Min Invas Ther & Allied Technol 2000: 9(3/4) 287–292

Aortic and venous valve for percutaneous insertion

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Summary

The purpose of this paper is to present *in vitro* and *in vivo* experimental evaluation of a new, artificial, bicuspid, aortic and venous valve. Valves were constructed from square stents with barbs covered by porcine small intestine submucosa (SIS). A valve 15 mm in diameter was tested in a flow model (2.5 l/min) with pressure measurement. A 100-ml rubber bag attached to a side arm of the flow model simulated heart ejection fraction. In acute (n=6) and short-term (n=3) experiments conducted in four swine and four dogs, valves ranging from 16 - 28mm in diameter were placed into the ascending aorta through 10 F sheaths; three were placed subcoronary and six in a supracoronary position. Function and stability of the valves were studied with pressure measurements and aortograms. Three short-term animals were sacrificed for gross and histologic evaluation at one, two and four weeks respectively. In an acute experiment, venous valves with four barbs were placed into the IVC through an 8 F guiding catheter in three dogs. For longer-term testing, valves were placed into the IVCs and iliac veins of three young swine. The animals were followed up after two weeks with venograms, then were sacrificed for gross and histologic evaluation.

Keywords

aortic valve, venous valve, stents and prostheses, interventional procedures, experimental, biomaterial

Introduction

Expandable stents have been widely used for more then 10 years in the treatment of obstructions in vascular and nonvascular systems. Expandable stents also have a great potential as carriers of percutaneously-placed intravascular devices. They have been explored as carriers for an inferior vena cava filter [1–6], a vascular occluder [7], a prosthetic venous valve [8], a Monodisk for closure of cardiac septal defects [9] and a prosthetic aortic valve [10–12]. Self-expandable Gianturco Z- stents served as carriers for most of these devices. We present a report on a new stent, a self-expandable square stent, and its potential as a carrier for a venous and aortic valve.

Square stent

The square stent was constructed in our research laboratory from stainless steel wire 0.006–0.02" diameter. Selection of the wire diameter depends on the desired size and degree of expansile force of the square stent. The selected wire was hand-bent, on a wooden template with fixed metal pegs enabling bending the wire into an exact square. Stent sizes ranging from 5 mm to 50 mm can be made. The corners of the square stent were coil-bent, to reduce stress and fatigue of the stent. When barbs are needed for better fixation of the square stent, one or both wire ends were extended 1–2 mm over the stent frame to form a barb(s) on one or both sides of the stent. One, two or more anchoring barbs can be attached to the other side of the square stent with metal cannullae. Square stents can be made as a single stent (Figure 1 a, b, c), or connected by an elongated barb into combination of two or more stents. These combinations can be made of stents of

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various sizes and lengths, and with different degrees of expansile force.

Venous and aortic valve

The square stent becomes a valve when the stent with barbs on all four corners is covered with low porous material, such as small intestine submucosa (SIS) or polytetrafluoroethylene (PTFE) (Figure 2 a, b, c). SIS provides an acellular framework that becomes remodeled by host tissue, while being degraded and reabsorbed over time [13]. This makes SIS a unique covering for intravascular devices.

Venous and aortic valve have the same construction and differ only by the sizes of the square stent and diameter of the wire from which they are made. The square stent has four barbs and its diagonal axis is constrained to the length of πr, forming a diamond (rhombus or two equal triangles) in order to fit in the vein or aortic circumference of $2\pi r$. For veins 15 mm in diameter, a diagonal axis of 20 mm square stent is constrained to 22 mm and for a 30 mm aorta diagonal axis of 40 mm square stent is constrained to 46 mm.

