Chirurgia Polska 2004, 6, 3, 133–138
ISSN 1507–5524

Pathology of the arterial wall after stent implantation: macroscopical and histological findings after interventional therapy in iliac and femoral arteries

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Abstract

After the explantation of 9 segments of iliac and femoral arteries with inlying stents macroscopical, radiological, histological and histochemical investigations were accomplished. The findings consisted of the identification of regular processes due to the contact between the stent struts and the arterial wall.
A smouldering inflammation in the area surrounding the filaments, the appearance of a proliferating neointima, the proof of a neoendothelium and a differing reaction to the stent depending on the varying quality of the arterial wall in contact were part of the findings. The clinical consequences are also discussed.

Key words: stents, pathological findings, inflammation, neointimal proliferation, neoendothelium

Introduction

Intraluminal interventions in the iliac and femoral arteries with and without the use of arterial stents are a widespread form of therapy for arterial occlusive disease. These procedures, if applicable, are nowadays accepted as the method of choice for iliac interventions. However, the insertion of stents into the femoral arteries is a point of ongoing discussion.

As a contribution to the discussion about stents in general, we present macroscopical and histological findings from specimens harvested by the explantation of stent containing arteries.

Material

From June 2000 until December 2003 we performed nine operations in which, for anatomical reasons, the explantation of arterial segments with an inlying stent was indicated. The segments originated from the following vascular regions: the common iliac artery — 1, the extenal iliac artery — 5, the femoral artery — 1 and the superficial femoral artery — 2. The following operations were performed: an interposition of a graft — 7, a cross-bypass — 1 and a retrograde ringcutter-desobliteration — 1. We combined specimen from the iliac and femoral region as the histological findings were absolutely identical. The specimen we obtained by ringcutter-desobliteration provided sufficient arterial wall material for a complete histological examination.

The examination consisted of a macroscopical description, radiological documentation as well as histological and immunhistochemical tests. The specimens had passed a fixation by formaldehyde. For the histological staining H.E., Ev. G. and FE-stains were used.

The immunhistochemical characterisation of cells and tissues was based on the use of the following markers: CD3, CD20, CD45RO, CD68, α-actin, vimentin and factor VIII.

Macroscopical findings

Explanted vascular sections showed the following characteristic macroscopic aspects where the stent had been in contact with the arterial wall. The inner surface

of the arterial wall presented a grey intraluminal structure of neointimal fibrosis. In addition, in some areas the stent filaments almost reached the luminal surface. We found allusions about the context of the thickness of the myofibrotic proliferation depending on the positioning in relation to calcifications and stent filaments. Radiological imaging proved to be very helpful (Fig. 1).

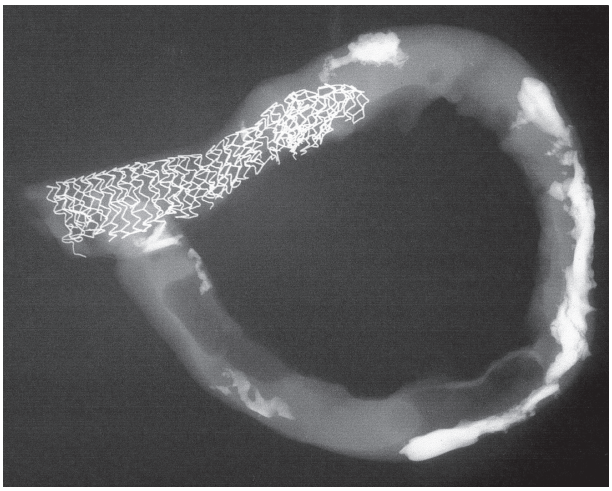

Figure 1. X-ray from a femoral artery with differing intensity of calcification and plaque formation — malpositioned stent

Regularly, the intimal layer proliferated in the surrounding area of the stent filaments (Fig. 2). Parietal thrombi as well as fresh thrombi in apposition to these were typical signs of the occluding process in the arterial lumen which took place in several episodes (Fig. 3). Unexpectedly, we were able to describe fairly the deficient opening of stents in contact with hard plaque. This we found in three specimens (Fig. 3).

