Prediction of early death after myocardial infarction in patients with reduced left ventricular ejection fraction. The search for new indications for cardioverter-defibrillator implantation (ICD)

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Kardiol Pol. 2021;
79 (12): 1343–1352;
DOI: 10.33963/KP.a2021.0177

Received:
September 6, 2021

Revision accepted:
December 11, 2021

Published online:
December 11, 2021

ABSTRACT

Background: The highest rate of death is in the first few weeks after myocardial infarction (MI). However, the assessment of indications for primary prevention implantable cardioverter-defibrillator (ICD) implantation should be postponed until at least 40 days after MI.

Aims: Our aim was to identify the subgroup of high-risk patients with reduced left ventricular ejection fraction (LVEF) who would benefit from primary prevention ICD implantation within 40 days of MI.

Methods: Out of 205 606 patients with MI, in this study, we included 18 736 patients treated invasively, with LVEF <40%, who survived until hospital discharge. Patients were divided into two groups according to the survival status at 40 days — patients who died within this period (n = 1331) and patients who survived (n = 17405).

Results: Among all patients who died within 12-months after MI, 37.7% did die during the first 40 days. Patients with cardiac arrest before hospital admission or within the first 48 hours of hospitalization (hazard ratio [HR], 3.35; 95% confidence interval [CI], 2.82–3.98; *P* <0.0001], cardiogenic shock before admission or during hospitalization (HR, 3.06; 95% CI, 2.62–3.59; *P* <0.0001), unsuccessful percutaneous coronary interventions (PCI; HR, 2.42; 95% CI, 2.11–2.84; *P* <0.0001), LVEF <20% (ref. LVEF ≥30%; HR, 2.75; 95% CI, 2.25–3.36; *P* <0.0001) had approximately threefold and patients with chronic kidney disease almost 1.5-times (HR, 1.25; 95% CI, 1.47–3.59; *P* = 0.0053) higher 40-day mortality compared to patients without these risk factors. The most striking differences in mortality between these subgroups were observed shortly after discharge.

Conclusions: The highest risk of death in patients with reduced LVEF who survived until hospital discharge occurred within the first 40 days after MI. There is a possibility to select patients with the worst prognosis and treat them more aggressively.

Key words: implantable cardioverter-defibrillator, myocardial infarction

Kardiol Pol 2021; 79, 12: 1343–1352

WHAT'S NEW?

There is the highest mortality within the first 40 days after myocardial infarction (MI). In our study, of all patients who did not survive the first year after acute MI, 37.7% died during the first 40 days. It means that one-third of patients die before LVEF reassessment and determining the indications for implantable cardioverter-defibrillator (ICD) or cardiac resynchronization therapy defibrillator (CTR-D) implantation in primary prevention. In our cohort, patients with MI were at approximately three-fold higher risk of 40-day mortality if they had (1) cardiac arrest before or within the first 48 hours of admission; (2) cardiogenic shock; (3) unsuccessful percutaneous coronary intervention (final thrombolysis in myocardial infarction [TIMI], 0–2 flow) and left ventricular ejection fraction (LVEF) <20% (compared to LVEF ≥30%). Furthermore, the risk of death in patients with LVEF between 20% and 30% compared to patients with LVEF >30% and patients aged over 65 years compared to younger ones was almost twice as high. Moreover, the risk of 40-day death in patients with chronic kidney disease was almost 1.5-times higher than other MI patients. The most significant differences in mortality between groups with and without the above-mentioned risk factors were observed in the short time after discharge.

INTRODUCTION

Over the last two decades, there has been a significant increase in the number of implantable cardioverter-defibrillator (ICD) implantation procedures. It has been proven that this therapy reduces mortality in patients with heart failure [1]. The current European Society of Cardiology (ESC) guidelines recommend ICD implantation as the standard treatment of patients with reduced left ventricular ejection fraction (LVEF) [2]. However, in patients who have recently had a myocardial infarction (MI), the assessment of indications for primary prevention ICD implantation should be postponed until at least 40 days after the acute coronary syndrome [3]. The IRIS (The Immediate Risk Stratification Improves Survival) and DINAMIT (the Defibrillator in Acute Myocardial Infarction Trial) studies showed that ICD implantation does not reduce all-cause mortality in this period but decreases the rate of death due to arrhythmia. However, the latter is offset by an increase in nonarrhythmic mortality [4, 5]. According to the ESC guidelines, primary prevention ICD implantation in this period should be considered in case of incomplete revascularization and reduced LVEF prior to MI [3]. Despite the high prevalence of the invasive management strategy in the treatment of acute coronary syndromes, which has led to an improvement in in-hospital outcomes, long-term mortality in post-MI patients is still unsatisfactory, especially in those with reduced LVEF. It has been shown that 7% of patients with MI who survive until hospital discharge die or experience nonfatal cardiac arrest within 6 months. Additionally, in the subgroup of MI patients with LVEF lower than 30%, the risk of death significantly increases during the first month after the event [6]. It must be noted that the most frequent cause of death in this group is ventricular arrhythmia [7]. Therefore, considering the highest rate of death and causes of death in the first few weeks after MI, we aimed to identify the group of high-risk patients with reduced LVEF who would benefit from primary prevention ICD implantation within 40 days of MI.