Two separate triangular pieces of SIS were sutured to the square frame with 7.0 Prolene monofilament, running sutures allowing for the gap between the diagonal axes. The valve was front-loaded into a guiding catheter; the 15 mm venous valve was loaded into an 8 F guiding catheter, the 40 mm aortic valve into a 10 F guiding catheter. For deployment a special

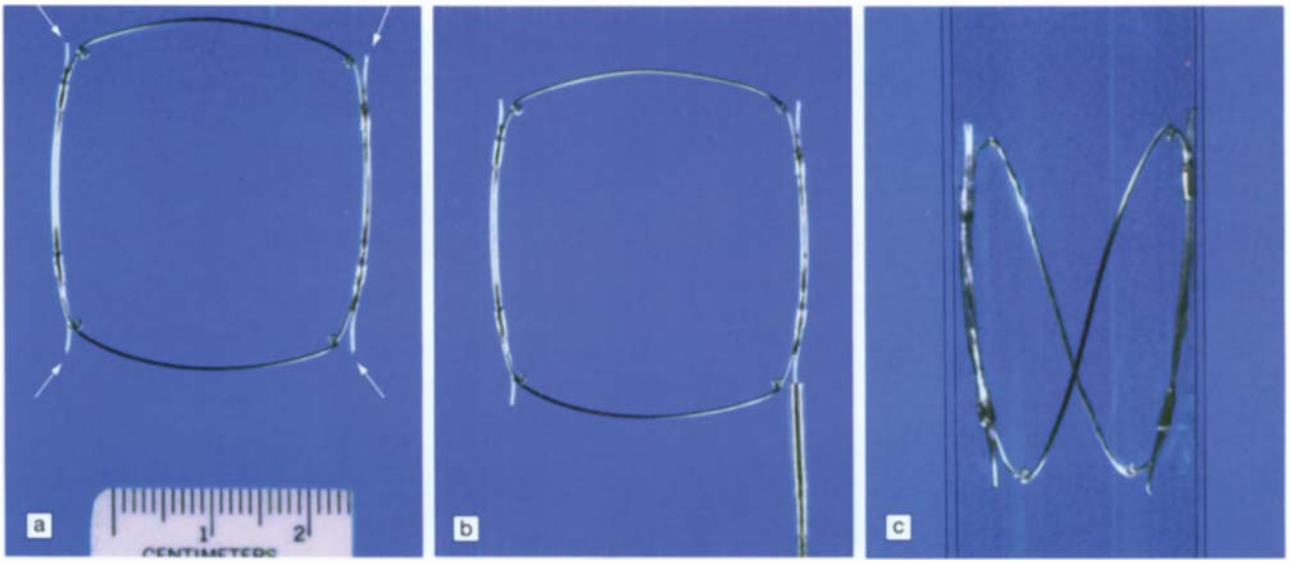

Figure 1. The square stent. **(a)** Single square stent 28 mm in length with four barbs for self-attachment to the vessel wall (arrows). **(b)** Square stent retained by wire pusher connected to one barb. **(c)** Square stent deployed into a tube 20 mm in diameter.

