Impact of Acute Total Occlusion of Culprit Artery on Outcome in NSTEMI – Results From a Large National Registry

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Abstract

Background

The impact of acute total occlusion (TO) of culprit artery in non-ST-segment elevation myocardial infarction (NSTEMI) is not fully established. We aimed to evaluate clinical and angiographic phenotype and outcome of NSTEMI patients with TO (NSTEMI\textsubscript{TO}) compared to NSTEMI patients without TO (NSTEMI\textsubscript{NTO}) and those with ST-segment elevation and TO (STEMI\textsubscript{TO}).

Methods

Demographic, clinical and procedure-related data of patients with percutaneous coronary intervention (PCI) performed in acute myocardial infarction between 2014 and 2017 from the Polish National Registry were analysed.

Results

We evaluated 131,729 patients: NSTEMI\textsubscript{NTO} (n=65,206), NSTEMI\textsubscript{TO} (n=16,209) and STEMI\textsubscript{TO} (n=50,314). NSTEMI\textsubscript{TO} group had intermediate results compared to NSTEMI\textsubscript{NTO} and STEMI\textsubscript{TO} regarding: mean age (68.78±11.39 vs 65.98±11.61 vs 64.86±12.04 (years), p<0.0001), Killip class IV on admission (1.69 vs 2.48 vs 5.03(%), p<0.0001), cardiac arrest before admission (2.19 vs 3.09 vs 6.02(%), p<0.0001) and death during PCI (0.43 vs 0.97 vs 1.76(%), p<0.0001) - for NSTEMI\textsubscript{NTO}, NSTEMI\textsubscript{TO} and STEMI\textsubscript{TO}, respectively. However, in NSTEMI\textsubscript{TO} we noticed: the longest time from pain to first medical contact (median 4.0 vs 5.0 vs 2.0 (hours), p<0.0001); left circumflex artery (LCx) most often as culprit lesion (14.09 vs 35.86 vs 25.42(%), p<0.0001) and lowest frequency of TIMI flow grade 3 after PCI (88.61 vs 83.36 vs 95.57(%), p<0.0001).

Conclusions

NSTEMI\textsubscript{TO} clearly differs from NSTEMI\textsubscript{NTO}. It appears as an intermediate condition between NSTEMI\textsubscript{NTO} and STEMI\textsubscript{TO}, although NSTEMI\textsubscript{TO} patients have the longest time delay to and the worst result of PCI which can be explained by the location of the culprit lesion in LCx.

Background

According to the European Society of Cardiology (ESC) guidelines patients with myocardial infarction (MI) and ST-segment elevation (STEMI) are eligible for emergency reperfusion therapy, whereas those with non-ST-segment elevation MI (NSTEMI) require further risk stratification and thus the qualification for invasive diagnosis and treatment is delayed.\textsuperscript{1} The STEMI-NSTEMI paradigm is based on the observation that ST-segment elevation (STE) on the electrocardiogram (ECG) in the majority of patients with MI is associated with acute total occlusion (TO) of infarct-related artery (IRA), while subtotal IRA occlusion leads mostly to ST-segment depression and negative T-waves on the ECG. However, when
qualification for emergent reperfusion therapy is based on the ECG criteria, we lose around 25% of patients with acute TO of IRA who do not present STE. NSTEMI patients are a very heterogeneous group in which ESC guidelines recommend urgent coronary angiography only in those with life-threatening ventricular arrhythmias, resistant angina pectoris and haemodynamic instability. These conditions may be accompanied by a total IRA occlusion, but this is not always the case. Thus, the percutaneous coronary intervention (PCI) may be deferred in significant subset of NSTEMI patients with TO of IRA which may result in delayed myocardial salvage and worse cardiovascular outcomes.

This study aimed to identify the key points of clinical characteristics, course of treatment and outcome of patients with NSTEMI with TO of IRA (NSTEMI_TO) by comparison with the two most outlying groups: patients with NSTEMI and non-occluded coronary artery (NSTEMI_NTO) and patients with STE and occluded IRA (STEMI_TO).

