Are Self-expanding Stents Superior to Balloon-expanded in Dilating Aortas? An Experimental Study in Pigs*

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Objective: To study the stent/vessel interaction and distensibility following the natural increase in vascular diameter using self-expanding and balloon-expanded stents.

Design: Open experimental study.

Setting: Animal laboratory, university hospital.

Materials and methods: Eight Palmaz (P) and eight Gianturco (G) stents were transluinally placed in the infrarenal aortas of 16 pigs. Pulsatile diameter changes above, at and below the stents were non-invasively monitored with an ultrasound phase-locked echo-tracking system before and immediately after stenting and at 4 and 18 weeks. Blood pressure was registered intra-arterially and stiffness (β) was calculated. Intravascular ultrasound (IVUS) was performed at 18 weeks.

Results: Median weight increased from 20 kg (19-26) to 93 kg (62-130). Diameter of the aorta increased 60%. In group P no pulsatile diameter change could be measured at the stent (β = 0°). In group G stenting increased stiffness from β 20.7 (9.2) to 43.2 (8.0) (p < 0.05). After 18 weeks stiffness returned to β 20.1 (12.4). Expanded, median diameter of the P stents was 7.4 (0.8) mm, not increasing after 18 weeks. Initial diameter of the G stents was 7.8 (1.0) mm, increasing 56% to 12.2 (2.3) mm (p < 0.05). IVUS revealed the G stents to be well attached to the vascular wall, but five P stents were detached within half of the circumference.

Conclusion: Self-expanding stents follow the pulsatile diameter change of the vessel wall, not adversely affecting distensibility after 18 weeks. They show good attachment despite 56% dilation. In contrast, the balloon-expanded stents do not show pulsatile movement and may detach during vessel diameter increase. This may be of importance when choosing stents for endovascular treatment of abdominal aortic aneurysms.

Key Words: Endovascular stents; Aorta; Ultrasound; Diameter; Distensibility.

Introduction

Intravascular stenting for treatment of atherosclerotic stenoses and occlusions has developed rapidly since the first description by Dotter in 1969.1 It has mainly been used as a complement to percutaneous transluminal angioplasty (PTA). In the last few years different kinds of stents, in combination with synthetic grafts, have been evaluated in the treatment of abdominal aortic aneurysms, both experimentally on animals2-6 and in clinical practice.7-11 Various factors, such as stent material, thrombogenicity, endothelialisation and problems relating to retrograde transluminal access have to be considered.12

Endovascular grafts have to be anchored to the aortic vessel wall with one or several stents. Both balloon-expanded4,5,7,10 and self-expanding2,3,6 stents have been utilised. The former have the theoretical advantage of a more rigid construction, theoretically enabling a faster endothelialisation,13 while the latter comply better to pulsatile diameter changes of the vessel wall and to any diameter change over time. The abdominal aorta of man continues to grow throughout...
This is due to age related changes of the vessel wall as a result of a disruption of elastic components, remodeling and increase in collagen concentration. Thus, when using stents in the aorta, as in endovascular grafting of abdominal aortic aneurysms, one has to consider the fact that the vessel may dilate, disrupting the attachment between stent and vessel wall. This may lead to dislodgement of the whole graft. Further, patients with established aortic aneurysms might have a generalised dilating disease\(^{15}\) with a tendency for dilation of non-aneurysmatic arteries.

The aim of this study was to evaluate the stent/vessel interaction following the natural increase in vascular diameter of growing pigs as a model for dilating arteries, and comparing balloon-expanded stents with self-expanding. For this we used a non-invasive phase-locked echo-tracking ultrasound technique. Intravascular ultrasound was also used to determine the attachment of the different stents to the vessel wall.