METHODS

SILCARD, PL-ACS, AMI-PL

In the present study, we analyzed data from 205 606 MI patients (both ST-segment elevation and non-ST-segment elevation myocardial infarction) derived from three combined medical registries: SILCARD (The Silesian Cardiovascular Database), PL-ACS (Polish Registry of Acute Coronary Syndromes), and AMI-PL (Acute Myocardial Infarction in Poland).

SILCARD was developed under the agreement between the Silesian Center for Heart Disease in Zabrze and the Regional Department of National Health Fund (NHF) in Katowice, Poland to conduct epidemiological analyzes and prepare scientific elaborations on the group of patients with cardiovascular diseases (CVD) in the Silesia Province. The design and rationale of the SILCARD database were described previously [8]. The reported data come from 310 hospital wards and 1863 outpatient clinics and contain information on 487 518 patients, 956 634 cardiovascular hospitalizations, and 61 906 964 outpatient visits.

The PL-ACS is a clinically driven registry established in 2003, gathering detailed data on in-hospital management, treatment modalities, and outcomes. Its design and introduction were a joint effort of the Silesian Center for Heart Diseases in Zabrze and the Polish Ministry of Health. Currently, over 630 000 hospitalizations for acute coronary syndrome are listed in the PL-ACS registry. Its detailed design has been described elsewhere [9].

The AMI-PL is a registry of administrative data gathered from all MI hospitalizations, containing data from the national healthcare provider. The database currently comprises information on over 550 000 hospitalizations from 2009. The detailed design of AMI-PL has been presented previously [10].

According to letter no. PCN/0022/KB/49/21, keeping the register is not a medical experiment and does not require the consent of the ethics committee.

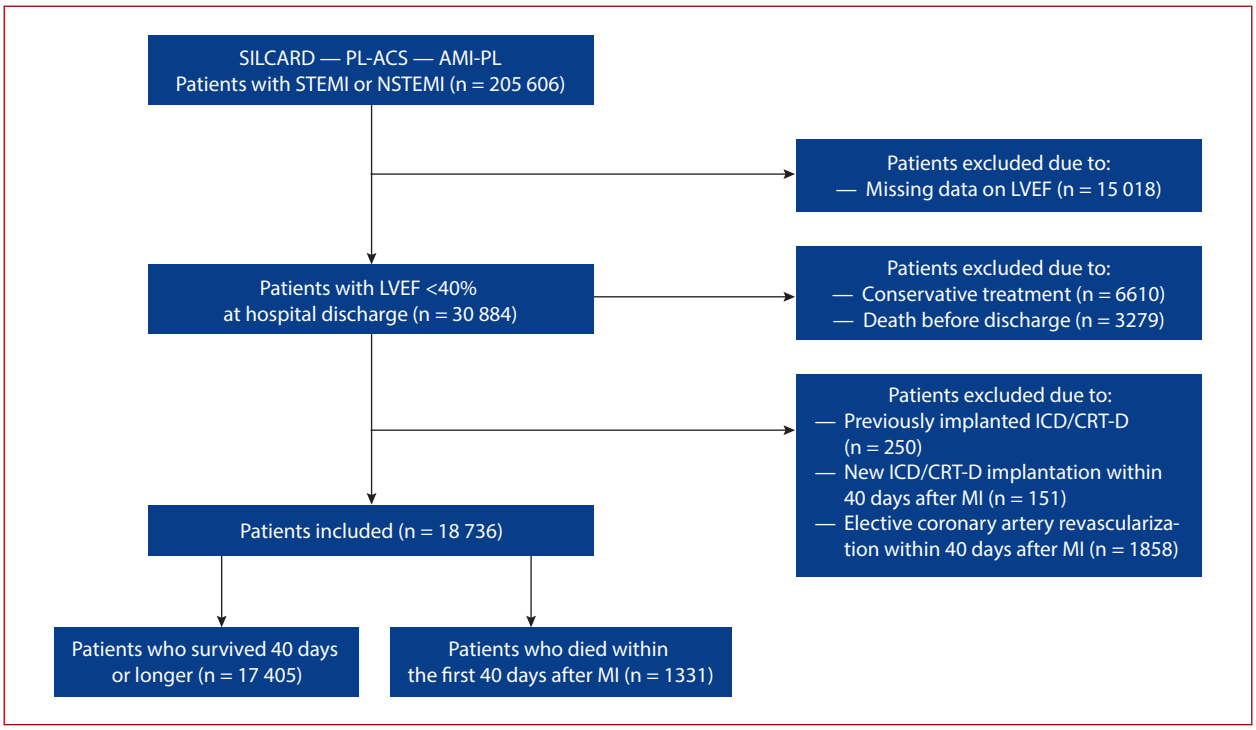

Figure 1. Flowchart of the study population

Abbreviations: AMI-PL, Acute Myocardial Infarction in Poland; CRT-D, cardiac resynchronization therapy defibrillator ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; MI, myocardial infarction; PL-ACS, Polish Registry of Acute Coronary Syndromes; SILCARD, The Silesian Cardiovascular Database

Study population

A flowchart of the study population is shown in Figure 1. Patients who were included in the study were hospitalized with MI treated invasively, had LVEF <40%, and survived until hospital discharge. The exclusion criteria were as follows: MI treated with fibrinolysis or conservatively, ICD or cardiac resynchronization therapy defibrillator (CRT-D) implanted before the index hospitalization or within 40 days after MI, elective coronary artery revascularization within 40 days after MI, and missing data on LVEF. In total, 18 736 patients were included. Patients were divided into two groups according to the survival status at 40 days — patients who died within this period (n = 1331) and patients who survived (n = 17 405). Selected clinical characteristics and angiographic parameters, as well as causes of rehospitalizations, were analyzed in both groups.

