Survival rate after acute myocardial infarction in patients treated with percutaneous coronary intervention within the left main coronary artery according to time of admission

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Abstract

The relationship regarding time of percutaneous coronary intervention (PCI) and clinical outcomes in patients with acute myocardial infarction (AMI) treated within the left main coronary artery (LMCA) is less investigated compared to the overall group of patients with AMI. Therefore, we aimed to assess the relationship between time of PCI (day- vs night-time) and overall mortality rate in patients treated due to AMI within the LMCA.

This cross-sectional study included 443,805 AMI patients hospitalized between 2006 and 2018 enrolled in the Polish Registry of Acute Coronary Syndromes. We extracted 5,404 patients treated within the LMCA. The number of patients were treated during daytime hours (7:00 am–10:59 pm) was 2809 while 473 patients underwent treatment during night-time hours (11:00 pm–6:59 am). Differences in cardiac mortality rates between night- and day-hours among patients treated with PCI during the follow-up period were assessed via the Kaplan–Meier method.

The 30-day (20.3% vs 14.9%, P = .003) and 12-month (31.7% vs 26.2%, P = .001) overall mortality rates were significantly greater among patients treated during night-time, which was confirmed by comparison using Kaplan–Maier survival curves (P = .001). The time of PCI was not found among predictors of survival in multiple regression analysis (hazard ratio: 1.22; 95% confidence interval: 0.96-1.55, P = .099).

Patients treated during night-time in comparison to the day-time are related to higher in-hospital, 30-day and 12-month mortality. This is probably largely a consequence that the night-time, in comparison to the day-time, of treatment of patients with AMI with PCI within the LMCA is and indicator of higher comorbidity and clinical acuity of patients undergoing therapy. Therefore, the night-time was not found to be an independent predictor of greater mortality rate during the 12-months follow-up period.

Abbreviations: ACS = acute coronary syndrome, AMI = acute myocardial infarction, DTB = door-to-balloon time, IABP = intraaortic balloon counterpulsation, LMCA = left-main coronary artery, NSTEMI = non-ST segment elevation myocardial infarction, PAD = peripheral arterial diseases, PCI = percutaneous coronary intervention, STEMI = ST segment elevation myocardial infarction, TIMI = thrombolysis in myocardial infarction.

Keywords: acute myocardial infarction, day- and night-time treatment, left-main coronary disease, long-term mortality, percutaneous coronary intervention

1. Introduction

Previously published studies in which the effect of time of percutaneous coronary intervention (PCI) on long-term clinical outcomes was assessed among an overall group of patients with different location of culprit lesion and diagnosis of acute coronary syndrome (ACS), have been widely investigated.^[1] It has been suggested that night-time may negatively influence long-term clinical outcomes when considering overall mortality, but

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these observations are not univocal and more recent publications neglect poorer outcomes in patients treated during night hours.^[2–4] Patients with acute myocardial infarction (AMI) treated within the left main coronary artery (LMCA) belong to a narrow group undergoing high-risk procedures that require an operator and a highly-skilled team and this group is related to worse clinical outcomes when compared to non-LMCA PCI.^[5] Therefore, we concluded that the time of PCI may have greater impact on long-term clinical outcomes in that selected group of patients treated with PCI within the LMCA when compared to the overall group of patients treated due to AMI independently of culprit lesion location.

The aim of the presented study is to assess the relationship between time of PCI (day- vs night-time) and overall mortality in patients treated due to AMI within the LMCA.

2. Methods

2.1. Study design and patient population

This observational cross-sectional study was performed among 443,805 patients hospitalised due to non-ST segment elevation myocardial infarction (NSTEMI) or ST-segment elevation myocardial infarction (STEMI). Patients from the current Polish Registry of ACS were prospectively enrolled between January 2006 and December 2018. This registry is run in cooperation with the Ministry of Health as well as the National Health Fund and was described in previously published studies.^[6] From the overall group of patients, 5404 consecutive patients treated within the stent placement into the LMCA were selected. After taking the exclusion criteria into consideration (missing data on time of procedure, previous coronary artery bypass grafting operation, cardiogenic shock at admission and/or door-to-balloon time (DTB) longer than 72 hours), the patients were divided according to time of PCI treatment: daytime hours (7:00

am-10:59 pm) - 2809 patients, and night-time hours (11:00 pm - 6.59 am) - 473 patients (Fig. 1). The protocol complied with the 1964 Declaration of Helsinki, and all participants provided their written informed consent for the percutaneous intervention. Due to the retrospective nature as well as anonymization of the collected data and registry, obtaining the consent of the Bioethics Committee was not required.

