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The value of chronic total occlusion in a non-infarct-related artery in patients with multi-vessel coronary artery disease undergoing acute coronary syndromes

Znaczenie obecności przewlekłe niedrożnej tętnicy wieńcowej, innej niż tętnica dozawałowa, u chorych z wielonaczyniową chorobą wieńcową i ostrym zespołem wieńcowym

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Słowa kluczowe

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Summary

Introduction. The coexistence of multi-vessel disease (MVD) and chronic total occlusion (CTO) in patients undergoing coronarography due to acute coronary syndrome (ACS) is suggested to worsen the overall prognosis.

Aim. The comparison of patients with ACS without and with a chronic total occlusion (CTO) in a non-infarct-related artery (non-IRA) regarding the clinical characteristics, the impact on left ventricular (LV) damage and long-term survival.

Material and methods. The study population consisted of 402 consecutive patients with MVD undergoing coronarography because of ACS.

Results. Up to one third of patients revealed at least one non-IRA CTO. Patients with CTO more often suffered from non-STE ACS ($p = 0.005$) and had higher risk because of age and comorbidities. In 25.56% of patients without CTO at least moderate LV failure was diagnosed only whereas in CTO patients it amounted to 48.5% ($p = 0.02$).

The average 490-day mortality in all MVD-patients was up to 13.18%. All-cause and cardiovascular mortality in CTO patients was 17 and 12.5% while in patients without CTO 11 and 9%, respectively ($p = 0.2$ and $p = 0.4$).

Conclusions. In patients with MVD undergoing coronarography because of ACS the presence of CTO in non-IRA as compared with patients without CTO has a significant impact on LV impairment and overall prognosis.

Streszczenie

Wstęp. Współistnienie wielonaczyniowej choroby wieńcowej oraz przewlekłe niedrożnej tętnicy wieńcowej pogarsza rokowanie odległe pacjentów.

Cel pracy. Porównanie pacjentów z ostrym zespołem wieńcowym pod względem obecności przewlekłe niedrożnej tętnicy (CTO), innej niż dozawałowa (non-IRA), w odniesieniu do charakterystyki klinicznej, wpływu na uszkodzenie lewej komory serca i przeżycie odległe.

Materiał i metody. Badana populacja składała się z 402 kolejnych pacjentów z wielonaczyniową chorobą wieńcową (MVD) poddanych pilnej koronarografii z powodu ostrego zespołu wieńcowego (ACS).

Wyniki. Blisko u jednej trzeciej pacjentów stwierdzono przynajmniej jedną przewlekłe niedrożną tętnicę (inną niż dozawałowa). Pacjentów z przewlekłe niedrożną tętnicą wieńcową znacznie częściej hospitalizowano z powodu ostrego zespołu wieńcowego bez uniesienia odcinka ST (non-STE ACS, $p = 0,005$), byli oni też w starszym wieku oraz mieli wyższe ryzyko całkowite z uwagi na choroby współistniejące. Co najmniej umiarkowane uszkodzenie lewej komory serca stwierdzono u 25,6% pacjentów bez przewlekłe niedrożnej tętnicy wieńcowej, natomiast u pacjentów z CTO odsetek ten sięgał 48,5% ($p = 0,02$).

Średnia, 490-dniowa, śmiertelność u wszystkich pacjentów z wielonaczyniową chorobą wieńcową wyniosła 13,18%. Śmiertelność całkowita oraz z przyczyn sercowo-naczyniowych u pacjentów z przewlekle niedrożną tętnicą wieńcową kształtowała się następująco: 17 i 12,5%, podczas gdy u pacjentów bez CTO wyniosła odpowiednio 11 i 9% ($p = 0,2$, $p = 0,4$).

Wnioski. U pacjentów z wielonaczyniową chorobą wieńcową poddanych pilnej koronarografii z powodu ostrego zespołu wieńcowego obecność przewlekle niedrożnej tętnicy wieńcowej, innej niż dozawałowa, ma istotny wpływ na uszkodzenie lewej komory serca oraz rokowanie odległe.