Statistical analysis

Qualitative parameters are presented as percentages while continuous parameters are presented as the median and interquartile range. Differences in categorical variables between the groups were tested using the χ^2 test with Pearson modification, whereas differences in continuous variables were tested using the U Mann-Whitney test. To assess the impact of particular parameters on 40-day mortality, a multivariable analysis was performed using step-down Cox proportional hazards regression modeling. The multivariable model included the following variables: age, sex, LVEF, sudden cardiac arrest before admission or during hospitalization, cardiogenic shock, a history of arterial hypertension, diabetes mellitus, chronic kidney disease, tobacco smoking, diagnosis of ST-segment elevation myocardial infarction (STEMI), multivessel coronary artery disease, and final thrombolysis in myocardial infarction (TIMI) flow 0–2 vs. 3. The results of the multivariable analysis are expressed as a hazard ratio (HR) with the corresponding 95% confidence interval (CI). For mortality at 12 months, the analysis with the Kaplan-Meier method with the log-rank comparison of curves was performed. The level of statistical significance was $P<0.05$ (two-tailed). Statistica 10 software (StatSoft Inc., Tulsa, OK, USA) was used for all calculations.

RESULTS

Clinical and angiographic characteristics

Patients who died during a 40-day follow-up were older and more frequently female. Moreover, they were more likely to have cardiac arrest before admission or within the first 48 hours of hospital admission, as well as pulmonary edema, cardiogenic shock, hypertension, diabetes mellitus, a previous stroke, peripheral arterial disease, and had both lower blood pressure on admission and LVEF. Patients who died were less frequently current smokers and were less

Table 1. Demographic and clinical characteristics of the study population

	Patients who survived 40 days (n = 17 405)	Patients who died within 40 days (n = 1331)	*P*-value
Age, years	69 (60–77)	74 (65–80)	<0.0001
Male sex, n (%)	11 884 (68.28)	875 (65.74)	0.056
Hypertension, n (%)	12 546 (72.08)	913 (68.6)	0.0064
Current or former smokers, n (%)	10 201 (58.61)	720 (54.11)	0.0013
Type 2 diabetes mellitus, n (%)	5803 (33.34)	520 (39.05)	<0.0001
Obesity, n (%)	3448 (19.81)	251 (18.87)	0.41
Previous MI, n (%)	5046 (28.99)	355 (26.67)	0.072
Previous PCI, n (%)	3483 (20.01)	211 (15.85)	0.0002
Previous CABG, n (%)	1046 (6.01)	56 (4.21)	0.007
Previous stroke, n (%)	870 (5.0)	132 (9.95)	<0.0001
PAD, n (%)	1173 (6.74)	140 (10.53)	<0.0001
STEMI, n (%)	9844 (56.56)	790 (59.35)	0.047
Atrial fibrillation on admission, n (%)	1558 (8.95)	34 (2.53)	0.001
Diabetes mellitus, n (%)	5803 (33.34)	520 (39.05)	<0.0001
Chronic kidney disease, n (%)	1897 (10.90)	233 (17.48)	<0.0001
Systolic blood pressure on admission, mm Hg	130 (105–147)	120 (100–140)	<0.0001
Diastolic blood pressure on admission, mm Hg	80 (70–100)	77 (65–80)	<0.0001
Heart rate, 1/min	80 (70–100)	90 (75–100)	<0.0001
LVEF, %	31 (27–35)	30 (20–35)	<0.0001
Sudden cardiac arrest before admission or within the first 48 hours of hospital admission, n (%)	599 (3.44)	254 (19.1)	<0.0001
Pulmonary edema, n (%)	1083 (6.22)	150 (11.24)	<0.0001
Cardiogenic shock, n (%)	731 (4.2)	220 (16.52)	<0.0001

Continuous variables are presented as median (interquartile range [IQR]). Dichotomous variables are presented as percentages

Abbreviations: CABG, coronary artery bypass grafting; PAD, peripheral artery disease; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; other — see Figure 1