2.2. Endpoints

The primary study endpoint included 30-day and 12-month mortality rate.

2.3. Statistical analysis

Continuous variables in 2 selected groups of patients were compared using Mann–Whitney *U* test. Categorical variables were compared with the use of the Chi-squared test. Differences in cardiac mortality rates between night- and day-hours among patients treated with PCI during the follow-up period were assessed via the Kaplan–Meier method and were compared using the log-rank test. Univariate and multivariate Cox regression analysis were conducted to analyze the predictors of 12-month mortality. This was a retrospective study based on the national registry and no sample size was calculated. Analyses were performed using the Statistica version 13.3 (TIBCO Software, CA). All statistical tests were 2-sided (the level of P < .05 was considered statistically significant).

3. Results

3.1. Study population

The authors did not observe any significant differences in the percentage of males and the mean age of patients treated during

Table 1

Clinical characteristics in patients with acute myocardial infarction and treated with percutaneous coronary intervention within main-left coronary artery according to time of procedure (day vs night).

Selected indices	D	Night	P-value	
Gender, males	67.64	67.02	.79	
Age, yr	70.79 (61.52-79.73)	69.73 (60.8–78.82)	.13	
Type of myocardial infarction				
STEMI	67.21	49.89	< .001	
NSTEMI	32.79	50.11		
Systolic blood pressure, mm Hg	130.0 (120.0–150.0)	130.0 (115.0–150.0)	.24	
Diastolic blood pressure, mm Hg	80.0 (70.0–90.0)	80.0 (70.0–90.0)	.75	
Killip-Kimball class grade				
	71.80	67.65	.014	
I	21.00	21.35		
III	7.19	10.99		
Door-to-balloon time, min				
- Overall group	112.0 (47.0-501.0)	53.0 (35.0–108.0)	< .001	
- STEMI	52 (31–100)	45 (30–73)	.004	
- NSTEMI	201 (70-915)	71.5 (40–177)	< .001	
Prior percutaneous coronary intervention	17.90	13.14	.011	
Prior myocardial infarction	23.43	19.07	.037	
Prior cerebral stroke	4.93	5.83	.44	
Peripheral arterial disease	9.33	8.76	.71	
Diabetes	29.09	29.81	.75	
Prior or present smoking	57.78	57.21	.82	

Data are presented as percentages or median (min, max), for age (lower-upper interquartile range).

NSTEMI = non-ST segment elevation myocardial infarction, STEMI = ST-segment elevation myocardial infarction.

day- and night-time hours (Table 1). The percentage of patients with STEMI was significantly higher during day hours when compared to night (67.21% vs 49.89%, P < .0001), while the rate of patients with NSTEMI at admission was higher during night time (32.79% vs 50.11%, P < .001). Those and other clinical features are presented in Table 1.

3.2. Procedural indices

There was a significant difference in the rate of patients with patent coronary arteries at admission expressed by the thrombolysis in myocardial infarction (TIMI) flow grade scale (P=.003). Those and other procedural indices are presented in the Table 2.

3.3. In-Hospital and long-term clinical outcomes

Considering in-hospital observations, patients treated with PCI of LMCA during night-time presented cardiogenic shock significantly more often (4.89% vs 10.19%, P<.001) and the frequency of in-hospital cardiac arrests was also significantly greater among patients treated during night-hours (7.31% vs

Table 2

Procedural indices and left ventricle ejection fraction in patients with acute myocardial infarction and treated with percutaneous coronary intervention within main-left coronary artery according to time of procedure (day vs night).