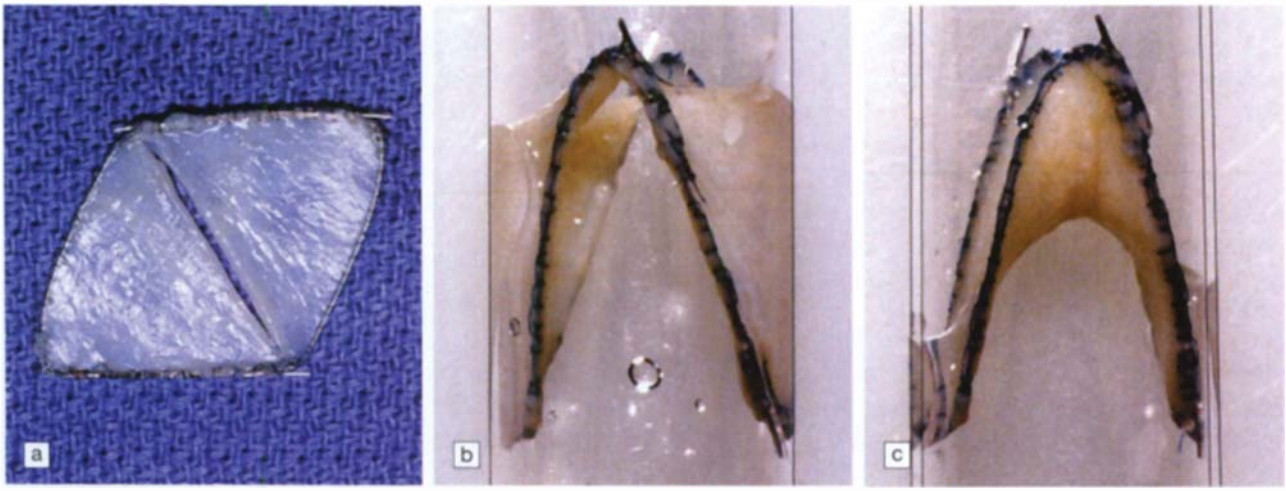

Figure 2. Valve design. **(a)** Non-restricted valve 20 mm in length with four barbs. **(b)** Deployed valve in a plastic tube, open position. **(c)** Deployed valve in a plastic tube, closed position.

pusher, with a small hook at its end was used. It assured valve placement in proper position and prevented its dislodgement by blood flow before its barbs engage into the vessel wall. The valve was self-expanding so that the valve automatically assumed its operational form upon insertion. When the valve was deployed, two valvular sinuses were created between the venous or aortic wall and SIS or PTFE-mounted leaflets on the square stent. The valve was open in systole to permit fluid flow. In diastole, the valve was closed as its two triangular leaflets sealed against each other to prevent fluid flow.

In vitro testing

SIS-covered 20 mm square-stent valves, with four barbs, were repeatedly tested in a flow model, 15 mm in diameter, for competency. Pressure was measured proximal and distal to the valve during prograde flow. The valves were exposed to retrograde hydrostatic pressure of 60 mmHg, provided by a water column in a plastic tube. For venous testing, continuous forward flow was approximately 250 mL min^{-1}. For aortic testing, continuous forward flow was 2.5 L min^{-1}. Valves were also tested with additional pulsatile flow. A 100 mL rubber bag, attached by a side arm at the lower end of the flow model, provided pulsatile flow. Manual compression of the bag was used to simulate the calf muscle pump and heart ejection fraction. To simulate the calf pump, a mild-force bag compression was applied for 2–3 s; to simulate the heart ejection fraction, a fast, < 1 s bag compression was used. The flow model was in a vertical position during testing.

At rest, without flow, the valve was closed, with a hydrostatic pressure of 61 mmHg below and 60 mm above the valve. With initiation of continuous non-pulsatile forward flow, the valve opened practically immediately with low venous or high arterial flow. The valve stayed in an open position during the whole duration of continuous flow. With pulsating flow, and either mild or strong force compression of the bag, the valve stayed open but closed immediately after the injection.

With the imitation of venous testing, pressures below the valve fell to 6–16 mmHg (median 11 mmHg) and returned to the original 60 mmHg after 24–32 s continuous flow. When pressure increased to 45 mm Hg, the valve opened partially and stayed open to the next pulsatile injection. The valve pressure was unchanged.

The aortic valve was tested at hydrostatic pressures of 100 mmHg. At rest without flow, the valve was closed by a hydrostatic pressure of 101 mmHg below and 100 mmHg above the valve. In pulsatile flow, immediately after a fast bag compression pressure above, it increased to 110 (± 5) mm Hg and below it decreased to 79 (± 7) mmHg.