Histological findings

The processing of specimens of iliac arteries with in-lying stents for histological examinations was quite difficult. Whereas the findings were clearly to be seen, for technical reasons it was almost impossible to prepare sections of metal containing iliac arteries with their big diameter in such a way that the resulting photographs could be presented in an acceptable way so that any spectator could draw conclusions from the presented pictures. As it was possible to prepare sections of carotid arteries in which the findings had been the same as in those specimens on which we report here, we decided to present the figures of carotid arteries which are representative for the findings to be described, as well for the macroscopic (compare Fig. 2A and B) as for the histological part.

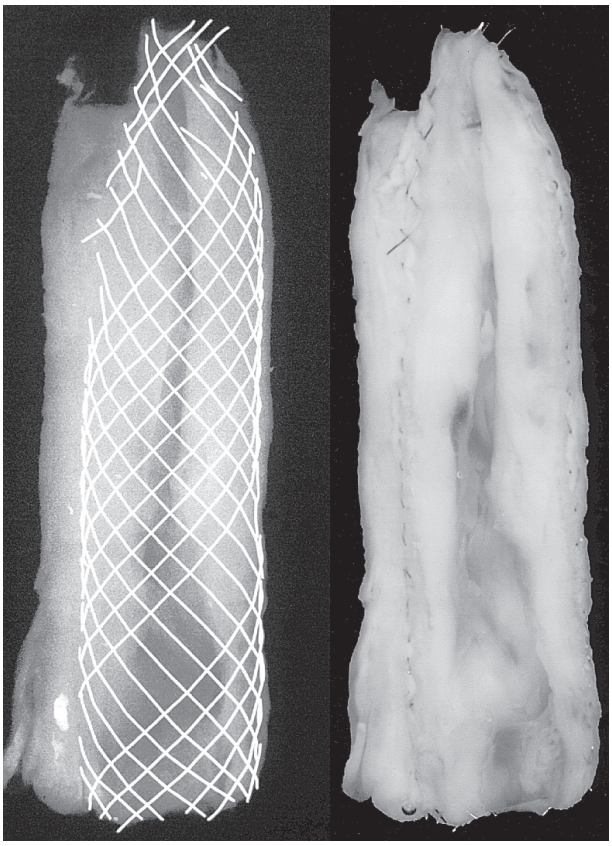

Figure 2A. Macroscopic aspect of a segment of a femoral artery with massive myofibrotic proliferation; on the left side, the radiological picture shows a little calcification

