Patients with heart failure and reduced ejection fraction: A sub-analysis from the 3-year Coordinated Myocardial Infarction Care Program (KOS-MI) registry

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ABSTRACT

Background: The Coordinated Care Program after Myocardial Infarction (KOS-MI) implemented in Poland has shown significant improvement in patient prognosis, ended in nationwide success, and got international attention. A similar program and methodology may be an attractive option for patients with heart failure (HF).

Aims: This study aimed to analyze whether a similarly structured program would also be beneficial for HF patients after myocardial infarction.

Methods: This is a multicenter retrospective study of 1972 patients hospitalized for MI. Almost half of patients (n = 963, 48.8%) participated in the KOS-MI program. In the total population, 467 patients presented with reduced ejection fraction HF (HFrEF ≤40%), and 237 (50.7%) participated in the program. Major adverse cardiovascular and cerebrovascular events were evaluated at a 3-year follow-up. Multivariate independent risk analysis was performed. We used propensity score matching for participants and non-participants in the KOS-MI program, resulting in 127 pairs.

Results: A 3-year follow-up (completed by 93% of patients), there was a 57% reduction in major adverse cardiovascular and cerebrovascular events (HR, 0.43; 95% CI, 0.31–0.6; *P* <0.001), 67% in mortality (HR, 0.33; 95% CI, 0.22–0.5; *P* <0.001), and 42% in hospital admissions for HF (HR, 0.58; 95% CI, 0.4–0.9; *P* <0.007) in the KOS-MI patients. There was no difference in the occurrence of MI (HR, 0.71; 95% CI, 0.37–1.34; *P* = 0.29), stroke (HR, 0.9; 95% CI, 0.18–4.45; *P* = 0.89), and repeated revascularization (HR, 0.6; 95% CI, 0.34–1.05; *P* = 0.07). Following propensity score matching 127, well-matched pairs between groups were created. Following adjustment, there was a statistically significant reduction in the risk of death (HR, 0.02; 95% CI, 0.29–0.89; *P* = 0.02) while other parameters were similar.

Conclusions: The KOS-MI program significantly improved HFrEF patients' prognosis up to 3 years post-treatment, even after its cessation after one year. Thus, implementing a dedicated comprehensive care program for HF patients is warranted.

Key words: cardiac rehabilitation, heart failure, myocardial infarction

WHAT'S NEW?

The Coordinated Care Program after Myocardial Infarction (KOS-MI) confirmed its success as a secondary prevention for patients after myocardial infarction. In the group of patients participating in KOS-MI with concomitant heart failure (HF), we noticed a 57% reduction in major adverse cardiovascular and cerebrovascular events, 67% in mortality, and 42% in hospital admissions for HF in three-year follow-up, even though participation in the program ends after one year. Creating another program, dedicated to HF patients, similar to KOS-MI, may be a beneficial solution for this group of patients.

INTRODUCTION

Heart failure (HF) affects 26 million people worldwide while in Poland in 2013–2018 almost 1.7 million people had HF, which is a growing medical and public health need [1, 2]. Rehabilitation is recommended both for patients after a heart attack and for patients with HF [3, 4]. In a cumulative report focusing on populations ≥60 years old, regular exercise has shown a 25%–40% reduction in the risk of cardiovascular disease mortality and 22%–35% reduction in all-cause mortality [5]. In 2017, the National Health Fund and the Ministry of Health introduced the Coordinated Care in Myocardial Infarction Program (KOS-MI) for patients after MI [6]. The results of the 3-year follow-up showed significant benefits for patients participating in this program [7]. Promising results prompted us to analyze whether a similarly structured program might also be beneficial for HF patients after MI.

METHODS

This is a multicenter, retrospective, observational study of 2084 patients admitted to the American Heart of Poland centers with a diagnosis of acute MI between November 1, 2017 to November 14, 2018. The study methodology was published previously [7]. Briefly, 112 patients were excluded from the cohort: 93 were transferred to the intensive care unit (ICU), and 21 died during hospitalization. The final analyzed population comprised 1972 patients, with 963 (48.8%) participating in the KOS-MI program. MI was diagnosed according to the third universal definition [8], while HF with reduced ejection fraction (HFrEF) was defined as EF ≤40% following ESC guidelines [3].

Of 1972 patients, 467 (23.7%) presented with HFrEF, and 237 (50.7%) were enrolled in the KOS-MI program (KOS-HF). All patients in the KOS-HF group participated in rehabilitation and completed the one-year program. The control group (nKOS-HF) comprised 230 (49.3%) patients with HFrEF not participating in the KOS-MI program (Figure 1).

