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Short- and long-term outcomes of percutaneous left atrial appendage occlusion in cancer patients

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ABSTRACT

Introduction and objectives: Percutaneous left atrial appendage occlusion (LAAO) is a viable option to mitigate bleeding and stroke risks in patients with atrial fibrillation (AF) who are not eligible for oral anticoagulation. Its safety and efficacy in cancer patients remain unclear due to their exclusion from trials. This study aimed to compare short- and long-term LAAO outcomes between cancer and non-cancer patients.

Methods: Retrospective single centre study of 361 consecutive patients who underwent LAAO between april-2010 and december-2023 were included. Short-term outcomes included periprocedural complications, 30-day hospital readmission and mortality. Long-term outcomes included the composite of stroke, bleeding, and mortality and each component assessed separately.

Results: The study included 93 cancer patients (54 % active, 46 % in remission) and 268 non-cancer patients. Baseline characteristics were similar, including ischemic and bleeding risk profiles (CHA_2DS_2-VASc: 4.5 ± 1.4 vs. 4.4 ± 1.5; HAS-BLED: 3.3 ± 0.9 vs. 3.2 ± 0.9), previous stroke and total bleeding events. Short-term outcomes showed no significant differences in periprocedural complications (7 % vs. 6 %), 30-day readmission (2 % vs. 3 %), or 30-day mortality (0 % vs. 1.5 %). Over 32 months, there was no significant difference regarding the composite endpoint ($p = 0.067$), stroke (SHR 0.54; $p = 0.25$) or bleeding events (SHR 1.36; $p = 0.35$). LAAO was effective in terms of stroke reduction in cancer and non-cancer patients ($p = 0.027$ and $p = 0.006$, respectively). All-cause mortality rates were higher in cancer patients ($p = 0.002$), mainly due to cancer progression and infections.

Conclusions: LAAO procedure was safe and effective in both populations. Cancer patients experienced higher rates of all-cause mortality, with no differences in stroke and bleeding outcomes between groups.

1. Introduction

Cancer patients are at increased risk of developing atrial fibrillation (AF) due to shared risk factors such as advanced age, obesity, systemic inflammation, and specific anti-cancer treatment.[1,2] The onset of AF in cancer patients is associated with an increased likelihood of thromboembolism and bleeding events, posing challenges in assessing the overall clinical benefit of anticoagulation. [3,4] Traditional stroke risk scores have not been validated in this population, requiring an individualized approach as recommended by guidelines. [4–6].

Given these limitations, there is an unmet need for alternative stroke prevention methods, particularly in cancer patients at high bleeding risk and in those with recurrent embolic events despite anticoagulation therapy. [4,7] Left atrial appendage occlusion (LAAO) has emerged as a

Abbreviations: **AF**, Atrial fibrillation; **CV**, Cardiovascular; **DAPT**, Dual-antiplatelet therapy; **LAAO**, Left atrial appendage occlusion; **PDL**, Peri-device leak; **SAPT**, Single-antiplatelet therapy.

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potential option[8–10]; however, data on its safety and efficacy in cancer patients are lacking due to their exclusion from clinical trials. Currently, there are few retrospective studies that have revealed contradictory findings, with some indicating higher risks of periprocedural complications[11,12], including stroke[13], bleeding[12] and in-hospital mortality[14] in cancer patients.

Therefore, we sought to compare the safety and effectiveness in short- and long-term outcomes among patients with and without cancer who underwent LAAO.

2. METHODS

The study was conducted in accordance with the Declaration of Helsinki and was approved by the local Ethics Committee.

2.1. Patient population

This was an observational and retrospective study that included consecutive patients who underwent LAAO between april-2010 and december-2023 at a single tertiary center. The closure devices used included the Amplatzer Cardiac Plug™ (Abbott®), Amulet™ (Abbott®), Watchman™ (Boston Scientific®), and LAmbre™ (Lifetech Scientific®), selected at the operators' discretion, with sizing based mainly on CT imaging or transoesophageal echocardiography (TEE). We identified patients with active or prior cancer, collecting details on their cancer history (active vs. remission), type/stage, and treatments. Active cancer was defined as receiving cancer therapies (surgery, chemotherapy, radiation, or hormonal therapy) within 6 months of LAAO or having untreated disease. We compared this cohort with patients undergoing LAAO in the same period without cancer history, evaluating short- and long-term outcomes.

2.2. Clinical data

Baseline characteristics, CHA_2DS_2-VASc (Congestive Heart Failure (HF), Hypertension, Age $\geq$ 75 years, Diabetes Mellitus, prior Stroke or Transient Ischemic Attack (TIA), Vascular disease, Age 65 to 74 years and female Sex) and HAS-BLED (Hypertension, Abnormal renal and/or liver function, Stroke, Bleeding history or predisposition, Labile INR, Age $>$ 65 years, Drugs and/or alcohol concomitantly) scores, antithrombotic medications, procedural details, and outcome results were collected.

2.3. Outcomes definitions

Short-term outcomes included in-hospital mortality, length of stay and periprocedural complications (i.e., vascular complications, cardiac tamponade treated with pericardiocentesis or surgery, stroke, device migration, bleeding and other complications). Furthermore, readmission (Cardiovascular (CV) causes or procedure-related) and mortality (CV and all-cause) rates were assessed at 30 days. Long-term outcomes included the composite of stroke, bleeding, and mortality (CV and all-cause) after at least 1 month follow-up, in addition to device-related complications.

Stroke was classified according to the VARC criteria. [15] When referring to bleeding events, we specifically address major bleeding events as described in the ESC consensus definitions for LAAO therapy studies. [16].

2.4. Definitions

Successful LAAO was defined as a device deployed and implanted in correct position, meeting all release criteria according to the manufacturer's instruction for use. Device-related thrombosis (DRT) was defined as a thrombus on the luminal side of the device in TEE or CT, regardless of clinical implications. Significant *peri*-device leak (PDL) was defined as a residual leak over 5 mm in TEE or CT.

