AORTIC LUMEN DIAMETER AND BLOOD PRESSURE CHANGES DYNAMICS AFTER REPLACING AORTA ABDOMINALIS WITH PROSTHESIS

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Abstract
The aim of this study was to find out the biointegration of innovative vascular prosthesis, made in Riga Technical University (RTU), in dog's abdominal aorta. The research is being performed in Veterinary Medicine Faculty of Latvia University of Agriculture since July 19. 2011. We used 9 female gender, 1-3 years old Beagle dogs in this study. The research is approved by the Latvian Republic Food and Veterinary Service. The study is carried out in the frame of European Social Fund co-financed project 'Establishment of interdisciplinary research groups for a new functional properties of smart textiles development and integrating in innovative products' (ESF No. 2009/0198/1DP/1.1.1.2.0./09/APIA/VIAA/148). 5-8 mm in diameter, 8 mm - 18 mm in length RTU produced aortic grafts were implanted retroperitoneal in dogs. Before the surgery the diameter of abdominal aorta was measured in cross sections, afterwards – cranial and caudal from the prosthesis, as well cross-section diameter of vascular graft was measured. Blood pressure was measured before the surgery and after the procedure on regular basis. Results are the following: there are no significant differences in aortic and graft diameter before and 1-2 months after the operation, there are no significant differences in systolic and diastolic blood pressure before and four months after the surgery at significance level $\alpha = 0.05$. The study shows that the innovative aortic prostheses don't change in diameter, and surgery like abdominal aorta transplantation doesn't cause significant variations in blood pressure. The study is being continued to find out later reactions to synthetic vascular graft.
Key words: vascular graft, synthetic prostheses.

Introduction

In medicine one of the major blood vessel diseases is atherosclerosis. As a result of atherosclerosis, the affected blood vessels become narrower and do not provide a complete tissue trophic of concrete area. Condition like this, decreases the patient's life quality. One of the options to restore normal blood circulation is to replace the pathologically affected blood vessels with synthetic prosthesis. The autologous blood vessels often are not enough to replace large blood vessels, so in such cases there is no other alternative as to replace the damaged blood vessel with an artificial prosthesis. During the last decades intensive development of prosthesis has taken place throughout the world. As A. Wesolow notes that there have been more than 450 different types of vascular prosthesis developed in the United States during the last 30 years (Wesolow, 2008). At the same time, using vascular prostheses in clinical practice, many failures have been associated not only with incorrect diagnoses, awkward operations, lack of patient compliance, infections, but also with the prosthesis design and inappropriate materials or incomplete work in the preclinical experimental verification.

Biomechanical and physiological properties of vascular prosthesis which are offered today do not conformwith human blood vessel properties. These wall structure characteristics do not allow the prosthesis to pulsate, resulting in failure to delete a high pulse wave fluctuations, and do not provide long-term hemodynamic processes in a live organism. Nowadays, one of the major medical problems is restoration of body functional unity after vascular reconstruction (Lukyanchikovs et al., 2010).

Successful introduction of new vascular prostheses with better rheological and immunological properties into clinical practice requires a comprehensive study of their properties in experimental animals *in vivo*. In such experiments there are no alternative methods *in vitro* (Podlaha et al., 2009).

New structure pulsating aortic prostheses are designed in Riga Technical University (RTU), under the supervision of the professor V. Kantsevicha. It is weaving technology, biocompatible with the surrounding tissue, inert, non-toxic polyurethane and polyester filament yarn used to make artificial blood vessels. In order to implement the aortic graft in human medicine, it is necessary to study their effects on the body and the possible resulting complications; therefore, the usage of laboratory animals is an integral part of this process (Lukyanchikovs and Kantsevicha, 2010)

One of the most serious postoperative complications is lumen narrowing of the implanted vascular prostheses caused by overgrowing with neointimal cells. The restricted artificial blood vessels phase also causes hemodynamic disturbances in the area around.

The aim of this study is to find out the biointegration of innovative vascular prosthesis, made in RTU, in dog's abdominal aorta. Biointegration in our study includes changes in vascular lumen cranial from the aortic graft, in graft place and caudal from it, and provides blood pressure and its changes

during postoperative period in dogs. In future we will investigate the animal body reaction to acceptance of the above mentioned innovative vascular prosthesis with histological and imunohistological examinations.