The primary endpoint was the occurrence of major adverse cardiac and cerebrovascular events (MACCE) including all-cause mortality, repeated MI, repeated revascularization, and stroke. The secondary endpoint was hospitalization for HF decompensation.

The KOS-MI Program incorporated 4 modules. The first module consisted of treatment of the MI and coordinating visits. The second involved daily or stationary rehabilitation. Electrotherapy constituted the third module. The last module involved a minimum of 3 consultations with a cardiologist in the Center and a final evaluation of care on the last visit [7, 9]. Standard medical information was gathered from the hospital's information system and the KOS-MI records. Long-term observation data were obtained from the National Registry of Acute Coronary Syndromes (PL-ACS) based on the National Health Fund Data.

The study protocol was compatible with the ethical guidelines of the 1975 Declaration of Helsinki and is part of a larger analysis approved by the Ethics Committee of the Beskid Medical Chamber in Bielsko-Biala (no. 2020/11/5/2).

The data were subjected to censorship from March 15, 2021, with the median observation time being showcased in the results.

Statistical analysis

Numerical data were expressed as means and standard deviations. Categorical data were presented as absolute numbers and percentages. The χ^2 test was used for the comparison of categorical data and student's t-test or the Mann–Whitney test were used for numerical data depending on the distribution. Survival and event-free survival curves were estimated using Kaplan–Meier survival analysis with a log-rank test for the comparison of curves. A *P*-value of 0.05 or less was considered statistically significant. Multivariate independent risk analysis and regression logistic model were performed. Statistica (v. 10; StatSoft. Inc. US) and MedCalc v. 18.5 (MedCalc. Belgium) were used for statistical analyses.

Propensity score matching and survival analysis were performed in R 4.3.1 using the MatchIt and survival packages respectively [10, 11]. The variables for analysis were selected based on their significant associations with the primary study endpoints, including clinical and demographic data impacting patient prognosis, such as medical procedures, comorbidities, and patient characteristics. These variables are listed in Figure 2. Due to the limited sample size, 1:1 nearest neighbor matching without replacement was selected as the matching method. A 0.10 caliper was chosen due to the resulting balance and the number of matched pairs. Data with missing values were removed from the analysis. The balance of the matched set was evaluated by the absolute standardized mean difference visualized by a love plot. Hazard ratios were calculated using the Cox proportional hazards model.

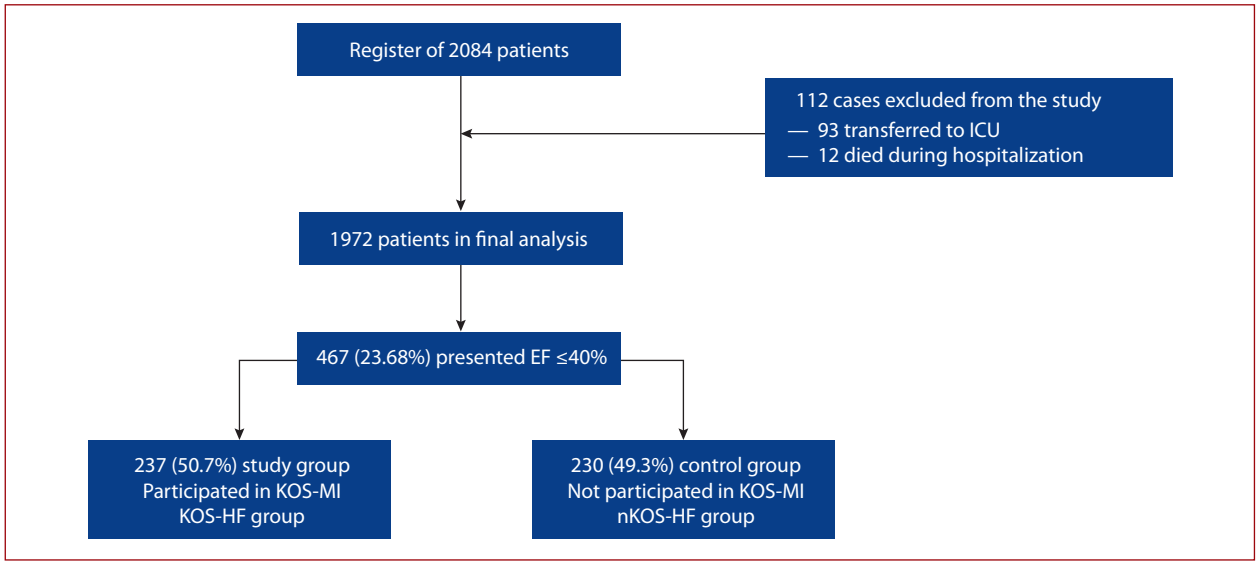

Figure 1. Study flowchart

Abbreviations: EF, ejection fraction; ICU, intensive care unit; KOS-MI, Coordinated Myocardial Infarction Care Program