2.5. Statistical analysis

Categorical variables were presented as numbers (percentages), while continuous variables were expressed as mean $\pm$ standard deviation. Statistical comparisons were conducted using the Student's *t*-test for continuous variables and the chi-square or Fisher's exact test for categorical variables. Both short- and long-term outcomes were assessed. Cumulative incidence functions and Fine-Gray competing risk regression models were employed to analyse stroke and bleeding events, adjusting for the competing risk of mortality. Results are presented as sub-distribution hazard ratios (SHR). For the composite endpoint and all-cause mortality analysis, Kaplan-Meier survival curves were used for time-to-event variables and compared with log-rank tests. Hazard ratios (HR) were calculated using Cox regression analysis. The variables for all-cause death were analysed separately in univariate Cox regression models, and those with a p-value less than 0.1 were included in multivariable Cox regression models. The observed annualized ischemic event rates were compared with the extrapolated annualized expected rates without any anticoagulation therapy, based on the mean CHA_2DS_2-VASc score before LAAO. [17] Similarly, the observed annualized bleeding rates were compared with the extrapolated annualized expected rates under anticoagulation use, based on the mean HAS-BLED score before LAAO. [18] Statistical significance was set at $p < 0.05$. Statistics were performed using R, version 4.2.2 (The R Foundation for Statistical Computing, Austria) and SPSS software version 26.0 (IBM Corporation).

3. RESULTS

3.1. Baseline characteristics

A total of 361 patients were included in the analysis: 26 % (n = 93) with cancer and 74 % (n = 268) without cancer. The baseline characteristics were similar between groups (Table 1).

Overall, the population had a high-risk profile for ischemic (CHA_2DS_2-VASc: 4.4 $\pm$ 1.4) and bleeding events (HAS-BLED: 3.3 $\pm$ 0.9), with no significant differences between cancer and non-cancer groups (CHA_2DS_2-VASc: 4.5 vs. 4.4; HAS-BLED: 3.3 vs. 3.2, p = 0.67). Patients with cancer had higher prevalence of history of genitourinary bleeding (9 % vs. 3 %, p = 0.013). The Amplatzer Cardiac Plug™ or Amulet™ devices were used in over half of the patients, with no differences in device types between the groups.

The most common indication for LAAO was high bleeding risk (55 % and 52 % with a history of major bleeding, and 18 % and 16 % with increased bleeding risk, in cancer and non-cancer patients respectively) and those with stroke despite appropriate anticoagulant treatment (23 % in cancer patients and 29 % in non-cancer patients, Supplementary Table 1).

Among cancer patients, 54 % (n = 50) had active disease at the time of device implantation, with the remain being in remission. Overall, cancers were more frequently localized to a single organ without evidence of spread (n = 74, 80 %). Additionally, 48 % (n = 45) had a history of surgical intervention, 30 % (n = 28) underwent chemotherapy, and 24 % (n = 22) received radiation therapy. The main cancer diagnoses included genitourinary (34 %), gastrointestinal (23 %) and breast (12 %) (Table 2).

3.2. Short-term outcomes

All LAAO procedures were successfully performed. There was no difference in the length of stay of hospitalization between groups (p = 0.69). Periprocedural complications occurred in 6 % of patients (n = 23), mainly due to vascular complications (2 %, n = 6) and cardiac tamponade (2 %, n = 6). Stroke, device migration, and bleeding were

Table 1
Baseline characteristics of cancer and non-cancer patients.

	Cancer patients (n = 93)	Non-cancer patients (n = 268)	p-value
Male sex	57 (61 %)	142 (53 %)	0.165
Age (years)	76 ± 7	75 ± 8	0.072
Hemoglobin (g/dL)	11.9 ± 1.7	12.2 ± 1.9	0.099
Creatinine (mg/dL)	1.3 ± 0.9	1.3 ± 1.1	0.897
Body mass index (kg/m^2)	28.8 ± 4.9	29.2 ± 5.7	0.563
Atrial Fibrillation			0.543
Paroxysmal	24 (26 %)	78 (29 %)	
Persistent/Permanent	69 (74 %)	190 (71 %)	
CHA_2DS_2-VASc score	4.4 ± 1.5	4.4 ± 1.3	0.667
Heart failure	25 (27 %)	63 (24 %)	0.525
Hypertension	79 (85 %)	215 (80 %)	0.313
Diabetes	34 (37 %)	76 (28 %)	0.139
Stroke/Transient ischemic attack	30 (32 %)	105 (39 %)	0.235
Thromboembolism	3 (3 %)	15 (6 %)	0.365
Vascular disease	23 (25 %)	47 (18 %)	0.131
Age ≥ 75 years	56 (60 %)	138 (52 %)	0.146
HAS-BLED score	3.3 ± 0.9	3.2 ± 0.9	0.523
Hypertension (uncontrolled)	4 (4 %)	10 (4 %)	0.806
Abnormal renal function	29 (31 %)	59 (22 %)	0.089
Abnormal liver function	3 (3 %)	28 (10 %)	**0.032**
Stroke/Transient ischemic attack	30 (32 %)	105 (39 %)	0.235
Bleeding	60 (65 %)	162 (60 %)	0.487
– Gastrointestinal	32 (34 %)	75 (28 %)	0.242
– Intracranial	17 (18 %)	53 (20 %)	0.753
– Genitourinary	8 (9 %)	7 (3 %)	**0.013**
– Pulmonary	1 (1 %)	8 (3 %)	0.309
– Other	2 (2 %)	20 (7.5 %)	0.065
Labile INR	3 (3 %)	11 (4 %)	0.714
Alcohol	6 (7 %)	19 (7 %)	0.835
Antiplatelet medications	16 (17 %)	46 (17 %)	0.993
– ASA	14 (15 %)	40 (15 %)	0.976
– Clopidogrel	7 (8 %)	21 (8 %)	0.924
– DAPT	5 (5 %)	15 (6 %)	0.936
NSAID use	2 (2 %)	3 (1 %)	0.463
Age > 65 years	88 (95 %)	238 (89 %)	0.102
Coronary artery disease	28 (30 %)	77 (29 %)	0.801
Prior CABG	3 (3 %)	14 (5 %)	0.433
Valvular heart disease	21 (23 %)	41 (15 %)	0.117
Cardiomyopathy	3 (3 %)	14 (5 %)	0.433
Obstructive sleep apnea	9 (10 %)	24 (9 %)	0.835
Chronic lung disease	13 (14 %)	23 (9 %)	0.135
Long term anticoagulation	33 (35 %)	111 (41 %)	0.314
– Acenocoumarol	6 (6 %)	20 (7 %)	0.745
– DOAC	26 (28 %)	88 (33 %)	0.383
– Other	1 (1 %)	3 (1 %)	0.972
LVEF, %	54 ± 9	53 ± 11.4	0.560
LAVI, ml/m^2	49 ± 10	47 ± 8	0.385
Amplatzer cardiac plug™ or Amulet™	47 (51 %)	139 (52 %)	0.825
Watchman™	24 (26 %)	89 (33 %)	0.185
LAmbre™	22 (24 %)	40 (15 %)	0.054