Table 2. Angiographic characteristics and in-hospital outcomes

	Patients who survived 40 days (n = 17 405)	Patients who died within 40 days (n = 1331)	*P*-value
Infarct-related artery, n (%)			
Left main	573 (3.29)	75 (5.64)	<0.0001
Left anterior descending	9031 (51.89)	687 (51.65)	
Diagonal branch	350 (2.02)	23 (1.73)	
Circumflex	2273 (13.06)	178 (13.38)	
Obtuse marginal branch	714 (4.1)	53 (3.98)	
Right coronary artery	3754 (21.57)	271 (20.38)	
Saphenous vein or arterial graft	343 (1.97)	20 (1.5)	
Not determined	366 (2.1)	23 (1.74)	
Multivessel coronary artery disease, n (%)	10 956 (62.95)	930 (69.9)	0.0044
PCI, n (%)	17 351 (99.69)	1,327 (99.7)	0.95
Final TIMI flow, n (%)			
0	517 (2.97)	180 (13.49)	<0.0001
1	261 (1.5)	58 (4.33)	
2	896 (5.15)	144 (10.82)	
3	15 732 (90.39)	951 (71.46)	
CABG, n (%)	54 (0.31)	4 (0.3)	0.94
Inotropes or vasopressors, n (%)	898 (5.16)	253 (19.01)	<0.0001
IABP, n (%)	369 (2.12)	143 (10.74)	<0.0001
Reinfarction, n (%)	101 (0.58)	19 (1.43)	0.0002
Major bleeding, n (%)	190 (1.09)	41 (3.08)	<0.0001

Abbreviations: IABP, intra-aortic balloon pump; other — see Table 1

likely to have previous coronary artery revascularization in comparison with individuals who survived 40 days (Table 1). In the group of patients who died, there was a higher percentage of patients with multivessel disease and the left main artery as an infarct-related artery. Patients who survived 40 days had more likely the left anterior descending artery as an infarct-related artery and a higher success rate of percutaneous coronary intervention (PCI) (Table 2). The success rate in the whole study population (TIMI 3 flow after PCI) was 89.03%.

Table 3. Pharmacological treatment at discharge

	Patients who survived 40 days (n = 17405)	Patients who died within 40 days (n = 1331)	*P*-value
ASA, n (%)	16 738 (96.17)	1239 (93.09)	<0.0001
Clopidogrel, n (%)	15 765 (90.58)	1154 (86.7)	<0.0001
ACE-I or ARB, n (%)	14 477 (83.18)	827 (62.13)	<0.0001
β-blocker, n (%)	15 365 (88.28)	932 (70.02)	<0.0001
Statin, n (%)	16 117 (92.6)	1103 (82.9)	<0.0001
Nitrate, n (%)	2277 (13.08)	145 (10.89)	0.022
LMWH, n (%)	943 (5.42)	180 (13.52)	<0.0001
Oral anticoagulant, n (%)	809 (4.65)	34 (2.53)	0.001
VKA	727 (89.86)	23 (67.65)	0.0001
NOAC	82 (10.14)	11 (32.35)	

Abbreviations: ASA, acetylsalicylic acid; ACE-I, angiotensin-converting-enzyme inhibitor; ARB, angiotensin II receptor blocker; LMWH, low-molecular-weight heparin; NOAC, non-VKA oral anticoagulant; VKA, vitamin-K antagonist

In-hospital treatment and outcomes and prescribed medicines at discharge

In patients who died in 40 days following MI, major bleeding and recurrent MI were more often observed. These patients were more likely to require inotropic support and intra-aortic balloon pumps (Table 2). Moreover, they were less likely to be prescribed antiplatelets, β-blockers, ACE inhibitors/angiotensin II receptor antagonists, statins, and nitrates. On the other hand, patients who survived 40 days were less frequently discharged on anticoagulants (Table 3).

Forty-day mortality and its predictors

Forty-day and 1-year mortality in patients with MI and LVEF <40% who survived until hospital discharge was 7.1% and 18.81%, respectively. The cumulative mortality rate in this group is shown in Figure 2. In the multivariable analysis, the independent predictors of 40-day mortality were as follows: cardiac arrest before hospital admission or within the first 48 hours of hospitalization, cardiogenic shock before admission or during hospitalization, unsuccessful PCI, lower LVEF, age >65 years, and chronic kidney disease (Table 4). Cumulative mortality rate curves for patients stratified according to independent predictors of death are depicted in Figures 2 and 3. We found ca. three-fold higher 40-day mortality in patients with cardiac arrest, cardiogenic shock, or unsuccessful percutaneous coronary intervention compared to patients without these complications.

Rehospitalizations within 40 days

There were significantly higher overall and cardiovascular 40-day readmission rates in patients who died during this period. Cardiac arrest was significantly more frequent, while stable coronary artery disease and unstable angina were significantly less frequent causes of readmission in this group, compared to patients who survived 40 days (Table 5). The median time from hospital discharge to readmission in patients who died and survived 40 days was 10 (5.25–18) and 24 (14–33) days, respectively.

DISCUSSION

In the present study patients with MI and reduced LVEF were analyzed. This group included 14.5% of all patients with MI, who had survived the in-hospital period. This percentage was slightly lower than described in other studies, i.e. 21.4% in the study by Zaman et al. [11]. The above-mentioned discrepancies might stem from the fact that in the present analysis, patients treated conservatively and patients with implanted ICD or CRT-D were excluded. Nevertheless, it is worth emphasizing, that every seventh patient with MI had LVEF <40% at hospital discharge. The ESC guidelines suggest a subsequent reassessment of LVEF 40 days after MI in these patients. After this period further therapeutic decisions should be made. Considering the results of our study, it seems that this recommendation should be re-examined. In our study, we showed, that approximately 38% of deaths in the first year after MI occur within the first 40 days. It means that one-third of patients die within the first year of MI before LVEF reassessment and starting adequate treatment, which could affect the survival of this group of patients. Thus, it seems reasonable to re-evaluate whether there is a subgroup of patients who should undergo ICD or CRT-D implantation in primary prevention before hospital discharge or shortly after MI.