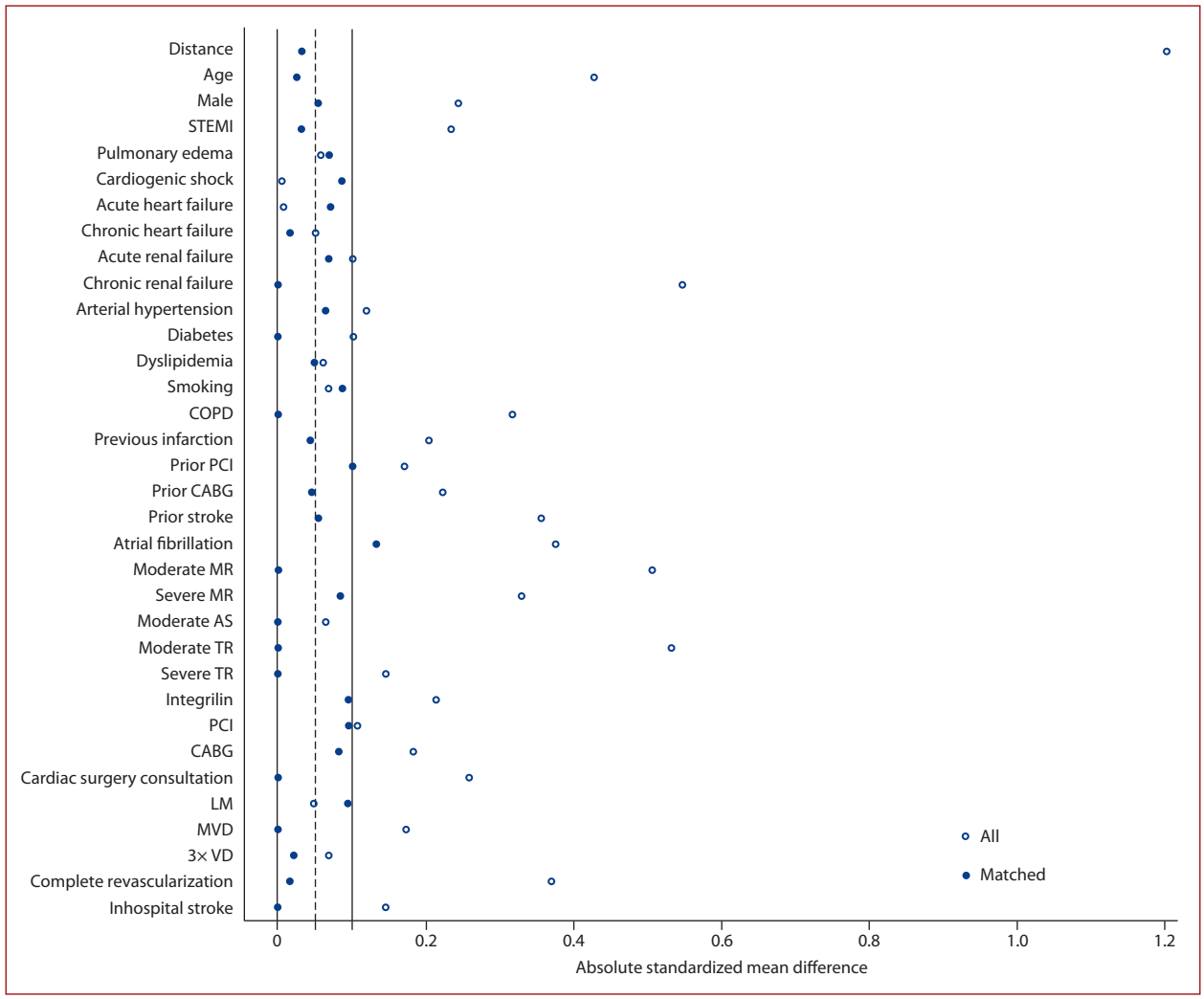

Figure 2. Love plot showing the resulting balance of covariates after propensity score matching

Abbreviations: AS, aortic stenosis; CABG, coronary artery bypass graft surgery; COPD, chronic obstructive pulmonary disease; LM, left main coronary artery; MR, mitral regurgitation; MVD, multivessel disease; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; TR, tricuspid regurgitation; 3 × VD – triple vessel disease

Table 1. Comparison of demographic and clinical characteristics between the HF-KOS and nHF-KOS groups

