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CLINICAL RESEARCH
Interventional cardiology

Percutaneous coronary intervention in cancer patients: a report of the prevalence and outcomes in the United States

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Aims This study aims to examine the temporal trends and outcomes in patients who undergo percutaneous coronary intervention (PCI) with a previous or current diagnosis of cancer, according to cancer type and the presence of metastases.

Methods and results Individuals undergoing PCI between 2004 and 2014 in the Nationwide Inpatient Sample were included in the study. Multivariable analyses were used to determine the association between cancer diagnosis and in-hospital mortality and complications. 6 571 034 PCI procedures were included and current and previous cancer rates were 1.8% and 5.8%, respectively. Both rates increased over time and the four most common cancers were prostate, breast, colon, and lung cancer. Patients with a current lung cancer had greater in-hospital mortality (odds ratio (OR) 2.81, 95% confidence interval (95% CI) 2.37–3.34) and any in-hospital complication (OR 1.21, 95% CI 1.10–1.36), while current colon cancer was associated with any complication (OR 2.17, 95% CI 1.90–2.48) and bleeding (OR 3.65, 95% CI 3.07–4.35) but not mortality (OR 1.39, 95% CI 0.99–1.95). A current diagnosis of breast was not significantly associated with either in-hospital mortality or any of the complications studied and prostate cancer was only associated with increased risk of bleeding (OR 1.41, 95% CI 1.20–1.65). A historical diagnosis of lung cancer was independently associated with an increased OR of in-hospital mortality (OR 1.65, 95% CI 1.32–2.05).

Conclusions Cancer among patients receiving PCI is common and the prognostic impact of cancer is specific both for the type of cancer, presence of metastases and whether the diagnosis is historical or current. Treatment of patients with a cancer diagnosis should be individualized and involve a close collaboration between cardiologists and oncologists.

Keywords PCI • Cancer • Complications • Mortality

Introduction

Cardiovascular diseases and cancer are the leading causes of death in developed countries, accounting for two-thirds of disease-related mortality.[1] They frequently co-exist in an increasingly aging population with shared risk factors such as tobacco use.[2,3] Despite advanced treatments that have improved survival rates across both conditions, cancer treatments are also known to have cardiovascular side effects.[4–7] Many chemotherapeutic agents are associated with angina, myocardial infarction (MI), and acceleration of pre-existing

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coronary artery disease (CAD),[8–11] and radiotherapy is associated with CAD through direct endothelial injury.[12,13] Furthermore, cancer is associated with a hypercoagulable state with increased platelet activation and aggregability, despite the increased prevalence of thrombocytopenia.[14,15]

Percutaneous coronary intervention (PCI) is the most common modality of coronary revascularization increasingly undertaken in multi-morbid patients.[16,17] These patients tend to be older,[18–21] with greater comorbid burden[18–20] and more extensive CAD.[19] A history of cancer is independently associated with increased risk of major adverse cardiovascular events[21,22] including cardiac mortality,[20] target lesion revascularization,[21] and major bleeding.[22,23,24]

There are limited data on clinical outcomes after PCI in patients with a coexistent diagnosis of cancer as many of the prior studies do not differentiate between current and prior diagnoses of cancer, cancer type, or the staging of cancer such the presence of metastases having pooled all cancer subtypes together. Additionally, most randomized controlled trials of cardiovascular care and outcomes exclude patients with active malignancy and treatment. The Nationwide Inpatient Sample offers an opportunity to evaluate the association between a current or historical cancer diagnosis and outcomes based on stage in the 'real-world' setting of a large, contemporary cohort of over 6 million US patients undergoing PCI. In this analysis, we examine temporal trends, clinical and procedural characteristics, indications for PCI, and clinical outcomes stratified by type of cancer diagnosis and stage over a 10-year period.

Methods

Data source

The data used in the current study are derived from the National Inpatient Sample (NIS) for hospital discharges in the United States between 2004 and 2014. The NIS is the largest all-payer inpatient health care database in the United States developed by the Healthcare Cost and Utilization Project (HCUP) and sponsored by the Agency for Healthcare Research and Quality (AHRQ). The NIS dataset contains hospital information on between 7 and 8 million yearly hospital discharges from 2004 onwards. Since 2012, the NIS samples discharges from all hospitals participating in HUCP, approximating a 20% stratified sample of all discharges from US community hospitals. The sampling strategy has changed over time in order to produce more generalizable estimates by reducing sampling bias. Before 2012 the NIS retained all discharges, but only from a sample of hospitals.

Study design

All individuals having a PCI between January 2004 and December 2014 were ascertained by identifying all eligible discharges with an International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) procedure codes of either 00.66 [*Percutaneous Transluminal Coronary Angioplasty (PTCA)*], 36.06 (*Insertion of non-drug-eluting coronary artery stent(s)*) or 36.07 (*Insertion of a drug-eluting coronary artery stent(s)*). Before a revision of the codes in 2005 the codes 36.01 (*Single vessel PTCA or coronary atherectomy without mention of thrombolytic agent*), 36.02 (*Single vessel PTCA or coronary atherectomy with mention of thrombolytic agent*), and 36.05 [*Multiple vessel PTCA or coronary atherectomy performed during the same operation, with or without mention of thrombolytic agent*] were also used. These codes were also included when identifying procedures in discharges from 2004 and 2005.

Records were eligible for inclusion if the discharge record showed that a PCI procedure had been performed during the hospitalization in a patient over the age of 18. Information on patient demographics were recorded for each hospital discharge including age, gender, race, admission type (elective or emergent), admission day (weekday or weekend), median household income according to ZIP code, the expected primary payer, and patient comorbidity conditions using the Elixhauser comorbidity index. Each discharge record had information on up to 30 diagnoses (15 between 2004 and 2008, 25 between 2009 and 2013, and 30 in 2014). These diagnosis codes were used to identify whether the patient had a primary diagnosis of an acute myocardial infarction (AMI), cardiogenic shock, ST-elevation myocardial infarction (STEMI), or non-ST-elevation myocardial infarction (NSTEMI) during hospitalization. Diagnostic codes were also used to identify other patient comorbidities including smoking, hypercholesterolaemia, and historical patient information.

Information regarding the PCI was determined from the procedure codes, including whether the PCI was a multi-vessel or single-vessel procedure and whether it involved bifurcation stenting. The use of adjunctive devices including intracoronary pressure wire, intravascular ultrasound, and an assist device [such as an intra-aortic balloon pump (IABP)] were also recorded. Where available stent type deployed (bare metal, drug-eluting) were identified.