To the best of our knowledge, there is no clear solution to the problem in the available literature. Randomized clinical trials assessing ICD effectiveness for primary prevention of sudden cardiac death within the first 40 days after MI have shown unambiguously no significant survival benefit from ICD implantation over optimal medical therapy. The way of randomization and timing of the procedure in these studies is worth analyzing. Patients recruited to the IRIS trial had acute MI 5–31 days before randomization. Approximately 7% of patients did not undergo ICD implantation despite allocation to the ICD group. Moreover, 9% of patients were discharged from the hospital before the planned procedure, and 1% of patients died before ICD implantation [4]. The inclusion criteria for the DINAMIT trial were acute MI 6–40 days before enrollment (18 days on average) and the possibility of ICD implantation within

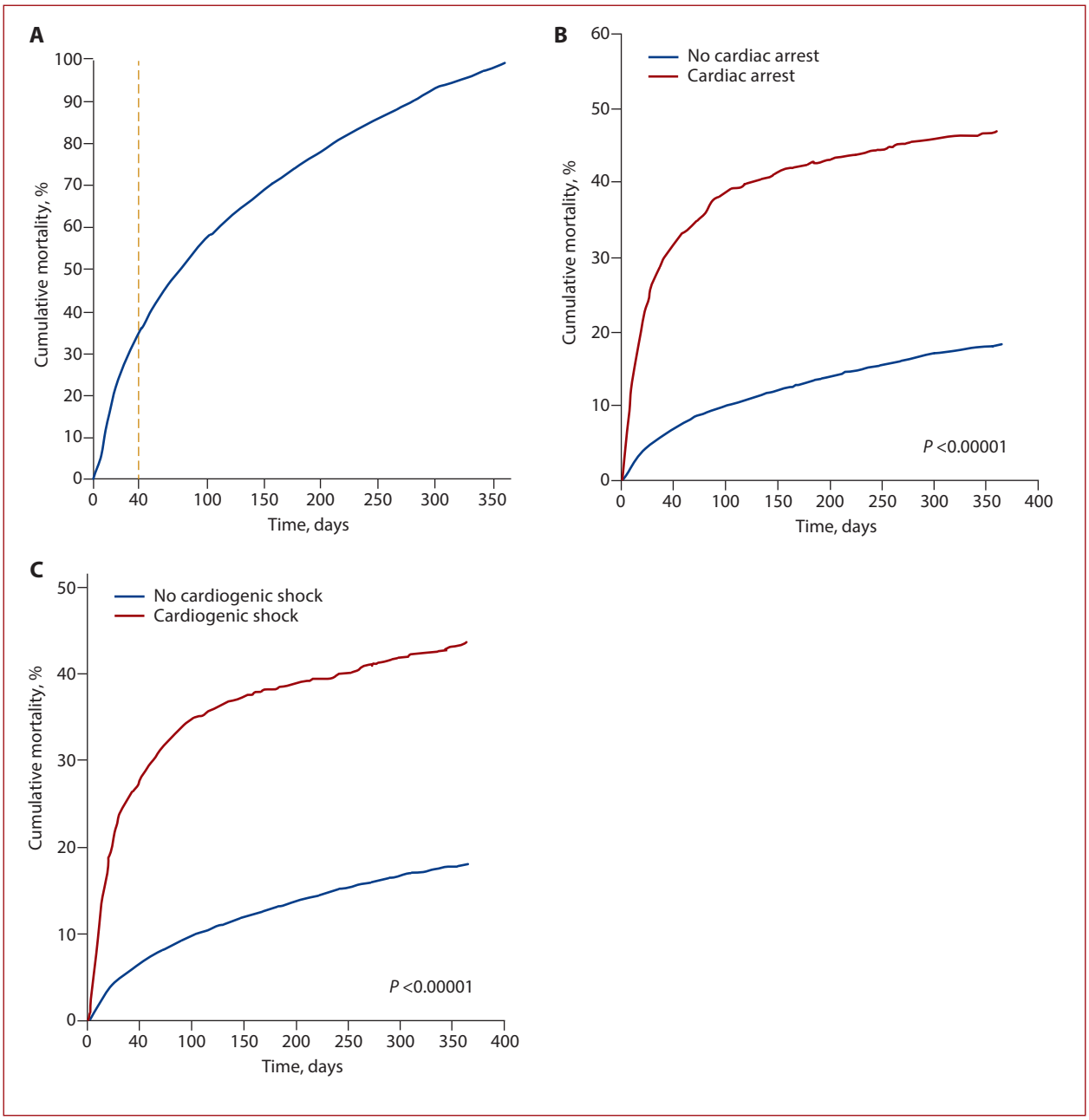

Figure 2. A. Kaplan-Meier curves for patients who died within 1 year of myocardial infarction. **B.** Kaplan-Meier curves for patients with and without cardiac arrest before admission or within the first 48 hours of hospitalization. **C.** Kaplan-Meier curves for patients with and without cardiogenic shock before admission or during hospitalization