Materials and Methods

In this study, 9 female, 1 to 3 years old, Beagle dogs, purchased from experimental animal farms in France were used. The experiment is confirmed by the Food and Veterinary Service of Republic of Latvia, and has a permission to be carried out. Pulsating 5-8 mm in diameter and 8 mm to 18 mm long RTU produced aortic grafts were implanted retroperitoneal in experimental animals.

Dogs were weighed and one hour before the surgery 5% or 10% 'Enroxil' (the active ingredient enrofloxacin) 5 mg kg^{-1} was injected i.m. to prevent infection. Non-steroidal anti-inflammatory agent 'Loxicom' (the active ingredient meloxicam) was administered orally appropriate to the animal's weight to reduce inflammation and pain one hour before surgery. As premedication 0.1% Atropine sulfate 0.02 mg kg^{-1} and 1% Acepromazine 0.1 mg kg^{-1}were used i.m. Diazepam 0.5% 0.25 mg kg^{-1} and 10% Ketamine 10 mg kg^{-1} were used i. v. for induction anesthesia. During the operation inhalation of anesthetic Isoflurane was used.

Animals on the operating table were positioned in the right lateral recumbent position and surgery area -lumbar vertebral area was aseptically prepared. Incision was done parallel to the lumbar vertebrae below the longest dorsal muscle (*M. longissimus dorsi)*, caudal from the, last, left rib. The skin, abdominal external oblique muscle (*M. Obliquus externa abdominis*), the abdominal internal oblique muscle (*M. Obliquus interns abdominis*), abdominal transverse muscle (*M. transversus abdominis)* were split dissecting abdominal aorta without cutting peritoneum. Two specially designed clamps were placed on the aorta for blood vessel surgery, about 4 to 5 cm away from each other, and blood flow was stopped. Three minutes before this action heparin was administered intravenously. Next, a transverse cut or piece resection in abdominal aorta was made to divide it in two parts. Then the innovative aortic prosthesis made in RTU was implanted. Total ischemic time ranged from 30 – 60 minutes. For aortic graft sewing 7/0 'Premilene', for muscle and skin sewing 2/0 'Serafit' and skin - 3/0 'Supramide' threads were used.

In post-operative period all animals got 5% or 10% 'Enroxil' 5 mg kg^{-1} injections i.m. once a day and anti-inflammatory agent 'Loxicom' appropriate to the animal's weight was administered orally for seven days. For five days analgesic drug 'Tramadol' 4 mg kg^{-1} 2-3 times a day was used i.m. too. Twice a day care of the wound with 3% hydrogen peroxide, or sodium chloride 0.9% solution was managed. After 14 days the stitches were removed. Ultrasound abdominal aortic diameter control was performed prior the surgery and two weeks after surgery in all animals. Further investigation repeated once a month throughout the postoperative period. Postoperative period lasts 6 months for 5 animals and 1 year for 4 animals. Blood pressure measurements were managed prior to the surgery and every month after the surgery in six dogs.

Ultrasound measurements were performed using PHILIPS HD11 ultrasound device. Before manipulations all animals got intramuscular Acepromazine injections 0.1 mg per body weight i.m. to facilitate investigations. During ultrasound examination dogs were placed in the right lateral recumbent position and area for measurement taking was prepared by clipping the hair behind the ribs and ventral from the longest dorsal muscles in 10 × 20 cm square expansion. Before surgery abdominal aortic diameter was measured in cross sections in one place, but after the aortic prosthesis implantation diameter in cross section of abdominal aorta was measured cranial and caudal from the prosthesis, as well cross-section diameter of vascular graft was measured. Cursors in all cases were placed in the middle of prosthesis and aortic wall. Prosthetic length, was measured longitudinally.

Blood pressure was measured using High Definition Oscillometry (HDO) device. Experimental animals were placed in a quiet, room. After five minutes when dogs were relaxed the blood pressure measurements were taken with first size dog cuff, as it is stated in the instruction enclosed. The cuff was placed on metacarpal area and on the base of tail. During manipulation this part of body on which the cuff was placed, was located on cardiac level ± 10 cm. Five measurements were taken in each investigation and average measurement was calculated.

