



Incidental detection of malignancy during preprocedural workup for transcatheter aortic valve implantation: A longitudinal cohort study

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The aim of this retrospective analysis was to investigate the prevalence and prognostic importance of incidental malignancy detected during pre-TAVI computed tomography. Among 579 patients, CT-work-up for TAVI exposed previously undetected malignancy in 4.5% of patients. TAVI patients with a new malignancy had a 2.9-fold increased risk of death at 1 year, and a 16 month shorter mean survival time compared to patients with no malignancy. (Am Heart J 2023;261:51–54.)

Transcatheter aortic valve implantation (TAVI) requires meticulous preprocedural planning. Computed tomography (CT) of the thorax, abdomen, and pelvis constitutes a cornerstone in the evaluation of anatomic feasibility and suitability for TAVI. As a collateral effect of comprehensive imaging, incidental findings can be detected during pre-TAVI workup. Previous studies reported clinically relevant incidental findings in up to half of all patients under evaluation for TAVI, but failed to quantify the prognostic relevance of these findings.^{1,2} Malignancy is the most relevant incidental finding and can importantly alter further clinical management and prognosis. The aim of the present study was to investigate the prevalence and prognostic importance of incidental malignancy detected during pre-TAVI CT.

Methods

Study design and population

The study was based on a prospectively collected data from an ongoing registry, which includes consecutive patients undergoing TAVI for severe, symptomatic aortic stenosis at Bern University Hospital in Switzerland. Details of the Bern TAVI registry have been reported previously.³ The study has been approved by the local ethics

committee and all patients provided written informed consent for participation. For the purpose of the present study, all patients undergoing TAVI between January 2015 and December 2016 and undergoing preprocedural CT were considered. Patients with known malignancy and patients with procedural death were excluded. No extramural funding was used to support this work.

Data collection and definitions

Data on incidental findings were retrospectively identified by systematic review of radiological reports of all TAVI CTs performed during the study period. Incidental findings were further evaluated if suspicious for malignancy, and the diagnosis of malignancy was verified by histopathology reports, tumor markers, or specific radiological tests. Incidental malignancies were categorized according to the organ system. Data on clinical management of malignancy was retrieved from discharge summaries. Standardized clinical follow-up was prospectively collected at 30 days, 1 year and 5 years after TAVI as previously described.³

Statistical analysis

Categorical variables are reported as frequencies and percentages. Continuous variables are presented as mean values \pm standard deviation (SD). Cumulative event curves were calculated using the Kaplan-Meier method and hazard ratios (HRs) with 95% confidence intervals (CIs) using Cox proportional hazards models. We performed a restricted mean survival time (RMST) analysis because it provides an integrated patient-oriented measure of the expected event-free survival time and is less liable to violations of the proportional hazards assumption.⁴ RMST was estimated from the non-parametric integration of the area under the Kaplan-Meier curves.

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One sentence summary: "Incidental malignancy is detected in 4.5% of patients undergoing workup for TAVI, and is associated with adverse five-year outcome."

Submitted December 16, 2022; accepted March 22, 2023

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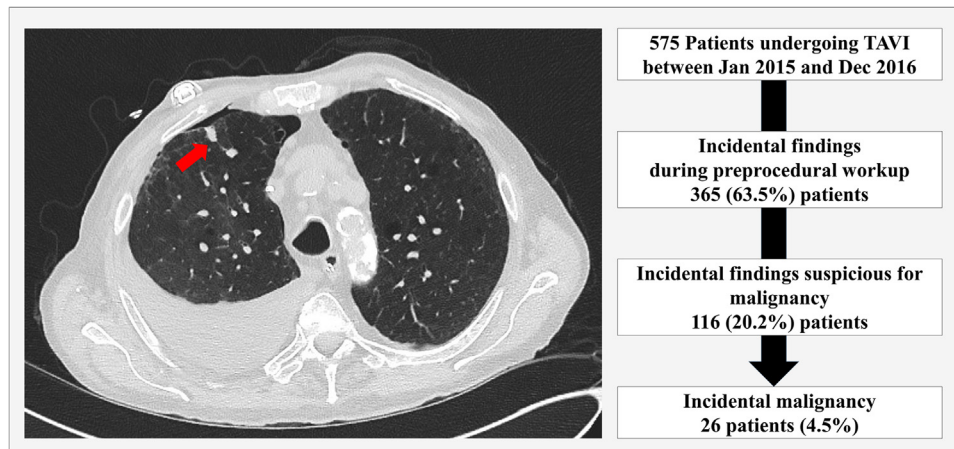
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0002-8703

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<https://doi.org/10.1016/j.ahj.2023.03.011>

