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Characteristics, management and outcome of patients with late-arrival STEMI in the Acute Coronary Syndrome Israeli Surveys (ACSIS)

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ABSTRACT

Introduction: Patients with ST-elevation myocardial infarction (STEMI) and late arrival (>12 h) after symptom onset, are at high risk for mortality and heart failure and represent a challenge for management. We aimed to define patient characteristics, management, and outcome of late-arrival STEMI in Israel over the last 20 years.
Methods: We analyzed data of late-arrival STEMI (12–48 h and > 48 h) from the biennial acute coronary syndrome Israeli Surveys (ACSIS), as well as time-dependent changes [early (2000–2010) Vs. late (2013–2021) period].
Results: Data regarding time from symptom onset to hospital arrival was available in 6,466 STEMI patients. Of these, 9.6 % arrived 12–48 h and 3 % >48 h from symptom onset. Late-arrival patients were more likely to be older women with diabetes and high GRACE score and less likely to have prior myocardial infarction.
In recent years, 95 % of patients arriving 12–48 h and 96 % of those arriving > 48 h had coronary angiography, as opposed to 75 % and 77 % in the early years ($p = 0.007$). Percutaneous coronary intervention (PCI) increased from 60 % and 55 % respectively to 85 % ($p \leq 0.001$).
TIMI-3 flow after primary PCI was 89–92 %, irrespective of arrival time. Late arrival patients (12–48 h but not > 48 h) who had PCI had better adjusted 1-year survival, HR 0.49 (95 %CI 0.29–0.82), $p = 0.01$.
Conclusions: Late-arrival STEMI patients have higher risk characteristics. Most late-arrival patients undergo coronary angiography and PCI and have TIMI-3 flow after primary PCI. In patients arriving 12–48 h after symptom onset PCI is associated with better survival.

1. Introduction

The main intervention to reduce mortality and complications in ST-elevation myocardial infarction (STEMI) is myocardial reperfusion using primary percutaneous coronary intervention (PCI). Since myocardial injury is a function of ischemia time, there is paramount importance in delivering reperfusion as early as possible. In the era of primary PCI, in-hospital mortality in STEMI patients varies between 4 and 12 % and reported 1-year mortality 11 % [1–4]. The prognosis of STEMI patients is dependent on many factors including age, left ventricular function, treatment strategy and complications, but most importantly on time to reperfusion.

Pre-hospital delay is the most important factor delaying time to reperfusion. In the United States, about 6 % of elderly patients are admitted to hospitals more than 12 h from symptom onset of acute myocardial infarction (MI) [5]. In Veterans it can reach up to 68 % of the patients [6]. Primary PCI is recommended in patients with STEMI presenting within 12 h of symptom onset [7,8]. For patients presenting later than 12 h from symptom onset, primary PCI is also recommended if there is clinical or electrocardiographic evidence of ongoing ischemia.

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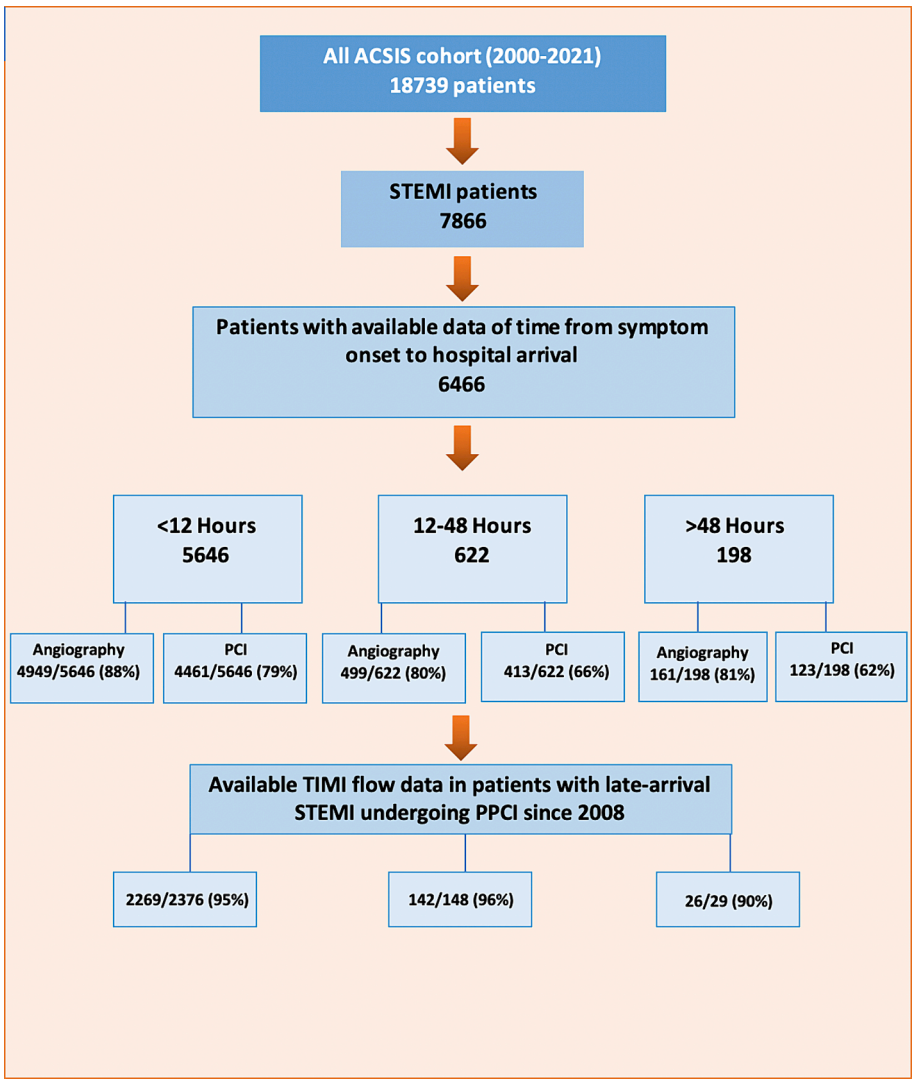

