JACC: CARDIOONCOLOGY VOL. 2, NO. 5, 2020
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ORIGINAL RESEARCH

Impact of Cancer in Patients Undergoing Transcatheter Aortic Valve Replacement

A Single-Center Study

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ABSTRACT

BACKGROUND The use of transcatheter aortic valve replacement (TAVR) in cancer survivors and patients with active cancer (AC) in cancer survivors and patients with active cancer (AC) is expanding, suggesting a need to adjust the indications and risk assessment pre-TAVR.

OBJECTIVES The purpose of this study was to determine the impact of cancer on peri-procedural complications and survival in a long-term, single-center cohort of patients treated with TAVR.

METHODS Patients treated with TAVR between January 2006 and December 2018 were grouped as follows: controls (patients without cancer), stable cancer (SC), and AC. The primary endpoints were peri-procedural complications and 30-day survival. A secondary endpoint was 10-year survival.

RESULTS A total of 1,088 patients (age 81 ± 5 years, 46.6% men) treated with transfemoral TAVR were selected: 839 controls, 196 SC, and 53 AC. Predominant malignancies were breast, gastrointestinal, and prostate cancer. No differences were observed between patients with cancer and controls regarding peri-procedural complications. Patients with AC had similar 30-day survival compared with controls and SC (94.3% vs. 93.3% vs. 96.9%, $p = 0.161$), but as expected, reduced 10-year survival. AC was associated with a 1.47 (95% CI 1.16 to 1.87) fold increased risk of all-cause 10-year mortality in multivariable adjusted models.

CONCLUSIONS TAVR should be performed in patients with cancer when indicated, considering that patients with cancer have similar periprocedural complications and short-term survival compared with control patients. However, patients with AC have worse 10-year survival. Future studies are needed to define cancer-specific determinants of worse long-term survival. (J Am Coll Cardiol CardioOnc 2020;2:735–43) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received February 3, 2020; accepted November 3, 2020.

ISSN 2666-0873 https://doi.org/10.1016/j.jaccao.2020.11.008

JACC: CARDIOONCOLOGY, VOL. 2, NO. 5, 2020
DECEMBER 2020:735–43

ABBREVIATIONS AND ACRONYMS

AC = active cancer

NYHA = New York Heart Association

SC = stable cancer

STS = Society of Thoracic Surgeons

TAVR = transcatheter aortic valve replacement

Major advances in the treatment of cancer, including combination chemotherapy, targeted molecular therapy, immune therapy, radiation, cancer prevention vaccines, and mitigation of treatment toxicities, have led to improved survival, resulting in a growing proportion of patients with aortic valve stenosis and concomitant cancer (1–8). Transcatheter aortic valve replacement (TAVR) might provide a feasible treatment option to increase life expectancy in this patient population (9,10). Patients at intermediate or high operative risk are recommended treatment with TAVR with equivalent outcomes to surgical aortic valve replacement according to current international guidelines (11,12). Recently, the safety of TAVR in surgical low-risk patients has been demonstrated in randomized trials (13,14); however, patients with cancer and an estimated life expectancy <2 years were excluded from major TAVR trials (15,16).

Patients with cancer show unique characteristics dependent on the tumor type and treatment that need to be considered when determining strategies for aortic valve replacement in patients with severe aortic stenosis; however, the presence of cancer is not reflected by surgical risk calculators (17). Data regarding periprocedural complications and short- and long-term survival in patients with cancer treated with TAVR are scarce. Nonrandomized studies have shown either similar outcomes following TAVR in cancer and control groups (9), or worse outcomes due to cancer progression after 1 year (18). In addition, incidental malignant findings in computed tomography have been shown to be an independent predictor of all-cause and noncardiovascular mortality, but not of cardiovascular mortality (10). Thus, the aim of this study was to determine the impact of active and stable cancer on peri-procedural complications and short- and long-term survival in a real-world, single-center cohort of patients treated with TAVR.

METHODS

PATIENT POPULATION. We analyzed all consecutive patients included in our dedicated local registry for transfemoral TAVR between January 2006 and December 2018. TAVR through transapical or transaortic procedures were excluded. The registry was initiated to observe and document procedural results and post-procedural outcomes of TAVR at our tertiary University Hospital Center. Three main groups were defined: 1) a control group, which included all patients who underwent TAVR without cancer; 2) a stable cancer (SC) group, which included all patients who underwent TAVR and had a stable cancer diagnosis; and 3) an active cancer (AC) group that included all patients who underwent TAVR and had an active cancer diagnosis. The AC group included patients with cancer diagnosed within the past 6 months, patients who had cancer-related therapy within the past 6 months, active metastatic disease, or active recurrence of the cancer. The SC disease subgroup included patients with cancer who did not match the AC definition. Patients in the 3 groups were not matched. The study was approved by the local ethics committee (No. 16-6894-BO).

