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Original Research

Evaluation of Hybrid Surgical Access Approaches for Pulmonary Valve Implantation in an Acute Swine Model

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Percutaneous implantation of the pulmonary valve through peripheral vascular access can be limited due to poor venous access, low patient weight, hemodynamic or rhythmic instability, and size constraints related to the valve. In such cases, hybrid procedures may provide alternatives. Because the most commonly used median sternotomy is unsuitable for chronic trials in large animals, we evaluated several hybrid approaches for pulmonary valve replacement in a swine model. We tested the feasibility of hybrid pulmonary valve implantation in pigs by using inhouse-generated valves containing bare-metal or nitinol stents. Valves consisted of bovine jugular veins, bovine pericardial valves, or sprayed polyurethane valves. Access was achieved through median sternotomy, lower partial sternotomy, transverse sternotomy, or right lateral thoracotomy. The delivery device was introduced in a transventricular manner. Implantation took place under fluoroscopic and epicardial echocardiographic guidance. We achieved implantation of the stented valve in 12 (92.3%) pigs, of which 5 (41.7%) of the implanted valves were in an optimal position. Paravalvular leakage occurred in 2 trials (16.7%). Lower partial sternotomy provided the best trade-off between feasibility and minimized trauma for long-term animal trials. Here we describe our experience with hybrid pulmonary valve implantation in an acute large-animal (swine) model. We demonstrate the feasibility of the procedure in terms of surgical technique and the perioperative management and preparation of the field for a chronic trial.

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The significance of the pulmonary valve is frequently underestimated.[8] However, it is the most commonly operated heart valve, especially in connection with congenital heart disease.[15] In addition, pulmonary regurgitation frequently remains after surgical repair of a pulmonary valve affected by congenital heart disease, such as tetralogy of Fallot, pulmonary atresia, or isolated pulmonary valve stenosis.[13] For a certain time period, this regurgitation seems to be well tolerated.[7,13] However, several studies have shown subsequent negative outcomes, including right ventricular volume overload, right ventricle dysfunction, arrhythmia, and sudden cardiac death.[7,10,14,23] As a consequence, pulmonary valve replacement has become more important. Until recently, a surgical approach was the only option to treat pulmonary regurgitation or stenosis after surgical repair of congenital heart disease affecting the pulmonary valve. Particularly when performed with the median sternotomy access, this approach offers the best overview of the operative site and the possibility to quickly choose to perform cardiopulmonary bypass (if necessary).[9,15]

Numerous diverse options have been developed for replacement of pulmonary valves, such as homografts,[1,21] Hancock[5] and Contegra[16] conduits (Medtronic, Minneapolis, MN), and other alternatives.[17,25,39] Common disadvantages are the limited durability of the replaced valve due to calcification with stenosis, regurgitation, and intimal peel as well as lack of growth.[7,9,15] Thus, these patients need many reoperations,[27] and every reoperation is associated with an increased risk of cardiac damage due to resternotomy, harmful bleeding, infection, and myocardial or neurologic injury from cardiopulmonary bypass.[27,36] Consequently, the correct timing of pulmonary valve replacement is of particular importance: soon enough to prevent right ventricular damage but late enough to keep reoperation rates low.[35]

In 2000, a new, less invasive technique[9] to prolong conduit lifespan and to treat valve stenosis or regurgitation was published:[32] a bovine jugular valve sutured into a platinum stent is implanted into the pulmonary valve position through percutaneous access of the femoral vein.[7,9] With this method, pulmonary valve stenosis or regurgitation can be corrected, and the risks associated with reoperation can be avoided.[27] Follow-up studies have demonstrated favorable results.[10,11,28] But despite these promising results, this new technique has several limitations. For example, low patient weight, poor vascular access, tortuous course of delivery sheaths, and hemodynamic and rhythm instability due to large delivery catheters can be challenging or even limiting factors to a percutaneous approach.[4,27,37]

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An alternative method to avoid these limitations is a hybrid approach, in which optimal access is provided surgically, whereas the procedure is performed in interventional technique.[37]

The standard access for most heart operations is the median sternotomy. However, the Governmental Animal Protection Committee did not approve median sternotomy for a previous chronic large animal trial in pigs because of the instability of the pectoral girdle after the operation; initially the sternum is very vulnerable and unstable after median sternotomy, even if closed anatomically correctly. To avoid this problem, an alternative means of access is required.

