Editorial

Editorial comment on the RESPOND study

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It was a real pleasure to write an Editorial comment for this issue of the *Journal of Thoracic Disease*. We read with great interest the paper of Volkmar Falk, submitted to the *European Heart Journal* describing the safety and efficacy of the transcatheter Lotus™ valve (Boston Scientific Corporation, Marlborough, Massachusetts, USA) (1). In Essen, we had the great opportunity to be involved within the early and first-in-man implantation of the predecessor of the Lotus™ valve, the Sadra™ TAVI (transcatheter aortic valve implantation) system, in collaboration with Raimund Erbel and Eberhard Grube in 2007. The above-mentioned paper summarized the results of a prospective, multi-centre, open-label and single-arm registry (RESPOND: Repositionable Lotus Valve System-Post Market Evaluation of Real World Clinical Outcomes) from 41 centres in Europe, New Zealand and Latin America in a total of 1,014 patients.

In general, the Lotus™ device represents a second-generation TAVI device, which consists of a pre-loaded, stent-mounted tissue valve prosthesis and catheter delivery system. The frame consists of braided nitinol wires with three bovine pericardial leaflets. The idea of this concept was that this new device offers the possibility to reposition or retrieve the device if it is not perfectly placed. The valve is illustrated in *Figure 1*. Moreover, the valve is surrounded by an adaptive seal (polymer membrane) to act against paravalvular leakage (PVL). By the way, especially this feature has meanwhile created a landmark legal battle between different medical companies. An aortic diameter of ≥20 to ≤27 mm could be covered by the Lotus™ valve. Generally speaking, the concept of this device can be quite vividly explained by the so called Chinese finger trap.

The paper what we refer to, aimed to describe for the first time, the use of the Lotus™ device in a large and "all-comer" patient population and to evaluate 30-day mortality and VARC-2 criteria (2). The paper comes with several new, positive, but also debatable aspects in the field of TAVI. In regard to the obtained results, it should be mentioned at first, that an independent echo core-lab was used to assess postoperative valve function. It should be mentioned, that the overall "intention-to-treat" population consisted of a total of 1,014 patients, but in 18 patients, no Lotus™ valve was implanted, which corresponds to 1.8%. Therefore, only 996 patients received a Lotus™ valve with a rate of 99.7% correct positioning. An ideal valve should cover all pathologies and should be suitable for every TAVI patient. The reasons for not implanting a Lotus™ valve were inability to track through the anatomy/device complication (n=10), procedural complication (n=6), incorrect sizing (n=1) or one unknown reason. On the other side however, it must be highlighted, that 11.7% of the "as-treated" group showed moderate to severe aortic regurgitation as the underlying pathology. In this respect, the Lotus™ device will definitively create new possibilities to treat also patients with aortic regurgitation, which has been also published so far (3).

The major innovation of the Lotus™ valve is based on the possible repositioning and retrievability of the device. This feature has been attempted in 296 (29.2%) of

Figure 1 Self-expandable Lotus™ valve.

the patients and was successful in 99.0%. In one patient, repositioning was twice unsuccessful due to malfunction of the device leading to persistent PVL. We need to ask, however, if we need such a function of retrievability or repositioning in the current armamentarium of self- or balloon-expandable TAVI prostheses. Of course, this question cannot be easily answered and is up to the individual operator to use it or not. However, within the paper, the reasons for resheathing or repositioning were not indicated quite detailed, or was it just used as they could? The authors argued, that, valve function can be assessed, although the device has not been fully released and if unsatisfactory, the valve can easily be re-sheated and re-implanted (1).

The patient population within the RESPOND registry consisted of a typical TAVI cohort, however, it should be stated that 13.3% of the patients had a history pacemaker implantation prior to the index procedure. The 30-day follow-up data, showed both an excellent rate of all-cause mortality (2.6%) and stroke (3.0%). In should be kept in mind however, that in 8.8% of the patients, an embolic protection system was used, which could have affected the results in both directions. Therefore, in can be concluded, that the Lotus™ valve comes with excellent, and to other published studies comparable, mortality and stroke rates.

The main highlights of the referenced paper are the rate of postoperative pacemaker implantation and the rate of PVL. Among all patients, the 30-day permanent pacemaker implantation rate was 30.0% (27.1%, 33.0%), but 34.6% (31.4%, 37.8%) among all patients without a history of prior pacemaker implantation. It is easy to see, that in the current era of high cost-effectiveness, postoperative pacemaker implantation rates of 30–40% are far above the normal limit and are out of the question. Of course, this might be related to the fact that all valves could have been highly calcified, which could be proven by the calcification score of the native aortic valve, but as the population was an "all-comer" population, it is more likely that the high recoil forces and the implantation height or position within the aortic annulus impacts the conduction system within the left ventricular outflow tract (LVOT) leading to postoperative permanent pacemaker implantation. By the use of balloon-expandable TAVI prostheses and especially when implanted quite "aortic", pacemaker implantation rates are as high as 3.7% (4).