Baseline demographics and risk scores, cardiovascular risk factors, medical history, and data about cancer (cancer type, diagnosis, stage, treatment), laboratory parameters, clinical examination, electrocardiography, echocardiography, and periprocedural outcomes were retrospectively collected. Data collection and monitoring regarding TAVR outcomes were assessed according to the Valve Academic Research Consortium 2 definitions (Supplemental Table 1) (19). Functional status was assessed using the Katz Index of activities of daily living (20). For surgical risk evaluation, both the European System for Cardiac Operative Risk Evaluation score (logistic EuroSCORE) and the Society of Thoracic Surgeons (STS) predicted risk of mortality score were used (21,22).

TAVR PROCEDURES. All procedures were performed in accordance with relevant guidelines and regulations. The indication for TAVR in the individual patient was a consensus decision of the multidisciplinary heart-team. TAVR was performed by a multidisciplinary heart-team in a hybrid operating room using standard techniques (23,24), predominantly under conscious sedation (25) with percutaneous femoral artery access and closure (26). One of the following Conformitè Europëenne-approved bioprostheses were implanted: Edwards Sapien XT 23 mm, 26 mm, 29 mm; Edwards Sapien S3 23 mm, 26 mm, 29 mm; Medtronic CoreValve and Medtronic Evolut R 23 mm, 26 mm, 29 mm, 34 mm. The prosthesis size was determined on the basis of preprocedural echocardiographic and multidetector computed tomographic findings.

The valve was positioned under fluoroscopic guidance and correct valve positioning was confirmed by aortic root angiography. To minimize the risk of valve mispositioning and left ventricular decompensation during occlusion of the outflow tract, transient rapid or transvenous right ventricular pacing (100 to 180 beats/min) was used during valve implantation. Following aortic valve implantation, coronary artery

blood flow was confirmed by aortic root angiography. The valve delivery system was removed from the femoral artery and percutaneous or surgical closure of the femoral vascular access site was performed. After the procedure, follow-up outpatient clinical visits were conducted at 3 months post-procedure and annually through our electronic database. Mortality data were obtained from our local death register for a maximum follow-up of 13 years.

ENDPOINT DEFINITION. The primary endpoints were peri-procedural complications following TAVR according to the Valve Academic Research Consortium 2 definitions and 30-day survival. A secondary endpoint was 10-year survival.

STATISTICAL ANALYSIS. Continuous variables are reported as mean ± SD) or median (interquartile range [IQR]) and categorical variables are reported as number of patients and percentages and stratified by control group, SC group, and AC group. For continuous variables, independent samples Student's *t*-test or Wilcoxon-Mann-Whitney *U* test was used, whereas for categorical variables, Fisher exact test was used to compare the control group and AC group. Likewise, cancer entities and peri-procedural complications were compared using the Fisher exact test. Survival curves were computed through Kaplan-Meier analysis using the log-rank test for both 30-day and 10-year all-cause mortality. A univariable and multivariable Cox regression analysis was used to determine the associations of the 3 study groups (control group as reference) with 10-year survival using the following models: 1) unadjusted; 2) adjusted for age and gender; and 3) further adjusted for STS score, patients with pre-procedural pacemaker, peripheral artery disease, and New York Heart Association (NYHA) functional class at baseline. All analyses were performed using SAS Software version 9.4 (SAS Institute Inc., Cary, North Carolina). Differences with p values <0.05 (2-sided) were considered statistically significant.

RESULTS

BASELINE CHARACTERISTICS OF THE STUDY GROUPS. A total of 1,088 patients were treated with transfemoral TAVR between January 2006 and December 2018 at our center. A total of 839 patients (77.1%) were included in the control group, 196 patients (18.0 %) in the SC group, and 53 patients (4.9%) in the AC group (**Central Illustration**).

The baseline characteristics of the 3 study groups are depicted in **Table 1**. Patients with AC were significantly younger compared with control patients. Patients with SC did not show any difference regarding age in comparison with the control group. Gender distribution, Logistic EuroSCORE, STS score, and frailty were similar between cancer groups and controls. Cardiovascular risk factors, including hypertension, diabetes mellitus, and obesity were comparable between the study groups. Medical history consisting of cardiac, vascular, pulmonary, and neurological disease was comparable between cancer groups and controls. Heart failure subclasses were similar between groups, but NYHA class at baseline was significantly higher in the control group. Laboratory and echocardiography parameters did not differ significantly between the groups (**Table 1**).