Selected indices	D	Night	P-value	
Left ventricle ejection fraction	45.0 (35.0–50.0)	45.0 (35.0–52.0)	.69	
Infarct related artery within LMCA	77.25	77.17	.97	
PCI other than LMCA	34.78	33.83	.69	
Intra-aortic balloon counterpulsation	4.45	5.50	.31	
In-hospital mode CABG	1.67	1.48	.76	
PCI within LMCA volume per 1 CathLab/yr	3.92 (2.67-5.36)	3.92 (2.5-6.2)	.85	
TIMI grade flow before PCI				
0	20.76	27.70	.003	
1	20.23	20.30		
2	23.01	22.62		
3	36.00	29.39		
TIMI grade flow after PCI				
0	2.76	3.46	.35	
1	1.23	2.16		
2	4.28	4.32		
3	91.73	90.06		

Data are presented as percentages or median (min, max).

CABG=coronary artery bypass grafting, CathLab=catheterization laboratory, LMCA=left main coronary artery, PCI=percutaneous coronary intervention, TIMI=thrombolysis in myocardial infarction.

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Table 3

In-hospital and long-term clinical outcomes in patients with acute myocardial infarction and treated with percutaneous coronary intervention within main-left coronary artery according to time of procedure (day vs night).

Follow-up events	D	Night	P-value	
In-hospital outcomes				
Cardiogenic shock	4.89	10.19	< .001	
In-hospital cardiac arrest	7.31	10.59	.014	
Major bleedings	1.82	1.27	.4	
In-hospital re-infarction	1.11	0.00	.022	
Target vessel revascularization	1.18	1.27	.86	
In-hospital mortality	10.57	14.38	.015	
Long-term outcomes				
30-d mortality	14.88	20.30	.003	
12-mo mortality	26.20	31.70	.001*	

Data are presented as percentages.

^{*} log-rank.

10.59%, P=.014). In-hospital mortality rate was significantly greater among patients treated during night-hours (10.57% vs 14.38%, P=.015). The 30-day mortality rate was significantly higher in patients treated during night-when compared to day-hours (14.88% vs 20.30%, P=.003). The 12-month mortality was also significantly greater in patients treated during night-time (26.20% vs 31.70%, P=.001) (Table 3, Fig. 2).

3.4. Predictors of long-term clinical outcomes

Using univariate Cox regression analysis, it was revealed that PCI LMCA during night-hours (P=.003), intra-aortic balloon counterpulsation (IABP) use (P<.001), prior MI (P<.001), PCI (P=.047) and cerebral stroke (P<.001) as well as peripheral arterial diseases (PAD) (P<.001), older age (P<.001), diabetes

Table 4

Relationship	of	selected	indices	with	12-month	mortality	-
univariate Co	x re	gression a	analysis.				

Selected predictor	HR	95% CI	P-value
PCI LMCA night vs d	1.31	1.1-1.57	.003
Intra-aortic balloon counterpulsation	2.86	2.27-3.59	< .001
Left ventricle ejection fraction, %	0.94	0.93-0.95	< .001
Systolic blood pressure, mm Hg	0.99	0.98-0.99	< .001
Diastolic blood pressure, mm Hg	0.98	0.98-0.99	< .001
Gender, males	1.01	0.88–1.17	.88
Prior myocardial infarction	1.38	1.18–1.6	< .001
Prior percutaneous coronary intervention	1.19	1.00-1.41	.047
Prior cerebral stroke	1.64	1.25–2.148	< .001
Peripheral arterial disease	1.68	1.36-2.07	< .001
Age, yr	1.04	1.03-1.05	< .001
Prior or present smoking	0.89	0.78-1.03	.11
Diabetes	1.22	1.05-1.4	.007
Killip–Kimball class grade III vs I and II	2.78	2.31–3.35	< .001
PCI of artery other than LMCA	1.14	0.99-1.34	.06
Door-to-balloon time, min.	1.0	1.0-1.0	.86
Type of myocardial infarction STEMI vs NSTEMI	1.04	0.9-1.2	.6
TIMI grade flow before PCI 0-1 vs 2-3	1.23	1.07-1.41	.002
PCI within LMCA volume per 1 CathLab/yr	1.0	0.97-1.03	.98

CathLab = catheterization laboratory, LMCA = left-main coronary artery, NSTEMI = non-ST segment elevation myocardial infarction, PCI = percutaneous coronary intervention, STEMI = ST-segment elevation myocardial infarction, TIMI = thrombolysis in myocardial infarction.

