

Worse long-term prognosis in myocardial infarction occurring at weekends or public holidays with insight into myocardial infarction with nonobstructive coronary arteries

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KEY WORDS

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EDITORIALS

by Lesiak, see p. 930;
Mamas and Bharadwaj,
see p. 932

ABSTRACT

INTRODUCTION The weekend effect in Polish patients with myocardial infarction (MI) treated in the current network of catheterization laboratories is poorly understood.

OBJECTIVES We sought to investigate long-term prognosis of patients with MI admitted at weekends or public holidays (NWDs) and on working days (WDs).

PATIENTS AND METHODS We enrolled 865 patients with MI hospitalized between 2012 and 2017. The long-term mortality within the median (IQR) time of 68.5 (36.7–78.4) months was determined in 223 patients (25.8%) admitted on NWDs and in 642 (74.2%) on WDs.

RESULTS Patients admitted on NWDs more often had ST-segment elevation MI (41.3% vs 30.8%; $P = 0.005$), left anterior descending artery as an infarct-related artery (38.1% vs 30.2%; $P = 0.031$) and incomplete reperfusion expressed as Thrombolysis in Myocardial Infarction flow grade 0/1 following primary angioplasty (6.8% vs 1.6%; $P < 0.001$) as compared with those hospitalized on WDs. Myocardial infarction with nonobstructive coronary arteries (MINOCA) occurred less often on NWDs (4% vs 9%, $P = 0.019$). The all-cause long-term mortality was higher in NWD patients as compared with those admitted on WDs (36.3% vs 28.4%; $P = 0.037$). By the Cox proportional hazards model with time-dependent covariates, MI on NWDs (hazard ratio, 1.027; 95% CI, 1.022–1.032; $P < 0.001$) but not MINOCA (hazard ratio, 0.971; 95% CI, 0.595–1.583; $P = 0.91$) was independently associated with long-term mortality.

CONCLUSIONS Patients hospitalized on NWDs as compared with those admitted on WDs had a larger ischemic territory and more often had transmural MI with incomplete epicardial reperfusion, which resulted in a higher long-term mortality. The latter outcome was not influenced by MINOCA.

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INTRODUCTION The weekend effect and its impact on the outcomes of myocardial infarction (MI) treatment has been intensively studied over the recent years. The first comprehensive report regarding the weekend effect was presented in 2001 by Bell and Redelmeier.¹ Based on their analyses of 3 789 917 broadly defined acute care admissions, they stated a significantly higher in-hospital mortality in various disease entities.¹ Previous findings have been summarized in 2 meta-analyses. Sorita et al² ascertained a higher in-hospital (odds ratio [OR], 1.05; 95% CI, 1.03–1.08) and 30-day mortality (OR, 1.05;

95% CI, 1.02–1.09) in patients admitted off-hours. According to their observations, these differences might have eventuated out of the substantially longer door-to-balloon time in ST-segment elevation MI (STEMI). Kwok et al³ have recently confirmed that with observations regarding a slightly higher early mortality in weekend admissions (OR, 1.06; 95% CI, 1.03–1.09). The hypothesis regarding the impact of the timing of admission on clinical outcomes has not been confirmed based on more recent studies.³

There is scarce evidence regarding the weekend effect in Polish patients. Słonka et al⁴

WHAT'S NEW?

The weekend effect means worse prognosis in patients admitted to hospitals during weekends. Its impact on myocardial infarction has been intensively studied over the recent years. Several hypotheses concerning this phenomenon have been proposed so far, but its etiology has not been fully elucidated. In the current study with over 5-year follow-up, it was shown that patients with myocardial infarction admitted at weekends or public holidays had higher long-term mortality than those hospitalized during working days and this effect was visible after the first year of observation. Patients admitted during nonworking days compared with those admitted during working days had more often ST-segment elevation myocardial infarction accompanied by more frequent myocardial infarctions with larger ischemic territory and incomplete epicardial blood flow not driven by operator experience. Simultaneously, myocardial infarction with nonobstructive coronary arteries was less often diagnosed on nonworking days, but this finding did not influence long-term mortality.

demonstrated similar rates of in-hospital complications as well as 2-year mortality in patients treated with percutaneous coronary intervention (PCI) in the daytime and during off-shift hours in the years 1998 to 2003. Noteworthy, the significantly higher rate of stent implantations was observed in the daytime group.⁴ A similar analysis of patients with STEMI collected in the EUROTRANSFER registry showed that thrombolytic therapy was more frequently administered to patients hospitalized off-hours (4.1% vs 2.3%; $P = 0.041$). Surprisingly, the time from chest pain onset to diagnosis of STEMI was shorter in the off-hours group by 10 minutes ($P = 0.007$); nevertheless, 1-year mortality rates were similar in both groups.⁵ Despite the above-mentioned observations, there are no available data solely describing the relationship between the current organization of cardiac catheterization laboratories in Poland working for 24 hours, 7 days a week and the long-term prognosis in patients with MI admitted on nonworking days. This problem has been partly raised by Walicka et al.⁶ In their recently published study, the authors determined the predictors of in-hospital mortality based on the large number of 2 855 029 nonsurgical hospitalizations.⁶ As was shown, vascular diseases were characterized by the highest mortality, whereas weekend admissions (Saturday: OR, 1.40; 95% CI, 1.36–1.43; Sunday: OR, 1.29; 95% CI, 1.26–1.32) and public holidays (OR, 1.25; 95% CI; 1.20–1.30) were independent predictors of in-hospital mortality.

