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RESEARCH LETTER

Outcomes and readmissions in patients with cancer undergoing catheter ablation for atrial fibrillation

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Approximately, 2–16% of patients with cancer have atrial fibrillation (AF), and it is associated with a two-fold higher risk of systemic thromboembolism or stroke and a six-fold higher risk of developing heart failure.[1] The use of anti-arrhythmic drugs (AADs) in patients with cancer is particularly challenging due to drug interactions with anti-neoplastic therapies leading to an increased propensity for QT prolongation and arrhythmias.[1] Catheter ablation for AF is safe, and it is associated with superior clinical results as compared to medical therapy.[2] However, there is limited data on the procedural safety and clinical outcomes of patients with cancer undergoing catheter ablation for AF. In this observational study, we examined the outcomes of patients with cancer undergoing catheter ablation in a nationally representative cohort of patients.

The National Readmissions Database (NRD) was analysed from 2016 to 2019 to identify patients ≥18 years old undergoing AF ablation as described previously.[3,4] The NRD is the largest, publicly available, all-payer inpatient database in the USA that contains longitudinal, nationally representative information on hospital readmissions for all ages and contains data from approximately 18 million discharges annually.[4] Due to the de-identified nature of the NRD dataset, the need for informed consent and Institutional Review Board approval was waived.

Patients were divided into three cohorts based on their cancer status: those with no cancer, those with active cancer [implantable cardioverter defibrillator (ICD) 10 CM codes: C00.x-C97.x], and those with prior history of cancer (ICD 10 CM codes: Z85.xx). The baseline characteristics were compared using a Pearson χ^2 test and Fisher's exact test for categorical variables, and a one-way analysis of variance for continuous variables. A multivariable regression model (logistic for categorical outcomes and linear for continuous outcomes) was utilized to assess the independent association of active cancer and a history of cancer with in-hospital, 30-day, 90-day, and 180-day outcomes after adjusting for age, sex, and comorbidities as reported in *Table 1*. Definitions of outcomes of interest are reported in *Table 1*, defined using their respective ICD-10 CM codes. The statistical analysis was performed using STATA 17.0, and a $P < 0.05$ was considered statistically significant.

Our cohort included 50 623 weighted AF ablation procedures (*Table 1*), of which 5923 (11.7%) were performed in patients with a history of cancer and 1468 (2.9%) were performed in patients with active cancer. Patients with active cancer and a history of cancer were older at the time of ablation as compared to patients with no cancer [74.3 (0.34) vs. 74.2 (0.17) vs. 68.8 (0.08) years, $P < 0.01$] and had a higher burden of key comorbidities including heart failure (65.3% vs. 54.5% vs. 52.4%, $P < 0.01$), renal failure (28.9% vs. 25.8% vs. 22.0%, $P < 0.01$), and chronic pulmonary disease (33.4% vs. 29.2% vs. 24.8%, $P < 0.01$) (*Table 1*).

Crude outcomes are shown in *Table 1*. On multivariable analysis, the presence of active cancer was associated with significantly higher odds of cardiovascular complications [adjusted odds ratio (aOR) 1.21; 95% confidence interval (CI): 1.02–1.49; $P = 0.04$], bleeding complications (aOR:1.73; 95% CI: 1.25–2.39; $P < 0.01$), pulmonary complications (aOR:1.55; 95% CI: 1.25–1.95; $P < 0.01$), longer length of stay (adjusted mean difference: + 2.35; 95% CI: + 1.55 + 3.16; $P < 0.01$) days and lower odds of routine home discharge (aOR:0.54; 95% CI: 0.45–0.65; $P < 0.01$), as compared to those without cancer.

Patients with active cancer had significantly higher odds of 30-day all-cause readmissions (aOR:1.32; 95% CI: 1.07–1.62; $P < 0.01$), 30-day bleeding-related readmissions (aOR:1.86; 95% CI: 1.08–3.20; $P = 0.02$), 90-day all-cause readmissions (aOR:1.28; 95% CI: 1.06–1.56; $P = 0.01$), 90-day bleeding-related readmissions (aOR:2.14; 95% CI: 1.35–3.42; $P < 0.01$),180-day all-cause (aOR:1.31; 95% CI: 1.05–1.64; $P = 0.01$), and 180-day bleeding-related readmissions (aOR:2.08; 95% CI: 1.23–3.51; $P < 0.01$), without any difference in atrial fibrillation/flutter, stroke, and heart failure-related readmissions. Patients with a history of cancer had similar odds of periprocedural complications along with 30-day/90-day/180-day readmissions as compared to those with no cancer.

