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Case report

# Evidence of leaflet injury during percutaneous aortic valve deployment

Rachid Zegdi [a,b,*], Patrick Bruneval [a,c], Didier Blanchard [d], Jean-Noël Fabiani [a,b]

[a] Université René Descartes, Paris V, France
[b] Assistance Publique-Hôpitaux de Paris, Service de Chirurgie Cardio-Vasculaire, Hôpital Européen Georges Pompidou, Paris, France
[c] Assistance Publique-Hôpitaux de Paris, Service d'anatomie pathologique, Hôpital Européen Georges Pompidou, Paris, France
[d] Assistance Publique-Hôpitaux de Paris, Service de Chirurgie Cardiologie, Hôpital Européen Georges Pompidou, Paris, France

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**Abstract**

It has been suggested that valved stent deployment during transcatheter aortic valve implantation may be responsible for traumatic injury to pericardial leaflets, especially with balloon expandable valved stents. However, such an injury has not been described nor reported so far. We here report the microscopic analysis of 4 Sapien-Edwards prostheses, 2 of which have been implanted in humans. There was no macroscopic evidence of traumatic injury to the pericardial leaflets of the percutaneous valves. However, pathological microscopic findings were observed in all of them. These mainly consisted of collagen fibers fragmentation and disruption. Areas of non- or mildly affected tissue were adjacent to areas of severely damaged tissue. The entire thickness of the leaflets might be involved. The severity of the lesions also differed among leaflets from a same prosthesis. Areas of plasmatic insudation were identified in one case. The disruption index was significantly higher in the Sapien group in comparison to the control group: 42.4% (14–63.5%) versus 17.5% (9.2–31%) ($p < 0.001$). Although of limited size sample, this study does prove that traumatic injury to leaflets occurs during percutaneous valves implantation. This should prompt physicians to wait for the long-term results of this new technology before extending the indications to low-risk patients.


*Keywords:* Aortic stenosis; Pericardium; Bioprosthesis

## 1. Introduction

Trans-catheter aortic valve implantation (TAVI) has been shown to be feasible in patients with severe aortic valve stenosis through either a retrograde trans-arterial or an antegrade trans-apical access. This new technology is currently under clinical investigation and there is a large consensus to restrict its use to high-risk surgical candidates [1].

It has been suggested that valved stent deployment during TAVI may be responsible for traumatic injury to pericardial leaflets, especially with balloon-expandable valved stents [2]. However, such an injury has neither been described nor reported so far.

## 2. Material and methods

Four Edwards Sapien valves (Edwards Lifesciences, Irvine, CA, USA) were used in this study. Sizes were 23 and 26 mm in two cases each. Two prostheses have been implanted in two high-risk surgical patients. One of these prostheses had been implanted trans-apically. However, the patient died from intractable apical bleeding immediately after implantation and the prosthesis was retrieved at post-mortem examination. In the second case, implantation was performed straightforwardly through a transfemoral access. However, retrograde intraventricular migration occurred within 3 h post-implantation. The patient underwent urgent surgical aortic valve replacement. During the surgical procedure, the prosthesis was gently retrieved through the aortic orifice after native valve resection.

In the first non-implanted case, the prosthesis had been crimped onto the balloon-tipped delivery catheter prior to arterial insertion of the introducer sheath. The procedure was aborted owing to inability to cross the iliac arteries. In the last case, the introducer and the delivery catheter with the crimped prosthesis had to be removed for a technical reason (the stiff guidewire was displaced and was no longer inside the left ventricle). The procedure resumed successfully with another introducer and delivery catheter. In these two last cases, the valved stent was deployed *ex vivo* at the same speed as in clinical practice.

These four Edwards Sapien prostheses (Sapien group) were promptly immersed in a glutaraldehyde solution and subsequently processed for pathological analysis. Samples were analyzed at ×5 and ×20 magnification after Sirius red and hematoxylin and eosin (H&E) staining. A disruption index was defined by the measurement of the relative contribution of

* Corresponding author. Address: Hôpital Européen Georges Pompidou – Service de Chirurgie Cardiovasculaire – 20, rue Leblanc – 75908 Paris, France. Tel.: +33 1 56 09 37 48; fax: +33 1 56 09 22 19.
*E-mail address:* rzegdi@hotmail.com (R. Zegdi).

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the disruption to the pericardial leaflet thickness. This index was determined on two random fields at ×20 magnification for each leaflet. The distances between collagen bundles were measured along 10 equally interspaced lines perpendicular to the long axis of the sample. On each line, the measured distances were summed and normalized to the length of the line. For each field, the mean value of the 10 normalized distances was defined as the disruption index (expressed in percentages).

