

EDITORIAL COMMENT

A Permanent Solution for a Temporary Problem

Transcatheter Valve-In-Valve Implantation for Failed Transcatheter Aortic Valve Replacement*

Lutz Buellesfeld, MD,† Eberhard Grube, MD‡

Bern, Switzerland; and Bonn, Germany

Over the past decade, transcatheter aortic valve replacement (TAVR) matured from an adventitious endeavor in the early years to an established and paradigm-changing treatment option for many patients with severe aortic valve stenosis.

However, lack of long-term data on device performance as well as the obvious presence of procedure-specific complications currently limit the expansion of this technology toward lower-risk patients outside controlled and randomized clinical trials.

See page 571

Fortunately, we are continuously increasing our understanding of both mechanisms and the impact of procedure-inherent risks, which enables us to take adequate measures to overcome these issues. Reduction of device profile sizes, improved screening standards, and better technical performances led to a significant decrease of access site complications. Improved implantation techniques lowered the rate of pacemaker implants, which is still higher for the Medtronic CoreValve (Medtronic, Minneapolis, Minnesota) than for the Edwards Sapien prostheses (Edwards Lifesciences, Irvine, California); but this complication does not translate into prognostic relevance (1). Finally, rates of embolic cerebral events are leveling down in more recent publications, probably related to improved operator skills and technical refinements. In addition, the advent of protection devices will further help to increase the safety of the procedure.

Against this background, aortic regurgitation after TAVR is one of the last remaining issues still underestimated in terms of its incidence and clinical relevance,

mainly for 3 reasons: 1) aortic regurgitation after TAVR is difficult to grade, given the lack of established evaluation criteria in this new setting; 2) the prognostic impact of aortic regurgitation in TAVR patients is largely unknown; and 3) we have only anecdotal reports on bail-out strategies to deal with aortic regurgitation after TAVR but no established concepts with prospective assessment and validation.

In this issue of *JACC: Cardiovascular Interventions*, Toggweiler et al. (2) present an interesting article reporting the results of a multicenter study on frequency, feasibility, and outcome of transcatheter valve-in-valve implantation with the balloon-expandable Edwards prosthesis in patients with significant aortic regurgitation after TAVR (so called “transcatheter heart valve [THV]-in-THV”). Lack of pre-specified criteria to perform this second implant and missing information on regurgitation evaluation methods are significant limitations of this study, but there are 2 main conclusions that should be highlighted: 1) severe aortic regurgitation is rare; and 2) interventional treatment of aortic regurgitation is doable.

Severe Aortic Regurgitation Is Rare

Post-procedural presence of aortic regurgitation in patients undergoing TAVR has been described since the introduction of this technique. In general, there are several mechanisms that cause valvular or paravalvular leakages, which must be understood and the actual one identified in order to properly address this issue in a given case. Paravalvular regurgitation is always the result of incomplete annular sealing of the device due to device misplacement, device-annulus mismatch, incomplete device expansion, or unfavorable degeneration or calcification patterns prohibiting full apposition (3) (Fig. 1). Valvular regurgitation is the result of restricted leaflet motion, leaflet destruction, and under- or overexpansion of the device, which affects normal leaflet dynamics.

Good news is that, severe aortic regurgitation in patients undergoing TAVR is rare. In a total of 760 TAVR patients, Toggweiler et al. (2) observed an incidence of 3% for severe aortic regurgitation, moderate aortic regurgitation in 10%, and less-than-moderate aortic regurgitation in 87% of cases. These numbers are well in line with previous publications, reporting moderate-to-severe and severe aortic regurgitation in 5% to 32% of TAVR patients (4–6). A total of 21 patients received a THV-in-THV to treat acute severe regurgitation, which equals 2.8% of the study population. Identified mechanisms were paravalvular in 18 cases, with implants too deep in 10 and too high in 8 cases, and valvular in 3. Of note, severe paravalvular aortic regurgitation in patients with optimal device implant depth was not observed in this study. However, the range of optimal implant depths was not pre-defined, which might have biased the investigators to classify implants as either too high or too low once severe aortic regurgitation was present, mistak-

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

From the †Department of Cardiology, Swiss Cardiovascular Center, Bern University Hospital, Bern, Switzerland; and the ‡Department of Medicine II, Bonn University Hospital, Bonn, Germany. Drs. Buellesfeld and Grube are both consultants and proctors of Medtronic.