Data provided as mean ± standard deviation or number (%). ASA: Acetyl salicylic acid; CABG: Coronary artery bypass grafting; DAPT: Dual antiplatelet therapy; INR: International Normalized Ratio; LAVI: Left Atrial Volume Index; LVEF: Left ventricular ejection fraction; DOAC: Direct oral anticoagulants; NSAIDs: Nonsteroidal anti-inflammatory drugs.

rare (≤1%). There were no significant differences between the groups (p = 0.97).

There was no significant difference in the 30-day readmission rate between patients with and without cancer (2 % vs. 3 %, p = 0.53). Thirty-day all-cause mortality was 1.5 % (n = 4 non-cancer patients): hemorrhagic stroke (n = 2, both on DAPT), HF decompensation (n = 1), and end-stage cirrhosis (n = 1). No deaths occurred in the cancer group at 30-day follow-up.

Table 2
Clinical profile of cancer patients.

Age at cancer diagnosis (years)	71 ± 8
Active at time of device implant	50 (54 %)
Remission at time of device implant	43 (46 %)
Progression of active cancer	
Localized	74 (80 %)
Metastatic	19 (20 %)
Treatment modalities	
Prior surgery	45 (48 %)
Chemotherapy	28 (30 %)
Radiation therapy	22 (24 %)
Hormonal therapy	7 (8 %)
Other	5 (5 %)
Type of cancer	
GENITOURINARY	**32 (34 %)**
Prostate	19 (20.5 %)
Bladder	6 (6.5 %)
Renal	4 (4 %)
Vulvar/ovarian/endometrial	3 (3 %)
GASTROINTESTINAL	**21 (23 %)**
Colorectal	14 (16 %)
Liver	3 (3 %)
Pancreatic	2 (2 %)
Gastric	2 (2 %)
BREAST	**11 (12 %)**
HEMATOLOGIC	**10 (11 %)**
Lymphoma	3 (3 %)
Myelodysplastic syndrome	3 (3 %)
Leukemia	2 (2 %)
Multiple myeloma	2 (2 %)
SKIN	**6 (6 %)**
Squamous/Basal cell	5 (5 %)
Melanoma	1 (1 %)
OTHER	**13 (14 %)**
Lung	6 (6 %)
Brain	5 (5 %)
Oropharyngeal	1 (1 %)
Liposarcoma	1 (1 %)

Data provided as mean ± standard deviation or number (%).

3.3. Long term-outcomes

The median follow-up time was 32 [16–52] months. There was no difference in the composite endpoint of stroke, bleeding, and all-cause mortality (log-rank p = 0.067) among cancer and non-cancer patients. The incidence of the individual endpoints of stroke (SHR: 0.54; 95 % CI: 0.19–1.55; p = 0.25) or bleeding events (SHR: 1.36; 95 % CI: 0.71–2.61; p = 0.35) were also similar between groups (Table 3 **and** Fig. 1).

In the cancer group, 2 % (n = 2) had recurrent stroke, compared to 3 % (n = 9) in the non-cancer group. Recurrent bleeding was seen in 12 % (n = 11) of cancer patients and 11 % (n = 29) of non-cancer patients, with nearly half (45 % cancer and 40 % non-cancer patients) on antithrombotic therapy.

When comparing the observed annualized ischemic event rate with the expected rate based on the CHA_2DS_2-VASc, a relative risk reduction (RRR) of 75 % in cancer (p = 0.027) and 60 % in non-cancer patients (p = 0.006) was observed. LAAO procedure was associated with a non-significant RRR of bleeding events of 10 % in cancer and 39 % in non-cancer patients (Fig. 2).

Regarding device-related complications, there were no differences between groups. Significant PDL (>5mm) occurred in 2 (2 %) cancer and 4 (2 %) non-cancer patients. DRT was identified in 1 (1 %) cancer and 2 (2 %) non-cancer patients (Table 3). One patient with DRT, not on antithrombotic therapy, experienced an ischemic stroke. The remaining DRT and PDL cases had no clinically evident impact during follow-up.

Although CV mortality was similar between groups (HR: 0.60; 95 % CI: 0.31–2.95; p = 0.94), cancer patients had higher all-cause mortality in the univariate Cox analysis (HR: 2.01; 95 % CI: 1.29–3.13; p = 0.002), mainly due to cancer progression (44 %) and infections (30 %). On the other hand, in the non-cancer group, the main causes of death were CV

Table 3
Short- and long-term outcomes stratified by cancer status.

