Intracoronary ultrasound-guided angioplasty for coronary chronic total occlusion

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Abstract

Background: Recanalisation for coronary chronic total occlusion (CTO) is associated with high rates of restenosis and reocclusion. The use of intracoronary ultrasound (ICUS) may improve immediate and long-term outcomes following recanalisation. To our knowledge, no study has examined the use of ICUS-guided balloon angioplasty in CTO.

Aim: To compare the results of ICUS-guided balloon angioplasty and ICUS-guided angioplasty with stent implantation in patients with CTO.

Methods: The study involved 51 CTO patients in whom optimal balloon angioplasty results were achieved according to quantitative coronary angiography (QCA). These patients then underwent ICUS-guided balloon angioplasty with the goal of achieving a minimal luminal cross-sectional area (MLCSA) of > 6.0 mm^2 and a residual plaque burden (RPB) of < 65%. Of the 51 patients, the ICUS criteria defining optimal balloon angioplasty were achieved in 23 patients and 7 patients did not undergo stent implantation due to calcification and/or small vessel diameters (group A – 30 patients). In 21 patients, the failure to achieve optimal ICUS parameters resulted in stent implantation with the goal of achieving in stent MLCSA > 9 mm^2 and > 55% of average total cross-sectional area of the vessel according to distal and proximal reference segments (group B). The two groups were similar in terms of clinical and angiographic characteristics.

Results: Balloon angioplasty which was regarded as optimal by QCA, was shown to be non-optimal by ICUS in 41 patients (80.4 %). The MLCSA was smaller in group A than group B (6.5 ± 1.5 vs. 8.9 ± 2.0 mm^2; p < 0.001). Restenosis was found in 8 (26.6%) group A patients and 4 group B patients (19%) (p > 0.05). The restenosis rate in 23 group A patients with optimal ICUS parameters was 8.6% (2 patients). Consecutive ICUS measurements showed a gradual increase in the total vessel area during the PCI procedure and at the 6-month follow-up (p < 0.05).

Conclusions: 1. Achieving an optimal balloon angioplasty result in CTO patients requires confirmation using ICUS. 2. In some patients immediate and long-term outcomes following ICUS-guided optimised balloon angioplasty are comparable to those of ICUS-guided stent implantation. 3. Direct measurement of a chronically occluded coronary artery at pre-intervention, during the intervention and at long-term follow-up may argue in favour of using ICUS in recanalisation of CTO. 4. ICUS-guided balloon angioplasty for CTO could be a method of choice in patients in whom long-term dual antiplatelet therapy is associated with a high probability of bleeding complications.

Key words: chronic total occlusion, coronary angioplasty, intracoronary ultrasound

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Introduction

Chronic total occlusion (CTO) of coronary arteries is found in 20-40% of angiograms [1, 2], and recanalisation of chronically occluded arteries comprises 7-16% of all percutaneous coronary interventions (PCI) [2, 3]. The CTO treatment success rates are lower than for other lesion types mainly due to the limited effectiveness and high restenosis rate, even after stent implantation [4, 5]. Thus, CTO recanalisation remains a critical issue to address in interventional cardiology.

Balloon angioplasty for CTO is associated with worse outcomes than stent implantation [4, 5]. Only the STOP trial found that the rate of restenosis was similar for both optimal balloon angioplasty according to quantitative coronary angiography (QCA) and stent implantation [6]. While drug-eluting stent (DES) implantation for CTO appears to be

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a promising treatment [7], the rate of in-stent restenosis is higher than for other lesions [8]. In addition, DES is associated with stent thrombosis, a relatively high reocclusion rate and the need for long-term double antiplatelet treatment.

While intracoronary ultrasound (ICUS)-guided angioplasty may provide additional benefits in recanalisation [9], it is rarely performed in CTO [10]. To our knowledge, no study has examined the use of ICUS-guided balloon angioplasty in CTO.

The present study compared the outcomes following ICUS-guided balloon angioplasty and ICUS-guided stent implantation in patients with CTO.

Methods

The study group included 51 patients who underwent optimal balloon angioplasty of a chronically occluded coronary artery. The CTO was defined as an occlusion more than 15 days old with TIMI 0 or 1 flow. Optimal balloon angioplasty was defined as a residual diameter stenosis < 20% according to QCA, a type C dissection or less, and absent early elastic recoil (loss > 50% of the initial gain in vessel diameter within 10 min after the last balloon inflation). The primary exclusion criteria were: suboptimal balloon angioplasty, a vessel diameter less than 2.5 mm, multivessel disease qualifying for bypass grafting, myocardial infarction in the preceding 15 days, decompensated heart failure, occlusion length > 30 mm and a type of occlusion decreasing the chance of success.

After achieving optimal balloon angioplasty, ICUS was performed and the size of the balloon was increased to match the maximal dimension defined by the formula: mean vessel diameter at occlusion (VDmean) – 10%. The goal was to achieve a minimal lumen cross-sectional area (MLCSA) at occlusion of > 6.0 mm^2 and a residual plaque burden (RPB) of < 65%. If these parameters were achieved, the vessel was not stented; otherwise a stent was implanted under ICUS guidance. The stent was implanted to cover all the occlusion site and dissection. Stent struts must have full apposition to the vessel wall and it was the intention to obtain minimal to maximal stent diameter ratio of 0.7. The goal was to achieve MLCSA in stent > 9 mm^2 and > 55% of average total cross-sectional area of the vessel according to distal and proximal reference segments.

The study protocol was approved by the Bioethics Committee of the Jagiellonian University Medical College (KBET/208/L/2002 of 21 March 2002), and all patients gave written informed consent.

Of the 51 patients, the ICUS criteria defining optimal balloon angioplasty were achieved in 23 patients. Additionally, 7 patients, for whom achieving optimal results was impossible and calcification and/or small vessel diameter prevented stent implantation, were included in the balloon angioplasty group in the final analysis (in accordance with the intention to treat) because the group best corresponded to a population with CTO. These 30 patients formed group A.

