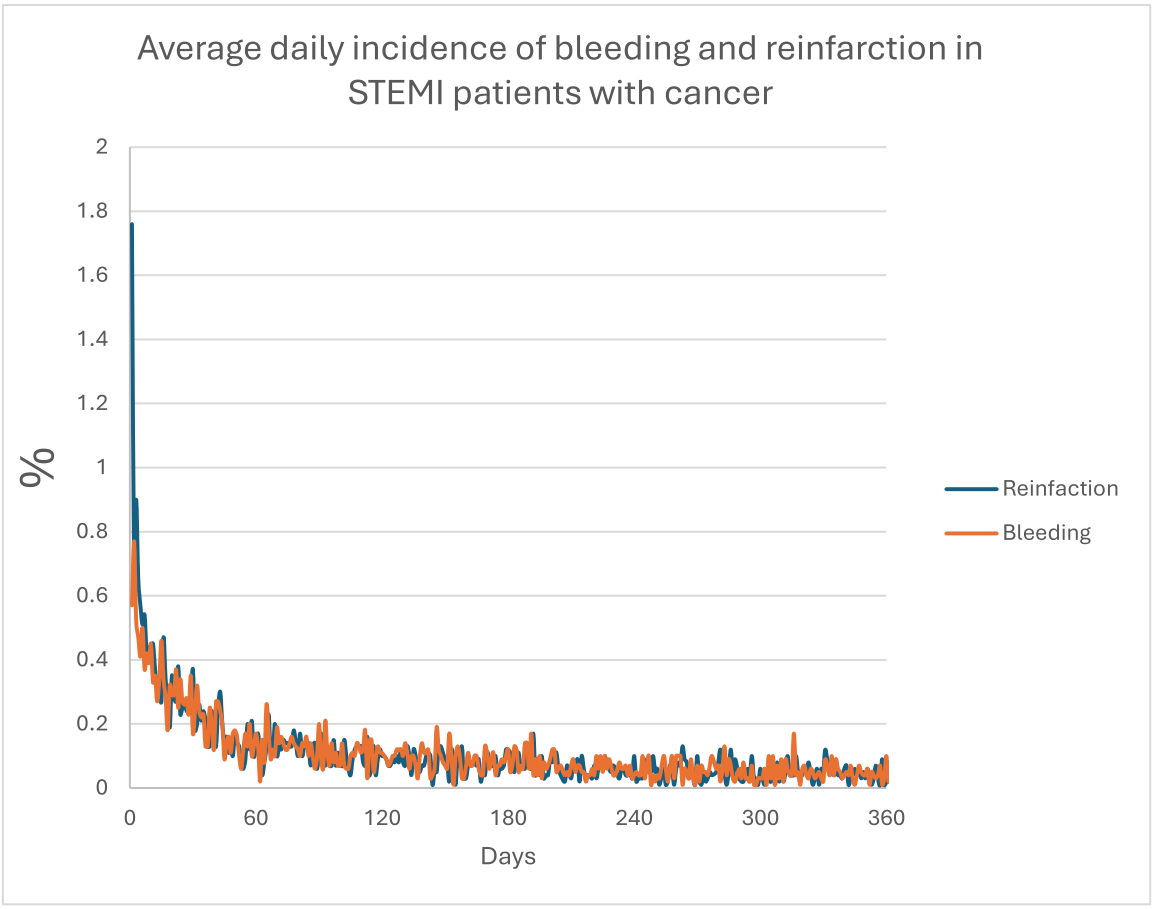


Figure 3 Competing risk models for re-infarction and bleeding events in patients who had PCI.

diagnosis procedure combination showed that cancer patients have higher risk of re-infarction.[40] Data from the National Heart, Lung, and Blood Institute Dynamic Registry, USA showed that among patients presenting with myocardial infarction, cancer patients had higher rates of recurrent infarction.[13] However, consistent with our study, a more recent study from the Coronary Revascularization Demonstrating Outcome Study in Kyoto showed that cancer was not associated with higher risk of ischaemic events.[14,41] Nevertheless, these studies have not considered whether the risk of ischaemic events varies amongst different cancer types. Our study shows that the rate of re-infarction at the first year varies depending on the cancer type from around 4% in breast cancer to around 6.9% in patients with lung and hematologic malignancies.