CANCER SUBTYPE CLASSIFICATION. A detailed characterization of cancer types and therapeutic regimens is provided in **Table 2**. Most prevalent malignancies were breast (n = 62, 24.8%), gastrointestinal (n = 48, 19.2%), prostate (n = 39, 15.7%), hematologic (n = 27, 10.8%), urinary tract (n = 26, 10.4%), and skin cancer (n = 24, 9.6%) (**Figure 1**). The distribution of the cancer types between AC and SC subgroups was not significantly different for cancer types, except for hematologic cancers being more frequent in the active cancer subgroup. Time from diagnosis of cancer was 3.2 ± 4.4 years in the AC subgroup compared with 10.5 ± 8.8 years in the SC subgroup. More patients in the AC group suffered from metastatic cancer compared with the SC diseases group (19% vs. 0.3%, $p < 0.001$). Significantly more patients in the stable cancer group had a history of tumor-related surgery (80% vs. 66%, $p = 0.040$). History of radiotherapy was present in 32% of the patients with AC compared with 22% in the SC group ($p = 0.139$). Active chemotherapy was performed only in AC patients (83%, $p < 0.001$), whereas a history of chemotherapy was present in 34% ($p = 0.010$) of the SC disease patients. Patients with SC were not receiving any cancer-related therapy at the time of TAVR.

PERI-PROCEDURAL COMPLICATION RATE IN THE STUDY GROUPS. Intraprocedural death was low in all study groups. Concerning structural complications, we observed no difference between the groups. Permanent pacemaker implantation rate did not differ significantly. Post-procedural stroke, bleeding, vascular access complications, and renal failure were comparable in the controls, SC, and AC groups (**Table 3**).

SHORT- AND LONG-TERM SURVIVAL RATES IN THE STUDY GROUPS. No significant differences in terms of survival across the controls, SC, and AC groups were observed for the first 30 days after TAVR (94.3% vs. 96.9% vs. 93.3%, $p = 0.161$). However, not entirely unexpected, the 10-year survival was significantly

TABLE 1 Baseline Characteristics of the 3 Study Groups: Control, SC, and AC

	Control Group (n = 839)	SC Group (n = 196)	AC Group (n = 53)	p Value (Control Group vs. AC Group)
Demographics and risk scores				
Age (yrs)	81.4 ± 5.4	81.8 ± 5.6	78.5 ± 6.4	<0.001
Female	458 (54.5)	94 (47.9)	29 (54.7)	0.985
Log. EuroSCORE	15.0 (9.7-23.1)	13.9 (9.1-24.7)	15.9 (7.5-23.5)	0.607
STS score	6.0 (3.5-6.8)	5.0 (3.7-6.3)	5.4 (3.3-6)	0.051
Frailty	111 (13.2)	23 (11.7)	8 (15.0)	0.698
Cardiovascular risk factors				
Hypertension	795 (94.7)	183 (93.3)	51 (96.2)	0.638
Diabetes mellitus	291 (34.6)	67 (34.1)	17 (32.0)	0.698
Obesity	459 (54.7)	99 (50.5)	30 (56.6)	0.788
Medical history				
Recent myocardial infarction	56 (6.6)	14 (7.1)	4 (7.5)	0.805
Stable coronary artery disease	534 (63.6)	120 (61.2)	29 (54.7)	0.191
Previous PCI	379 (45.5)	85 (43.3)	24 (45.2)	0.969
Previous CABG	109 (12.9)	19 (9.6)	5 (9.4)	0.452
Unstable angina	17 (2.0)	6 (3.0)	1 (1.8)	0.943
Pre-procedural pacemaker	123 (14.6)	25 (12.7)	3 (5.6)	0.068
Atrial fibrillation	183 (21.8)	41 (20.9)	7 (13.2)	0.161
Peripheral artery disease	180 (20.2)	27 (13.7)	17 (32.0)	0.071
Pulmonary hypertension	219 (26.2)	60 (30.6)	19 (35.8)	0.124
COPD	184 (21.9)	48 (24.4)	15 (28.3)	0.282
Neurological dysfunction	49 (5.8)	16 (8.1)	3 (5.6)	0.956
Chronic renal disease	53 (6.3)	17 (8.6)	5 (9.4)	0.810
Clinical status				
NYHA functional class II	82 (9,8)	24 (12.2)	12 (22.6)	0.031
NYHA functional class III	639 (76.8)	140 (71.4)	36 (67.9)	
NYHA functional class IV	108 (12.9)	31 (15.8)	5 (9.4)	
Heart failure classification				
HFpEF	581 (69.2)	139 (70.9)	34 (62.2)	0.671
HFmrEF	132 (15.7)	29 (14.7)	12 (24.5)	
HFrEF	126 (15.0)	27 (14.2)	8 (13.2)	
Laboratory parameters				
Hemoglobin (g/dl)	12.0 ± 1.6	12.0 ± 1.7	11.9 ± 1.7	0.739
Echocardiography parameters				
LVEF <30%	45 (5.3)	12 (6.1)	5 (9.4)	0.213
LVEF 30%-50%	230 (27.4)	44 (22.4)	18 (33.9)	
LVEF >50%	564 (67.2)	140 (71.4)	30 (56.6)	
LVEF (%)	51.3 ± 11.1	51.1 ± 11.2	48.8 ± 11.8	0.118
Mean PG (mm Hg)	43.9 ± 15.6	44.7 ± 15.3	46.9 ± 16.4	0.171
AVA continuity equation (cm^2)	0.7 (0.6-0.8)	0.6 (0.6-0.7)	0.6 (0.6-0.8)	0.235
AVA planimetry (cm^2)	0.6 (0.6-0.7)	0.7 (0.6-0.7)	0.6 (0.6-0.8)	0.454
sPAP (mm Hg)	46.0 ± 11.3	46.3 ± 12.7	46.5 ± 12.5	0.745