Therefore, the main aim of our current study was to evaluate in an acute pig model different means of access for minimally invasive pulmonary valve replacement that would be suitable for a future, chronic trial. A secondary objective was to obtain preliminary data regarding possible valves and stents for use in this model. The results from this current study assessing various means of access can then be used in future chronic trials in pigs to facilitate more precise evaluation of an increased number of valves and stents during minimally invasive pulmonary valve implantation.

Materials and Methods

Animals. This study used male and female German Landrace×Piétrain crossbred and purebred German Landrace pigs (*Sus scrofa domesticus*; conventional husbandry; age, 3 to 4 mo; body weight, 25.5 to 41.5 kg; $n = 13$) purchased from the university farm (Oberschleissheim, Germany). All experiments were conducted in the laboratory for Surgical Research at the Walter Brendel Centre of Experimental Medicine at Ludwig-Maximilian University (Munich, Germany). The study protocol was approved and accepted by the local Governmental Commission on the Care and Use of Animals.

The pigs were preoperatively housed at the animal facilities of the Institute for Surgical Research at the Walter Brendel Centre of Experimental Medicine. Each box stall (1.5 m × 2.0 m) housed 2 animals, with access to an additional roofless run (4.0 m × 4.0 m). The air temperature was between 22 and 24 °C with an average humidity of 24%. The pigs were fed once daily with a commercial pelleted pig feed suitable for laboratory animals, with unrestricted access to water. Preoperative fasting was maintained for 12 h; water remained available.

Anesthesia and surgical preparation. The anesthesia and surgical preparation protocols have already been described in detail.[29,30] In short, premedication comprised azaperone (2 to 10 mg/kg IM), ketamine (10 to 15 mg/kg IM), and atropine (0.5 to 1 mg IM). After ear vein cannulation, midazolame (0.1 mg/kg IV) was administered, and then general anesthesia was induced and maintained with propofol (induction, 1 to 2 mg/kg IV; maintenance, 4 to 10 mg/kg IV hourly) and fentanyl (induction, 0.02 mg/kg IV [maximum]; maintenance, 0.045 mg/kg IV hourly). To prevent ventricular arrhythmia, amiodarone (20 mg/kg IV daily) and intravenous magnesium were administered. Heparin was injected intravenously before vessel preparation (5000 IU) and before thoracotomy (10,000 IU), with additional acetylsalicylic acid (500 mg) as thromboembolic prophylaxis. Furthermore, pancuronium bromide (4 mg IV) was given before sternotomy or thoracotomy for muscle relaxation and paralysis during opening of the thoracic cavity.

The pigs were endotracheally intubated under laryngoscopy; tube size varied according to animal size and weight. Volume-controlled ventilation was performed, with a positive end-expiratory pressure of 4 mm Hg. The FiO_2 was 100% initially; after normalization of oxygen saturation, oxygen flow was reduced to maintain FiO_2 around 45%. Arterial blood samples were taken to monitor paO_2, $paCO_2$, and pH. Throughout the procedure, the electrocardiogram and vital parameters including blood pressure, heart rate, oxygen saturation, and temperature were monitored continuously.

Surgical preparation was performed as described elsewhere.[29,30] The planned operative areas were shaved: the right or left neck for dissection and the respective area for thoracotomy or sternotomy. First, the external carotid artery and jugular vein were exposed surgically; the artery was cannulated by using a 7-French introducer sheath, whereas vein cannulation used an 11-French introducer sheath. Arterial and central venous pressures were monitored continuously.

Surgical approach. We used 4 different thoracotomy methods to gain access to the heart for valve implantation. In 5 cases, a median sternotomy was performed, in which the animal was placed in dorsal recumbency and an incision made prior to sternotomy. The pericardium was opened by using a 10- to 12-cm craniocaudal incision, the heart was exposed, and pericardial positioning sutures were fastened on each side. For puncture preparation, 2 pursestring sutures (4-0 polypropylene) were applied on the right ventricular wall very close to the acute margin.