A cancer diagnosis on each of the included records was identified using clinical classifications software (CCS) developed by HCUP. These codes categorize ICD-9 codes into clinically meaningful categories, which can be used to search for particular conditions. A diagnosis of cancer on the record was identified by using CCS codes between 11 and 44, all corresponding to different cancer types.[25] Individual ICD-9 codes within each CCS code were utilized in order to categorize the diagnosis into a current diagnosis, where the patient had an active diagnosis during hospital admission or historical cancer diagnosis, where the ICD-9 code identified a personal history of the cancer type.

Clinical outcomes

In-hospital clinical outcomes including: in-hospital mortality, cardiac complications, post-operative stroke, bleeding, and vascular complications were identified. The length of stay on the discharge record and the total billed hospitalization charge for each individual discharge were recorded. As the total billed charge is not representative of the hospital services cost, a charge to cost conversion ratio was used in order to covert the reported charges into the actual cost for the payer.

Procedural complications and safety indicators were identified using ICD-9-CM codes in any secondary diagnosis field. Cardiac complications included iatrogenic and pericardial complications or need for bail out or emergency coronary artery bypass grafting (CABG). Bleeding complications included gastrointestinal, retroperitoneal, intracranial, intracerebral haemorrhage, unspecified haemorrhage, and whether a blood transfusion was required, Supplementary material online, *Table S1*.

Statistical analysis

Statistical analysis was performed on STATA/MP version 14.0. Continuous variables are presented as median and interquartile range, due to skewed data, and categorical data are presented as number and percentage. Where missing data were less than 10% of the covariate data, the observations with missing data were removed. Data were assumed to be missing at random. For all analyses, the survey estimation commands were used (by using the svy prefix in analyses conducted in Stata), this followed the recommendations from AHRQ for analysis of survey data to account for the complex survey design of the NIS database. The use of sampling weights are required because the design of the study means that different observations may have

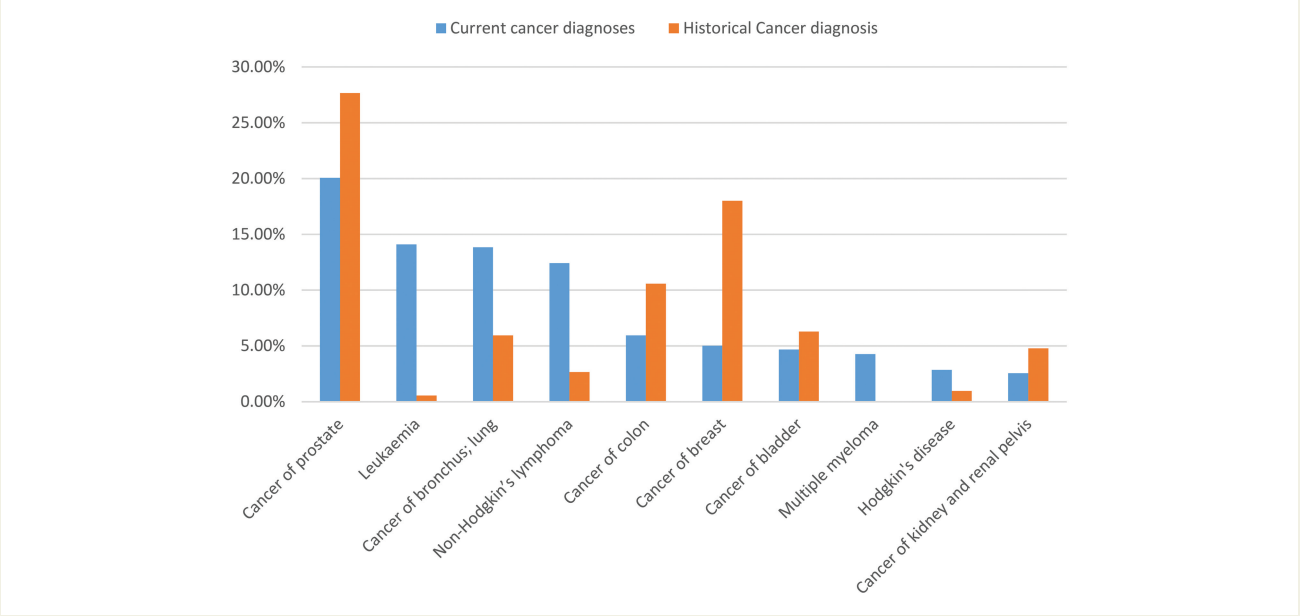


Figure 1 Percentages of top 10 prevalent current cancer diagnoses, along with historical prevalence of each type of cancer.

different probabilities of selection. Due to the redesign of the NIS data and the alternative sampling strategy used before 2012, these weights needed to be updated from the original sampling weights for 2004–2011 in order for the analysis to be conducted across all included years. Due to records being sampled by hospitals rather than individuals, clustering of records within hospitals was taken into account in the survey estimation. This was done by defining each hospital to be the primary sampling unit. For calculation of national estimates and correct variances, sampling weights for each individual discharge that were provided by the AHRQ were used.

Multivariable analyses were conducted to investigate the impact of the patient having a current or historical diagnosis of cancer compared to those records with no cancer on (i) in-hospital mortality, (ii) any defined complication, and (iii) a composite of any of the considered complication. Logistic regression models were fitted in order to investigate the impact of a current cancer diagnosis on in-hospital death or an in-hospital complication, either post-operative bleeding, vascular complication, cardiac complication, or a stroke/transient ischaemic attack (TIA).

The four most prevalent cancers, prostate, breast, colon, and lung cancers, were studied. Analyses were conducted to look at the impact of a current or historical cancer diagnosis of each cancer type compared to no cancer diagnosis. After this, the focus turned more specifically to patients with a current cancer diagnosis of the four most prevalent cancers. Within these cancer diagnoses, the presence or absence of metastases was considered. In order to assess the impact of the cancer diagnosis, all models were adjusted for potential confounders. These included age, gender, median income, expected payer, elective admission, primary diagnosis of MI, STEMI/NSTEMI diagnosis, diagnosis of shock, use of an assist device or IABP, the type of stent used, multi-vessel PCI and year of hospitalization, as well as the Elixhauser comorbidities, smoking status, and previous MI, PCI, CABG, or stroke.

Although the main interest lay in the four different cancer types, the effect of patients having a current or historical cancer diagnosis (of any type) was also considered.

Results

A total of 7 121 387 PCI procedures were undertaken between 2004 and 2014. Discharges with less than 10% missing data for included outcomes as well as covariates including age, gender, and PCI indication were excluded, so that 6 571 034 procedures were included in the final analysis. In total, approximately 7% of the procedures were removed due to missing data, Supplementary material online, *Figure S1*.