In this study we sought to investigate whether the occurrence of MI at weekends or public holidays influences the long-term prognosis in Polish patients treated in a high-volume university center and to determine the potential causes of these relationships.

PATIENTS AND METHODS We enrolled 865 consecutive patients hospitalized between 2012 and 2017 in our hospital with a MI diagnosis and in

whom coronary angiography was performed. A total of 223 (25.8%) were admitted on a nonworking day (NWD) including weekends (Saturdays or Sundays) (200 [23.1%]) or public holidays (23 [2.7%]). In turn, 642 (74.2%) patients were admitted on a working day (WD) (FIGURE 1). Patient age, anthropometric data, medical history, clinical presentation, baseline laboratory measurements, and data regarding the course of hospitalization were collected.⁷ Patients were classified as STEMI or NSTEMI in accordance with current guidelines.^{8,9} Renal failure was diagnosed when the creatinine clearance calculated by means of the Cockcroft–Gault formula was lower than 60 ml/min.¹⁰ Between 2 and 4 days after admission, left ventricular ejection fraction (LVEF) was assessed by 2-dimensional transthoracic echocardiography at rest.¹¹

A detailed evaluation of both the infarct-related artery (IRA) as well as the result of the primary PCI procedure were performed based on angiography done for each artery in 2 contralateral projections.¹² Two experienced and blinded physicians reviewed each coronary angiogram. In case of disagreement between the 2 physicians, a third opinion was sought, and a conclusion was drawn.^{13,14} Myocardial infarction with nonobstructive coronary arteries (MINOCA) has been defined by the universal criteria of MI and no lesion of 50% or greater on coronary angiography.¹⁵ Moreover, patients with MINOCA were analyzed for the presence of insignificant stenosis in epicardial arteries and were divided into 2 groups with 1) normal coronary arteries or minimal intracoronary irregularities with stenosis of less than 30% or with 2) mild to moderate lesions of at least 30% and less than 50%.¹⁶ Epicardial blood flow was evaluated by means of the Thrombolysis In Myocardial Infarction (TIMI) scale in all patients.¹⁷ TIMI epicardial blood flow grade 2 or 3 without flow limiting dissection not covered by the stent was recognized as the optimal PCI result, whereas TIMI flow grade 0 or 1 was the equivalent of incomplete epicardial reperfusion.^{17–19} According to the commonly accepted American College of Cardiology Foundation / American Heart Association / American College of Physicians clinical competence statement, operators performing less than 50 PCIs per year, 50 to 100 PCIs per year, or more than 100 PCIs per year were defined as low, intermediate-, or high-volume, respectively.^{20,21}

Long-term follow-up of all-cause mortality was obtained from the Polish National Death Registry. The study protocol was complied with the Declaration of Helsinki and was approved by the local ethics committee. All patients included in the study gave their informed consent.

Statistical analysis Statistical analyses were performed with the SPSS Statistics software (version 25.0.0.2, IBM, Armonk, New York, United States). Continuous variables were first checked for normal distribution and expressed as median (interquartile range) or mean (SD), whereas

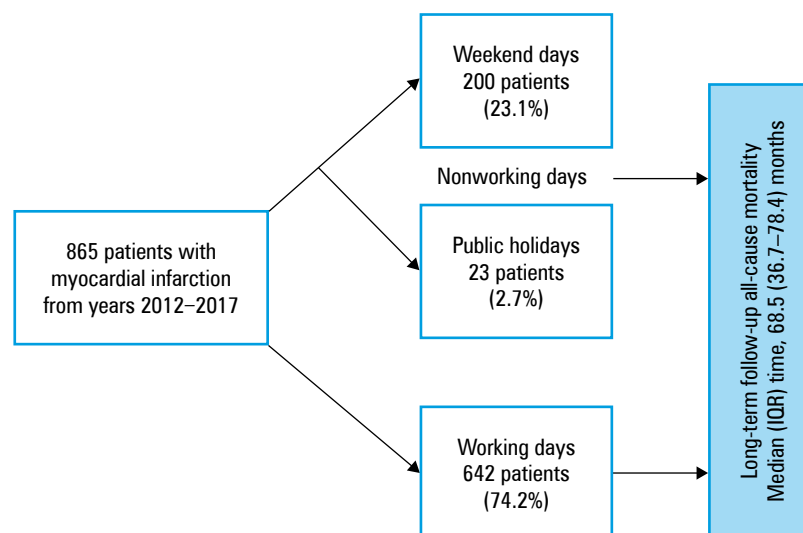


FIGURE 1 The study flow-chart
Abbreviations: IQR, interquartile range

categorical variables as number (percentage). Continuous variables were compared by the *t* test or the Mann–Whitney test if the distribution was normal or different than normal, respectively. Categorical variables were analyzed by means of the χ^2 test or the Fisher exact test. Kaplan–Meier curves of all-cause mortality in the study groups were performed and compared with the log-rank test. Finally, the proportional hazard assumption was verified with the model interaction of the covariate of interest with time. If such a variable turned out to be significant, the proportional hazard assumption would be violated.²² Afterwards, the Cox proportional hazards model with time-dependent covariates was performed to find the independent determinants of all-cause mortality. A 2-tailed *P* value of less than 0.05 was considered statistically significant.