In one case, a transverse sternotomy was performed (Figure 1). The animal was placed in dorsal recumbency. A transverse incision was located at the caudal base of the forelegs; the left and right mammary arteries were harvested and ligated. After sternotomy, the pericardium was incised by using a 10- to 12-cm craniocaudal cut, and both the pericardial positioning sutures on each side and the 2 pursestring sutures at the puncture site were applied to the right ventricular wall of the heart. In another case, a right lateral thoracotomy was performed, in which the pig was placed in left lateral recumbency. The skin incision was L-shaped and located at the upper part of the fifth rib. After thoracotomy, the pericardium was incised by using a 10- to 12-cm craniocaudal cut and fixed with sutures on each side. Finally, 2 pursestring sutures (4-0 polypropylene) were applied on the anterior aspect of the right ventricular wall. In the remaining 5 cases, a lower partial sternotomy was used (Figure 2). The pig was placed in dorsal recumbency, a skin incision was made, and only the lower two thirds of the sternum were opened; the cranial part remained unmanipulated and stable. After the pericardium was opened by using a 10- to 12-cm craniocaudal incision, pericardial positioning sutures were placed on each side, the 2 purse-string sutures were applied to the puncture area of the heart on the right ventricular wall.

A radiopaque strap, fixed with 2 stitches above the pulmonary annulus, was placed for easier localization of the pulmonary valve during fluoroscopy.

Imaging. The entire procedure was performed under fluoroscopic (ExpoScop 8000, Ziehm, Nürnberg, Germany) and epicardial echocardiographic (Hewlett-Packard, Andover, MA) guidance. Preoperatively, an ultrasonic probe in the 2- to 4-MHz range (model s4, Philips Healthcare, Andover, MA) and an ultrasonic probe in the 5- to 12-MHz range (model s12, Philips Healthcare) were applied intraoperatively directly at the heart.

Stents and valves. We tested several valved stents for use in this study. In 10 cases, 26-, 30-, and 39-mm balloon expandable cobalt chromium stents were used. In the 2 remaining cases, a self-expandable nitinol stent was used.

Three types of valves were used in these procedures: conventional valves from a bovine jugular vein or pericardial valve, as well as a novel sprayed polyurethane valve.

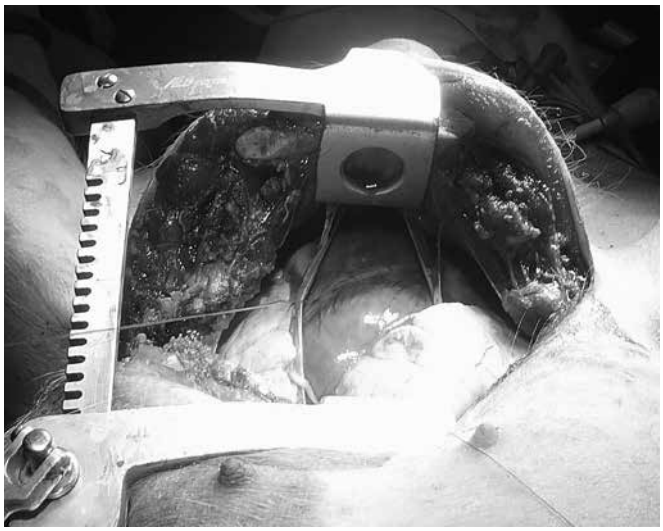

Figure 1. Surgical overview by using transverse sternotomy to gain access to the heart for minimally invasive transventricular pulmonary valve implantation; the heart is visible through the opened pericardium, which has been fixed with positioning sutures.

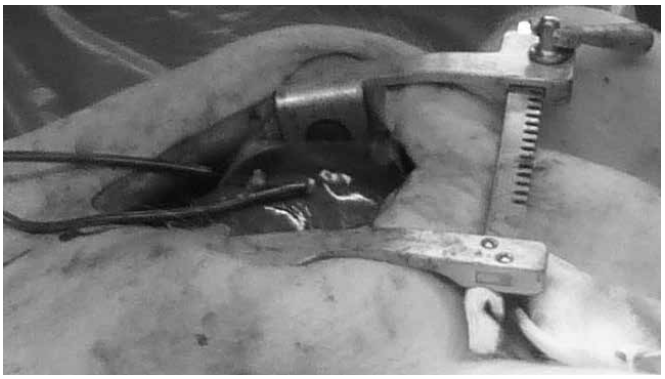

Figure 2. Lower partial sternotomy as a means to gain access to the heart for minimally invasive transventricular pulmonary valve implantation; pursestring sutures and a tourniquet are already applied.

Procedural details. To reach the right ventricle, one of the thoracotomy methods described earlier was used. The stented valve was implanted on the beating heart through direct access to the right ventricle under fluoroscopic and epicardial echocardiographic guidance.