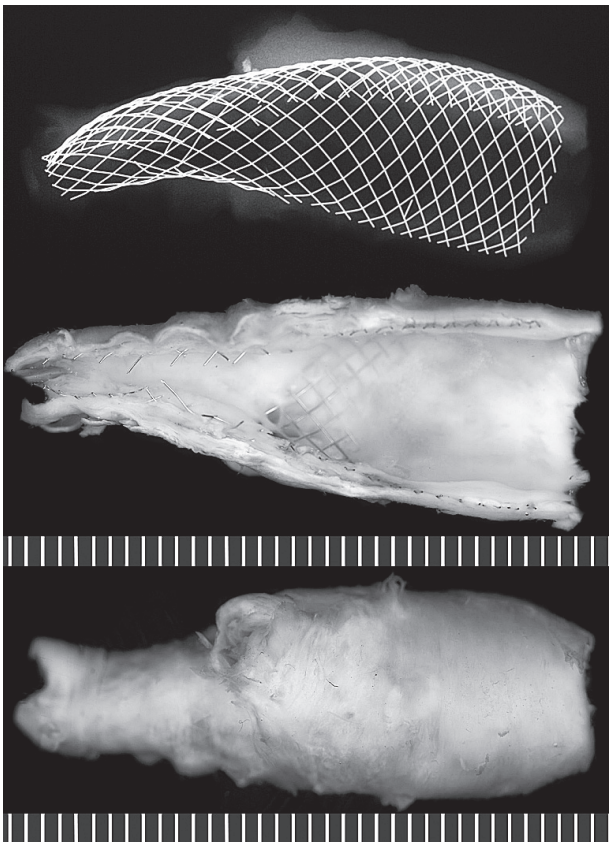

Figure 2B. Beside the grey intraluminal structure of the neointimal fibrosis, it is possible to identify areas where the stent filaments almost reach the luminal surface. This specimen from a carotid artery is quite comparable to Figure 2A

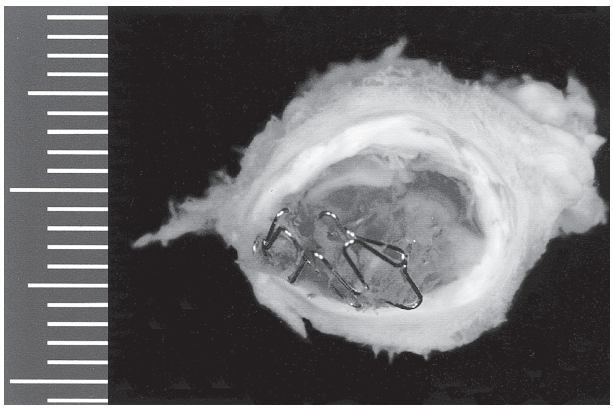

Figure 3. Transversal cut of an iliac artery with deplaced stent, neointimal proliferation and occluding multilayer thrombus

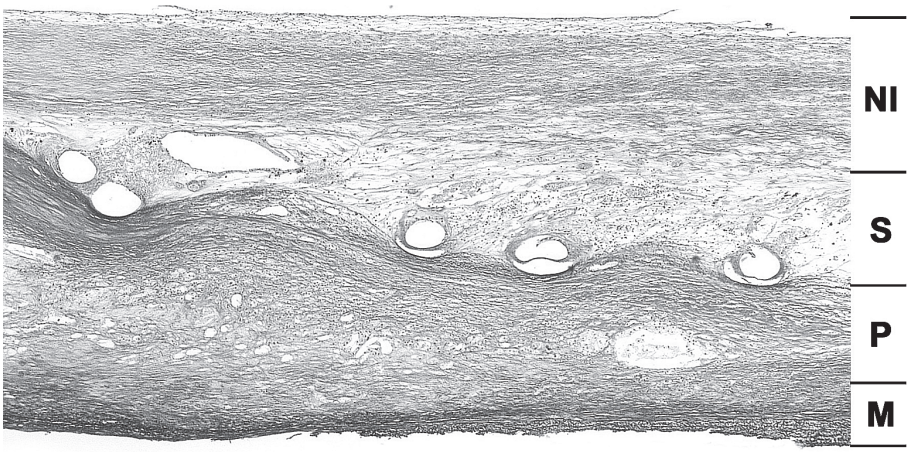

Figure 4A. Histological overview after the disengagement of 6 stent filaments. Beneath the one-cell-layer of a luminal neoendothelium lies a neointima (NI) with a matrix rich in fibres. There are wave shaped deformations due to the expanding stent filaments (S) in a preexisting fibrous plaque (P), remains of the original media (M)

