Prospective registry evaluating safety and efficacy of cobalt-chromium stent implantation in patients with *de novo* coronary lesions

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Abstract

Background: Cobalt-chromium (Co-Cr) stents are a new type of endovascular prostheses characterised by better mechanical properties than traditional stainless steel stents.

Aim: To assess the safety and efficacy of percutaneous coronary interventions (PCI) using the new Co-Cr Kos stent (Balton, Poland).

Methods: A total of 59 patients with coronary artery diseases (76% men, aged 60±9 years, diabetes – 16.9%, smoking – 62.7%, 11.8% – acute myocardial infarction) underwent PCI for *de novo* lesions in native coronary vessels. The patients were followed for 6 months for the occurrence of cardiac events. Quantitative coronary angiography was performed at baseline and after 6 months.

Results: In total, we implanted 62 stents in 59 coronary arteries. The mean diameter of the stents was 3.18±0.18 mm, and length – 14.62±2.12 mm. During a one-month follow-up period no cardiac events were noted. During a 6-month follow-up no death or new myocardial infarction were recorded. Control angiography was done in 55 (92%) subjects. Repeated target vessel revascularisation due to recurrent angina or in-stent restenosis was required in 10 (17%) patients; however, off-line core evaluation found significant re-narrowing in implanted stents (>50% diameter stenosis) only in 6 cases (10.9%). The mean late vessel lumen loss was 0.55±0.6 mm and stenosis 25.2±17.9%.

Conclusions: Implantation of the new Co-Cr Kos stent during PCI is safe and effective.

Key words: coronary artery disease, stent, PTCA, restenosis

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Introduction

Coronary angioplasty with stent implantation is currently one of the basic modalities of invasive treatment in patients with symptomatic coronary artery disease (CAD). There are many types of bare metal stents available made of 316L stainless steel. Recently, vascular endoprostheses based on cobalt-chromium (Co-Cr) alloys have been increasingly often introduced into clinical practice. Due to favourable mechanical properties, the use of Co-Cr alloys allows reduction of stent strut thickness without any compromise in stent radial forces and radiopacity. Such enhancements enable the reduction of endoprostheses' profile, increase their flexibility, and consequently facilitate stent implantation into tortuous vascular segments or in the case of severe obstructive lesions. Reducing stent strut thickness may also be of importance in lowering the risk of restenosis [1, 2].

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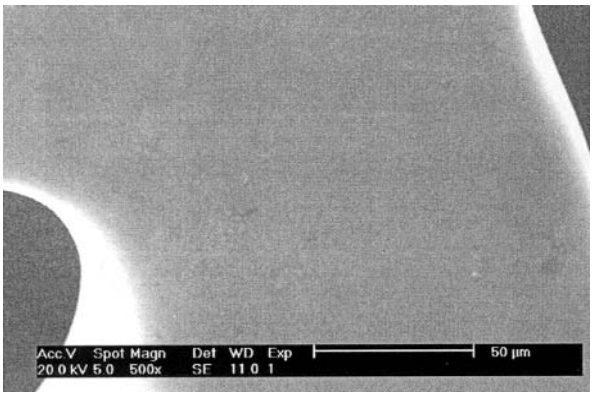

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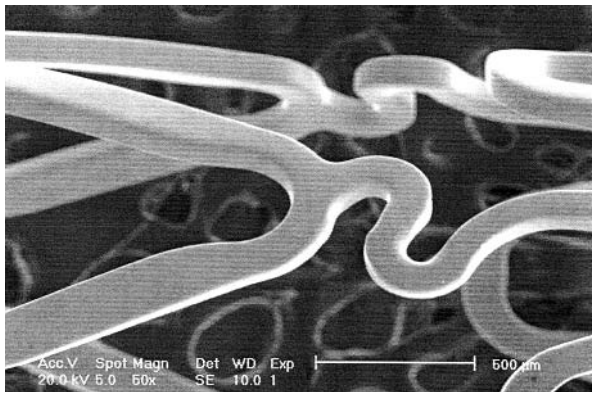

Figure I. The structure of the Kos stent

These advantages justify more common interest in the use of stents based on Co-Cr alloys.