Before implantation, the stented valve was either crimped on the balloon catheter or placed in the implantation device for self-expandable stents. To implant a valve that was sutured in a balloon expandable stent, the 23- or 26-mm Ascendra transapical delivery system (Edwards Lifesciences, Irvine, CA) was used. The self-expandable nitinol stent with valve was placed by using the Talent implantation device (Medtronic, Santa Rosa, CA).[3]

To gain access to the right ventricle, the prepared Teflon-armed pursestring suture–framed area was lanced. First, a guide wire was launched, to direct the implantation route. Then, a 7-French sheath and Judkins catheter were inserted and subsequently exchanged for a stiff Cook wire. After that, the implantation sheath with the mounted stented valve was introduced by using the wire. Under fluoroscopic control, the stent was placed precisely on the marked annulus of the native valve (Figure 3).

The bare metal stent was implanted by using balloon dilatation; the valved nitinol stent was implanted by withdrawing the cover sheath. After removal of the implantation device, the right ventricle was closed by tightening the pursestring sutures.

Measurements. Various hemodynamic measurements were performed by using the Swan–Ganz catheter during the procedure: after access of the jugular vein and external carotid artery, just before valve implantation, and finally after implantation, when the implantation device was completely removed and the right ventricle was closed. Parameters measured included arterial blood pressure, central venous pressure, right ventricular pressure, pulmonary arterial pressure, and wedge pressure; blood gas analysis was performed before and after valve implantation.

Before implantation, the annulus of the native pulmonary valve was measured by using echocardiography. After implantation, ultrasonography was used to examine stent position, paravalvular leakage, possible valve insufficiency, and stenosis.

Endpoint. After the final measurements, the pigs were euthanized through intravenous administration of potassium chloride during general anesthesia, and the procedure was terminated. After heart explantation, the position of the valved stent, its anchorage, and damage of the valve or the stent (such as stent fracture, valve deformation, and possible new valve insufficiency) were assessed.

Statistical analysis. For statistical analysis, SPSS version 23 (IBM, Armonk, NY) and Microsoft Excel 2013 (Microsoft, Redmond, WA) were used. Continuous variables are presented as mean ± 1 SD. For categorical variables, percentages of the categories are given.

Results

Implantation of the pulmonary valve was achieved in 12 (92.3%) of the 13 swine. The remaining animal died during a very complicated intubation process and the consequences thereof (tracheal perforation, pneumothorax), well before the trial. Therefore, no access method was chosen in this case.

A summary of all trials with details regarding the laboratory animals, access method, implanted stent and valve, and procedure duration is given in Table 1. The different approaches for gaining access to the heart are compared in Table 2.

One major complication during the procedure was the occurrence of ventricular fibrillation, which occurred in all cohorts—in 3 of the 5 pigs that underwent median sternotomy, in the 2 pigs that underwent sternotomy (either right lateral or transverse), and in 1 of the 5 swine that underwent lower partial sternotomy. During median sternotomy, ventricular fibrillation occurred after valve implantation in 2 pigs and when the Judkins catheter was used to place a wire in the remaining animal. During right lateral thoracotomy, bleeding control of the arteria thoracica interna triggered ventricular fibrillation. With transverse sternotomy, ventricular fibrillation occurred due to coronary artery obstruction when placing the introducer sheath. Placement of pursestring sutures at the right ventricle triggered ventricular fibrillation during lower partial sternotomy. External defibrillation interrupted ventricular fibrillation in 4 cases, but the remaining 2 cases of ventricular fibrillation did not revert despite treatment. Whereas 1 of the 2 cases of refractory ventricular fibrillation occurred after valve implantation and therefore did not affect the implantation procedure, the other case started after access to the heart was achieved, prior to valve implantation. As a result, the valve-carrying stent eventually was implanted into a dead pig.

The overall diameter (mean ± 1 SD) of the native pulmonary annulus in the 12 pigs (measured by using ultrasonography) was 16.7 ± 4.0 mm. Stent diameter ranged from 19 to 30 mm.