Methods

We analysed the data of patients with MI assembled within 48 months (2014–2017) into the ORPKI - Polish National Database of Invasive Coronary Procedures, coordinated by Jagiellonian University Medical College and endorsed by the Association of Cardiovascular Interventions of the Polish Cardiac Society. All clinical data was collected by the operator and then uploaded into database after each procedure. The diagnosis of NSTEMI, STEMI, recognition of IRA, all clinical decisions during the coronary invasive procedure and definition of periprocedural complications remained to the uploading ORPKI operators’ experience and knowledge according to current ESC guidelines.

Acute TO of IRA was defined in our study as Thrombolysis In Myocardial Infarction (TIMI) 0 flow during coronary angiography in patients with MI. To achieve the aim of the study we compared 3 groups of patients: NSTEMI_TO, NSTEMI_NTO and STEMI_TO and excluded from the analysis patients: with STEMI and non-occluded coronary artery (STEMI_NTO), without significant coronary artery stenosis, not treated with PCI and diagnosed as chronic total occlusion of IRA.

Our study was an observational, non-experimental, retrospective analysis and was performed in accordance with relevant guidelines and regulations. Only anonymized data was subjected to the research analysis and according to Regulation 2016/679 of the European Parliament and of the Council (EU) from 27 April 2016 on the protection of individuals with regard to the processing of personal data and on the free movement of such data, and with art. 9 Sect. 2 this study did not require any additional ethics board approval. All subjects of our study gave informed consent for personal data processing by the Association of Cardiovascular Interventions of Polish Cardiac Society before percutaneous coronary intervention.

Statistical analysis
Categorical variables are presented as numbers and percentages. Continuous variables were expressed as mean, standard deviation (SD) or median and interquartile range (IQR). Normality of continuous variables was assessed by the Kolmogorov–Smirnov–Lilliefors test. Equality of variances was assessed using the Levene's test. Differences between three groups were compared using the classical one-way analysis of variance (ANOVA) or the Welch's ANOVA depending on the equality of variances for normally distributed variables. The Kruskal-Wallis test was used for ordinal or non-normally distributed continuous variables. Categorical variables were compared by the Pearson's chi-square test. All post-hoc analyses were performed using the Benjamini-Hochberg procedure for controlling the False Discovery Rate (FDR). Two-sided p-values < 0.05 were considered statistically significant. All calculations were done with JMP®, Version 14.2.0 (SAS Institute Inc., Cary, NC, USA).

Results

Results of 245,869 coronary angiographies performed in patients with MI were entered to the ORPKI registry. After exclusion of patients: a) without significant stenosis of coronary arteries, b) without occlusion of IRA in STEMI, c) without PCI treatment; d) with chronic total occlusion of IRA and e) with multivessel PCI treatment a total number of 131,729 patients with single-vessel PCI constituted the study group. Among them 65,206 (80.09%) patients with NSTEMI had no TO of IRA (TIMI > 0), while totally occluded IRA (TIMI = 0) were found in 16,209 (19.91%) patients with NSTEMI and in 50,314 (48.21%) with STEMI. The study flowchart is shown in Fig. 1.

Clinical characteristic of the study groups

Patients with NSTEMI_TO were younger than those with NSTEMI_NTO but older than patients with STEMI_TO. The percentage of smokers was the highest in STEMI_TO, lower in NSTEMI_TO and the lowest in NSTEMI_NTO. The prevalence of chronic diseases (arterial hypertension, diabetes, chronic kidney disease, chronic obstructive pulmonary disease) was the highest in NSTEMI_NTO group, lower in NSTEMI_TO group and the lowest in STEMI_TO. All of the aforementioned differences were significant (p < 0.0001). Similar tendency was observed in the history of previous coronary revascularization (PCI or CABG), MI or stroke, which were the most frequent in patients with NSTEMI_NTO, less frequent in NSTEMI_TO and the least frequent in STEMI_TO group (p < 0.0001).

