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STRUCTURAL

Clinical Bioprosthetic Heart Valve Thrombosis After Transcatheter Aortic Valve Replacement

Incidence, Characteristics, and Treatment Outcomes

John Jose, MD, DM,[a,b] Dmitriy S. Sulimov, MD,[a] Mohamed El-Mawardy, MD,[a] Takao Sato, MD,[a,c] Abdelhakim Allali, MD,[a] Erik W. Holy, MD,[a] Björn Becker, MD,[a] Martin Landt, MD,[a] Julia Kebernik, MD,[a] Bettina Schwarz, MD,[a] Gert Richardt, MD,[a] Mohamed Abdel-Wahab, MD[a]

ABSTRACT

OBJECTIVES The aim of this study was to determine the incidence, characteristics, and treatment outcomes of patients diagnosed with clinical transcatheter heart valve thrombosis.

BACKGROUND Limited data exists on clinical or manifest transcatheter heart valve thrombosis. Prior studies have focused on subclinical thrombosis.

METHODS A retrospective analysis was conducted of prospectively collected data from a single-center registry that included 642 consecutive patients who underwent transcatheter aortic valve replacement between 2007 and 2015 (305 patients had self-expanding valves; balloon-expandable, n = 281; mechanically expanding, n = 56). Long-term oral anticoagulation (OAC) was indicated in 261 patients, while 377 patients received dual-antiplatelet therapy post-procedure. All patients underwent scheduled clinical and echocardiographic follow-up.

RESULTS The overall incidence of clinical valve thrombosis was 2.8% (n = 18). No patient on OAC developed thrombosis. Of the detected thrombosis cases, 13 patients had balloon-expandable, 3 had self-expanding, and 2 had mechanically expanding valves. Thrombosis occurred significantly more often with balloon-expandable valves (odds ratio: 3.45; 95% confidence interval: 1.22 to 9.81; p = 0.01) and following valve-in-valve procedures (odds ratio: 5.93; 95% confidence interval: 2.01 to 17.51; p = 0.005). Median time to diagnosis of valve thrombosis was 181 days. The median N-terminal pro-brain natriuretic peptide level was 1,318 pg/ml (interquartile range: 606 to 1,676 pg/ml). The mean transvalvular gradient and valve area were 34 ± 14 mm Hg and 1.0 ± 0.46 cm^2, respectively. Computed tomography showed hypoattenuating areas with reduced leaflet motion. Initiation of OAC resulted in significant reduction of transvalvular gradient and clinical improvement. No deaths were related to valve thrombosis.

CONCLUSIONS Clinical transcatheter heart valve thrombosis is more common than previously considered, characterized by imaging abnormalities and increased gradients and N-terminal pro-brain natriuretic peptide levels. It occurred more commonly after balloon-expandable transcatheter aortic valve replacement and valve-in-valve procedures. OAC appeared to be effective in the prevention and treatment of valve thrombosis. Randomized control trials are needed to define optimal antithrombotic therapy after transcatheter aortic valve replacement. (J Am Coll Cardiol Intv 2017;10:686–97) © 2017 by the American College of Cardiology Foundation.

From the [a]Heart Center, Segeberger Kliniken (Academic Teaching Hospital of the Universities of Kiel, Lübeck, and Hamburg), Bad Segeberg, Germany; [b]Christian Medical College Hospital, Vellore, Tamil Nadu, India; and the [c]Tachikawa General Hospital, Nagaoka, Japan. Drs. Abdel-Wahab and Richardt have received institutional research grants from St. Jude Medical and Biotronik. Dr. Abdel-Wahab is a proctor for Boston Scientific. Dr. Richardt has received lecture fees from Edwards Lifesciences and Boston Scientific.

Transcatheter aortic valve replacement (TAVR) is an innovative, minimally invasive procedure that has become the standard of care for patients with severe aortic stenosis who are either inoperable or at high risk. With short-term efficacy and safety established in several trials in the past decade (1–4), recent research efforts have focused on durability and long-term outcomes after TAVR. There are few studies on modes of transcatheter heart valve (THV) failure, such as endocarditis or thrombosis, and consequently the current state of knowledge on this important aspect is fragmented. Although more than 200,000 TAVRs have been performed worldwide in the past 10 years (5), THV thrombosis remains a poorly characterized phenomenon.

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Several sporadic cases of THV thrombosis were recently reported and have generated significant research interest on this entity (6–12). The most data so far on THV thrombosis were recently published by Latib et al. (13), reporting an overall incidence of 0.61% in a multicenter experience. However, design limitations of this registry precluded any detailed analysis regarding antithrombotic therapy, device type, or comparison with surgical rates. It was also believed that the risk for thrombosis was significantly underestimated in this registry analysis. In another recent report, Makkar et al. (14) analyzed computed tomographic (CT) data from patients in a clinical trial and 2 single-center registries and provided data on possible subclinical thrombosis. More recently, a 10% incidence of subclinical THV thrombosis was identified in patients undergoing implantation of balloon-expandable valves (SAPIEN 3, Edwards Lifesciences, Irvine, California) (15). Both these latter studies focused on subclinical THV thrombosis and relied mainly on CT examination performed relatively early after TAVR, for diagnosing thrombosis. However, risk for THV thrombosis is likely to be a continuous hazard that cannot be wholly assessed with a single CT examination. Well-designed longitudinal evaluation studies are needed to truly identify the magnitude and natural history of this problem.

The Heart Center at Segeberger Kliniken has had a well-established TAVR program since 2007, with a pre-defined clinical and echocardiographic follow-up schedule for patients after TAVR. In a retrospective analysis of prospective data from the center's database, we aimed primarily to estimate the incidence of clinical or manifest THV thrombosis in a general TAVR population. Secondary objectives of our study were to describe the timing, characteristics, predictors, and treatment outcomes of patients diagnosed with clinical THV thrombosis.

ABBREVIATIONS AND ACRONYMS

CT = computed tomographic

NT-proBNP = N-terminal pro-brain natriuretic peptide

TAVR = transcatheter aortic valve replacement

THV = transcatheter heart valve

METHODS

STUDY DESIGN AND PARTICIPANTS. For this retrospective analysis, we identified a total of 649 consecutive TAVR procedures (n = 642) performed between September 2007 and August 2015 at the Heart Center at Segeberger Kliniken. Although baseline characteristics, procedural data, treatment details, and clinical outcomes, including follow-up data, for all patients were collected prospectively for the institute's TAVR database, the analysis was retrospective. The institutional database is approved by the local ethics committee, and informed consent was obtained from all patients. The study was conducted in accordance with principles of good clinical practice. All procedures followed were in accordance with ethical standards of the responsible committees on human experimentation (institutional and national) and with the Declaration of Helsinki of 1964, as revised in 2013. Flow of patients in this analysis is shown in **Figure 1**.

DEVICE AND PROCEDURE TYPES. TAVR was performed using 1 of the following devices: balloon-expandable (SAPIEN XT and SAPIEN 3, both Edwards Lifesciences), self-expanding (CoreValve and Evolut R, both Medtronic, Minneapolis, Minnesota; Biovalve, Biotronik, Bülach, Switzerland; JenaValve, Jena Valve Technology, Munich, Germany; and Symetis, Symetis, Geneva, Switzerland), or mechanically expanding (Lotus, Boston Scientific, Marlborough, Massachusetts). TAVR was performed through transfemoral, transsubclavian, transapical, or transaortic routes. In most patients, it was done under conscious sedation without transesophageal echocardiographic guidance. Pre-dilatation was done at the operator's discretion. Valve-in-valve procedures were not excluded from this analysis.

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