The remaining 21 patients showed non-optimal ICUS parameters and underwent stent implantation (group B). The two groups were similar in terms of clinical characteristics and angiographic features (Table I). Repeat coronary angiography and ICUS were performed 6 months after initial procedure. Binary restenosis was defined as stenosis > 50% according to QCA. Examples of the procedures in both groups are presented in Figure 1 and 2.

Coronary angiography, ventriculography and angioplasty were performed using a digital Integris HM 3000 system (Philips Medical Systems, Holland) and dedicated software (ACA DCI, Philips Medical Systems, Holland) for quantitative angiography. On-line QCA measurements were taken after successful recanalisation and achieving optimal balloon angioplasty according to the operator. A radiological projection with the minimal lumen diameter (MLD) at the level of the stenosis was chosen for further analysis. Off-line measurements were taken after the intervention. The mean of three consecutive measurements was used for analysis.

The ICUS was performed using an electronic Oracle-In Vision (EndoSonics Corporation, United States) system and Jovus Avanar F/X ultrasound probes (Jomed, Volcano Therapeutics, United States). After intracoronary injection of 250 μg nitroglycerine, ICUS was performed by manual advancement of a diagnostic catheter about 20 mm beyond the occlusion site and automatic pullback at a speed of 0.5 mm/s. Images were recorded and analysed as recommended by the ACC and ESC [11]. Two recordings were made, the second one using the croma flow system. Proximal and distal reference sites were defined as the sites with minimal narrowing by angiography maximally up to 10 mm from the occlusion site without side branches.

Measurements were taken immediately after recanalisation, during the optimisation of balloon angioplasty and after its completion, after stent implantation and the optimisation of stenting, and during repeat examination at 6 months. The ICUS was performed in the chronically occluded coronary artery only. Measurements were taken at the maximal occlusion site and at proximal and distal reference sites. A semi-automatic computer system was used to calculate the following parameters: LD (lumen diameter; minimal = MLD, maximal = LD max, mean = LD mean); VD (vessel diameter; minimal = VD min, maximal = VD max, mean = VD mean); LA (lumen area), VA (vessel area) and PA (plaque area) using the formula PA = VA – LA; residual plaque burden (RPB) defined as the ratio of lumen area to total vessel area using the formula [(1-LA/VA) × 100%] or PA/VA; minimal lumen cross-sectional area (MLCSA); remodelling index (RI); and the ratio of total vessel area to average lumen area at distal and proximal reference sites (negative remodelling was defined as RI < 1.0, positive remodelling as RI > 1.0). Atherosclerotic plaques were classified as soft, hard, calcified or mixed, based on tissue echogenicity. Calcifications were classified as deep or superficial, and the arc of the calcified plaque was measured. Dissection after PCI was

Table I. Clinical characteristics and angiographic features

Parameter	Total n = 51	Group A n = 30	Group B n = 21	p
Age [years]	57.4 ± 9.7	59.7 ± 10.2	54.2 ± 8.1	0.045
Males (n) Females (n)	45 6	25 5	20 1	NS
Duration of occlusion [months]	4.9 ± 3.6	5.0 ± 3.9	4.9 ± 3.2	NS
CCS class I	11	6	5	NS
II	31	18	13	NS
III	9	6	3	NS
IV	0	0	0	NS
CCS class (mean)	2.0 ± 0.6	2.0 ± 0.6	2.0 ± 0.6	NS
Diabetes mellitus	12	9	3	NS
Hypertension	40	25	15	NS
Hyperlipidaemia	51	30	21	NS
BMI	27.6 ± 4.9	27.4 ± 3.2	28.9 ± 4.5	NS
Smoking	16	9	7	NS
Positive family history	22	13	9	NS
Duration of CHD [years]	2.7 ± 4.5	2.9 ± 5.0	2.4 ± 3.8	NS
Prior myocardial infarction				NS
anterior	18	11	7	NS
inferior	21	11	10	NS
lateral	2	1	1	NS
Previous PCI	5	3	2	NS
LVEF (%)	48.7 ± 10.6	50.0 ± 10.6	46.8 ± 10.6	NS
Location of occlusion, n (%)				NS
LAD	26 (51.0)	17 (56.7)	9 (42.9)	
RCA	18 (35.3)	9 (30.0)	9 (42.9)	
Cx	7 (13.7)	4 (3.3)	3 (14.2)	
Calcification, n (%)	17 (33.3)	12 (40)	5 (23.8)	NS
Type of occlusion, n (%)				NS
blunt	15 (29)	10 (33.3)	5 (23.8)	
tapered	36 (71)	20 (66.7)	16 (76.2)	
TIMI flow grade 0, n (%) TIMI flow grade 1, n (%)	27 (52.9) 24 (47.1)	16 (53.3) 14 (46.7)	11 (52.4) 10 (47.6)	NS
Side branch at site of occlusion, n (%)	32 (62.7)	19 (63.3)	11 (52.3)	NS
Proximal reference [mm]	2.9 ± 0,6	2.8 ± 0.5	3.0 ± 0.6	NS
Length of occlusion [mm]	16.2 ± 6.4	15.7 ± 6.3	17.0 ± 6.7	NS

Abbreviations: CCS – Canadian Cardiovascular Society, BMI – body mass index, CHD – coronary heart disease, PCI – percutaneous coronary intervention, LVEF – left ventricular ejection fraction, LAD – left anterior descending artery, RCA – right coronary artery, Cx – circumflex artery, TIMI – thrombolysis in myocardial infarction

classified according to Honye et al. [12]. The ICUS images and off-line QCA measurements were evaluated by two independent observers, and only concordant results were taken for analysis; a consensus was reached between the observers in cases of discordance.