Clinical status on admission in NSTEMI_TO group was more severe than in NSTEMI_NTO group but less serious than in STEMI_TO group. More advanced Killip classes occurred with the highest frequency in patients with STEMI_TO, lower frequency in NSTEMI_TO and the lowest frequency in NSTEMI_NTO. Cardiac arrest before admission was more frequent in patients with STEMI_TO compared to NSTEMI_TO, and more frequent in NSTEMI_TO than in NSTEMI_NTO (See Table 1).
Table 1
Clinical characteristics of the study groups. \( p < 0.0001 \) for all analyses of the study groups by the Kruskal–Wallis one-way analysis of variance

<table>
<thead>
<tr>
<th></th>
<th>NSTEMI(_{\text{NTO}}) ( (N = 65,206) )</th>
<th>NSTEMI(_{\text{TO}}) ( (N = 16,209) )</th>
<th>STEMI(_{\text{TO}}) ( (N = 50,314) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean (SD)</td>
<td>68.78 (11.39)</td>
<td>65.98 (11.61)</td>
<td>64.86 (12.04)</td>
</tr>
<tr>
<td>Male gender, n (%)</td>
<td>42.380 (65.19%)</td>
<td>11.215 (69.53%)*</td>
<td>34.133 (68.00%)</td>
</tr>
<tr>
<td>Weight (kg), mean (SD)</td>
<td>79.98 (17.49)</td>
<td>81.64 (17.54)</td>
<td>80.52 (16.67)</td>
</tr>
<tr>
<td>Smokers, n (%)</td>
<td>14.075 (21.59%)</td>
<td>4.303 (26.55%)</td>
<td>14.842 (29.50%)</td>
</tr>
<tr>
<td>Arterial hypertension, n (%)</td>
<td>47.872 (73.42%)</td>
<td>11.222 (69.23%)</td>
<td>29.912 (59.45%)</td>
</tr>
<tr>
<td>Diabetes, n (%)</td>
<td>17.774 (27.26%)</td>
<td>3.737 (23.06%)</td>
<td>8.729 (17.35%)</td>
</tr>
<tr>
<td>Kidney disease, n (%)</td>
<td>5.633 (8.64%)</td>
<td>948 (5.85%)</td>
<td>1.647 (3.27%)</td>
</tr>
<tr>
<td>COPD(^b), n (%)</td>
<td>1.718 (3.61%)</td>
<td>343 (2.90%)$</td>
<td>659 (1.75%)</td>
</tr>
<tr>
<td>Previous stroke, n (%)</td>
<td>2.877 (4.41%)</td>
<td>671 (4.14%)#</td>
<td>1.687 (3.35%)</td>
</tr>
<tr>
<td>Previous PCI, n (%)</td>
<td>17.433 (26.74%)</td>
<td>3.027 (18.67%)</td>
<td>6.010 (11.94%)</td>
</tr>
<tr>
<td>Previous CABG, n (%)</td>
<td>4.300 (6.59%)</td>
<td>835 (5.15%)</td>
<td>814 (1.62%)</td>
</tr>
<tr>
<td>Previous MI, n (%)</td>
<td>18.406 (28.23%)</td>
<td>3.550 (21.90%)</td>
<td>6.493 (12.90%)</td>
</tr>
<tr>
<td>Killip class III(^c), n (%)</td>
<td>1.051 (2.25%)</td>
<td>325 (2.47%)</td>
<td>1.431 (3.33%)</td>
</tr>
<tr>
<td>Killip class IV(^c), n (%)</td>
<td>787 (1.69%)</td>
<td>326 (2.48%)</td>
<td>2.162 (5.03%)</td>
</tr>
<tr>
<td>Cardiac arrest before admission, n (%)</td>
<td>1.208 (2.19%)</td>
<td>477 (3.09%)</td>
<td>2.962 (6.02%)</td>
</tr>
<tr>
<td>Cardiac arrest during angiography, n (%)</td>
<td>151 (0.27%)</td>
<td>82 (0.53%)</td>
<td>19 (0.04%)</td>
</tr>
</tbody>
</table>

Data are presented as mean and standard deviation (SD) or number (n) and percentage (%).

NSTEMI\(_{\text{NTO}}\): non-ST-segment elevation myocardial infarction without total occlusion of culprit artery; NSTEMI\(_{\text{TO}}\): non-ST-segment elevation myocardial infarction with total occlusion of culprit artery; STEMI\(_{\text{TO}}\): ST-segment elevation myocardial infarction with total occlusion of culprit artery; COPD: chronic obstructive pulmonary disease; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; MI: myocardial infarction.