Between 2004 and 2014, there was a modest increase in the number of PCI procedures performed on patients with a current cancer diagnosis over time, although a greater increase was observed in patients with a historical cancer diagnosis, from around 4.8% in 2004 up to 7.2% in 2014 (Supplementary material online, *Figure S2*). The prevalence of the top 10 current cancer diagnoses in patients undergoing PCI, alongside the corresponding prevalence for a diagnosis for each cancer in the past medical history (historical prevalence) are depicted in *Figure 1*. Prostate cancer had the highest prevalence of both current and historical cancer diagnoses. A complete distribution of cancer types is given in Supplementary material online, *Table S2*, and a closer look at how the proportions of each of the top 10 cancer types make up the current and historical cancer diagnoses is given in Supplementary material online, *Table S3*.

Four most common cancer diagnoses

In patients who underwent PCI, the four most common malignancies were prostate, breast, colon, and lung cancer. A selection of the clinical demographics and characteristics of these cancer types stratified by type of diagnosis, current or historical, are presented in *Table 1*, with the full table given in Supplementary material online, *Table S4*. Approximately 98% of patients diagnosed with breast cancer were

Table 1 Characteristics of records with four different current and historical cancers diagnoses and patients with no cancer diagnosis (shortened version)

	Prostate cancer		Breast cancer		Colon cancer		Lung cancer		No cancer
	Current (n = 23 071)	Historical (n = 99 994)	Current (n = 5763)	Historical (n = 64 983)	Current (n = 6746)	Historical (n = 37 839)	Current (n = 15 801)	Historical (n = 21 312)	(n = 6 086 339)
Patient characteristics									
Median age (years) [IQR]	74 [97,80]	75 [68,80]	70 [62,77]	74 [66,80]	72 [65,79]	75 [67,81]	69 [63,76]	71 [64,77]	64 [55,73]
Gender—male	100%	100%	0.2%	0.2%	64.2%	64.2%	65.3%	61.5%	66.4%
White	64.2%	69.3%	62.6%	68.8%	62.8%	69.5%	66.6%	73.6%	62.5%
Black	7.8%	6.4%	8.8%	6.9%	7.8%	5.1%	7.3%	5.0%	6.4%
Hispanic	4.2%	3.6%	4.5%	3.6%	4.3%	3.8%	2.9%	2.6%	5.5%
Missing ethnicity	20.4%	17.1%	19.8%	17.2%	21.5%	17.8%	19.8%	16.0%	20.4%
Admission types—elective	29.2%	25.4%	24.7%	23.9%	30.5%	25.0%	22.7%	25.1%	27.3%
Admission day, weekday	85.4%	83.8%	83.1%	83.4%	84.0%	83.8%	82.1%	84.2%	83.9%
Median ZIP income									
1st quartile	23.9%	21.5%	26.7%	23.8%	30.0%	25.3%	28.3%	24.8%	26.5%
2nd quartile	25.9%	25.1%	28.8%	26.7%	27.5%	26.8%	27.7%	27.8%	26.9%
3rd quartile	25.3%	25.6%	25.1%	25.3%	24.5%	24.1%	24.7%	25.1%	24.8%
4th quartile	24.9%	27.6%	19.4%	24.2%	18.4%	23.9%	19.2%	22.3%	21.8%
Expected primary payer									
Medicare	76.0%	78.2%	69.9%	76.4%	71.7%	77.0%	69.1%	74.7%	49.7%
Private	19.4%	18.3%	20.7%	18.5%	18.5%	17.9%	20.7%	19.1%	35.6%
Procedure details									
Single-vessel PCI	71.5%	73.8%	73.1%	75.8%	69.5%	74.2%	71.6%	75.3%	72.8%
Multi-vessel PCI	19.2%	19.3%	17.9%	17.1%	17.8%	18.6%	17.8%	17.7%	17.8%
Bifurcation stenting	1.8%	2.1%	2.0%	1.9%	1.2%	2.0%	1.9%	1.8%	1.7%
Use of assist device or IABP	3.4%	2.6%	4.3%	2.6%	5.6%	2.3%	6.7%	3.4%	3.3%
Bare metal stent	31.5%	23.0%	36.3%	22.4%	46.8%	26.8%	49.6%	27.6%	21.6%
Drug-eluting stent	63.3%	73.0%	57.1%	73.1%	38.4%	68.9%	39.3%	67.1%	73.7%
Unknown stent type	7.7%	6.3%	7.83%	6.53%	15.88%	6.70%	12.82%	7.3%	6.9%
Both stent types used	2.5%	2.3%	1.26%	2.06%	1.18%	2.45%	1.76%	2.0%	2.2%
Intravascular ultrasound	5.0%	5.4%	3.9%	5.6%	5.0%	4.8%	4.4%	5.0%	4.9%
Record characteristics									
Primary diagnosis AMI	36.8%	39.2%	44.0%	40.4%	36.1%	40.3%	47.6%	38.3%	41.1%
STEMI diagnosis during hospitalization	19.8%	18.4%	22.6%	19.1%	26.0%	18.1%	30.4%	17.8	23.1%
NSTEMI diagnosis during hospitalization	24.0%	25.0%	28.5%	25.8%	28.3%	26.4%	30.1%	26.8%	22.7%
Diagnosis of shock	2.9%	1.9%	3.4%	2.4%	6.0%	2.3%	6.7%	3.3%	2.8%
Median length of stay, days, median [IQR]	2 [1,4]	2 [1,4]	3 [1,5]	2 [1,4]	4 [2,10]	2 [1,4]	4 [2,8]	2 [1,4]	2 [1,4]