Fig. 1. Study population flowchart. ACSIS = Acute Coronary Syndrome Israeli Surveys, PCI = percutaneous coronary intervention, PPCI = primary PCI, STEMI = ST elevation myocardial infarction.

Based on the evidence from the Occluded Artery Trial (OAT), routine PCI of an occluded infarct-related artery in patients presenting with STEMI > 48 h after symptom onset is not indicated, in the absence of ongoing chest pain [8,9].

In patients presenting 12–48 h from symptom onset without evidence of ongoing ischemia, there is no consensus as to whether PCI is beneficial. The BRAVE-2 study showed improved myocardial salvage and 4-years survival with primary PCI compared with conservative treatment alone in this group [10,11]. The BRAVE-2 study had limitations. It was started in 2001 and had a relatively small sample size (n = 347). Observational data from the FAST-MI (French Registry of Acute ST-elevation and non-ST-elevation Myocardial Infarction) in patients with STEMI presenting within 12–48 h, showed a significant lower rate of all-cause death at 1 month (2.1 % vs. 7.2 %) and after a median follow-up of 58 months (30.4 Vs. 78.7 per 1000 patient-years) with an invasive strategy in comparison to conservative treatment [12,13]. The European society of cardiology (ESC) guidelines recommend that primary PCI should be considered in patients presenting 12–48 h after symptom onset [8]. However, the American college of cardiology/American heart association (ACC/AHA) guidelines consider PCI in stable late-arrival (>24 h) STEMI patients none-beneficial [7].

There is little real-life data regarding the utility of coronary angiography and PCI in late arrival STEMI. The aim of this study was to determine patient characteristics, management and outcome in late arrival STEMI, and to compare outcomes of late arrival patients who had coronary angiography and PCI with those who didn't, using a large Israeli national database spanning more than 20 years.

2. Methods

The current study included all consecutive patients from the acute coronary syndrome (ACS) Israeli Surveys (ACSIS) conducted between 2000 and 2021, who presented with STEMI and had data regarding time from chest pain onset to hospital admission. The ACSIS registry is a biennial prospective survey enrolling consecutive patients from all 26 coronary care units operating in Israel over a 2-month period [14]. Data were recorded on prespecified case report forms for all admitted patients diagnosed with ACS. Informed consent was obtained from all patients. The institutional review board (IRB) of all participating hospitals approved the survey, which was performed according to the Helsinki Declaration. The pre-specified demographic, cardiovascular risk factors, co-morbidities, medications, and clinical data were recorded along with admission and discharge diagnoses as defined by the attending physicians based on clinical, electrocardiographic, and biochemical criteria. To better understand the management and outcomes of patients with late-arrival STEMI, we compared data from two time periods: early

Table 1
Patient characteristics.