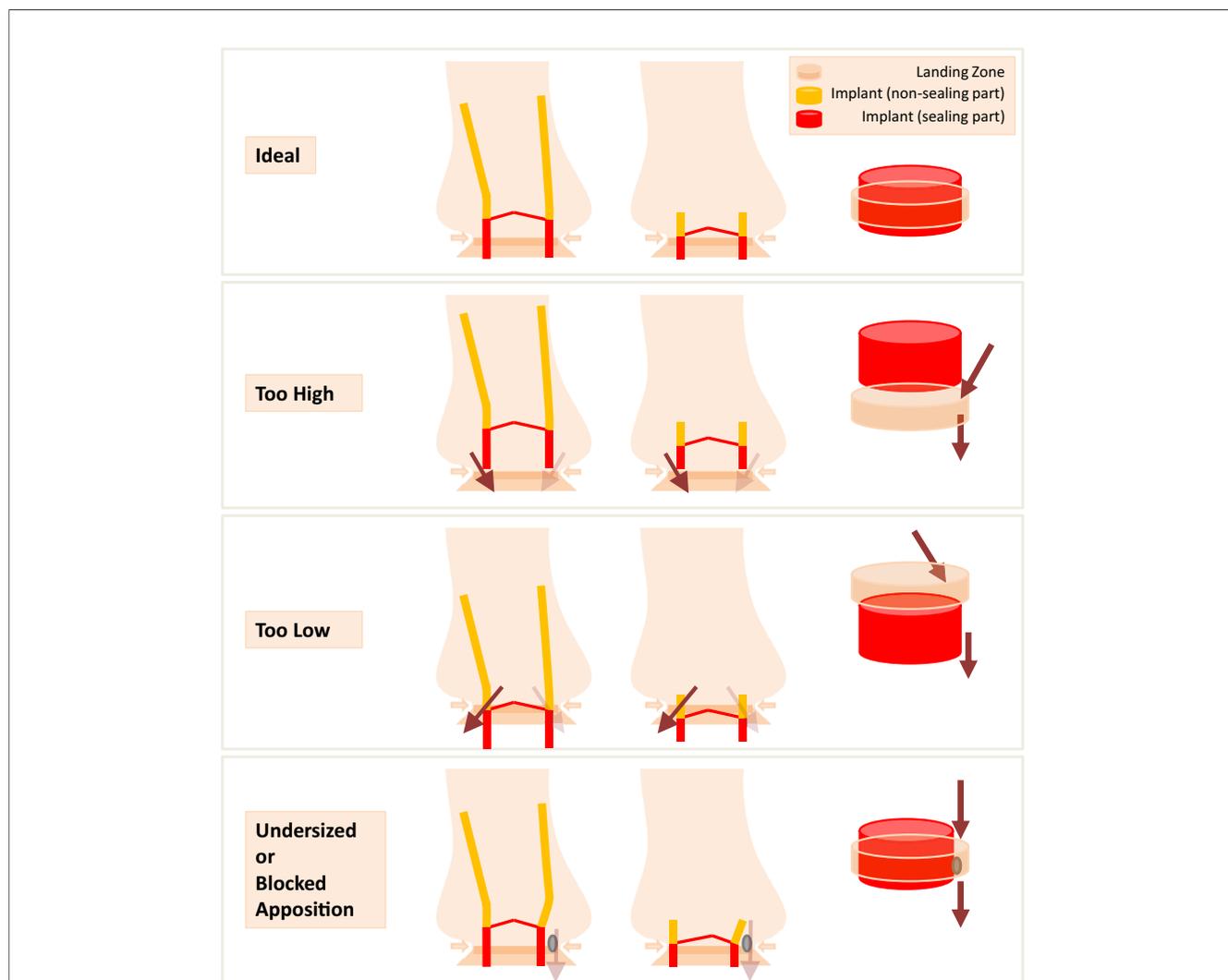


Figure 1. Selected Mechanisms of Paravalvular Regurgitation After Transcatheter Aortic Valve Replacement