There is limited data on outcomes of AF ablation in patients with cancer, and our study provides important insights using a large national claims-based database. The significant findings include:

(1) In patients undergoing catheter ablation for AF, 11.7% had a history of cancer, and 2.8% had active cancer.

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Table 1 Baseline characteristics, outcomes, and procedure-related complications stratified by cancer status

Variable no. (%)	No cancer ($n = 43\,232$, 85.4%)	History of cancer ($n = 5923$, 11.7%)	Active cancer ($n = 1468$, 2.9%)	*P*-value
Females	44.9%	50.8%	40.5%	<0.01
Age (standard error) years	68.8 (0.08)	74.2 (0.17)	74.3 (0.34)	<0.01
CHA_2DS_2-VASc score				
≤3	50.0%	35.2%	31.0%	<0.01
4	14.2%	14.6%	16.5%	
5	13.9%	18.9%	20.6%	
≥6	22.2%	31.3%	31.8%	
Type of cancer				
Oesophageal cancer	—	0.7%	1.7%	—
Colorectal cancer	—	7.3%	3.9%	—
Lung cancer	—	6.3%	14.3%	—
Breast cancer	—	25.6%	7.6%	—
Uterine cancer	—	4.3%	0.7%	—
Prostate cancer	—	19.3%	12.1%	—
Leukaemia	—	0.9%	18.8%	—
Lymphoma	—	4.4%	10.6%	—
Comorbidities				
Anaemia	2.9%	3.5%	6.2%	<0.01
Congestive heart failure	52.4%	54.5%	65.3%	<0.01
Valvular heart disease	23.6%	29.1%	28.3%	<0.01
Chronic obstructive pulmonary disease	24.8%	29.2%	33.4%	<0.01
Prior myocardial infarction	8.7%	9.5%	8.8%	0.43
Prior stroke	10.0%	12.6%	10.9%	<0.01
Prior percutaneous coronary intervention	1.1%	1.3%	1.4%	0.62
Prior coronary artery bypass graft	7.3%	8.6%	8.4%	0.06
Diabetes	28.0%	25.3%	31.3%	<0.01
Hypertension	78.4%	82.0%	81.9%	<0.01
Liver disease	2.9%	3.1%	5.7%	<0.01
Renal failure	22.0%	25.8%	28.9%	<0.01
Peripheral vascular disorder	13.6%	15.2%	16.7%	<0.01
Coagulopathy	5.8%	6.1%	12.3%	<0.01
Obesity	24.9%	20.6%	18.1%	<0.01
Prior ICD	6.9%	6.7%	7.3%	0.86
Prior permanent pacemaker	10.4%	14.6%	15.9%	<0.01
Long-term anticoagulation	52.7%	61.5%	49.2%	<0.01
Outcomes				
In-hospital mortality	0.9%	0.6%	2.0%	<0.01
Adjusted odds ratio (OR)[a]	Reference	0.56 (0.33–1.05), $P = 0.06$	1.63 (0.93–2.83), $P = 0.08$	
Any cardiovascular complication[b]	13.2%	14.5%	19.6%	<0.01
Adjusted OR[a]	Reference	0.95 (0.54–1.07), $P = 0.41$	1.21 (1.02–1.49), $P = 0.04$	
Any peripheral vascular complication[c]	2.6%	2.9%	2.5%	0.62
Adjusted OR	Reference	1.14 (0.89–1.45), $P = 0.29$	1.02 (0.65–1.61), $P = 0.93$	
Any bleeding complication[d]	3.7%	4.3%	7.6%	<0.01
Adjusted OR[a]	Reference	1.09 (0.88–1.35), $P = 0.43$	1.73 (1.25–2.39), $P < 0.01$	
Any pulmonary complication[e]	10.3%	11.1%	18.6%	<0.01
Adjusted OR[a]	Reference	0.96 (0.83–1.10), $P = 0.55$	1.55 (1.24–1.95), $P < 0.01$	