LIST OF ABBREVIATIONS:

ACS	–	Acute Coronary Syndrome
STEMI	–	ST Segment Elevation Myocardial Infarction
NSTEMI	–	Non ST Segment Elevation Myocardial Infarction
UA	–	Unstable Angina
MVD	–	Multi-vessel Coronary Disease
CTO	–	Chronic Total Occlusion
Non-IRA	–	Non-Infarct-Related Artery
MI	–	Myocardial Infarction
PCI	–	Percutaneous Coronary Intervention
LV	–	Left Ventricle
EF	–	Ejection Fraction
TIMI	–	Thrombolysis In Myocardial Infarction
CABG	–	Coronary Artery Bypass Graft

INTRODUCTION

Unstable angina (UA), myocardial infarction with ST segment elevation (STEMI) and myocardial infarction without ST segment elevation (NSTEMI) constitute the core of acute coronary syndromes (ACS). According to the number of haemodynamically relevant narrowed vessels in angiography one may distinguish a single or multi-vessel coronary artery disease (MVD). The second one is found in approximately 45-80% of patients with ACS (1, 2). The presence of multi-vessel disease is believed to be an independent risk factor with worse outcome and prognosis in patients with ACS (3, 4). Chronic total occlusion of coronary artery (CTO) occurs in about 15-30% of patients with coronary artery disease (CAD) (5). The coexistence of MVD and CTO in other than infarct related coronary artery (non-IRA) in patients with ACS in some studies is suggested to worsen the overall prognosis (6). Therefore, in our study we tried to assess these variables in patients undergoing all types of ACS.

AIM

The comparison of patients with ACS without and with a chronic total occlusion (CTO) in a non-infarct-related artery (non-IRA) regarding the clinical characteristics, the impact on left ventricular (LV) damage and long-term survival.

MATERIAL AND METHODS

The study is retrospective and all data and records were summoned up based on material obtained within standard medical procedures.

The study population consisted of 402 consecutive MVD patients who were hospitalized in 2009-2011 in our Cardiology Department after coronary angiography because of ACS. The presence of more than 50% lesion diameter stenosis in at least two of the epicardial coronary arteries was regarded as multi-vessel coronary disease. CTO in a non-IRA was defined as a total vessel occlusion lasting more than 3 months with the TIMI 0-1 blood flow grade in the artery not responsible for ACS. The CTO vessel diameter over 2 mm was taken into account only. The coronarographic assessment was performed by two invasive cardiologists independently. Ejection fraction (EF) was managed to evaluate echocardiographically during index hospitalization in 92% of patients. An average 490-day (median 322) follow-up data were derived from both hospital documentation and telephone interviews.

Statistical analysis

Continuous variables were presented as mean value \pm standard deviation, median and the Student's t-test analyses were performed. Categorical variables were expressed as numbers and/or percentages. The chi-square test with Yates correction for discontinuity or Fisher's exact test were used for comparative statistics. Graphic Kaplan-Meier method was used to describe survival in follow-up. P-value equal to or less than 0.05 was considered as statistically significant.

RESULTS

Ultimately 402 consecutive patients with MVD undergoing ACS were enrolled in this study. In as much as 33.8% of all patients a non-IRA CTO was present.

CTO patients were older at the time of ACS, statistically more frequently presented renal insufficiency, peripheral atherosclerosis, myocardial infarction in the history, previous CABG and were more often in their worse clinical status at admission evaluated by Killip-Kimball scale (tab. 1). More likely they also suffered from diabetes ($p = 0.08$).

Graphical and statistical analysis of ACS distribution is shown in figure 1. A higher incidence of STEMI was observed in patients without CTO ($p = 0.08$) while in those with non-IRA CTO a myocardial infarction without ST segment elevation was the most common cause of ACS ($p = 0.005$). 48.5% of patients with CTO had at least moderate LV damage ($EF < 45\%$) echocardiographically as compared with only 25.56% patients without CTO ($p = 0.02$, fig. 2).