(P=.007), higher grade of Killip–Kimball class (P<.001) and patency of culprit artery before PCI assessed with the TIMI scale (grade 0–1) (P=.002) were among predictors of increased mortality rate at 12 months. Among the factors significantly related to lower mortality rate at 12 months, the authors found: greater left ventricle ejection fraction (P<.001), higher systolic (P<.001) and higher diastolic blood pressure (P<.001) (Table 4).





Figure 3. Predictors of 12-month overall mortality in patients with acute myocardial infarction and treated with percutaneous coronary intervention within the left main coronary artery.

With multiple Cox regression analysis, it was confirmed lower left ventricle ejection fraction (P < .001), lower systolic blood pressure (P < .001), older age (P < .001), IABP use (P < .001), and PAD (P < .001) were among the significant predictors of grater mortality rate at 12 months. However, significance between night- and day-time of LMCA PCI and mortality rate at 12-months was not noted (Fig. 3).

4. Discussion

The time of PCI in patients with AMI and among those treated with PCI within the LMCA is related to the overall 30-day and 12-month survival rate, which is significantly higher in patients treated during night-time. Using multiple Cox regression analysis, it was confirmed that lower left ventricle ejection fraction and lower systolic blood pressure at admission, older age, IABP use and diagnosed PAD are among significant predictors of greater mortality rate at 12-months, but no statistical significance for the time of PCI (night- vs day-time) was noted.

The main aim of the study was to evaluate the results of PCI within LMCA treatment depending on the time of the procedure (day-time vs night-time). The results of the study may be of considerable importance in the planning of PCI within LMCA

procedures. In the case of worse treatment results during the night-time compared to the day-time, PCI in selected patients in whom PCI can be postponed may then be scheduled for working hours in the morning. Of course, the clinical condition of the patient is of great importance, and the fact that PCI within LMCA is performed during the night-time in patients who often cannot wait, which undoubtedly translates into long-term treatment results. In several studies, it has been demonstrated that 3-vessel disease or LMCA should be preferably treated with cardiac surgical revascularisation in comparison to PCI in patients with stable angina regarding lower rates of the combined end-point of main adverse cardiac and cerebrovascular events at 1 year.^[7] However, there are some factors such as age, which can substantially blur differences in clinical outcomes dependent on the dissemination of coronary artery disease, which was presented in a non-randomized study.^[8] Despite this, unprotected LMCA disease in patients with ACSs is related to high mortality rate due to frequent hemodynamic or arrhythmic instability.^[9] In this high-risk group of patients, percutaneous therapy is preferred over surgical procedures. Surgical treatment (coronary artery bypass grafting) is usually performed at a later time following diagnosis, and mostly, in the group of low-risk patients.^[9]

The studies published at the beginning of this millennium have already shown that in the overall group of patients with AMI, admission on weekends is associated with higher mortality and lower implementation of invasive cardiac procedures.^[10] Patel et al demonstrated that mortality rate in patients treated with emergency PCI and culprit lesion primary located in the LMCA depend on the extent of its occlusion.^[11] It was observed that patients treated within unprotected LMCA occlusion are burdened with greater mortality rate when compared to patients with patent LMCA considering in-hospital (43.3% vs 20.6%, P < .001), 1- (52.8% vs 32.4%, P < .001) and 3-year mortality rates (73.9% vs 52.3%, P < .001).^[10] The greater mortality at following years in the group of patients with totally occluded LMCA before PCI was mainly attributed to the presence of cardiogenic shock, no-reflow, acute left ventricle dysfunction, LMCA occlusion, and renal failure.^[11] It could also be concluded that the difference in survival rate between these 2 groups decreased in following years of the observational period and may be attributed to poor survival among extremely high-risk patients treated during night-hours, which was also clearly visible in the presented analysis.

