A new external stent – intimal proliferation and apoptosis in the vein graft in the animal model

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Abstract

Background: We have previously showed that the extravascular dacron mesh stent wrapped around a vein graft and implanted into the arterial system prevented the hypertrophy of the graft's wall, impeded the overgrowth of the intima and decreased the proliferation rate of venous graft cellular elements.

Aim: To determine the role of cellular proliferation and apoptosis in the process of remodelling in the stent in an animal model in a 12-week period.

Methods: Male sheep (n = 21) received by transplantation the hybrid graft (group 1) or carotid artery radial vein grafts (group 2). A hybrid graft was composed of a radial vein, collagen fibrin glue and highly flexible torlen/dacron mesh tubing. Grafts were retrieved on day 5, 9 and then week 4, 6, 8, 10, 12, respectively. A proliferation process was assessed using a Ki-67 antigen kit. The presence of apoptosis was detected using a TUNEL kit, strictly according to the manufacturer's manual.

Results: The number of proliferating cells has presented a decreasing trend in both groups, whereas the mean quantity of apoptotic cells increased over a 12-week period ($p < 0.001$) in both groups. Proliferation was more prominent during the first 5 weeks in both groups. The trend had a tendency to reverse during the last 7 weeks of observation. The ratio of proliferating to apoptotic cells differed between groups (1.6 vs. 1.9 on day 5 and 0.2 vs. 0.6 in week 12, in group 1 and group 2, respectively). No linear correlation between proliferation and apoptosis was observed ($p > 0.05$).

Conclusions: Different kinetics in the trico hybrid graft group in comparison with the radial vein graft group was observed, with a more prominent cellular turnover in the trico hybrid graft. Apoptosis in an unprotected vein wall was overcomed by the proliferation process. In trico hybrid vein grafts, beneficial remodelling of the intimal layer was predominantly dependent on inhibition of intimal proliferation rather than the effect of changes of the apoptosis ratio. There was no linear correlation between proliferation and apoptosis in the investigated grafts.

Key words: coronary disease, coronary vein graft, hybrid graft, remodelling, proliferation, apoptosis

Kardiol Pol 2009; 67: 1210-1217

Introduction

Recent data suggest that revascularisation strategies result in a significant decrease in mortality as compared to pharmacological treatment for all patients with coronary artery disease (CAD). Moreover, patients with a 3-vessel CAD may benefit from coronary artery bypass grafting (CABG) more than patients undergoing percutaneous coronary intervention (PCI) [1]. Some investigators reported that patients with multivessel CAD had similar outcomes (including symptoms of myocardial ischemia or stroke) in follow-up studies after CABG and PCI procedures. However, a number of interventions was significantly higher in the PCI group [2, 3]. It has been also highlighted that despite promising short-term and midterm outcomes after drug-eluting stent implantation, there are no convincing data regarding long-term safety and efficacy of this technique [4].

During the first year after CABG almost 20% of implanted vein grafts will get occluded [5] and throughout ten years about 50% of by-passes will be occluded due to vascular thickening and development of atherosclerotic lesions [6]. In response to the local hemodynamic conditions, vein grafts undergo a specific sequence of adaptations after arterialisation. The process is regulated by proliferation and cell death, with a pivotal role of apoptosis. Westerband et al. [7] estimated that the average proliferative index was

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Received: 19 February 2009. **Accepted:** 05 August 2009.

1.34% in human vein grafts which were retrieved between 3 and 18 months after CABG.

We previously found that the extravascular dacron mesh stent wrapped around a vein graft and implanted into the arterial system prevented the hypertrophy of the graft's wall, impeded the overgrowth of the intima and decreased the proliferation rate of venous graft cellular elements [8, 9]. However, little is known about cell death in this model.

Apoptosis contributes to the pathogenesis of various cardiac abnormalities (e.g. myocardial ischemia, arrhythmias and heart failure). Therefore, a cardiac surgeon should give some attention to the role of apoptosis, its mechanisms, and clinical implications. This knowledge may influence the surgeon's approach in clinical practice and improve the patient's outcome.