For statistical analysis average ± standard error was calculated and a T- test for paired samples in Microsoft Excel program was used.

Results and Discussion

By summarizing the results of blood pressure and calculating the average values ± standard deviation, we obtained data that are demonstrated in Table 1. The following table shows systolic blood pressure dynamics, where the average systolic blood pressure before aortic operation is 156.88 ± 5.01 mmHg and a minimal 140.8 mmHg to a maximal 166.80 mmHg. After the operation, it ranges from an average of 162.13 ± 10.12 to 139.65 ± 6.25 mmHg, and a minimal of 117.8 mmHg to a maximal 186.0 mmHg. Normal systolic blood pressure in dogs is 120 mmHg (Reece,

Table 1

Sistolic blood pressure (sys) dynamics measured on the base of tail

Animal name	sys (mmHg) before operation ± stand. error	sys (mmHg) 1-3 days after operation ± stand. error	sys (mmHg) 1 month after operation ± stand. error	sys (mmHg) 2 month after operation ± stand. error	sys (mmHg) 3 month after operation ± stand. error	sys (mmHg) 4 month after operation ± stand. error
Brille	166.8 ± 4.77	186.00 ± 4.92	174.40 ± 2.61	156.60 ± 4.11	153.80 ± 6.64	155.60 ± 5.14
Pienene	141.50 ± 7.81	160.80 ± 1.35	156.20 ± 3.24	122.40 ± 4.80	146.20 ± 3.18	144.40 ± 2.94
Minne	163.40 ± 3.38	165.80 ± 3.46	131.20 ± 3.87	149.40 ± 1.63	131.80 ± 4.31	133.80 ± 2.35
Knīpa	140.80 ± 4.05	179.40 ± 4.00	142.00 ± 5.29	117.80 ± 0.58	126.80 ± 4.55	129.80 ± 2.63
Smukā	166.20 ± 3.67	120.00 ± 2.34	122.60 ± 1.24	117.80 ± 2.13	-	-
Bumbulīte	162.60 ± 17.15	175.20 ± 6.65	163.00 ± 1.65	169.00 ± 2.03	-	-
average ± st.error	156.88 ± 5.01	162.13 ± 10.12	148.36 ± 8.11	142.50 ± 8.15	139.65 ± 6.25	149.90 ± 5.78
minimum	140.80	120.00	122.60	117.80	126.80	129.80
maximum	166.80	186.00	174.40	169.40	153.80	155.60

1997; Garančs, 2006). However, the blood pressure is a variable rate and there is a wide variation between dog breeds. For example, the Labrador Retriever dogs systolic blood pressure is 118 ± 17 mmHg, but Greyhaunds have 149 ± 20 mm Hg. In Beagle dogs systolic blood pressure ranges 140 ± 15 mmHg, but even between individuals normal blood pressure can vary, and each animal can have its own. To determine the exact blood pressure, the measuring should be done in healthy animals on a regular basis (Egner et al., 2007).

Based on the above stated information, the average data in this study complies with the reference values. Before the surgery the systolic blood pressure in most experimental animals is higher than it is mentioned in literature, but it can be explained with an additional stress, since this kind of manipulation was performed for the first time on these animals. It should be noted that animals with high blood pressure respond nervously to strangers such as the veterinarian (Marino et al., 2011). Increased systolic pressure 1-3 days after the surgery can be explained by the additional stress since during the post operative period the animals were in another room. Of course, the surgery remains the tissue injury and there is pain response (despite the use of analgesics) to which animals also respond with increased blood pressure (Egner et al., 2007; Reece, 1997). Subsequent blood pressure measurements as shown in Table 1. display the fact that the systolic blood pressure returns to normal and complies with the reference values mentioned above. In all tables there are some empty cells because the study continues and missed measurements are not done yet.

We wanted to find out if there are significant differences between the systolic blood pressure measurements before surgery and in the postoperative period. The result by statistical calculating shows that in all cases no significant difference at significance level $\alpha = 0.05$ was found.