\( p < 0.0001 \) for all post-hoc analyses with following exceptions:

\[*p = 0.0003 for post-hoc comparison between NSTEMI\(_{\text{TO}}\) and STEMI\(_{\text{TO}}\);\]

\[#p = 0.1283 for post-hoc comparison between NSTEMI\(_{\text{NTO}}\) and NSTEMI\(_{\text{TO}}\);\]

\[\$p = 0.0002 for post-hoc comparison between NSTEMI\(_{\text{NTO}}\) and NSTEMI\(_{\text{TO}}\).\]
<table>
<thead>
<tr>
<th>NSTEMI(_{NTO})</th>
<th>NSTEMI(_{TO})</th>
<th>STEMI(_{TO})</th>
</tr>
</thead>
<tbody>
<tr>
<td>((N = 65,206))</td>
<td>((N = 16,209))</td>
<td>((N = 50,314))</td>
</tr>
</tbody>
</table>

data available for: \(a\) – 131,452 patients, \(b\) – 96,952 patients, \(c\) – 102,807 patients, \(d\) – 119,955 patients

**Time delays in MI treatment within study groups**

Direct transport to the catheterization laboratory (Cath lab) was most common in STEMI\(_{TO}\) group, less common in NSTEMI\(_{TO}\) and the rarest in NSTEMI\(_{NTO}\). Time from pain to first medical contact (FMC) was longer in NSTEMI\(_{TO}\) group than in both STEMI\(_{TO}\) and NSTEMI\(_{NTO}\) group. Time periods (from pain to balloon inflation and from FMC to inflation) were the shortest in STEMI\(_{TO}\), intermediate in NSTEMI\(_{TO}\) and the longest in NSTEMI\(_{NTO}\) group. Time from FMC to inflation < 90 min and time from FMC to inflation < 120 min were observed most frequent in patients with STEMI\(_{TO}\), less frequent in NSTEMI\(_{TO}\) and least frequent in NSTEMI\(_{NTO}\) (Table 2, Fig. 2).
Table 2
Comparison of patient- and system-related delays to the primary PCI. p < 0.0001 for all analyses of the study groups by the Kruskal –Wallis one-way analysis of variance

<table>
<thead>
<tr>
<th></th>
<th>NSTEMI_{NTO}</th>
<th>NSTEMI_{TO}</th>
<th>STEMI_{TO}</th>
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<tbody>
<tr>
<td></td>
<td>(N = 65,206)</td>
<td>(N = 16,209)</td>
<td>(N = 50,314)</td>
</tr>
<tr>
<td>Direct transport to Cath lab, n (%)</td>
<td>3.682 (6.66%)</td>
<td>1.412 (9.14%)</td>
<td>1.2645 (25.69%)</td>
</tr>
<tr>
<td>Time from:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain to the FMC, median (IQR)</td>
<td>4.00 (2.00–11.00)</td>
<td>5.00 (2.00–14.00)</td>
<td>2.00 (1.00–5.53)</td>
</tr>
<tr>
<td>Pain to inflation, median (IQR)</td>
<td>14.42 (7.00–30.98)</td>
<td>12.48 (6.38–27.00)</td>
<td>4.00 (2.33–8.50)</td>
</tr>
<tr>
<td>FMC to inflation, median (IQR)</td>
<td>6.00 (2.42–17.00)</td>
<td>4.17 (2.00–9.67)</td>
<td>1.40 (0.97–2.25)</td>
</tr>
<tr>
<td>FMC to inflation &lt; 90 min, n (%)</td>
<td>7.008 (14.05)</td>
<td>2.618 (18.61)</td>
<td>24.268 (53.07)</td>
</tr>
<tr>
<td>FMC to inflation ≤ 120 min, n (%)</td>
<td>9.553 (19.16)</td>
<td>3.445 (24.48)</td>
<td>31.098 (68.01)</td>
</tr>
</tbody>
</table>

Data are presented as median and interquartile range (IQR) or number (n) and percentage (%);