RESULTS Clinical characteristics The baseline characteristics of the enrolled patients are shown in [TABLE 1](#). Patients in NWD and WD groups were similar in terms of demographic data, cardiovascular risk factors, history of MI, stroke, prior percutaneous and / or surgical coronary revascularization, and the distribution of Killip class on admission. The significant differences were observed in the clinical presentation of MI. STEMI was more frequent on NWDs (41.3% vs 30.8%; *P* = 0.005) accompanied by higher values of baseline creatine kinase (median [IQR], 202 [112–527] IU/l vs 169 [105–335] IU/l; *P* = 0.02) and isoenzyme MB of creatine kinase (median [IQR], 24 [16–61] vs 21 [14–39] IU/l, *P* = 0.003) as compared with those admitted on WDs. There were no differences in the remaining laboratory parameters on admission ([TABLE 1](#)).

Angiographic features The angiographic analysis showed significant differences in the distribution of the IRA in compared groups (*P* = 0.003) ([TABLE 2](#)). The left anterior descending artery (LAD) or the diagonal branch (38.1% vs 30.2%) as well as

the right coronary artery (38.6% vs 32.6%) were more often identified as IRA in patients admitted during NWDs as compared with WDs. In contrast, patients with IRA of the left circumflex artery or marginal branch were treated more frequently on WDs as compared with NWDs (22.4% vs 15.7%). Interestingly, IRA remained more often undetermined in those admitted on WDs (10.6% vs 4.5%; *P* = 0.006). There were no differences in terms of applied revascularization in both groups. In patients treated with primary PCI, incomplete epicardial reperfusion expressed as TIMI blood flow grade 0/1 was found more frequently in the NWD group as compared with the WD group (6.8% vs 1.6%; *P* < 0.001) ([TABLE 2](#)). Among patients treated with PCI, there were no significant differences in operators volume (*P* = 0.15). The majority of patients were revascularized by high-volume operators: on NWDs, it was 66.3% of PCIs and on WDs, 71.9%.

In-hospital and long-term mortality and its determinants There were no differences between patients admitted on NWDs as compared with WDs in terms of length of hospitalization (median [IQR], 5 [4–8] days vs 6 [3–8] days; *P* = 0.66) and in-hospital mortality (2.7% vs 3%; *P* = 0.84).

The median (IQR) time of follow-up was similar in patients hospitalized on NWDs and WDs (68.7 [37.4–79.2] months vs 68.4 [36.4–78.2] months; *P* = 0.40). At 1 year, mortality rate was 13.5% in those admitted on NWDs and 11.5% on WDs (log-rank *P* = 0.46, [FIGURE 2A](#)), whereas after the first year of follow-up mortality rate was 26.8% versus 19%, respectively (log-rank *P* = 0.027, [FIGURE 2A](#)). Finally, all-cause long-term mortality was higher in patients who were treated on NWDs as compared with WDs (36.3% vs 28.4%, log-rank *P* = 0.037) ([FIGURE 2A](#)). There were no differences in the subgroup analysis regarding the type of MI ([FIGURE 2B](#) and [2C](#)), with only nonsignificant trend towards a higher long-term mortality in patients with STEMI hospitalized on NWDs

TABLE 1 Characteristics of the study patients

Characteristic		Nonworking days (n = 223)	Working days (n = 642)	P value
Demographic data				
Male gender		161 (72.2)	437 (68.1)	0.25
Age, y		68 (58–78)	69 (61–78)	0.35
Body mass index, kg/m ²		27.5 (25–31.6)	27.7 (24.8–30.8)	0.57
Cardiovascular risk factors and history				
Diabetes mellitus		85 (38.3)	240 (37.5)	0.83
Hypertension		190 (85.6)	567 (88.6)	0.24
Dyslipidemia		182 (82)	543 (84.8)	0.31
Renal failure		33 (14.8)	106 (16.5)	0.54
Active smoking		55 (24.8)	149 (23.3)	0.66
Chronic heart failure		78 (35.1)	209 (32.7)	0.51
Prior stroke		15 (6.8)	42 (6.6)	0.92
Prior myocardial infarction		68 (30.6)	179 (28)	0.45
Prior revascularization	Percutaneous coronary intervention	39 (17.6)	119 (18.6)	0.93
	Coronary artery bypass surgery	8 (3.6)	26 (4.1)	
	Both percutaneous coronary intervention and coronary artery bypass surgery	6 (2.7)	21 (3.3)	
Killip class on admission	I	173 (77.9)	514 (80.1)	0.71
	II	32 (14.4)	74 (11.5)	
	III	6 (2.7)	24 (3.7)	
	IV	11 (5)	29 (4.5)	
Left ventricular ejection fraction, %		50 (40–55)	50 (40–55)	0.33
Clinical presentation	NSTEMI	131 (58.7)	444 (69.2)	0.005
	STEMI	92 (41.3)	198 (30.8)	
Laboratory tests on admission				
Troponin, ng/ml		0.109 (0.035–0.487)	0.110 (0.029–0.379)	0.14
Creatine kinase, IU/l		202 (112–527)	169 (105–335)	0.02
Isoenzyme MB of creatine kinase, IU/l		24 (16–61)	21 (14–39)	0.003
Sodium, mEq/l		140 (138–142)	140 (138–142)	0.91
Potassium, mEq/l		4.1 (3.8–4.4)	4.1 (3.9–4.5)	0.09
Hemoglobin, g/dl		14.2 (13.1–15.1)	14 (12.7–15)	0.16
Hematocrit, %		41.9 (39–44.7)	41.6 (38.2–44.4)	0.25
MCV, fl		89.7 (86.6–93.3)	89.4 (86.4–92.5)	0.19
White blood cells, × 10 ³ /μl		9.3 (7.4–11.6)	9.2 (7.4–11.8)	0.90
Platelet count, × 10 ³ /μl		222 (190–261)	220 (182–278)	0.98
Glucose, mmol/l		7.1 (5.9–9.4)	6.8 (5.7–8.9)	0.08
Creatinine, μmol/l		88 (76–104)	89 (77–105)	0.72
Glomerular filtration rate, ml/min		71 (58.8–86.5)	70.3 (56–86)	0.49
Total cholesterol, mmol/l		4.6 (3.7–5.4)	4.4 (3.6–5.2)	0.13
LDL cholesterol, mmol/l		2.7 (1.7–3.5)	2.5 (1.6–3.4)	0.09
HDL cholesterol, mmol/l		1.2 (1–1.7)	1.3 (1–1.7)	0.73
Triglycerides, mmol/l		1.2 (0.9–1.7)	1.3 (0.9–1.7)	0.91