Top row: ideal implant of CoreValve (Medtronic, Minneapolis, Minnesota) and Edwards (Edwards Lifesciences, Irvine, California) prostheses. **Last column** indicates the match of landing zone and sealing part of the device; **second row:** implant too high, allowing for focal or circumferential regurgitation from outside; **third row:** implant too deep, allowing for focal or circumferential regurgitation from inside; **bottom row:** undersized prosthesis or presence of morphological characteristics preventing ideal device apposition.

only neglecting alternative causes of paravalvular aortic regurgitation.

Finally, the study points out that significant aortic regurgitation is poorly tolerated. This is a typical clinical finding, because pressure-adapted ventricles can hardly cope with rapid volume overload, particularly in the presence of additional underlying myocardial pathologies such as ischemic heart disease. Consequently, severe aortic regurgitation was associated with cardiogenic shock in 52% of patients, with need for cardiopulmonary support and resuscitation in a substantial number of cases. So there is no doubt that severe aortic regurgitation is a relevant issue with significant clinical impact. Interestingly, there is increasing evidence from other reports that, not only severe, but any kind of post-procedural

aortic regurgitation seems to be linked to a worsened outcome (6,7). Therefore, we probably have to rethink our current strategies on how we are dealing with nonsevere aortic regurgitation, potentially lowering the threshold to take corrective measures to reduce or eliminate post-procedural leakage.

In summary, severe aortic regurgitation is rare but often dramatic; and the prognostic impact of aortic regurgitation is probably underestimated.

Interventional Treatment of Aortic Regurgitation Is Doable

In theory, various options are available to handle aortic regurgitation after TAVR, depending on the underlying

mechanism. Several techniques have been described in anecdotal reports, including medical treatment only, post-dilation, post-dilation with oversized balloons, pull-up maneuvers for the self-expanding CoreValve prosthesis using a snare, implantation of a second prosthesis (THV-in-THV), implantation of focal occluders, or conversion to conventional surgery (Fig. 2).

From the conceptual standpoint, THV-in-THV is useful in cases of device misplacement too high or too low as well as cases with valvular regurgitation. The reasonably high success rate of 90% (19 of 21) reported by Toggweiler et al. (2) with reduction of aortic regurgitation in all cases nicely demonstrates the value of this approach. Short-term mortality at 30 days tended to be increased compared with

patients without need for a second prosthesis (14.3% vs. 7.3%), but survival at 12 months was comparable (76% vs. 78%). The authors finally concluded that THV-in-THV for treatment of significant aortic regurgitation is feasible and results in satisfactory short- and mid-term outcome.

This corroborates the results of previously published experiences using both the Edwards as well as the Medtronic CoreValve prostheses. However, it does not mean that THV-in-THV is generally the best and only way to go. This approach is actually prone to fail in cases with alternative causes such as device-annulus mismatch or 'hostile' calcification patterns. For instance, if the first prosthesis is too small, the second will not correct for this. One could select a larger size prosthesis to implant at a