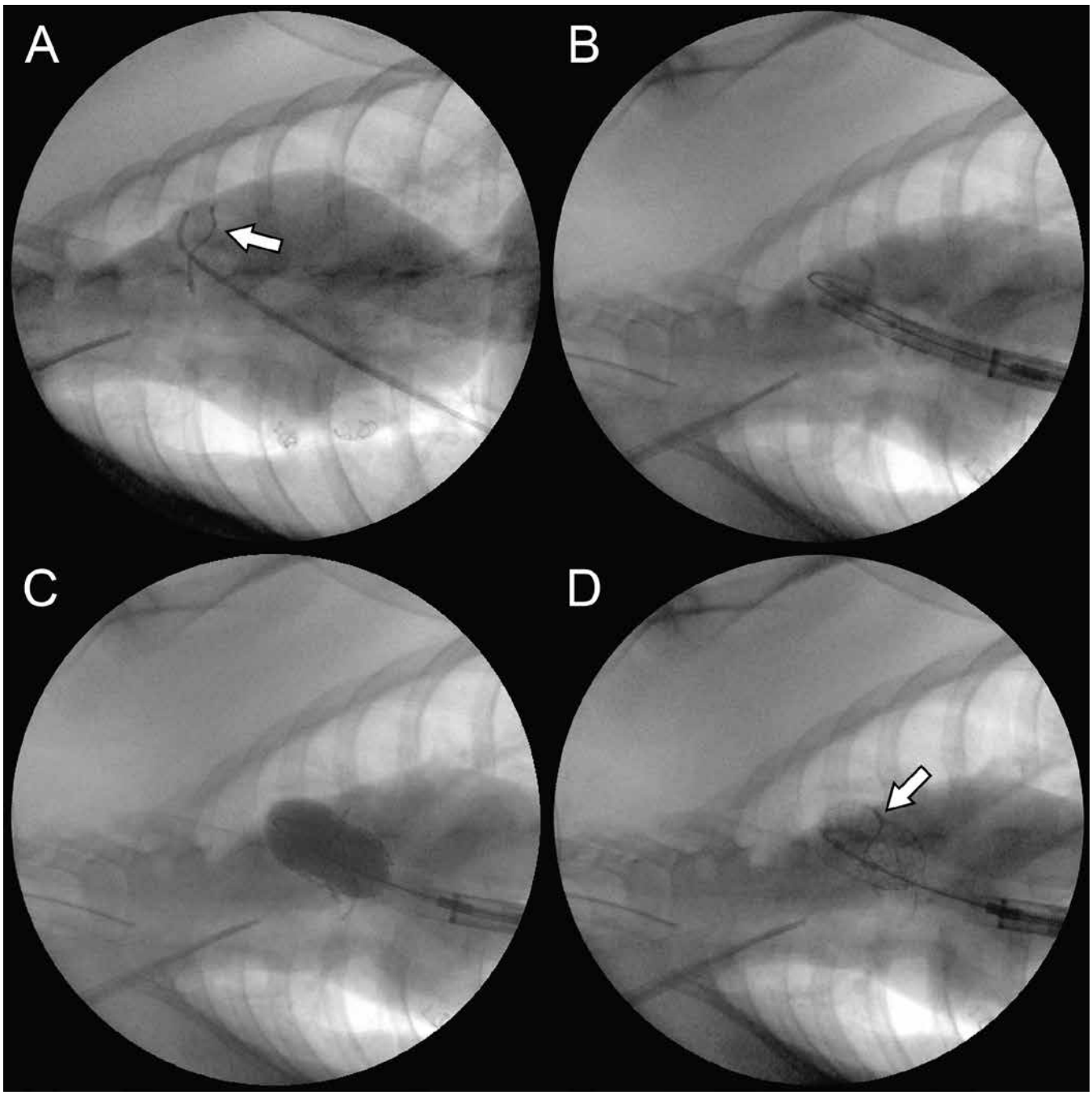

Figure 3. Intraprocedural cineangiograms. (A) Preimplantation overview. The white arrow indicates a radiopaque strap, fixed above the pulmonary annulus, for localizing the pulmonary valve during fluoroscopy. (B) Crimped stent with attached valve placed in pulmonary position before balloon dilatation. (C) Implantation of valved stent through balloon dilatation. (D) Implanted valved stent placed in pulmonary position according to the pulmonary annulus mark (radiopaque strap). White arrow indicates radiopaque strap that is fixed above the pulmonary annulus.

Table 3 contains the hemodynamic data before valve implantation; Table 4 includes the measurements afterward. The difference between the calculated RV to PA gradient before and after valve implantation was 9.7 ± 16.5 mm Hg. In 2 pigs (16.7%), the implanted stented valve was too large for the native annulus. The stented valve was optimal placed in 5 of the 12 cases (41.7%; Figure 4).