In 1 published study regarding a group of patients with STEMI treated with PCI, it was demonstrated that there was no relationship between in-hospital and long-term mortality (48 months) concerning on- and off-hour admissions.^[12] However, using stratified analysis, it was shown that off-hour admissions were significantly associated with increased mortality in the highrisk sub group of patients when compared to the low- and moderate-risk subgroup of patients.^[12] Also, in the study published by Jneid et al, no significant differences concerning in-hospital mortality rates were observed among the overall group of patients treated with PCI due to AMI according to offand regular-hours.^[13] In an older study, it was demonstrated that patients with STEMI and treated with PCI are related to significantly longer times to treatment during off-hours when compared to regular hours.^[14] This was also confirmed in the large meta-analysis performed by Sorita et al on a large number of patients (1,892,424 patients with AMI). It was suggested that patients presenting AMI during off-hours are at risk of greater mortality, and that patients with STEMI present longer DTB times.^[15] No differences in clinical outcomes among patients with STEMI and treated with PCI during off- and regular-hours were found in regions with well-organized and efficient STEMI networks focused on reperfusion.^[16] In another publication by Dasari et al. analysing a group of over 40,000 patients treated with PCI due to STEMI, in-hospital mortality was equal for offhour arrival and on-hour arrival, and was estimated to be at 4.2% for both groups.^[17] However, the authors found that riskadjusted all-cause mortality was higher for patients admitted during off-hours (OR: 1.13; 95% CI: 1.02-1.26).^[17] This was confirmed in the current study, where more high-risk patients were admitted to hospital during night-hours and their prognosis was thus worse. In some studies, a direct relation was demonstrated between clinical outcomes and the time of PCI in the overall group of patients treated due to STEMI. In the study published by Glaser et al examining 685 consecutive patients treated due to STEMI with PCI, the in-hospital death rate was greater when the patient was admitted during off- compared to on-hours (7.0% vs 4.4%).^[2] Also, the accumulation MACE rate was higher among patients treated during off- in comparison to on-hours (16.2% vs 6.8%). As a partial explanation of those differences, it was calculated that patients admitted during offhours were more likely to experience with cardiogenic shock and multivessel coronary artery diseases, and were equally likely to

demonstrate complete occlusion of the infarct-related artery.^[2] The outcomes remained poorer among patients treated during off-hours, even when the procedure was immediately successful.^[2]

The in-hospital mortality rate in patients with STEMI due to unprotected LMCA stenosis remains high and was previously estimated to be at 47.8%. Using multiple regression analysis, age, diabetes, and TIMI grade flow other than 3 after PCI were found to be among significant predictors.^[18] In another, more recently published study, patients with STEMI and treated with PCI within LMCA were at risk of higher in-hospital mortality rate when compared to the overall group of patients treated with PCI of other coronary arteries than LMCA. This was mainly sanctioned due to the fact that patients treated within the LMCA had higher rates of cardiogenic shock and cardiac arrest.^[19] Furthermore, the mortality rate was highest in the group of patients with concurrent LMCA and non-LMCA PCI, and was higher when compared to the isolated LMCA PCI and non-LMCA PCI.^[19] In a recently published study by Chieffo et al, it was demonstrated that overall in-hospital mortality rate for all patients undergoing PCI within LMCA was 1.4%, while after the mean 17-month follow-up period, the mortality rate was 8.3%.^[20] In yet another study, high in-hospital mortality rate was confirmed in patients with AMI and PCI within unprotected LMCA (40%). The l mortality during the mean 44.6 months of follow-up period was 52.7%.^[21] Among the predictors of inhospital mortality, the authors found cardiogenic shock, lack of TIMI 3 grade flow after PCI and collateral circulation of grade 2 or 3. While among the predictors of the overall mortality, only cardiogenic shock remained.^[21] In a different study, the complexity and extent of dissemination of coronary artery stenosis were additionally confirmed as predictors of 1- and 3year mortality in patients with STEMI and treated due to unprotected LMCA disease.^[22] The in-hospital mortality rate was 30.8%, 1-year mortality was 44.4% and 3-year mortality was 54.3%.^[22] That was higher when compared to the currently presented group of patients, where the overall in-hospital mortality rate was 10.57% for day and 14.38% for night-hours, and at 30 days: 14.88% vs 20.3%, and 12 months: 26.2% and 31.7%, respectively. The mortality rates were lower, besides the fact that the percentage of patients without patent coronary arteries was higher in the current study when compared to that mentioned above. The study did not include the percentage of patients in particular Killip-Kimball class grades.^[22]

Another small study performed on patients with STEMI and unprotected LMCA disease with the mean follow-up of 15.8 months revealed 30-day mortality at 39.7% and mid-term mortality at 44%, which was also significantly higher when compared to the presently analysed group. Among the predictors of 30-day mortality authors, cardiogenic shock at presentation, age above 75 years and post-PCI TIMI flow<3 were confirmed by the authors.^[23] While among the independent predictors of midterm mortality, cardiogenic shock at presentation, age>75 years, and post-PCI grade flow<3 were found.^[23]