Values are mean ± SD, n (%), or median (Q1-Q3).

AC = active cancer; AVA = aortic valve area; CABG = coronary artery by-pass graft; COPD = chronic obstructive pulmonary disease; HFpEF = heart failure with preserved ejection fraction; HFmrEF = heart failure with midrange ejection fraction; HFrEF = heart failure with reduced ejection fraction; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; PM = pacemaker; PG = peak gradient; SC = stable cancer; sPAP = systolic pulmonary artery pressure; STS = Society of Thoracic Surgery.

reduced in the AC group compared with SC group and control groups (56.6% vs. 77.6% vs. 76.5%, p = 0.003). The 10-year survival was similar between controls and SC group. Figure 2 depicts the Kaplan-Meier 10-year distribution of survival curves among the 3 groups. In Cox regression analysis, AC was associated with more than a 40% excess risk of all-cause 10-year mortality. Effect sizes remained stable after adjustment for age and gender, as well as multivariable adjustment (Table 4).

We assessed the influence of metastasis on survival in the cancer group. Patients with metastatic disease

had a reduced 10-year survival compared with those without metastasis (46.7% vs. 74.4%, p = 0.008). We determined if one cancer type had worse mortality compared with other cancer types, and found no cancer type to be significant. This may have been because of the small number of patients in each cancer type group (Supplemental Table 2).

DISCUSSION

The rationale for this analysis was to determine the impact of active and stable cancer on periprocedural complications and short- and long-term survival in a single-center cohort of patients treated with TAVR. The main findings are: 1) a high percentage of patients (22.9%) treated with TAVR had cancer; 2) TAVR is safe in patients with cancer, with similar periprocedural complication rates compared with patients without cancer; 3) patients with cancer showed 30-day survival rates similar to controls; and 4) patients with AC had reduced 10-year survival rates compared with SC and control patients treated with TAVR, an observation that was significant after multivariable adjustment.

Patients with cancer experience important alterations of normal physiology due to an accentuated inflammatory status (27), immune system changes (28), and alteration of the hemostatic balance (29). These factors need to be carefully considered before considering TAVR in this population. Current guidelines (11,12) indicate aortic valve replacement in patients with symptomatic severe aortic stenosis in the "absence of comorbidities or general conditions that make benefit unlikely." The heart valve team needs to agree on the benefit of aortic valve replacement, and decide whether TAVR or surgical aortic valve replacement is indicated based on preprocedural calculated risk and clinical status. TAVR is indicated over surgical aortic valve replacement in patients with high or intermediate surgical risk with an anticipated survival of more than 12 months. Many patients with cancer today have a good prognosis due to optimized medical treatment.