Tab. 1. Patient characteristics

Medical data	no CTO (n = 266)	CTO (n = 136)	p
Age: average ± SD (median)	65.1 ± 11.3 (63)	69.2 ± 11.9 (70)	< 0.001
Male	65.50%	72.80%	0.3
Post MI	19.50%	59.60%	< 0.001
Post PCI	14%	20.60%	0.14
Post CABG	0%	10.30%	< 0.001
Diabetes	12.80%	20.60%	0.08
Hypertension	83%	88.20%	0.7
Hyperlipidemia	79.30%	78%	0.9
Renal failure	5.30%	16.20%	0.001
Peripheral atherosclerosis	3.60%	9.60%	0.04
Killip-Kimball 2-4 Class	3.40%	9.60%	0.02

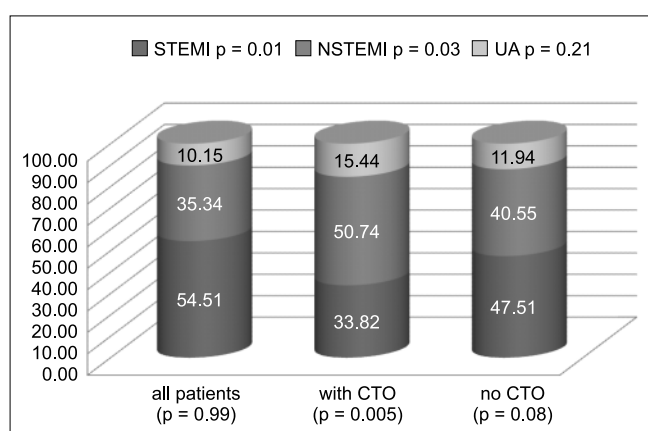


Fig. 1. ACS distribution

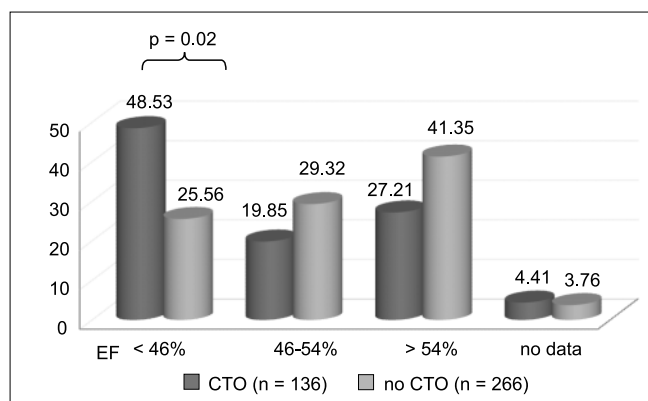


Fig. 2. Percentage EF distribution

The average 490-day mortality in the group of 402 patients with MVD was 13.18% (p = 0.15). In CTO patients Kaplan-Meier estimates of all-cause and cardiovascular mortality amounted to 17 and 12.5%, and in patients without CTO to 11 and 9%, respectively (log-rank test p = 0.2/Cox F-Test p = 0.04 and log-rank test p = 0.4/Cox F-Test p = 0.09).

The survival curves are shown graphically in figure 3.

DISCUSSION

It is known that patients with MVD have unfavourable overall prognosis but the coexistence of CTO in

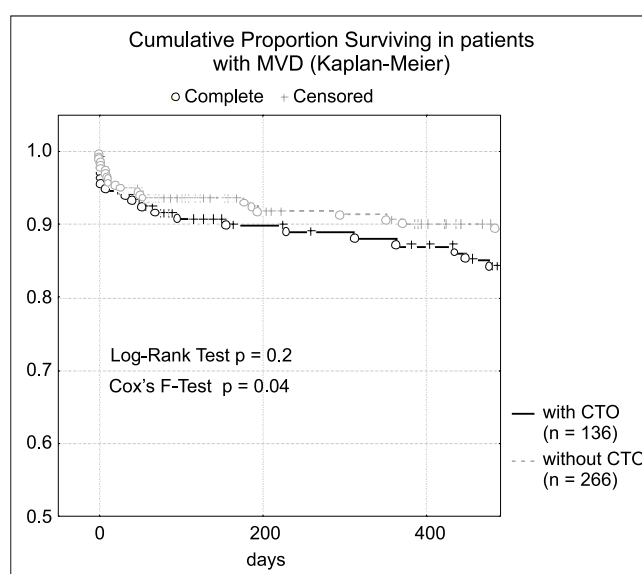


Fig. 3. The survival curves in patients with MVD (all-cause mortality)