The aim of our study was to evaluate the efficacy and safety of Co-Cr stents (Kos; Balton Sp. z o.o.) in the treatment of symptomatic angina pectoris.

Methods

Stent characteristics

The Kos stent (Figure 1) is made of L-605 Co-Cr alloy (composition: cobalt 51%, chromium 20%, nickel 10%, tungsten 15%, others 4%). Manufacturing method is similar to the Chopin stent. It is a Co-Cr alloy tube cut off with the use of a laser. Surface smoothness (Figure 1) is achieved by polishing using electrochemical methods.

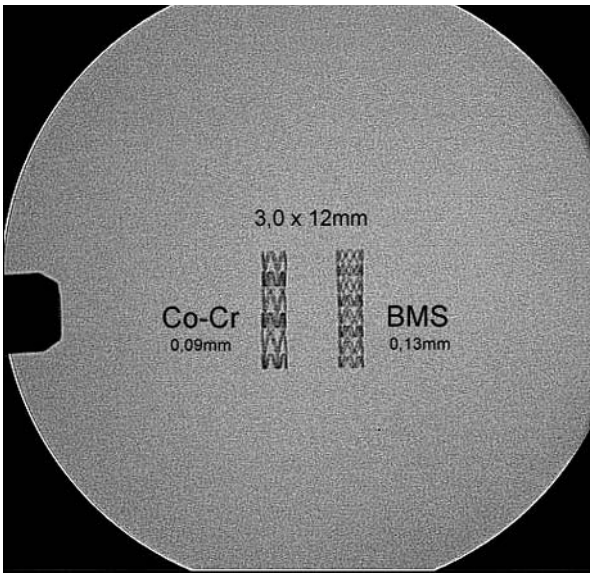

Figure 2. Radiopacity of the Kos stent (Co-Cr) compared with a standard bare metal stent (BMS)

Strut thickness is 0.09 mm. Stent profile of the device pre-mounted on the balloon catheter is 0.38 mm. After stent deployment, length loss does not exceed 0.5%, while diameter loss is less than 2%. Moreover, it features a small area of vessel wall coverage (14-19%). In spite of the thinner struts, the Kos stent has good radiopacity (Figure 2).

Patients

Fifty-nine consecutive patients suffering from symptomatic CAD with significant stenosis (>50% of vessel lumen diameter) seen in coronary angiography and selected for coronary stent implantation were enrolled in the study (Table I). Seven (11.8%) patients were admitted to hospital due to acute myocardial infarction (MI), 22 (37.3%) had unstable angina, and the remaining patients (50.9%) presented stable angina. Prior to intervention, coronary artery stenosis severity was assessed visually by an operator.

Table I. Demographic data of 59 studied patients

Parameter	
Male gender	45 (76.3%)
Age [years]	60±9.4
Hypercholesterolaemia	32 (54.2%)
History of CAD in the family	15 (25.4%)
Smoking	37 (62.7%)
Diabetes mellitus	10 (16.9%)
Hypertension	21 (35.6%)
History of myocardial infarction	22 (3.3%)
Stable coronary artery disease	30 (50.8%)
Unstable coronary artery disease	22 (37.3%)
Acute myocardial infarction	7 (11.8%)

Only *de novo* coronary lesions with stenosis ≥50% and <100%, type A and B_1, and reference vessel diameter ≥2.8 mm and ≤4.0 mm were selected. According to the study protocol, coverage of the whole atherosclerotic plaque with a stent of maximum 18 mm length was recommended. Patients with contraindications for aspirin (ASA), ticlopidine or clopidogrel, with left main stem involvement or known hypersensitivity to Co-Cr alloys were excluded from the study. The study was approved by the Local Bioethical Committee of the Silesian Medical Academy.

Percutaneous coronary intervention (PCI)

After informed consent was obtained the patients received 150 mg of ASA and 500 mg of ticlopidine b.i.d. or 75 mg of clopidogrel, started at least 24 hours before intervention (except for unstable angina pectoris and acute MI patients). During the procedure, a 100 U/kg bolus of unfractionated heparin was injected, adjusted if necessary to keep ACT above 300 seconds. Double antiplatelet therapy was continued for 30 days following PCI.