**Materials and Methods**

Sixteen pigs (mean weight 20 kg, range 19–26) were anaesthetised with 2.5% thiopenthal-sodium (Pentothal® Natrium, Abbot Laboratories, North Chicago, Illinois, U.S.A.). After induction, the animals were intubated and ventilated with a Siemens-Elema respi- rator (model 900, Siemens Elema, Stockholm, Sweden) using a mixture of 30% oxygen and 70% \(\text{N}_2\text{O}\). A slow continuous infusion of midozalam (Dormicum®, Roche, Basel, Switzerland) and ketamine (Ketalar®, Kabi Pharmacia, Uppsala, Sweden) and intermittent doses of xylazin-chlorid (Rompun® vet, Bayer AG, Leverkusen, Germany) were used to maintain anaesthesia. Each pig received a single dose of benzylpenicillin procain (Streptocillin vet®, Boehringer Ingelheim, Agrovet A/S, Hellerup, Denmark). Approximately 1000 ml Ringer solution and 500 ml dextran (Macrodex®, Kabi Pharmacia, Uppsala, Sweden) were administered during the procedure.

With the pig in the supine position on a radiolucent operating table, a skin incision was made in the right groin. The common femoral artery and its branches were exposed. 5000 IU of heparin (Lövens, Ballerup, Denmark) were used to maintain anaesthesia. Each pig received a single dose of benzylpenicillin procain (Streptocillin vet®, Boehringer Ingelheim, Agrovet A/S, Hellerup, Denmark). Approximately 1000 ml Ringer solution and 500 ml dextran (Macrodex®, Kabi Pharmacia, Uppsala, Sweden) were administered during the procedure.

A data acquisition system consisting of a personal computer type 386 (Express, Tokyo, Japan) and a 12-bit analogue to digital converter (Analogue Devices, Norwood, Mass, U.S.A.) was used to maintain anaesthesia. Each pig received a single dose of benzylpenicillin procain (Streptocillin vet®, Boehringer Ingelheim, Agrovet A/S, Hellerup, Denmark). Approximately 1000 ml Ringer solution and 500 ml dextran (Macrodex®, Kabi Pharmacia, Uppsala, Sweden) were administered during the procedure.

The pulsatile diameter changes in the abdominal aorta (AA) were non-invasively monitored using an electronic echo-tracking instrument (Diamove, Teltec AB, Lund, Sweden), interfaced with a real-time ultrasound scanner (EUB-240, Hitachi, Tokyo, Japan).\(^{16}\) This scanner was fitted with a 3.5 MHz linear transducer for measuring the AA. An echo-tracking phase-locked loop circuit restores the position of an electronic gate relative to the moving echo. The small compensatory steps of the gate yield the echo movement per unit time. The instrument is equipped with dual echo-tracking loops, which enable two separate echoes from opposite vessel walls to be tracked simultaneously. The difference in signals between them instantaneously indicate any change in vessel diameter. The smallest detectable movement is \(8 \mu\text{m}\)\(^{17}\) and the time resolution is about 1.2 ms. When insonating metallic stents, the echoes from the stent, rather than from the wall, dominate.

Strain, or fractional diameter change, is defined as

\[
\text{Strain} = \frac{D_{\text{systolic}} - D_{\text{diastolic}}}{D_{\text{diastolic}}}
\]

Stiffness \((\beta)\)\(^{18}\) is defined as

\[
\beta = \frac{\ln \left( \frac{P_{\text{systolic}}}{P_{\text{diastolic}}} \right)}{\left( \frac{D_{\text{systolic}} - D_{\text{diastolic}}} {D_{\text{diastolic}}} \right)}
\]

In this equation \(P_{\text{systolic}}\) and \(P_{\text{diastolic}}\) are the
maximum systolic and end-diastolic blood pressure levels and In (P systolic / P diastolic) the natural logarithm for the systolic/diastolic pressure ratio. D systolic and D diastolic are the corresponding vessel diameters.

Stiffness (β), as an expression of distensibility, was established by Hayashi et al.\(^{19}\) and based on the observation that there is a linearity between the logarithm of pressure ratio and strain in the physiological pressure range, thus without pressure dependence. It was later modified by Kawasaki et al.\(^{18}\) to be used in vivo. The low pressure-dependence of stiffness (β) has been confirmed during in vivo studies in man.\(^{14}\) Distensibility is defined as the inverse of stiffness (β). Both a structural variable, the intrinsic elasticity of the vessel wall, and a functional variable, mean arterial pressure, is included in this definition. These two variables are necessary to include when measuring distensibility since it is not possible to correct it to a common mean arterial pressure. With the renal arteries localised and the catheter placed at that level, the top of the catheter was visualised by ultrasound and the abdominal aorta 2-3 cm above the tip was insolated. After three pulsatile diameter change registrations of acceptable quality, the catheter was withdrawn distally to the intended place of stenting, 2-3 cm below the most distal renal artery, and diameter registrations were repeated.