Continued

Table 1 *Continued*

	Prostate cancer		Breast cancer		Colon cancer		Lung cancer		No cancer
	Current (*n* = 23 071)	Historical (*n* = 99 994)	Current (*n* = 5763)	Historical (*n* = 64 983)	Current (*n* = 6746)	Historical (*n* = 37 839)	Current (*n* = 15 801)	Historical (*n* = 21 312)	(*n* = 6 086 339)
Median total charge ($) [IQR]	$18 125 [$13 380, $25 857]	$17 573 [$13 223, $24 060]	$18 303 [$13 711, $25 789]	$17 713 [$13 200, $24 513]	$22 641 [$14 792, $37 833]	$17 615 [$13 062, $24 595]	$21 431 [$14 927, $32 155]	$17 817 [$13 049, $24 558]	$17 396 [$12 930, $24 186]
Comorbidities									
Hypercholesterolaemia	13.2%	14.2%	12.4%	13.7%	10.4%	13.4%	9.8%	10.8%	13.5%
Smoking	28.2%	33.9%	27.0%	26.9%	23.7%	31.0%	48.6%	52.4%	35.5%
Anaemias	13.9%	10.5%	17.9%	14.0%	34.1%	14.6%	21.4%	12.5%	8.3%
Congestive heart failure	1.5%	0.8%	2.4%	0.9%	8.8%	0.9%	5.2%	1.8%	0.9%
Chronic pulmonary disease	16.4%	15.6%	19.1%	18.1%	18.1%	16.9%	50.8%	48.5%	15.2%
Diabetes	28.2%	28.3%	37.0%	34.8%	31.6%	36.2%	25.7%	28.2%	33.4%
Hypertension	71.2%	74.9%	71.3%	76.6%	64.2%	76.2%	61.7%	67.7%	69.5%
Fluid and electrolyte disorders	9.5%	8.0%	12.5%	11.9%	19.7%	10.5%	19.7%	10.8%	9.2%
Obesity	7.0%	7.7%	12.5%	11.5%	7.9%	10.3%	5.6%	6.9%	12.4%
Peripheral vascular disorder	12.8%	11.6%	9.5%	10.9%	11.1%	12.0%	16.4%	18.0%	10.2%
Metastatic cancer	9.2%	1.0%	15.1%	1.4%	24.1%	2.1%	23.2%	2.1%	N/A
Previous MI	13.5%	15.4%	11.9%	12.0%	9.9%	15.3%	13.0%	16.4%	13.1%
Previous PCI	18.0%	22.1%	13.3%	18.8%	13.2%	21.8%	15.9%	23.8%	18.7%
Previous CABG	9.0%	10.6%	4.4%	5.9%	4.6%	8.9%	4.8%	7.9%	7.3%
Previous TIA/stroke	4.4%	6.1%	3.9%	6.4%	4.1%	6.0%	4.7%	5.6%	3.7%

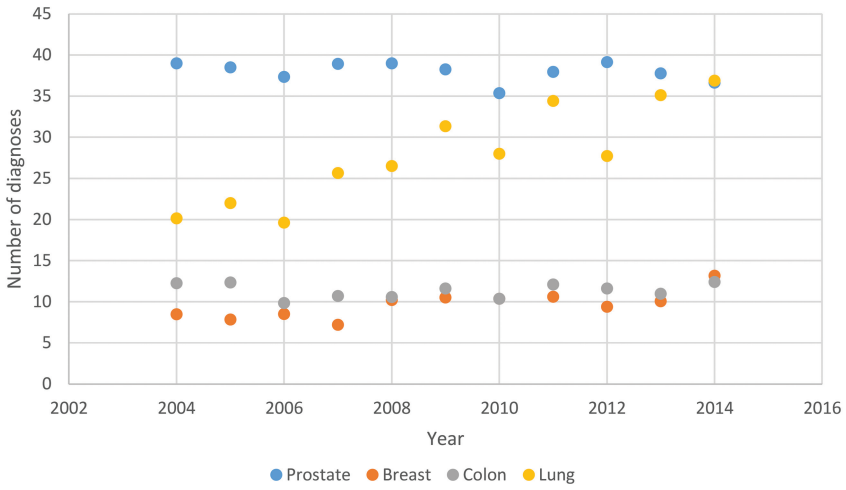


Figure 2 Prevalence rates of current prostate, breast, colon, lung diagnoses per 10 000 records of patients who were diagnosed with cancer.

female, while diagnoses of colon and lung cancer had a broader sex distribution, although there were consistently more males than females across all diagnoses (ranges between 61.5% and 65.3%). Records with a historical cancer diagnosis had a higher median age across all the considered cancer types, and all of the median ages of records with any form of cancer diagnosis were higher than those with no cancer diagnosis. Across all considered diagnoses (current, historical, and no cancer) the majority of individuals were of white ethnicity, ranging between 62.5% and 73.6%. Records with a diagnosis of breast or lung cancer were more likely to have a primary diagnosis of MI. Across all four types of cancer, patients with either a current or historical diagnosis of cancer, the prevalence of comorbid conditions such as anaemia, renal failure, chronic pulmonary disease, and peripheral vascular disease was greater than in patients with no cancer diagnosis.

There was up to a decade difference in the median ages of patients with and without metastases across the four different cancer types (range 64–75 years) (Supplementary material online, *Table S5*). Patients without the presence of metastases were more likely to be admitted as an elective procedure while patents with a cancer diagnosis and metastases were more likely to be admitted with an initial diagnosis of an AMI and during weekends. The prevalence rates of the four cancer types diagnoses per 10 000 records over the included years is depicted in *Figure 2*. The number of patients with prostate, breast, and colon cancer remain fairly stable; however, over time there is a much larger increase in the number of patients with lung cancer, from 20 people per 10 000 records to over 35 people per 10 000 records.

Clinical outcomes

Patients with a current cancer diagnosis had higher rates of in-hospital mortality or in-hospital complications than patients with a historical diagnosis of cancer (*Table 2*). There were worse outcomes in patients with a current or historical cancer diagnosis for all four cancer diagnoses compared to patients with no prior history of cancer. In patients with a current diagnosis of lung cancer, there was an increased risk of in-hospital mortality (odds ratio (OR) 2.81, 95% confidence interval (95% CI) 2.37–3.34) or any in-hospital complication (OR 1.21, 95% CI 1.10–1.36), while a current diagnosis of colon cancer was independently associated with increased odds of any complication (OR 2.17, 95% CI 1.90–2.48) or bleeding (OR 3.65, 95% CI 3.07–4.35) but not mortality (OR 1.39, 95% CI 0.99–1.95). A current diagnosis of breast cancer was not significantly associated with either in-hospital mortality or any of the complications studied and prostate cancer was only associated with increased risk of bleeding (OR 1.41, 95% CI 1.20–1.65) (*Table 3*). A historical diagnosis of lung cancer was independently associated with an increased OR of in-hospital mortality (OR 1.65, 95% CI 1.32–2.05) (*Table 3*).

Crude in-hospital mortality and procedural complication rates were consistently greater for patients with metastases for all of the cancer diagnoses studied compared to those patients with a current diagnosis of cancer without metastases, with the exception of colon cancer where rates were similar (*Table 4*). Supplementary material online, *Tables S6, S7, and S8* show the demographics, mortality/complications and models results, for the same analyses conducted as above but with all patients with a current or historical cancer diagnosis, not just one of the top 4 cancers.

Multivariate analyses were conducted to examine the impact of cancer type and the presence of metastases on in-hospital mortality and post-procedure complications (*Table 5*). For patients with a current cancer diagnosis without the presence of metastases there was no difference in in-hospital mortality with a diagnosis of prostate, breast cancer, or colon cancer compared to no cancer diagnosis. In contrast, patients with lung cancer had a two-fold increase in the odds of in-hospital mortality (OR 2.44, 95% CI 2.01–2.96). In patients with metastases diagnoses of prostate, colon and lung cancer were independently associated with increased odds of in-hospital mortality and all four cancers were associated with increased odds of specific in-hospital procedural complications (*Table 5*).