The aim of this study was to determine the role of cellular proliferation and apoptosis in the process of remodelling in the vein covered with dacron stent on an animal model over a 12-week period.

Methods

Experimental model

The research was performed after the approval of the local Ethical Committee on Animal Research had been obtained. Animals were treated according to the European Convention on Animal Care. The specimens were assessed prospectively after the stent implantation in all animals at the following time points: day 5 and 9, and week 4, 6, 8, 10 and 12.

A total number of 21 male sheep of the same breed, aged 8 to 10 months and weighing 35-40 kg were enrolled into the study. In cooperation with the manufacturer, we designed a 4 mm diameter prosthesis made out of polyester fibre (torlen/dacron) as a mesh. This extravascular stent (patent pending) is very resistant to bending and has the ability to change in diameter according to the acting (mainly along the long axis) forces. The stent model was described in detail previously [8, 9]. The animal model was chosen on the basis of similarity between the vein graft wall in humans and large animals and simplicity of external stenting procedures [10]. The method we implemented was based on the experience of Angelini et al. [11] who were the first to describe external stenting of a saphenous vein implanted into the common carotid artery on a pig model.

Surgical technique

In brief, after premedication (Atropin 1 mg/20 kg body weight *s.c.*, Xylazine 2% 0.8 ml *i.v.*), animals were given intravenous anaesthesia (Pentobarbital/Vetbutal 0.25 ml/kg b.w. *i.v.*, Metamizol/Biovetalgin 5-10 ml *i.v.*). The animals were mechanically ventilated (FiO_2 of 0.21-0.30) and a gastric tube was introduced to prevent flatulence.

Heparin was administrated *i.v.* (5000 units) and the radial vein was harvested. All side branches were obliterated with the 4-0 silk ligature. The vein with a diameter of 3-4 mm formed the biological component of the hybrid graft. Then, it was wrapped with the mesh and glued to it with the use of the tissue fibrin glue Beriplast (Canteon, Mannheim, Germany).

A 10-15 cm long fragment of a carotid artery was bypassed with the hybrid graft and then cut and ligated to start the blood flow exclusively through the graft. The end to side anastomoses were performed with the use of prolene 7-0 (Ethicon, Somerville, USA). The same procedure was applied to the opposite side of the neck, where the vein graft covered only with tissue glue (without the polyester mesh) was used. Although the glue may alter mechanical conditions within the graft, we decided to use it in the control group because it has some influence on the metabolic condition of the graft (including haemostasis, inflammation and anaphylaxis) [12]. Animals were extubated on the operating table and allowed to recover. The applied surgical method was described previously [8, 9].

Histology and immunochemistry

Samples of vessels were divided into proximal, medial and distal parts, and at least three samples from each part were obtained for particular examination. This procedure was applied to obtain representative samples from each part of the graft. Cross sections were analysed using an optical microscope (specimens were previously flushed with 0.9% NaCl and preserved for 20 h in 4% formaldehyde with phosphate buffer) and evaluated in a transmission electron microscope. The cross sections were dehydrated and embedded in paraffin. Cross sections for histology were stained with eosin, haematoxylin and van Gieson solution to make the elastic fibres visible.

Proliferation of the cells was assessed with the use of the Ki-67 monoclonal antigen (Ki-67 Antigen Kit, Novocastra, Newcastle upon Tyne, UK) strictly according to the manufacturer's manual. The specimens were fixed overnight in 10% neutral-buffered formalin (phosphate buffer). The samples were subsequently passed through graded alcohol solutions, processed three times in xylene and finally embedded in paraffin blocks. 5 µm thick slices were placed on Apes-coated slides, deparaffinised and rehydrated. To unmask the antigen, sections were boiled in 0.01 M citrate buffer (pH 6.0) in a microwave oven for 10 min at 800 W. For quenching of endogenous peroxidase activity, tissue sections were blocked with normal rabbit serum for 10 min and incubated with primary antibodies for 60 min at 25°C. Next, biotinylated secondary antibodies and ABC reagent were added (30 min, 25°C each). DAB and H_2O_2 were used as peroxidase substrates. Finally, tissues were stained with haematoxylin, dehydrated and coverslipped.

