Predictors of restenosis in patients treated with angioplasty for subclavian artery occlusive disease

Czynniki predykcyjne restenozy u chorych uprzednio leczonych angioplastyką z powodu zwężenia tętnicy podobojczykowej

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Abstract

Background: Subclavian angioplasty (PTA) is widely used in the treatment of subclavian (SAS) and innominate (IAS) artery obstruction, however factors influencing long-term outcome are not well determined.

Aim: To assess incidences and predictors of restenosis after SAS/IAS PTA.

Methods: PTA was attempted in 168 (73 M) patients, aged 61.6 ± 8.3 years with angiographically confirmed SAS/IAS ≥ 50%, and symptoms of cerebral ischemia, upper limb claudication, subclavian-coronary steal or for obtaining blood pressure control.

Results: PTA was successful in 159 (94.6%) patients and 164 lesions; including 141 (100%) stenotic lesions and 23 (71.9%) out of 32 occlusions. Mean stenosis grade was reduced from 75.7 ± 15.7% to 12.3 ± 10.9% ($p < 0.01$). Balloon angioplasty was performed in 11 (6.9%), single stent was implanted in 134 (84,3%), and 2 stents within one lesion in 14 (8,8%) patients. Complete symptom resolution was observed in 90.6% of patients after successful PTA.

A 6 months follow-up period was completed by 151 patients (44.7 ± 19.6 months). Twenty-one (13.9%) restenoses ≥ 50% occurred, including 1 (9.1%) out of 11 after balloon angioplasty, 15 (11.8%) out of 127 after one stent implantation, and 5 (38.5%) after 2 stents implantation for one lesion ($p = 0.029$). Nineteen symptomatic restenoses were successfully treated with repeated angioplasty. Multivariable analysis revealed that independent predictors of restenosis were implantation of 2 stents ($p = 0.046$), smaller stent diameter ($p = 0.029$), and increased hs-CRP level ($p < 0.001$). A trend to association with younger age was observed ($p = 0.06$).

Conclusions: Angioplasty is a safe and effective method for the treatment SAS/IAS and leads to symptom reversal in majority of patients. Hs-CRP level, stent diameter, 2 stents implanted for one lesion are independent predictors of restenosis.

Key words: angioplasty, subclavian artery stenosis, restenosis

Streszczenie

Wstęp: Angioplastyka (PTA) zwężenia tętnicy podobojczykowej (SAS) i/lub pnia ramienno-głowowego (IAS) stała się leczeniem z wyboru w wyselekcjonowanej grupie chorych.

Cel: Określenie częstości i czynników predykcyjnych restenozy u chorych poddanych angioplastyce SAS/IAS.

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Metody: Do PTA zakwalifikowano 168 chorych (73 mężczyzn), w wieku 61,6 ± 8,3 roku, ze stwierdzoną angiograficznie niedrożnością lub zwężeniem SAS/IAS ≥ 50% i objawami niedokrwienia mózgu, chromaniem kończyny górnej, zespołem podkradania wieńcowo-podobojczykowego w celu umożliwienia kontroli ciśnienia tętniczego.

Wyniki: Zabieg PTA był skuteczny u 159 (94,6%) chorych oraz w 164 zmianach, w tym 141 (100%) zwężeniach i 23 (71,9%) spośród 32 niedrożności SAS/IAS. Średni stopień zwężenia wynosił 75,7 ± 15,7% przed oraz 12,3 ± 10,9% po PTA SAS/IAS ($p < 0,05$). Balonową angioplastykę wykonano u 11 (6,9%) chorych, u 134 (84,3%) wszczepiono jeden stent, a u 14 (8,8%) – 2 stenty do zaopatrzenia jednej zmiany. Całkowite ustąpienie dolegliwości zaobserwowano u 90,6% chorych po skutecznej PTA.

Spośród 151 chorych podczas co najmniej 6-miesięcznego okresu obserwacji (44,7 ± 19,6 miesięcy), u 21 (13,9%) stwierdzono ponowne zwężenie SAS/IAS ≥ 50%, w tym u jednego (9,1%) z 11 po balonowej angioplastyce, 15 (11,8%) ze 127 po implantacji jednego stentu oraz u 5 (38,5%) z 13 po implantacji 2 stentów do zaopatrzenia jednego zwężenia ($p = 0,029$). Dziewiętnastu chorych z nawrotem objawów poddano powtórnej PTA.

Zidentyfikowano następujące niezależne czynniki prognostyczne restenozy: implantacja 2 stentów ($p = 0,046$), mała średnica stentu ($p = 0,029$) oraz stężenie hs-CRP ($p < 0,001$). Wykazano trend do korelacji z restenozą u młodszych chorych ($p = 0,06$).

Wnioski: Angioplastyka jest efektywną metodą leczenia SAS/IAS i przyczynia się do ustąpienia objawów klinicznych niedokrwienia u większości chorych. Restenoza wykazuje silny związek z liczbą implantowanych stentów oraz średnicą stentu, a także stężeniem hs-CRP.

Słowa kluczowe: angioplastyka, zwężenie tętnicy podobojczykowej, restenoza

Introduction

The PTA of subclavian artery stenosis (SAS) and/or innominate artery stenosis (IAS) has become the treatment of choice in patients with symptoms of the posterior fossa ischemia, claudication of the upper extremities and in patients referred for CABG with internal mammary artery implantation [1-4]. The procedure has a high rate of immediate efficacy and leads to prompt (immediate) relief of symptoms caused by SAS and IAS [1-7].

Long term benefit is limited by restenosis which is reported in up to 18% of patients [5, 7-9]. Some clinical, angiographic and procedural parameters are described in the literature as factors associated with restenosis [5, 10, 11]. The problem is interesting, because in carotid arteries, which have similar localization and diameter, restenosis occurs three times less often [12]. Experimental and clinical studies indicate that also an inflammatory process plays an important role in pathogenesis of restenosis after stent implantation [13, 14]. In the case of PTA of SAS/IAS the problem is additionally complicated by late restenosis, which occurs one year after PTA [5, 8, 15].

The aim of the current study was to identify predictors of restenosis and to assess their prevalence in patients treated with angioplasty of subclavian artery stenosis.