Statistical analysis

Statistical analysis was performed using STATISTICA 6.1 PL software (StatSoft Inc., United States). Unpaired Student's t-tests were used to compare two samples, and Mann-Whitney U test was used for non-normal data distribution. Paired Student's t-tests were used to compare paired data, and the Wilcoxon signed rank test for paired comparisons was used for non-normal distributions. Chi-square tests were used to analyse relationship between qualitative variables. Statistical differences were assessed using analysis of variance with repeated measures. The Friedman test was performed if the data failed to meet the assumptions. A p value < 0.05 was taken to indicate significance.

Results

Short- and long-term observation

There were no in-hospital major adverse cardiac or cerebral events (i.e., death, myocardial infarction, stroke or symptom-driven revascularisation). Mild elevation of CK and CKMB (< 3 times normal) was observed in one group A patient and two group B patients.

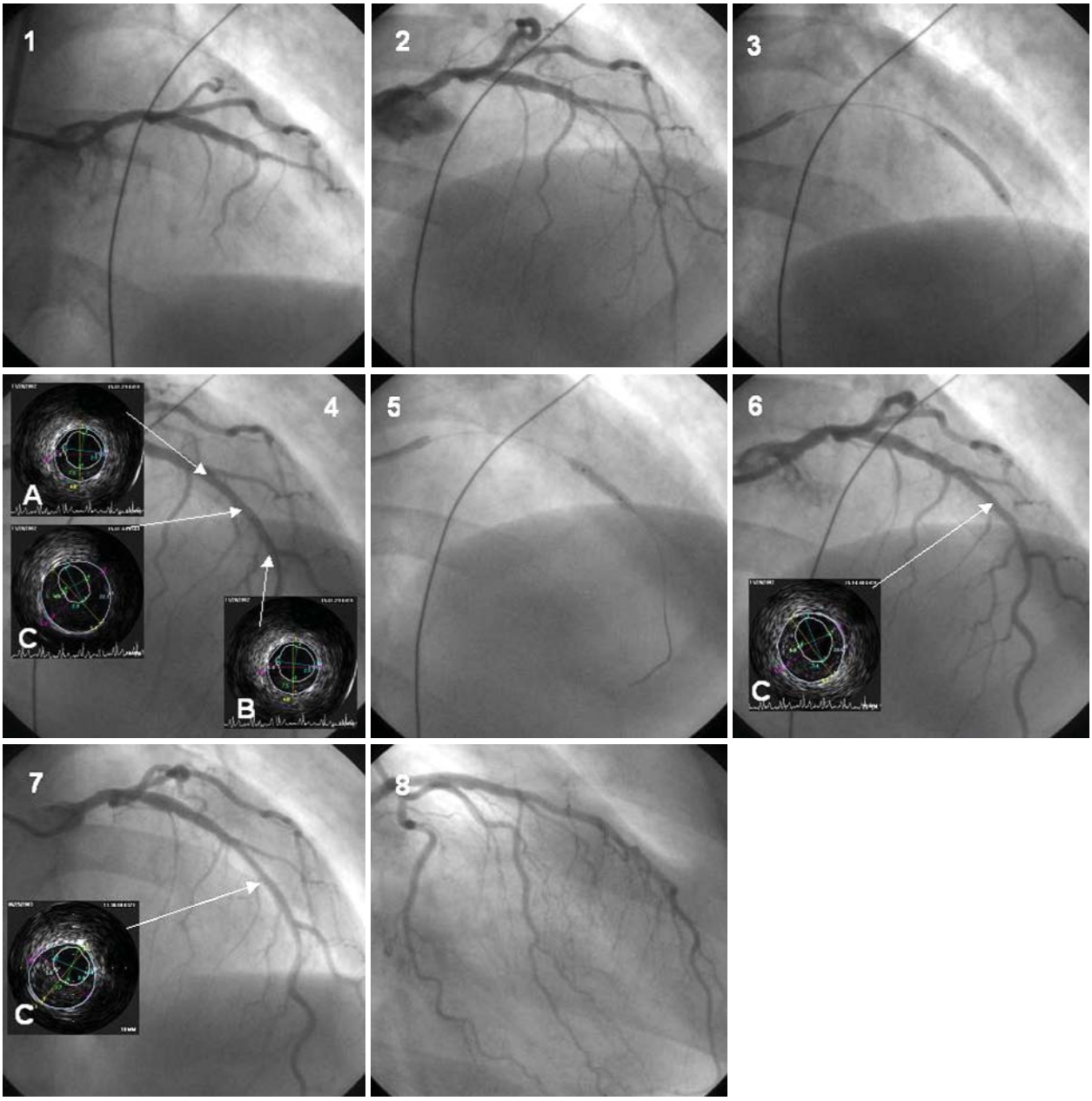

Figure 1. Patient 70-year-old, male. **1** – occlusion of the middle part of the left anterior descending coronary artery; **2** – artery after 1.5 mm balloon predilatation; **3** – artery after dilatations with bigger balloons; **4** – optimal result of balloon angioplasty according to QCA, in ICUS MLCSA smaller than 6 mm^2; **5** – dilatation with bigger balloon according to ICUS measurements; **6** – still optimal angiographic result, no progression of dissection, the optimal result confirmed in ICUS; **7, 8** – control angiography after 6 months, good long-term result, no restenosis, angiographic result confirmed in ICUS

A – proximal reference, B – distal reference, C – MLCSA at the site of the occlusion, D – MLCSA at the site of the occlusion after optimisation

Table II summarises the 6-month follow-up results. There was one sudden cardiac death, and this occurred 3 months after PCI in a group B patient who had a reduced left ventricular ejection fraction (30%). Restenosis was identified in 8 (26.6%) group A patients and 4 (19%) group B patients. The restenosis rate in 23 group A patients with optimal ICUS parameters was 8.6% (2 patients). Major adverse cardiac or cerebral events (MACCE) occurred in 9 (30%) group A and 6 (28.6%) group B patients.