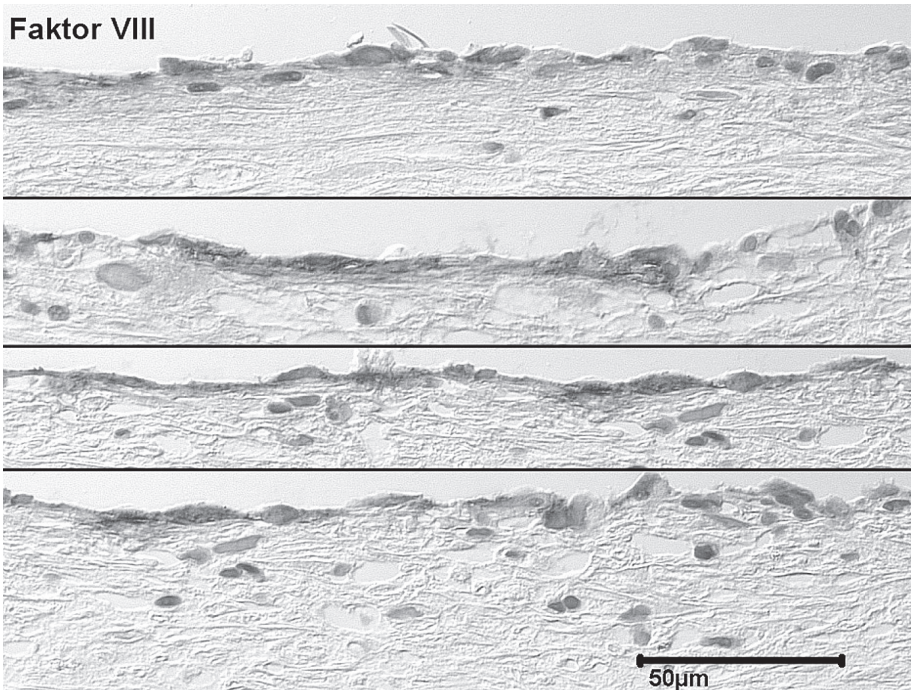

Figure 4B. Neoendothelium as a factor-VIII positive one-cell-layer

The metal filaments which were pressed by their centrifugal power of expansion into the arteries' walls or plaques were surrounded and most times covered by a myofibrotic layer which was covered on the inner surface by a neoendothelium (Fig. 4). We found typical wave-shaped marks in the intima and medial layer of the arterial wall after the implantation of stents. These findings seemed to be independent of the period the stent had remained implanted and could be demonstrated as early as 4 weeks after surgery as well as after more than one year of contact between the implant and the biological tissue (Fig. 4).

Additional histological findings consisted of three classes:

The first was the proliferation of myofibroblasts in a membrane-like area that could be called neointima. It consisted predominantly of α-actin-positive myofibroblasts and a matrix of type-III-collagene. Next to the stent filaments we found a chronically smouldering inflammation with an adjacent heavy proliferation of myofibroblasts. In some cases this led to a subtotally stenosing proliferation of neointima.

The second category of findings consisted of a vascularisation of the neointima itself with fibrosis and arteriosclerosis of these vessels.

The third column of reactions we saw in the accumulation of T-lymphocytes and macrophages which were storing hemosiderin. In contact to the adventitia lay multi nuclear giant cells of the foreign body type. A typical vasculitis was not observed.

Two results were outstanding. In plaques which were rich in atheroma and lipids the reaction to the stent filaments was less impressive. When the stent filaments however, came in contact with original arterial wall or fibrous plaque then the reaction to this contact was considerably augmented.

A differentiated histochemical analysis was subsequently performed. Changes in the accumulation of cells that had been shown by the above-mentioned markers were registered. Here we saw that obviously CRP, PDGF, IFN-γ and TNF-α acted as a kind of trigger for the development of restenosis.

The following figures (Fig. 5–7) demonstrate the reaction to the stent made visible by the proof of cells that are responsible for the reaction to stent filaments described here.

By proving the absence of B-cells that would have been reactive to CD20, the possibility of acute inflammation could be excluded (Fig. 7C).

The reaction to stents was more intense when the diameter of the stent was small in comparison to the arterial diameter. In our specimens stents never displayed inert behaviour.