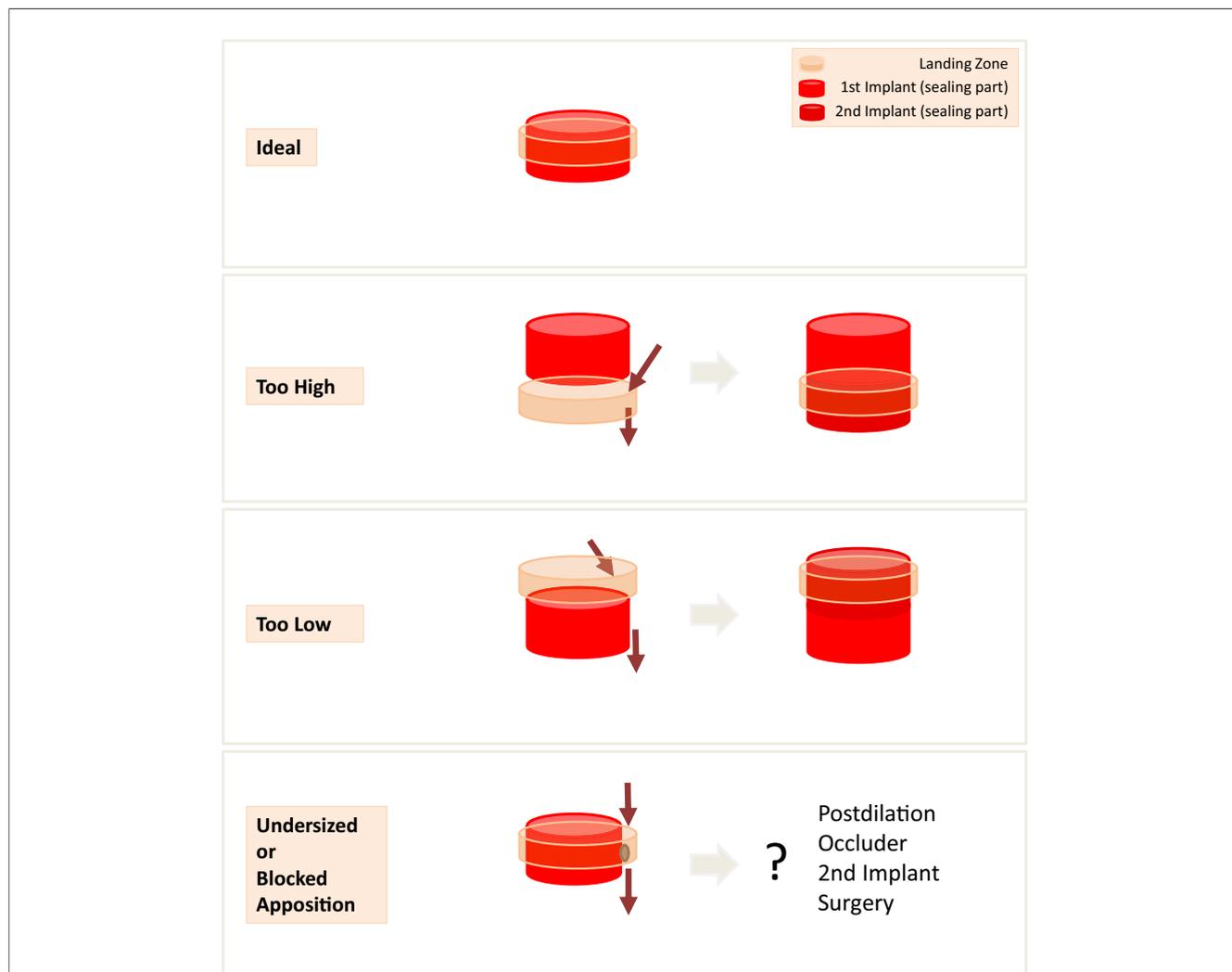


Figure 2. Bail-Out Options for Paravalvular Regurgitation

Top row: ideal match of landing zone and sealing part of the device; **second row:** if implant is too high, second implant at a deeper position extends the sealing part toward the original landing zone (of note, avoid complete sinus isolation to protect coronary artery perfusion); **third row:** if implant is too deep, implant at the same or slightly higher position extends the sealing part toward the original landing zone; **bottom row:** various options must be considered in case of undersizing or lack of complete apposition.

deeper position in the outflow tract, but outflow tract dimensions may exceed annulus dimensions, allowing again for paravalvular gaps, and underexpansion of the valve in the upper part will stress the leaflets, potentially affecting long-term performance. In this scenario, other treatment options must be considered.