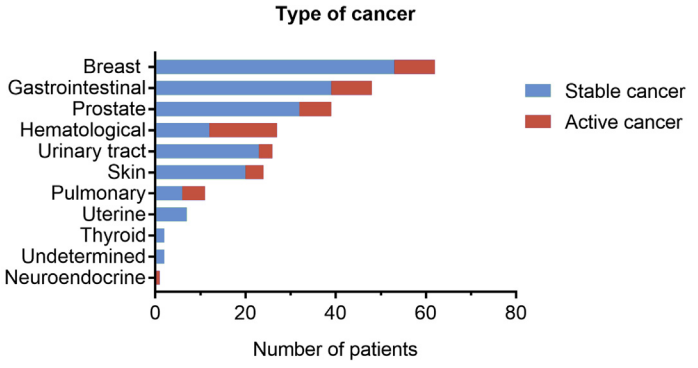
However, decision making for patients with cancer is complex, as current guidelines and risk scores do not reflect cancer-specific characteristics. Most patients with cancer were excluded from studies that led to the actual indications for TAVR (16,30,31); however, our data suggest that the AC patient population could still benefit from valve intervention, as patients with AC had similar postprocedural complication and 30-day survival rates compared with patients with SC and with the general population.

TABLE 2 Cancer Types and Therapeutic Regimen of the SC and AC Groups

	SC Group (n = 196)	AC Group (n = 53)	p Value
Cancer characterization			
Breast cancer	53 (27)	9 (16.9)	0.153
Gastrointestinal cancer	39 (19.8)	9 (16.9)	0. 639
Prostate cancer	32 (16.3)	7 (13.2)	0.584
Urinary tract cancer	23 (11.7)	3 (5.6)	0.219
Skin cancer	20 (10.2)	4 (7.5)	0.565
Hematological cancer	12 (6.1)	15 (28.3)	<0.001
Pulmonary cancer	6 (3)	5 (9.4)	0.054
Uterine cancer	7 (3.5)	0 (0)	0.330
Thyroid cancer	2 (1)	0 (0)	0.838
Undetermined cancer	2 (1)	0 (0)	0.838
Neuroendocrine	0 (0)	1 (1.8)	0.141
Multiple cancers	9 (4.5)	4 (7.5)	0.392
First diagnosis (yrs)	10.5 ± 8.8	3.2 ± 4.4	<0.001
Metastatic cancer	6 (0.3)	10 (19)	<0.001
Therapeutic regimen			
History of surgery	156 (80)	35 (66)	0.040
History of radiotherapy	42 (22)	17 (32)	0.139
History of chemotherapy	67 (34)	0 (0)	0.010
Active chemotherapy	0 (0)	44 (83)	<0.001
Proteasome inhibitors	0 (0)	9 (16.6)	0.003
Hormonal therapy	0 (0)	8 (15)	0.004
Alkylating agents	0 (0)	6 (11.3)	0.008
Platinum-based	0 (0)	6 (11.3)	0.008
Anthracyclines	0 (0)	5 (9.4)	0.012
Tyrosine kinase inhibitors	0 (0)	4 (7.5)	0.018
Antimicrotubule agents	0 (0)	3 (5.6)	0.031
Immune checkpoint inhibitors	0 (0)	2 (3.7)	0.059
5-fluoruracil	0 (0)	1 (1.18)	0.141

Values are n (%) or mean ± SD.
Abbreviations as in Table 1.

FIGURE 1 Type of Cancer



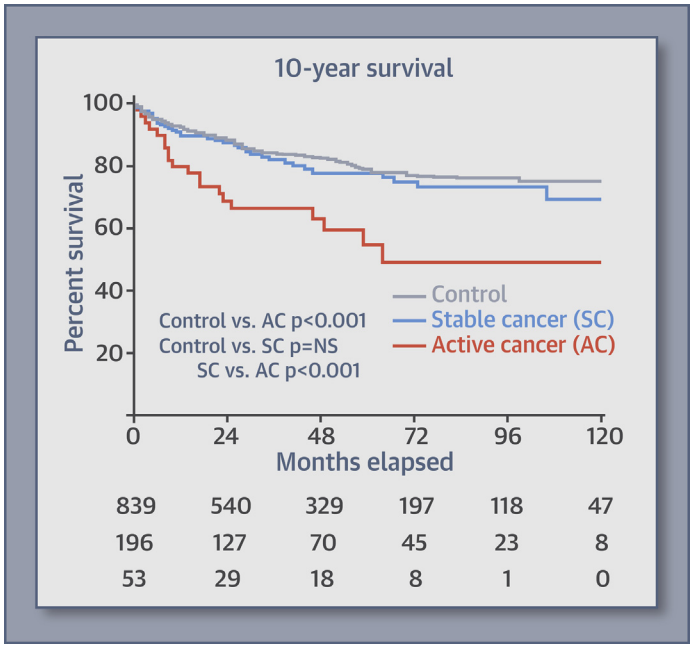
Type of cancer and distribution between active **(red)** and stable **(blue)** cancer in the cancer group are shown. Most common cancer types were breast, gastrointestinal, prostate, hematologic, and urinary tract. Most patients had stable cancer. Only the hematologic cancer group included statistically significantly more patients with active than stable cancer.