In the current study, compared to other studies assessing the relationship between clinical outcomes in patients with AMI treated with PCI and the time of admission to hospital, we selected a very narrow and specific group of patients treated within the LMCA. These patients are preferably treated, when possible, during day-hours, which is proceeded, if possible or reasonable, by cardiac surgical consultation. Additionally, in other studies concentrating on this issue, off-hours were most frequently defined as weekends and weekdays during night-shifts, which were usually after 5:00 pm or, in some publications, patients treated during night-hours independently of the day of the week. We extracted a very narrow group of patients treated very late (after 11:00 pm) and early in the morning (before 7:00 am) which is not common in this type of analysis and is difficult to compare with other studies. Moreover, PCI within LMCA is performed when the situation is at a dead-end and when patients absolutely require PCI. This creates an extremely high-risk group of patients whose prognosis is poor by design. The experience of operators performing procedures during night-shifts and their physical condition is another factor. The difference in the clinical condition of patients at baseline, expressed for example, in Killip-Kimball grade certainly affects bias, but it is also compensated by other factors, for example, shorter DTB time at night-time. We deliberately did not perform propensity score matching analysis because it would be an artificial division in our opinion. However, when looking at DTB time in NSTEMI patients included in the presently analysed study, the data seem not to reflect the real-world practice, being very short time in NSTEMI patients. However, this only applies to the night hours, where a large proportion are clinically severe and in the higher grades of the Killip class. For NSTEMI patients treated with PCI during the day-time, the mean DTB time is much longer compared to STEMI patients. Considering the time of cardiac arrest and cardiac shock, unfortunately, we do not have their exact times. Most of the cardiogenic shocks occurred on the same day as PCI (median 0; min 1; max 10 days after PCI), similar to cardiac arrests (median 0; min 2; max 19 days after PCI). It should be noted that as soon as possible revascularization can prevent both complications, and the prognosis in the event of cardiogenic shock or cardiac arrest before PCI within LMCA is undoubtedly associated with worse prognosis.

Data on percutaneous left ventricle assist devices has been collected in PL-ACS since mid-2016. At that time, there was not a single patient with PCI LMCA who had percutaneous left ventricle assist device who had MI. Similarly, extra corporeal membrane oxygenation data were collected over the same period and applied to 1 patient. This could affect the results and bring some bias. The approach to treating patients with IM within LMCA depends largely on the location of the centre and the preferences of the operator on duty, both the cardiac surgeon and the interventional cardiologist. Rather, in most cases, patients are treated percutaneously, but this is also influenced by the location of the centre, and patients in centres with a cardiac surgery department or nearby seems to be more willingly treated by surgeons, but this is usually a small percentage. However, we do not have accurate data on this matter in the analysed register. No correction for this data may also affect the bias.

Another limitation of the current study is the PCI concomitant other than LMCA, although the frequency of such PCIs was similar in both groups and did not differ statistically significantly, the type of such PCI could have an impact on bias. According to the current recommendations of American and European cardiological societies, full revascularization at baseline is not recommended, especially in patients with cardiogenic shock. However, in selected patients PCI within the left coronary artery may reduce the patient's exposure to complications during the next stage of percutaneous intervention. Another factor in favor of performing a concomitant PCI during PCI of LMCA at baseline may be, for example, the difficulty or impossibility of the stent delivery to further segments of the branch of the left coronary artery in subsequent stages. The ethnic differentiation has not been carried out because we do not have such data and due to the fact that almost 100% of patients included into the analysis are Caucasian.

In conclusion, patients treated during night-time in comparison to the day-time are related to higher in-hospital, 30-day and 12month mortality. This is probably largely a consequence that the night-time, in comparison to the day-time, of treatment of patients with AMI with PCI within the LMCA is and indicator of higher comorbidity and clinical acuity of patients undergoing therapy. Therefore, the night-time was not found to be an independent predictor of greater mortality rate during the 12months follow-up period. Based on the analysis performed, it seems that there is a tendency towards poorer clinical outcomes among patients treated during night-time, for this reason it seems advisable to perform PCI within LMCA in day-hours in patients with NSTEMI if possible and reasonable.

Author contributions

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