After considering the effect of metastases on mortality and complications, we also considered the effect for patients undergoing radiotherapy, given in Supplementary material online, *Table S9*, although

Table 2 Prevalence of mortality and complication data for each of the considered cancers, for both current and historical diagnoses

	Prostate cancer		Breast cancer		Colon cancer		Lung cancer		No cancer diagnosis
	Current ($n = 23\,071$)	Historical ($n = 99\,944$)	Current ($n = 5763$)	Historical ($n = 64\,983$)	Current ($n = 6746$)	Historical ($n = 37\,839$)	Current ($n = 15\,801$)	Historical ($n = 31\,312$)	($n = 6\,086\,339$)
In-hospital mortality	2.1%	1.2%	2.5%	1.6%	4.8%	1.8%	7.4%	2.6%	1.6%
Any complication	11.6%	9.2%	13.7%	10.8%	30.2%	10.5%	19.1%	11.0%	8.8%
Bleeding	4.9%	3.5%	6.8%	5.0%	21.2%	4.5%	11.0%	4.8%	3.1%
Vascular complication	0.9%	0.8%	0.7%	1.2%	2.0%	0.9%	1.2%	0.8%	1.0%
Cardiac complication	4.0%	2.8%	3.5%	2.4%	8.8%	2.6%	4.7%	2.6%	3.0%
Post-operative stroke	3.3%	3.3%	4.2%	3.6%	2.8%	3.7%	4.7%	3.9%	2.8%

Table 3 Adjusted[a] odds ratios (95% confidence interval) for in-hospital mortality and complications for patients with a current or historical diagnosis of the four considered cancers

	Prostate cancer vs. no cancer	Breast cancer vs. no cancer	Colon cancer vs. no cancer	Lung cancer vs. no cancer
Current cancer diagnosis				
In-hospital mortality	1.02 (0.81,1.30)	1.05 (0.69,1.60)	1.39 (0.99,1.95)	2.81 (2.37,3.34)
Any complication	1.09 (0.98,1.21)	1.01 (0.84,1.21)	2.17 (1.90,2.48)	1.21 (1.10,1.36)
Bleeding	1.41 (1.20,1.65)	1.09 (0.84,1.39)	3.65 (3.07,4.35)	1.79 (1.56,2.05)
Vascular complication	0.84 (0.63,1.13)	0.43 (0.22,0.88)	1.08 (0.72,1.62)	0.68 (0.49,0.94)
Cardiac complication	1.10 (0.94,1.29)	0.90 (0.63,1.27)	1.45 (1.16,1.81)	0.73 (0.60,0.88)
Post-operative stroke	0.90 (0.76,1.06)	1.15 (0.85,1.54)	0.62 (0.44,0.86)	1.13 (0.94,1.36)
Historical cancer diagnosis				
In-hospital mortality	0.76 (0.66,0.87)	0.81 (0.69,0.95)	0.99 (0.83,1.21)	1.65 (1.32, 2.05)
Any complication	1.01 (0.95,1.06)	0.90 (0.85,0.96)	0.96 (0.89,1.04)	0.96 (0.97,1.06)
Bleeding	1.20 (1.10,1.31)	0.97 (0.89,1.06)	1.04 (0.92,1.17)	1.18 (1.01,1.38)
Vascular complication	0.86 0.73,1.02)	0.89 (0.76,1.04)	0.85 (0.67,1.07)	0.62 (0.45,0.86)
Cardiac complication	1.01 (0.92,1.10)	0.86 (0.76,0.97)	0.92 (0.79,1.07)	0.81 (0.66,0.99)
Post-operative stroke	0.89 (0.82,0.97)	0.86 (0.79,1.10)	0.96 (0.84,1.08)	0.94 (0.79,1.10)

[a]Adjustment for age, gender, median income, elective admission, day of admission (weekend/weekday), median ZIP income, expected payer, primary diagnosis of MI, STEMI/NSTEMI diagnosis, diagnosis of shock, hypertension, or hypercholesterolaemia, if the patient smokes, Elixhauser comorbidities, use of an assist device or intra-aortic balloon pump, use of a bare metal or drug-eluting stent, bifurcation stenting, fractional flow reserve, single or multi-vessel PCI, previous MI, CABG, PCI or stroke, and year of hospitalization.

numbers were small, 601 individuals received radiotherapy in the 4 most common cancers (1.2%). Patients undergoing radiotherapy appear to do worse than without, this is most clear in patients who have prostate, lung and colon cancer. There were no complications in patients identified as undergoing radiotherapy in patients with breast cancer.

The type of stent used was also considered and the mortality and complications for BMS and DES are given for the 5 966 770 patients, after the removal of patients whose stent type was unknown of both types were identified in the same admission (Supplementary material online, *Table S10*). Patients appear to have better outcomes when fitted with a DES rather than a BMS. Finally, we considered only hospitalizations between 2012 and 2014 to compare as there may be changes in both PCI intervention and cancer treatment across all included years. The results, given in Supplementary material online, *Table S11* across both current and historical diagnoses of the four cancer types and do not materially change in this new analysis.

Length of stay and healthcare costs

The median lengths of stay (IQR) are higher for all four cancer types in the presence of metastases compared to the absence of metastasis (Supplementary material online, *Table S4*). Patients with lung or colon cancers have the longest length of stay with median values of between 3 and 7 days. An increased median cost (USD) of hospitalization for all four cancer types compared to patients with no cancer diagnosis was observed, with the presence of metastases consistently associated with the highest median hospitalization costs. The greatest

Table 4 Prevalence of mortality and complication data for each of the considered cancers, stratified by the presence or absence of metastasis

	Prostate cancer (n = 23 071)		Breast cancer (n = 5763)		Colon cancer (n = 6746)		Lung cancer (n = 15 801)	
	Metastasis presence		Metastasis presence		Metastasis presence		Metastasis presence	
	No (n = 20 970)	Yes (n = 2134)	No (n = 4893)	Yes (n = 870)	No (n = 5121)	Yes (n = 1625)	No (n = 12 132)	Yes (n = 3669)
In-hospital mortality	1.7%	5.6%	2.0%	5.1%	4.7%	5.1%	6.5%	10.3%
Any complication	1.1%	1.7%	1.2%	2.3%	3.1%	2.9%	1.8%	2.4%
Bleeding	4.3%	10.9%	4.9%	17.8%	22.3%	17.8%	9.2%	16.6%
Vascular complication	0.9%	0.9%	0.8%	0%	2.1%	1.8%	0.9%	2.0%
Cardiac Complication	4.1%	2.5%	3.8%	1.7%	8.0%	11.3%	4.8%	4.3%
Post-operative stroke	3.2%	3.9%	4.1%	5.0%	2.7%	2.9%	4.6%	5.1%