Fresh bovine pericardium was obtained from a slaughterhouse. Fat was first removed and samples were immersed and stored in a 0.625% glutaraldehyde solution. Ten macroscopically normal fragments (0.30–0.40 mm thickness – control group) were processed for pathologic analysis the same way as the Sapien prostheses.

Results were expressed as median (range). Comparison between quantitative variables was performed with the Mann–Whitney test.

## 3. Results

There was no macroscopic evidence of traumatic injury to the pericardial leaflets of the percutaneous valves: there were no laceration, no dehiscence and no tears. However, pathologic microscopic findings were observed in all of them. These mainly consisted of collagen fiber fragmentation and disruption (Fig. 1).

Areas of non- or mildly affected tissue were adjacent to areas of severely damaged tissue. The entire thickness of the leaflets might be involved. The traumatic lesions, however, were more pronounced at the level of the sub-mesothelium (Fig. 1). The severity of the lesions also differed among leaflets within the same prosthesis.

The prosthesis that migrated toward the left ventricle showed leaflet thrombosis (Fig. 2). Areas of plasmatic insudation were seen close to the leaflets' surfaces (Fig. 2).

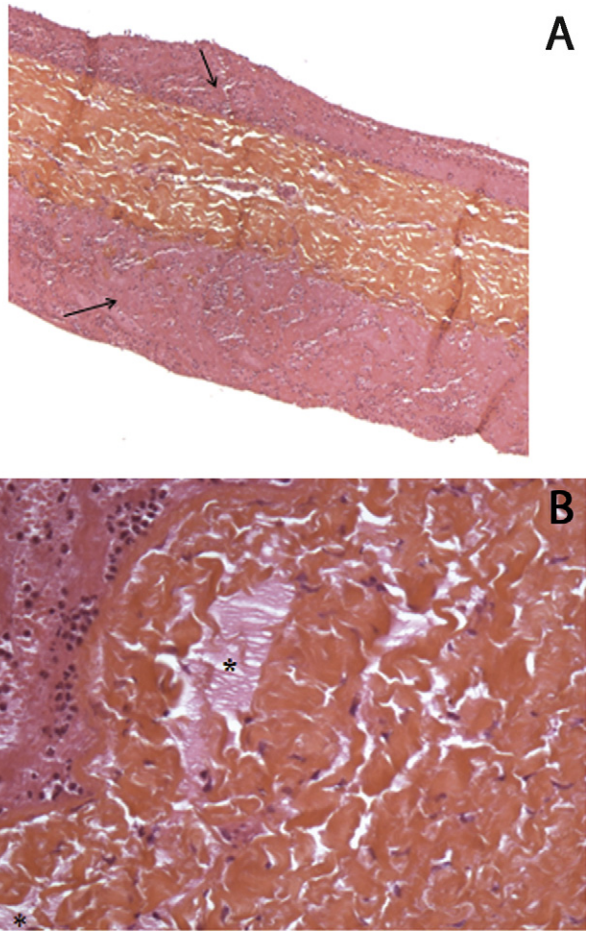


Fig. 2. Microscopic aspect (at low (A) and high (B) magnification – H&E stain) of a pericardial leaflet from a balloon-expandable Sapien-Edwards valve that migrated after its implantation in a patient. The leaflet is covered by thrombosis (*arrows*). Areas of plasmatic insudation are seen close to the leaflet's surface (*).

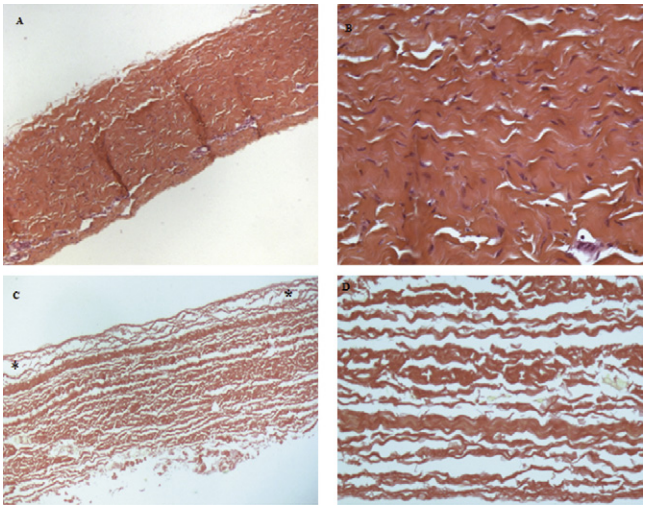

Fig. 1. Typical microscopic aspect of pericardium from the control group (A and B) and a balloon-expandable Sapien-Edwards valve (C and D). In this latter, disruption (*) of the collagen fibers is present across the whole thickness of the leaflet and predominates at the sub-mesothelium level. (Sirius red stain; ×5 (A–C) and ×20 (B–D).