The PCI procedure was performed using standard techniques. A primary lesion predilatation was not mandatory and the choice to do it or not was left to the discretion of the operator.

Follow-up angiography

According to the study protocol, a follow-up angiography was performed in each patient 6 months after the primary procedure. For clinical reasons control angiography was allowed earlier, and if it was done, its results were used for study analyses.

Angiographic analysis

Three angiograms of the target lesion were performed in each patient – the first one directly prior to the coronary intervention, the second directly after PCI, and the third within a 6-month follow-up period.

All angiograms were evaluated by an independent investigator employed at our centre but not participating in the study. They were assessed by means of quantitative analysis employing Medis software. Calculations were done based on calibration with a catheter filled with contrast medium by means of automatic measurement with manual adjustment if necessary. All calibrations were based on the mean of two different projection measurements. Vessel reference diameter (RD) was calculated as the mean artery diameter measured proximally and distally to the target lesion. Vessel percent diameter stenosis (%DS) was defined as minimum lumen diameter (MLD) to artery reference diameter ratio. Late lumen loss (LS) was assessed as difference of MLD in the angiogram performed immediately after stent implantation and study performed within the 6-month follow-up period. In-stent restenosis (ISR) was defined as restenosis exceeding 50% of the vessel RD (%DS >50%) at the site of stent implantation or within proximal or distal 3 mm.

Study endpoints

Primary endpoint of the study was angiographic binary ISR detected during 6-month follow-up and the need for symptom driven repeat target lesion revascularisation (TLR).

Secondary endpoints included the magnitude of late lumen loss, all-cause mortality, myocardial infarction, either STEMI or NSTEMI, and symptomatic acute or subacute in-stent thrombosis.

Results

Kos stent implantation and early clinical course

In three (4.8%) out of 62 patients who underwent PCI with stenting, the study protocol was violated, resulting in them being excluded from further analysis; they were however included in clinical follow-up. Finally, 59 patients were studied and 62 Kos stents were implanted. Direct stenting was performed in 27 (45.8%) cases and 32 (54.2%) interventions were preceded by balloon predilatation. In 3 (4.8%) cases, the procedures were complicated by artery dissection requiring an extra Co-Cr stent deployment carried out also according to the study protocol.

Mean stent diameter was 3.18±0.18 mm and mean length 14.62±2.12 mm. Mean deployment pressure was 12.5±1.4 atm. In one (1.6%) case, the stent slipped off the balloon during direct stenting of critical stenosis in the torturous segment of the circumflex artery. The stent was withdrawn successfully and predilatation--facilitated successful stenting using the same type of stent was carried out. Characteristics of the lesions and their location are presented in Table II.

None of the patients required urgent surgical revascularisation or repeat PCI during index hospitalisation. No symptomatic acute or subacute in-stent thrombosis, MI or deaths occurred.

Follow-up

Control coronary angiography according to the protocol was performed in 55 (93.2%) patients. Three patients were lost to angiographic follow-up due to consent withdrawal, but none of them manifested any clinical symptoms of restenosis. They were not included in further analyses. One patient died of stroke during follow-up.

None of the patients developed acute MI during 6-month follow-up. Angina recurrence was observed in 10 (17%)

Table II. Characteristics of vascular lesions

		n	%
Location	LAD	29	49.2
	RCA	17	28.8
	CX	12	20.3
	OM	1	1.7
Disease	one vessel	49	83.1
	two vessel	8	13.6
	three vessel	2	3.3
Lesion type	A	29	49.2
	B_1	30	50.8
Calcified lesions		18	30.5

Abbreviations: LAD – left anterior descending artery, RCA – right coronary artery, CX – circumflex branch of the left coronary artery, OM – obtuse marginal branch

patients and in all of them repeat coronary angiography revealed significant coronary lesions. Repeat target lesion PCI was carried out in 10 cases (TLR=18.1%). However, post-hoc digital analysis of the angiograms revealed significant stenosis at the site of the target lesion only in 6 (10.9%) patients. In the remaining 4 patients, repeat PCI turned out to be done for borderline restenosis (%DS 40-50%), accompanied by angina. Mean late lumen loss in the study population was 0.55 mm and mean in-stent restenosis reached 25.2%. The results of digital angiogram analysis are outlined in Table III.