Table 4. Predictors for 40-day mortality — a multivariable analysis

	HR (95% CI)	*P*-value
Sudden cardiac arrest before admission or within the first 48 hours of hospital admission	3.35 (2.82–3.98)	<0.0001
Unsuccessful PCI	2.42 (2.11–2.84)	<0.0001
Cardiogenic shock before admission or during hospitalization	3.06 (2.62–3.59)	<0.0001
LVEF <20%[a]	2.75 (2.25–3.36)	<0.0001
LVEF 20%–30%[a]	1.90 (1.68–2.16)	<0.0001
Age >65 years	1.82 (1.59–2.07)	<0.0001
Chronic kidney disease	1.25 (1.07–1.47)	0.0053

[a]Vs. LVEF ≥30%

Abbreviations: CI, confidence interval; HR, hazard ratio; other — see Table 1 and Figure 1

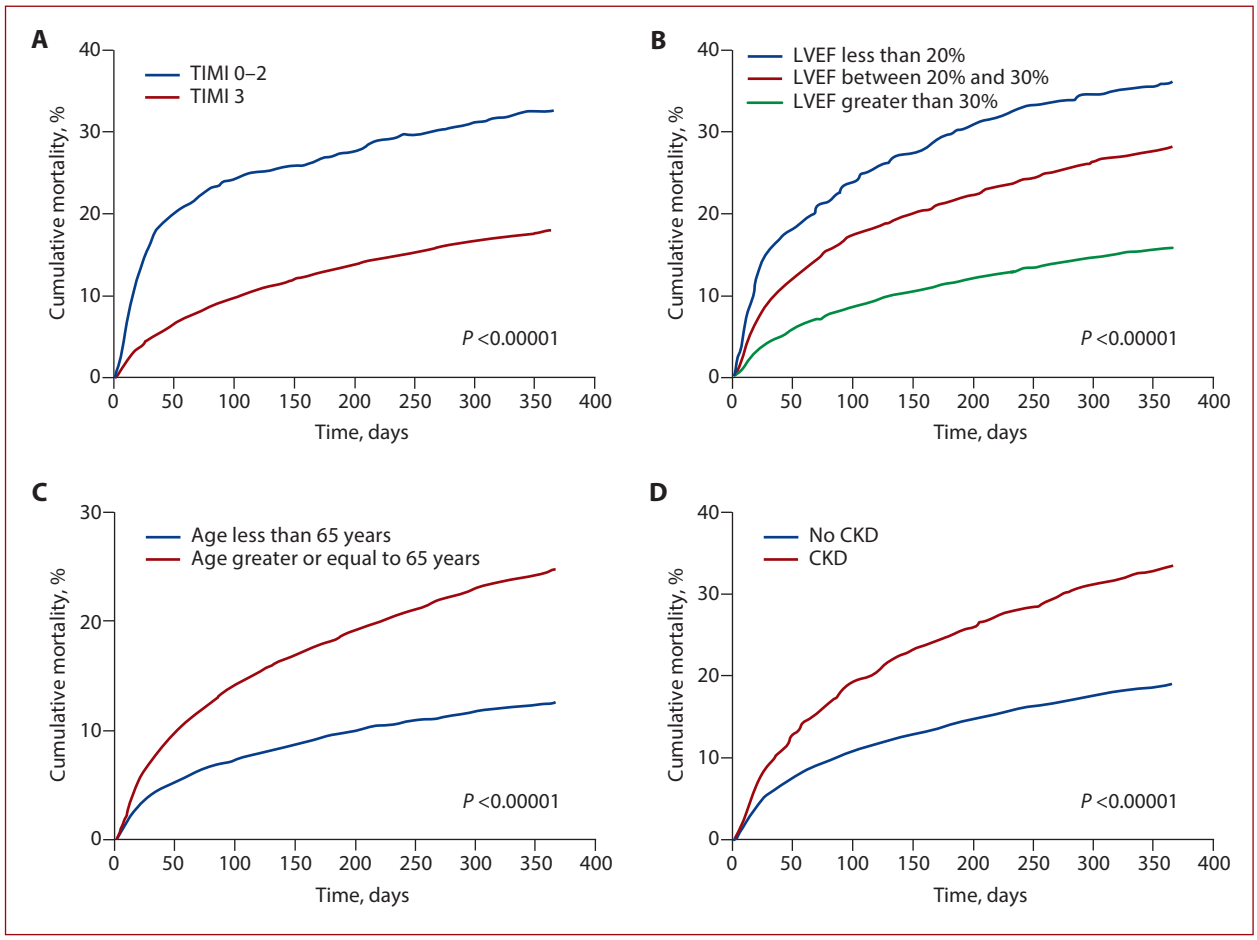

Figure 3. A. Kaplan-Meier curves for patients stratified by final TIMI flow. **B.** Kaplan-Meier curves for patients stratified by left ventricular ejection fraction. **C.** Kaplan-Meier curves for patients stratified by age. **D.** Kaplan-Meier curves for patients with and without CKD

