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Transcatheter Aortic Valve Implantation. Where are we?

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Prospering from the know-how of percutaneous coronary angioplasty, coronary stents and the vast surgical experience with bioprosthetic valves, transcatheter aortic valve implantation (TAVI) – also called percutaneous aortic valve replacement or PAVR - has become a daily clinical reality. It was initially performed via the complex and hazardous antegrade transseptal approach in 2002, which has been replaced by the retrograde transfemoral or antegrade transapical technique[1-4]. In the beginning, the transfemoral approach required surgical access and/closure of the femoral artery, but became the first truly percutaneous technique of aortic valve replacement in 2006[5]. In 2007 the CoreValve company and Edwards Lifesciences obtained CE mark approval for their bioprosthetic percutaneous heart valves with the specification that these valves are intended for patients with a high or prohibitive risk for surgical valve replacement (AVR) or who cannot undergo AVR. Since then an exponential increase of the number of TAVI has occurred. This is what we currently know with certainty. The rest is less certain.

The precise number of patients treated, the number of valves implanted and the number of institutions which perform TAVI, are not known. The exponential growth is remarkable in the absence of sound scientific data indicating or proving the safety and efficacy. The information stems from either physician or industry observational studies which by the nature of their design and execution do not meet the rigorous clinical and scientific standards of randomised trials in which a steering committee carries final responsibility of the data and reporting[6-11].

These observational studies nevertheless reveal the feasibility and applicability of TAVI, which is one of the prerequisites for a treatment to be successful. They also forecast the direction of TAVI and its role in the treatment of patients with aortic stenosis. Even in the absence of a true proof of safety and efficacy, the continuous and ingenious changes in the hardware most likely will be one of the major forces that boost its application, and to which patients and society will positively respond.

As already alluded to, the basis of treatment entails more than practical matters. Many parties are involved with distinct interests and responsibilities. The mandate of the FDA is to "promote the public health by ensuring that medical devices are safe, effective, and available in a timely manner"[12]. This implies that we as physicians, who have the final responsibility for the patients, must provide the evidence. It is a complex issue which contains many questions; the "what", the "how", the "why"…

What do we need to know from a clinical point-of-view? It is more than safety and efficacy, it is also the answer to the question of who should or should not receive TAVI (definition of the responder and non-responder). This may seem an odd question in light of the patients who are currently treated. Still, some of these elderly patients or patients with numerous comorbidities will fare well, and others will not. Patient stratification is important to save patients from being exposed to the risks of a procedure without enjoying the benefit. It is all too easy to think about these studies in terms of endpoints or outcome measures of interest, or about how to define these endpoints and the methods of assessment, as well the type of

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bio-statistical analyses that are needed. It is much more complex on a practical level to carry out these studies, but it is nonetheless possible.

Irrespective of design (observational or randomised), they need to be multicentric and require a complex infrastructure of data collection, verification and analysis. We can follow the example of the Euro Heart Survey and carry out a similar initiative in the framework of the EuroPCR[13,15]. Using EuroPCR, with its stated mission "to contribute to the advancement of education and information in the field of cardiovascular interventions with the aim of reducing the burden of cardiovascular disease" also allows collaboration with industry, regulatory bodies and other authorities. Such an initiative will also allow a scrutiny of the aetiology of some of the periprocedural complications and adverse events during follow-up, whether the event is patient-, procedure- or device-related, in addition to the definition of responder and non-responder. This, in term, will offer proposals for improvement in the domains of indication, procedure and technology. We may then move to less sick or older patients in whom the objective of TAVI is not only improvement in quality-of-life or independence for all Activities Daily Living (ADL), but quality-of-life and longevity.

These population-based studies may also help to understand and/or predict a number of specific procedure related complications, which should receive more attention. For instance, what is the fate of mitral regurgitation if present before TAVI, does TAVI provoke late AV conduction abnormalities which may explain the occurrence of witnessed sudden death as seen in some patients, what are the effects of the almost ubiquitous paravalvar aortic regurgitation after TAVI on the left ventricular function and survival? We seem to accept a moderate degree of aortic regurgitation after TAVI, yet, aortic stenosis is more than a valve disease. The myocardium is involved as well. It makes the question even more intricate when one considers the combined histological effects of age and elevated afterload on the myocardium. When using the CoreValve Revalving system (CRS), of which the frame is 5 cm high, one may question whether we can always easily perform coronary angioplasty when needed after valve implantation. Although the diamonds of the frame are large enough to allow passage of a 6 or 7 Fr guiding catheter, this may not always be straightforward. If true, it may lead to innovations in the technology from which both the patient and the application of TAVI may benefit.

At present, the size of the valve that is implanted is based upon guidelines provided by the manufacturer. Yet, they currently lack a clinical and scientific basis. Specific studies are needed to elucidate the principles upon which the size of the valve is to be selected[15,16]. This obviously also holds for the balloon that is used to crack or stretch the commissures before the valve is inserted.

The list of questions is endless, which is further illustrated by the study reported in this issue[17]. It is a call upon our responsibility and accountability to perform TAVI in the right environment, and to set-up or participate in appropriately organised and designed studies that address a clinical need.

Only then shall we be capable and successful in bringing TAVI where it should be.

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