Material

The study included 168 patients (94 male, 74 female), aged 61 ± 8.3 years (range: 38-80), who underwent PTA of SAS/IAS recruited from a group of 238 patients with angiographically proven stenosis or occlusion of subclavian or innominate artery. 173 lesions were qualified for PTA (bilateral lesions in 5 patients) including: 132 (78.7%) lesions in left subclavian artery, 30 (17.8%) – in right subclavian artery and 11 (6.5%) – in innominate artery.

Seventy patients without clinical symptoms of stenosis or occlusion and no additional indications for the procedure were qualified for conservative treatment.

Symptoms of the posterior fossa ischemia were present in 27 (16%) patients, claudication of the upper extremity in 23 (13.6%) and both: claudication and ischemia symptoms in 101 patients (60.1%) respectively. In 3 patients (1.8%) PTA was performed due to coronary-subclavian steal syndrome after CABG, and in 2 (1.2%) patients PTA was performed prior the scheduled CABG with implantation of the internal mammary artery to left anterior descending artery. In 4 patients with bilateral SAS the only indication for PTA was inability to measure blood pressure. In 5 (3%) patients without symptoms of ischemia from the posterior region of the cerebrum and no claudication, but with occlusion of the internal carotid artery, PTA was performed to increase brain perfusion diminished after stroke.

Isolated SAS/IAS was present in 39 (23.2%) of the 168 patients referred for PTA. In the remaining 129 (76.8%) patients there were stenoses in arteries in other localizations for instance: in carotid arteries, coronary arteries, renal arteries and/or lower extremities arteries. In 87 (51.8%) cases stenosis of ≥ 50% in at least one coronary artery was present, in 35 (20.8%) stenosis ≥ 50% in lower extremities arteries and in 13 (7.7%) in renal artery ≥ 50%, respectively. Moreover, in 68 (40.5%) patients there was coexisting stenosis of ≥ 50% in one of carotid arteries (internal or common) or in vertebral artery contralateral to SAS/IAS. Percutaneous and/or surgical revascularization procedure within at least one peripheral artery excluding posterior fossa was performed in 95 (56.2%) patients.

Methods

Angiography of the SAS/IAS was performed immediately before the procedure, with the use of COROSCOP system (Siemens). The stenosis was visualized in at least 2 views and the quantitative assessment of the stenosis was performed with the use of Quantcor QCA V2.0.

In all patients transfemoral access was achieved with the use of a guiding catheter or a long guiding sheath 6-8 F. Additional access trough brachial or radial artery was used in patients with chronic subclavian artery occlusion (guiding catheter, long guiding sheath 5-6 F). Guide wires with the diameter of 0.014-0.035 inch were used depending on the severity of SAS/IAS, anatomical conditions and operator's preferences. The technique of the procedure was as follows: a guide wire was passed through stenosis or occlusion site followed by vessel lumen dilatation with a balloon catheter with or without stent implantation. If technically feasible direct stenting, without postdilatation was preferred. Balloon-expandable stainless steel stents were preferred and the diameter of the stent was adjusted to reference diameter of the artery. Self-expandable stent was chosen for treatment of ostial infundibuliform SAS, long lesions (> 30 mm) and in peripheral localizations – in places where steel stents could be deformed or crushed by the clavicle during moving. When a self-expandable stent was used the diameter was 1-2 mm bigger than the reference diameter of the artery. Optimal result of the procedure was defined as a residual stenosis < 30% with gradient < 10 mm Hg.

When lesions with large plaque burden localized in the neighborhood of vertebral artery were treated, vertebral artery was protected with a guide wire, and in lesions covering vertebral artery, kissing balloons technique with simultaneous inflation of two balloons was used. Neuroprotection devices (proximal: PAES GORE NPS or distal: Angioguard filter) were used when an antegrade flow in the vertebral artery was observed, or the lesion was localized in the ostium of the artery, large thrombus was seen or the lesion was localized in IAS.

All patients received aspirin (75 mg/d) and ticlopidine (2 × 250 mg/d) or clopidogrel (75 mg/d) at least 3 days before an elective procedure. In the case of urgent procedure patients received loading dose of aspirin (325 mg) and clopidogrel (300 mg). Standard doses of heparin were administrated during the procedure. After the procedure treatment with aspirin was recommended indefinitely and with clopidogrel/ticlopidine for 3 months, respectively.

Monitoring after the procedure

All patients underwent follow-up evaluation 3-6, 12 months after treatment of SAS/IAS with PTA and once a year thereafter. The assessment included: clinical and neurological examination, blood pressure measurements on the right and left arm and ultrasound study with the use of duplex Doppler technique with evaluation of flow in the arteries.

Restenosis evaluation

Restenosis was diagnosed on the basis of the following data: recurrent clinical symptoms, blood pressure difference between arms > 20 mm Hg and the result of ultrasound study revealing steal syndrome from the subclavian artery and 2-fold difference in the peak systolic velocity at the site of the procedure when compared with the result immediately after PTA [16]. In patients with clinical symptoms of restenosis, balloon angioplasty of SAS/IAS was performed during control angiography. In selected cases restenosis was treated with cutting balloon or with drug eluting stent implantation.

Laboratory study

The following laboratory analyses were performed in all patients at admission: total cholesterol level, LDL and HDL cholesterol level, high sensitivity C-reactive protein (hs-CRP) and leukocytosis.

Results

Forty five (26.8%) patients had a history of myocardial infarction and 44 (26.2%) patients had a history of stroke or TIA. Dyslipidaemia was present in 152 (90.5%), patients, smoking in 139 (82.7%), diabetes in 40 (23.8%), hypertension in 126 (75%) and obesity in 26 (15.5%) patients, respectively.

Successful PTA of SAS/IAS was performed in 159 (94.6%) of 168 patients referred for the procedure (tab. 1). In 5 patients bilateral PTA was performed. The success rate in treatment of stenosis was 100% and in occlusions achieved 71.9%, respectively (successful treatment of 23 out of 32 occlusions). Mean degree of stenosis before the procedure was 75.7 ± 15.7% and decreased to 12.3 ± 10.9% ($p < 0.001$) after PTA. Residual stenosis did not exceed 30% in any patient.