Pilot animal study

Aortic valve

In acute (n = 6) and short-term experiments (n = 3) conducted in four swine and four dogs, valves ranging from 16–28 mm in diameter were placed into the ascending aorta through 10 F sheaths; three were placed in the subcoronary and six in the supra-coronary position (Figure 3 a, b). Function and stability of valves was studied with pressure measurements and aortograms. Three animals were sacrificed for short-term gross and histologic evaluation at 1, 2 and 4 weeks, respectively.

All the animals survived the initial post-implant period. The animals tolerated the procedure well and no arrhythmias or aortic pressure changes were observed. Valve movements were regular and there was no gradient across the valve. In two short-term animals with valves placed in the sub coronary position, one of the cusps of the native valve was trapped between the square stent and the aortic wall. This created considerable regurgitation and an appropriate model for evaluating SIS-valve efficacy. Both animals maintained systemic pressures of 92/74 (± 9) mmHg and 110/80 (± 11) mmHg. None of the square stent valves caused stenoses and only small contrast regurgitation was seen in two animals. Left ventricular end-diastolic pressures were unchanged after stent-valve implantation in all animals.

All nine prosthetic valves were undamaged by the implantation procedure. Aortic rupture was seen in one of the nine animals after 1 week. Aortograms revealed minimal regurgitation and no interference with coronary blood flow in all animals. Postmortem examination revealed the valves to be securely anchored. Histologic evaluation at 2 and 4 weeks revealed early remodeling of SIS with fibrocytes, fibroblasts and endothelial cells.

Venous valve

Venous valves were tested in an acute experiment on three dogs using a preloaded 20 mm square stent valve. The valve was placed into the 15 mm inferior vena cava (IVC) through an 8 F guiding catheter from the transjugular approach. Function of the valves and their stability was studied in the supine and upright positions, with injection of contrast medium and pressure measurement below and above the valve (Figure 4 a, b). For

longer-term testing, valves were placed into the IVC and iliac veins of three young swine via the transjugular approach. Animals were followed for 6 weeks by venograms and pressure measurement, and were then sacrificed for gross and histologic evaluation.