Data are presented as median (interquartile range) or number (percentage).

Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein; MCV, mean corpuscular volume; NSTEMI, non-ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction

as compared with those admitted on WDs (log-rank $P = 0.067$).

In the study population, age, gender, admission day, creatinine level, type of MI, IRA, TIMI epicardial flow after PCI, and LVEF were identified as potentially associated with long-term mortality. Moreover, covariates of NWDs as

compared with WDs and LAD as compared with non-LAD have been verified as time-dependent variables. By the Cox proportional hazards model with time-dependent covariates, apart from age, higher creatinine level, lower LVEF, also MI admissions at NWD (hazard ratio [HR], 1.027; 95% CI, 1.022–1.032; $P < 0.001$) remained independently

TABLE 2 Angiography and revascularization in the study groups

Characteristic		Nonworking days (n = 223)	Working days (n = 642)	P value
Infarct-related artery	Left main	7 (3.1)	27 (4.2)	0.003
	Left anterior descending/diagonal branch	85 (38.1)	194 (30.2)	
	Left circumflex/marginal branch	35 (15.7)	144 (22.4)	
	Right coronary artery	86 (38.6)	209 (32.6)	
	Undetermined	10 (4.5)	68 (10.6)	
Diagnosis of MINOCA		9 (4)	58 (9)	0.02
Treatment	Percutaneous coronary intervention	190 (85.2)	513 (79.9)	0.21
	Coronary artery bypass surgery	4 (1.8)	18 (2.8)	
	Conservative	29 (13)	111 (17.3)	
TIMI flow after percutaneous coronary intervention	2/3	177 (93.2)	505 (98.4)	<0.001
	0/1	13 (6.8)	8 (1.6)	
Operator volume	>100 percutaneous coronary interventions /year	126 (66.3)	369 (71.9)	0.15
	50–100 percutaneous coronary interventions /year	64 (33.7)	144 (28.1)	

Data are presented as number (percentage) of patients.

Abbreviations: MINOCA, myocardial infarction with nonobstructive coronary arteries; TIMI, thrombolysis in myocardial infarction

TABLE 3 Determinants of long-term mortality

Independent variable	Univariable model			Multivariable model		
	HR	95% CI	P value	HR	95% CI	P value
Age, per 1 year	1.057	1.045–1.071	<0.001	1.046	1.033–1.058	<0.001
Male vs female	0.989	0.762–1.283	0.93	0.816	0.616–1.08	0.16
MINOCA, yes vs no	0.793	0.502–1.254	0.32	0.971	0.595–1.583	0.91
NWD vs WD ^a	1.323	1.018–1.791	0.04	1.027	1.022–1.032	<0.001
Creatinine, per 1 µmol/l	1.003	1.002–1.005	<0.001	1.01	1.007–1.014	<0.001
LAD vs non-LAD ^a	1.01	0.86–1.187	0.9	1.005	0.809–1.372	0.70
TIMI 2/3 vs 0/1	0.368	0.207–0.655	<0.001	0.629	0.348–1.136	0.12
LVEF, per 1%	0.95	0.942–0.959	<0.001	0.962	0.953–0.972	<0.001

a Time-dependent covariate

Abbreviations: HR, hazard ratio; LAD, left anterior descending artery; LVEF, left ventricular ejection fraction; NWD, nonworking day; WD, working day; others, see [TABLE 2](#)

associated with mortality rate ([TABLE 3](#)). Admissions on NWDs as compared with WDs were associated with increased mortality rate within the second (HR, 1.96; 95% CI, 1.10–3.45; $P = 0.023$) and the third (HR, 2.08; 95% CI, 1.01–4.35; $P = 0.047$) year following MI, whereas LAD IRA was associated with an increased mortality rate in the first year following MI (HR, 1.65; 95% CI, 1.12–2.44; $P = 0.012$).