NSTEMI_{NTO}: non-ST-segment elevation myocardial infarction without total occlusion of culprit artery;
NSTEMI_{TO}: non-ST-segment elevation myocardial infarction with total occlusion of culprit artery;
STEMI_{TO}: ST-segment elevation myocardial infarction with total occlusion of culprit artery; Cath lab: catheterization laboratory;

p < 0.0001 for all post-hoc analyses;

data available for: a – 119,955 patients, b – 107,435 patients, c – 109,566 patients, d – 109,664 patients;

Results of coronary angiography

To minimize confounding factors influencing the electrocardiographic presentation of MI we decided to make angiographic analysis only for patients with PCI of single native vessel disease: left anterior descending artery (LAD) n = 45,008; left circumflex artery (LCx) n = 29,479; right coronary artery (RCA) n = 29,479. The frequency rates of culprit lesion for LAD, LCx, RCA and other arteries (n = 10,223 include subset of patients who do not fulfil criteria of single native vessel disease PCI) within NSTEMI_{NTO}, NSTEMI_{TO} and STEMI_{TO} groups are shown in Fig. 3. NSTEMI_{TO} was related predominantly to LCx artery occlusion, on the contrary LAD occlusion as a culprit lesion was observed the least often in this group. In patients with STEMI_{TO} LCx occlusion was infrequent, while occlusion of RCA or LAD was prevalent. NSTEMI_{NTO} was related most often to LAD as the culprit lesion, less commonly to RCA and the least often to LCx (p for contingency analysis < 0.0001).

Analyses of PCI results
The successful revascularization outcome defined as TIMI flow grade after PCI in the NSTEMI\textsubscript{TO} group was worse than in STEMI\textsubscript{TO} and NSTEMI\textsubscript{NTO} (Table 3). TIMI flow grade 3 in IRA after PCI was reached with the lowest frequency and TIMI flow grade 0 after PCI was noticed with the highest occurrence rate in NSTEMI\textsubscript{TO} group compared with both STEMI\textsubscript{TO} and NSTEMI\textsubscript{NTO} groups. No-reflow phenomenon, cardiac arrest during PCI and death during invasive procedure in NSTEMI\textsubscript{TO} were less frequent than in STEMI\textsubscript{TO} but more frequent than in NSTEMI\textsubscript{NTO}. Higher total radiation dose and total amount of contrast used during procedure were observed in NSTEMI\textsubscript{TO} compared with NSTEMI\textsubscript{NTO} and STEMI\textsubscript{TO}.

<table>
<thead>
<tr>
<th></th>
<th>NSTEMI\textsubscript{NTO} (N = 65,206)</th>
<th>NSTEMI\textsubscript{TO} (N = 16,209)</th>
<th>STEMI\textsubscript{TO} (N = 50,314)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIMI 3 after PCI\textsuperscript{a}, n (%)</td>
<td>62.114 (95.57)</td>
<td>13.483 (83.36)*</td>
<td>44.494 (88.61)</td>
</tr>
<tr>
<td>TIMI 2 after PCI\textsuperscript{a}, n (%)</td>
<td>1.678 (2.58)</td>
<td>834 (5.16) *</td>
<td>2.921 (5.82)</td>
</tr>
<tr>
<td>TIMI 1 after PCI\textsuperscript{a}, n (%)</td>
<td>531 (0.82)</td>
<td>333 (2.06) *</td>
<td>971 (1.93)</td>
</tr>
<tr>
<td>TIMI 0 after PCI\textsuperscript{a}, n (%)</td>
<td>672 (1.03)</td>
<td>1.525 (9.43) *</td>
<td>829 (3.64)</td>
</tr>
<tr>
<td>No reflow after PCI, n (%)</td>
<td>315 (0.48)</td>
<td>218 (1.34%) *</td>
<td>878 (1.75%)</td>
</tr>
<tr>
<td>Total amount of contrast (mL), median (IQR)</td>
<td>160.00 (120.0; 200.0)</td>
<td>170.00 (138.0; 220.0)</td>
<td>160.00 (130.0; 200.0)</td>
</tr>
<tr>
<td>Total radiation dose (mGy), median (IQR)</td>
<td>859.00 (486.0; 1.453.0)</td>
<td>978.00 (570.0; 1.633.0)</td>
<td>842.00 (480.0; 1.419.0)</td>
</tr>
<tr>
<td>Cardiac arrest during PCI, n (%)</td>
<td>361 (0.55)</td>
<td>175 (1.08) *</td>
<td>1.198 (2.38%)</td>
</tr>
<tr>
<td>Death during PCI, n (%)</td>
<td>281 (0.43)</td>
<td>158 (0.97) *</td>
<td>885 (1.76%)</td>
</tr>
</tbody>
</table>