We also observed that cancer increases the risk of major bleeding by around 50% at 1 year post-discharge. This is consistent with the prior findings from the nationwide Swedish quality registries, which showed that cancer is strongly associated with severe bleeding in patients presenting with AMI.[42] Cancer can increase bleeding risk either directly through formation of fragile blood vessels formed because of cancer-induced angiogenesis, or by indirectly increasing the risk of bleeding remote from the cancer site.[43] In patients with AMI, bleeding risk may be increased due to concomitant use of anti-platelets therapy. Notably,



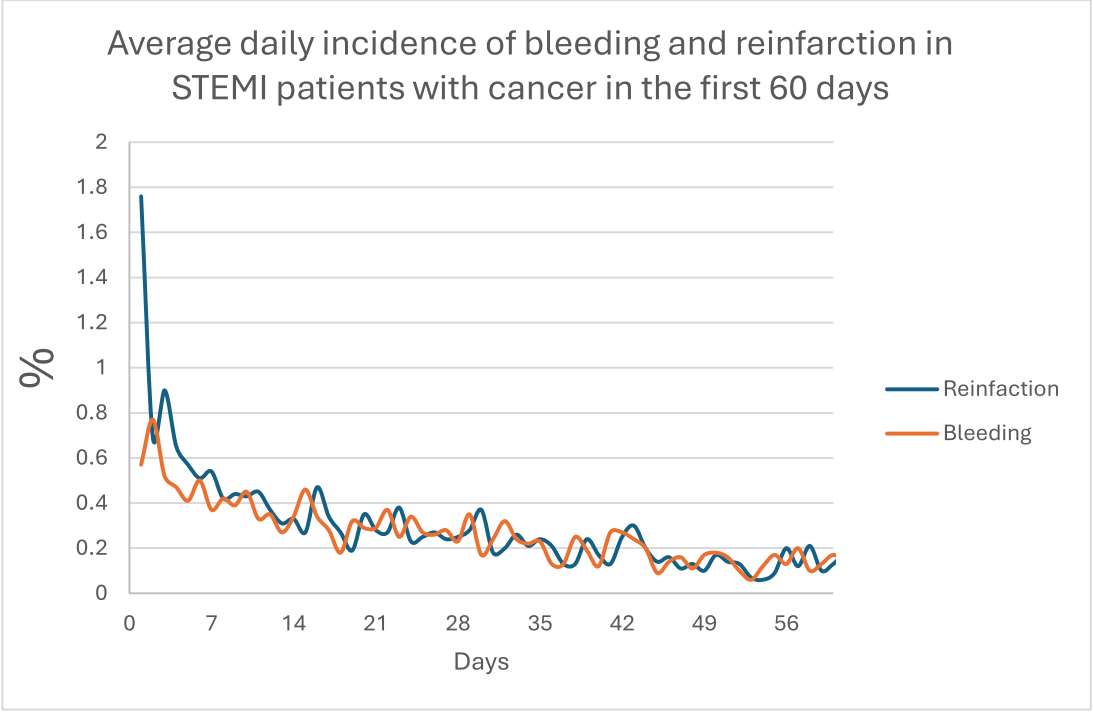


Figure 4 Daily incidence rate of re-infarction and bleeding in STEMI patients with cancer.