Outcomes	Cancer patients	Non-cancer patients	p-value
Short-term outcomes			
In-hospital			
Length of stay, days	2.5 ± 4.1	2.3 ± 4.9	0.691
Length of stay > 2 days	15 (16 %)	33 (12 %)	0.350
Periprocedural complications	6 (7 %)	17 (6 %)	0.971
– Vascular complications	1 (1 %)	5 (2 %)	1.000
– Cardiac tamponade	3 (3 %)	3 (1 %)	0.189
– Stroke	1 (1 %)	2 (0.7 %)	1.000
– Device migration	0 (0 %)	2 (0.7 %)	1.000
– Bleeding	1 (1 %)	3 (1 %)	1.000
– Other	0 (0 %)	2 (0.7 %)	1.000
All-cause mortality	1 (1 %)	0 (0 %)	0.258
CV mortality	1 (1 %)	0 (0 %)	0.258
30-day			
Readmission	2 (2 %)	11 (4 %)	0.528
Diagnoses			
– Bleeding	1 (1 %)	4 (2 %)	1.000
– Stroke	1 (1 %)	3 (1 %)	1.000
– Decompensated HF	0 (0 %)	2 (0.7 %)	1.000
– Cardiac tamponade	0 (0 %)	1 (0.4 %)	1.000
– Cellulitis of access site	0 (0 %)	1 (0.4 %)	1.000
All-cause mortality	0 (0 %)	4 (1.5 %)	0.576
CV mortality	0 (0 %)	0 (0 %)	1.000
Long-term outcomes			
Stroke	4 (4 %)	24 (9 %)	0.148
– Recurrent	2 (2 %)	9 (3 %)	0.636
Bleeding	13 (13 %)	31 (12 %)	0.540
– Recurrent	11 (12 %)	29 (11 %)	0.790
– Epistaxis	1 (1 %)	3 (1 %)	0.520
– Gastrointestinal	2 (2 %)	12 (5 %)	0.317
– Genitourinary	5 (5 %)	1 (0.4 %)	**0.020**
– Intracranial	1 (1 %)	6 (2 %)	0.483
– Other	2 (2 %)	1 (0.4 %)	0.452
– Anemization	2 (2 %)	8 (3 %)	0.673
Device-related complications	3 (3 %)	6 (3 %)	0.700
– PDL	2 (2 %)	4 (2 %)	0.651
– DRT	1 (1 %)	2 (1 %)	1.000
All-cause mortality	31 (33 %)	64 (20 %)	**0.010**
CV mortality	4 (4 %)	11 (4 %)	0.935

Data provided as mean ± standard deviation or number (%). CV: Cardiovascular; DRT: Device-related thrombosis; HF: Heart Failure; PDL: Peri-device leak.

(28 %), infections (21 %), and bleeding events (19 %). In the multivariate Cox analysis, independent predictors of all-cause mortality included body mass index, diabetes, chronic kidney disease, post-procedural bleeding, and cancer. (Fig. 3). Details of the univariate analysis are shown in Supplementary Table 2.

When analysing the different types of LAAO devices, there were no significant differences in long-term outcomes **(**Supplementary Table 3**).**

3.4. Pattern of antithrombotic treatment

Before device implantation, 35 % of cancer patients and 41 % of non-cancer patients were on anticoagulation therapy (p = 0.314).

Approximately one-third of patients in both groups were discharged on single-antiplatelet therapy (SAPT), another third on dual-antiplatelet therapy (DAPT), and the remaining third on anticoagulation therapy. At 6 months, no differences in post-LAAO antithrombotic treatment were observed. In the cancer group, 39 % were on SAPT, 39 % were free of treatment, 20 % were on anticoagulants and 2 % on DAPT. In the non-cancer group, 40 % were on SAPT, 33 % were free of treatment, 24 % were on anticoagulants and 2 % on DAPT (Supplementary Table 4).

When considering only high bleeding risk patients (68 cancer patients and 183 non-cancer patients), the majority of both cancer (63 %, n = 43) and non-cancer (64 %, n = 117) patients were free from antithrombotic therapy at 6 months follow-up.

3.5. Active cancer vs remission cancer

No differences in baseline characteristics were found between patients with active cancer and those with a prior history of cancer (Supplementary Table 5). Short-term outcomes showed no significant differences in post-LAAO complications (10 % vs. 5 %, p = 0.33) or hospital stay length (p = 0.11). One patient in each group was readmitted within 30 days, with no deaths occurring. Long-term outcomes showed no differences in the composite endpoint (log-rank p = 0.088), stroke (SHR: 1.50; 95 % CI: 0.13–16.75; p = 0.84), or bleeding events (SHR: 1.94; 95 % CI: 0.61–6.19; p = 0.26) (Fig. 4). However, all-cause mortality was higher in the active cancer group (log-rank p = 0.010), while CV mortality was similar (log-rank p = 0.34).

3.6. Cancer type and treatment modalities

There were no differences in HAS-BLED and CHA_2DS_2-VASc scores among different cancer types. There were also no differences in stroke rates among cancer types, but genitourinary cancer was associated with more bleeding events (SHR: 3.21; 95 % CI: 1.05–9.79; p = 0.04). Hematologic cancer had worse outcomes with higher all-cause mortality (HR: 2.76; 95 % CI: 1.13–6.75; p = 0.026). Metastatic cancer did not have more strokes or bleeding event (**Supplementary Fig. 1**). Treatment modalities, including surgery, chemotherapy, radiation or hormonal therapy, did not affect long-term outcomes after LAAO across all types of cancer.

4. Discussion

The main findings of our study are (Fig. 5): (1) Short-term outcomes, including periprocedural complications and the long-term composite endpoint of stroke, bleeding, and all-cause mortality, were similar between cancer and non-cancer patients, as were the individual endpoints of stroke and bleeding. (2) Cancer patients exhibited higher long-term all-cause mortality, primarily due to cancer progression and infections, while CV mortality remained similar between the groups; (3) LAAO effectively reduced ischemic events in both cancer and non-cancer patients, with a higher RRR observed in cancer patients. These findings are particularly relevant in the context of advancements in cancer therapies, which have significantly improved patient prognosis. [19].

In the recent years, LAAO has emerged as a viable option to mitigate bleeding risks associated with anticoagulation, particularly in patients with contraindications, and to reduce the risk of recurrent embolic events during anticoagulant therapy. [4,7,20,21] The PROTECT-AF, PREVAIL, and PRAGUE-17 studies have demonstrated that percutaneous LAAO reduces the risk of major bleeding and death compared to warfarin[8,22,23] and is noninferior to direct oral anticoagulants (DOAC) for stroke and major bleeding. [24] However, cancer patients were not specifically included or described in these trials, making it challenging to ascertain the utility of LAAO in this population. Although there is increasing information regarding the efficacy and safety of LAAO in “real-world” practice, few retrospective studies involve cancer patients, and the results are controversial. [11,13,25].