Optimisation outcomes

Table III summarises the angiographic features of the study population. There were no between-group differences

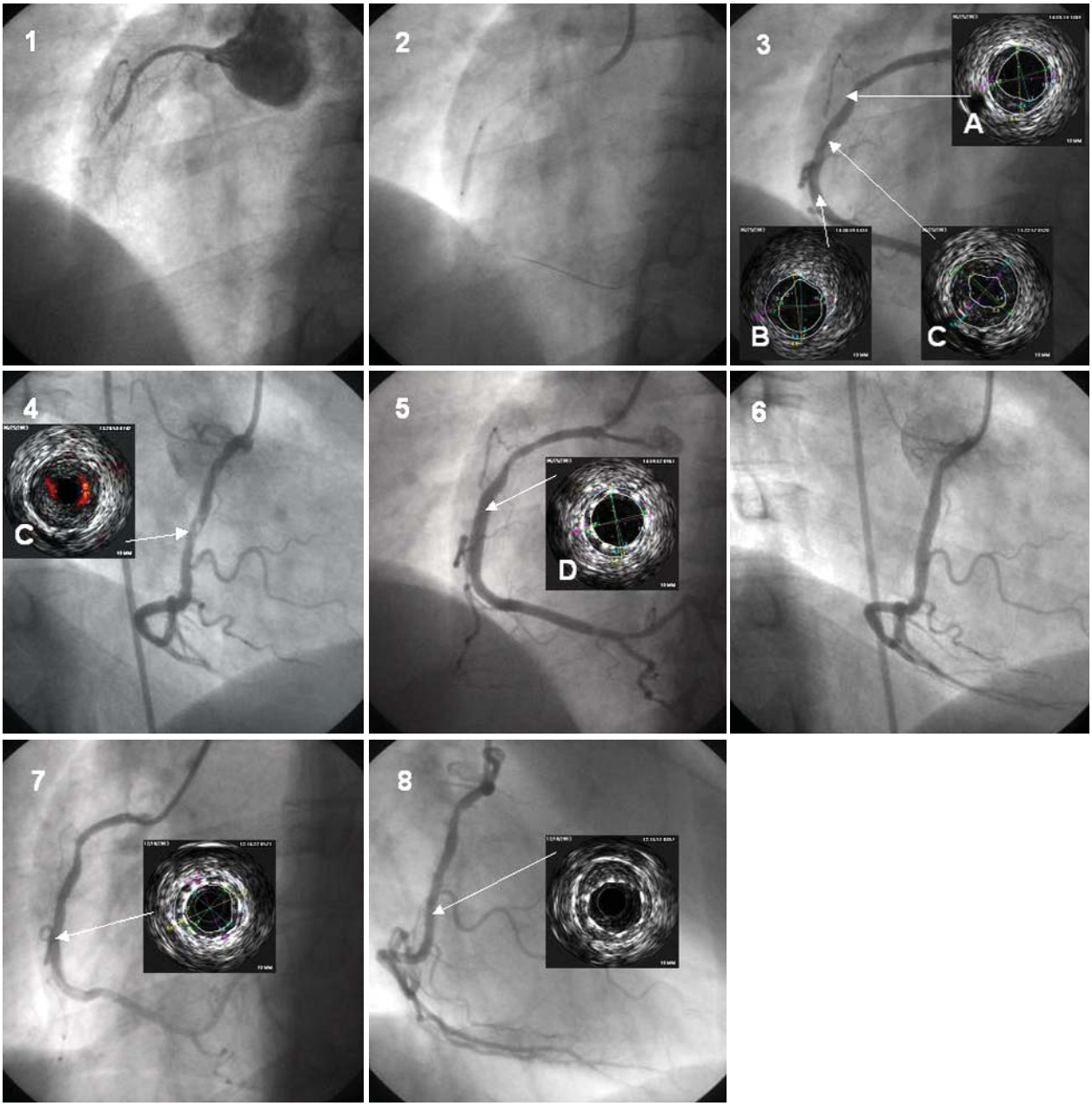

Figure 2. Patient 55-year-old, male. **1** – occlusion of the middle part of the right coronary artery; **2** – artery after recanalisation and 1.5 mm balloon predilatation; **3**, **4** – artery after further predilatations; optimal result of balloon angioplasty according to QCA, in ICUS MLCSA smaller than 6 mm^2; **5**, **6** – artery after stent implantation, optimal result confirmed in ICUS; **7**, **8** – control angiography after 6 months, good long-term result, no restenosis, angiographic result confirmed in ICUS

A – proximal reference, B – distal reference, C – MLCSA at the site of the occlusion, D – in-stent MLCSA

at baseline. The ratio of balloon nominal size to the reference lumen diameter according to QCA was 1.3 ± 0.2 for the whole group and 1.3 ± 0.2 for the balloon angioplasty group. The assumed balloon catheter size was 3.73 ± 0.59, and in practice the maximal size was 3.4 ± 0.4 mm. The total vessel diameter (VD mean) at the level of occlusion measured using ICUS was 4.1 ± 0.6 mm, whereas the average reference vessel diameter measured using QCA was 2.6 ± 0.5 mm. The ratio of average reference vessel diameter using QCA to true vessel diameter measured using ICUS was 0.62.

Ultrasound results

The only difference in baseline ultrasound parameters was that soft plaques were more common in group A than group B (Table IV). The amount of residual plaque burden at the proximal (48.5 ± 9.5%) and distal reference (53.2

± 9.2%) segments was high, indicating a high degree of atherosclerosis in the study population.