Discussion

Metal materials used for stents, such as steel or nitinol, are believed to react more or less inertly in the host. In the nine specimens of iliac and femoral arteries described here, that had to be removed because of total arterial occlusion and for the sake of reconstruction of arterial blood flow, we found that there was no inert behaviour displayed. The reactions to metal filaments of stents were absolutely comparable to those results previously described for coronary and carotid arteries [1, 2]. As these results were unanimous, the reaction of arterial walls to stents can be described as regular. The regularity of these reactions can be proved by

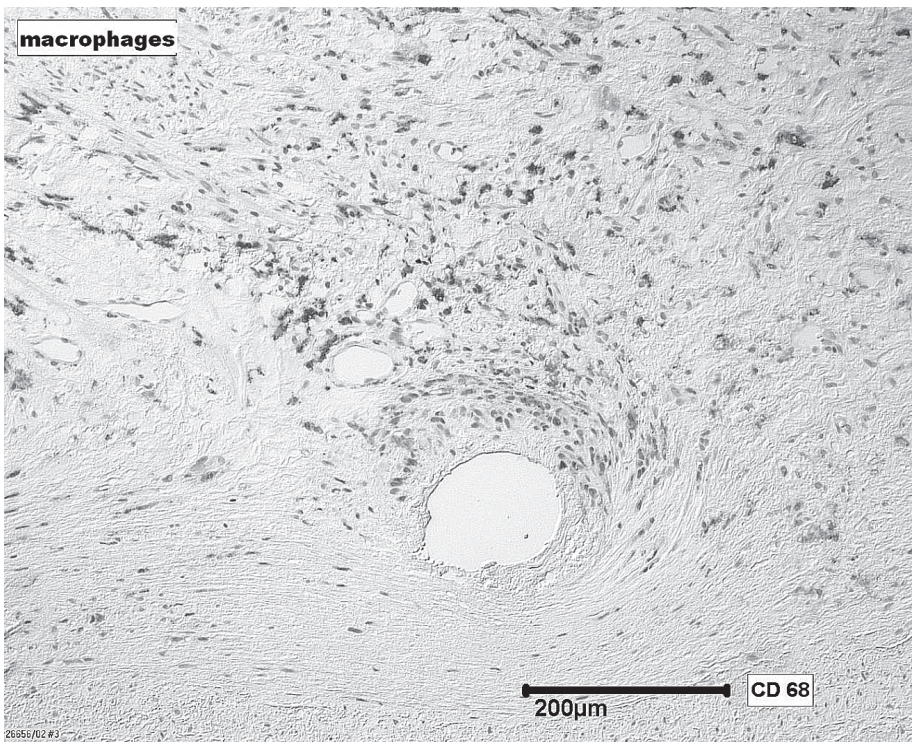

Figure 5. CD 68-positive macrophages in a perifilamentary area of inflammation

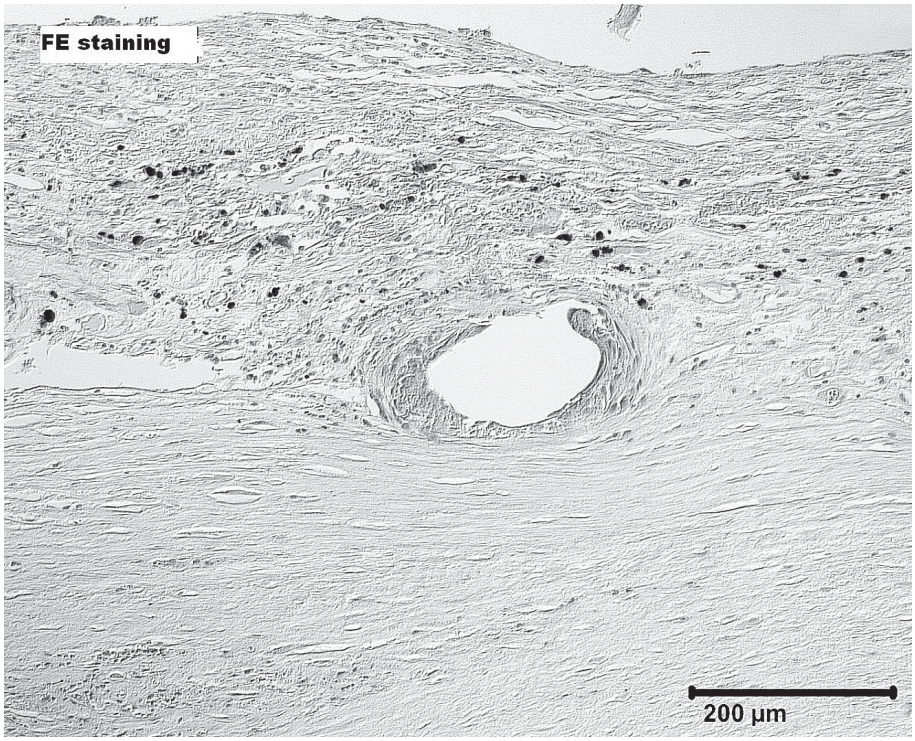

Figure 6. Siderin storing macrophages in a perifilamentary area of inflammation

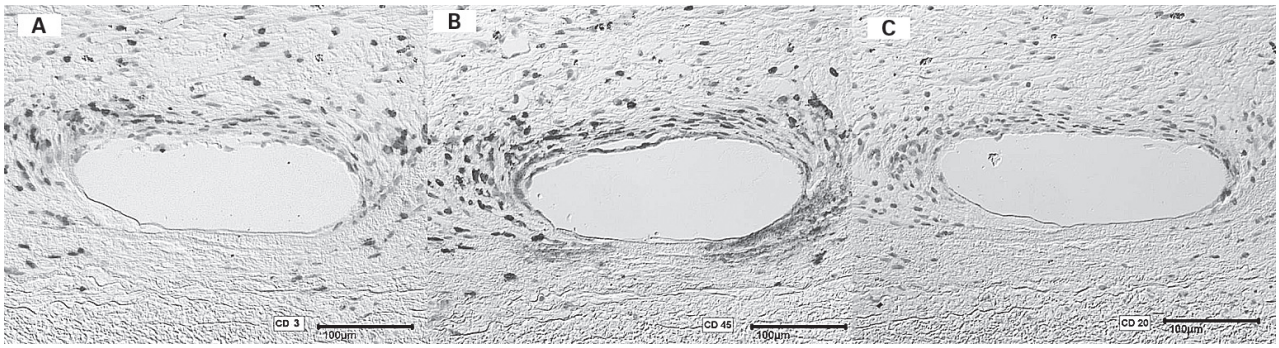

Figure 7A-C. Immunhistochemical imaging of perifilamentary inflammatory infiltrations, prevelantly from CD 3- and CD 45-positive T-lymphocytes (A+B), CD 20-negative reaction to B-lymphocytes (C)

the histological and histochemical identification of cells that are expressing mediators which trigger a well-described reaction of chronic smouldering inflammation and the following formation of a neointimal layer that is sometimes excessive. Such extreme reactions were also found in other vascular regions, for instance in coronary stents in more than 30% [3]. The clinical importance however may differ in other areas as the thrombi that surrounded the stent struts in the iliac, as well as in the carotid arteries, might be more dangerous in the supraaortic region [2].

In contrast to other authors [4] our results concerning the iliac arteries were very similar to those in the coronary specimens. We interpreted the thrombi in the occluded arteries as a reaction to the reduced arterial flow caused by the proliferation of the neointima, which in some specimens was almost lumen-occluding by itself. It is a morphological alteration which those authors described to be pathognomonic for coronary arteries.

The fact that the reaction to a stent was more intense when its diameter was small in relation to the artery, was interpreted as being due to the minor fixation resulting in more irritating struts which, in addition, were more exposed to the bloodstream with a more intensive interaction between humoral factors and stents [1].

We found different kinds of reaction depending on the plaque consistency. The reaction seemed to be depending on the existence of soft or fibrous plaque. This might be seen as a certain hint on some regularity in the tissue reaction to stents depending on the morphology of the arterial wall. One of the conclusions of this investigation is the question whether in the future it might be possible to identify the quality of the arterial wall by diagnostic procedures before any intervention might be performed. Is it possible in the future to achieve better long term results by a more differentiated indication for a stent implantation?