In regard to PVL, of course, the described rates of PVL are extremely low (absent or trace in 92.0%, mild in 11.1% and 0.3% moderate and none severe PVL). One could assume that no post-dilatation was performed in the RESPOND registry in contrast to most other TAVI prostheses. It should be mentioned however, that both baseline and discharge echo core-lab data were available for 89.7% of the patients. The RESPOND registry reported extremely low PVL rates, which are comparable to our prior published results with the balloon-expandable Sapien 3™ prosthesis (Edwards Lifesciences, Irvine, CA, USA), which is also equipped with a sealing skirt. We resulted in a PVL rate of less than mild in 97.8%, 2.2% moderate and also no severe PVL was observed. Interestingly, Falk *et al.* did not report, how the aortic dimensions were assessed. Of course, cardiac multislice-CT was recommended, but detailed data are missing. One could assume, that all participating centers did a meticulous CT and echo screening prior to the TAVI procedure. From our personal experience, not only the sealing technology leads to the desired result of minimizing PVL, but also exact and precise imaging. It is often observed, that patients present with "borderline" aortic annuli between two valve sizes, and it is up to the operators choice to choose the smaller or larger valve, or to postdilate or overinflate the balloon during implantation.

Most recently, a paper has been published comparing the valve performance of the mechanically expanding Lotus™ valve and the balloon-expandable Sapien 3™ prosthesis. Interestingly, less PVL were observed by the use of the Lotus™ prosthesis in comparison to the Sapien 3™ valve (P=0.02). Also on multivariate analysis, the use of the Lotus™ valve was associated with less PVL (OR 0.41 m;

P=0.03) (5), despite a lower cover index with the Lotus™ valve. However, Soliman *et al.* neither present the rate of intraoperative valve retrieval or repositioning of the Lotus™ valve, nor the rate of postoperative permanent pacemaker implantation.

In summary, second-generation TAVI devices, such as the Lotus™ valve, come with excellent 30-day mortality and stroke rates and were absolute safe and efficient in comparison with to other currently available TAVI systems on the market. Postoperative PVL rates might be lower due to the anti-leakage sealing capability and possibility of repositioning of the Lotus™ valve in comparison with other second-generation TAVI devices, but has to be proven in larger, and if possible, randomized trials. On the other hand however, postoperative permanent pacemaker implantation rates are far above the upper limit of other currently available TAVI prostheses on the market. This big issue should be kept in mind when moving into an intermediate or even low-risk TAVI population.

In conclusion, most of the current systems available come with excellent outcomes and were easy to handle, so is the Lotus™ device. Nevertheless, each individual operator should feel comfortable with his local conditions and valve experience, as TAVI results vary quite substantial between different centres. With new generations of TAVI prostheses, mortality rates are excellent, the problem of PVL has been almost resolved, stroke rates are extreme low, and although the rates of permanent pacemaker implantation vary sometimes extreme between different valves substitutes, currently, the only unsolved issue is structural valve deterioration in the long-run, which might be also affected by pre-mounted/pre-crimped and dry-stored valves in the future. The new version of the Lotus™ valve, which is under evaluation to date, incorporates the Depth Guard™ technology, which aims to reduce LVOT interaction, thereby minimizing the risk for permanent pacemaker implantation.

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Footnote

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References

1. Falk V, Wöhrle J, Hildick-Smith D, et al. Safety and efficacy of a repositionable and fully retrievable aortic valve used in routine clinical practice: the RESPOND Study. Eur Heart J 2017. [Epub ahead of print].
2. Meredith Am IT, Walters DL, Dumonteil N, et al. Transcatheter aortic valve replacement for severe symptomatic aortic stenosis using a repositionable valve system: 30-day primary endpoint results from the REPRISE II study. J Am Coll Cardiol 2014;64:1339-48.
3. Wöhrle J, Rodewald C, Rottbauer W. Transfemoral aortic valve implantation in pure native aortic valve insufficiency using the repositionable and retrievable lotus valve. Catheter Cardiovasc Interv 2016;87:993-5.
4. Wendt D, Al-Rashid F, Kahlert P, et al. Low Incidence of Paravalvular Leakage With the Balloon-Expandable Sapien 3 Transcatheter Heart Valve. Ann Thorac Surg 2015;100:819-25.
5. Soliman OI, El Faquir N, Ren B, et al. Comparison of valve performance of the mechanically expanding Lotus and the balloon-expanded SAPIEN3 transcatheter heart valves: an observational study with independent core laboratory analysis. Eur Heart J Cardiovasc Imaging 2017. [Epub ahead of print].