Insight into the population of patients with MINOCA

A subanalysis of all studied patients revealed that MINOCA was diagnosed more frequently on WDs than on NWDs (9% vs 4%; $P = 0.019$). Direct comparison of patients with MINOCA treated on NWDs and WDs showed no significant differences in demographic data, cardiovascular risk factors, prior MI, stroke or PCI, and the distribution of Killip class on admission ([TABLE 4](#)). None of the MINOCA patients had prior coronary artery

bypass surgery. In the MINOCA population, clinical presentation of NSTEMI dominated in both NWD as well as WD admissions (100% vs 84.5%; $P = 0.25$). Interestingly, Takotsubo cardiomyopathy as a mechanism of MINOCA occurrence was diagnosed only in 2 patients admitted on WDs. In both groups, no differences were found in baseline cardiac necrotic markers and in the distribution of insignificant lesions in coronary arteries on angiography ([TABLE 4](#)). The length of hospitalization in both MINOCA groups hospitalized on NWDs and on WDs was similar (median [IQR], 4 [3–5] days vs 4 [3–7] days; $P = 0.85$). There were no in-hospital deaths in the compared groups.

The median (IQR) time of long-term follow-up was similar in both MINOCA subgroups (83.3 [72.9–85.5] months vs 77.3 [70.8–84] months, $P = 0.38$). There was no significant difference in all-cause mortality between NWD versus WD population (22.2% vs 31%; $P = 0.35$; [FIGURE 3A](#)). There

TABLE 4 Characteristics of the study patients with myocardial infarction and nonobstructive coronary arteries

Characteristic		Nonworking days (n = 9)	Working days (n = 58)	P value
Male gender		3 (33.3)	29 (50)	0.29
Age, y		70 (59–74)	72.5 (66–78)	0.81
Body mass index, kg/m ²		29.1 (26–31.3)	26.8 (23.8–30.1)	0.41
Diabetes mellitus		5 (55.6)	15 (25.9)	0.08
Hypertension		9 (100)	54 (93.1)	0.55
Dyslipidemia		6 (66.6)	45 (77.6)	0.37
Renal failure		2 (22.2)	13 (22.4)	0.68
Glomerular filtration rate, ml/min		68.2 (11.7)	64.5 (21.6)	0.62
Active smoking		3 (33.3)	6 (10.3)	0.09
Chronic heart failure		3 (33.3)	19 (32.8)	0.62
Left ventricular ejection fraction, %		52.5 (43.5–60)	55.0 (42.5–60)	0.79
Prior stroke		1 (11.1)	3 (5.2)	0.44
Prior myocardial infarction		2 (22.2)	13 (22.4)	0.68
Prior PCI		1 (11.1)	11 (19)	0.49
Killip class on admission	I	8 (88.9)	46 (79.3)	0.67
	II	1 (11.1)	7 (12.1)	
	III	0	3 (5.2)	
	IV	0	2 (3.5)	
Clinical presentation	NSTEMI	9 (100)	49 (84.5)	0.25
	STEMI	0	9 (15.5)	
Takotsubo cardiomyopathy		0	2 (3.5)	0.75
Baseline cardiac necrotic markers	Troponin, ng/ml	0.055 (0.03–0.24)	0.064 (0.023–0.245)	0.75
	Creatine kinase, IU/l	175 (126–183)	131 (89–266)	0.39
	Creatine kinase MB fraction, IU/l	21 (20–26)	19 (14–28)	0.33
Coronary angiography	<30% stenosis	6 (66.7)	31 (53.5)	0.36
	30%–50% stenosis	3 (33.3)	27 (46.5)	

Data are presented as median (interquartile range) or number (percentage).

Abbreviations: PCI, percutaneous coronary intervention; others, see [FIGURE 1](#) and [TABLES 1 and 2](#)

were also no differences in long-term mortality between patients with MINOCA and MI with obstructive coronary artery in the whole analyzed groups (29.9% vs 30.5%; $P = 0.28$; [FIGURE 3B](#)) as well as in patients admitted on WDs (31% vs 28.1%; $P = 0.74$; [FIGURE 3C](#)) and on NWDs (22.2% vs 36.9%; $P = 0.12$; [FIGURE 3D](#)). Finally, MINOCA proved not to be an independent predictor of long-term mortality ([TABLE 3](#)).

DISCUSSION As shown in this study, the admission of patients with MI to a high-volume university center on NWDs was independently associated with a higher long-term mortality and this effect was visible after the first year since MI. Patients hospitalized during NWDs as compared with those admitted on WDs had a larger ischemic territory and more often transmural MI. As a consequence, the complete epicardial reperfusion was significantly less common in patients admitted on NWDs despite similar experience of PCI operators. Moreover, a diagnosis of MINOCA was more likely on WDs but the latter finding did not influence long-term mortality.