The ICUS-guided optimisation resulted in increased MLCSA in both groups, to 6.5 ± 1.5 mm^2 in group A and to 8.9 ± 2.0 mm^2 in group B (Table V). The MLCSA was larger in the stent group than in the balloon angioplasty group. Despite the optimal angiographic result by QCA, the residual plaque burden (RPB) was large and similar for both groups (group A = 67.3 ± 8.4%, group B = 65.4 ± 7.4%; p > 0.05). Optimisation reduced the RPB in both groups, to 53.6 ± 8.3% for group A and 45.2 ± 8.0% for group B, and the group B value was lower than the group A value (p < 0.001).

At 6 months there was a reduction in MLCSA compared to the final MLCSA after angioplasty for both group A (6.2 ± 1.3 mm^2) and group B (7.8 ± 2.3 mm^2), with the latter being larger (p < 0.05). Repeat examination revealed enlarged plaque areas and residual plaque burdens for both groups.

Both groups showed an increase in total vessel area. The total vessel area at the proximal and distal reference sites were compared with the maximal and minimal vessel area at the level of occlusion in group A patients without restenosis (Figure 3 and Table VI). This analysis revealed an increase in the total vessel area at the proximal and distal reference sites and at the level of occlusion when taking consecutive measurements during the intervention, i.e. the total vessel area was larger after optimisation of the procedure as compared with the baseline value. At 6 months, there were further increases at every measurement point. A similar analysis performed in the stent implantation group revealed an increase in the total vessel area at the proximal and distal reference sites during the intervention and at 6 months (Figure 3 and Table VII). While the total vessel area at the level of occlusion was larger after stent implantation, there was no significant difference at long-term follow-up.

Table II. Six-month follow-up results

	Group A n = 30	Group B n = 21
Death	0	1
Myocardial infarction	0	0
Stroke	0	0
Progression of atherosclerosis [%]	2	1
Clinical restenosis, n (%)	2 (6.7)	1 (4.7)
Angiographic restenosis, n (%)	6 (20)	3 (14.3)
Restenosis in total, n (%)	8 (26.7)	4 (19.0)
Repeat revascularisation, n (%)	9 (30)	5 (23.8)
PCI	8	5
CABG	1	0
MACCE, n (%)	9 (30)	6 (28.5)

Abbreviations: PCI – percutaneous coronary intervention, CABG – coronary artery bypass grafting, MACCE – major adverse cardiac and cerebral events
p > 0.05 for all intergroup comparisons

Factors influencing restenosis

In patients from group A, the MLCSA was smaller in patients with rather than without restenosis (5.1 ± 0.8 vs. 6.7 ± 0.8 mm^2 ; p < 0.001) while the amount of residual plaque burden was larger (61.1 ± 8.4 vs. 53.2 ± 8.3%, respectively; p = 0.03). There were no significant differences in PA and VA between patients with and without restenosis. In the group B patients, the MLCSA

Table III. Qantitative coronary angiography parameters for groups A and B at baseline and at 6 months

		Group A	Group B	p
MLD	baseline	0	0	
	final	2.6 ± 0.4	3.2 ± 0.5	< 0.001
	p	< 0.001	< 0.001	
	at 6 months	1.7 ± 0.7	2.3 ± 0.8	0.02
% diameter stenosis	baseline	100	100	NS
	final	15.1 ± 4.1	11.7 ± 7.4	0.004
	p	< 0.001	< 0,001	
	at 6 months	41.0 ± 22.8	35.7 ± 20.1	NS
Proximal reference [mm]	baseline	2.9 ± 0.5	3.0 ± 0.7	NS
	final	3.0 ± 0.5	3.6 ± 0.7	< 0.001
	p	NS	NS	
	at 6 months	3.1 ± 0.5	3.5 ± 0.7	NS
Distal reference [mm]	after 1st inflation	2.3 ± 0.5	2.2 ± 0.6	NS
	final	2.8 ± 0.5	3.2 ± 0.6	0.004
	p	NS	NS	
	at 6 months	2.6 ± 0.7	3.1 ± 0.5	0.008
Immediate gain [mm]		2.6 ± 0.4	3.2 ± 0.5	< 0.001
Late lumen loss [mm]		0.9 ± 0.7	0.9 ± 0.70	NS
Final lumen gain [mm]		1.7 ± 0.7	2.3 ± 0.8	0.02

Abbreviations: MLD – minimal lumen diameter

Table IV. Ultrasound characteristics

		Total	Group A	Group B	p
Qualitative analysis					
Plaque					
	soft	18	14	4	NS
	hard	15	7	8	
	calcified	16	8	8	
	mixed	2	1	1	
Plaque					
	soft	18	14	4	0.042
	other	33	16	17	
Calcification					
	absent	11	7	4	NS
	superficial	3	3	0	
	intermediate	8	5	3	
	deep	13	6	7	
	mixed	16	9	7	
Calcium arc [°]		142.4 ± 118.0	151.5 ± 131.9	130.0 ± 98.6	NS
Occlusion site					
MLCSA [mm^2]		5.1 ± 1.7	5.0 ± 1.6	5.2 ± 1.8	NS
PA [mm^2]		9.2 ± 3.1	9.2 ± 2.9	9.1 ± 3.4	NS
VA [mm^2]		14.3 ± 4.2	14.2 ± 3.6	14.3 ± 4.7	NS
RPB [%]		66.2 ± 7.8	67.3 ± 8.4	65.4 ± 7.4	NS
Proximal reference segment					
MLCSA [mm^2]		8.3 ± 2.7	8.0 ± 2.3	8.7 ± 3.0	NS
PA [mm^2]		7.5 ± 2.7	8.1 ± 3.0	6.7 ± 2.3	NS
VA [mm^2]		15.8 ± 3.6	16.1 ± 3.6	15.4 ± 3.7	NS
RPB [%]		48.4 ± 9.5	52.1 ± 10.2	45.7 ± 10.0	NS
Distal reference segment					
MLCSA [mm^2]		6.1 ± 2.4	6.0 ± 2.5	6.2 ± 2.2	NS
PA [mm^2]		6.4 ± 3.2	6.8 ± 2.3	5.9 ± 3.0	NS
VA [mm^2]		12.5 ± 4.3	12.8 ± 3.4	12.1 ± 4.6	NS
RPB [%]		53.2 ± 9.2	54.9 ± 8.8	51.0 ± 9.7	NS