In the control group, the tissue appearance was better preserved (Fig. 1). Wavy collagen bundles were clearly seen. Fractures of collagen fibers were occasionally noticed.

The disruption index was significantly higher in the Sapien group in comparison to the control group: 42.4% (14–63.5%) versus 17.5% (9.2–31%), respectively ($p < 0.001$). There was no statistically significant difference in tissue damage severity (as reflected by the disruption index) between prostheses that had been implanted in patients (two prostheses, six leaflets and 12 fields analyzed) compared with those not implanted: 38.3% (14–63.5%) versus 47.6% (35.8–58.3%), respectively ($p = 0.15$).

## 4. Discussion

Collagen fiber fragmentation and disruption are pericardial lesions that have already been described in explants of failed Ionescu–Shiley's bioprostheses [3]. In the present preliminary study, the lesions described are likely of traumatic origin. They were found immediately after valve deployment. Their marked severity contrasted with the

normal macroscopic appearance of the leaflets after valved stent deployment.

It is unlikely that the traumatic lesions to leaflets were the result of a misuse of the devices. First, injury was found in each of the four prostheses evaluated. Second, manipulation of the prosthesis and the delivery catheter was performed by an adequately trained team with a large experience in TAVI (more than 120 cases performed).

These lesions may have occurred during the crimping and/or the deployment of the prosthesis. During the crimping process, the bovine pericardium is severely folded and compressed. During dilation of the prosthesis, the bovine tissue is subjected to compression and friction against the stent. This is probably why the observed lesions were found to predominate at the level of the 'smooth' surface of the pericardium, which is in direct contact with the stent (when the leaflets are in an open position).

It is difficult to say at the present time whether these traumatic lesions will have an impact on prosthesis durability. This injury was associated with plasmatic insudation within the leaflets, which might secondarily favor leaflet calcification [3].

Rare cases of severe acute intraprosthetic regurgitation have been reported during Edwards Sapien valve implantation. A traumatic injury to the leaflets might be a plausible cause in some of these cases. However, anatomic confirmation was not (and could not be) described, as these cases were successfully managed by valve-in-valve implantation [4].

The medium (5 years) and long-term (10—15 years) durability of percutaneous valves are currently unknown. The present data suggest that this might not be as long (i.e., comparable to surgical bioprostheses) as anticipated. It seems reasonable to wait for long-term data before extending indications of TAVI to patients with low-operative risk.

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Editorial comment

# Pericardial leaflet injury in transcatheter aortic valve implantation: trick or treat

*Keywords:* Pathology; Pericardium; Trans-catheter aortic valve implantation; Valve disease

Trans-catheter aortic valve implantation (TAVI) was introduced in the clinical setting to avoid sternotomy and cardiopulmonary bypass for treatment of aortic stenosis in high-risk patients, otherwise destined to imminent fatal outcome.

Recently, the indication was extended to endovascular treatment of failed bioprostheses (valve-in-valve implantation) to avoid re-operation.

Biological xenograft tissue, because of its pliability to folding during implantation, is employed within a stent, and pericardium appears to be the best.

Pericardium is mostly composed of collagen tissue (fibrosa). The fibrosa is much thicker in bovine pericardium than in porcine cusps, and the amount of hydroxyproline (the main amino acid of collagen) is double in pericardium versus natural aortic cusps [1]. The collagen fibers possess a natural waviness, which allows elasticity during cardiac cycles (Fig. 1).

Unlike the traditional pericardial valve xenografts, in which the pericardium is gently manipulated to mold cusps mimicking the native aortic valve, in TAVI, either through the trans-arterial or the trans-apical approach, the pericardial valve is folded ('crimped') to minimize the size while reaching the final set in the aortic root. In addition, the prosthetic valve is dilated by ballooning, flattening the pericardium against the stent, to attach the stent itself to the aortic root without suturing, so as to avoid device escape and periprosthetic leak.

TAVI is considered a 'compassionate' procedure reserved for terminal patients with severe aortic stenosis, at high risk for surgical valve replacement.

However, as the operation was revealed to be technically feasible and relatively easy to be accomplished, the question arises whether it might be indicated also in low-risk patients, thus becoming a reliable alternative option for any patient with aortic stenosis, who dislikes sternotomy, general anesthesia, and cardiopulmonary bypass.

At present, the attention has been focused mostly on stent profile and performance. The hospital mortality risk has been