Discussion

Stent implantation is currently an integral part of most PCI procedures. Many types of endoprostheses are used in clinical practice, with similar outcomes reported. Some of them have similar structure, but some represent completely different design. Due to comparable outcomes of bare metal stents, endoprosthesis designers currently focus on enhancing flexibility and lowering system profile to improve safety and efficacy of PCI procedures [3]. It enables PCI to be performed on tortuous coronary arteries and facilitates crossing through severe obstructive lesions.

These theoretical requirements are met by Co-Cr alloy, which for more than ten years has been used to construct implants and prostheses having direct contact with bones, soft tissues and blood [4]. The clear advantages of Co-Cr alloy include high strength, endurance, biocompatibility and enormous radiopacity. These features have allowed stents to be manufactured with thinner struts, lower profile and large radial force accompanied by maximal elasticity without loss of either stent radial force or ability to successfully cover lesions compared to traditional ones. In the opinion of the operators participating in our study, the examined stents share such features.

Clinical and angiographic results in our patients with stents implanted into *de novo* lesions of native coronary arteries seem to confirm the high efficacy of treatment using this type of stents. Only in one case did an attempt to deploy a stent fail, which definitively must be considered a good result. Procedural efficacy was 100%. Moreover, no events of acute thrombosis in the examined stents were observed. A low rate of in-stent restenosis (10.9%) and small late lumen loss (0.55 mm) make this stent comparable to other devices in the same category. A favourable feature of the examined stent system is also a low rate of marginal dissections (n=3; 5%) requiring additional stent implantation. This may be a result of the thinnest stent struts and favourable shape of the balloon catheter preventing damage of the vessel wall distal and proximal to the stent deployment site.

The results of this registry may indicate the advantages of a new stent type based on Co-Cr alloy. Rough comparison of the presented registry results to the findings of Chopin classical bare metal stent registry

Table III. The results of QCA analysis performed in 55 patients during 6-month follow-up

	Before implantation	After implantation	After 180 days
RD [mm]	2.94±0.69	2.95±0.50	2.73±0.42
MLD [mm]	1.07±0.38	2.45±0.40	1.90±0.56
%DS [%]	63.72±8.69	12.53±7.09	25.22±17.87
Lesion length [mm]	9.57±0.79	–	7.33±4.17
AG [mm]	–	1.38±0.44	–
LLL [mm]	–	–	0.55±0.47
BR	–	–	10.9% (n=6)

Abbreviations: RD – reference diameter, MLD – minimal lumen diameter, %DS – % diameter stenosis, AG – acute gain of vessel lumen, LLL – late lumen loss, BR – angiographic binary restenosis (exceeding >50% of lumen)

performed previously by our team seems to confirm such speculation [5]. The patient population was similar in the present and the latter study (n=101, lesions A/B_1 type 73%, diabetes mellitus 18.2%). Direct comparison between these registries may indicate higher efficacy of endoprostheses based on Co-Cr alloy (Kos vs. Chopin: restenosis rate – 10.9 vs. 18.6%; LLL – 0.55 vs. 0.77 mm; TLR – 18.1 vs. 23.5%)

During 6-month follow-up no events associated with possible unfavourable biocompatibility related to the used Co-Cr alloy were noted. Our findings are consistent with results of clinical follow-up of patients who underwent Co-Cr prosthesis implantation in the soft tissues and bones. It suggests excellent biocompatibility of Co-Cr alloys. Cobalt-chromium alloy does not induce excessive tissue proliferation as observed in the studies with devices using extra aurum or nitinol alloys to improve stent radiopacity and flexibility [6, 7].