Figure 1



Study flowchart and sample case showing incidental findings on preprocedural computed tomography (Red arrow). TAVI = transcatheter aortic valve implantation. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

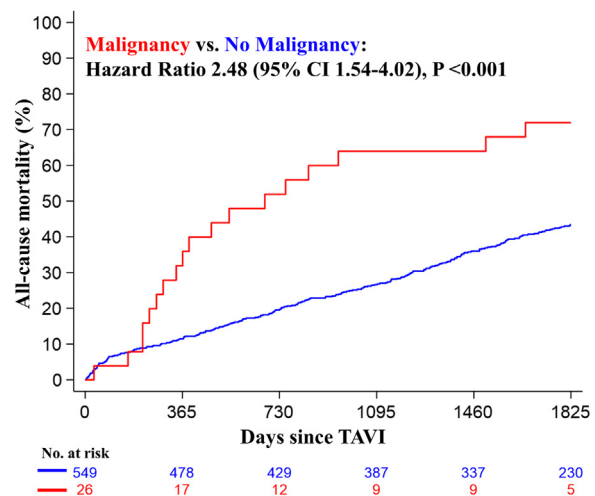
All *P*-values were 2-sided, and a *P*-value < .05 was considered significant for all tests. All statistical analyses were performed with Stata 15.1 (StataCorp, College Station, TX).

Results

Among 579 patients undergoing CT prior to TAVI between January 2015 and December 2016, 575 were included in the present study. Incidental findings were reported in 365 patients (63.5%). Malignancy was suspected in 116 patients (20.2%) and confirmed in 26 patients (4.5%) (Figure 1). Among patients with incidental malignancy, cancer staging was available in 11 patients (stage I/II: 7 and stage III/IV: 4), while 15 patients refused further investigations for the purpose of staging of disease. Patient with incidental malignancies detected during pre-evaluation for TAVI were comparable to patients with no malignancy with regards to age (81.0 ± 6.6 years vs 81.6 ± 6.7 years, $P = .703$), sex (females 46.2% vs 50.6%, $P = .692$), and cardiovascular comorbidities. Malignancy was most commonly found in the lung 7 (27%) and the urogenital system 7 (27%) followed by the gastrointestinal system 3 (16%). Sixteen patients (61.5%) declined oncological therapy, while 10 patients underwent treatment (chemotherapy $n = 9$, radiation therapy $n = 4$, or tumor surgery $n = 5$).

Clinical follow-up was complete in 96.2% of patients at 5 years. Among 26 patients with incidental malignancy, 18 patients died during the study period (cancer-related death 12; cardiovascular death 5; and unknown 1). All cause death was significantly higher in patients with malignancy compared with those without malignancy at 1 year (31.9% vs 11.4%, HR 2.87, 95% CI 1.37-

Figure 2



Kaplan-Meier curves for all-cause death. Hazard ratios and *P*-values were calculated with the use of Cox proportional hazards models. TAVI = transcatheter aortic valve implantation.

6.00, $P = .005$) and at 5 years (72.0% vs 43.4%, HR 2.48, 95% CI 1.54-4.02, $P < .001$) (Figure 2). The RMST of patients with incidentally detected malignancy was 488 days (95% CI 216-759) shorter compared to patients with no malignancy.

Discussion

The salient findings of this study can be summarized as follows. First, incidental malignancy was detected in

4.5% of patients during pre-evaluation for TAVI. Second, almost one-third of patients with incidentally detected malignancy during pre-TAVI CT died within 1 year after TAVI. The risk of death within 1-year after TAVI was 2.9 times increased compared to patients with no malignancy, and the RMST after TAVI was 16 months shorter compared to patients with no malignancy.

In the present study, the observed prevalence of incidental findings, significant incidental findings, and incidental malignancy was 63.5%, 20.2%, and 4.3%, respectively, which is consistent with previous reports.^{1,2,5} Notably, less than 1 in 10 patients with an incidental finding was eventually diagnosed with malignancy. Several studies have investigated the clinical impact of incidental findings. A recent meta-analysis concluded that significant incidental findings, defined as an incidental finding that was potentially pathological and required further investigation or treatment prior to TAVI, were not associated with mortality up to 3 years, but were associated with an increased risk of mortality when evaluated at ≥ 4 years.⁵ In the present study, we observed that a new diagnosis of malignancy during pre-TAVI work-up had an important impact on prognosis that materialized already within the first year after TAVI. Our findings are consistent with a previous report that examined the clinical impact of active cancer in patients undergoing TAVI. In the latter study, patients with cancer had a more than 2-fold increased mortality after TAVI compared with those without cancer (HR: 2.37, 95% CI: 1.74-3.23).⁶ Our results suggest that incidentally detected malignancy may be the main driver of adverse outcome in patients with incidental findings during TAVI work-up while other incidental findings may be less prognostically relevant.