Continued

Table 1 *Continued*

Variable no. (%)	No cancer (*n* = 43 232, 85.4%)	History of cancer (*n* = 5923, 11.7%)	Active cancer (*n* = 1468, 2.9%)	*P*-value
Any neurological complication[f]	1.3%	1.0%	0.8%	0.20
Adjusted OR[a]	Reference	0.69 (0.47–1.01), *P* = 0.06	0.44 (0.17–1.16), *P* = 0.09	
Discharge to home	75.5%	70.6%	54.6%	<0.01
Adjusted OR[a]	Reference	1.08 (0.98–1.20), *P* = 0.10	0.54 (0.45–0.65), *P* < 0.01	
Length of stay	4.8 (0.05) days	4.9 (0.09) days	8.2 (0.41) days	<0.01
Adjusted mean difference (MD)[a]	Reference	− 0.38 (−0.68 - + 0.19) days, *P* = 0.11	+2.35 (+1.55 - + 3.16) days, *P* < 0.01	
30-day all-cause readmissions	10.3%	11.1%	15.0%	<0.01
Adjusted OR[a]	Reference	0.98 (0.86–113), *P* = 0.81	1.32 (1.07–1.62), *P* < 0.01	
30-day atrial fibrillation/flutter-related readmissions	2.7%	2.6%	2.5%	0.87
Adjusted OR[a]	Reference	1.01 (0.74–1.34), *P* = 0.99	1.02 (0.64–1.56), *P* = 0.98	
30-day heart failure-related admissions	3.0%	3.2%	3.0%	0.85
Adjusted OR[a]	Reference	0.88 (0.69–1.13), *P* = 0.33	0.78 (0.51–1.21), *P* = 0.27	
30-day stroke-related readmissions	0.2%	0.2%	0.3%	0.66
Adjusted OR[a]	Reference	0.76 (0.34–1.69), *P* = 0.50	1.42 (0.43–4.65), *P* = 0.56	
30-day bleeding-related readmissions	0.6%	0.9%	1.5%	<0.01
Adjusted OR[a]	Reference	1.17 (0.74–1.86), *P* = 0.49	1.86 (1.08–3.20), *P* = 0.02	
90-day all-cause readmissions	17.1%	19.5%	23.9%	<0.01
Adjusted OR[a]	Reference	1.02 (0.90–1.15), *P* = 0.76	1.28 (1.06–1.56), *P* = 0.01	
90-day atrial fibrillation/flutter-related readmissions	4.3%	4.5%	4.4%	0.87
Adjusted OR[a]	Reference	1.09 (0.86–1.39), *P* = 0.48	1.09 (0.73–1.63), *P* = 0.66	
90-day heart failure-related admissions	4.7%	5.3%	5.3%	0.38
Adjusted OR[a]	Reference	0.93 (0.75–1.15), *P* = 0.52	0.88 (0.61–1.28), *P* = 0.52	
90-day stroke-related readmissions	0.4%	0.5%	0.7%	0.31
Adjusted OR[a]	Reference	1.23 (0.68–2.24), *P* = 0.48	1.58 (0.63–3.96), *P* = 0.33	
90-day bleeding-related readmissions	1.1%	1.5%	2.8%	<0.01
Adjusted OR[a]	Reference	1.20 (0.82–1.75), *P* = 0.34	2.14 (1.35–3.42), *P* < 0.01	
180-day all-cause readmissions	22.8%	25.7%	31.6%	<0.01
Adjusted OR[a]	Reference	1.04 (0.91–1.18), *P* = 0.59	1.31 (1.05–1.64), *P* = 0.01	
180-day atrial fibrillation/flutter-related readmissions	5.5%	5.8%	5.9%	0.79
Adjusted OR[a]	Reference	1.14 (0.87–1.48), *P* = 0.34	1.19 (0.79–1.79), *P* = 0.39	
180-day heart failure-related admissions	5.7%	6.7%	7.5%	0.11
Adjusted OR[a]	Reference	0.97 (0.77–1.23), *P* = 0.81	1.06 (0.71–1.57), *P* = 0.77	
180-day stroke-related readmissions	0.5%	0.8%	0.6%	0.30
Adjusted OR[a]	Reference	1.33 (0.71–2.48), *P* = 0.38	1.23(0.31–3.34), *P* = 0.97	
180-day bleeding-related readmissions	1.4%	1.9%	3.7%	<0.01
Adjusted OR[a]	Reference	1.14 (0.78–1.67), *P* = 0.50	2.08 (1.23–3.51), *P* < 0.01	