Although Co-Cr stents are commonly used, the results of only two registries with this type of endoprosthesis are available. The first one, the Guidant registry, assessed efficacy and safety of Multilink-Vision stents implanted in 267 patients with *de novo* coronary lesions [8]. Outcome measures for these stents (LLL 0.83 mm, %DS 29.2%, TLR 4.3%) were the most favourable from among the whole group of Guidant stents, which may reflect the beneficial effects of reduced stent strut thickness on severity of vessel wall damage followed by 'repair' neointima proliferation. Similar results (LLL 0.94 mm, %DS 15.7%, TLR 3.4%) were reported for Co-Cr Driver stents manufactured by Medtronic in the registry involving implantation of endoprostheses in a group of 298 patients [9]. In both these studies, a low rate of repeat intervention in the target vascular segments was reported, suggesting their high clinical efficacy. However, attention must be paid to higher LLL and rate of ISR compared to our results. This difference may be a result of higher percentage of vascular lesions of unfavourable type B_2 and C morphology (registry Driver B_2/C – 50.7%, and registry Vision B_2/C – 40%, respectively).

The main limitation of our study is the relatively small number of patients, which may have affected the results. Including more patients would increase the reliability of our findings and allow comparisons with the results of mentioned Co-Cr stent registries.

When discussing the results of our study, the relatively high number of patients undergoing repeat PCI due to non-significant borderline in-stent restenosis must be stressed. It is likely a result of using only visual assessment of stenosis severity during the procedure, but also of clinical suggestion that chest pain must be of coronary origin. It leads to a significant increase of TLR rate that may make study results unreliable. Thus, it seems essential that, especially in the case of clinical studies on efficacy of various intravascular endoprostheses, more careful attention must be paid to the management of borderline lesions. In these cases objective QCA measurements (although not considered ideal) and/or assessment of coronary flow reserve by means of fractional flow reserve measurement can be performed to choose the best therapy. This could limit the number of unnecessary coronary procedures and improve the accuracy of analysis of clinical trials.

Conclusions

Our experience suggests high efficacy of the Balton Kos™ coronary stent, featuring a relatively low restenosis rate and high clinical effectiveness.

References

1. Kastrati A, Mehilli J, Dirshinger J, et al. Intracoronary stenting and angiographic results: strut thickness effect on restenosis outcome (ISAR-STEREO) trial. *Circulation* 2001; 103: 2816-21.
2. Pache J, Kastrati A, Mehilli J, et al. Intracoronary stenting and angiographic results: strut thickness effect on restenosis outcome (ISAR-STEREO-2) trial. *J Am Coll Cardiol* 2003; 41: 1283-8.
3. Colombo A, Stankovic G, Moses JW. Selection of coronary stents. *J Am Coll Cardiol* 2002; 40: 1021-33.
4. Donachie M. Biomedical alloys. *Advanced Materials and Processes*, 1998. 7: 63-5.
5. Buszman P, Żurakowski A, Kinasz L, et al. The new Polish stent Chopin. Assessment of safety and efficacy in the treatment of de-novo coronary lesions using percutaneous angioplasty. *Kardiol Pol* 2005; 62: 456-9.
6. vom Dahl J, Haager PK, Grube E, et al. Effects of gold coating of coronary stents on neointimal proliferation following stent implantation. *Am J Cardiol* 2002; 89: 801-5.
7. Hoffmann R, Mintz GS, Haager PK. Relation of stent design and stent surface material to subsequent in-stent intimal hyperplasia in coronary arteries determined by intravascular ultrasound. *Am J Cardiol* 2002; 89: 1360-4.
8. Kereiakes DJ, Cox DA, Hermiller JB, et al. Usefulness of a cobalt chromium coronary stent alloy. *Am J Cardiol* 2003; 92: 463-6.
9. Sketch MH Jr, Ball M, Rutherford B, et al. Evaluation of the Medtronic (Driver) cobalt-chromium alloy coronary stent system. *Am J Cardiol* 2005; 95: 8-12.