	HF-KOS n = 237	HF-nKOS n = 230	*P*-value
Age, mean (SD)	65.8 (11.5)	70.9 (10.3)	<0.001
Male, n (%)	179 (75.5)	154 (66.9)	0.04
STEMI, n (%)	142 (59.9)	104 (45.2)	0.001
NSTEMI, n (%)	95 (40.1)	126 (54.8)	0.001
Killip III, n (%)	3 (1.3)	7 (3)	0.18
Killip IV, n (%)	8 (3.4)	8 (3.5)	0.95
Acute heart failure, n (%)	12 (5.1)	15 (6.5)	0.50
Congestive heart failure, n (%)	88 (37.1)	84 (36.5)	0.89
Ejection fraction, mean (SD)	35,4 (6.2)	34,8 (6.2)	0.29
Acute kidney injury, n (%)	3 (1.3)	6 (2.6)	0.29
Chronic kidney disease, n (%)	14 (5.9)	42 (18.3)	<0.001
Hypertension, n (%)	140 (58.7)	148 (64.4)	0.21
Diabetes mellitus, n (%)	67 (28.3)	76 (33)	0.26
Dyslipidemia, n (%)	151 (63.7)	147 (63.9)	0.96
Smoking, n (%)	37 (15.6)	33 (14.4)	0.70
COPD, n (%)	5 (2.1)	14 (6.1)	0.03
Prior MI, n (%)	35 (14.8)	52 (22.6)	0.03
Prior PCI, n (%)	26 (10.9)	38 (16.5)	0.08
Prior CABG, n (%)	7 (2.9)	16 (6.9)	0.05
History of stroke, n (%)	5 (2.1)	16 (6.9)	0.01
Atrial fibrillation, n (%)	24 (10.1)	48 (20.9)	0.001

Abbreviations: CABG, coronary artery bypass graft surgery; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction; SD, standard deviation

Table 2. Angiographical characteristics

	HF-KOS n = 237	HF-nKOS n = 230	*P*-value
Coronary angiography, n (%)	237 (100)	218 (94.8)	<0.001
PCI, n (%)	208 (87.8)	186 (80.9)	0.04
CABG, n (%)	21 (8.9)	15 (6.5)	0.34
LM disease, n (%)	30 (12.7)	33 (14.4)	0.59
Multivessel disease, n (%)	145 (61.2)	165 (71.9)	0.01
Complete revascularization after two stages, n (%)	130 (54.9)	86 (37.3)	<0.001

Abbreviations: LM, left main coronary artery; other — see Table 1

RESULTS

The baseline detailed demographic and clinical characteristics were divided into the study group (KOS-HF) and the control group (nKOS-HF) (Table 1). Mean (standard deviation) ejection fraction (EF) measured on admission in the HF-KOS group was 35.4% (6.2) vs. 34.8% (6.2) in the nKOS-HF group. A comparison of the groups in terms of angiographical data is shown in Table 2.

In multivariable analysis, KOS-MI participation independently decreased mortality in the HF patients (OR, 0.31; 95% CI, 0.2–0.5; *P* <0.001) (Figure 3).

At 1-year follow-up, we observed a significant difference between the groups, nKOS-HF vs. KOS-HF, in the occurrence of MACCE (HR, 0.58; 95% CI, 0.34–0.99); mortality was close to significance (HR, 0.5; 95% CI, 0.23–1.08). There was no significant difference in the occurrence of MI (HR, 0.63; 95% CI, 0.24–1.62), HF decompensation (HR, 0.68; 95% CI, 0.39–1.20), or repeated revascularization (HR, 0.75; 95% CI, 0.33–1.72). These results were obtained using one-dimensional models on the groups after propensity score matching.

At year three, the follow-up was complete in 93%. The median observation time was 2.8 years (interquartile range 2.6–3.1). There was a significant difference between the groups, nKOS-HF vs. KOS-HF, in the occurrence of MACCE (43.1% vs. 22%; *P* <0.001), death (30.4% vs. 11.5%; *P* <0.001), and HF decompensation (28.9% vs. 18.5%; *P* = 0.007). There was no significant difference in the occurrence of MI (10.3% vs. 7.5%; *P* = 0.29), repeated revascularization (14.2% vs. 8.8%; *P* = 0.07), or stroke (1.5% vs. 1.3%; *P* = 0.89) (Figure 4).

Following propensity score matching, 254 patients were selected, forming 127 well-matched pairs, with a standardized difference of fewer than 10% in each studied parameter. The absolute standardized mean difference for each covariate between the KOS treatment groups is presented with a love plot (Figure 2).