In 2 trials (16.7%), paravalvular leakage could be measured after implantation. The first case occurred due to the 'hammock effect'[28] after median sternotomy; the second case occurred due to kinking of the stent in the proximal lumen after lower partial sternotomy. In all 12 animals, a bench test[8] after heart explantation and removal of the implanted valve showed no insufficiency of the stented valve. Stent fracture occurred in just 1 case (8.3%).

Discussion

Patients with congenital heart disease involving the pulmonary valve need several reoperations throughout their lifetimes.[2,27] In these cases, preservation of the patient's own valve or, after surgical repair, preservation of the conduit is of great importance.[13,33,34] The innovative method to percutaneously

Table 1. Summary of all trials, with details regarding access method, valve and stent types, and duration of the procedure

Animal	Weight (kg)	Mode of access	Valve type	Stent	Procedural time (hh:mm)
PK1	31	median	jugular vein	bare metal	02:30
PK2	38	median	jugular vein	bare metal	01:55
PK3	31	transverse	jugular vein	bare metal	02:19
PK4	41	right lateral	jugular vein	bare metal	03:24
PK5	26	median	pericardial	bare metal	02:40[a]
PK6	25.5	median	pericardial	bare metal	01:40
PK7	35	median	pericardial	bare metal	04:30
PK8	34	lower partial	polyurethane	nitinol	02:30
PK9	41	lower partial	polyurethane	nitinol	03:20
PK11	38.5	lower partial	pericardial	bare metal	03:15
PK12	41.5	lower partial	polyurethane	bare metal	01:55[b]
PK13	40	lower partial	polyurethane	bare metal	03:05
Mean ± 1 SD	35.2 ± 5.8	—	—	—	02:45 ± 00:48

Animal PK10 was not analyzed because it died before the trial.
[a]PK5 developed lethal ventricular fibrillation right after the valve implantation; the reported time represents the duration from hemodynamic measurements before the intervention through thoracotomy and valve implantation (no hemodynamic measurements after the intervention)
[b]PK12 developed lethal ventricular fibrillation after the lower partial sternotomy during the puncture preparation; the reported time represents the duration from hemodynamic measurements before the intervention through thoracotomy and valve implantation (no hemodynamic measurements after the intervention)

Table 2. Comparison of the different approaches to gain access to the heart for hybrid valve implantation.

	Aorta	Pulmonary artery	Right atrium	Left atrium	Right ventricle	Left ventricle	Complications
Median sternotomy	++	++	++	++	++	++	↓
Transverse sternotomy	—	—	+	- -	++	++	↑
Right lateral thoracotomy	—	- -	++	- -	++	+	↑
Lower partial sternotomy	+	+	++	+	++	++	↓

++, very good visibility; +, sufficient visibility; –, moderate visibility; —, poor visibility; ↑, numerous complications; ↓, fewer complications

implant a pulmonary valve via peripheral venous access offers a new, less invasive treatment method to prolong conduit lifespan and to treat valve stenosis or regurgitation.[32] However, known challenges and limitations associated with the percutaneous approach include low patient weight, poor vascular access, rhythm disturbances, and hemodynamic compromise due to the passage of large delivery catheters in small infants.[4,37]

A hybrid approach that combines the benefits of surgery and intervention might avoid these problems.[37] Compared with the percutaneous approach, the clear advantages of the hybrid approach include (i) more rapid access for rescue cardiopulmonary bypass and (ii) the opportunity to perform banding or secure stitches during the same procedure as for valve implantation.[12]

Following the axiom that 'smaller is better,'[37] some case reports describe minimally invasive pulmonary valve implantation through a subxyphoidian approach or transverse mini-thoracotomy.[18,20] More frequently published is the hybrid approach, comprising median sternotomy and direct valve implantation by means of right ventriculotomy. One group recently demonstrated the feasibility of implanting a self-expandable, valved stent off-bypass in the pulmonary position in 6 adult pigs.[43] Two other groups published their experiences with median sternotomy and direct off-bypass transventricular pulmonary valve implantation.[6,38]

In the current study, we initially used the median sternotomy as approach to prove the feasibility of implanting the pulmonary valve via a direct ventriculotomy in our setting. In addition, we used this approach to establish the best possible surgical overview for comparison. We were able to confirm the previously described results[6,38,43] regarding implantation of a pulmonary valve through median sternotomy and direct transventricular access. Although median sternotomy offers the best surgical overview and cardiac approach, it breaks the 'smaller is better' rule.[37] In addition, median sternotomy is unsuitable for long-term trials involving pigs because the Governmental Animal Protection Committee has not approved median sternotomy for a chronic large animal trial in pigs given the instability of the pectoral girdle after the operation. Therefore, the primary goal in our acute porcine model was to develop and evaluate various access pathways for minimally invasive transventricular pulmonary valve implantation. Important criteria for optimal access are an ideal surgical overview, comparable to the median sternotomy, with an easy approach to the right ventricle and pulmonary artery, sternal stability, a low complication rate, high safety, and easy reproducibility.