Prospektywny rejestr oceniający skuteczność i bezpieczeństwo leczenia chorych ze zmianami *de novo* w naczyniach wieńcowych przy użyciu stentów kobaltowo-chromowych

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Streszczenie

Wstęp: Stenty wieńcowe zbudowane ze stopów kobaltowo-chromowych (Co-Cr) są nowym rodzajem endoprotez o korzystniejszych właściwościach mechanicznych niż tradycyjne stenty metalowe.

Cel: Ocena skuteczności i bezpieczeństwa zabiegów przezskórnych interwencji wieńcowych (PCI) z użyciem stentów wieńcowych kobaltowo-chromowych Kos firmy Balton.

Metodyka: Do badań włączono kolejnych 59 chorych z objawową chorobą wieńcową. Siedmiu (11,8%) chorych stanowiło grupę pacjentów przyjętych z powodu ostrego zawału mięśnia sercowego (MI), a 22 (37,3%) z powodu objawów niestabilnej dławicy piersiowej. Średni wiek chorych wynosił 60±9 lat, cukrzyca występowała u 17% chorych, nikotynizm – u 63%, hipercholesterolemia – u 54%, obciążenie rodzinne – u 25% chorych. Do badania kwalifikowano tylko zmiany typu *de novo* w naczyniach wieńcowych ze stenozą ≥50% i <100% typu A i B_1 o referencyjnej średnicy naczynia ≥2,8 mm i ≤4,0 mm. Protokół badania zalecał pokrycie całej blaszki miażdżycowej przez stent o maksymalnej długości 18 mm. Protokół badania zakładał implantację badanego stentu do zmian *de novo* w naczyniach natywnych, 6-miesięczną obserwację kliniczną oraz kontrolną koronarografię po 6 mies. U każdego pacjenta wykonywano 3 angiogramy docelowej zmiany – jeden bezpośrednio przed interwencją, drugi bezpośrednio po zakończeniu zabiegu i trzeci podczas 6-miesięcznej kontroli. Wszystkie angiogramy analizowane były przez niezależnego badacza za pomocą cyfrowej automatycznej analizy ilościowej przy użyciu programu Medis. Głównym punktem końcowym badania były angiograficzne cechy restenozy (ISR) w obrębie stentu podczas kontrolnej koronarografii oraz potrzeba wykonania ponownej rewaskularyzacji w obrębie implantowanego stentu (ang. *target lesion revascularization*, TLR) w okresie 6-miesięcznej obserwacji z powodu nawrotu dolegliwości stenokardialnych. Do drugorzędowych punktów końcowych zaliczono późną utratę światła, wystąpienie zgonu, MI z uniesieniem odcinka ST, MI bez uniesienia odcinka ST oraz objawów ostrego lub podostrego wykrzepienia w obrębie stentu.

Wyniki: Łącznie implantowano 62 stenty o średniej średnicy 3,18±0,18 mm i długości 14,62±2,12 mm. W okresie miesięcznej obserwacji żaden chory nie wymagał wykonania ponownego zabiegu rewaskularyzacji wieńcowej, nie notowano również epizodów niestabilnej dławicy piersiowej i MI. W okresie 6-miesięcznej obserwacji w badanej populacji nie stwierdzono zgonów ani objawów MI. Kontrolną koronarografię wykonano u 55 (92%) chorych. W 10 (17%) przypadkach wykonano zabieg re-PCI obejmujący zmianę docelową (TLR). Cyfrowa analiza angiogramów wykazała jednak obecność istotnego nawrotu zwężenia w obrębie docelowego segmentu u 6 chorych (10,9%). U pozostałych 4 chorych zabiegi PCI wykonane zostały z powodu obecności granicznych wartości nawrotu zwężenia (stopień zwężenia: 40–50%) oraz współistnienia dolegliwości stenokardialnych. Późna utrata światła wynosiła średnio 0,55±0,6 mm, a średnie zwężenie 25,2±17,9%.

Wnioski: Stent wieńcowy Kos jest bezpieczną i efektywną endoprotezą wewnątrznaczyniową umożliwiającą przeprowadzenie skutecznych zabiegów PCI.

Słowa kluczowe: choroba niedokrwienna serca, stent, restenoza

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