[a]Adjusted for the following variables: age, gender, hypertension, diabetes mellitus, peripheral vascular disease, chronic lung disease, heart failure, chronic liver disease, prior stroke, history of percutaneous coronary intervention, history of coronary artery bypass graft, chronic renal failure, anaemia, CHA2DS2-VASc score, obesity, prior permanent pacemaker, prior implantable cardioverter defibrillator, and long-term anticoagulation.
[b]Cardiovascular complications (including cardiac arrest, heart block, myocardial infarction, pericardial effusion, cardiogenic shock, and pericardial effusion requiring intervention).
[c]Peripheral vascular complication (including arteriovenous fistula, pseudoaneurysm, and access site haematoma).
[d]Bleeding complications (gastrointestinal bleeding, blood transfusion, and retroperitoneal bleeding).
[e]Pulmonary complications (including respiratory failure, pneumothorax, pleural effusion, and pneumonia).
[f]Neurological complications (including ischaemic stroke, haemorrhagic stroke, and transient ischaemic attack).

Table 2 Studies analysing the safety and efficacy of catheter ablation in patients with cancer

Study (years)	Study design	Patients (*n*)	History of cancer/ active cancer (*n*)	Age (mean)	Female (%)	Type of cancer (%)	Primary outcome	Results and conclusion	Follow-up(months)
Giustozzi *et al.*[13] (2021)	Retrospective single centre	184	21/-	64.3	33.0	Gastrointestinal (36%), breast (23%), and genitourinary (18%)	Clinically relevant bleeding, defined as the composite of major and clinically relevant non-major bleedings observed during 30 ± 5 days after the catheter ablation procedure.	Clinically relevant bleeding after catheter ablation for AF is more frequent in cancer survivors than in patients without cancer	1
Eitel *et al.*[14] (2021)	Retrospective single centre	140	62/8	71.3	44.3	Genitourinary cancer (30%), breast cancer (28.6%), haemato-oncologic cancer (12.9%), gastrointestinal cancer (11.4%), head or neck cancer (5.7%), and lung cancer (2.9%)	Complications were defined as periprocedural when occurring intra-procedural, post-procedural during the hospital stay or until 30 days after the procedure. Complications were classified as major complications if permanent injury, interventional treatment, prolonged hospital stay, repeat hospitalization for more than 48 h, or death occurred, as described in the consensus statement for catheter ablation of AF. Bleeding complications were classified as described in the criteria of the International Society on Thrombosis and Haemostasis as major bleeding or clinically relevant non-major bleeding.	High arrhythmia-free survival with low frequencies of periprocedural complications was observed in patients with a history of cancer undergoing cryo-balloon ablation. Procedural safety and arrhythmia-free survival were comparable to patients without cancer disease.	12

Continued

Table 2 *Continued*

Study (years)	Study design	Patients (*n*)	History of cancer/ active cancer (*n*)	Age (mean)	Female (%)	Type of cancer (%)	Primary outcome	Results and conclusion	Follow-up(months)
Ganatra *et al.*[11] (2023)	Retrospective single centre	502	205/46	65.5	50.0	Breast cancer (29.9%), lung cancer (6.0%), prostate cancer (22.3%), lymphoma (10.0%), and other cancer (31.9%)	Freedom from atrial fibrillation (with or without anti-arrhythmic drugs or need for repeat ablation) at 12 months post-ablation in patients with a history of cancer compared to controls.	The success rate, defined as freedom from recurrent AF, with or without AAD, and the need for repeat ablation at 12 months post-ablation, in patients with cancer was similar to that observed in non-cancer controls. At the same time, safety outcomes, including post-procedural bleeding, pulmonary vein stenosis, stroke, and cardiac tamponade within the first 3 months after catheter ablation, were also similar to non-cancer controls.	12
Thotamgari *et al.*[10] (2023)	Retrospective multi-centre	47 765	750/-	67.1	42.0	Haematological malignancy (60%), respiratory tract (16%), gastrointestinal (12%), breast (6%), and urinary tract (6%)	Mortality, major periprocedural cardiac complications including acute heart failure, acute myocardial infarction, cardiac arrest, cardiogenic shock, acute pericarditis, heart block, major bleeding, retroperitoneal bleeding, pulmonary embolism, and acute kidney injury.	Patients with cancer undergoing catheter ablation for atrial fibrillation had significantly higher odds of in-hospital mortality, major bleeding, and pulmonary embolism as compared to those without cancer.	In-hospital stay

(2) Compared to patients without cancer, having a diagnosis of active cancer was associated with a higher adjusted odds of periprocedural complications and higher odds of 30-day/90-day/180-day all-cause readmissions and bleeding-related readmissions as compared to patients without cancer.
(3) There was no significant difference in the odds of periprocedural complications and 30-day/90-day/180-day readmissions in patients with a history of cancer as compared to those without cancer.