Abbreviations: MLCSA – minimal luminal cross-sectional area, PA – plaque area, VA – vessel area, RPB – residual plaque burden

was similar for both patients with and without restenosis (7.9 ± 1.3 vs. 9.1 ± 2.1 mm^2; $p > 0.05$). The amount of residual plaque burden was larger in patients with restenosis compared to those without restenosis (47.9 ± 4.7 vs. 39.7 ± 8.5%; $p = 0.01$). In both groups, restenosis correlated with the MLCSA at the level of occlusion achieved during the intervention ($r = 0.35$; $p < 0.05$), minimal vessel area at the distal reference site, plaque type ($r = 0.31$; $p < 0.05$), and arc angle of the calcified plaque ($r = 0.53$; $p < 0.01$). Additionally, in group A there was a correlation between restenosis and the MLCSA at the distal reference site ($r = 0,57$; $p < 0.01$).

Negative and positive remodelling was found in 35 (68.6%) group A and 16 (31.4%) group B patients. Negative remodelling was found in 26 (74%) patients with CTO at ≥ 3 months. Positive remodelling was found in 8 (26%) patients with CTO > 3 months. Negative remodelling correlated with in-stent restenosis ($r = 0.53$; $p < 0.01$).

Discussion

Despite several years of experience in the invasive treatment of CTO, restenosis rates remain unacceptably high, ranging from approximately 10% for DES [8] up to 55% for bare metal stents [5, 13]. Therefore, we investigated whether the use of ICUS would reduce the restenosis rate.

Contrast angiography is a routine tool for visualising coronary arteries during the intervention and for assessing outcomes [14]. Predictive angiographic factors of restenosis after PCI are minimal lumen diameter (MLD) and diameter stenosis (%DS) after the intervention. Thus, the goal of intervention is to produce the largest lumen diameter after

Table V. Ultrasound characteristics at the site of occlusion before and after optimisation and at follow-up for groups A and B

		Group A	Group B	p
MLCSA [mm^2]	baseline	5.0 ± 1.6	5.2 ± 1.8	NS
	p	< 0.001	< 0.001	
	after optimisation	6.5 ± 1.5	8.9 ± 2.0	< 0.001
	p	< 0.001	< 0.001	
	at 6 months	6.1 ± 1.3	7.8 ± 2.3	< 0.001
PA [mm^2]	baseline	9.2 ± 2.9	9.1 ± 3.4	NS
	p	< 0.001	< 0.001	
	after optimisation	8.1 ± 3.5	7.1 ± 3.3	NS
	p	< 0.001	< 0.001	
	at 6 months	9.1 ± 2.9	10.8 ± 2.4	NS
VA [mm^2]	baseline	14.2 ± 3.6	14.3 ± 4.7	NS
	p	0.002	0.004	
	after optimisation	14.6 ± 4.2	15.9 ± 4.7	NS
	p	0.04	0.006	
	at 6 months	15.2 ± 3.4	18.6 ± 3.9	0.008
RPB [%]	baseline	67.3 ± 8.4	65.4 ± 7.4	NS
	p	< 0.001	< 0.001	
	after optimisation	53.6 ± 8.3	45.2 ± 8.0	< 0.001
	p	0.004	< 0.001	
	at 6 months	58.8 ± 7.9	57.4 ± 8.8	NS

Abbreviations: MLCSA – minimal luminal cross-sectional area, PA – plaque area, VA – vessel area, RPB – residual plaque burden

the procedure, according to the 'bigger is better' hypothesis, and immediate residual percent stenosis below 20% [15].

The traditional matching of the balloon catheter size to the size of the reference vessel diameter measured by QCA provides optimal results in only approximately 35% of patients [16], and optimal angiographic results are not always synonymous with optimal dilatation [17]. The present study confirmed that the optimal result in QCA after angioplasty of CTO (i.e. an immediate residual stenosis below 20%) was not a predictor of an adequate vessel lumen. In most patients (80.4%) the minimal lumen cross-sectional area after aggressive balloon angioplasty remained small (< 5 mm^2). Hancock et al. achieved similar angiographic features in 30 balloon angioplasty patients (reference vessel size 3.5 mm, MLD 2.8 mm and residual stenosis 20.3%) and reported restenosis in 40% of patients, twice that of the present study [18].

The ICUS is the gold standard for monitoring progression and regression of atherosclerosis in coronary arteries and for evaluating mechanisms of restenosis after PCI [19]. This technique provides measurements of the true vessel size and allows correct size matching for balloon catheters and stents. The ICUS-measured diameters are usually larger than those measured using QCA, but if negative remodelling is present, the diameter may be similar or even smaller. Angiographically normal coronary artery segments used as reference in QCA contain 40-50% of calcium [20]. Diffuse atherosclerosis in CTO with restricted blood flow at initial angiography does not provide an accurate measurement of vessel diameter [21]. In the present study, the ratio of the reference vessel segment measured by QCA to the true vessel size measured by ICUS was 0.62, which is similar to other investigations [22]. Furthermore, CTO is frequently associated with negative remodelling [23]. Nishida et al. found negative remodelling in 9 (56%) patients out of 16 subjects with a CTO duration < 3 months and in all 11 patients with a CTO duration > 3 months [24].