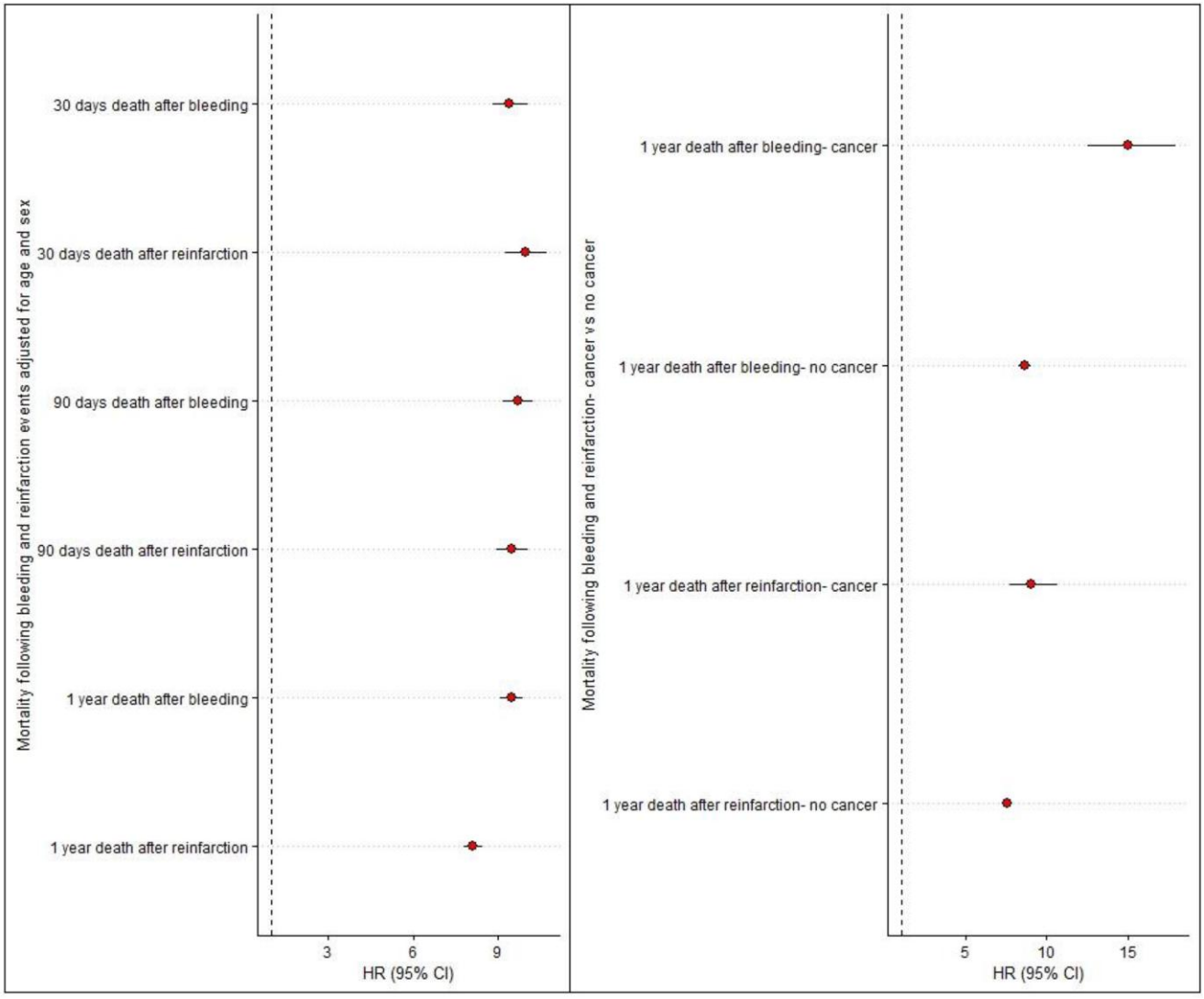


Figure 5 Risk of death following bleeding and re-infarction.

colon cancer has the highest rate of bleeding at 1 year with almost 1 out of 12 patients requiring hospital admission for major bleeding. The mechanism underlying the higher risk of bleeding in colon cancer patients may point towards a causative role of DAPT, as aspirin has topical and systemic effects on the gastrointestinal mucosa, which lead to mucosal damage and bleeding in both the upper and lower gastrointestinal tract.[44,45]

The Academic Research Consortium for High Bleeding Risk define high bleeding risk as major bleeding rate more than 4% at the first year.[9] According to this definition, active cancer is considered a major criterion and might alone qualify a patient at high bleeding risk. This statement, appear fully justified by the event rates observed in our population, where major bleeding occurred in 6.5% of patients with active cancer. This holds particularly true for patients with colon cancer, lung cancer, and prostate cancer. Therefore, mitigation of the risk of bleeding in STEMI patients with cancer is of paramount importance.[7,46] Duration and type of DAPT may be modulated to optimize the balance between bleeding and ischaemic risk in these patients. There is growing evidence that a shorter duration of DAPT (for 1–3 months) in high bleeding risk patients lowers bleeding and cardiovascular mortality without increasing ischaemic events.[47,48] Hence, a shorter treatment duration, followed by aspirin or P2Y12 inhibitor monotherapy in patients with active cancer appears particularly appropriate. Whether modulation of DAPT intensity, de-escalating potent P2Y12 inhibitors to clopidogrel, or a lower drug dose requires further study and is currently evaluated in multiple randomized controlled trials.[7] Finally, whether aspirin or P2Y12 inhibitor monotherapy should be preferred in cancer patients should be better explored in future studies.

