



BAISHIDENG PUBLISHING GROUP INC

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242 Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com <http://www.wjgnet.com>

Name of Journal: *World Journal of Cardiology*

ESPS Manuscript NO: 27677

Manuscript Type: Case Report

We would like to thank reviewers for their comments. They were very constructive and helped to improve the manuscript substantially.

Reviewer #1:

The authors describe a very late transcatheter aortic valve replacement (TAVR) thrombosis with favorable evolution after anticoagulation. This is a very interesting report and reinforces that all patients undergoing TAVR should be monitored for incremental increases in transvalvular mean gradient by TTE and places "in the eye of the storm" the need to define a specific antithrombotic regimen post-TAVR to reduce the risk of incident valve hemodynamic deterioration (VHD). I have some comments. Please report which kind of Sapien valve was implanted to the patient. I suppose you implanted Sapien XT using the NovaFlex delivery system since Sapien 3 with commander delivery system was developed since 2013. (*Prog CV Dis* 2014; 56:583-95). Sapien 3 valve have significantly lower paravalvular leak (PVL) due to its outer skirt and longer frame height. Please clarify. The causal relationship between moderate PVL and transcatheter heart valve thrombosis is quite speculative. I recommend to include a very recently paper and its editorial that analyze the incidence timing and predictors of VHD after TAVR in 1521 pts (*JACC* 2016; 67:644-55 and 656-8). Del Trigo et al reported that there was a mild but significant increase in transvalvular gradients

over time after TAVR (0.3±4.99 mmHg/year). The lack of anticoagulation therapy, a greater body mass index (> 27 kg/m²) and the use of a 23-mm transcatheter valve were associated with higher rates of VHD post-TAVR. Please reformulate the discussion in the light of this very recently paper. Additional comments: remove "avec" in the first paragraph of the last page. Add the reference of the GALILEO trial.

The THV was an Edward SAPIEN. This was the generation prior to SAPIEN XT.

This was added in the first paragraph of the case report description:

...using a first-generation balloon-expandable Edwards SAPIEN...

This was added in the third paragraph of the discussion:

Moderate PVL could be associated with a different flow pattern over the leaflets and in the left main that could lead to THV thrombosis and accelerated progression of atherosclerosis although this relationship is speculative.

This was added in the third paragraph of the discussion:

Valve hemodynamic deterioration (VHD), defined by an increase in mean TPG of more than 10 mmHg over time, was observed more frequently in patients with smaller THV (23 mm) and those not receiving oral anticoagulation.⁴ Most of these patients did not have a progressive deterioration after the first year. VHD does not seem to be part of a continuum towards THV thrombosis and this later remains unpredictable. However, the pathophysiology of VHD may include some degree of sub-clinical leaflet thrombosis.

This was added in the second paragraph of the discussion:

...and the GALILEO (rivaroxaban; NCT02556203) ...

Reviewer #2:

Interesting case report The manuscript will need some language polishing: (...)TEE and 4D CT scan early "avec" THV implantation; should be a heightened clinical awareness, 64 years-old woman,they have remained unchanged after nine months etc...

The authors may wish to mention other ongoing studies on anti platelet-antithrombotic regimen after TAVR (beside the GALILEO trial): The ARTE trial, POPular-TAVI, REAC-TAVI, Atlantis study... The reported incidence of THV thrombosis in the manuscript by Latib et al in Circ CV Interv is 0.61% (not 0.65%) The authors mention that cardiac CT scan may be the optimal diagnostic test for THV thrombosis. Is this really the case? Reference 4 does not necessarily support this statement. Please justify

This was added in the second paragraph of the discussion:

The ARTE (clopidogrel; NCT01559298) and REAC-TAVI (ticagrelor vs. clopidogrel; NCT02224066) trials are evaluating different antiplatelet strategies and the GALILEO (rivaroxaban; NCT02556203) and ATLANTIS (apixaban; NCT02664649) studies are looking at the effect of non-vitamin K oral anticoagulant following TAVR. Similarly, the POPular-TAVI trial (NCT02247128) is evaluating the effect of adding clopidogrel for 3 months post-implantation in patients with and without ongoing vitamin-K oral anticoagulation treatment.

This was corrected in the first paragraph of the discussion:

Even though estimated incidence is low (0.61%), consequences can be catastrophic if appropriate therapy is not initiated promptly.

This was added in the first paragraph of the discussion:

In a series of 3 pathology-proven THV thrombosis, TEE was also negative in each cases. However, Makkar et al. showed that 4D-CT and TEE had a diagnostic concordance of 100% in 10 patients presenting reduced leaflets motion following TAVR. Whether 4D-CT is the optimal imaging modality remains to be proven.

Reviewer #3:

The video's could not be played. The link was not available. Minor errors: Page 5: line 4: Please consider " after" instead of " avec" . Page 5: line 9: Please replace rivoroxaban with rivaroxaban. There are no other comments on the manuscript.

The videos have been sent to the editor by e-mail because the submission website was not able to accomodate them. Hopefully, you will get access to the videos this time.

This was corrected in the first paragraph of the discussion:

Reports have revealed subclinical leaflet thrombosis detected by TEE and 4D CT scan early after THV implantation

This was corrected in the second paragraph of the discussion:

... and the GALILEO (rivaroxaban; NCT02556203) and ...

Reviewer #4:

interesting case report on a new clinical problem this case is illustrative and gives additional information on the potential course of TAVR thrombosis how was the left main at the time of the implantation of the valve? this rapid evolution of the left main stenosis in intruiging. did you have IVUS imaging before or after stenting?

No IVUS was done.

This was added in the second paragraph of the discussion:

...the angiographic appearance was more in favor of disease progression of a previous non-significant lesion seen on the per-TAVR angiogram

Reviewer #5:

Intersting