The presence of apoptosis was detected using a TUNEL kit (In Situ Cell Death Detection Kit, Roche,

Table I. Percentage of proliferating and apoptotic cells per field of vision in both examined groups

Time point	Proliferation			Apoptosis		
	radial vein group	trico hybrid graft group	p	radial vein group	trico hybrid graft group	p
Day 5	8.1 ± 2.4	6.0 ± 2.3	0.003	4.3 ± 1.5	3.8 ± 1.3	0.2
Day 9	8.1 ± 2.2	8.7 ± 2.9	0.5	4.4 ± 1.8	4.0 ± 1.4	0.3
Week 4	7.8 ± 1.9	8.1 ± 2.4	0.6	6.4 ± 2.2	6.2 ± 2.4	0.5
Week 6	7.5 ± 2.6	5.6 ± 3.8	0.04	8.4 ± 3.0	7.1 ± 2.4	0.1
Week 8	6.9 ± 2.0	5.2 ± 3.4	0.03	9.2 ± 3.7	8.2 ± 3.5	0.4
Week 10	6.3 ± 2.3	1.7 ± 1.0	< 0.0001	9.0 ± 3.4	8.2 ± 3.3	0.4
Week 12	5.4 ± 1.9	1.7 ± 0.7	< 0.0001	9.4 ± 3.1	8.2 ± 2.6	0.2

Germany) for detection of terminal deoxynucleotidyl transferase-mediated dUTP-biotin, strictly according to the manufacturer's manual. For the TUNEL technique, sections were dewaxed and rehydrated by heating at 60°C followed by washing in xylene and rehydration through a graded series of ethanol and double distillated water. Then, the tissue sections were incubated for 20 min at 25°C with a proteinase K working solution and boiled in 200 ml of 0.1 M citrate buffer (pH 6.0) in a microwave oven for 5 min at 350 W. The slides were cooled and immersed for 30 min at 20°C in 0.1 M Tris-HCl (pH 7.5), containing 3% BSA and 20% normal bovine serum. Then, the slides were rinsed twice with PBS and TUNEL reaction mixture (with terminal deoxynucleotidyl transferase – EC 2.7.7.31) was added on sample. After incubating for 60 min at 37°C in a humidified atmosphere in the dark, the slides were rinsed 3 times with PBS. Finally, tissues were stained with haematoxylin, coverslipped and analysed under a microscope. Negative control (without terminal deoxynucleotidyl transferase – EC 2.7.7.31) and positive control (cells incubated with DNase I) were prepared per protocol.

The assessment of percentages of stained, proliferating and apoptotic cells' nuclei was performed with the use of a light optic microscope. Usually, approximately 100 nuclei were found in one field of vision. Counting was stopped once a number of 1000 was reached or when all cells in a particular section were evaluated.

Table II. Correlation between proliferation and apoptosis

Time point	Radial vein group	Trico hybrid graft group
Day 5	0.071 (0.7)	0.193 (0.4)
Day 9	–0.140 (0.5)	–0.039 (0.8)
Week 4	–0.005 (0.9)	–0.019 (0.9)
Week 6	–0.004 (0.9)	0.103 (0.6)
Week 8	–0.151 (0.5)	–0.424 (0.06)
Week 10	0.060 (0.8)	0.025 (0.9)
Week 12	–0.075 (0.7)	0.292 (0.2)

Values are the Pearson coefficient of correlation and (in parentheses) a 'p' value

Statistical analysis

The results were analysed using Statistica 7.1 (StatSoft, Cracow, Poland) software procedures. Descriptive statistics are presented as percentages, means, and standard deviations. Bivariate analyses for group comparisons of continuous variables were performed using parametric or non-parametric tests for independent and dependent variables, as appropriate. Normal distribution was confirmed using the Shapiro-Wilk test. Additionally, the Tukey post hoc tests were used, when applicable. The correlation was assessed using the Pearson and Spearman correlation coefficients. A p value < 0.05 was considered significant.