non-IRA makes their situation even worse. The pathophysiological background of this fact is surely multifactorial. The nature of ACS results in microvascular ischemia and if the IRA is also a source of collateral circulation to the area previously supplied by vasculature of chronically occluded artery the LV impairment is much more extended (7). Of note, there are also clinical and angiographic differences between CTO lesions among the 3 major coronary arteries which eventually affects the long-term survival after PCI (8, 9). Thus, not only the presence of CTO but its location as well seem to be significant. One can not also pass over the post-reperfusion blood flow disturbances and the cardiomyocyte damage that obviously are more pronounced while CTO is present. Besides, the permanent myocardial ischemia might be a substrate for many different supraventricular and/or ventricular arrhythmias that may lead towards worsening quality of life and a lot of complications, diseases and even SCD.

In our study patients with MVD hospitalized because of all sorts of ACS were analyzed. Patients with non-IRA CTO compared with patients without CTO were older

at the time of index ACS, demonstrated more cardiovascular risk factors and co-morbidities (10) and had advanced atherosclerotic disease that remains consistent with other studies. In patients with CTO significantly more frequent cause of ACS was non-STEMI, whereas in patients without CTO – STEMI. Due to more cardiovascular risk factors in patients with CTO a significantly greater degree of LV damage, worse overall prognosis and the tendency to higher mortality were observed.

In the previous registries and studies it has been demonstrated that a CTO in a non-IRA MVD patients undergoing primary PCI because of STEMI is an independent predictor of early and late mortality (11, 12). On the contrary, MVD alone (without CTO) was only a weak factor of early mortality (6). Moreover, concurrent CTO in a non-IRA in STEMI patients and the presence of cardiogenic shock on admission exert adverse effect on early and late survival rate (13). Three-vessel disease, cardiogenic shock and CTO coexistence in non-IRA in the setting of STEMI individuals were also confirmed as independent risk factors for over one year cardiac mortality (14). In almost all former trials concurrent CTO involved a reduced residual LVEF that firmly influenced on poor prognosis and adverse cardiovascular events (6, 11-14). An interest was also manifested in NSTEMI patients with MVD presenting with concurrent CTO. It was found that within this group the CTO presence is an independent predictor of 12 month mortality as well (15, 16).

The results on cardiovascular risk factors and the extent of LV damage in MVD patients with CTO coincide with our study findings. However, since in our observation patients undergoing all kinds of ASC were enrolled, the higher prevalence of all-cause and cardiovascular mortality in CTO population was observed as compared to studies concerning STEMI individuals only. These numbers are adequately smaller but yet similar to those regarding trials with NSTEMI patients that fully reflects the greater proportion of NSTEMI with CTO individuals

in our study. As one may expect patients with NSTEMI have worse overall prognosis than STEMI individuals that biased our results (17, 18). Nevertheless, our findings regarding mortality were not statistically significant (in terms of log-rank test) that partially could be due to a large heterogeneity of ACS patients (prior researchers concentrated either on NSTEMI or STEMI populations only) and partly as a result of small target group.

Based on above observations and willing to prevent from worse clinical outcome in these patients there are suggestions to perform PCI of CTO of coronary arteries which is proven to be safe (19) (while performed by experienced invasive cardiologists), in many ways profitable (probably reflecting less adverse LV remodeling (20)) and above all, improved survival (21, 22) as compared to conservative treatment. The main questions still remaining unanswered are the timing of the procedure, the extent of revascularization and degree of subsequent benefit (23). They need a clear and unequivocal reply we hope to obtain gradually in the forthcoming results of on-going studies (24).

CONCLUSIONS

In patients with MVD undergoing coronarography because of ACS the presence of CTO in non-IRA as compared with patients without CTO has a significant impact on LV impairment and overall prognosis.

LIMITATIONS

The comparatively short observation time and lack of echocardiographic assessment of all patients could have had a significant influence on the analysis. Not having taken into consideration the CTO vessels of diameter smaller than 2 mm, the extent of collateral vasculature and primary or secondary arterial branches could also ultimately affect our results. And, of course, the relatively small group of all patients in this study and its heterogeneity could be a reason for some statistically insignificant results.

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