Our study provides several observations that may allow better understanding of the potential mechanism behind the weekend effect in patients with MI. Undoubtedly, one of the most important issues is the higher frequency of incomplete epicardial reperfusion expressed as TIMI flow grade 0 or 1 on NWDs; nevertheless, a sub-optimal recanalization of the IRA was not an independent predictor of death during long-term follow-up most likely due to an interaction with the type of IRA. As has been shown by Henriques et al,²³ the PCI failure occurred more often in patients hospitalized during off-hours (6.9% vs 3.8%; $P < 0.01$). Glaser et al²⁴ performed a meticulous analysis of angiographies conducted which showed a higher incidence of major dissection and less frequent use of stents, coronary imaging techniques, and mechanical thrombectomy in patients treated off-hours.²⁴ In the research devoted to the weekend effect, TIMI flow grade 3 has been consequently indicated as an independent predictor of favorable prognosis.^{4,25,26} Previous studies indisputably proved that complete post-PCI TIMI flow was an accurate predictor of

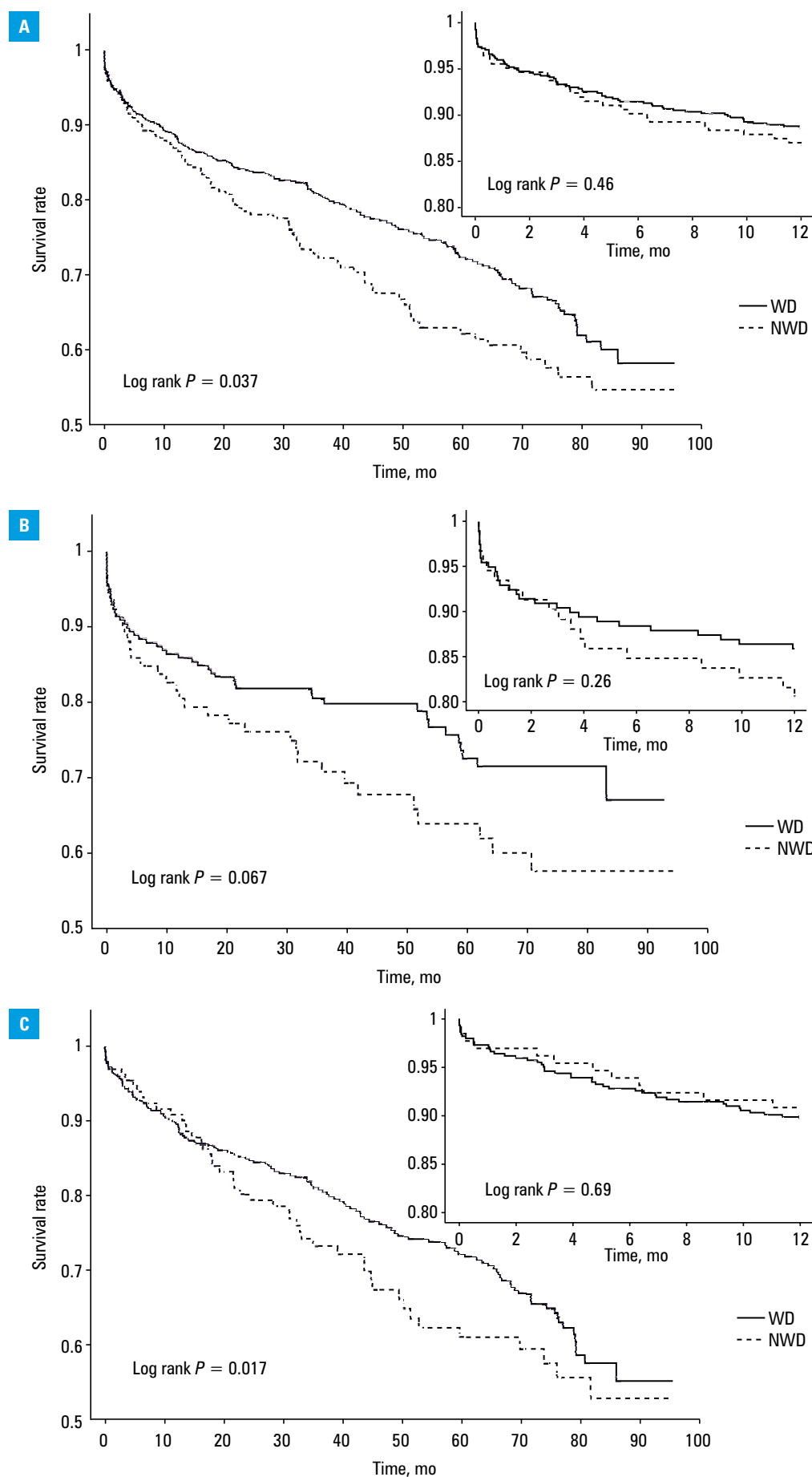


FIGURE 2 Survival rates on working and nonworking days. The whole study population (**A**), patients with ST-segment elevation myocardial infarction (**B**), and patients with non-ST-segment elevation myocardial infarction (**C**) with 1-year and the whole long-term follow-up. Abbreviations: see [TABLE 3](#)