Current guidelines recommend the review and reporting of incidental findings, as the importance of incidental findings will increase as the life expectancy of patients undergoing TAVI increases.^{7,8} On the downside, work-up of potential malignancy leads to significant costs, patient anxiety, and arguably delays in TAVI. The latter may directly interfere with prognosis, and is of particular concern given the overdiagnosis of incidental findings suspicious of malignancy. In contrast, incidental detection of malignancy allows for an earlier diagnosis and timely treatment that may result in a favorable prognosis for the individual patient. Indeed, previous studies have reported that there is no delay in time to TAVI in patients with significant incidental findings.⁵

The diagnosis of incidental malignancy during TAVI work-up requires an individualized treatment strategy and a shared-decision making process. TAVI is considered futile in patients with a life expectancy of less than 1 year.⁹ Weighting the probabilities of cardiac vs cancer-related death is however often challenging. At the same time, TAVI may be warranted for symptom relief, and may reduce the risk of cancer treatment. Indeed, 40% of pa-

tients with incidental malignancy underwent oncological therapy after TAVI in the present study. Further studies are needed to evaluate the prognostic effect of oncological treatment following TAVI in patients with incidental malignancy, especially in younger population.

Limitation

The findings of the present analysis should be interpreted in light of several limitations. First, the present study includes only patients that underwent TAVI. Patients that did not undergo TAVI after a new diagnosis of malignancy are not reflected in the present registry. The reported prevalence of incidental malignancy may therefore be underestimated. Second, the study reports on patients undergoing TAVI in 2015 and 2016. Consequently, elderly patients with significant comorbidities were included. The reported prevalence may therefore not be generalizable to younger patients at lower risk. Third, even though clinical events were independently adjudicated, the number of cases with incidental malignancy was relatively small. Therefore, it is difficult to interpret the significance of cancer contributing to death and we cannot differentiate direct mortality from cancer from mortality associated with treatment of cancer. Finally, we could not determine the cancer staging in all patients with incidental malignancy. The higher mortality in patients with incidental malignancy may be overestimated by the presence of patients at the advanced cancer stage (stage III/IV), who have a life expectancy of less than 1 year. Patients with advanced stages of cancer may have been referred to TAVI rather than surgery.

Conclusion

In conclusion, CT-work-up for TAVI exposed previously undetected malignancy in 4.5% of patients. TAVI patients with a new malignancy had a 2.9-fold increased risk of death at 1 year, and a 16 month shorter mean survival time compared to patients with no malignancy.

Funding

No funding.

Conflict of interest

Dr Windecker reports research and educational grants to the institution from Abbott, Amgen, Astra Zeneca, BMS, Bayer, Biotronik, Boston Scientific, Cardinal Health, CardioValve, CSL Behring, Daiichi Sankyo, Edwards Lifesciences, Guerbet, InfraRedx, Johnson & Johnson, Medtronic, Medtronic, Novartis, Polares, OrPha Suisse, Pfizer, Regeneron, Sanofi-Aventis, Sinomed, Terumo, V-Wave. Dr Windecker serves as unpaid advisory board member and/or unpaid member of the steering/executive group of trials funded by Abbott, Abiomed, Amgen, Astra Zeneca, BMS, Boston Scientific, Biotronik, Cardiovalve,

Edwards Lifesciences, MedAlliance, Medtronic, Novartis, Polares, Sinomed, V-Wave and Xeltis, but has not received personal payments by pharmaceutical companies or device manufacturers. He is also member of the steering/executive committee group of several investigator-initiated trials that receive funding by industry without impact on his personal remuneration. Dr Windecker is an unpaid member of the Pfizer Research Award selection committee in Switzerland and of the Women as One Awards Committee. Dr Pilgrim reports research grants to the institution from Edwards Lifesciences, Boston Scientific and Biotronik, personal fees from Biotronik and Boston Scientific, and other from HighLife SAS, he received travel reimbursement from Medira and is a proctor for Medtronic. Dr Gräni receives funding from the Swiss National Science foundation, InnoSuisse, CAIM and GAMBIT foundation. Dr Okuno reports speaker fees from Abbott. Dr Heg has no personal conflicts; his employer, CTU Bern, University of Bern, has a staff policy of not accepting honoraria or consultancy fees. However, CTU Bern is involved in design, conduct, or analysis of clinical studies funded by not-for-profit and for-profit organizations. In particular, pharmaceutical and medical device companies provide direct funding to some of these studies. For an up-to-date list of CTU Bern's conflicts of interest see http://www.ctu.unibe.ch/research/declaration_of_interest/index_eng.html. All other authors have no relationships relevant to the contents of this article to disclose.

Acknowledgments

None.

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