In 11 patients balloon angioplasty was performed. One stent was used in 139 cases of SAS/IAS and 2 or more stents in one artery were implanted in 14 patients. In 13 patients the ipsilateral vertebral artery and/or right common carotid artery were protected with a guide wire or with the use or a neuroprotection system. In 5 patients proximal neuroprotection system was used (PAES, GORE NPS). In one female patient common carotid artery was protected with the use of Angioguard filter. Moreover, in 13 patients (8.2%) with concomitant critical stenosis of vertebral artery, angioplasty of this artery with stent implantation was performed. Five out of 9 patients with unsuccessful opening of left subclavian artery occlusion were referred for surgical treatment with implantation of

Table 1. PTA procedure – success rate and procedure details
Tabela 1. *Zabieg PTA – skuteczność i dane proceduralne*

Number of patients/number of lesions treated with PTA SAS/IAS	168 patients/173 lesions
Bilateral PTA	5 patients
Vascular access transfemoral access double-site access (transfemoral and transbrachial/transradial)	 153 15
Success rate – per patients/per procedure in stenoses in occlusions	159 (94.6%)/164 (94.8%) 141/141 (100%) 23/32 (71.9%)
Mean degree of SAS/IAS before PTA (range 51-100) after PTA (range 0-29)	 75.7 ± 15.7% 12.3 ± 10.9%
Balloon angioplasty (per patients/per lesions)	11 (6.9%)/11
Stent implantation (per patients/per lesions)	148 (93.1%)/153
Direct stenting (% of lesions with stents)	61/153 (39.9%)
Number of SAS/IAS with stent implantation	142/11
Number of implanted stents 1 stent for one lesion ≥ 2 stents for one lesion	 139 14
Mean stent length (range 9-88 mm)	24.6 ± 11.6
Mean stent diameter (range 5-10 mm)	7.6 ± 1.2
Steel stent	128 (83.7 %)
Self expandable stent	25 (16.3 %)
Vertebral artery angioplasty	13 (8.2 %)
Protection of the vertebral artery/common carotid artery with a guide wire with PAES neuroprotection syste filter in the right common carotid artery during PTA IAS	13 (8.2 %) 7 (4.4 %) 5 (3.1 %) 1 (0.7 %)
Mean fluoroscopy time [min] in occlusions in stenoses	19.7 ± 14.8 34.7 ± 20.8 16.0 ± 9.8

carotid-subclavian bypass. Details concerning the procedure are presented in table 1.

Periprocedural complications occurred in 8 patients (4.8%) including stroke in the posterior perfusion region with persistent amaurosis in one patient (0.6%), hyperperfusion syndrome with intracranial bleeding in one patient (0.6%), acute ischemia of the upper extremity requiring implantation of the additional stent at the dissection site in one female patient (0.6%) and bradycardia with blood pressure drop in one patient (0.6%). In one female patient occlusion of aorto-femoral bypass was observed. Moreover, in several patients hematomas at the vascular access site into femoral or axillary artery were observed. In 3 patients (1.8%) large hematomas were observed what required prolonged hospitalization. No deaths occurred during 30-days follow-up period.

The release of claudication was observed in all patients after successful PTA and dizziness as well as vertigo resolved in 116 (90.6%) patients out of 128 patients with these symptoms prior to the procedure. Mean difference between systolic blood pressure measured on the brachial artery decreased from 36.1 ± 19.4 mm Hg to 11 ± 5.9 mm Hg ($p < 0.001$) and for diastolic blood pressure from 18.8 ± 17.8 mm Hg to 10 ± 4.9 mm Hg ($p < 0.001$), respectively. Difference between systolic blood pressure values ≥ 20 mm Hg and diastolic ≥ 10 mm Hg were observed in 21 patients (13.2%) after successful PTA, that was due to occlusion or critical stenosis (near total) of the contralateral SA/IA. The mean systolic velocity in the subclavian artery and/or in the innominate artery after the procedure was 1.51 ± 0.59 m/s.

During 6-month follow up after successful PTA there were 2 cardiovascular deaths (one sudden cardiac death, one death due to myocardial infarction). Six-month follow-up period was completed for 151 patients. During mean follow-up period of 44.7 ± 25.9 months (range 6108) restenosis ≥ 50% of SAS/IAS occurred in 21 (13.9%) patients, including two cases (18.2%) of restenosis in 11 procedures in innominate artery, one restenosis (3.7%) for 27 procedures in right subclavian artery and 18 cases