TABLE 3 Periprocedural Complications in the Control, SC, and AC Groups

Complication	Control Group (n = 839)	SC Group (n = 196)	AC Group (n = 53)	p Value Control Group vs. AC Group
Intraprocedural death	2 (0.2)	0 (0)	0 (0)	0.722
Structural complications				
Coronary obstruction	6 (0.7)	0 (0)	0 (0)	0.537
Myocardial infarction, n (%)	13 (1.5)	1 (0.5)	0 (0)	0.361
Ventricular perforation	8 (0.9)	0 (0.9)	1 (1.8)	0.509
Tamponade	7 (0.8)	1 (0.8)	0 (0)	0.504
Valve in valve	28 (3.3)	3 (3.3)	2 (3.7)	0.864
Any structural complication	62 (7.3)	5 (2.5)	3 (5.6)	0.639
Pacing rate				
Permanent pacemaker implantation	133 (15.8)	38 (19.3)	5 (9.4)	0.210
Stroke	28 (3.3)	7 (3.6)	3 (5.6)	0.370
Bleeding complications				
All grade bleeding	127 (15.1)	28 (14.3)	7 (13.2)	0.703
Life-threatening bleeding	25 (3)	3 (1.5)	3 (1.8)	0.278
Major bleeding	51 (6.1)	12 (6.1)	2 (3.7)	0.500
Minor bleeding	51 (6.1)	12 (6.1)	3 (5.6)	0.201
Vascular access complications	122 (14.5)	28 (14.2)	8 (15)	0.911
Acute renal failure	158 (18.8)	25 (12.7)	10 (18.8)	0.994

Values are n (%).
Abbreviations as in Table 1.

FIGURE 2 The 10-Year Kaplan-Meier Survival Curves in Control, SC, and AC Groups



The Kaplan-Meier survival curves after 10 years of follow-up for the control group (gray), stable cancer (SC) group **(blue)**, and active cancer (AC) group **(red)**. The survival rate was 76.5% in the control group, 77.6 % in the SC group, and 56.6% in the AC group.

Peri-procedural complications were low in both the cancer and control groups. In patients with AC and SC, TAVR appears to be similarly safe as in the general population. Higher peri-procedural bleeding rates in patients with cancer were previously described (32), potentially related to dysfunctional platelet function in patients with cancer or bleeding from the cancer itself to be related to higher complication rates. This was not confirmed by our study. Bleeding complications were low in the cancer group as well as in the noncancer group and did not differ significantly, even though a high percentage of gastrointestinal cancer and hematological cancer was present in our study group.

Ten-year follow-up revealed similar survival rates in controls and patients with SC, but reduced survival rates in patients with AC. Other studies demonstrated similar 1-year results in a single-center cohort study of 749 patients with a total of 47 patients with cancer (9). A multicenter trial presented worse 1-year outcomes in 222 patients with cancer from a cohort of 2.700 TAVR patients mainly driven by the progression of cancer (32). We observed the same effect regarding long-term survival of patients with AC, which remained significant after adjusting for potential confounders. Another study also showed similar 30-day mortality, but worse 1-year mortality in a cohort of 99 patients with AC and 251 patients with history of cancer compared with 1,471 patients without known cancer (33). These short-term findings were also consistent with ours. These other studies (32,33) have confirmed that this higher mortality rate in patients with AC is driven by cancer progression.

Treatment decisions in patients with severe aortic stenosis and cancer are complex, but treatment of noncancer conditions can allow for the best standard of cancer care, including surgery and administration of new promising medications, like immune checkpoint inhibitors and targeted therapies. Current guidelines also recommend postponing or canceling noncardiac surgery if severe aortic stenosis is symptomatic and recommend surgical aortic valve replacement or TAVR before noncardiac surgery, including cancer surgery (11,12,34).