NSTEMI\textsubscript{NTO}: non-ST-segment elevation myocardial infarction without total occlusion of culprit artery; NSTEMI\textsubscript{TO}: non-ST-segment elevation myocardial infarction with total occlusion of culprit artery; STEMI\textsubscript{TO}: ST-segment elevation myocardial infarction with total occlusion of culprit artery; TIMI: Thrombolysis in myocardial infarction; PCI: percutaneous coronary intervention

p < 0.0001 for post-hoc all analyses with following exception: *p = 0.0005 for post-hoc comparison between NSTEMI\textsubscript{TO} and STEMI\textsubscript{TO}; \textsuperscript{a} – data available for 131,385 patients

Discussion

To the best of our knowledge we conducted the largest single study analysis dedicated to NSTEMI\textsubscript{TO} phenomenon (16,209 patients). The previous meta-analyses on this topic included 10,415 patients (7
studies) and 17,212 patients (25 studies) with NSTEMI<sub>T0</sub> respectively.<sup>6–7</sup>

Our study results suggest that NSTEMI<sub>T0</sub> may be considered as an intermediate condition between NSTEMI<sub>NTO</sub> and STEMI<sub>T0</sub>. However, the following features make NSTEMI<sub>T0</sub> group exceptional:

- The longest time delay to obtain proper medical care (patients with NSTEMI<sub>T0</sub> reached FMC when STEMI<sub>T0</sub> patients had already finished their PCI),
- LCx as the most frequent infarct related artery,
- The worst final result of PCI.

Numerous studies showing the differences in baseline clinical presentation between patients with STEMI and NSTEMI. In the OPERA Registry correlates of mid- and long term mortality were similar for NSTEMI and STEMI patients.<sup>8</sup> This leads to the conclusion that we should not consider STEMI and NSTEMI as two different diseases but rather as a ischemic continuum due to subtotal or total occlusion of coronary artery with different ECG manifestation.<sup>9–10</sup> Total occlusion of IRA can occur in both STEMI and NSTEMI patients. There are numerous studies which have compared acute total occlusion of IRA with non-total occlusion of IRA but mostly within NSTEMI subset of patients.<sup>11–12</sup> Our goal was to compare three manifestations of acute MI: NSTEMI<sub>NTO</sub>, NSTEMI<sub>T0</sub> and STEMI<sub>T0</sub> thus for the first time we have compared three groups instead of two.

Considering the baseline characteristic, patients with NSTEMI<sub>T0</sub> in our study constituted an intermediate group between NSTEMI<sub>NTO</sub> and STEMI<sub>T0</sub>. In comparison to STEMI<sub>T0</sub> they were older and had higher prevalence of cardiovascular risk factors and chronic diseases. When comparing NSTEMI<sub>T0</sub> to NSTEMI<sub>NTO</sub>, they were younger and had lower prevalence of cardiovascular risk factors and chronic diseases. These findings are in accordance with other studies, where patients with NSTEMI, in comparison to STEMI, were older and had more often chronic diseases.<sup>13–14</sup> According to the baseline characteristic our NSTEMI<sub>T0</sub> group was definitely closer to STEMI<sub>T0</sub> than NSTEMI<sub>NTO</sub> group. Patients with STEMI<sub>NTO</sub> were excluded due to large group heterogeneity. To summarize the results of prehospital management, participants with NSTEMI<sub>T0</sub> generally were not considered as candidates for direct transportation to the Cath lab in contrary to STEMI<sub>T0</sub> patients (9.41% vs 25.69%). Additionally, ischemia-time, i.e. time from pain to balloon inflation, as well as time from FMC to balloon inflation were longer in NSTEMI<sub>T0</sub> than in STEMI<sub>T0</sub> group. Duration of ischemia is a major determinant of infarct size and subsequent mortality.<sup>3,15</sup> In almost all studies included in the meta-analysis of Khan et al. patients with NSTEMI<sub>T0</sub> had a mean delay to invasive procedure longer than 24 hours and in comparison to NSTEMI<sub>NTO</sub> increased risk of both major adverse cardiovascular events and mortality.<sup>6</sup> Mean time from pain to inflation in our study was approximately 30 hours (data not presented) and also was similar to presented by Khan et. al.<sup>6</sup>
Time from pain to FMC was the longest in NSTEMI TO group, even longer than in NSTEMI NTO group. In NSTEMI TO group patients postponed decision to seek medical help probably because of younger age (than in NSTEMI NTO group) and lack of previous experience with stenocardial pain. Longer time delay from pain to FMC in NSTEMI TO than in STEMI TO may be explained by lower severity of symptoms due to lower extent of ischemia in case of LCx occlusion (typical for NSTEMI TO in our study) in contrary to LAD or dominant RCA occlusion typical for STEMI TO.