In our study, cancer and non-cancer patients undergoing LAAO had similar baseline characteristics, with both groups exhibiting high thromboembolic risk, primarily driven by advanced age, CV comorbidities, and prior stroke, as well as high bleeding risk, reflecting that most patients had experienced a major bleed before. Compared with the landmark PROTECT-AF[23] and PREVAIL[22] trials that excluded patients who had contraindications to antithrombotic therapy, our cohort was at higher bleeding risk. However, the bleeding risk was comparable to that in the more contemporary PRAGUE-17 trial. [24].

Concerning indications for LAAO, a history of major bleeding and stroke while on anticoagulant treatment were the most common in both groups, consistent with observations in other registries. [26].

Periprocedural complications occurred in 6 % of patients, with no

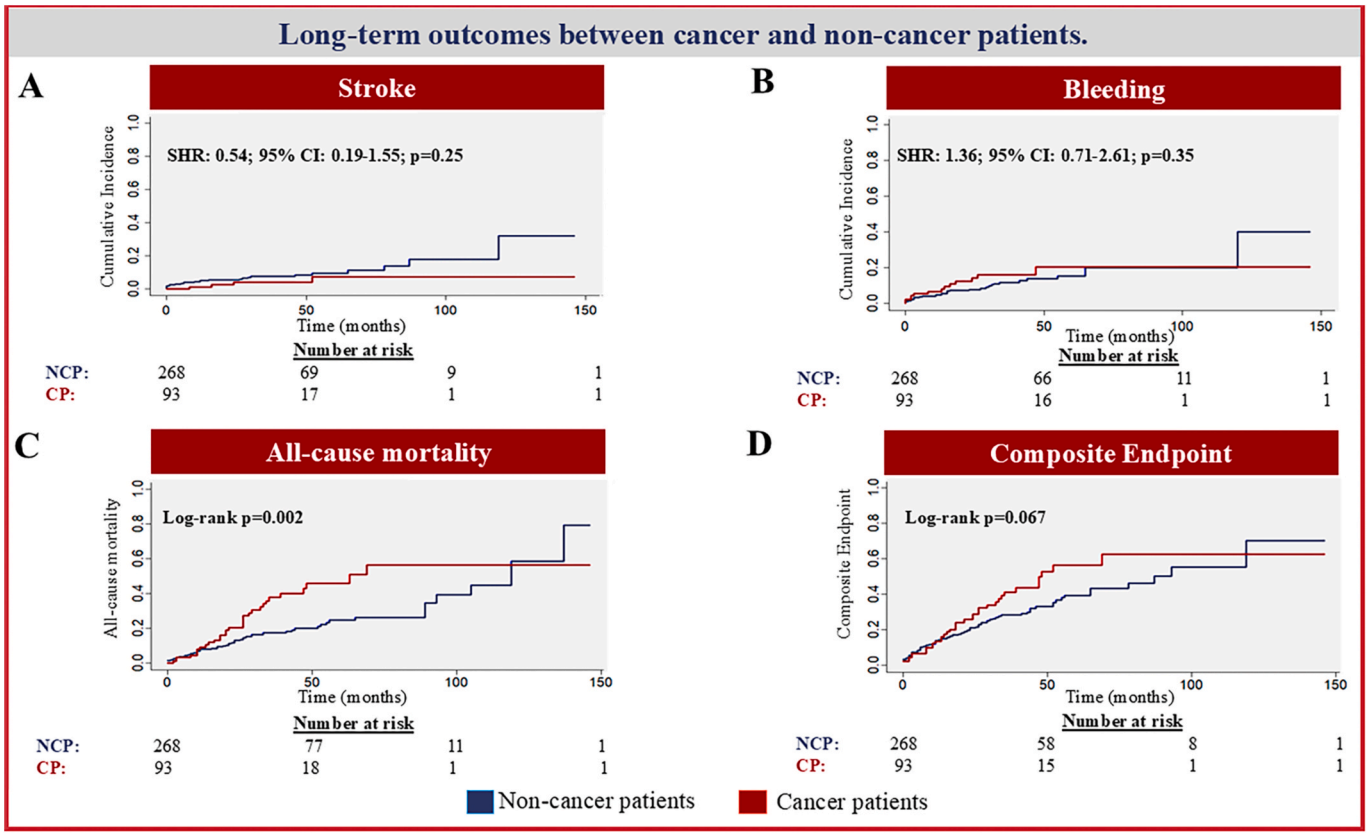

Fig. 1. Long-term outcomes between cancer and non-cancer patients. Fine and Gray cumulative incidence function curves (A and B) and Kaplan–Meier curves (C and D). CP: Cancer patients; NCP: Non-cancer patients.