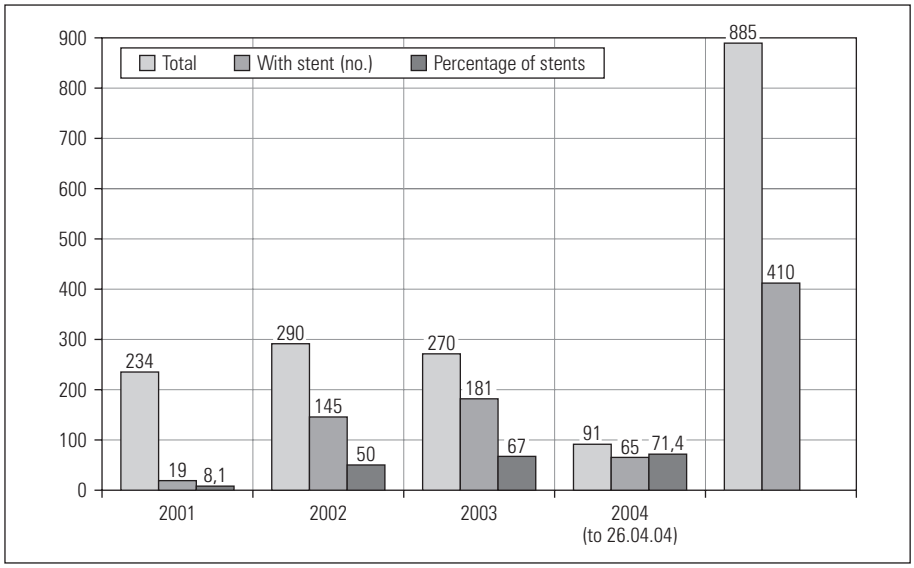

Figure 8. Number of angioplasties in the iliac arteries in the years 2001–2004 in the Radiological Department of the DRK-Kliniken Mark Brandenburg

To find out about the quantitative importance of total occlusions after stent implantation in iliac and femoral arteries we observed the number of implantations which where done in our institution at the same time when we were explanting these specimens. The number of implantations can be found in Figure 8.

The frequency of stent implantations in the iliac and femoral arteries at our institution is certainly increasing due to the better materials and stents which are now available. Compared to the number of implantations, the number of cases of total occlusive disease after stenting is not excessive, even if we admit that the number of operations after the total occlusion of stents is more than those in which we could explant the arterial segments with an inlying stent. More often, we bypassed the occluded segment and the estimated number of bypassed occlusions was three times higher than the number of explanted specimens. Nevertheless, all these total occlusions do not add up to the amount of implanted stents. So in our opinion, it is possible to conclude that the long-expected era of the mass explantation of occluded stents will not arrive.

The final conclusion should be that by explanting and examining specimens as we did here, it is possible to arrive at findings that are relevant to various clinical points of view. If vascular surgeons have to remove arterial segments, grafts or stents, they should not dispose of them but preserve them, if possible in cooperation with pathologists who have a special interest in vascular pathology.

References

1. Muller KM, Schmitz F. Morphological findings after stent implantation in the carotid artery. Pathologe 2004; 25: 108–115.
2. Toma N, Matsushima S, Murao K *et al.* Histopathological findings in a human carotid artery after stent implantation. Case report. J Neurosurg. 2003; 98: 199–204.
3. Grewe PH, Thomas D, Machraoui A *et al.* Coronary morphologic findings after stent implantation. Am J Cardiol. 2000; 85: 554–558.
4. Ishibashi-Ueda H, Yutani C, Imakita M *et al.* Histologic comparison of coronary and iliac atherectomy tissue from cases of in-stent restenosis. Angiology 1999; 50: 977–987.

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Praca wpłynęła do Redakcji: 01.09.2004 r.