Results

The process of remodelling, including proliferation and apoptosis, was assessed in the examined groups over a 12-week period in both vein layers (intimal and medial) jointly. The number of proliferating cells presented a decreasing trend during the observation in both groups. Moreover, a significantly lower proliferation ratio was observed after 5 days, 6, 8, 10 and 12 weeks in the trico hybrid graft group (group 1) in comparison with the radial vein graft group (group 2) (Table I). The mean number of apoptotic cells increased over a 12-week period with no statistically significant differences between examined groups (Table I).

The mean quantity of proliferating cells was changing in a 12-week period in a significant way, with differences between the following time points in group 2: week 12 vs. days 5, 9, weeks 4 and 6 (post hoc analysis). In group 1, the differences were observed between: day 5 vs. day 9, weeks 10 and 12; day 9 vs. weeks 6, 8, 10 and 12; week 4 vs. weeks 6, 8, 10 and 12; and finally, week 6 vs. weeks 10 and 12 (post hoc analysis). Similar results were found as far as the apoptosis was concerned.

However, statistically significant differences were observed between the following time points in both groups: day 5 vs. weeks 6, 8, 10 and 12; and between day 9 vs. weeks 6, 8, 10 and 12 (post hoc analysis).

Figure 1 shows the relationship between the number of proliferating and apoptotic cells in both groups. Proliferation was more prominent in both groups during the first five weeks. The trend was reversed in the last 7 weeks of observation. It is worth mentioning that the balance between proliferation and apoptosis was achieved after the same time of 5 weeks in both groups. However, the ratio of proliferating to apoptotic cells was entirely different in group 1 in comparison with group 2. At the beginning of the study (day 5) it was 1.6 in group 1 and 1.9 in group 2. After 12 weeks, the ratio was 0.2 in group 1 and 0.6 in group 2. In consequence, the ratio was 3 times higher in the radial vein group, indicating different kinetics and more prominent cellular turnover in the trico hybrid graft group.

Thickness of the wall increased consecutively in the follow-up observation in both groups; in the radial vein graft from 311.5 ± 61.9 µm to 957.8 ± 105.3 µm ($p < 0.001$ for trend) and in the hybrid graft from 278.2 ± 74.9 µm to 680.8 ± 166.5 µm ($p < 0.001$ for trend), and the differences in the thickness of the wall between groups were significant at all time points ($p < 0.05$ for all). The correlation between the mean number of proliferating cells and the wall thickness was $R = -0.95$ ($p < 0.001$) in the radial vein and $R = -0.88$ ($p < 0.001$) in the hybrid grafts. The correlation between the number of apoptotic cells and the wall thickness was $R = 0.96$ ($p < 0.001$) in the radial vein and $R = 0.96$ ($p < 0.001$) in the hybrid graft.

The results of the analysis of correlation between proliferation and apoptosis are presented in Table II. The coefficients of linear correlation were weak and not significant. Histological examples of proliferating and apoptotic cells in both types of grafts are presented in Figures 2-5.

Discussion

The study aimed to assess the role of cellular proliferation and apoptosis in the remodelling process within two types of grafts over a 12-week period. A novelty of our study is to describe the degree of cellular turnover in a new external stent graft with regard to the role of apoptosis and proliferation. The appropriate assessment of cellular turnover in our graft in a long time may be a valuable method in assessment of graft stenosis development.

We found different cellular kinetics in the trico hybrid graft compared to the radial vein graft. Although we reported a decrease in the number of proliferating cells with an increase in the mean quantity of apoptotic cells, there was no direct relationship between the number of proliferating and apoptotic cells. The equal number of proliferating and apoptotic cells was observed 5 weeks after grafting in both groups. Thickness of the wall increased consecutively during the follow-up observation in both groups. So, there was a negative correlation between the mean number of proliferating cells and the wall thickness, and the correlation between the number of apoptotic cells and the wall thickness was positive in both groups.