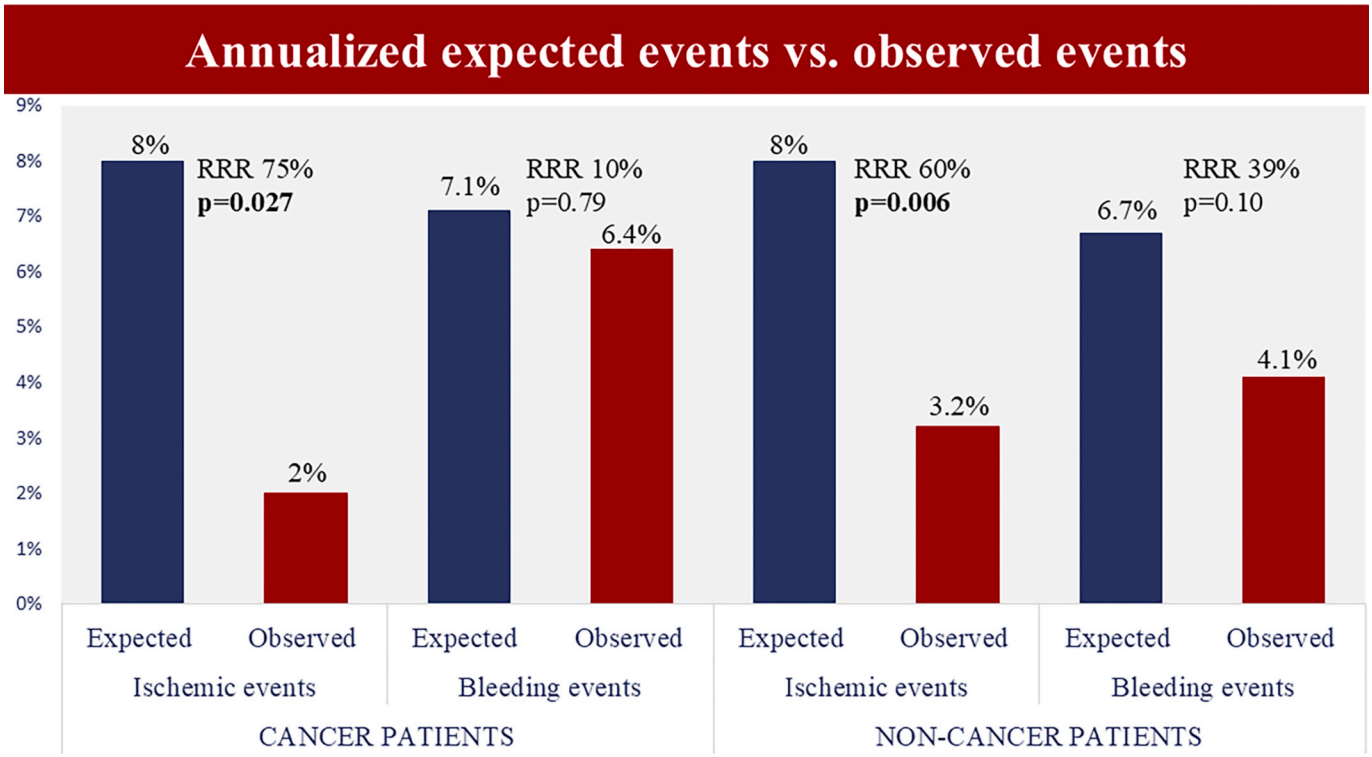

Fig. 2. Annualized expected events vs. observed events. A relative risk reduction (RRR) in ischemic events of 75 % in cancer patients (p = 0.027) and 60 % in non-cancer patients (p = 0.006) was observed. The LAAO procedure was associated with a non-significant RRR of bleeding events of 10 % in cancer patients and 39 % in non-cancer patients.

Variable	HR	95% CI	p-value
Age	1.02	0.98-1.05	0.315
Male sex	1.56	0.95-2.55	0.077
BMI	0.93	0.88-0.98	0.009
Diabetes	1.80	1.12-2.91	0.015
Vascular disease	1.26	0.78-2.05	0.341
HAS-BLED score	1.22	0.94-1.58	0.139
Chronic Kidney Disease	1.67	1.02-2.73	0.042
Post-procedural stroke	1.49	0.83-2.69	0.184
Post-procedural bleeding	2.50	1.52-4.10	0.000
Neoplasia	1.77	1.11-2.82	0.015

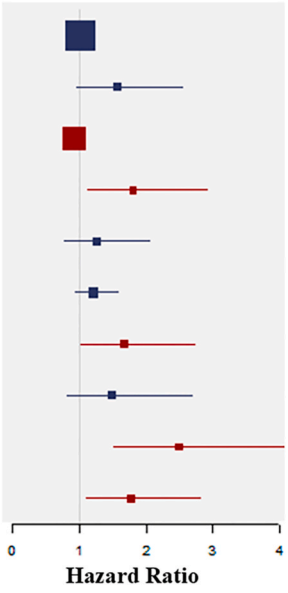

Fig. 3. Forest plot of multivariate analysis for independent predictors associated with all-cause mortality. Significant predictors of increased all-cause mortality included body mass index (BMI), diabetes, chronic kidney disease, post-procedural bleeding, and neoplasia.