Table 5 Adjusted[a] odds ratios (95% confidence interval) for in-hospital mortality and complications for patients with a current diagnosis of the four considered cancers with and without the presence of metastases

	Prostate cancer vs. no cancer	Breast cancer vs. no cancer	Colon cancer vs. no cancer	Lung cancer vs. no cancer
No metastases present				
In-hospital mortality	0.95 (0.75,1.20)	0.94 (0.61,1.43)	1.20 (0.84,1.72)	2.44 (2.01,2.96)
Any complication	1.06 (0.96,1.18)	0.97 (0.81,1.17)	2.07 (1.79,2.38)	1.16 (1.04,1.29)
Bleeding	1.32 (1.12,1.56)	1.00 (0.78,1.29)	3.33 (2.77,4.00)	1.61 (1.40,1.87)
Vascular complication	0.83 (0.61,1.12)	0.42 (0.21,0.87)	1.04 (0.67,1.61)	0.66 (0.48,0.91)
Cardiac complication	1.14 (0.96,1.34)	0.95 (0.66,1.34)	0.55 (1.23,1.95)	0.78 (0.64,0.96)
Post-operative stroke	0.88 (0.75,1.04)	0.12 (0.83,1.51)	0.59 (0.42,0.84)	1.09 (0.89,1.32)
Metastases present				
In-hospital mortality	1.53 (1.09,2.15)	1.51 (0.94,2.44)	1.95 (1.31,2.88)	3.94 (3.04,5.11)
Any complication	1.31 (1.11,1.55)	1.20 (0.96,1.50)	2.55 (2.15,3.02)	1.43 (1.22,1.67)
Bleeding	1.91 (1.52, 2.39)	1.44 (1.08,1.94)	4.81 (3.89, 5.96)	2.33 (1.92,2.83)
Vascular complication	0.95 (0.58,1.56)	0.48 (0.23,1.02)	1.19 (0.72,1.98)	0.76 (0.46,1.24)
Cardiac complication	0.85 (0.64,1.14)	0.71 (0.48,1.05)	1.17 (0.85,1.60)	0.59 (0.44,0.78)
Post-operative stroke	1.03 (0.78,1.38)	1.31 (0.91,1.88)	0.69 (0.47,1.02)	1.27 (0.96,1.67)

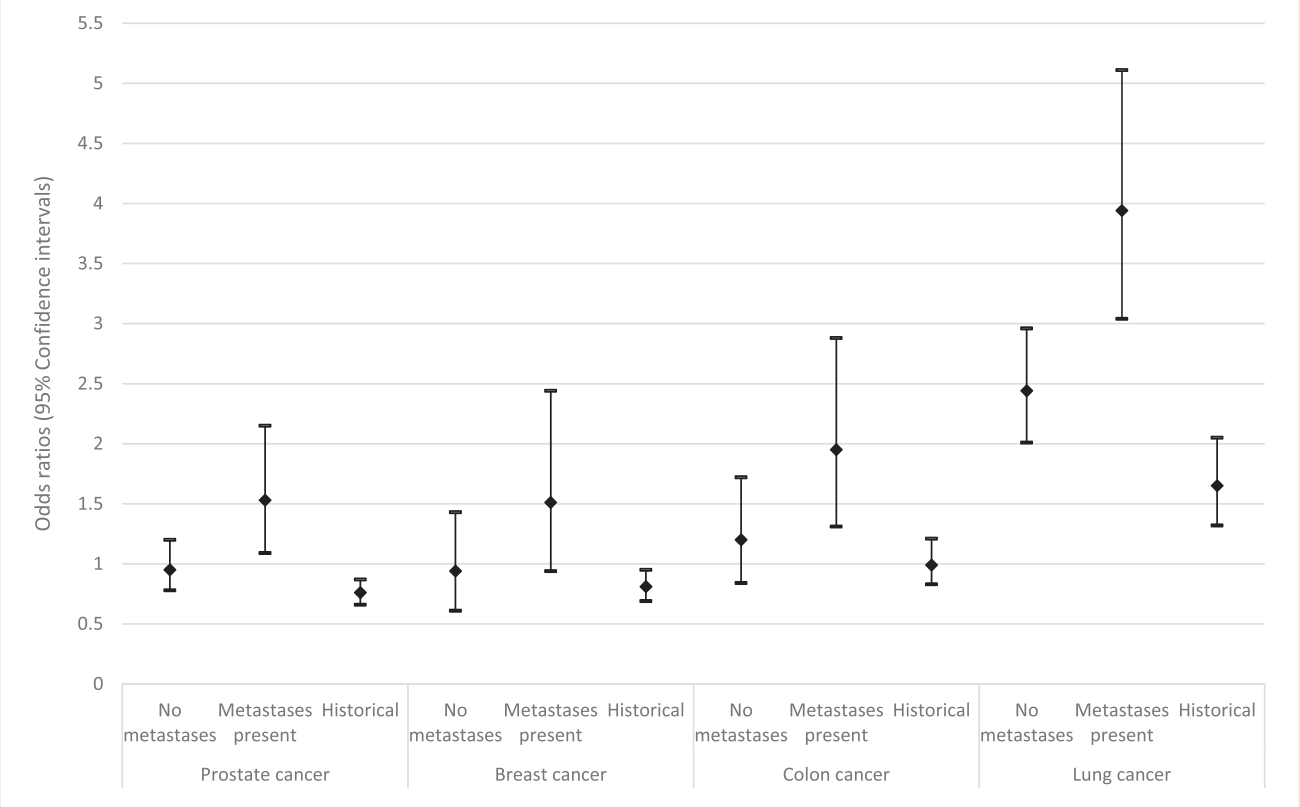
[a]Adjustment for age, gender, median income, elective admission, day of admission (weekend/weekday), median ZIP income, expected payer, primary diagnosis of MI, STEMI/NSTEMI diagnosis, diagnosis of shock, hypertension, or hypercholesterolaemia, if the patient smokes, Elixhauser comorbidities, use of an assist device or intra-aortic balloon pump, use of a bare metal or drug-eluting stent, bifurcation stenting, fractional flow reserve, single or multi-vessel PCI, previous MI, CABG, PCI or stroke, and year of hospitalization.

costs were seen in patients with colon or lung cancer, with metastasis, whose median costs were $23 941 (IQR $15 497–$40 632) and $23 627 (IQR $16 175–$35 031), respectively. Supplementary material online, *Figures S3* and *S4* show the differences in length of stay and costs for patients with current and historical cancer diagnoses.