At three years, there was a statistically significant lower risk of death (HR, 0.52; 95% CI, 0.29–0.89; *P* = 0.02) while there was a trend toward lower MACCE occurrence (HR, 0.6; 95% CI, 0.4–0.9; *P* = 0.11). There was no statistically significant difference in the occurrence of HF decompen-

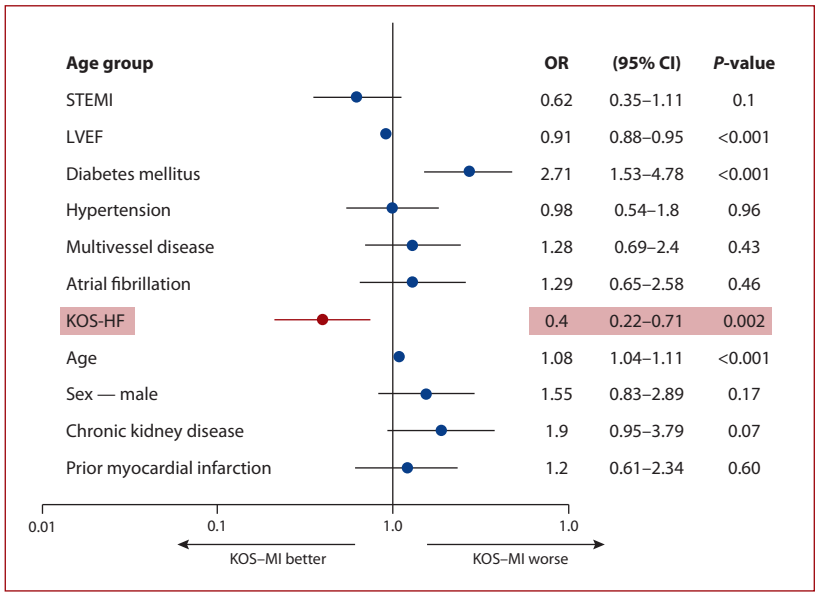

Figure 3. Independent predictors of mortality — multivariate analysis

Abbreviations: CI, confidence interval; LVEF, left ventricular ejection fraction; OR, odds ratio; other — see Figures 1 and 2

sation (HR, 0.74; 95% CI, 0.46–1.17; $P = 0.73$), MI (HR, 0.79; 95% CI, 0.38–1.65; $P = 0.97$), repeated revascularization (HR, 0.65; 95% CI, 0.33–1.28; $P = 0.81$), or stroke (HR, 1; 95% CI, 0.06–16.04; $P = 1$) (Table 3). Kaplan–Meier survival analysis for matched data is presented in Figure 5.

DISCUSSION

In a sub-analysis of the KOS-MI registry [7], involving post-MI patients with HF with reduced ejection fraction on admission, participation in the coordinated care program led to a significant 48% reduction in mortality after 3 years. However, other endpoints like MI incidence and HF-related hospitalization, while initially reduced, lost statistical significance after propensity score matching and reducing the sample size.

The KOS-MI Program was created for patients after MI to coordinate and provide comprehensive patient care. Many publications focusing on the Coordinated Care in Myocardial Infarction Program confirmed that the prognosis of patients participating in this program was better than in the non-participating group [7, 12–15]. Kubielas et al. [12] conducted a survival analysis on 180 000 post-MI patients, with 13.6% being part of the KOS-MI Program. Their results showed a 29% reduction in one-year mortality among program participants [12]. Wita et al. [13] showed that KOS-MI improves prognosis by boosting cardiac rehab participation, lowering MACCE, achieving full revascularization, and increasing ICD implantation rates. Further analysis demonstrated a 45% reduction in MACCE at 3-month follow-up [14], and 2-year data on MI patients indicated a 30% risk reduction in mortality and 14% for MACCE [15]. Over three years, KOS-MI participants experienced significant benefits, including a 25% reduction in MACCE ($P = 0.008$), a 38% decrease in mortality ($P = 0.008$), a 28% decline in hospital admissions for HF ($P = 0.049$), and a 29% decrease in repeated revascularization ($P = 0.04$) [7].

EF is an important factor for HF patients, and it can significantly affect the outcomes of individuals who have undergone revascularization procedures after experiencing a MI [16]. The European Society of Cardiology recommends exercise training (class I) for MI and HF, backed by evidence of enhanced exercise capacity in HFrEF patients [3, 4]. Our study aimed to determine if patients with HFrEF (≤40% LVEF) participating in KOS-MI also experienced substantial program benefits. Despite the program's focus on post-MI patients, our results indicate that those with concurrent HFrEF experienced a 57% MACCE reduction, a 67% decrease in mortality, a 30% reduction in recurrent MI, and a 42% drop in HF hospitalization. These outcomes are particularly impressive, considering the program's discontinuation after one year.