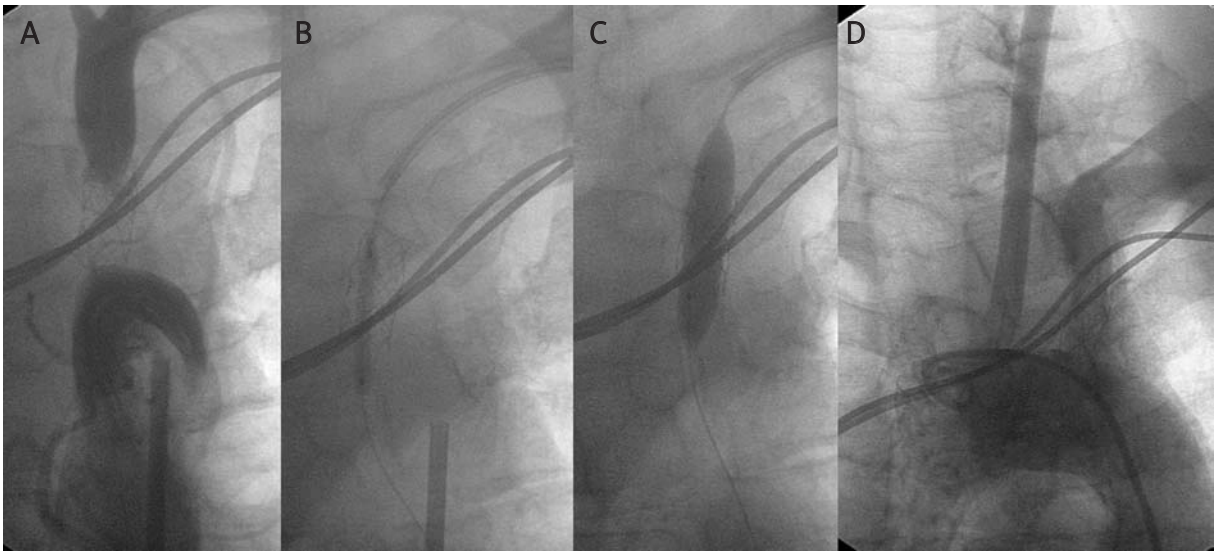

Fig. 1. A – diffuse restenosis in an implanted stent 7/16 mm causing its occlusion 8 months after PTA. Leads of a pacemaker system are also seen. Bilateral vascular access through radial and femoral artery, **B** – unsuccessful attempt with transfemoral access of passing through an occlusion site in subclavian artery. Opening of the artery through transradial access with a 0,014 guide wire, predilatation with coronary balloon 2.5/20 mm, **C** – subsequent balloon dilatation 6.0/20 mm from transradial access, **D** – final effect

***Ryc. 1. A** – rozlana restenoza w obrębie implantowanego stentu 7/18 mm powodująca jego niedrożność w 8 miesięcy po PTA. Widoczne elektrody implantowanego stymulatora. Podwójny dostęp z tętnicy promieniowej i udowej. **B** – z dostępu przez tętnicę udową nie udało się sforsować liderem miejsca niedrożności tętnicy podobojczykowej. Udrożnienie z dostępu promieniowego – liderem 0,014 predylatacja balonem wieńcowym 2,5/20 mm. **C** – kolejne poszerzenie balonem 6,0/20 mm z dostępu promieniowego. **D** – wynik końcowy*

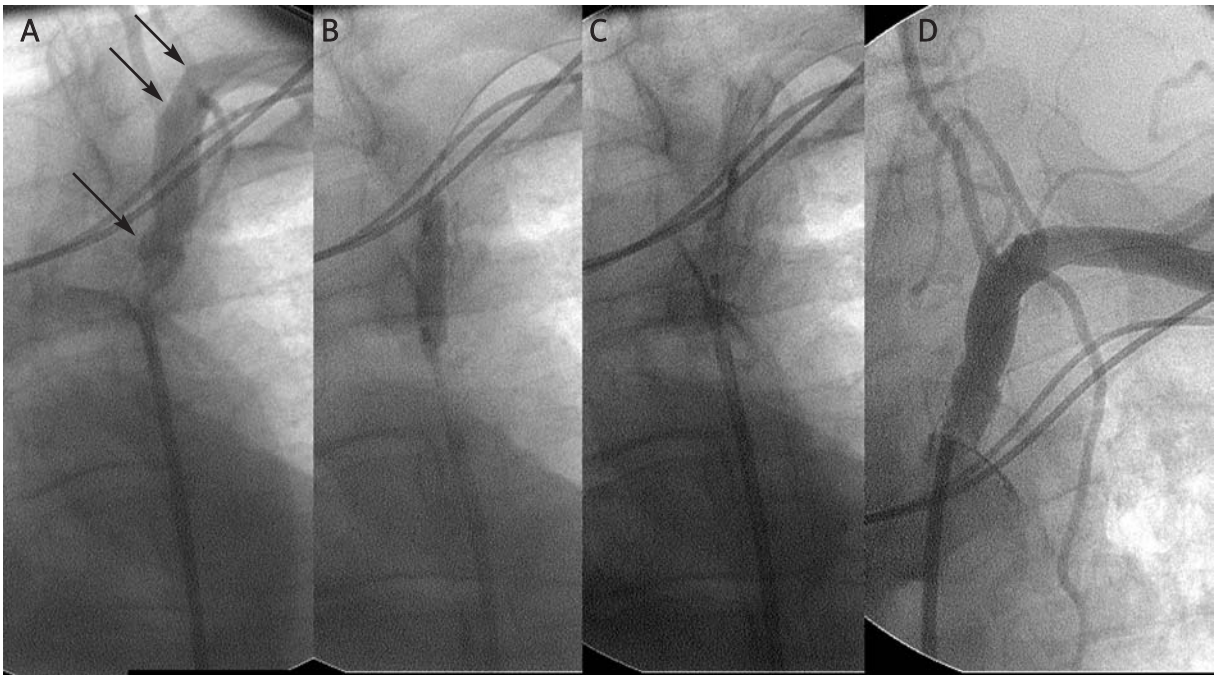

Fig. 2. A – result after further 8 months in the same patient. Local restenosis in the proximal part of the implanted stent (arrow) and neointima proliferation distal to the implanted stent (2 arrows). **B** – angioplasty with a conventional balloon through transfemoral access. **C** – implantation of stent 7.0/18 mm overlapping previously implanted stent at the site of neointima proliferation distal to previously implanted stent – stent positioning. **D** – final result

***Ryc. 2. A** – obraz po kolejnych 8 miesiącach u tego samego chorego. Lokalna restenoza w proksymalnej części implantowanego stentu (strzałka) oraz rozrost neointimy dystalnie do implantowanego stentu (2 strzałki). **B** – angioplastyka balonem konwencjonalnym z dostępu udowego. **C** – implantacja stentu 7,0/18 mm „na zakładkę" w miejsce rozrostu neointimy, za uprzednio implantowanym stentem – pozycjonowanie stentu. **D** – wynik końcowy*