Discussion

In this analysis of over 6 million PCI procedures, close to 1 in 10 patients undergoing PCI had either a current or historical diagnosis of cancer, with prostate, breast, colon, and lung cancers, the four most common cancer types encountered. A current diagnosis of lung cancer was independently associated with a two-fold risk of in-hospital mortality, while a current diagnosis of colon, breast, and prostate cancer (in the absence of metastases) was not associated with an increase in-hospital mortality risk. We also observed that patients with a current diagnosis of colon cancer are at the greatest risk of major bleeding events. Patients with metastatic cancer, irrespective of cancer type have a poorer prognosis post-PCI and are at increased risk of in-hospital mortality and PCI complications, including major bleeding events. Finally, a historical diagnosis of cancer is not associated with adverse outcomes once differences in baseline characteristics are adjusted, with the exception of lung cancer.

There are limited data regarding outcomes of patients undergoing PCI with a current or historical diagnosis of cancer. Such patients are



Take home figure The prognostic impact (odds ratio and 95% confidence intervals) of a historical diagnosis of cancer, current cancer with no metastases and current cancer with metastases on in-hospital mortality for prostate, breast, colon, and lung cancer.

often excluded from randomized controlled trials, and cancer history is not captured in national PCI registries. Many of the prior analyses that have studied the prognostic impact of cancer on PCI outcomes been reported from single centres[19,21] limited by small sample sizes. They therefore lack the granularity to evaluate temporal trends or the relationship between cancer type, nature of cancer diagnosis (current or historical), the presence of metastases, and clinical outcomes. Our analysis reveals that over the past decade, patients with either a historical or current diagnosis of cancer are increasingly encountered in contemporary PCI practice. Cancer patients are living longer,[26] and their exclusions in clinical trials leave us with limited data regarding optimal percutaneous management of their coronary disease, which we treat with limited understanding of their clinical outcomes and using extrapolation from non-cancer patients' data. Irrespective of whether the cancer diagnosis is current or historical, these patients are on average older by up to a decade in line with previous studies,[19,20] and are more likely to have prevalent comorbid conditions that are associated with adverse outcomes.[27–30] In addition, patients with certain cancer subtypes, particularly lung and breast cancer, are much more likely to undergo PCI in the setting of an AMI, reflecting the reluctance of interventional cardiologists to undertake elective PCI procedures in these patients.

While previous work has shown that a diagnosis of cancer is associated with death,[19,20,31] re-infarction,[14] major bleeding,[14] and target lesion revascularization,[17] our analysis is the first to provide outcome data stratified by current vs. historical cancer diagnoses in the four most common cancer types and by the presence and the absence of metastases (*Take home figure*). We reveal that a current diagnosis of lung cancer (in the absence of metastases) is independently associated with a two-fold increase in in-hospital mortality and PCI complications, including major bleeding. Colon cancer had the greatest association with major bleeding complications (OR 3.65, 95% CI 3.07–4.35). One explanation for increased bleeding would be cancer-specific responses to dual-antiplatelet therapy in the setting of PCI, particularly in the GI tract, as reported previously using the NIS database.[23] Interestingly, a current diagnosis of breast cancer (in the absence of metastases) was not independently associated with any of the clinical outcomes studied once differences in baseline characteristics were adjusted, and a current diagnosis of prostate cancer was independently associated with an increase in major bleeding (OR 1.32, 95% CI 1.12–1.56) but not other endpoints. In the presence of metastases, all four cancer subtypes were independently associated with mortality, PCI complications, and major bleeding events. Lung cancer with metastases has the greatest impact on clinical outcomes, and was independently associated with a four-fold increase in mortality, followed by colon cancer with a two-fold increased mortality. Colon cancer with metastases had the strongest independent association with major bleeding events, with almost a five-fold increase in risk observed (OR 4.81, 95% CI 3.89–5.96).

The adverse in-hospital outcomes following PCI observed in patients with a current cancer diagnosis are likely to be multifactorial. Malignancy is associated with a hypercoagulable state as cancer cells are able to activate the coagulation cascade and secrete acute phase reactants[32] placing cancer patients at high thrombotic risk. This may be further exacerbated by interrupting antiplatelet therapy for surgery. Thrombocytopenia,[33,34] malignant gastrointestinal,[35] or metastatic hepatic disease can significantly increase bleeding risk in cancer patients. Comorbid conditions such as anaemia due to impaired erythropoiesis, haemolysis, chemotherapy, nutritional deficiencies, and immune-mediated mechanisms[36] serve to further increase both ischaemic and haemorrhagic risk. Major bleeding and thrombotic events are known to be associated with mortality,[37–39] and the increases in the rate of these events in patients with cancer may contribute to the adverse outcomes that we report. Operator recognition of the high ischaemic and haemorrhagic risk of this group may explain the increased use of PTCA alone or bare metal stents (BMS) that we and others have observed.[19,20] Interestingly, both in-hospital mortality and major bleeding events were significantly greater for all four cancer subtypes in patients who received a BMS compared to a drug-eluting stent (Supplementary material online, *Table S10*). This may suggest a degree of selection bias, where those patients that were felt to be at greatest bleeding risk or in those in whom it was likely that DAPT had to be interrupted were treated with BMS, which reflect the poorer outcomes in this group.

Importantly, a historical diagnosis of prostate, breast, or colon cancer was not independently associated with an increased risk of adverse outcomes, contrary to lung cancer which was associated with both an increased risk of mortality (OR 1.65, 95% CI 1.32–2.05) and bleeding complications (OR 1.18, 95% CI 1.01–1.38). While previous work has not studied outcomes in this patient population undergoing PCI, analysis of cancer survivors in the Surveillance, Epidemiology and End Results (SEER) database suggests that lung cancer survivors had the highest rate of cardiovascular death at 5 years.[40] Interestingly, the most common cause of death for lung cancer 'survivors' was primary lung cancer, even 20 years after a diagnosis of lung cancer[41] suggesting that in lung cancer survivors, lung cancer may not be truly 'cured' or there is a high rate of lung cancer recurrence that may place them at increased risks of both ischaemic and haemorrhagic events.