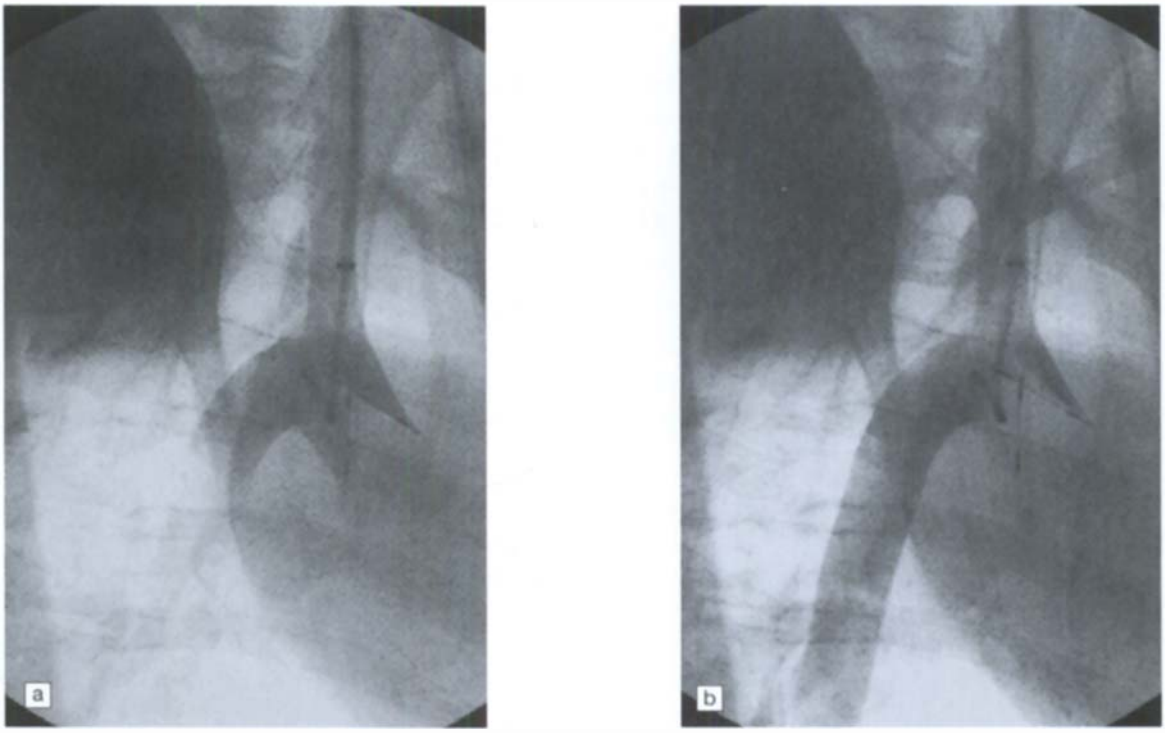

Figure 3. Aortic valve aortogram showing competency of the supra coronary placed prosthetic aortic valve. **(a)** Diastole. **(b)** Systole.

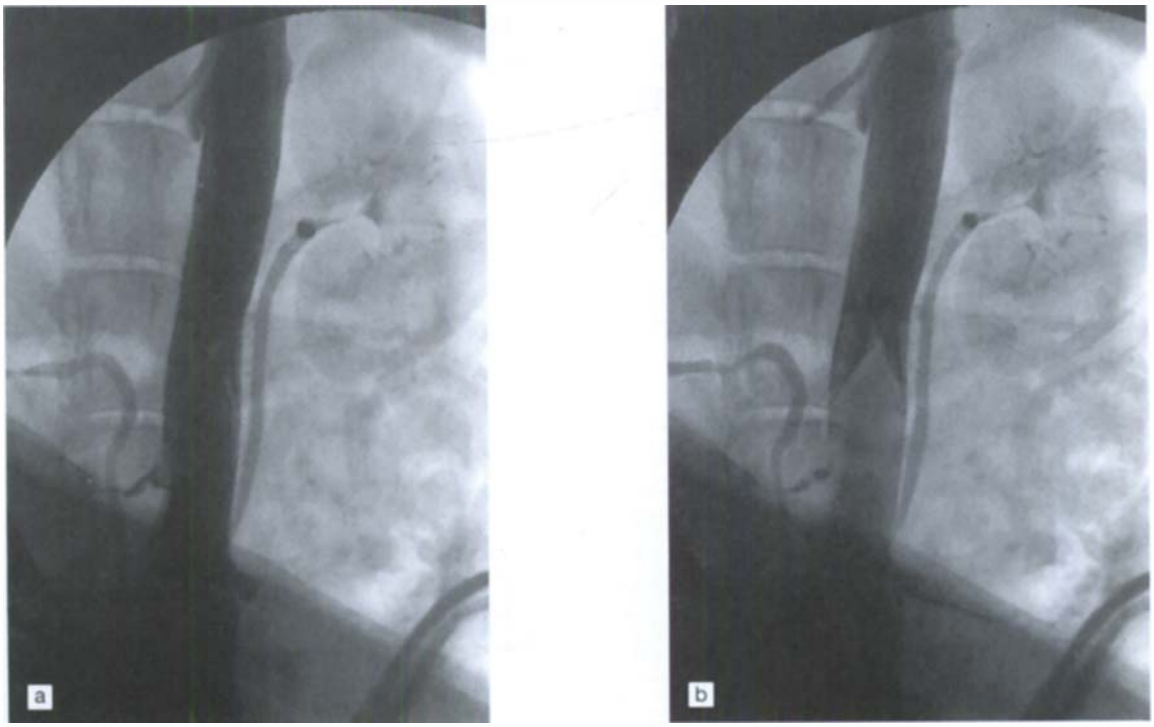

Figure 4. Venous valve cavogram in upright position with injection of contrast agent from the right femoral vein. **(a)** Early phase of injection shows valve patency with flow to upper IVC. **(b)** Late phase of contrast injection shows valve closure.