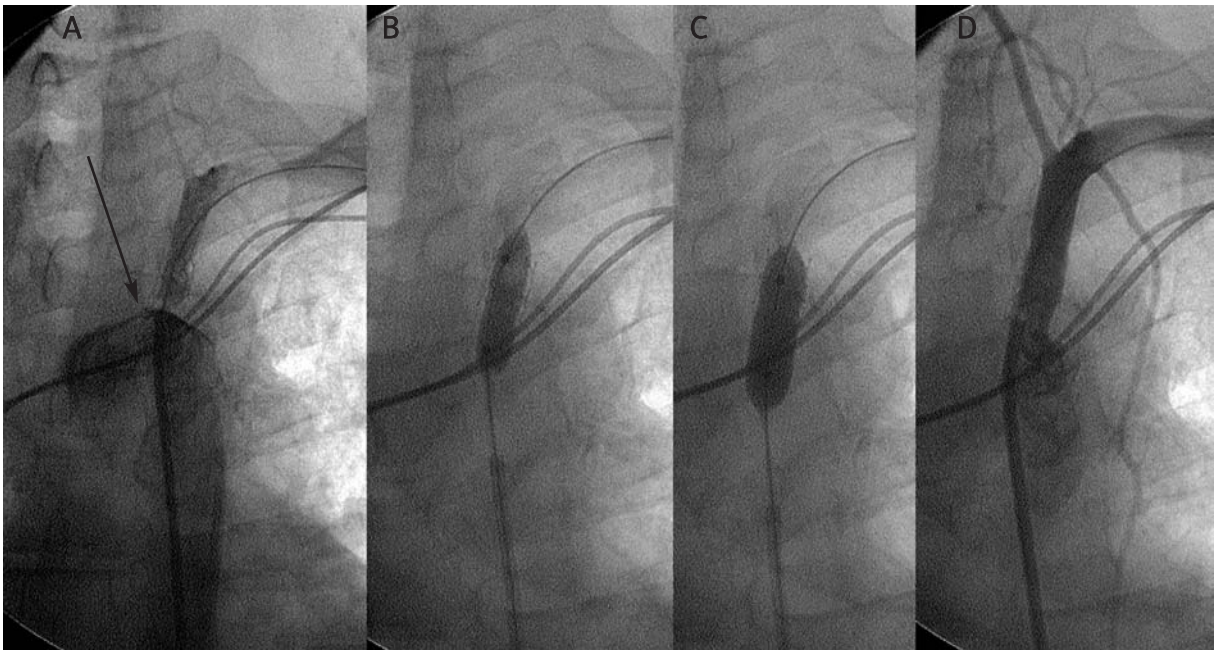

Fig. 3. A – result after subsequent 10 months in the same patient. Subsequent (3th) restenosis in the proximal part of implanted stent (arrow). **B** – angioplasty with a cutting balloon 7 mm through transfemoral access. **C** – dilatation with a conventional balloon, pressure 12 atm. **D** – final result

***Ryc. 3. A** – obraz po kolejnych 10 miesiącach u tego samego chorego. Kolejna (3.) restenoza w proksymalnej części implantowanego stentu (strzałka). **B** – angioplastyka balonem tnącym 7 mm z dostępu udowego. **C** – dodatkowe poszerzanie balonem konwencjonalnym 8,0/20 mm, ciśnieniem 12 atm. **D** – wynik końcowy*

(15.3%) of restenosis in 118 procedures in left subclavian artery ($p = 0.588$). Restenosis in procedures performed for artery occlusion occurred in 2 out of 23 patients (8.7%) and in PTA performed for treatment of artery stenosis in 19 out of 141 patients (13.5%) ($p = 0.525$).

Among patients who underwent balloon angioplasty ($n = 11$) restenosis was observed in one patient (9.1%). In patients who underwent angioplasty with one stent implantation ($n = 127$) restenosis occurred in 15 patients (11.8%), and in individuals with implantation of 2 or more stents for treatment of one lesion in SAS/IAS ($n = 13$) in 5 patients (38.5%), respectively ($p = 0.029$).

Restenosis during first year of follow-up was diagnosed in 10 patients at the mean time of 6.8 ± 2.0 months (range 5-11 months) after the procedure. In the rest of the group, restenosis was identified during second or third year of follow-up at the mean time 21.4 ± 7.4 months (range 13-35) after PTA. Clinical symptoms of restenosis occurred in 20 out of 21 patients. Repeated PTA was performed in 19 patients. 2 patients were referred for conservative treatment. In 7 patients out of 19 who underwent repeated PTA (36.8%) to treat restenosis, recurrence of restenosis occurred. In 5 patients from this group (15.8%) restenosis recurred 3 or 4 times (in 2 patients repeated procedure was performed with cutting balloon and one female patient was referred for surgical treatment with aorto-subclavian bypass). In one patient drug eluting stent was implanted at the site of restenosis.

Representative images demonstrating procedures in patients with restenosis are presented in fig. 1-5.

A univariate analysis demonstrated that out of 38 variables (clinical, laboratory, angiographic and procedural) the following parameters are associated with restenosis: younger age ($p = 0.001$), high level of hs-CRP ($p < 0.001$), high leukocytosis ($p = 0.009$), implantation of 2 or more stents in one artery ($p = 0.006$), smaller diameter of stent ($p = 0.001$) and lower levels of HDL cholesterol ($p = 0.044$) (tab. 2). Multivariable backward stepwise regression analysis revealed that the following parameters were independent risk factors of restenosis: hs-CRP level ($p < 0.001$), stent diameter ($p = 0.029$) and implantation of 2 or more stents for treatment of one lesion ($p = 0.046$) (tab. 3). Also a trend toward an association with younger age was demonstrated ($p = 0.06$).

Discussion

Percutaneous transluminal revascularization procedures of subclavian artery and innominate artery are an effective and common method of treatment of SAS/IAS. After successful PTA complete relief of symptoms is observed in 76-89% patients. In the rest of patients an improvement in clinical symptoms is present [1-7]. In the current study, we demonstrated complete relief of symptoms in 90.6% patients.