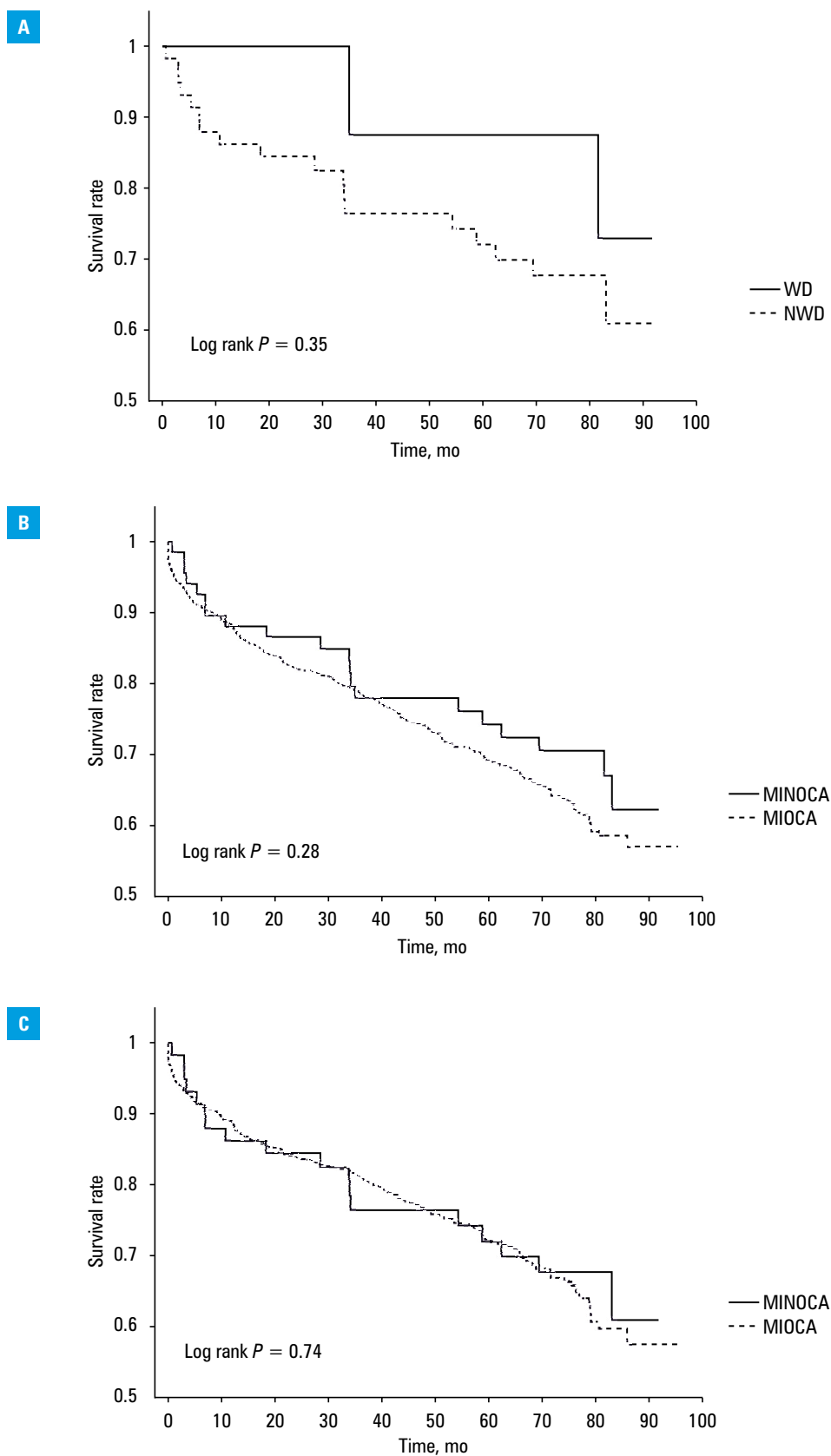


FIGURE 3 The long-term survival rates in the population of patients with myocardial infarction with nonobstructive coronary arteries: **A** – patients with myocardial infarction with nonobstructive coronary arteries (MINOCA) on working and nonworking days; **B** – patients with MINOCA as compared with those with myocardial infarction with obstructive coronary arteries (MIOCA), **C** – patients with MINOCA as compared with those MIOCA on working days
Abbreviations: see [TABLE 3](#)

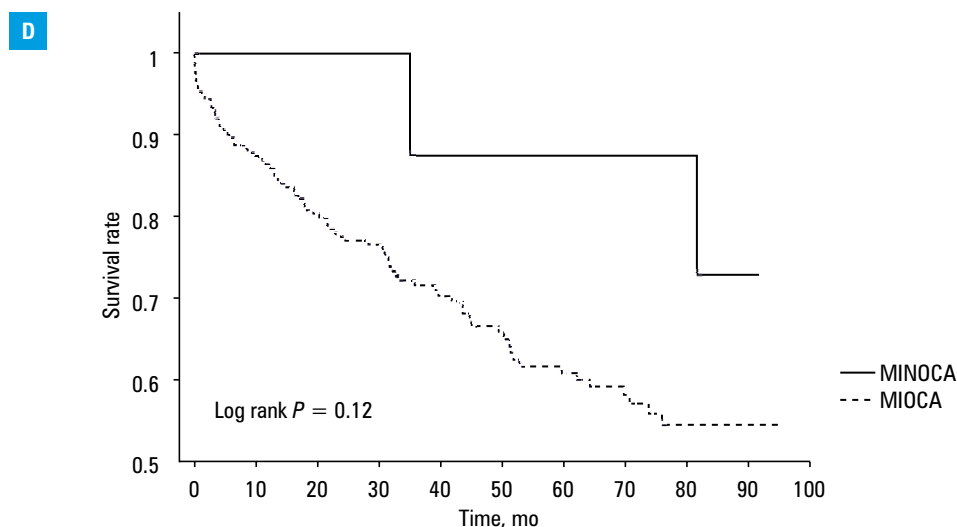


FIGURE 3 The long-term survival rates in the population of patients with myocardial infarction with nonobstructive coronary arteries: **D** – patients MINOCA versus MIOCA on nonworking days
Abbreviations: see [TABLE 3](#)