It was previously documented that the luminal diameter of the vein graft is dependent on changes in the number of cells and the amount of extracellular matrix in the wall [13-15]. Generally, cell proliferation and cell death are in balance. The cellular turnover involves cell migration from the adventitia to the media, medial proliferation with a peak observed several days after arterialisation, and less effective apoptosis at later time points [16]. The reduction

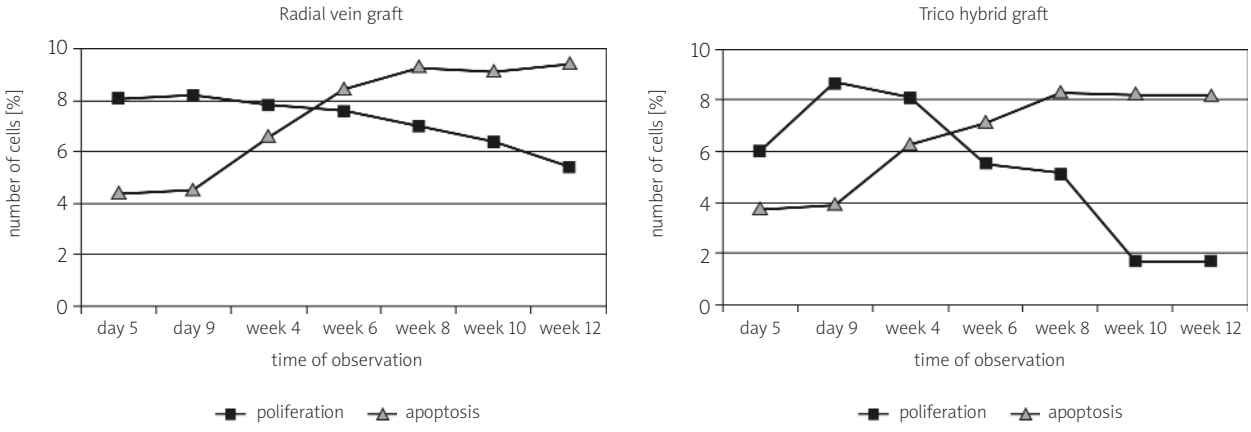

Figure 1. Percentage of proliferating and apoptotic cells per field of vision in both examined groups in a 12-week observation period

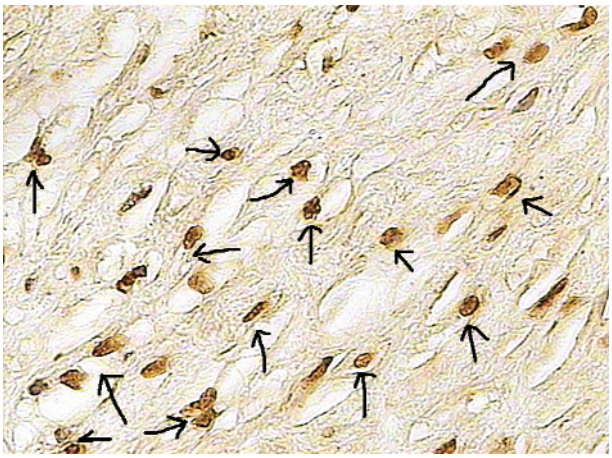

Figure 2. Apoptotic cells in the radial vein graft after 10 weeks (arrows)

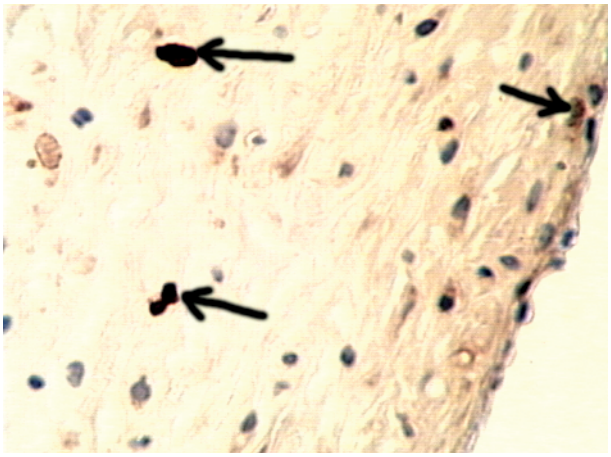

Figure 3. Proliferating cells in the radial vein graft after 10 weeks (arrows)