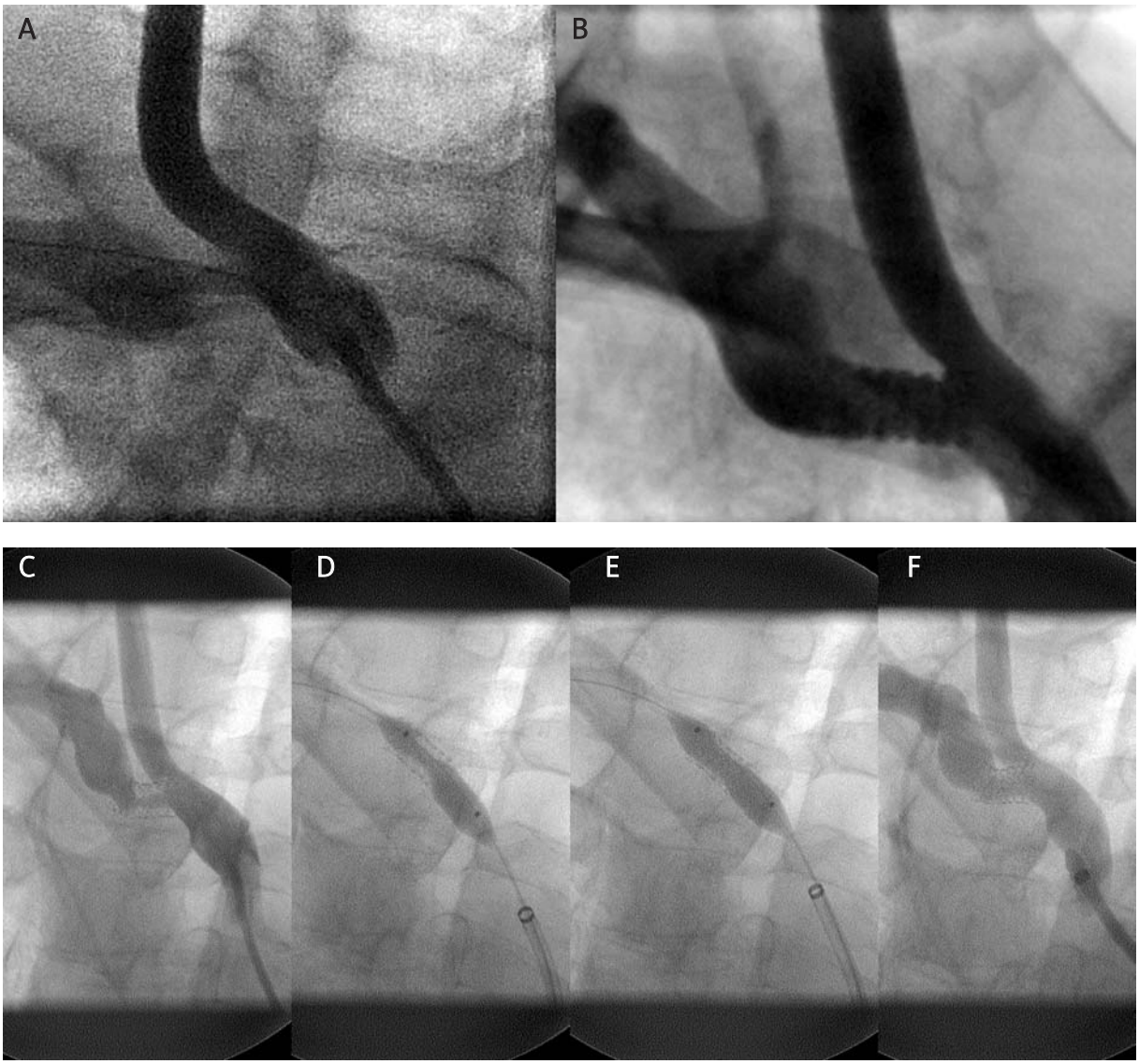

Fig. 4. A – tight stenosis in right subclavian artery. **B** – result of angioplasty with stent implantation 7.0/15 mm. **C** – the same patient after 16 months – diffuse restenosis in stent with a significant vessel lumen reduction. Transfemoral access. **D**, **E** – angioplasty with the use of cutting balloon 7.0/20 mm, pressure 8-10 atm. **F** – final result

***Ryc. 4. A** – ciasne zwężenie tętnicy podobojczykowej prawej. **B** – obraz po angioplastyce z implantacją stentu 7,0/15 mm. **C** – ten sam chory po 16 miesiącach – rozlana restenoza w stencie z istotną redukcją światła. Dostęp z tętnicy udowej. **D**, **E** – angioplastyka za pomocą balonu tnącego 7,0/20 mm, ciśnienie 8–10 atm. **F** – wynik końcowy*

Success rate in PTA of SA/IA is currently up to 100%, and in cases with occlusions in 46-100% (in centers with high experience it exceeds 70%) [5, 7, 10, 11, 17, 18]. In the current study, bilateral vascular access through femoral and radial/brachial artery during PTA enabled reaching success rate of 72% in cases with artery occlusions.

Complications are reported in 2.7-17.8% patients and include most frequently complications related with vascular access (2-9%) and peripheral embolism (0-2.7%). The rate of stroke does not exceed 2%, and deaths occur sporadically [2, 5, 7, 10, 15, 18, 19]. Serious complications include aortic dissection or blood extravasation with mediastinal bleeding in attempts of opening of chronic occlusions [15]. In the current study no deaths in periprocedural period were observed and serious compilations (i.e. stroke, intracranial bleeding, occlusion of the artery with stent and occlusion of aorto-femoral bypass) occurred in 4 patients (2.4%). Complications related to vascular access site (i.e. large hematoma) occurred in 3 patients out of 168 patients