We evaluated a transverse sternotomy approach that included an extended, lateral subxiphoidal incision[26] to provide sufficient cardiac visibility. As early as 1971, researchers have chosen a transverse approach for heart transplantations in pigs.[41] They described the access for their indication as being optimal, but because of the amount of tissue cut and exposed, this method is also most traumatic.[41] The transverse sternotomy that we used in our current trial did not provide ideal access to the pulmonary artery and aorta. A high complication rate paralleling the trauma of the approach was confirmed by the high hemodynamic instability and ventricular fibrillation during the procedure.

Table 3. Hemodynamic data before valve implantation

Animal no.	BP (mm Hg)	RVP (mm Hg)	PAP (mm Hg)	PCWP (mm Hg)	Calculated systolic RV to PA gradient (mm Hg)
PK1	91/52 – 66	33/10 – 17	31/15 – 21	13	2
PK2	107/73 – 90	35/8 – 19	32/17 – 23	13	3
PK3	96/52 – 71	30/6 – 15	25/14 – 19	11	5
PK4	115/66 – 84	45/8 – 26	45/24 – 36	14	0
PK5	89/47 – 60	17/10 – 14	19/13 – 17	11	–2
PK6	90/49 – 64	31/8 – 17	22/18 – 20	11	9
PK7	126/46 – 68	35/1 – 14	37/17 – 25	7	–2
PK8	96/54 – 71	24/0 – 10	24/12 – 18	6	0
PK9	114/76 – 93	34/0 – 14	30/14 – 21	7	4
PK11	109/52 – 69	34/0 – 13	30/1 – 12	8	4
PK12	111/47 – 67	35/0 – 15	30/9 – 20	13	5
PK13	103/49 – 65	28/0 – 11	23/3 – 13	5	5
Mean	104/55 – 72	32/4 – 15	29/13 – 20	10	3
SD	12/10 – 11	7/4 – 4	7/6 – 6	3	3

Animal no. shows all test animals; PK10 not analyzed (test animal which died before the trial); BP: blood pressure; RVP: right ventricular pressure; PAP: pulmonary arterial pressure; PCWP: pulmonary capillary wedge pressure; RV: right ventricular; PA: pulmonary arterial; SD: standard deviation; Values of BP and PAP are shown as systolic/diastolic – mean ; RVP is shown as systolic/diastolic – end-diastolic.

Table 4. Hemodynamic data after valve implantation

Animal no.	BP (mm Hg)	RVP (mm Hg)	PAP (mm Hg)	PCWP (mm Hg)	Calculated systolic RV to PA gradient (mm Hg)
PK1[a]	50/30, 38	37/9, 18	n/a	n/a	n/a
PK2	69/48, 55	28/6, 19	29/16, 20	12	–1
PK3	82/33, 45	29/4, 18	31/20, 26	11	–2
PK4	68/44, 56	65/8, 31	35/22, 28	13	30
PK5[b]	n/a	n/a	n/a	n/a	n/a
PK6	82/46, 58	37/0, 16	26/12, 18	6	11
PK7	99/46, 63	50/0, 19	10/2, 5	4	40
PK8	91/46, 57	48/1, 19	33/16, 22	6	15
PK9[a]	n/a	41/8, 18	30/14, 22	8	11
PK11[a]	67/56, 60	40/0, 20	37/16, 27	n/a	3
PK12[c]	n/a	n/a	n/a	n/a	n/a
PK13	80/36, 51	29/5, 16	21/11, 16	11	8
Mean	76/43, 54	40/4, 19	28/14, 20	9	13
SD	15/8, 8	12/4, 4	8/6, 7	3	14