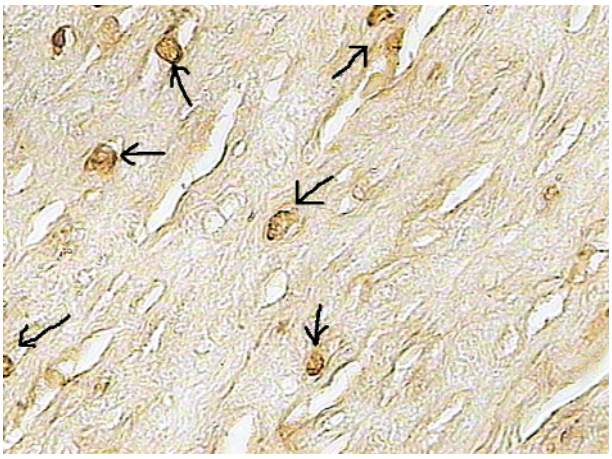

Figure 4. Apoptotic cells in the hybrid graft after 10 weeks (arrows)

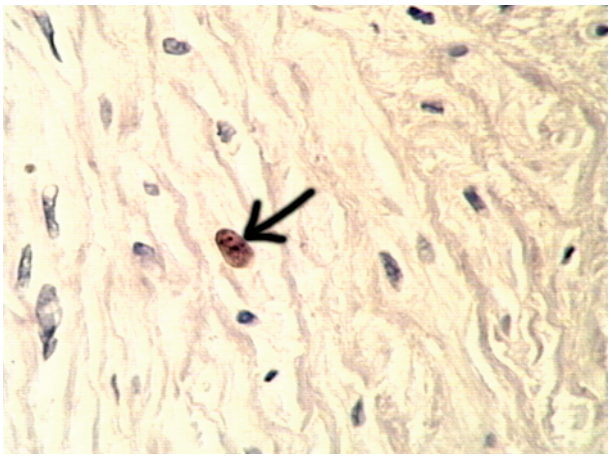

Figure 5. Proliferating cells in the hybrid graft after 10 weeks (arrow)

in vascular wall cells appears in relation to both necrosis and apoptosis. Apoptosis seems to be more prominent than necrosis within the very first hours after arterialisation of the vein graft, especially in relation to contractile smooth muscle cells [15]. It was reported that when proliferation was superior to apoptosis, hypertrophy occurred (e.g. hypertensive left ventricular hypertrophy). When opposite trend is present, like in aortic aneurysms or atherosclerotic plaques, atrophy is more prone [15].

Rodriguez et al. [17] showed that atrophy appeared in the saphenous vein graft within the first 48 hours after arterialisation. In that study, apoptosis was higher in non-smooth muscle cells than in smooth muscle cells (49.9 ± 7.8 vs. 14.5 ± 3.5%) after 8 hours. Smooth muscle cell proliferation was low in a 48-hour observation period, whereas non-smooth muscle cell proliferation increased to 22 ± 5.4% within 48 h. The different kinetics of remodelling observed was also believed to be responsible for the replacement of the media with fibrous tissue.

In an experimental rat model, Westerband et al. [7] reported that cellular proliferation and apoptosis were most intense within the first week after arterialisation of the vein graft. On day 1, apoptosis exceeded proliferation and the ratio of proliferating cells to apoptotic cells was 0.33. Then, after 3 days, the ratio was 2.0. The balance in the number of apoptotic and proliferating cells was observed after 7 days and later maintained comparably low in a 30-day observation period (< 1% after 21 days). Moreover, after 7 days, similar topographic profiles were also noted in relation to apoptosis and proliferation. The cells were mainly dispersed throughout the media and the adventitia. At later time points, cellular proliferation continued to be present in both layers, whereas apoptotic cells were found mostly in the developing neointima. In discussion, the authors [7] claimed that the mismatch observed between proliferation and apoptosis during the first week could explain cellular accumulation early in the development of intimal hyperplasia. Another

explanation was that proliferation required more time (14-18 h) than apoptosis (approximately 2 h). And finally, apoptotic cells had been quickly removed by neighbouring macrophages, so the number of apoptotic cells was underestimated.