Abbreviations: CKD, chronic kidney disease, other — see Table 4

Table 5. 40-day readmissions and procedures during follow-up

	Patients who survived 40 days (n = 17 405)	Patients who died within 40 days (n = 1331)	*P*-value
Readmission rate, n (%)	3563 (20.47)	695 (52.25)	<0.0001
Readmission for cardiovascular disease, n (%)	3084 (17.72)	617 (46.38)	<0.0001
Causes of readmissions, n (%)			
Atrial fibrillation	75 (2.43)	8 (1.32)	<0.0001
Supraventricular arrhythmias	25 (0.81)	3 (0.44)	
Ventricular arrhythmias (except for sudden cardiac death)	19 (0.61)	2 (0.32)	
Conduction disorders	35 (1.13)	11 (1.76)	
Sudden cardiac arrest	18 (0.59)	68 (11.02)	
Pulmonary embolism	14 (0.45)	5 (0.88)	
Valvular heart disease	110 (3.56)	16 (2.64)	
Heart failure	1130 (36.64)	239 (38.77)	
Myocardial infarction	230 (7.46)	60 (9.69)	
Unstable angina	366 (11.87)	19 (3.08)	
Stable coronary artery disease	897 (29.09)	73 (11.89)	
Other	165 (5.36)	112 (18.19)	
Procedures performed during follow-up, n (%)			
Coronary angiography	2026 (11.64)	11 (0.81)	<0.001
PCI	1004 (5.77)	2 (0.15)	<0.0001
CABG	132 (0.76)	0 (0)	0.27
Cardiac ablation	38 (0.22)	0 (0)	0.55

Abbreviations — see Table 1

7 days of randomization. Approximately 6% of patients allocated to the ICD group did not undergo device implantation. The mean time between randomization and the procedure was 6.3 ± 7.3 days [5]. It should be noted that in both studies, survival analysis was conducted from the moment of randomization and not from the MI [4, 5]. The Multicenter Automatic Defibrillator Implantation Trial (MADIT)-II, based on which the ESC recommends ICD implantation at least 40 days after MI, showed a significant reduction of overall mortality compared to optimal medical therapy only after approximately 9 months of ICD therapy. It is noteworthy that 88% of patients who underwent ICD implantation were included in the study >6 months after MI [1]. It appears from the above data that patients included in the trials, on which ESC guidelines were based, did not reflect the "real-world" population. Some patients may have died before recruitment or between randomization and ICD implantation. Nowadays, in the era of interventional treatment of MI, patients are discharged from the hospital early (usually on the 4th or 5th day), and the early start post-hospital period is characterized by a high risk of death in some patients. In our study, the eligibility criteria analogous to those for randomized clinical trials regarding ICD implantation after MI were not applied. Elimination of these limitations should enable researchers to establish the role of primary prevention ICD implantation in reducing early sudden cardiac deaths after MI.

Over the last few years, wearable cardioverter-defibrillators (WCDs) have emerged as a bridge to ICD implantation in patients at risk of sudden cardiac death soon after MI. A recent randomized clinical trial (Vest Prevention of Early Sudden Death Trial [VEST]) included patients with acute myocardial infarction and LVEF of 35% or less. It has been shown that there was no difference in arrhythmic deaths (sudden death or death from ventricular tachyarrhythmia) between participants assigned to receive a WCD and the control group. However, there was significantly lower all-cause mortality in the device group. It should be pointed out that patients were enrolled up to 7 days after hospital discharge and participants in the device group wore the device, on average, only 14 hours a day. Of the 48 patients in this group, 36 patients who died were not wearing the device at the time of the incident. These facts may explain the negative results of the VAST trial. Nonetheless, data from the trial confirm that the highest risk of arrhythmic death occurs during the first 30 days after MI. Therefore, in certain patients, WCDs might reduce mortality if they are worn for the recommended time per day [12]. In 2019, experts of the Heart Rhythm Section of the Polish Cardiac Society gave their opinion on the use of WCDs in Poland. They suggest that up to three months after MI, WCD therapy can be considered in patients with a history of sustained VT or VF during the first 48 hours of ACS, cardiogenic shock or pulmonary edema, and with a history of asymptomatic permanent VT [13]

Forty-day mortality

In our study, we showed that 40-day mortality after MI is still very high (during this period occurs approximately one-third of all deaths within the first year). Our results are consistent with previous reports. In the VALsartan In Acute myocardial iNfarcTion (VALIANT) trial, the highest risk of death was within the first week after MI. During the first month of MI, the risk of cardiovascular death or nonfatal cardiac arrest was 1.4%, but between months 6 and 12, the risk declined to 0.27% per month [6]. We found independent predictors of 40-day mortality, which enabled us to identify patients with a greater risk of death early after MI.

Sudden cardiac arrest

In our analysis, the strongest predictor of early death was sudden cardiac arrest before admission or within the first 48h of hospital admission. The risk of death early after hospital discharge in this group was 3-times higher compared to patients without cardiac arrest. Other studies have not confirmed this finding. It has been shown that patients with MI complicated by out-of-hospital cardiac arrest who are alive at hospital discharge have a similar risk of death compared to the other MI patients [14, 15]. This might be the reason for the abovementioned discrepancies. To the best of our knowledge, there are no studies that aimed to analyze the relationship between in-hospital cardiac arrest and early mortality after discharge in a population similar to our cohort.