Time delay to achieve the opening of the occluded artery in NSTEMI TO group in comparison to STEMI TO was amplified during in-hospital management what is noticeable as the pronounced difference (almost three times longer median time from FMC to balloon inflation in NSTEMI TO group).

In contrast, patients with NSTEMI TO in comparison to NSTEMI NTO were earlier considered as candidates for invasive management. The potential explanation is more severe clinical presentation caused by total artery occlusion. Higher frequency of cardiac arrest before admission and more advanced Killip class in NSTEMI TO group than in NSTEMI NTO group in our study confirms this hypothesis. Similar results were obtained by Shin et al. in the COREA-AMI Registry. Other commonly used parameter of time delay in MI is the percentage of patients who receive PCI within 120 min. since the onset of symptoms. In our study almost 70% of STEMI TO, but only 25% of NSTEMI TO patients had PCI within 120 minutes. Terkelsen and other investigators confirmed that time delay to PCI worsened prognosis causing increased risk of mortality especially in patients with totally occluded artery.

In our NSTEMI patients approximately 20% had acute coronary artery occlusion which is less than previously reported by Khan (25.5%) and Hung (34%). This difference may be explained by the fact that we defined NSTEMI TO more restrictive, analysing only patients with TIMI 0 flow, whereas Khan and Hung included patients with TIMI 0–1. Previous studies examining the distribution of occluded artery in NSTEMI TO patients indicated RCA or LCx being mostly responsible artery for NSTEMI TO. In our study we found that LCx is the most typical localization of the culprit lesion responsible for MI in the NSTEMI TO group. The distribution of the IRA differs between trials when STEMI cases are compared to NSTEMI, i.e. in STEMI there is underrepresentation of LCx as IRA, whereas in NSTEMI TO occlusion of LAD occurs the least often. We must acknowledge that ECG has unsatisfactory sensitivity to diagnose coronary artery total occlusion, especially in posterolateral distribution. It has been shown that the presence of STE on ECG enables to detect acute coronary TO in 70%-92% of cases for the LAD and RCA, but the ability of 12 lead ECG to diagnose LCx-related MI with coronary occlusion of IRA is below 50%. Explanation is that LCx supplies the region of the heart placed more distally to the chest wall with no corresponding leads in standard ECG.

In our study patients with NSTEMI TO demonstrated more severe clinical condition on admission than those with NSTEMI NTO (more advanced Killip class, higher prevalence of death and cardiac arrest prior...
admission or during invasive procedure, no-reflow phenomenon), which is in concordance with prior studies showing that prognosis of patients with total occlusion without ST segment elevation is worse than in NSTEMI <sub>NTO</sub> patients. We confirmed that the outcome after PCI (lower frequency of achieving TIMI 3 and higher frequency of TIMI 0) in NSTEMI <sub>TO</sub> is even inferior to STEMI <sub>TO</sub>. Possible explanation is that unrecognized acute coronary artery occlusion is associated with high morbidity and mortality and the outcome in this group is worse than in those who received timely revascularization.