better long-term outcomes in patients with MI, especially in STEMI.²⁷

The poor general clinical condition of admitted patients was also indicated as potentially associated with the weekend effect. That issue has been explored by Isogai et al²⁸ who found that the weekend effect was noticeable in Killip class II–IV, but not in Killip class I. We did not find a similar relationship and the baseline clinical condition expressed as Killip class was similar in both compared groups. Moreover, almost an identical distribution of cardiovascular risk factors and comorbidities was noted in the study groups. On the other hand, the percentage of patients with STEMI admitted during NWDs was higher by 10% and associated with higher baseline enzymatic injury suggesting longer time of effective ischemia as compared with WDs. Khoshchreh et al²⁹ found that STEMI on WDs and NWDs constituted 13.1% and 17.9% of patients with acute coronary syndromes, respectively, and Martin et al³⁰ reported 50.7% and 58.7%, respectively. Also myocardial infarctions with larger area at risk expressed as the left anterior descending artery territory were presented more frequently on NWDs than WDs. These findings are probably the consequence of the fact that STEMI and high-risk NSTEMI are immediately treated invasively according to the current guidelines whereas lower-risk patients might be postponed to a post-weekend WD. Thus, larger infarcts treated invasively on NWDs have created higher long-term risk associated with potential stent thrombosis, restenosis, or reintervention as compared with WD admissions.

Previous studies also suggested that the difference in patient prognosis might be associated with a reduced in-hospital staff service and weekend duties which are performed by less experienced operators.^{31,32} The experience of PCI operator is a well-recognized prognostic factor

in patients treated invasively.^{33–35} On the other hand, it is a difficult issue to measure the quality of performed medical procedures. In our study, to evaluate the experience of PCI operators, we chose the most commonly used parameter of annual PCI volume that was counted for each of the PCI operators working in our center. As was shown by Ahmed et al³⁶ this parameter, but not years of experience, determines the important prognostic factor which is the needle-to-balloon time. Nevertheless, our study did not show any differences in the competence of individual operators performing procedures on NWDs and WDs. Noteworthy, our study covers the years 2012 to 2017 during which the catheterization laboratories network in Poland provided a high-quality service for patients with MI.³⁷ Our center is also classified as one of the highest-volume institutions, and in the analyzed group, primary angioplasty was performed in over 80% of cases.³⁷

It is unclear why the survival curves associated with the weekend effect diverge after the first year since MI but not from the beginning ([FIGURE 2A](#)). It is difficult to explain this phenomenon directly on the basis of the study results. One may speculate that after the first year following MI, when dual antiplatelet therapy was stopped and the risk of recurrent ischemic events increased, in the group of patients admitted on NWDs with larger, non-optimally reperfused infarcts, it was much more pronounced. Also, the multivariable model confirmed time-dependence of the weekend effect. Therefore, further research is required to explain this observation.

Interestingly, in this study, also a higher prevalence of undetermined IRA and diagnosis of MINOCA was documented during WDs. Difficulties in determination of IRA are often associated with its spontaneous recanalization without visible residual stenosis, which is a proven favorable

prognostic factor.^{17,19} Although MINOCA was less often diagnosed on NWDs, it was not associated with higher long-term mortality. As has been shown in the SWEDEHEART registry, MINOCA occurred most frequently in the morning (incidence rate ratio [IRR], 1.70; 95% CI, 1.63–1.84) and on Mondays (IRR, 1.28; 95% CI, 1.18–1.38) and also less often at weekends.³⁸ Comparably to our study, the time of MINOCA occurrence did not affect the long-term prognosis.³⁸ That circadian onset is probably associated with the pathophysiology of MINOCA.³⁹ It is a complex disease entity and circadian stress might constitute its direct trigger. However, we did not observe differences in the incidence of Takotsubo cardiomyopathy being a common MINOCA etiology and an entity extremely close to the stress factor.^{40,41} Nevertheless, this observation was based on a relatively small group of MINOCA patients, therefore this and previous findings require conformational studies on the role of chronobiology in the pathophysiology of MINOCA.

Our study has several limitations. First, we have included a relatively small group of patients, limited to a single high-volume university center, which may misrepresent the results of the Polish population. This applies especially to the tertiary centers in which the operators have a significantly lower annual operator volume.^{33,34,42} Second, due to lack of access to complete data, we did not analyze the door-to-balloon or ischemic times as well as the influence of nighttime admissions on outcomes.^{2,43} However, the higher baseline cardiac necrotic markers suggest expected longer delay during NWDs. Third, we did not analyze the cause of death in long-term follow-up because of the registry data limitations.^{44–46}

Conclusions Patients with MI admitted on NWDs, as compared with those hospitalized during WDs, had a larger ischemic territory and more often had transmural MI with incomplete epicardial reperfusion, which was associated with a higher long-term mortality. Although MINOCA was less often diagnosed on NWDs, this finding did not influence long-term mortality. The continuous efforts should be undertaken to ensure the comparable outcomes for all patients with MI regardless of the time of presentation also in high-volume centers.

ARTICLE INFORMATION

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CONTRIBUTION STATEMENT KS conceived the concept of the study. KS, KN, and JZ contributed to the design of the research. KS and KN performed the review of literature and were involved in data acquisition. All authors analyzed and interpreted the data. JN and JZ supervised data processing. JZ coordinated funding for the project. All authors edited and approved the final version of the manuscript.

CONFLICT OF INTEREST None declared.

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