Diastolic blood pressure results and the average values ± standard deviation are shown in the following data Table 2. The following table shows diastolic blood pressure dynamics, where the average diastolic blood pressure before aortic operation is 82.16 ± 4.50 mmHg and a minimal 69.8 mmHg to a maximal 98 mmHg. After the operation, it ranges from an average of 88.83 ± 8.13 to 69.56 ± 6.04 mmHg and minimal from 43 mmHg to a maximal 109.6 mmHg. Normal diastolic blood pressure in dogs is mentioned to be 70 mm Hg (Reece, 1997; Garančs, 2006). Similar to systolic blood pressure the diastolic blood pressure varies between animal species too. In Beagles it is 79 ± 13 mmHg, of course in this case the animal's individual characteristics and environmental conditions should be taken into account as in measuring systolic blood pressure (Egner et al., 2007).

In the data in Table 2. and Figure 2. we can see that the diastolic and systolic blood pressures are above normal reference range before surgery and 1-3 days after surgery, but later it returns to normal and corresponds to the values described in the literature. The reasons for this phenomenon is the same as mentioned in the systolic blood pressure, because both of these pressures and their changes has the same causes.

The diastolic blood pressure results are shown graphically in Figure 2. It shows the individual animal's response to external as well as internal conditions. Animals individual diastolic blood pressure curve is a marked decline and hikes. Comparing the average values before and after surgery we found no significant differences at $\alpha = 0.05$.

Ultrasound findings are reported in Tables 3., 4., 5. Diameter of the prosthesis before the surgery and 1 and

Table 2

Diastolic blood pressure (dia) dynamics measured on the base of tail

Animal name	dia (mmHg) before operation ± stand. error	dia (mmHg) 1-3 days after operation ± stand. error	dia (mmHg) 1 month after operation ± stand. error	dia (mmHg) 2 month after operation ± stand. error	dia (mmHg) 3 month after operation ± stand. error	dia (mmHg) 4 month after operation ± stand. error
Brille	90.60 ± 3.18	85.40 ± 4.96	91.00 ± 4.91	81.40 ± 3.48	81.20 ± 3.36	90.80 ± 2.08
Pienene	74.00 ± 6.77	91.80 ± 5.03	71.40 ± 5.60	73.00 ± 5.75	79.00 ± 2.70	66.00 ± 1.48
Minne	74.80± 2.85	99.20 ± 8.73	83.00 ± 3.76	75.20 ± 4.85	70.20 ± 2.20	74.80 ± 2.05
Knīpa	69.80 ± 1.46	109.60 ± 4.29	74.00 ± 3.25	44.00 ± 0.83	69.80 ± 4.77	64.80 ± 3.87
Smukā	98.00 ± 7.16	55.40 ± 2.03	62.40 ± 0.67	62.60 ± 2.27	-	-
Bumbulīte	85.80 ± 5.59	104.00 ± 5.94	76.20 ± 2.03	82.2 0± 1.65	-	-
average ±st.error	82.16 ± 4.50	88.83 ± 8.13	76.33 ± 4.01	69.56 ± 6.04	75.05 ± 2.95	74.10 ± 5.99
minimum	69.80	55.40	62.40	43.00	69.80	64.80
maximum	98.00	109.60	91.00	82.20	81.20	90.80

2 months after the surgery do not differ significantly at $\alpha = 0.05$. The statistical comparison for future months will be done when necessary measurements from all animals will be obtained, since the animals were not operated simultaneously.

In studies available histological and immunohistochemical evaluation of vascular prostheses are described. One of the major problems after explantation of the prosthesis is intimal hyperplasia found in vascular prostheses made from various material (Ao et al., 2000; Podlaha et al., 2009). Intimal hyperplasia is the cause for narrowing of the blood vessel lumen. In this study, narrowing of the lumen is not noticed during two months, but it is also important to determine lumen changes over time. Testing of commercial polyester prostheses three months after implantation revealed neointimal hyperplasia in varying degrees, and in individual animals prosthetic lumen was closed. Authors explained it by differences in experimental animal species (Uberrueck et al., 2005). In general, polyester, polytetrafluoroethylene, poliurethane prosthesis has been used for many years and found to be suitable for large vessel transplantation. The problems begin when replanted blood vessels are < 5 mm in diameter (Rashid et al., 2004; Alcantara et al., 2005).

