JACC: ADVANCES VOL. 2, NO. 1, 2023

EDITORIAL COMMENT

Heart Valve Team Conundrum

The Optimal Management Strategy of Severe Aortic Stenosis in Cancer Patients*

Pompilio Faggiano, MD,[a] Roberto Lorusso, MD, PhD,[b] Stefano Carugo, MD,[c,d] Andrea Faggiano, MD[c,d]

Cancer and aortic valve stenosis (AS) are 2 of the leading causes of death in developed countries.[1] The concomitant occurrence of cancer and severe AS is a common medical scenario with several mechanisms contributing: shared underlying risk factors, inflammatory state, and valve-toxic effects of cancer therapy, especially chest radiotherapy. This clinical setting should prompt the clinician to investigate any possible cardiovascular side effects induced by cancer therapy such as left ventricular dysfunction or coronary atherosclerosis, which may consequently influence the management choice. Not surprisingly, AS outcomes are worse in patients with cancer. More than 50% of mortality is cancer-related but, despite this, cancer patients not undergoing treatment for severe AS have a significantly worse prognosis.[2] The complexity of the 2 diseases, the poor prognosis and the spectrum of treatment options arise a major clinical dilemma.[3] The clinician faces several questions, sometimes with considerable ethical implications.

IS CANCER-RELATED LIFE EXPECTANCY SUFFICIENT TO JUSTIFY A VALVE REPLACEMENT PROCEDURE?

For this procedure not to be futile, patients should generally have a postprocedural life expectancy of 1 year or greater. However, accurately estimating prognosis is often difficult in this patient population, especially given the rapidly expanding therapies for cancer. The presence of metastatic cancer is typically associated with a shorter life expectancy. Interestingly, a recent work from Japan has shown that in the event of metastatic disease, if radical cancer treatment is anyway feasible, the prognosis is still satisfactory. Conversely, metastatic patients who cannot undergo radical cancer treatment have a poor prognosis after transcatheter aortic valve implantation (TAVI).[4] Only a close collaboration between the Heart Team and the oncologist allows to properly estimate patient prognosis and allocate appropriate management.

CAN PATIENTS UNDERGO CANCER TREATMENT DESPITE SEVERE SYMPTOMATIC AS AND/OR ARE THEY INELIGIBLE FOR VALVE REPLACEMENT BECAUSE OF CANCER?

This aspect is crucial in the therapeutic decision-making (DM) process. It is imperative to define what the priority is: treating first cancer or AS. Where patients can safely receive effective oncologic treatment in the presence of severe AS, it is reasonable to consider them for valve replacement as soon as *malignancy remission* is confirmed.[3] Indeed, the history of a cancer in remission impacts the prognosis of patients with AS significantly less than an active cancer.[2]

*Editorials published in *JACC: Advances* reflect the views of the authors and do not necessarily represent the views of *JACC: Advances* or the American College of Cardiology.

From the [a]Cardiothoracic Department, Fondazione Poliambulanza, Brescia, Italy; [b]Cardio-Thoracic Surgery Department, Heart and Vascular Centre, Maastricht University Medical Centre, and Cardiovascular Research Institute Maastricht, Maastricht, the Netherlands; [c]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy; and the [d]Department of Cardio-Thoracic-Vascular Area, Foundation IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan, Italy.

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.