Several studies have underscored the importance of post-MI care in improving HF outcomes. Niedziela et al. [17] found a significant 48% reduction in readmissions over three years with a comprehensive post-MI care program in their KOS-MI registry sub-analysis. Gąsior et al. [18] demonstrated a 25% increase in overall survival and a 29% reduction in readmissions by implementing managed care strategies after acute MI.

Currently, Poland lacks a program dedicated to HF patients. According to the Polish Society's 2016 report, only one in 22 HF patients are rehabilitated [19]. Studies confirm cardiac rehabilitation benefits for HF patients, such as reducing mortality and rehospitalization rates. Early initiation after cardiovascular events also lowers rehospitalization and MI risk in 1–2 years. However, rehabilitation is underutilized globally, particularly exercise training [20–22]. Meta-analyses confirmed the exercise-biomarker link in HF, highlighting the role of exercise in the reduction in N-terminal pro B-type natriuretic peptide (NT-proBNP) levels [25, 26]. In Conraads' study, combined exercise training over four months was linked to a significant NT-proBNP

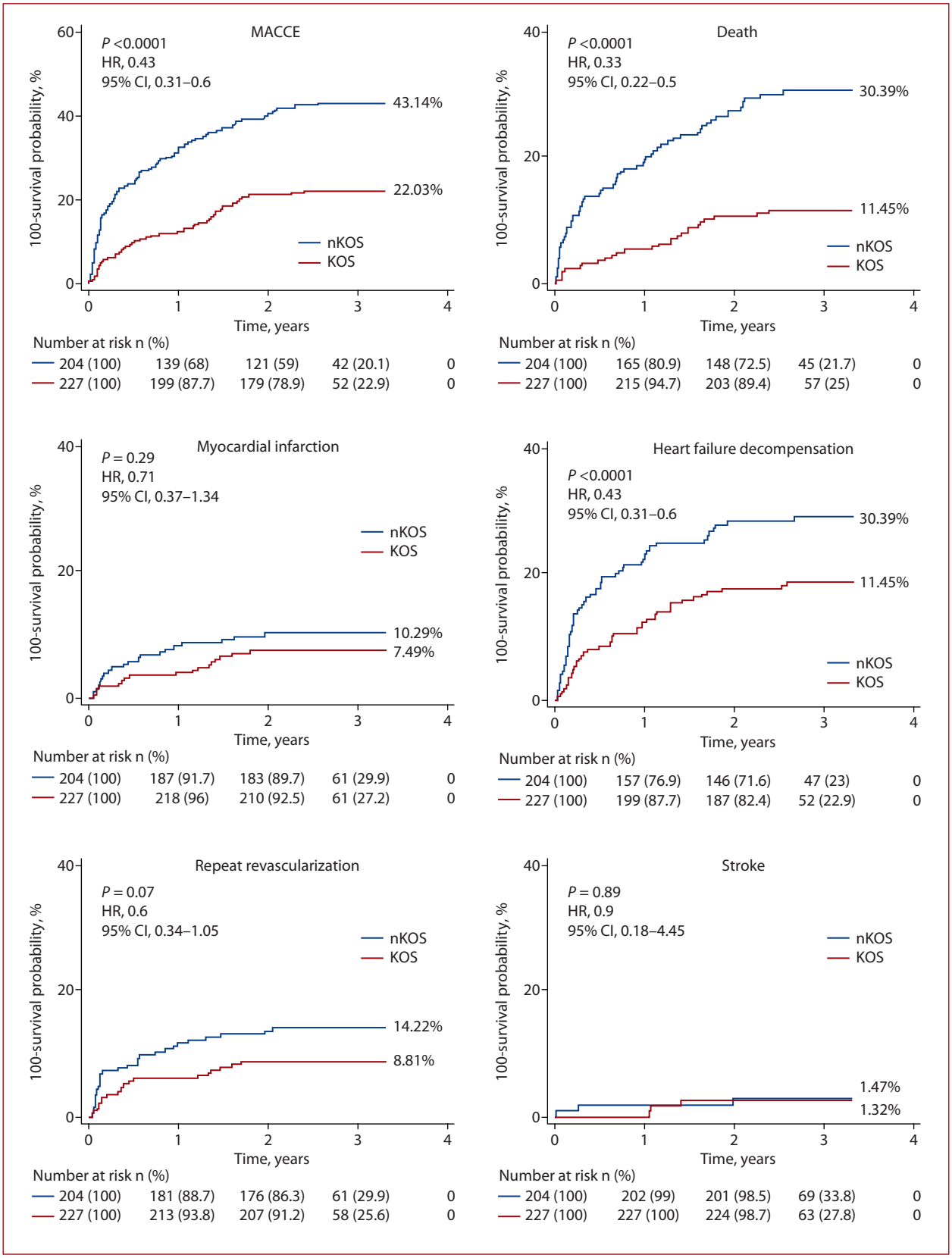

Figure 4. Three-year outcomes in the unadjusted population. Kaplan–Meier analyses with a low-rank test. **A.** Major adverse cardiac and cerebrovascular events (MACCE). **B.** Overall survival. **C.** Heart failure hospitalization. **D.** Recurrent myocardial infarction. **E.** Repeated revascularization. **F.** Stroke

Table 3. Propensity score matching results

	HF-KOS n = 127, n (%)	HF-nKOS n = 127, n (%)	HR	95% CI	*P*-value
MACCE	36 (28.3)	47 (37)	0.6058	0.3993–0.9192	0.11
Death	19 (15)	34 (26.8)	0.5167	0.2991–0.8926	0.02
HF	32 (25.2)	33 (25.9)	0.7398	0.4648–1.178	0.73
MI	13 (10.2)	13 (10.2)	0.7945	0.3822–1.652	0.97
RR	14 (11)	15 (11.8)	0.6493	0.3302–1.277	0.81
Stroke	1 (0.8)	1 (0.8)	1.003	0.06277–16.04	1

Abbreviations: HF, heart failure; MACCE, major adverse cardiac and cerebrovascular events; MI, myocardial infarction; RR, repeated revascularization

