

# Clinical characteristics and treatment profiles of patients after acute myocardial infarction with left ventricular ejection fraction below 40%: a short 2018–2019 report on the PL-ACS registry

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**Introduction** Cardiovascular diseases are the main cause of death in developed countries.<sup>1</sup> Coronary artery disease (CAD) accounts for around two-third of cases of left ventricular systolic dysfunction (LVSD) and heart failure with reduced ejection fraction (HFrEF).<sup>2,3</sup>

Acute myocardial infarction (AMI) is the leading cause of LVSD increasing the risk of HFrEF and worse clinical outcomes.<sup>4</sup> Therefore, optimal hospital treatment of AMI and proper discharge therapy is a key issue in patients with LVSD or HFrEF.

In this short communication, we analyzed the population of patients with AMI using the Polish Registry of Acute Coronary Syndromes (PL-ACS). Our objective was to assess the clinical and treatment characteristics of patients with left ventricular ejection fraction (LVEF) below 40% at discharge regardless of whether they had HFrEF before AMI, developed HFrEF as a complication of AMI during

hospitalization, or were discharged free of HFrEF despite reduced LVEF.

**Methods** The rationale and methodology of the PL-ACS registry were described elsewhere.<sup>5</sup> As we presented the subanalysis of the already approved registry study, no ethics committee approval was required. The registry included 755 947 patients with AMI, among whom EF was reported in 42 504, and 8287 (19.5%) of them presented EF below 40%. Finally, we included 7647 consecutive patients hospitalized between January 2018 and December 2019 and discharged alive with LVEF below 40%.

**Statistical analysis** Categorical variables were presented as percentages. Normally distributed continuous variables were expressed as mean (SD), and those with distribution other than normal—as median (interquartile range [IQR]).

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**TABLE 1** Drugs received by the study patients (n = 7647) at discharge

Drug	Patients, %
ASA	95.9
P2Y12 inhibitor	86
Anticoagulants (oral or LMWH) <sup>a</sup>	22.4
Nitrates	8.1
β-Blocker	87.5
ACEI	75.8
ARB	5.9
ARNI	1.4
ACEI, ARB, or ARNI <sup>b</sup>	79.7
MRA	33.2
Ivabradine	3.5
Diuretic	67
Statin	80.9
Fibrate	0.4
Ezetimibe	0.9
Calcium blocker	10.5
α-Blocker	2.3
PPIs	66.5
VKA	4.2
NOAC	11.5
LMWH	7
Insulin <sup>c</sup>	42.4
Oral antidiabetic <sup>c</sup>	47.1
Biguanide (metformin) <sup>c</sup>	28

a Possible use of low-molecular-weight heparin and oral anticoagulants at the same time; therefore, the sum of percentages for oral anticoagulants and low-molecular-weight heparin is greater than that of anticoagulants.

b Possible sequential use of an angiotensin-converting enzyme inhibitor, an angiotensin II receptor blocker, and / or an angiotensin receptor neprilysin inhibitor

c In diabetic patients

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor; ASA, acetylsalicylic acid; LMWH, low-molecular-weight heparin; MRA, mineralocorticoid receptor antagonist; PPI, proton pump inhibitor

**Results and discussion** The mean (SD) age of the study patients was 69.4 (10.8) years, and 71.2% of them were men. On admission, 60.9% of the patients presented with non-ST-segment elevation myocardial infarction, and 39.1% with ST-segment elevation myocardial infarction. A history of AMI was reported in 35.1% of individuals. Among the study patients, 84.3% already underwent percutaneous coronary intervention, whereas 2.1% had coronary artery bypass graft. Before admission, a history of heart failure was present in 24.9% of the patients, among whom 3.5%, 1.3%, and 2.6% were previously implanted with an implantable cardioverter-defibrillator (ICD), a cardiac resynchronization therapy defibrillator (CRT-D), or a pacemaker,

respectively. Furthermore, 21% of the study patients had a history of paroxysmal or persistent atrial fibrillation.

The most frequent comorbidities were hypertension (72.6%), hyperlipidemia (47.6%), diabetes (35.1%), chronic kidney disease (14%), peripheral artery disease (10%), and a history of stroke (8.5%).

Resuscitated cardiac arrest was reported in 4% of the study patients before admission and in 1.4% during hospitalization. A total of 69.6% of the patients presented with Killip class I, whereas 20.1%, 7%, and 3.3% with Killip class II, III, or IV, respectively. On admission or during hospitalization, 2.3% and 2.7% of the patients developed cardiac shock or were treated

for pulmonary edema, respectively. Left ventricular augmentation with an intra-aortic balloon pump was performed in 0.7% of the patients. The degree of left ventricular dysfunction (Killip class) as part of the ANIN risk score seemed to be a crucial predictor of long-term all-cause and cardiovascular mortality.<sup>6</sup>

On admission, sinus rhythm was present in 84.5% of the patients (median [IQR] heart rate, 80 [70–98] bpm).

All patients underwent coronary angiography (the radial approach was used in 79.9% of them). Multivessel disease was diagnosed in a total of 49.4% of the patients and in 81.3% treated with percutaneous coronary intervention, whereas 4.5% and 4.2% were eligible for urgent or elective coronary artery bypass graft, respectively. 12.4% of the patients who were ineligible for coronary intervention received pharmacologic treatment.

During hospitalization, a pacemaker, an ICD, or a CRT-D were implanted in 0.5%, 0.5%, and 0.07% of the patients, respectively.