The importance of the multidisciplinary approach of patients with cancer and cardiovascular disease has been emphasized by the birth and maturation of the field of cardio-oncology (8,35). Many cardio-oncology studies focus on the management of heart failure after cancer therapy (36), or on the cardiovascular adverse events of new cancer therapies (37–39), whereas studies regarding the management of patients with cancer and severe aortic stenosis are underrepresented. This study brings increased clinical evidence to optimize decision

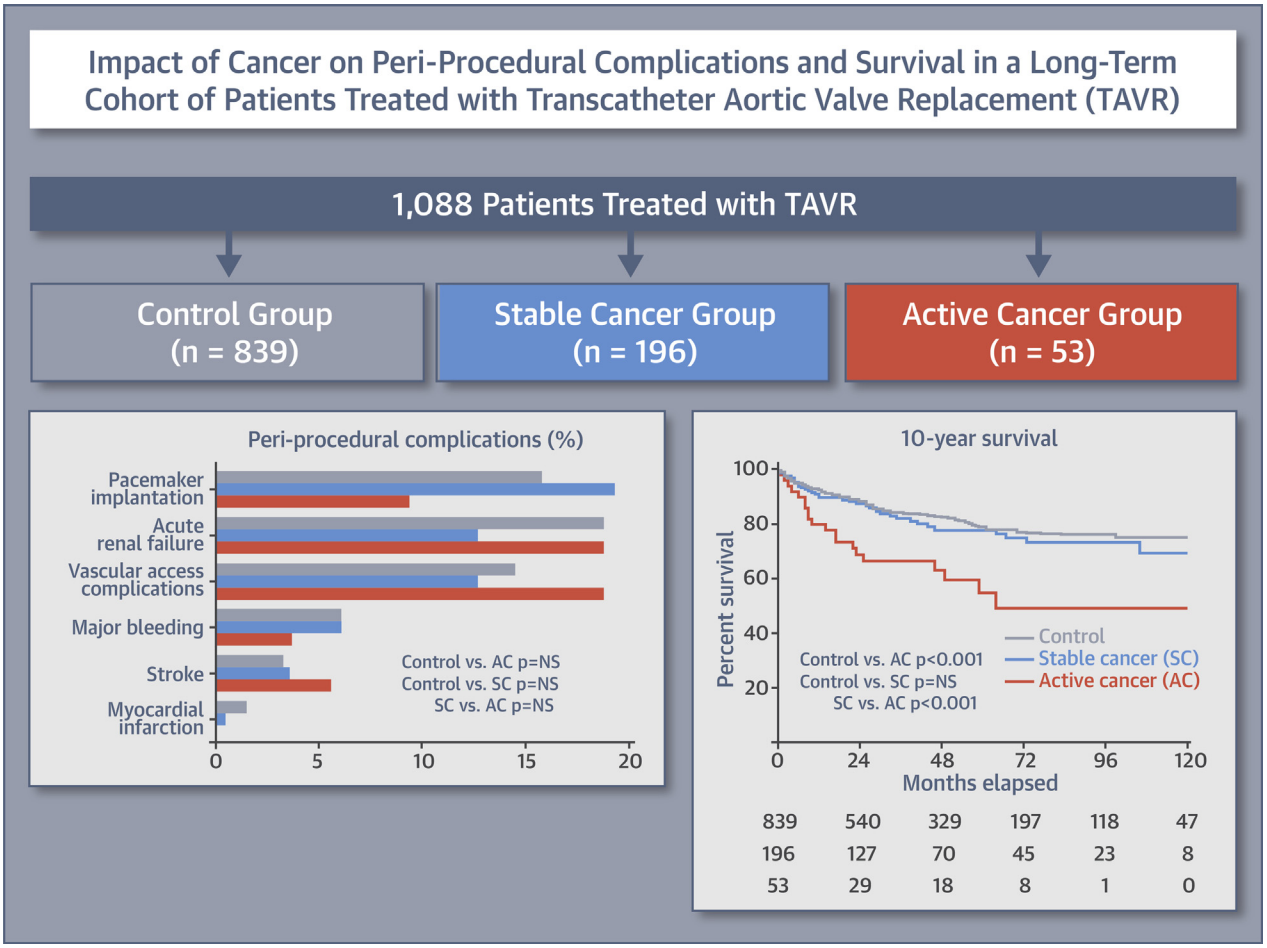
TABLE 4 Association With Cancer and 10-Year Survival by Univariable and Multivariable Cox Regression Analysis

	Control Group (n = 839)		SC Group (n = 196)		AC Group (n = 53)	
	HR (95% CI)	p Value	HR (95% CI)	p Value	HR (95% CI)	p Value
Unadjusted	1.00 (ref.)	N/A	0.92 (0.66-1.29)	0.661	1.45 (1.16-1.80)	<0.001
Age- and gender-adjusted	1.00 (ref.)	N/A	0.94 (0.68-1.32)	0.754	1.43 (1.15-1.77)	0.001
Multivariable-adjusted*	1.00 (ref.)	N/A	0.92 (0.66-1.29)	0.659	1.47 (1.16-1.87)	0.001

*Multivariable model included baseline age, gender, STS score, pre-procedural pacemaker, peripheral artery disease, and NYHA functional class.