Many contemporary risk scores consider a wide range of comorbid conditions to risk stratify patients undergoing PCI,[28,30,42,43] however none of the contemporary scores consider cancer diagnoses despite the fact that the prognostic impact of a cancer diagnosis is greater than that of many of the covariates included in these scores. Patients with prior history or current history of cancer undergoing PCI should be considered a high-risk group, and special consideration should be given to whether the PCI is warranted or can be delayed until cancer treatment is complete, allowing for the safe use of antiplatelet regimes and stent platforms as advocated by the SCAI expert consensus statement.[9] The recent European Society of Cardiology (ESC) Position Paper on cancer treatments and cardiovascular toxicity provides a framework through which patients with a current cancer diagnosis should be managed.[44] The position statement highlights that identification of patients with pre-existing CAD and other cardiovascular diseases upfront is important, particularly prior to initiating chemotherapeutic regimes, as pre-existing CAD substantially increases the risk of developing treatment-related CAD. Patients who develop an acute coronary syndrome or symptomatic coronary disease while thrombocytopenic particularly during chemotherapy are a particular challenge and need case-by-case multidisciplinary management. In patients treated by PCI who are subsequently found to have a malignancy, minimal duration of dual-antiplatelet therapy is advocated to limit bleeding risk. The ESC position paper highlights that patient management of this high-risk group should be individualized on the basis of indication for PCI, and the nature and type of cancer diagnosis involving a close collaboration between cardiologists and oncologists.[44]

Our work has a number of limitations. As with any administrative database, coding errors are always a potential source of bias as is underreporting of secondary and co-morbid diagnoses. The dataset does not record the timing of the cancer diagnosis in relation to the index PCI, which may be particularly relevant in the historical cancer cohort, where a prior diagnosis of cancer a decade ago may have very different prognostic implications to a more recent diagnosis. Furthermore, the NIS does not provide information on cancer subtype or grade that are known to have important prognostic implications. The NIS does not capture causes of mortality, therefore it is not clear whether the excess mortality risk that we report is due to an increased risk of cardiovascular mortality or whether merely reflects cancer deaths, although we report an independent increase in risk of PCI complications as well as major bleeding events. The outcome measures available from the NIS relate only to in-hospital outcomes and do not capture longer-term follow-up of mortality and other adverse events that are important to understand in patients with cancer, particularly in those whose outcomes may be limited by metastases. Furthermore, there is no formal adjudication of events and outcome measures such as major bleeding are not based on international definitions of bleeding such as Bleeding Academic Research Consortium (BARC) or thrombolysis in myocardial infarction (TIMI). While there is a considerable granular data relating to the PCI admission, full procedural details are not recorded in the NIS therefore limiting insights into differences in angiographic findings, PCI procedural techniques, and clinical outcomes. Additionally, no pharmacological information is recorded on NIS preventing further assessment of antiplatelet and anticoagulant choices as well as disparities in the use of guideline-directed evidence-based therapies in patients with cancer, or the use of cancer drug therapies, many of which have cardiotoxic actions themselves, which may contribute to the adverse outcomes. Finally, in keeping with all observational registry work, the possibility of unmeasured or unrecognized confounders may contribute to the adverse outcomes.

In conclusion, patients with a current or historical diagnosis of cancer represent 10% of patients undergoing PCI in the United States. After adjusting for differences in baseline characteristics, patients with cancer have worse short-term clinical outcomes compared to non-cancer patients. The prognostic impact of cancer is specific both for the type of cancer, presence of metastases, and whether the diagnosis is historical or current. Treatment of patients with a cancer diagnosis should thus be individualized recognizing that cancer is a prothrombotic and proinflammatory state with a higher risk of complications and should involve a close collaboration between cardiologists and oncologists.

Supplementary material

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

Conflict of interest: none declared.

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CARDIOVASCULAR FLASHLIGHT

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A rare case of cardiac foreign body

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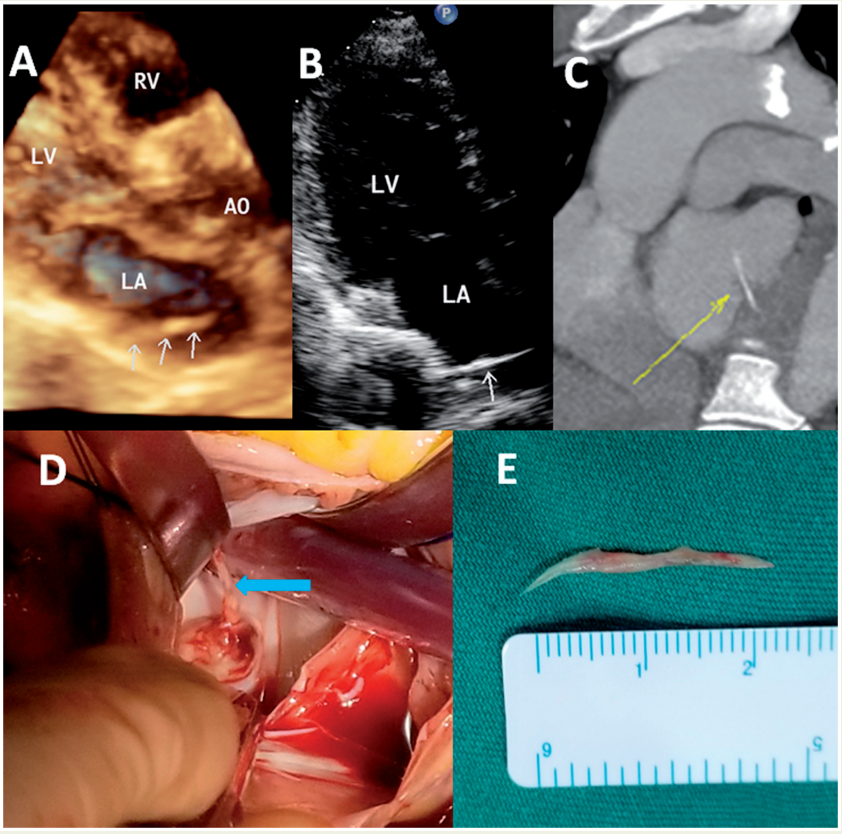

A 58-year-old woman was admitted to local hospital for severe abdominal pain 1 week ago. The abdominal pain was slightly relieved after symptomatic treatment. Then, she began to have fever 2 days ago and the maximum body temperature reached 38.4°C. No chest discomfort was experienced in the course. For further treatment, the patient visited our hospital. Physical examination revealed high temperature (38°C), acute face, moderate abdominal tenderness, normal heat rate, and blood pressure. The three-dimensional and two-dimensional transthoracic echocardiography showed a foreign body (length 20 mm) in the left atrium (*Panels A* and *B*, Supplementary material online, *Video S1* and *S2*). Emergency computed tomography revealed a foreign body in the oesophagus and left atrium as well (*Panel C*). Retrospecting her medical history, the patient had fish soup just before the unset of abdominal pain, so we supposed that the foreign body may be a fish thorn. Two days later, the patient underwent surgery of the foreign body removal under cardiopulmonary bypass. During operation, a 20 mm fish thorn was found to have penetrated into the left atrium through the second narrow part of the oesophagus (*Panels D* and *E*). The operation was successful, and postoperative anti-infective and other symptomatic treatment were given.

As far as we known, this is an extremely rare case about a quite uncommon cardiac foreign body, which was a fish thorn penetrating into the heart through the oesophagus. Currently, the patient was stable and we will continue to follow her outcome.

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