Unsuccessful PCI

In the present study, we showed that patients with unsuccessful PCI had almost 3-fold higher 40-day mortality compared to subjects with final TIMI flow 3 in the infarct-related artery. The multivariable analysis indicated that unsuccessful PCI was an independent predictor of death. Unsuccessful PCI leads to greater myocardial injury and, as a consequence, to reduced LVEF. This, in turn, results in an increased risk of serious life-threatening arrhythmias. These findings have been previously reported [16].

Cardiogenic shock

Cardiogenic shock complicating acute MI is associated with a less favorable prognosis. Shah et al. [17] evaluated the relationship between cardiogenic shock and mortality in patients who were alive at hospital discharge. They found that the highest risk of death occurred within the first 60 days after hospital discharge. During the 40-day follow-up, mortality was approximately 1.5-times higher compared to patients without cardiogenic shock. The FAST-MI (French Registry on Acute ST-elevation and non-ST-elevation Myocardial Infarction) study provided similar results [18]. Our results are consistent with these reports. We showed that in MI patients with cardiogenic shock, the highest mortality occurs within 40 days following MI. The reason for this might be the fact that patients who develop cardiogenic

shock are older, have more comorbidity burden, lower LVEF, more frequently unsuccessful PCI, and more frequent out-of-hospital and in-hospital sudden cardiac arrest than patients without this complication [17, 18].

Left ventricular ejection fraction

Left ventricular ejection fraction is an important predictor of mortality in patients with MI. Margolis et al. analyzed the LVEF of 2086 STEMI patients assessed within 72 hours of episode onset. Patients with LVEF lower than 40% had approximately 6-times higher 30-day mortality than those with LVEF >40% [19]. In the VALIANT study, MI patients with LVEF<40% or radiological evidence of heart failure were included. The rate of sudden cardiac death, including resuscitated sudden cardiac death, at 30 days was 2.3% and less than 1% in patients with LVEF ≤30% and >30%, respectively. The risk of major adverse cardiovascular events increased by 21% for each 5% decrease in LVEF [6]. Similarly, the present study demonstrated that reduced LVEF was associated with higher 40-day mortality.

Age

In our study, we observed that patients' age was an independent predictor of death within 40 days. The relative risk of death in patients aged over 65 years was almost twice as high as in younger patients. This may be due to a linear relationship between mortality after MI and age. This risk increases significantly for each subsequent year of age [19].

Rehospitalizations in the 40-day follow-up

Most rehospitalizations in patients with MI occur early after hospital discharge. Kim et al. [20] reported that two-thirds of readmissions in STEMI patients occurred up to 14 days of hospital discharge. The median time to readmission in this study was 9 days. The readmission rate for MI or heart failure was higher in this period compared to subsequent periods. Additionally, the MINAP registry (Myocardial Ischemia National Audit Project) provided similar findings [21]. In the present study, the 40-day readmission rate was 22%, which was higher than in other studies [20, 21]. The reason might be the fact that only patients with LVEF <40% were included in our study. In our analysis, heart failure was the most frequent cause of readmission, followed by acute coronary syndromes. Moreover, patients who died up to 40 days after MI were significantly more frequently readmitted for sudden cardiac arrest than patients who survived. We had no detailed data about the mechanism of sudden cardiac death. However, considering epidemiological data regarding patients with left ventricular systolic dysfunction after MI, we can suspect that most of them died of ventricular fibrillation or pulseless ventricular tachycardia. Therefore, it seems that primary prevention ICD implantation might reduce 40-day mortality in these patients.

Limitations

The data on causes of readmission within 40 days were derived from an administrative database, which has some limitations [22]. According to the ICD-10 classification, the principal diagnosis reported to the National Health Fund most often reflects the real reason for hospitalization. However, the reporting systems are not standardized. For example, the order and number of diagnoses are subjectively reported, therefore, some disease entities can be omitted. Moreover, the classification often does not determine the subcategories of individual diseases, which hinders the precise determination of all the diagnoses.

Another limitation of the study might be the lack of information on the causes of death in all patients. We would like to emphasize that we report all-cause mortality, not cardiac mortality. However, given the short time from discharge to death, it can be assumed with a high probability that these were sudden cardiac deaths and not consequences of chronic diseases.

CONCLUSIONS

The highest risk of death in patients with reduced LVEF occurs within 40 days after MI. These deaths constitute one-third of all deaths that occur during the first year. The development of an optimal treatment strategy and possible ICD implantation during this period, in a certain group of patients, can be another step toward reducing mortality.

Article information

Conflict of interest: None declared.

How to cite: Pres D, Tajstra M, Mitkowski P, et al. Prediction of early death after myocardial infarction in patients with reduced left ventricular ejection fraction. The search for new indications for cardioverter-defibrillator implantation. Kardiol Pol. 2021; 79(12): 1343–1352, doi: 10.33963/KP.a2021.0177.

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