Two additional results of our study in NSTEMI <sub>TO</sub> group are noteworthy, i.e.: increased total radiation dose and higher amount of contrast media during PCI compared with both STEMI <sub>TO</sub> and NSTEMI <sub>NTO</sub>. It may be due to predominance of LCx as IRA in NSTEMI <sub>TO</sub>. Fetterly et al. showed that PCI of LCx correlates with increased total radiation dose due to anatomy and need for specific oblique projections consuming higher radiation doses. Furthermore, it has been proven that patients with longer time to reperfusion (NSTEMI <sub>TO</sub> patients in our study) are prone to receive significantly more contrast media during PCI.

**Study limitations**

Our study has several limitations. First, we should deduce very cautiously about detailed in-hospital prognosis because our analysis is based on data from the structured registry of prespecified clinical and periprocedural data spectrum only, without longitudinal follow-up, but with the largest number of evaluated patients. Second, the registry was created and fulfilled by several operators, also quality of data depends on their individual knowledge; however only the most experienced operators collected the data.

**Conclusions**

Approximately one-fifth of NSTEMI patients had acute total coronary artery occlusion (NSTEMI <sub>TO</sub>). According to the clinical characteristics NSTEMI <sub>TO</sub> seems to be an intermediate condition between NSTEMI <sub>NTO</sub> and STEMI <sub>TO</sub>. However, it should be emphasized that NSTEMI <sub>TO</sub> patients have the longest time delay to PCI and the worst final result of PCI, which at least partially can be explained by the most common location of the culprit lesion in LCx. Therefore, patients with NSTEMI should undergo strict evaluation for signs indicating possible acute total coronary artery occlusion (e.g. younger age, lower cardiovascular risk, less chronic diseases but more severe clinical presentation on admission) and should have additional ECG leads (V7-V9) and echocardiographic wall motion abnormalities assessment to avoid time delay to and improve the results of revascularization.

**Abbreviations**

CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; CTO: chronic total occlusion; ECG: electrocardiogram; ESC: European Society of Cardiology; FMC: first medical contact; IRA: infarct-related artery; LAD: left anterior descending artery; LCx: left circumflex artery; MI: myocardial
infarction; NSTEMI\textsubscript{NTO}: non-ST-segment elevation myocardial infarction without occluded infarct-related artery; NSTEMI\textsubscript{T0}: non-ST-segment elevation myocardial infarction with occluded infarct-related artery; ORPKI: Polish National Database of Invasive Coronary Procedures; PCI: percutaneous coronary intervention; RCA: right coronary artery; STE: ST-segment elevation; STEMI\textsubscript{T0}: ST-segment elevation myocardial infarction with occluded infarct-related artery; TIMI: Thrombolysis In Myocardial Infarction; TO: total occlusion of infarct-related artery.

**Declarations**

**Ethics approval and consent to participate**

Our study was an observational retrospective analysis of anonymized electronic data from Polish National Database of Invasive Coronary Procedures which is available for members of Association of Cardiovascular Interventions of the Polish Cardiac Society. Therefore in this study only anonymized data was subjected to the research analysis and according to Regulation 2016/679 of the European Parliament and of the Council (EU) from 27 April 2016 on the protection of individuals with regard to the processing of personal data and on the free movement of such data, and with art. 9 section 2 this study did not require any additional ethics board approval.

**Consent for publication**

Not applicable.

**Availability of data and materials**

The datasets used and/or analysed during the current study are publicly available from the Jagiellonian University Medical College and the Association of Cardiovascular Interventions of the Polish Cardiac Society.

**Competing interests**

The authors declare that they have no conflict of interest.

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**Authors' contributions**

M.T., W.W. and M.R. designed the study. All authors wrote the main manuscript text. M.T., D.D., Z.S., S.B., W.W.2, M.G. and M.R. performed coronary angiographies later included in the ORPKI database. M.T., W.W. and K.P. performed statistical analyses. M.T., W.W., T.D. and J.P. prepared figures. All authors reviewed the manuscript.
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References


Figures
Figure 3

The frequency rate of culprit lesion for: left anterior descending artery (LAD), left circumflex artery (LCx), right coronary artery (RCA) and other arteries within study groups. p < 0.0001 for all analyses of study groups by the Kruskal-Wallis one-way analysis of variance, p < 0.0001 for all post-hoc analyses, p for contingency analysis < 0.0001.