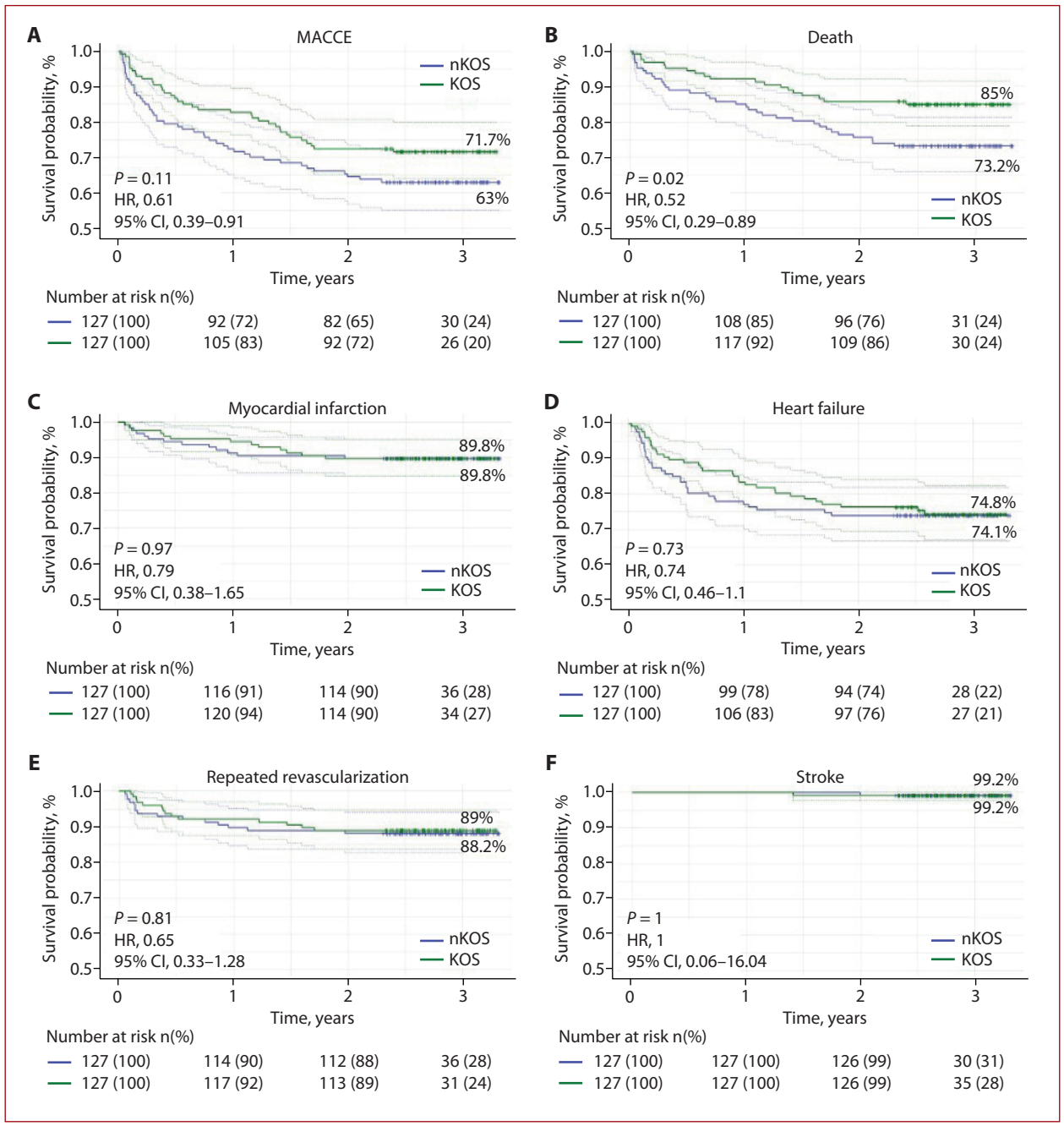

Figure 5. Propensity score matching — Kaplan–Meier survival analysis. **A.** Major adverse cardiac and cerebrovascular events (MACCE). **B.** Overall survival. **C.** Recurrent myocardial infarction. **D.** Heart failure hospitalization. **E.** Repeated revascularization. **F.** Stroke-free survival

level reduction without adverse remodeling effects [23]. Comparing endurance-resistance training with endurance training in post-PCI HF patients, both were safe and reduced NT-proBNP levels vs. standard care [24].

Haddadzadeh et al. [27] showed in a trial that personalized cardiac rehabilitation beginning one month after MI discharge notably improved EF over 12 months. Establishing interdisciplinary coordinated care for multifaceted HF symptomatology demands a multidisciplinary approach [28]. Lee et al. [29] highlighted that early integrated treatment significantly lowers mortality compared to primary care without physician consultation (HR, 0.75; 95% CI, 0.64–0.87; P <0.001) [29].

Recent studies indicate that both palliative and interdisciplinary care approaches for HF patients enhance their quality of life and reduce the use of healthcare resources [30]. Approximately 25% of patients discharged after HF are readmitted within 30 days, placing a burden on individuals and healthcare systems alike [31]. The New Hanover Regional Medical Center aimed to reduce the rate of 30-day HF patient rehospitalization through coordinated care and achieved positive outcomes by expanding services [32]. Day-care HF units appear to be an efficient choice for patients with recurrent HF-related hospitalization, offering the potential to improve outcomes and reduce healthcare costs for insurers [33]. Krishna [34] indicated that a multispecialty team model confers greater benefits than isolated service provision. Mizukawa et al. [35] found that collaborative management outperformed self-management education and usual care. Collaborative management led to better quality of life, lower readmission rates (20% vs. usual care 57.9% and self-management education 27.8%), and improved