**Stent placement**

After complete withdrawal of the Cordis catheter, eight pigs received self-expanding Gianturco stents (G) (Cook Inc., Bloomington, Ind., U.S.A.), 15 mm in relaxed diameter and 12 cm long. Another eight pigs received balloon-expanded Palmaz stents (P) P308 (Johnson & Johnson Interventional Systems Co., Warren, NJ, U.S.A.), 15 mm long and expandable to 8-12 mm. The wires of the Palmaz stents were 0.13 mm thick and care was taken to achieve maximum expansion within the limits of the vessel, using a 40 mm long and 10 mm wide Cordis Opta 5 balloon catheter (Cordis Europe NV, Roden, the Netherlands). When the balloon could not be expanded further and the vessel was seen to bulge on the fluoroscope, the balloon was emptied and the catheter withdrawn. Correct deployment below the renal arteries was performed under fluoroscopic monitoring. The Cordis catheter was again introduced and ultrasonic diameter registrations repeated in the suprarenal aorta, at the stent and halfway between the stent and the aortic bifurcation. After withdrawal of the catheter, the arteriotomy was closed with interrupted sutures and the animals were allowed to recover. At 4 and 18 weeks the animals were anaesthetised again, and a Cordis catheter introduced through an arteriotomy in the left common femoral artery. Pulsatile diameter change and blood pressure were registered as mentioned above. At 18 weeks intravascular ultrasound (IVUS) and angiography were added to the procedure after which the animals were sacrificed.

**Intravascular ultrasound**

An IVUS examination was performed with a 20 MHz transducer mounted on the tip of a 8 French catheter (CVIS Cardiovascular Imaging Systems Inc., Sunnyvale, CA, U.S.A.). Proximal to the transducer a rotating mirror reflects the ultrasound beam to 360 degrees on the vessel, producing transsectional images displayed on a monitor and stored on a SVHS video recorder (Panasonic AG 7350). The catheter was introduced into the vessel through the arteriotomy in the left common femoral artery and advanced into the aorta to the site of the renal arteries. From here the catheter was withdrawn through the stented region of the aorta. The attachment of the stent to the aortic wall was evaluated. The location of the stent in relation to the renal vein and the most distal of the renal arteries was evaluated.

**Statistics**

Results are expressed as median (interquartile range, IQR). Mann Whitney U-test was used for statistical analysis between groups and Wilcoxon signed rank test for analysis within groups. The level of significance was chosen at p < 0.05 (*). The study was approved by the Animal Ethics Committee of Lund University and the animals were cared for according to the European Convention for Laboratory Animal Care.

**Results**

All animals except one recovered fully between procedures. Pig no. 9 (with a G stent) became paraplegic between measurements at 4 and 18 weeks and had to be killed. Autopsy revealed no dislocation of the stent or occlusion explaining the paralysis.
This pig is excluded in the statistical analysis. The mean weight of the pigs increased from 21 kg (19-25) to 32 kg (25-38) at 4 weeks and 95 kg (62-130) at 18 weeks. There were no differences in weight between the two groups at any time.

Fig. 1a shows an original recording of the diameter change in the infrarenal aorta in one of the animals before stent deployment. The corresponding blood pressure curve is also shown. In Fig. 1b the diameter change and blood pressure curve of the same animal immediately after deployment of a self-expanding Gianturco stent is shown. The diameter change is smaller compared with pre-stenting. Fig. 1c shows an original recording of the diameter change in the infrarenal aorta in an animal receiving a balloon-expanded Palmaz stent. No diameter change could be registered over the stent.