Animal PK10 was not analyzed because it died before the trial; BP: blood pressure; RVP: right ventricular pressure; PAP: pulmonary arterial pressure; PCWP: pulmonary capillary wedge pressure; RV: right ventricular; PA: pulmonary arterial; SD: standard deviation; Values of BP and PAP are shown as systolic/diastolic, mean; RVP is shown as systolic/diastolic, end-diastolic.
[a]PK1, PK9 and PK11: missing data not available (n/a) due to measurement error
[b]PK5 died due to ventricular fibrillation right after valve implantation
[c]PK12 died due to ventricular fibrillation after the lower partial sternotomy during the puncture preparation

Right lateral thoracotomy is a well-known access method among those used for studies on atrial septal defect closure.[24] In sheep, right lateral thoracotomy typically is used for right heart procedures, [19] but this route gave sufficient access to pigs' right atrium and ventricle only. The obvious disadvantages with this method are the lack of access to the pulmonary artery and aorta and the increased complication rate.

We found here that lower partial sternotomy is an ideal approach for a transventricular valve implantation. The upper part of the sternum is not opened, and the stability of the pectoral girdle and thorax is retained. Both ventricles, pulmonary artery, and aorta are sufficiently accessible. This access method exhibited high reproducibility and a low complication rate. Another group chose this same approach for transapical mitral valved stent implantation in pigs.[31] Regardless, for all approaches in pigs, the valve was implanted safely, without any demonstrable damage after explantation.

A relevant complication associated with the different access methods was the development of ventricular fibrillation, which occurred in 6 animals overall: 3 times in connection with median sternotomy and once each in connection with right lateral thoracotomy, transverse sternotomy, and lower partial sternotomy. In just one case—right lateral thoracotomy—was the chosen access method the trigger for ventricular fibrillation. Regarding

Figure 4. Explanted heart; longitudinal cut along the right ventricular outflow tract. View from pulmonary artery to right ventricle; the implanted stented valve is in the optimal pulmonary position. The pulmonary annulus is marked with a radiopaque strap.

transverse sternotomy, the use of the introducer sheath triggered ventricular fibrillation. A possible reason for this effect might be a narrow approach or adverse angle for implantation. For the 3 other cases associated with median sternotomy, ventricular fibrillation occurred after or during valve implantation itself, regardless of the access method. The last case of ventricular fibrillation occurred after lower partial sternotomy, during placement of the pursestring sutures in preparation for implantation, irrespective of the method of access.

For studying valve replacement, multiple animal models exist. Although the ovine model might be considered the 'gold standard,'[22] the porcine model offers several advantages, including economic and husbandry benefits;[40] anatomic similarities of the porcine heart to humans';[22,40] and the resemblance to human anatomy in regard to the shape of the thoracic cavity and orientation of the heart,[42] all of which make pigs a more suitable laboratory animal for our study.

Because we focused mainly on different methods of access to the heart, we considered sheep a suboptimal laboratory animal for our study because of its very narrow sternum, which makes median sternotomy rather unfavorable for cardiac studies due to technical difficulties.[19] In contrast, in pigs, median sternotomy[40,43] and lower partial sternotomy are, as shown in our current study, technically feasible without restrictions. In addition, transverse sternotomy or lateral thoracotomy are technically feasible but carry greater risk for possible complications. The possible complications that arose in our study with the various access methods might likewise occur in similar hybrid approaches in humans.

This study has several limitations. It is a single-center investigation, with few test animals. First, due to the few test animals, not every stent could be used with every valve in connection with every possible access method: with 12 test animals, we used 3 valve types (pericardium, bovine jugular vein valve, and sprayed polyurethane), 2 types of stent (balloon and self-expandable), and 4 access methods. Therefore, no specific conclusion with regard to the prosthesis can be made. Second, the clinical relevance of some of the valves we used is currently rather low, given that they were fairly newly developed and not yet established. For specific evaluation of several different valve types, a long-term animal trial is required. Third, the low number of test animals limited the statistical analysis that was possible. Fourth, to achieve more profound and statistically significant results in terms of feasibility, a greater number in animals is necessary. Especially concerning the question whether a hybrid approach is safer than a traditional approach, a greater number of test animals and a chronic trial model are required.

In conclusion, the current study describes our experience with different approaches to a hybrid method of pulmonary valve implantation in an acute large animal model. We were able to demonstrate the feasibility of the procedure, especially in terms of optimal surgical access method and perioperative management. By testing different methods for accessing the heart, we ascertained the most preferable approach for future long-term large animal trials in pigs concerning not only the pulmonary valve but also the right side of the heart.

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