Supplementary data were published by Moore et al. [18] who found that a step increase in tensile stress and strain in a rat vein graft model was associated with an increase in the percentage of TUNEL-positive cells up to 30 days with a peak 1 and 24 h after the graft implantation. These findings are in agreement with the results from another experimental rat model in which an increased apoptotic index (percentage of apoptotic cells in relation to all cells) was demonstrated as early as 3 hours and as long as 1 month after coronary occlusion [19]. Liu et al. [20] reported that the initial cell death in a vein graft was followed by an increase in the percentage of proliferating cells (from 1.55% on day 1 to 5.6% on day 30, with a peak of 11.93% on day 5). When mechanical stretch was reduced using a polytetrafluoroethylene sheath to restrain the vein graft, the percentage of proliferating cells reduced (0.76%, 1.7% and 0.47 on days 1, 5 and 30, respectively) [20]. The use of the hybrid graft in our study may result in a similar effect observed.

In a rabbit model in a 4-week study, Meyerson et al. [21] demonstrated the nonlinear nature of the cellular proliferative response to shear stress. They reported that vein graft neointimal thickening was accelerated in the regions of low shear stress far beyond that predicted by a simple linear model. They also suggested that the process was responsible for the rapid progression of neointimal lesions in failing bypass grafts [21]. Accordingly, we assume that the lack of linear correlation in our study (low values of Pearson coefficients of correlation) may be explained in a corresponding way.

Interesting results were presented by Vijayan et al. [22] who investigated the effects of a biodegradable external stent on porcine vein graft thickening. They reported that after 1 month the hybrid stent-graft demonstrated a significant decrease in neointimal and medial thickening (0.038 mm and 0.09 mm, respectively) compared with the unstented control (0.13 mm and 0.301 mm, respectively). The difference remained significant after 6 months [22].

Limitations of the study

There are some limitations of the study. First, the TUNEL technique was employed to assess apoptosis. Although this is an acknowledged method in many researches, one ought to be aware of its limitations (i.e. low specificity, unknown number of necessary DNA strand brakes for detection, increase in false positives from necrotic cells). For these reasons, it should be paired with or replaced by another assay. Localisation of activated caspase-3 is now seen as a more accurate alternative to TUNEL [23]. Second, methodology varies between experimental researches significantly, so between-study comparisons are limited; types of animal models and molecular methods used within them have some impact on the results.

Conclusions

In conclusion, vascular remodelling involves both cell proliferation and death in the investigated grafts. In the study we showed different kinetics with a more prominent cellular turnover in the hybrid graft compared to the radial vein graft. Apoptosis in an unprotected vein was overcome by the proliferation process. It should be underlined that in trico-hybrid vein grafts, beneficial remodelling of the intimal layer predominantly depends on inhibition of intimal proliferation rather than changes of the apoptosis ratio over time. This suggestion supports the idea of overstretch injury triggering apoptosis in a vein graft wall [16].

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Nowy stent zewnętrzny – rola procesów proliferacji i apoptozy komórek śródbłonka w pomoście żylnym w modelu zwierzęcym

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Streszczenie

Wstęp: Z uwagi na wysokie ryzyko zamknięcia żylnych pomostów aortalno-wieńcowych, wykazane w obserwacjach prospektywnych, coraz częściej poszukuje się rozwiązań na poziomie komórkowym, które będą istotnie ograniczać rozwój tego niekorzystnego zjawiska. Jedną z metod jest możliwość wglądu w szereg mechanizmów adaptacyjnych zachodzących w żylnych graftach implantowanych do krążenia tętniczego. W modulowanie tego zjawiska zaangażowane są procesy proliferacji komórek błony wewnętrznej i środkowej oraz śmierci tych komórek, głównie w mechanizmie apoptozy. Takiej oceny dokonuje się najczęściej w odpowiednio dobranym modelu zwierzęcym. W poprzednich doniesieniach wykazaliśmy, że zewnętrzny stent skonstruowany z siateczki dakronowej pokrywającej biologiczny pomost wykonany z żyły odpromieniowej i implantowany do krążenia tętniczego ogranicza degenerację tegoż pomostu. Niewiele jednak wiadomo na temat udziału procesu apoptozy w protekcji pomostu żylnego powleczonego stentem zewnętrznym przed zamknięciem jego światła.