Table 1 shows the diameters of the aorta above and at the stents, and between the stent and the bifurcation at the time of stenting, after 4 and 18 weeks. There were no differences in suprarenal or distal aortic diameters at any time between the G and P stents. The distal aortic diameter in group P was not measured at time of stenting. Since there was an average decrease of 19% between the suprarenal and distal aortic diameters in group G, the distal aortic diameter in group P was calculated by subtracting 19% from the corresponding suprarenal diameters. During the 18 weeks there was a significant diameter increase of about 60% in the aorta ($p < 0.05$). Fig. 2a shows the diameter increase in the infrarenal aorta during the 18 weeks. Fig. 2b shows the corresponding diameters of the two different types of stent that were used. Note the 56% diameter increase in the G stent ($p < 0.05$) while group P remained unchanged.

Strain measured at the intended place of stenting was 0.022 (0.021) in group P and 0.025 (0.019) in group G. After 18 weeks strain was 0.024 (0.011) in group G. Strain was zero in group P as no movement could be detected here. Due to variations in blood pressure in some animals, only six from group P and five from group G could be used for calculations of stiffness ($\beta$). In group P no pulsatile diameter change could be measured over the stents, neither immediately after stenting nor at 4 or 18 weeks, stiffness ($\beta$) = $\infty$. In group G stenting acutely increased stiffness from $\beta$ 20.7 (9.2) to 43.2 (8.0) ($p < 0.05$) (Fig. 3). The stiffness over the stents slowly declined with $\beta$ 35.2 (12.9) at 4 weeks and $\beta$ 20.1 (12.4) at 18 weeks. For comparison the stiffness of the suprarenal aorta is depicted, showing a non-significant decrease from $\beta$ 9.5 (10.3) to 6.9 (10.7) in group G and 13.2 (11.4) to 5.4 (1.4) in group P. The distal aorta was significantly stiffer than the suprarenal aorta in both groups, at 18 weeks $\beta$ being 20.6 (10.6) vs. 5.4 (1.4) ($p < 0.05$) in group P and 25.7 (16.5 vs. 6.9 (10.7) ($p < 0.05$) in group G.

IVUS was performed at 18 weeks in 14 pigs (7 Palmaz and 7 Gianturco). One of the P pigs was not examined because of technical difficulties. All seven G stents were well attached to the vessel wall in the
Table 1. Aortic wall and stent diameters (Palmaz, balloon-expanded and Gianturco, self-expanding) during aortic diameter increase in growing pigs

<table>
<thead>
<tr>
<th></th>
<th>Palmaz (n=8)</th>
<th>Gianturco (n=7)</th>
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<tr>
<td></td>
<td>Suprarenal</td>
<td>Stent</td>
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<td></td>
<td>aortic diameter</td>
<td>diameter</td>
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<tr>
<td>Before stenting</td>
<td>9.2 (1.4)</td>
<td>8.0 (0.6)</td>
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<tr>
<td>At stenting</td>
<td>9.1 (1.3)</td>
<td>7.4 (0.8)</td>
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<tr>
<td>After 4 weeks</td>
<td>10.4 (0.7)*</td>
<td>8.1 (1.2)</td>
</tr>
<tr>
<td>After 18 weeks</td>
<td>14.8 (1.5)*</td>
<td>7.9 (1.5)</td>
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*p < 0.05 compared with diameter at stenting.

whole circumference (Fig. 4a) while five P stents were detached from the aortic wall from 90 to 360° of the circumference (Fig. 4b) and from 50–100% of the length. One P stent was well attached to the aortic wall and the attachment of one P stent could not be evaluated because of poor image quality. There was no sign of any stent migrating distally, not even among those which were detached. At angiography performed at 18 weeks, a leakage of contrast medium between the detached stents and the vessel wall was seen in some of the animals, confirming the findings of the IVUS. The renal vein and the most distal renal artery was visualised in all animals and their relation to the stent evaluated. All stents were located distal to the renal arteries.