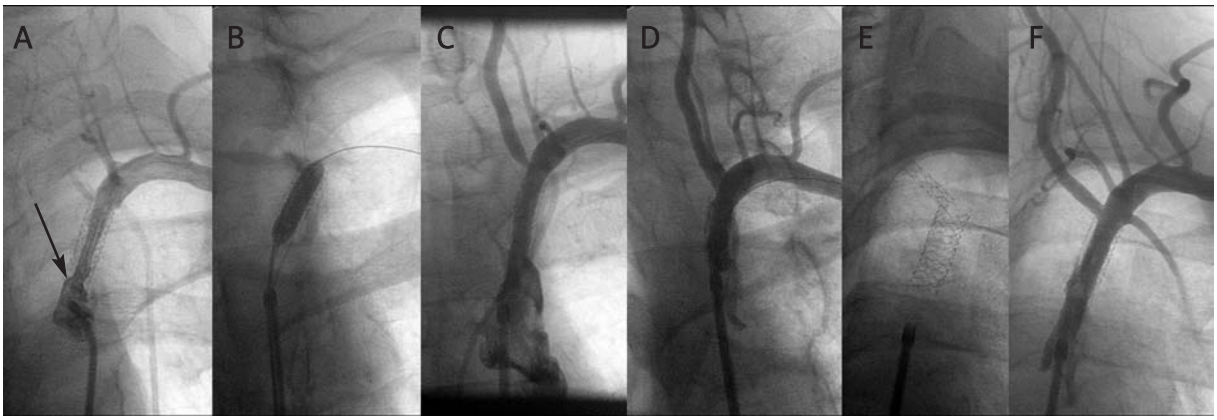

Fig. 5. A – diffuse restenosis in the implanted 6/18 mm stent (QA 61%) 8 months after PTA. Baseline gradient across stenosis was 80 mm Hg and 1 min after the end of exercise (hand grip) 110 mm Hg, respectively. Reverse flow in vertebral artery, which ostium is located in the direct neighborhood of the stent (arrow). **B** – dilatation with a conventional balloon 5.0/20 mm and 7.0/20 mm; vertebral artery is protected with a guide wire. **C** – result after several dilatations. Small residual stenosis, but displacement of a part of the atherosclerotic plaque in vertebral artery ostium causes its significant stenosis. **D** – result of direct drug eluting stent (3.0/13 mm) implantation in vertebral artery. **E, F** – final result with and without contrast administration. A protrusion of the stent of about 1 mm from vertebral artery into subclavian artery is seen. Baseline gradient after the procedure was 12 mm Hg

***Ryc. 5. A** – rozlana restenoza w obrębie implantowanego stentu 6/18 mm (QA 61%) w 8 miesięcy po PTA. Gradient spoczynkowy przez zwężenie 80 mm Hg, powysiłkowy po 1 min wysiłku* (hand grip) *110 mm Hg. Odwrócony przepływ w tętnicy kręgowej, która odchodzi tuż za stentem (strzałka). **B** – poszerzanie balonem konwencjonalnym 5,0/20 mm i 7,0/20 mm, tętnica kręgowa zabezpieczona liderem. **C** – obraz po kilku inflacjach. Niewielkie rezydualne zwężenie, ale przesunięcie części blaszki miażdżycowej w obręb ujścia tętnicy kręgowej powoduje jej istotne zwężenie. **D** – obraz po implantacji do tętnicy kręgowej w trybie „direct stenting" stentu pokrywanego lekiem 3,0/13 mm. **E, F** – obraz końcowy bez i po podaniu kontrastu. Widoczne wysunięcie stentu w tętnicy kręgowej o ok. 1 mm do światła tętnicy podobojczykowej. Gradient spoczynkowy po zabiegu 12 mm Hg*

(1.8%) who underwent PTA. In order to diminish risk of serious embolic complications it seems reasonable to use neuroprotection systems in selected patients especially in lesions involving vertebral artery ostium, patients without protective steal syndrome in the vertebral artery and in stenosis of innominate artery [5, 20-22]. Use of the distal neuroprotection systems with filters or occlusive balloons was reported by e.g. by Staikov et al., Vitec et al., and Shah et al. [20-22]. In our center we use proximal protection system with a guide wire GORE NPS (former Parodi Anti Emboli system) in high risk lesions including those with thrombus. The procedure includes temporal occlusion of the proximal portion of subclavian artery with a balloon, which causes reverse blood flow in vertebral artery and enables safe stent implantation [5].

Long term results of PTA of SAS/IAS is determined first of all by recurrence of clinical symptoms caused by restenosis and atherosclerosis-related events in other arterial vascular beds.

The rate of restenosis after stent implantation ranges from 6 to 18% and the mean is 12-14% [5-11, 15, 18]. Sawada et al. demonstrated restenosis in 29.4% patients 3-6 months after balloon angioplasty of SAS [24]. On the other hand, Schillinger et al. demonstrated low restenosis rate one year after stent implantation, but unfortunately the study revealed no superiority of angioplasty with stent implantation over balloon angioplasty during second and third year of follow-up, which was caused by late restenosis [8]. On the basis of the results of current study it seems justified to perform balloon angioplasty, and to perform stenting only in lesions, with suboptimal balloon angioplasty result (for example: dissection, high residual stenosis > 30%, thrombus) [5, 8, 9, 11, 25].

Risk factors of restenosis are not clearly identified. In few studies the following variables are mentioned: lesion length, residual stenosis after the procedure, smaller diameter of implanted stent, systolic blood pressure difference between the upper extremities [5, 10, 15, 24]. However, there are studies questioning the presence of any predictors of restenosis [11]. To our knowledge, there was no study evaluating potential association between inflammatory process and stent neointimal hyperplasia in subclavian and innominate artery, while such an association between in-stent restenosis and inflammation has been described for coronary arteries [13, 14]. From numerous clinical, laboratory, angiographic and procedural variables (tab. 2), which were analyzed in the current study the following factors were associated with restenosis: younger age, high hs-CRP level, higher leukocytosis, implantation of two or more stent for one lesion, smaller stent diameter, low HDL level. On the other hand, multivariable analysis revealed that only hs-CRP level (what could confirm an important role of inflammation), small stent diameter, implantation of 2 or more stents for one lesion and younger age were independent risk factors of restenosis. Younger age as a risk factor can indicate more severe progression

Table 2. Comparison of patients with restenosis ≥ 50% and patient without restenosis. Data are presented for 151 patients with at least 6-month follow-up
Tabela 2. *Porównanie chorych, u których wystąpiła restenoza ≥ 50% i chorych bez nawrotu zwężenia. Analiza dotyczy 151 chorych, u których obserwacja trwała przynajmniej 6 miesięcy*