After removing previously implanted polytetrafluoroethylene prosthesis in humans, prosthesis capsule thickening and the internal lumen narrowing of the prosthesis were found. In some cases formations of aneurysms (Formichi, 1988) were found. In this study, the aortic diameter was measured before and after the prosthesis, because we believe that there is a possibility that lumen diameter can change morphologically in post operative period. Our results show that the aortic lumen diameter before prosthesis implantation does not differ significantly with aortic lumen diameter cranially and caudally

Table 3

Aortic prosthesis diameter dynamics

Animal name	Prosthesis diameter prior operation/ cm	Prosthesis diameter 2 weeks after operation/ cm	Prosthesis diameter 1 month after operation/ cm	Prosthesis diameter 2 month after operation/ cm	Prosthesis diameter 3 month after operation/ cm	Prosthesis diameter 4 month after operation/ cm	Prosthesis diameter 5 month after operation/ cm
Fiksā	0.500	-	0.496	0.496	0.443	0.458	0.509
Poga	0.500	-	0.397	0.365	0.364	0.376	0.443
Melnīte	0.500	-	0.467	0.481	0.475	0.474	0.548
Brille	0.500	0.500	0.491	0.479	0.520	0.533	-
Pienene	0.500	0.477	0.463	0.467	0.467	0.522	-
Minne	0.500	0.467	0.467	0.436	0.424	-	-
Knīpa	0.800	0.672	0.684	0.670	-	-	-
Smukā	0.800	0.670	0.681	0.681	-	-	-
Bumbulīte	0.800	0.684	0.687	0.687	-	-	-

Table 4

Aortic diameter dynamics cranial from prosthesis

Animal name	Aortic diameter prior operation/ cm	Aortic diameter 2 weeks after operation/ cm	Aortic diameter 1 month after operation/ cm	Aortic diameter 2 month after operation/ cm	Aortic diameter 3 month after operation/ cm	Aortic diameter 4 month after operation/ cm	Aortic diameter 5 month after operation/ cm
Fiksā	0.780	-	0.790	0.795	0.788	0.760	0.775
Poga	0.688	-	0.720	0.740	0.763	0.784	0.776
Melnīte	0.811	-	0.837	0.833	0.849	0.833	0.892
Brille	0.826	0.769	0.760	0.812	0.820	0.785	-
Pienene	0.882	0.859	0.920	0.872	0.855	0.971	-
Minne	0.753	0.786	0.827	0.812	0.780	-	-
Knīpa	0.758	0.793	0.753	0.726	-	-	-
Smukā	0.721	0.701	0.731	0.731	-	-	-
Bumbulīte	0.727	0.714	0.784	0.784	-	-	-

Table 5

Aortic diameter dynamics caudal from prosthesis

Animal name	Aortic diameter prior operation/ cm	Aortic diameter 2 weeks after operation/ cm	Aortic diameter 1 month after operation/ cm	Aortic diameter 2 month after operation/ cm	Aortic diameter 3 month after operation/ cm	Aortic diameter 4 month after operation/ cm	Aortic diameter 5 month after operation/ cm
Fiksā	0.780	-	0.760	0.769	0.760	0.744	0.780
Poga	0.688	-	0.747	0.726	0.707	0.776	0.773
Melnīte	0.811	-	0.846	0.826	0.826	0.830	0.820
Brille	0.826	0.841	0.815	0.794	0.776	0.802	-
Pienene	0.882	0.811	0.763	0.828	0.795	0.846	-
Minne	0.753	0.820	0.814	0.814	0.859	-	-
Knīpa	0.758	0.694	0.688	0.678	-	-	-
Smukā	0.721	0.811	0.727	0.727	-	-	-
Bumbulīte	0.727	0.838	0.819	0.819	-	-	-

from prostheses one and two months after the operation at $\alpha = 0.05$. Mentioned aortic diameter changes are shown in Tables 4. and 5.

Conclusions

1. The study shows that the innovative aortic prostheses do not change in diameter after two month from the surgery.
2. Surgery like abdominal aorta transplantation does not cause significant variations in blood pressure during post operative period.
3. To find out later reactions to synthetic vascular graft, further observations are recommended.

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