Cel: Ocena wpływu dwóch przeciwstawnych zjawisk – proliferacji i apoptozy, na rozwój zmian degeneracyjnych w opisanym modelu.

Metody: Badania wykonano w grupie 21 owiec, po uzyskaniu akceptacji Komisji ds. Doświadczeń na Zwierzętach. Zastosowano standardowe procedury indukcji oraz podtrzymania znieczulenia i uznane techniki chirurgiczne. Do wnętrza siateczki dakronowej wprowadzano fragment żyły odpromieniowej, wypreparowanej z lewej kończyny przedniej, a następnie sklejano je klejem tkankowym. Tak przygotowany graft implantowano do krążenia tętniczego poprzez wykonanie zespolenia koniec do boku do tętnicy szyjnej (grupa badana), zarówno dystalnie, jak i proksymalnie. Następnie podwiązywano i przecinano tętnicę pomiędzy zespoleniami, uzyskując przepływ przez pomost. Symetrycznie, na drugiej tętnicy szyjnej wykonywano identyczne zespolenie, jednak bez zastosowania siateczki z tworzywa sztucznego (grupa kontrolna obserwacji). Materiał biologiczny pobierano do badań histologicznych i immunocytochemicznych 5 i 9 dni oraz 4, 6, 8, 10 i 12 tygodni po wykonaniu pomostu. Proliferację oceniano dzięki reakcji immunocytochemicznej z monoklonalnym przeciwciałem Ki-67, natomiast apoptozę monitorowano metodą TUNEL.

Wyniki: Liczba komórek proliferujących malała systematycznie w obserwacji 12-tygodniowej, podczas gdy liczba komórek ulegających apoptozie wyraźnie rosła ($p < 0,001$). Trendy te były widoczne zarówno w pomostach powleczonych, jak i niepowleczonych siateczką dakronową. Przewagę liczby komórek proliferujących nad apoptotycznymi stwierdzono w obu grupach w pierwszych 5 tygodniach obserwacji, po którym to czasie trend ulegał odwróceniu na rzecz komórek ulegających apoptozie (7 kolejnych tygodni). Stosunek liczby komórek proliferujących do apoptotycznych istotnie różnił się między grupami: w graftach z siateczką wynosił 1,6 w 5. dniu obserwacji i 0,2 w 12. tygodniu badania, podczas gdy w pomostach bez siateczki wynosił odpowiednio: 1,9 oraz 0,6. Nie stwierdzono korelacji pomiędzy liczbą komórek proliferujących i ulegających apoptozie w żadnej z grup.

Wnioski: W przebudowę ściany pomostu żylnego zaangażowane są zarówno procesy proliferacji, jak i apoptozy, przy czym w pomoście powleczonym stentem zewnętrznym wykonanym z dakronu obserwuje się odmienną dynamikę procesów biorących udział w przebudowie błony wewnętrznej i środkowej. Apoptoza w pomoście niezabezpieczonym siateczką jest zdominowana przez proces proliferacji, co może sprzyjać wcześniejszej jego okluzji. Korzystna przebudowa warstw naczynia, widoczna w obserwacji prospektywnej w pomoście powleczonym stentem zewnętrznym, zależy w przeważającej mierze od zahamowania proliferacji, podczas gdy wpływ apoptozy wydaje się mniej istotny. W modelu nie stwierdzono istotnej korelacji pomiędzy liczbą komórek proliferujących i ulegających apoptozie.

Słowa kluczowe: choroba wieńcowa, wieńcowy pomost żylny, pomost hybrydowy, przebudowa, proliferacja, apoptoza

Kardiol Pol 2009; 67: 1210-1217

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Praca wpłynęła: 19.02.2009. **Zaakceptowana do druku:** 05.08.2009.