Cancer and AF appear to have a bidirectional relationship, likely due to common risk factors.[5] The incidence of AF has been found to be 3.0–4.5 times higher within the first year of a cancer diagnosis compared to later years.[6] Conversely, an increased risk of cancer among patients presenting with AF has also been appreciated.[6] The prognosis with AF has been shown to be worse among cancer patients compared to those without cancer, with a two-fold higher adjusted risk for thromboembolic complications, and a six-fold higher adjusted risk for heart failure.[6] The underlying processes that explain the link between these two diseases remain unknown but might be biologically explained by the pro-inflammatory state, electrolyte, and fluid imbalance, and the possible presence of frailty.[7,8] Atrial fibrillation has also previously been shown to be associated with poor outcomes in patients undergoing inpatient chemotherapy and among patients undergoing chimeric antigen receptor T cell therapy as well as patients undergoing haematopoietic stem cell transplants.[9] A recent study by Thotamgari *et al.*[10] including 750 patients with cancer from the national inpatient sample database demonstrated that patients with cancer undergoing AF ablation had higher odds of in-hospital mortality along with periprocedural major bleeding and pulmonary embolism (*Table 2*). Our study additionally compares outcomes of patients with a history of cancer to those without cancer and also analyses hospital readmission rates in patients with active cancer or a history of cancer to those without cancer. Another single-centre study by Ganatra *et al.*[11] including 502 patients with cancer undergoing AF ablation showed that patients with cancer had similar odds of arrhythmia recurrence without any difference in the periprocedural complications compared to those without cancer (*Table 2*). Of note, the abovementioned study did not differentiate between the outcomes of patients with active cancer to those with a history of cancer, which might have contributed to the differences in the periprocedural outcomes as compared to our study.

One of the major risks related to AF ablation is radiation exposure, in particular, the effects of ionizing radiation exposure which is both deterministic and stochastic.[5] The latter is especially important in young patients with increased radiosensitivity and a longer life expectancy, as well as in patients who undergo a large cumulative radiation dose for long, difficult, or recurrent treatments.[5] The radiation exposure, on the other hand, could result in a large cumulative dosage and a lifelong radiation risk for the electrophysiological staff.[12] Therefore, it is important to reduce the amount of ionizing radiation that patients and personnel are exposed to. Although, in recent years, the development and widespread use of electro-anatomical mapping systems in conjunction with transoesophageal or intracardiac echocardiography during AF ablation has resulted in a significant reduction in ionizing radiation exposure but the lack of awareness of radiation exposure still persists.[12] In this scenario, the awareness of radiation doses and risks, also during interventional cardiology procedures, is essential today to apply the risk-benefit assessment and to reinforce the principles of justification and optimization in clinical practice.[12]

Our findings are best interpreted in the context of their limitations. This includes the lack of patient-level data verification due to the use of a de-identified database, the retrospective observational cohort study design, the possibility of coding errors due to the use of ICD codes, the presence of unmeasured confounding, and the lack of longer-term follow-up. Also, we lacked data on the type, dose, and duration of chemotherapy and/or radiotherapy received by patients with active cancer or a history of cancer. Furthermore, we were unable to stratify outcomes based on the type of ablation strategy utilized (radiofrequency vs. cryo-energy). Therefore, our study findings should be considered hypothesis-generating at best.

In conclusion, our study identifies the association between active cancer and higher odds of periprocedural complications and all-cause and bleeding-related readmissions in patients undergoing AF ablation and suggests the need for multi-disciplinary decision-making and individually tailored therapeutic approaches given the benefits and risks of the procedure in this high-risk cohort of patients. Further prospective studies are required to confirm these findings and explore the outcomes of AF ablation in patients with cancer.

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Data availability

The authors confirm that the data supporting the findings of this study are available upon reasonable request from the authors.

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