ISSN 2772-963X https://doi.org/10.1016/j.jacadv.2022.100190

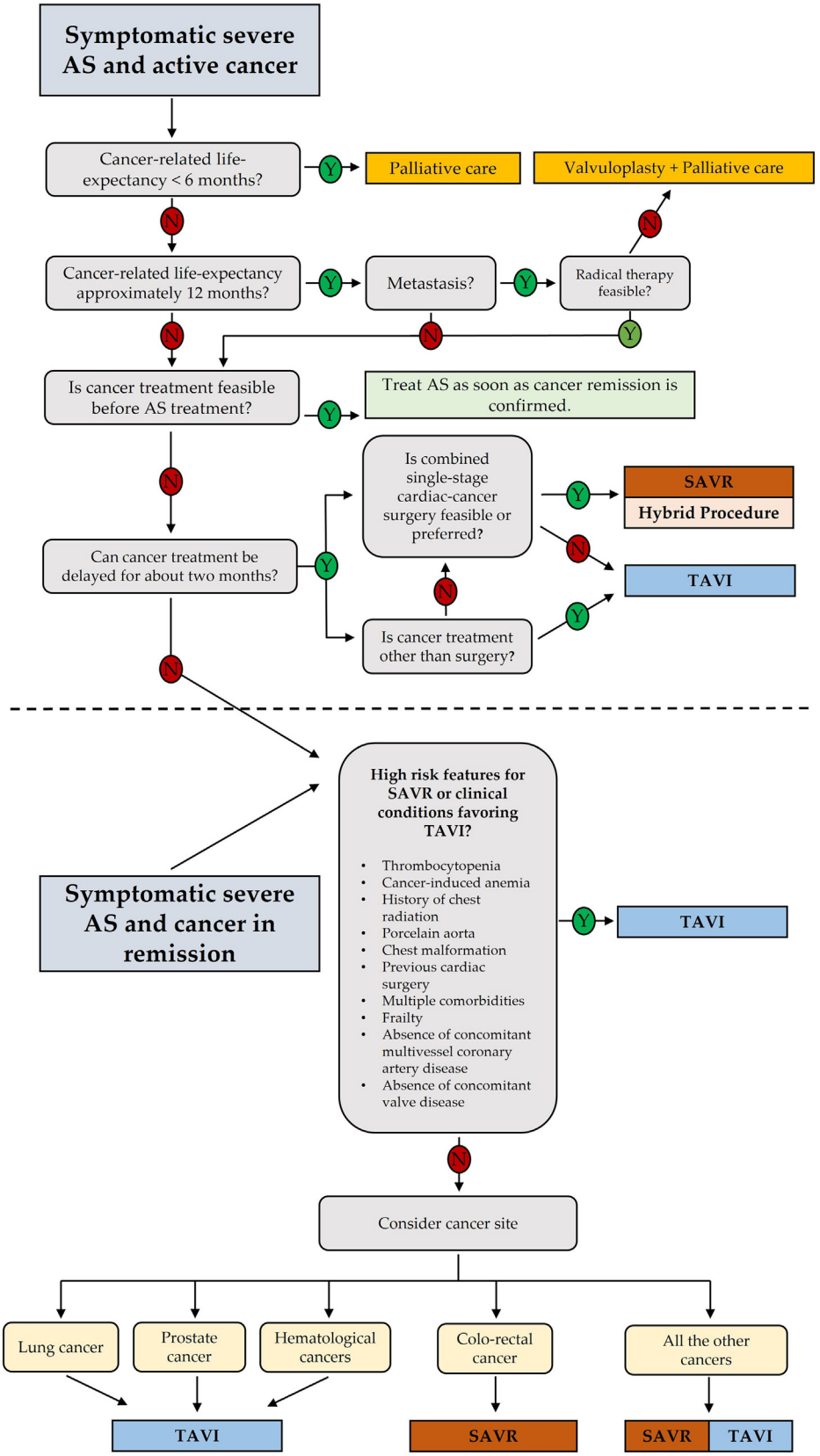
Conversely, where cancer treatment is necessary, but aortic stenosis needs to be addressed before cancer interventions, the timing of AS treatment requires consideration. Often cancer treatment cannot be delayed for 2 months as is necessary after a surgical valve replacement (SAVR). Consequently, the urgency to anticipate the oncological therapy as soon as possible is a sufficient clinical criterion to direct the treatment of AS toward a TAVI procedure, able to minimize the delays in cancer care from 2 months to ≅2 weeks. A reasonable exception to this DM process could be the possibility that the planned cancer treatment is radical surgery and that combined single-stage cardiac-oncological surgery is safely feasible.[5] Especially in the presence of left ventricular dysfunction, aortic regurgitation, or critical coronary artery disease, oncological surgery has a high intraoperative risk of acute decompensation. Such situations could require a combined single-stage oncological-valve treatment, not necessarily entirely surgical. In this setting, procedures conducted in the hybrid operating room ("hybrid procedures") would allow to carry out in rapid succession TAVI, with or without percutaneous coronary intervention, and cancer surgery.

WHAT IS THE MOST APPROPRIATE AORTIC VALVE REPLACEMENT PROCEDURE IN CANCER PATIENTS? SAVR OR TAVI?

Where immediate oncological treatment is not needed or cancer is in remission, nonurgent clinical DM helps identify the most suitable aortic valve replacement procedure. With the exception of patients with symptomatic severe AS caused by radiation, in which TAVI is recommended by the guidelines,[6] the standard treatment remains SAVR, although cancer patients are generally considered poor candidates for cardiac surgery mainly because of comorbidities that increase morbidity and mortality. It is worth considering that usually valve surgery requires extracorporeal circulation which seems to induce immunosuppression and increase inflammation. However, the relationship between the use of extracorporeal circulation and cancer progression has not yet been clearly demonstrated.[7] Furthermore, in the DM process, it is necessary to assess whether high-risk features for SAVR that make TAVI more appropriate are present. For example, cancer-induced thrombocytopenia or anemia, porcelain aorta, previous cardiac surgery, and frailty are all factors that tip the balance toward TAVI.[8] A recent meta-analysis shows that TAVI may be a safe and effective therapeutic option for cancer patients affected by severe AS, with short-term mortality and perioperative complications rate similar between cancer patients and controls.[9] A recent study found that TAVI and SAVR had similar in-patient mortality and 30-day readmission, while TAVI was associated with lower vascular complications, acute kidney injury, cardiogenic shock, and respiratory complications despite more comorbidities at baseline.[10]