Discussion

In the present study of self-expanding and balloon-expanded stents in an experimental porcine model, it was found that self-expanding stents follow the pulsatile diameter change of the vessel wall and do not adversely affect the distensibility of the vessel wall 18 weeks after placement. Despite a substantial increase in vessel diameter, self-expanding stents have good wall attachment as shown with intravascular ultrasound. In contrast, balloon-expanded stents do
not show any pulsatile diameter change after placement and may detach if the aorta dilates. Since the first report of transluminal graft implantation for treatment of abdominal aortic aneurysms, several studies on this topic have been published. The technique is still in a phase of development and the long term results are not yet fully clear. It is therefore of importance to study different materials and methods in an effort to find and develop those with which optimal results can be achieved.

To our knowledge only one study of the elastic properties of vessel walls after deployment of a self-expanding stent in vivo has been published, showing an immediate decrease of distensibility after stenting with wallstents in the iliac arteries of fully grown dogs. The method used in that study was an absolute induction angiometer which is invasive and may affect the blood flow. Ultrasound phase-locked tracking, the method used for measurement of diameter in the present study, is non invasive and well suited for investigating major arteries both in man and animals. The variability of the technique is small and the method reliable for accurate measurement of pulsatile diameter change. With simultaneous intra-arterial blood pressure measurement, pressure values of the vascular segment examined are obtained and the mechanical properties of the vessel wall or stent can be characterised (Fig. 1). For this we have chosen stiffness (β), distensibility being defined as the inverse of this index.

Due to age related changes of the vessel wall, the abdominal aorta of healthy man continues to dilate about 25% throughout adult life. This may be even more pronounced in patients with abdominal aortic aneurysms. When placing a graft anchoring stent in the aorta below the renal arteries, one has to consider the fact that the vessel may dilate, leading to detachment of the stent. In the present study on growing pigs, used as a model for dilating arteries, a dilation of approximately 60% was found in the normal aorta (Fig. 2a). The diameter of the G stent increased significantly by 56% and the IVUS revealed good integrity between the stent and the vessel wall (Fig. 2b and 4a). The balloon-expandable Palmaz (P) stents, on the other hand, remained unchanged during the same period and intravascular ultrasound showed that the Palmaz stents were detached from the aortic wall along various portions of its circumference (Fig. 2b and 4b).

Of great importance for the long-term patency of stents is the endothelialisation of the surface of the implanted material. A balloon-expanded stent is a stable, non-shifting frame (Fig. 1c), theoretically more advantageous for endothelial cell proliferation than the flexible self-expanding stent. In the high flow system of the aorta the risk of thrombus formation due to slow endothelialisation is, however, low and this is not of importance when choosing type of stent. More important might be compliance matching as proposed by Abbott et al. in the case of arterial grafts.

When placing the stents in the infrarenal aorta there was an immediate and distinct increase in stiffness (β). Because the P stent did not show any pulsatile diameter change at all, and stiffness (β) is calculated with diameter change as one factor, no values of stiffness (β) could be obtained (Fig. 3). The prompt increase of stiffness (β) in group G is consistent with the results by Back et al. In our study on dilating arteries, the stiffness (β) gradually decreased towards that of the surrounding aorta showing no significant difference after 18 weeks. This is probably due to the advantageous mechanical properties of the G stent in
this setting and a sign of good integration of the stent into the abdominal aortic wall. As the stent expands with the growing aorta, the stiffness (β) of the stent decreases and is probably gradually more determined by the intrinsic distensibility of the aortic wall surrounding it.

Previous studies have shown a potential use of IVUS especially in the follow-up of endovascular treatments, such as percutaneous transluminal angioplasty and stent deployment. Recently it has also been proposed as a control procedure after transluminal graft implantation. Our findings, as confirmed by angiography, indicate that IVUS may be used in the evaluation of stent/vessel wall attachment (Figs. 4a and b). The location of the stent in relation to the renal arteries can also be visualised.

In conclusion, this study of stent/vessel interaction on a porcine model of dilating arteries shows that self-expanding stents follow the pulsatile diameter change of the vessel wall and do not adversely affect the distensibility after 18 weeks. Despite a significant increase in aortic diameter, they maintain good wall attachment as shown with IVUS. In contrast, the balloon-expanded stents do not show any pulsatile movement after placement and may detach when the vessel diameter increases. These findings may be of importance when choosing stents in the transluminal endovascular treatment of abdominal aortic aneurysms.

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