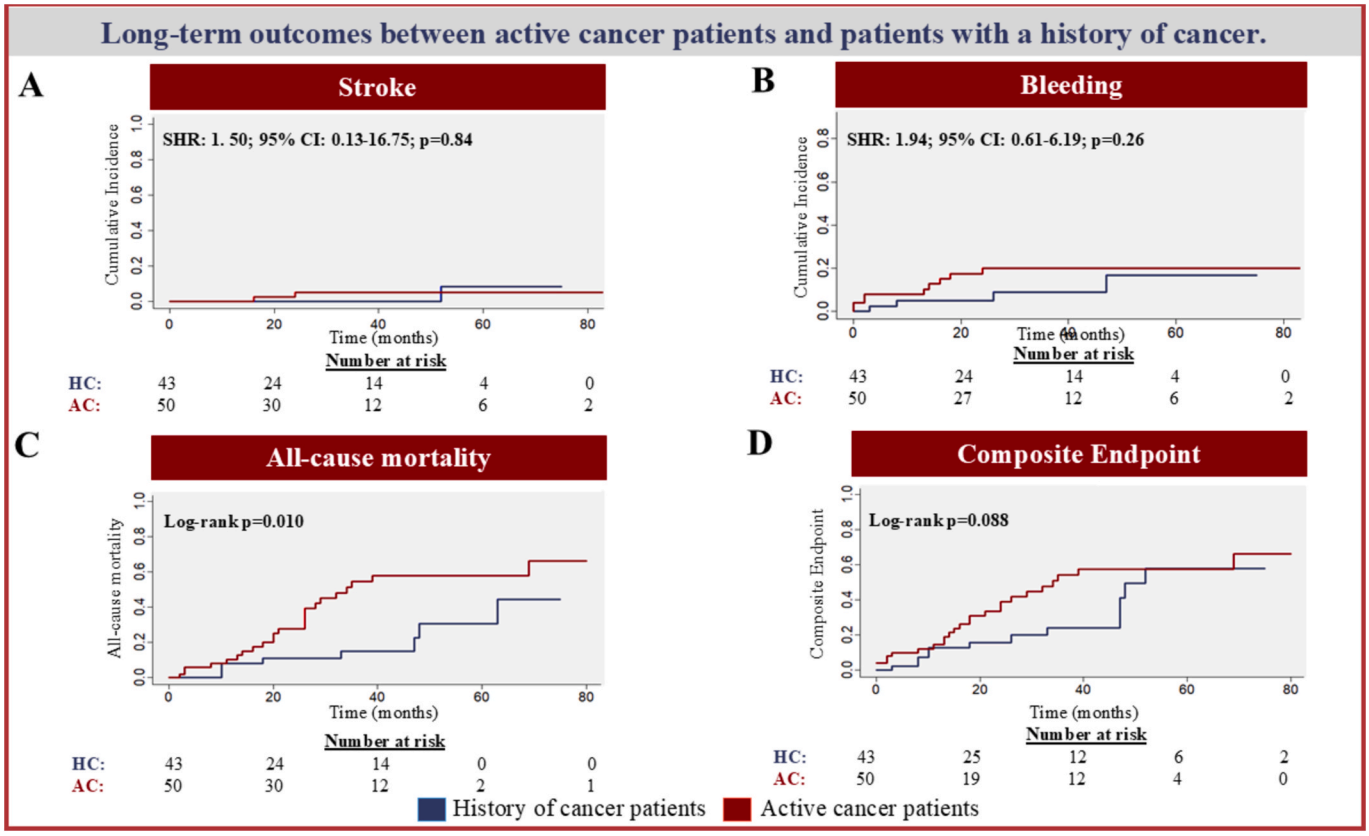

Fig. 4. Long-term outcomes between active cancer patients and patients with a history of cancer. Fine and Gray cumulative incidence function curves (A and B) and Kaplan–Meier curves (C and D). AC: Active cancer; HC: History of cancer.

differences between groups. In-hospital stroke was rare (≤1%). These findings differ from other studies which showed higher periprocedural complications in cancer patients, including increased vascular complications, [11] thromboembolic events, [11,13] cardiac tamponade, and major bleeding events. [12] In our study, only one (0.3 %) cancer patient experienced a major complication, cardiac tamponade, which resulted in death. This very low mortality rate is consistent with observations from other studies[13,21,27] and may be related to appropriate patient selection for the procedure, [28] accurate device sizing using TEE and CT in many cases, [29] and the experience of the operators. [30].

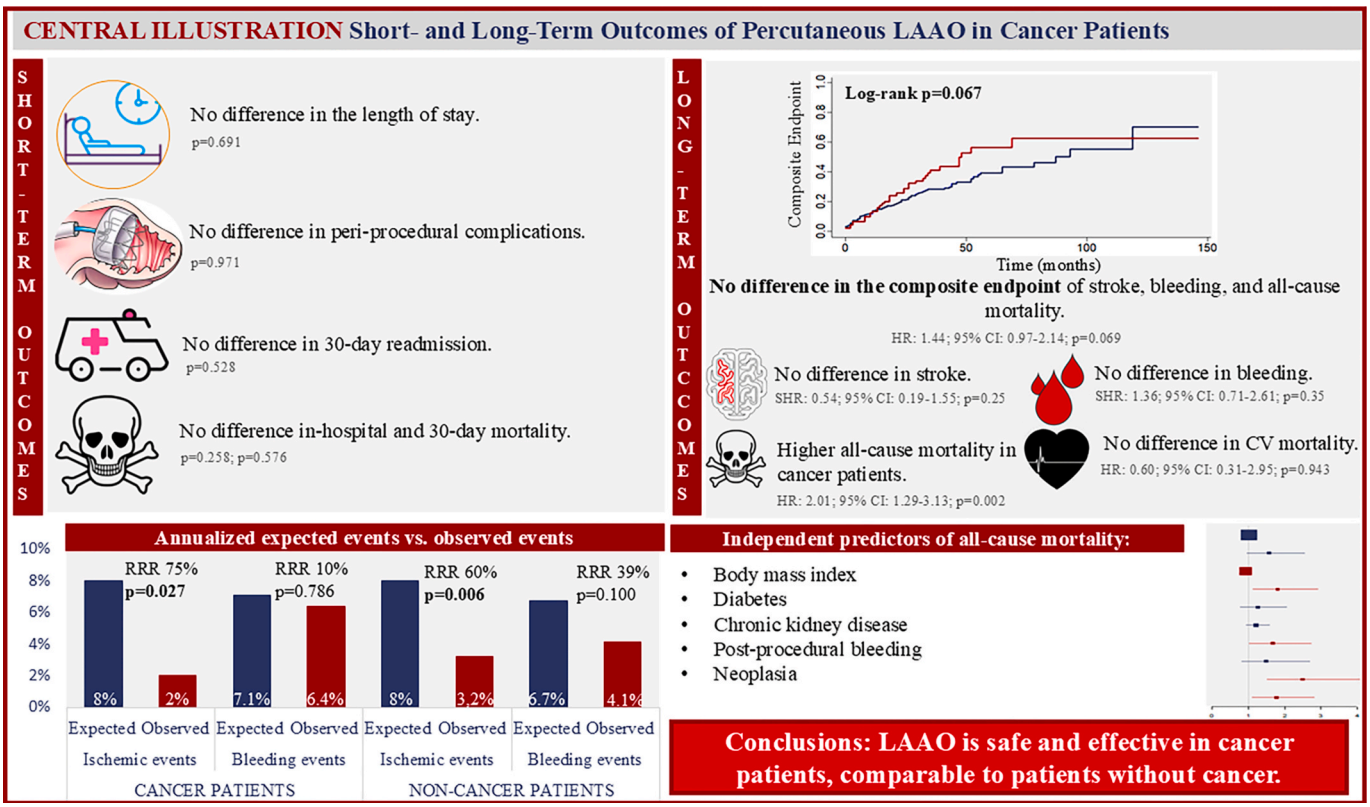

Fig. 5. Central illustration. Summary of short- and long-term outcomes of left atrial appendage occlusion in patients with and without cancer. CV: Cardiovascular; LAAO: Left Atrial Appendage Occlusion; RRR: Relative risk reduction.

We found one early readmission for ischemic stroke (patient on SAPT) and one for bleeding (patient on anticoagulation) in the cancer group, with no differences compared to the non-cancer group. This suggests that LAAO's short-term effectiveness is acceptable and similar to other studies. [11,13].