In this issue of *JACC: Advances*, Ullah et al[11] conducted a large nationwide analysis evaluating trends and outcomes of TAVI vs SAVR in cancer patients affected by solid tumors. As expected, using the Nationwide Inpatient Sample United States of America database, the authors found a steep yearly increase in the utilization of TAVI from 2011 to 2018 irrespective of the type of cancer. Indeed, by the year 2015, the proportion of TAVI procedures surpassed the corresponding proportion of SAVR procedures reflecting the tendency of clinicians to rely more on TAVI in this setting. This is not surprising considering that the minimally invasive nature of TAVI may lead clinicians to prefer it to SAVR in complex and fragile patients. Interestingly, the authors found different outcomes of TAVI vs SAVR according to the different tumor site. Compared with SAVR, TAVI was associated with a similar or lower rate of major adverse cardiovascular events, stroke, and in-hospital mortality in all different types of cancers except for colon-rectal cancer. As emphasized by the author, the higher odds of major adverse cardiovascular events and stroke with TAVI among colon-rectal cancer patients were mainly driven by the older and female population. Among all cancer types, TAVI in patients with prostate cancer had the most favorable outcomes compared with SAVR. Taking into consideration the time period 2002 to 2018, TAVI was associated with a higher rate of permanent pace-maker implantation. It is reasonable to believe that the use of new-generation TAVI could decrease this complication over time also among cancer patients. Unfortunately, being the results from a national database, they intrinsically lack of important clinical information, which would probably allow a further individualized management strategy. Moreover, the study does not include patients with hematological cancers, which seems to be more prone to perioperative complications after heart surgery.[12] Despite the above-mentioned limitations, this analysis adds some missing information to solve the conundrum of the optimal management strategy of severe AS in cancer patients.

FIGURE 1 **Algorithm for the Management of Symptomatic Severe Aortic Stenosis in Cancer Patients**



AS = aortic valve stenosis; SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve implantation.

In light of the current literature and of the new data from Ullah et al, we propose a DM algorithm for the management of symptomatic severe AS in cancer patients. As illustrated by **Figure 1**, in the case of active cancer, once it is ascertained that cancer-related life expectancy is >1 year, that cancer treatment is not feasible before AS treatment, and that cancer treatment can be delayed for at least 2 months, the DM process is comparable to cancer in remission. At this point, we suggest evaluation for the presence of high-risk features for SAVR and/or clinical conditions favoring TAVI. Where such conditions are not present, the choice between TAVI and SAVR rests in the judgment of the heart team, including consideration that tumor site can influence management strategy.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr Pompilio Faggiano, Cardiothoracic Department, Fondazione Poliambulanza, Via Leonida Bissolati, 57, Brescia 25124, Italy. E-mail: cardiologia@pompiliofaggiano.it.

REFERENCES

1. Frattini S, Troise G, Fucci C, et al. Aortic valve stenosis and cancer: a common and complex association. *Expert Rev Cardiovasc Ther*. 2021;19(4):289-299.

2. Minamino-Muta E, Kato T, Morimoto T, et al. Malignant disease as a comorbidity in patients with severe aortic stenosis: clinical presentation, outcomes, and management. *Eur Heart J Qual Care Clin Outcomes*. 2018;4(3):180-188.

3. Balanescu SM, Balanescu DV, Donisan T, et al. The onco-cardiologist dilemma: to implant, to defer, or to avoid transcatheter aortic valve replacement in cancer patients with aortic stenosis? *Curr Cardiol Rep*. 2019;21(8):83.

4. Kojima Y, Higuchi R, Hagiya K, et al. Prognosis of patients with active cancer undergoing transcatheter aortic valve implantation: an insight from Japanese multicenter registry. *Int J Cardiol Heart Vasc*. 2022;40:101045.

5. Fu Q, Li QZ, Liang DG, et al. Early and long-term results of combined cardiac surgery and neoplastic resection in patients with concomitant severe heart disease and neoplasms. *Chin Med J (Engl)*. 2011;124(13):1939-1942.

6. Lyon AR, López-Fernández T, Couch LS, et al. 2022 ESC guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS). *Eur Heart J*. 2022;43(41):4229-4361.

7. Lorusso R, Vizzardi E, Johnson DM, et al. Cardiac surgery in adult patients with remitted or active malignancies: a review of preoperative screening, surgical management and short- and long-term postoperative results. *Eur J Cardiothorac Surg*. 2018;54:10-18.

8. Windecker S, Okuno T, Unbehaun A, et al. Which patients with aortic stenosis should be referred to surgery rather than transcatheter aortic valve implantation? *Eur Heart J*. 2022;43:2729-2750.

9. Marmagkiolis K, Monlezun DJ, Cilingiroglu M, et al. TAVR in cancer patients: comprehensive review, meta-analysis, and meta-regression. *Front Cardiovasc Med*. 2021;8:641268.

10. Kadri AN, Bernardo M, Assar SZ, et al. Surgical versus transcatheter aortic valve replacement in patients with malignancy. *Cardiovasc Revasc Med*. 2021;23:59-65.

11. Ullah W, Thalambedu N, Zahid S, et al. Trends and outcomes of TAVI and SAVR in cancer and noncancer patients: a nationwide analysis. *JACC Adv*. 2023;2:100167.

12. Samuels LE, Kaufman MS, Morris RJ, et al. Open heart surgery in patients with chronic lymphocytic leukemia. *Leuk Res*. 1999;23(1):71-75.

KEY WORDS aortic valve stenosis, cancer, TAVI, SAVR