	Patients with restenosis n = 21	Patients without restenosis n =130	p (χ^2)
Follow-up period [months ± SD]	55.7 ± 28.4	43.9 ± 24.5	0.047
Procedure data			
Degree of SAS/IAS before PTA [% ± SD]	73.9 ± 15	75.0 ± 15.3	0.750
Degree of SAS/IAS after PTA [% ± SD]	15.9 ± 8.2	14.2 ± 11.3	0.518
PTA of the left SAS vs. right SA or IAS	18/3	100/35	0.361
SAS occlusion, n (%)	2 (9.5)	19 (14.6)	0.532
Predilatation (per number of stents), n (%)	12/20 (60)	74/125 (59.2)	0.946
Balloon angioplasty, n (%)	1 (4.8)	10 (7.7)	0.631
Implantation of one stent for one lesion, n (%)	15 (71.4)	112 (86.2)	0.088
Implantation of ≥ 2 stents for one lesion, n (%)	5 (23.8)	8 (6.2)	0.007
Diameter of implanted stent [mm ± SD]	6.8 ± 1.04	7.71 ± 1.16	0.001
Length of the implanted stent [mm ± SD]	23.8 ± 16.4	24.31 ± 9.24	0.843
Deployment pressure [atm ± SD]	12.2 ±3.79	11.7 ± 3.1	0.524
Blood pressure measured on upper extremities			
Difference in mean SBP before PTA [mm Hg ± SD]	40.5 ± 15	34.5 ± 20.4	0.204
Difference in mean DBP before PTA [mm Hg ± SD]	21.7 ± 19.8	17.7 ± 17.8	0.353
Difference in mean SBP after PTA [mm Hg ± SD]	–0.24 ± 15.6	6.47 ± 23.5	0.208
Difference in mean DBP after PTA [mm Hg ± SD]	4.52 ± 16	3.76 ± 13.9	0.819
Comorbidities			
Peripheral artery occlusive disease (lower extremities), n (%)	3 (14.3)	28 (21.5)	0.445
Renal artery stenosis ≥ 50%, n (%)	1 (4.8)	12 (9.2)	0.498
ICA stenosis ≥ 50% or contralateral VA stenosis, n (%)	9 (42.9)	55 (42.3)	0.962
Coronary artery disease	10 (47.6)	69 (53.1)	0.642
Number of coronary arteries with stenosis ≥ 50%	2.14 ± 1.6	1.91 ± 1.5	0.512
Male sex, n (%)	11 (52.4)	72 (55.4)	0.797
Age [years ± SD]	55.4 ± 8.05	61.7 ± 8.0	0.001
Obesity [BMI ≥ 30 kg/m^2], n (%)	3 (14.3)	21 (16.2)	0.828
Prior myocardial infarction, n (%)	5 (23.8)	53 (40.8)	0.138
Prior cerebral ischemic incident, n (%)	4 (19)	34 (26.2)	0.486
Hyperlipidaemia, n (%)	19 (90.5)	118 (90.8)	0.966
Smoking, n (%)	14 (66.7)	111 (85.4)	0.035
Diabetes, n (%)	3 (14.3)	35 (26.9)	0.216
Hypertension, n (%)	14 (66.7)	98 (75.4)	0.397
Laboratory studies			
Triglyceride level [mmol/l ± SD]	1.84 ± 1.2	1.70 ± 1.1	0.578
Total cholesterol [mmol/l ± SD]	5.0 ± 1.2	5.37 ± 1.5	0.288
LDL cholesterol [mmol/l ± SD]	3.14 ± 0.85	3.31 ± 1.05	0.474
HDL cholesterol [mmol/l ± SD]	1.12 ± 0.29	1.26 ± 0.30	0.044
hs-CRP [mg/dl ± SD]	12.5 ± 11.4	4.26 ± 4.62	0.000
Leukocytosis [thousands ± SD]	8.8 ± 2.5	7.4 ± 2.1	0.009
Ultrasound study			
Systolic velocity SAS/IAS after PTA	1.65 ± 0.69	1.44 ± 0.50	0.092
Systolic velocity in VA after PTA	0.63 ± 0.28	0.49 ± 0.17	0.082
Diastolic VA after PTA	0.19 ± 0.13	0.17 ± 0.07	0.408

Abbreviations: DBP – diastolic blood pressure, ICA – internal carotid artery, SBP – systolic blood pressure, VA – vertebral artery – velocity in vertebral artery ipsilateral to PTA SAS/IAS
Skróty: DBP – ciśnienie tętnicze rozkurczowe, ICA – tętnica szyjna wewnętrzna, SBP – ciśnienie tętnicze skurczowe, VA – prędkość w tętnicy kręgowej po stronie PTA SAS/IAS

of atherosclerosis and more severe inflammation in this group. Recognizing the role of inflammation in SA/IA restenosis is a novel concept, both in Polish and international studies.

In contrast to other vascular beds restenosis was not more frequent after treatment of occlusion, which is in concordance with the previous studies [5, 15, 25, 26]. On the other hand, in over a half of patients with restenosis,

Table 3. Multivariable backward logistic regression analysis. Independent risk factors of SAS/IAS restenosis after PTA

Tabela 3. *Wieloczynnikowa analiza metodą krokowej regresji wstecznej. Niezależne czynniki ryzyka restenozy w SAS/IAS po PTA*

	BETA	Error BETA	HR (CI)	p
Intercept				0.018
hs-CRP level before the procedure	0.41	0.08	**1.51** (1,29-1.76)	< 0.001
Implantation of 2 stents for one lesion	0.16	0.08	**1.17** (1.01-1.37)	0.046
Stent/stents diameter	–0.18	0.08	**0.84** (0.71-0.98)	0.029
Age	–0.16	0.08	**0.85** (0.73-0.99)	0.06

recurrence of symptoms occurred and caused symptoms in the second or third year of follow-up, which was observed by other authors [8, 15]. It indicates the necessity of long term follow-up of patients including medical interview, bilateral upper arm blood pressure measurements and systematic ultrasound study with flow assessment in SAS/IAS [17, 27]. We have previously demonstrated, that doubling velocity in SAS/IAS in comparison to the result of the ultrasound study performed immediately after procedure is characterized by high concordance with angiography when restenosis > 50% is considered [17].

Symptomatic restenosis after balloon angioplasty is treated with stent implantation and restenosis within stent in treated with balloon angioplasty [5, 8, 15, 28]. Treatment with cutting balloon have also been described [29], what was performed in 2 patients in the current study with recurrent restenosis. Moreover, in one female patient with 4 episodes of restenosis, we have decided to implant drug eluting stent. The follow-up period of this patient is 6 months (no restenosis) but it is too early to make a conclusion concerning long term benefit. It seems that recurrent restenosis, in this study occurring in 37% patients with restenosis is another topic requiring further investigations.

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