The main strength of this study is the large sample size derived from multiple centres from national registries designed specifically for purposes of research and quality improvement. It also provides insights on the long-term outcomes, but it has limitations. The observational design of this study limits causality conclusions. It was not possible to identify the exact staging of the cancer because it is not routinely captured in the database. Part of the study population includes patients treated before emergence of some of the modern techniques in PCI and cancer therapy. The database also fails to capture the duration of anti-platelets use after discharge, which limit the identification of

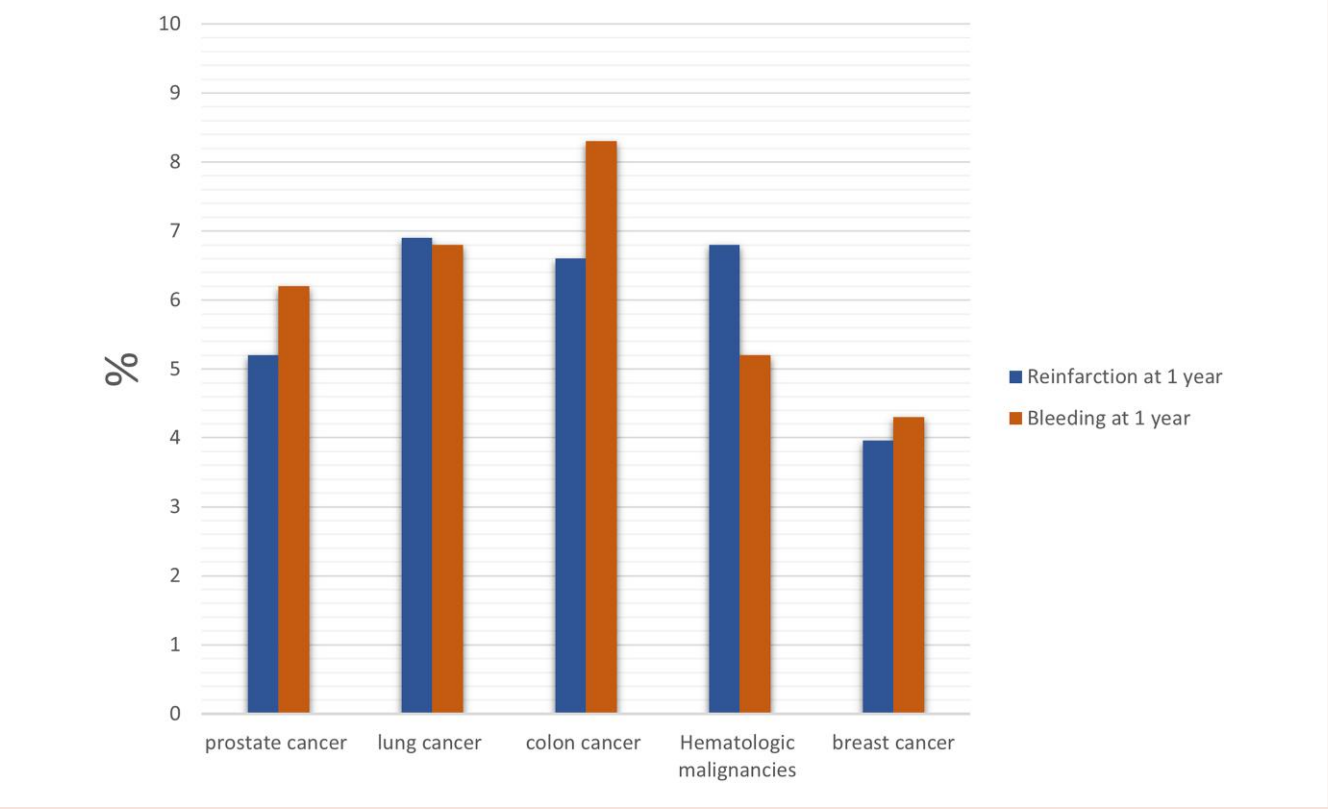


Figure 6 Bleeding and re-infarction events at 1 year in different types of cancer.

patients who had re-infarction due to DAPT cessation. The registry also lacks data on cancer treatment at various stages of disease, which limit our ability to evaluate the impact of treatment on bleeding and ischaemic risk.

To conclude, the findings of this study have important implications as it shows that cancer patients STEMI with active cancer are at significant higher risk of bleeding rather than re-infarction. Clinicians should pay more attention to the risk of bleeding and try to mitigate the risk of bleeding by limiting the duration of anti-platelets in high bleeding risk patients especially patients with colon cancer.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

Supplementary material

Supplementary material is available at *European Heart Journal Open* online.

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