rehospitalization-free survival (P = 0.02). In contrast, Koutlas et al. [36] noted in their coordinated care study a 62% decrease in admissions and a 73% reduction in hospital stay duration for HF patients (n = 47; P <0.001), which also led to economic savings for the healthcare facility. The Australian SHAPE study highlighted the role of general practitioners in enhancing care for HF patients [37] and recognized cardiac rehabilitation for its significant contribution to coordinated care [38]. Telemedicine enhances multidisciplinary care by improving coordination, timely delivery, and follow-up, enabling comprehensive patient management for better outcomes [39].

Poland had 750 000 HF patients before 2020, and this number was expected to increase to 1.2 million (25% rise). To address post-hospitalization care gaps and improve patient supervision, Polish cardiology experts introduced the KONS holistic care model. It aims to detect HF early, slow its progression, and enhance patient quality of life by integrating outpatient care, interventions, medications, rehabilitation, and telemedicine. Coordinating physicians create personalized pre-discharge plans to bridge gaps, manage the growing patient population, and enhance HF care in Poland [40]. We believe that implementing KONS, dedicated to managing HF regardless of concurrent MI, could greatly improve prognosis. Combining tailored rehabilitation, regular cardiological consultations and as-needed visits will improve early symptom detection and treatment adjustments such as diuretic dosing.

CONCLUSIONS

The results of our analysis showed improved prognosis in patients with HFrEF up to 3-year follow-up, particularly all-cause mortality, despite program termination at 12 months. Further exploration on a larger sample group is necessary, also in patients with HF with preserved ejection fraction (HFpEF ≥50%) and those with HF with mid-range ejection fraction (HFmrEF 41%–49%). Given the above finding, we believe that a program modeled on the KOS-MI program should be implemented for HF patients.

Article information

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