Device-related complications during follow-up is aligned with the reported incidence in the literature (2–4 %).[31] One patient with DRT, not on antithrombotic therapy, experienced an ischemic stroke. In the other cases, short-term anticoagulation was resumed without subsequent stroke or bleeding episodes. PDL, with a reported incidence in the literature of 10–26 %,[32] occurred in six patients (2 %) in our cohort, all of whom were managed conservatively without any clinical sequelae.

Our study shows no significant difference in stroke risk among groups during follow-up, similar to others studies, [25,27] with the incidence being low (4 % in our cohort). [22,23] Only 2 % (n = 2) of cancer patients and 3 % (n = 9) of non-cancer patients experienced recurrent strokes after LAAO. The observed annualized ischemic event rates after this procedure remained lower than expected according to baseline CHA_2DS_2-VASc, with a RRR of 75 % in cancer patients and 60 % in non-cancer patients, supporting the effectiveness of LAAO in stroke prevention. [22,23,33] It is worth mentioning that even with similar CHA_2DS_2-VASc scores, the reduction in ischemic risk was greater in the cancer group. These patients are likely more protected because they have a higher baseline risk that conventional risk scores may not fully capture, due to the prothrombotic environment associated with oncologic disease. [4,6] While LAAO effectively reduces arterial thromboembolic events, it does not prevent venous thromboembolism, so maintaining anticoagulation in these patients is crucial, requiring a careful balance with bleeding risk. [34].

The incidence of bleeding events was 13 % (n = 13) in the cancer cohort and 12 % (n = 31) in the non-cancer cohort, aligning with rates reported in previous studies. [25,27] Notably, the majority of these patients experienced recurrent bleeding, with rates of 85 % (n = 11) in the cancer group and 94 % (n = 29) in the non-cancer group. Most bleeding events (64 %, n = 28) occurred after the first 6 months, when the majority of patients (84 %, n = 36) were already free of antithrombotic therapy. This suggests that the high baseline hemorrhagic risk is a significant factor, especially since 89 % (n = 39) of these patients had undergone LAAO due to a history of major bleeding or increased bleeding risk.

In our cohort, bleeding events were similar to the expected rate based on the HAS-BLED score for patients on anticoagulation therapy. This may be because the HAS-BLED score underestimates the true bleeding risk in cancer patients, potentially masking a reduction in bleeding risk after LAAO and stopping antithrombotic agents. It can also be attributed to the high baseline hemorrhagic risk, making these patients prone to new bleeding episodes. Additionally, it is noteworthy that post-procedural bleeding emerged as an independent predictor of all-cause mortality. However, withholding antithrombotic therapy in these patients may reduce the bleeding burden, while they remain protected from the majority of ischemic events by LAAO. [33].

It is important to recognize that LAAO devices require short-term antithrombotic therapy post-procedure, [4] which can pose a challenge in this patient population. Increasing evidence suggests that a short duration of DAPT without anticoagulation[35–37] or low dose DOAC[38,39] post-LAAO are safe and may be more likely used in cancer patients with high bleeding risk. Randomized trials should assess whether percutaneous epicardial LAA exclusion safely reduces stroke risk in cancer patients with absolute contraindications to antithrombotic treatment, [40,41] while potentially increasing the risk of complications derived from a more invasive approach in this frail and comorbid population.

As expected, cancer patients had higher all-cause mortality, with approximately one-third dying during the follow-up period, primarily due to cancer progression and infections. Neoplasia was also identified as an independent predictor of all-cause mortality. In this population

with limited life expectancy, metrics such as freedom from stroke, major bleeding, and device-related complications may be more meaningful than long-term survival when considering LAAO. [28,42].

Patients with active cancer had higher all-cause mortality rates but did not have increased composite endpoint, stroke or bleeding risks, contrasting with literature. [34] Although the literature indicates thrombotic risk varies by cancer type, [43] our cohort showed no difference in stroke rates. However, genitourinary cancers were associated with a higher incidence of bleeding, likely due to their prevalence as the most common cancer type linked to an inherently high bleeding risk. [44].

Additionally, hematologic cancers had higher mortality. Furthermore, unlike previous reports, [34] treatment modalities did not impact long-term outcomes.

In summary, our results align with studies demonstrating that LAAO is safe and effective, [8,22,23] showing similar composite endpoint, stroke and bleeding rates in both cancer patients and non-cancer patients. [25,27] However, our findings contrast with studies reporting higher in-hospital mortality[14], stroke[13], and periprocedural complications[11,12] in cancer patients.

Physicians should consider LAAO as a valuable option for cancer patients. It is important to recognize that not all cancer patients have the same risk for bleeding or clotting, which affects the decision to use anticoagulation. A multidisciplinary, patient-centred approach is crucial. [42].

5. Limitations

This study has several limitations. Conducted at a single center, the findings are less generalizable. The non-randomized, retrospective design introduces biases and confounding factors. Additionally, considerable heterogeneity in cancer type and staging, along with a small sample size—particularly within specific cancer types and treatments—precluded robust subgroup analyses. Although ESC cardio-oncology guidelines suggest using the HAS-BLED and CHA_2DS_2-VASc scores, they may underestimate risks in cancer patients. [4–6] Despite having the longest follow-up in this field, it was still relatively short, precluding long-term outcome conclusions.

Our study contributes to the sparse literature on LAAO in cancer patients, with strengths including detailed bleeding risk data and comprehensive treatment information. However, further research, particularly randomized controlled trials, is needed to confirm these findings, evaluate the balance between reducing stroke risk and increasing other procedure-related complications, identify which cancer patients benefit most from LAAO, and determine the best post-LAAO antithrombotic therapy for this high-risk patient population.

6. Conclusions

Our data suggest that LAAO is safe and effective in both cancer and non-cancer patients, with similarly low incidences of complications, readmissions, composite endpoints, bleeding, and stroke in both short-term and long-term follow-ups. Notably, the cancer group had a higher RRR in ischemic events. Cancer patients exhibited higher all-cause mortality, mainly due to cancer progression and infections. These findings support the use of LAAO in cancer patients. Randomized clinical trials are needed to confirm these findings.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2024.101585.

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