The ICUS demonstrated that restenosis after balloon angioplasty was mainly due to a reduction in arterial diameter referred to as pathological remodelling. The SURE study demonstrated that remodelling is a two-phase process; adaptive vessel enlargement within one month

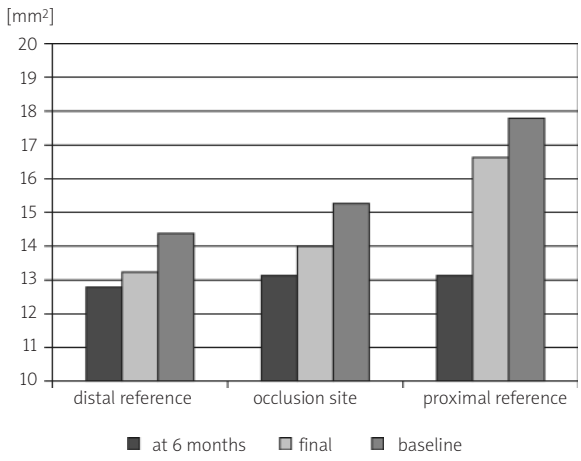

Figure 3. Total vessel area (VA) for group A (balloon angioplasty)

Table VI. Total vessel area (VA) for group A (balloon angioplasty)

	Distal reference	Occlusion site	Proximal segment
Baseline [mm^2]	12.8 ± 3.4	13.1 ± 3.5	16.1 ± 3.6
p	< 0.001	< 0.001	< 0.001
Final [mm^2]	13.2 ± 4.0	14.0 ± 3.6	16.7 ± 4.3
p	< 0.001	< 0.001	< 0.001
At 6 months [mm^2]	14.4 ± 3.7	15.3 ± 3.5	17.8 ± 4.3

Table VII. Total vessel area (VA) for group B (stent implantation)

	Distal reference	Occlusion site	Proximal reference
Baseline [mm^2]	12.1 ± 4.6	15.0 ± 3.3	15.4 ± 3.7
p	< 0.001	< 0.001	< 0.001
Final [mm^2]	13.5 ± 4.6	16.6 ± 4.5	17.1 ± 37
p	< 0,001	NS	< 0.001
At 6 months [mm^2]	15.5 ± 4.3	16.9 ± 4.1	19.5 ± 2.9

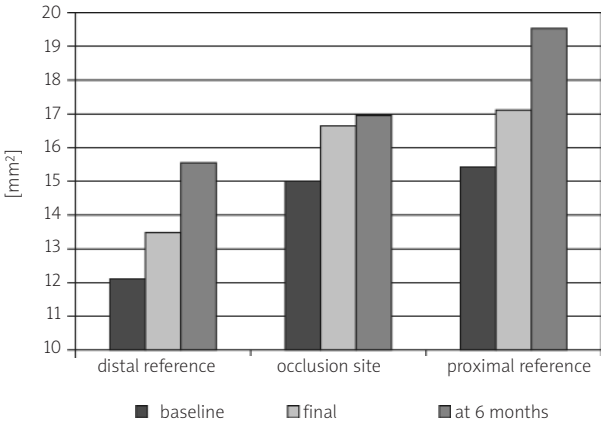

Figure 4. Total vessel area (VA) for group B (stent implantation)

after angioplasty followed by vessel constriction within 1-6 months [25]. In the present study positive remodelling (i.e. adaptive vessel enlargement) was still found in patients without restenosis at 6 months after angioplasty.

To the best of our knowledge, the present report is the first to describe the use of ICUS optimising balloon angioplasty in CTO. Previous studies that used ICUS-guided angioplasty for subtotal lesions reported good early and late results [26-28]. The superiority of the ICUS guidance over the QCA approach in non-occlusive lesions was also confirmed in the DIPOL study. The observed success rate during ICUS-guided POBA was 29.1% [29]. Abizaid et al. performed ICUS-guided balloon angioplasty of 438 lesions in 284 patients and achieved an optimal angioplasty result in 47% of patients [30]. In the present study, using similar criteria, optimal results were achieved in 49% of patients. The reasons for the improved ICUS-guided balloon angioplasty results were a reduced residual plaque burden and an increased vessel lumen at the site of stenosis. There was no deterioration in the dissection index after angioplasty; indeed the vessel size increased. Mintz et al. demonstrated that plaque compression or axial plaque redistribution is a mechanism of lumen enlargement during ICUS-guided balloon angioplasty [31]. This mechanism may play a role in soft plaques, whereas in cases of mixed and hard plaques there is an increase in the vessel area or plaque rupture. While the mechanism for optimisation is similar in CTO, there is an additional gradual increase in vessel size during the intervention. This is a first instance of gradual enlargement of a chronically occluded coronary artery. The vessel at the site of occlusion may be collapsed at baseline. The proximal and distal segments dilate as a result of improved blood flow and release of vasodilating substances, induced additionally by nitroglycerine, administrated during the procedure. Mechanical expansion using balloons of increasing size enhances the magnitude of dilatation at the site of occlusion. The present study showed that ICUS provides more accurate information on the actual vessel size as compared with QCA, both at the site of occlusion and at the proximal and distal reference segment. Werner et al. obtained similar results [10]. We found that optimisation of stent implantation by ICUS guidance also improved immediate and late outcomes, which reduced the rate of restenosis which is consistent with previous studies [32, 33].

Unlike other investigations, the present study identified no reocclusion. This is probably because ICUS allowed direct visualisation of the arterial wall and detection of dissection, which is not possible using angiography, prompting stent implantation.

The significant differences in vessel size measured by QCA and ICUS found in the present and a number of other

studies should be taken into account when stenting chronically occluded arteries, because underestimation of vessel size will consequently increase the rate of restenosis. Balloon angioplasty remains an important alternative despite many innovations in interventional techniques. Stents are not used in clinical practice in some CTO patients [34]. The present study objectively confirmed a gradual increase in vessel area both during the procedure and at 6 months after balloon angioplasty in CTO patients, and these observations indicate that further studies are warranted. A 1 : 1 ratio of stent to artery diameter is usually recommended in CTO, which may lead to underestimation of stent size and accounts for the high in-stent restenosis rate. However, choosing a larger stent without ICUS guidance and defining the type of remodelling may cause vessel rupture in the presence of negative remodelling. The historically high rate of restenosis in CTO patients may be due to angiography results leading to underestimation of the stent size required for treatment.