Good valve function was observed in all animals. There was no pressure gradient through the valve in the supine position. A pressure gradient of 12–15 mmHg developed immediately in upright position, with less pressure below the valves. All veins remained patent at 6 weeks and smooth incorporation of the SIS valves into the vein wall was observed. Valves mimicked natural vein valves. Histologic evaluation demonstrated host tissue replacement and collagen tissue stroma remodeling, with variable fibrocytes, fibroblasts and some inflammatory cells. Vascular endothelial cells covered valve leaflets.

Discussion

The catheter balloon-valve principle was suggested in 1980. The concept was balloon periodical closure of the insufficient aortic valve orifice, using a system attached to an aortic balloon-pump control unit [14]. A completely revolutionary concept, a catheter-based aortic valve, was introduced in 1992 with a percutaneously introduced ball-valve [10]. Whereas in the previous systems the inserted valve remained connected to the introducing catheter, the deployed ball valve stayed in the aorta without any support of the catheter. The ball valve consisted of a modified Z-stent, serving as a valve cage, and a detachable balloon as valve. The cage was deployed first, followed by introduction of the detachable balloon. Animal experiments showed good potential for this ball-valve [10]. The 'stent valve' bioprosthesis was introduced in 1992 [11]. It consisted of an explanted porcine valve, fixed on a wire stent-skeleton. The whole system was compressed and mounted on a modified balloon catheter for valvuloplasty, it was then placed into the aortic position using a sheath with an outer diameter of 13.6 mm. Balloon inflation was used to press the wire skeleton against the aortic wall. Testing was performed both for the supracoronary and infracoronary positions [11]. A similar model, with a valve made from the porcine pericardium mounted on a stent base, was tested successfully in animals. This model required a 24 F catheter for introduction [12]. The size of the delivery catheter for the disc valve (10 F sheath) is similar to that for delivery of the ball-valve and much smaller then the size of the stent-valve bioprostheses delivery catheters (24–41 F). A percutaneously-introduced disc valve was described in 1999 [15]. As with the ball-valve and stent-valve bioprostheses, the disc valve was delivered with a catheter, but stayed in place on its own.

The square stent was designed to be an intravascular implant-device carrier [16]. In order to squeeze a device through a delivery catheter small enough for percutaneous delivery, the stent structure must have a low profile and the covering material must be thin. Devices placed within the aorta must also have adequate strength and durability to withstand the aortic pressure of the blood flow. The main effort of the engineering involved was to construct the optimal stent framework with the lowest profile and enough expandable force to distend the covering material and secure hemostatic apposition of the occluder or valve to the artery, aorta or vein. We have shown that, with the square stent as a carrier, it is possible to introduce an aortic or venous valve covered with SIS percutaneously through a 6–10 F guiding catheter.

In a pilot study, only square stents covered with SIS were tested as venous or aortic valves. Square stents can also be covered with other materials, such as PTFE or Dacron.

Square stents and square-stent-based devices are radiopaque and easy to place. Once the device is anchored against the vessel wall, it is released and the pusher catheter with the retention wire is removed. After deployment, the square stent self-centres, self-adapts and self-attaches with four barbs to the wall of tubular structure.

The square stent is a new device with the potential to improve minimally-invasive treatment as a venous and aortic valve. The valve design is bicuspid and mimics natural valve anatomy. Initial studies showed that percutaneously-placed SIS square-stent valves are promising one-way valves, capable of sustaining aortic and venous back-pressure, while allowing forward-flow with minimal resistance.

Whether square-stent advantages in design, as a carrier for aortic and venous valves, will translate into long-term clinically-useful intravascular devices remains to be determined. More experimental studies are necessary to evaluate their long-term potential for possible future clinical use.

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