It is quite remarkable that none of these alternative regurgitation mechanisms—provided that they were not overlooked—were observed in the present study, which requires ideal screening, ideal device selection, and very favorable native valve morphologies. Previously published reports on aortic regurgitation after TAVR indicate that this ideal environment does not usually exist. Therefore, it is still the full bundle of treatment options outlined in the preceding text that must be considered in these patients. In summary, interventional treatment of aortic regurgitation is doable, but mechanisms must be understood.

Future Perspective

Aortic regurgitation after TAVR is a procedure-related issue that is certainly underestimated and currently not always addressed in an adequate fashion. New standards for valve assessment are needed to identify TAVR patients requiring additional efforts to deal with this complication. Because echocardiographic means are limited in describing severity of paravalvular aortic regurgitation, particularly in cases with circumferential or multiple jets, hemodynamic assessment gains importance and seems to be predictive for future events (8).

THV-in-THV is a suitable technique to deal with aortic regurgitation after TAVR in selected cases if the underlying mechanism allows for this approach, predominantly in device misplacements and valvular regurgitation. However, we are talking about a temporary problem as device misplacement is shortly going to be eliminated by the introduction of repositionable prostheses, which enable intra-procedural positional adjustments. In addition, future devices should and will provide dedicated paravalvular sealing mechanisms, which are made to fill gaps between the device frame and the native valve.

Finally, three- and four-dimensional imaging tools will facilitate a precise assessment of the aortic valve anatomy, further reducing the incidence of annulus-device mismatch.

Therefore, once dedicated devices and ideal screening tools are established, there is not much room left for regurgitation. In the meantime, papers like the present one are certainly appreciated, because it is at least good to see that we are able to deal with our own complication.

Reprint requests and correspondence: Dr. Eberhard Grube, Department of Medicine II, Bonn University Hospital, Sigmund Freud Strasse 25, Bonn 53105, Germany. E-mail: grubee@aol.com.

REFERENCES

1. Buellesfeld L, Stortecky S, Heg D, et al. Impact of permanent pacemaker implantation on clinical outcome among patients undergoing transcatheter aortic valve implantation. *J Am Coll Cardiol* 2012. In press.
2. Toggweiler S, Wood DA, Rodés-Cabau J, et al. Transcatheter valve-in-valve implantation for failed balloon-expandable transcatheter aortic valves. *J Am Coll Cardiol Intv* 2012;5:571–7.
3. Takagi K, Latib A, Al-Lamee R, et al. Predictors of moderate-to-severe paravalvular aortic regurgitation immediately after CoreValve implantation and the impact of postdilatation. *Catheter Cardiovasc Interv* 2011;78:432–43.
4. Smith CR, Leon MB, Mack MJ, et al., for the PARTNER Trial Investigators. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med* 2011;364:2187–98.
5. Yan TD, Cao C, Martens-Nielsen J, et al. Transcatheter aortic valve implantation for high-risk patients with severe aortic stenosis: a systematic review. *J Thorac Cardiovasc Surg* 2010;139:1519–28.
6. Abdel-Wahab M, Zahn R, Horack M, et al. Aortic regurgitation after transcatheter aortic valve implantation: incidence and early outcome. Results from the German Transcatheter Aortic Valve Interventions Registry. *Heart* 2011;97:899–906.
7. Kodali SK, Williams MR, Smith CR, et al., for the the PARTNER Trial Investigators. Two-year outcomes after transcatheter or surgical aortic-valve replacement. *N Engl J Med* 2012 Mar 26 [E-pub ahead of print].
8. Sinning JM, Hammerstingl C, Vasa-Nicotera M, et al. Aortic regurgitation index defines severity of peri-prosthetic regurgitation and predicts outcome in patients after transcatheter aortic valve implantation. *J Am Coll Cardiol* 2012;59:1134–41.

Key Words: aortic valve disease ■ aortic valve stenosis ■ transcatheter aortic valve replacement.