CI = confidence interval; HR = hazard ratio; NYHA = New York Heart Association; STS = Society of Thoracic Surgeons; other abbreviations as in Table 1.

CENTRAL ILLUSTRATION Transcatheter Aortic Valve Replacement in Patients With Cancer



Lind, A. et al. J Am Coll Cardiol CardioOnc. 2020;2(5):735–43.

Impact of cancer on peri-procedural complications and survival in a long-term cohort of patients treated with transcatheter aortic valve replacement (TAVR). This study analyses a cohort of 1,088 patients treated with TAVR followed over a maximum period of 13 years, divided into a control group (n = 839), a stable cancer (SC) group (n = 196), and an active cancer (AC) group (n = 53). Peri-procedural complications were present at comparable rates among control group, SC group, and AC group (columns graph below). Patients with AC had similar 30-day survival rates compared with patients with SC and with controls, but reduced 10-year survival rates (Kaplan-Meier surviving curves below). NS = not significant.

making in patients with cancer and severe aortic stenosis. To date, algorithms for the management of this patient population are scarce and the need of evidence-based guidelines is of tremendous importance.

When evaluating patients with cancer, the importance of doing no harm and the reality of limited resources raise questions about whether we should perform TAVR even if we could perform TAVR. Therapeutic futility has been defined as a lack of medical efficacy, particularly when the therapy is unlikely to produce its intended clinical result, as judged by the physician; or lack of a meaningful survival, as judged by the personal values of the patient (40). Performing TAVR is a technical question in nature and may be distilled into measurable facts. The question of whether we should perform TAVR is less straightforward and includes value judgments and uncertainty that extend beyond the individual cardiologist's or surgeon's technical or clinical expertise and therefore need to be discussed with a broader heart-team including cancer therapy specialists and with the patient (41).

This analysis includes many patients treated with TAVR over extended follow-up time, in a nonselected manner, with multiple comorbidities and a broad range of cancer types as typically seen in clinical practice, and describes in a detailed manner the impact of cancer on periprocedural complication and survival in patients treated with TAVR. This could serve as a basis to motivate additional studies in cancer and TAVR. Furthermore, our findings emphasize an important need of cancer-specific risk factors and scores that need to be taken into consideration before TAVR.

STUDY LIMITATIONS. The study was conducted as a retrospective, single-center cohort study. Over a period of 13 years, the interventional strategies, as well as the TAVR devices used for the intervention, have changed. However, considering the change in guidelines that occurred in 2012 to 2017 that recommended TAVR for patients with high operative risk, and 2017 that recommended TAVR for patients with intermediate risk, patients with cancer in the present study are represented equally across the entire time period. However, cancer therapy has changed significantly during the past years, leading to differences of therapy-related complications. Although data on tumor type were available, staging data were not. Moreover, cancer-specific prognosis was not able to be calculated. Because of the retrospective nature of the study, we could not find the specific cause of death for 159 deaths from a total of 263 deaths. The date of death was documented, but not the specific cause, when death occurred outside our clinic. A comparison of patients with cancer treated with TAVR and treated conservatively, without surgery, was also not available.

CONCLUSIONS

TAVR, when indicated, can be safely performed in patients with severe aortic stenosis and cancer, with similar periprocedural complications in patients with or without cancer. Furthermore, cancer patients have similar short-term survival, but reduced long-term survival in the AC group compared with SC and controls. This study brings increased evidence to inform decision making in patients with cancer and severe aortic stenosis. Future studies are needed to identify cancer-specific variables that are important to consider as prognostic factors in patients with cancer being evaluated for TAVR and to develop algorithms to inform the management of this growing population.

AUTHOR DISCLOSURES

Dr. Mincu was supported by the European Society of Cardiology through a Research Grant (R-2016-013). All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: TAVR appears to be safe in patients with severe aortic stenosis and active cancer, with similar periprocedural complications and 30-day survival as stable cancer patients and in control patients without cancer. Patients with active cancer had reduced long-term survival rates compared with stable cancer and control patients.

TRANSLATIONAL OUTLOOK: Future studies are needed to identify cancer-specific variables that are important to consider as prognostic factors in patients with cancer being evaluated for TAVR and to develop algorithms to inform the management of this growing population.

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KEY WORDS aortic stenosis, cancer, guidelines, outcomes, risk prediction, transcatheter aortic valve replacement, treatment planning, valvular disease

APPENDIX For supplemental tables, please see the online version of this paper.