The present strategy may be particularly useful in patients with a high risk of bleeding complications in whom combined treatment with two antiplatelet agents (e.g. aspirin and thienopyridine) required after stent implantation is contraindicated. Patients requiring surgery shortly after recanalisation may also be suitable candidates.

The inclusion criterion for the present study of a CTO duration > 15 days was consistent with the definition of CTO at the time the study was undertaken [35]. Although the current CTO definition involves a longer duration, the present study remains relevant since the average time of occlusion duration for the whole group was 4.9 months and 67% of occlusions were of > 3 months duration. The major limitation of the present study relates to the pre-selection of patients thought to have a high probability of balloon angioplasty success in CTO. Good outcomes cannot be achieved in all patients who may have smaller vessels and a longer duration of occlusion.

Conclusions

1. Achieving an optimal balloon angioplasty result in CTO patients requires confirmation using ICUS.
2. In some patients immediate and long-term outcomes following ICUS-guided optimised balloon angioplasty are comparable to those of ICUS-guided stent implantation.
3. Direct measurement of a chronically occluded coronary artery at pre-intervention, during the intervention and at long-term follow-up may argue in favour of using ICUS in recanalisation of CTO.
4. The ICUS-guided balloon angioplasty for CTO could be a method of choice in patients in whom long-term dual antiplatelet therapy is associated with a high probability of bleeding complications.

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Udrażnianie przewlekłych okluzji tętnic wieńcowych pod kontrolą ultrasonografii wewnątrzwieńcowej

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Streszczenie

Wstęp: Zabiegi udrożnienia przewlekłych okluzji tętnic wieńcowych (CTO) wiążą się z wysoką częstością restenozy i reokluzji. Zastosowanie ultrasonografii wewnątrzwieńcowej (ICUS) może poprawiać bezpośrednie i odległe wyniki tych zabiegów. Do tej pory nie oceniano zastosowania angioplastyki balonowej pod kontrolą ICUS w CTO.

Cel: Porównanie wyników angioplastyki balonowej pod kontrolą ICUS z implantacją stentu pod kontrolą ICUS u chorych z CTO.

Metody: Do badania włączono 51 chorych z CTO, u których w ocenie ilościowej angiografii wieńcowej (QCA) uzyskano optymalny wynik angioplastyki balonowej. Chorzy zostali poddani angioplastyce balonowej pod kontrolą ICUS, której celem było uzyskanie minimalnego pola powierzchni światła naczynia (MLCSA) powyżej 6,0 mm^2 oraz wielkości rezydualnej blaszki miażdżycowej (RPB) poniżej 65%. Z grupy 51 pacjentów kryteria ICUS definiujące optymalną angioplastykę balonową osiągnięto u 23 osób, natomiast u 7 nie implantowano stentu z powodu zwapnień i/lub małego wymiaru naczynia (grupa A – 30 chorych). U 21 pacjentów angioplastyka balonowa nie pozwoliła na osiągnięcie optymalnych parametrów ICUS, czego następstwem była implantacja stentu. Za optymalny wynik implantacji stentu uznawano MLCSA w stencie > 9 mm^2 oraz > 55% średniego pola powierzchni naczynia ocenianego na podstawie dystalnego i proksymalnego segmentu referencyjnego (grupa B). Analizowane grupy nie różniły się istotnie pod względem parametrów klinicznych i angiograficznych.

Wyniki: Optymalny w ocenie QCA wynik angioplastyki balonowej okazał się nieoptymalny w ocenie ICUS u 41 chorych (80,4%). Wartość MLCSA stwierdzona w grupie A była mniejsza niż w grupie B (6,5 ± 1,5 *vs* 8,9 ± 2,0 mm^2; $p < 0,001$). Restenoza wystąpiła u 8 (26,6%) chorych w grupie A oraz 4 (19%) osób w grupie B ($p > 0,05$). Częstość restenozy wśród 23 chorych z grupy A, u których osiągnięto kryteria ICUS definiujące optymalną angioplastykę balonową, wynosiła 8,6% (2 pacjentów). Kolejne pomiary ICUS wykazały stopniowy wzrost całkowitego pola powierzchni naczynia w czasie zabiegu udrożnienia oraz w okresie 6-miesięcznej obserwacji odległej ($p < 0,05$).

Wnioski: 1. Optymalny w angiografii wynik udrożnienia CTO metodą angioplastyki balonowej wymaga potwierdzenia w ICUS. 2. W określonej grupie chorych optymalizacja wyniku angioplastyki balonowej CTO pod kontrolą ICUS pozwala na uzyskanie wyników bezpośrednich i odległych porównywalnych z wynikami zabiegów angioplastyki z implantacją stentu pod kontrolą ICUS. 3. Możliwość bezpośredniej oceny wielkości przewlekle zamkniętego naczynia w ICUS przed zabiegiem, w czasie zabiegu oraz w okresie obserwacji odległej może wskazywać na potrzebę częstszego stosowania ICUS w zabiegach udrożnienia CTO. 4. Udrożnienie CTO metodą angioplastyki balonowej pod kontrolą ICUS może się stać leczeniem z wyboru u chorych, u których długotrwałe podwójne leczenie przeciwpłytkowe wiąże się z dużym ryzykiem powikłań krwotocznych.

Słowa kluczowe: przewlekłe okluzje tętnic wieńcowych, angioplastyka wieńcowa, ultrasonografia wewnątrzwieńcowa

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