At discharge, 35.6% of the study patients presented with New York Heart Association (NYHA) functional class I, whereas 48.9%, 13.4%, and 2.1% with NYHA class II, III, or IV respectively. The median (IQR) LVEF was 31% (27%–35%), mean (SD) left ventricular diastolic dimension 55 (10) mm, and severe or mild mitral regurgitation was observed in 2.6% and 11.2% of the patients, respectively.

According to the recent European Society of Cardiology guidelines, patients after AMI with reduced LVEF and HFrEF should receive pharmacotherapy related to AMI, drugs that can alter a history of LVSD, and medication relieving symptoms, indicated for secondary prevention and treatment of comorbidities.<sup>5</sup> Detailed data on pharmacotherapy applied at discharge is shown in TABLE 1.

Registries provide limited data on medication in patients surviving AMI with LVSD or HFrEF. Most of them do not stratify for LVEF,<sup>7</sup> limit inclusion to already established ischemic HFrEF excluding asymptomatic LVSD,<sup>8</sup> or include patients with mixed etiology of HFrEF.<sup>9</sup> Therefore, differences between patient characteristics make comparisons difficult.

The use of  $\beta$ -blockers and angiotensin-converting enzyme inhibitors (ACEIs) is recommended in LVSD or HFrEF.<sup>10</sup> The Portuguese Registry of Acute Coronary Syndromes (Pro-ACS) recruited patients with ischemic HFrEF,<sup>11</sup> but excluded those with a history of HFrEF before AMI, while such patients in our study represented 24.9% of the participants. The clinical characteristics of both populations were similar, except diabetes not reported in the Pro-ACS registry. The comparison of the PL-ACS and Pro-ACS registry data showed that antiplatelet treatment proved to be comparable with

acetylsalicylic acid administration: 95.9% in the PL-ACS registry versus 98.2% in the Pro-ACS registry, and P2Y12 inhibitor use was lower in the PL-ACS registry: 86% versus 98.6%, which was probably related to the difference in the frequency of surgical treatment: 8.7% in the PL-ACS registry versus 0% in the Pro-ACS registry. The use of statins was lower in the PL-ACS registry: 80% versus 93.4%. In the PL-ACS registry compared with the Pro-ACS registry, the frequency of  $\beta$ -blocker and ACEI/angiotensin II receptor blocker (ARB)/angiotensin II receptor neprilysin inhibitor (ARNI) therapy in patients with LVEF less than 40% was 77.7% versus 87.5% and 85% versus 79.7%. The difference in the use of ACEIs/ARBs/ARNIs might be related to inclusion of patients with a history of HFrEF in the PL-ACS registry, although the prevalence of acute HF complicating AMI was similar in both registries. In the QUALIFY survey focusing on HFrEF of various etiologies,  $\beta$ -blockers (96.7%) and any renin-angiotensin-aldosterone system blockers (91.9%) were used more often compared with data from the PL-ACS registry.<sup>12</sup>

Diuretics are recommended to improve symptoms and exercise capacity in HFrEF.<sup>10</sup> Compared with the QUALIFY survey, diuretics were less often used in our study cohort: 67% versus 86%. However, a higher proportion of the QUALIFY survey population was symptomatic, and nearly 90% of those patients presented with NYHA class II or III.<sup>12</sup>

Mineralocorticoid receptor antagonists (MRAs) should be used in symptomatic HFrEF despite treatment with ACEIs/ARBs/ARNIs and  $\beta$ -blockers.<sup>5</sup> In the PL-ACS registry, the Pro-ACS registry, and the QUALIFY survey, the frequency of MRA administration was 33.2%, 35.7%, and 73.2%, respectively.<sup>12</sup> The higher rate of MRA use in the QUALIFY survey may be explained by inclusion of a more symptomatic population with HFrEF (NYHA class: I, 13%; II, 46%; III, 36%; and IV, 5%). The main inclusion criterion for the PL-ACS and Pro-ACS registries was LVEF less than 40%, independently of symptoms.<sup>9</sup>

The same difference in patient characteristics may explain the variability of ivabradine use. Ivabradine is recommended in symptomatic patients with LVEF less than or equal to 35%, sinus rhythm, and a resting heart rate higher than or equal to 70 bpm despite treatment with evidence-based drugs.<sup>10</sup> According to the PL-ACS registry and the QUALIFY survey, ivabradine was prescribed in 3.5% and 13.9% of patients, respectively, whereas the proportion of patients on this drug was not reported in the Pro-ACS registry.<sup>11,12</sup>

Lack of reimbursement for ARNIs in Poland accounts for the prescription rate of these drugs reaching only 1.4% in the PL-ACS registry. Following the European Society of Cardiology guidelines, ARNIs are recommended

as replacement drugs for ACEIs in HFrEF still symptomatic despite optimal treatment with an ACEI, a  $\beta$ -blocker, and an MRA.<sup>10</sup>

Implantable cardioverter-defibrillator implantation is recommended in HFrEF (NYHA class II–III) with LVEF less than or equal to 35% after 3 months of optimal medical therapy. In the PL-ACS registry, 25.5% of the patients had HFrEF before ACS, and further 29.8% developed HFrEF during hospitalization (Killip class II–IV). Thus, about half of the patients were free of HFrEF and 29.8% did not complete the required medical treatment. The rate of ICD and CRT implantations in the PL-ACS registry was very low.<sup>10</sup>

**Conclusions** Despite clear recommendations for pharmacologic treatment and device therapy, a still too small proportion of patients surviving AMI with LVEF below 40% and HFrEF or only asymptomatic LVSD do receive such therapy.

## ARTICLE INFORMATION

**CONFLICT OF INTEREST** None declared.

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