	<12 h(n = 5,646)	**12–48 h(** n = 622)	**>48 h(** n = 198)	**P for trend**
Age (y)	60 [52–70]	63 [53–73]	64 [55–73]	<0.001
Gender (male)	4592 (81.3)	469 (75.4)	149 (75.3)	<0.001
Diabetes mellitus	1612 (28.6)	204 (32.9)	84 (42.4)	<0.001
Hypertension	2709 (48.1)	331 (53.3)	113 (57.1)	0.001
Current smokers	2722 (48.4)	275 (44.4)	72 (37.1)	<0.001
Family history of CAD	1415 (26.3)	124 (20.7)	42 (22.2)	0.004
Prior MI	1168 (20.7)	97 (15.6)	27 (13.8)	<0.001
Prior PCI	1036 (18.4)	65 (10.5)	16 (8.1)	<0.001
Chronic renal failure	332 (5.9)	40 (6.4)	14 (7.1)	0.393
s/p CVA/TIA	338 (6.0)	40 (6.4)	16 (8.1)	0.244
GRACE score > 140	5.6 %	7.4 %	11.5 %	0.006
Self-evacuation	1750 (31.1)	281 (45.4)	101 (51.0)	<0.001
Time from CP onset to admission (hours)	2.2 [1.3–3.5]	20.4 [15.1–27.7]	74.1 [54.1–103.3]	<0.001
Vital signs on FMC				
Admission Killip ≥ 2	779 (14.0)	88 (14.4)	31 (15.8)	0.48
Heart rate	77 [65–90]	80 [68–95]	81 [70–97]	<0.001
Systolic blood pressure	138 [120–157]	137 [117–154]	139 [119–157]	0.57
LVEF class (%)				
NORMAL (LVEF > 50 %)	1620 (33.4)	145 (27.4)	50 (29.1)	0.009
MILD (LVEF 40–50 %)	1759 (36.2)	193 (36.5)	66 (38.4)	0.616
MODERATE (LVEF 30–40 %)	1115 (23.0)	139 (26.3)	43 (25.0)	0.127
In-hospital complications				
CHF mild-moderate (Killip-2)	597 (10.6)	68 (11.0)	23 (11.7)	0.601
Pulmonary edema (Killip-3)	334 (5.9)	46 (7.4)	17 (8.6)	0.041
Post MI angina/re-ischemia	229 (4.1)	42 (6.8)	20 (10.2)	<0.001
New atrial fibrillation	338 (6.0)	47 (7.6)	19 (9.6)	0.013
High degree (2-3o) AVB	211 (3.7)	30 (4.8)	14 (7.1)	0.009

AVB = atrioventricular block, CAD = coronary artery disease, CHF = congestive heart failure, CP = chest pain, CVA = cerebrovascular accident, FMC = first medical contact, LVEF = left ventricular ejection fraction, MI = myocardial infarction, PCI = percutaneous coronary intervention, TIA = transient ischemic attack.

(2000–2010) and late (2013–2021). Specifically, we compared patients who arrived within 12 h to those who arrived between 12–48 h or over 48 h. Data regarding coronary angiography, PCI (both primary and late) and TIMI flow in the infarct-related artery before and after primary PCI were recorded. Clinical outcomes included 30-day major adverse cardiovascular events (MACE) and 1-year all-cause mortality. MACE included 30 days death, ACS including stent thrombosis, stroke and urgent revascularization. Data regarding outcomes were determined by hospital chart review, telephone contact, clinical follow-up, and by matching identification numbers of patients with the Israeli National Population Registry (for 30-day and 1-year mortality).

2.1. Statistical Methods

Patient characteristics were presented as n (%) for categorical variables and median [IQR] for normal/non-normal distributed continuous variables. A chi-square test for trend was used for comparison of categorical variables. Analysis of variance with 1 degree of freedom was performed for comparison of normally distributed continuous variables, and Kendall rank correlation, for non-normal distribution. For comparisons of 2 groups (yes vs. no angiography, etc.), a chi-square test was used for categorical variables and *t*-test or Mann–Whitney–Wilcoxon test as appropriate for normal/nonnormal distributed continuous variables.

To assess relationship between study groups and outcomes, multivariable logistic regression model was performed for the outcome of 30-day MACE, and a Cox proportional hazards model for 1-year mortality, adjusted for clinically relevant covariates with $p < 0.05$ in the univariable tests. Interaction between periods and study-groups was assessed.

Table 2
Rate of coronary angiography and PCI in late arrival STEMI.

Study groups	**<12 h(** n = 5,646)	**12–48 h(** n = 622)	**>48 h(** n = 198)
Angiography	4949/5646 (87.7 %)	499/622 (80.2 %)	161/198 (81.3 %)
Early period (2000–2010)	3145/3803 (82.7 %)	343/458 (75 %)	116/151 (76.8 %)
Late period (2013–2021)	1804/1843 (98 %)	156/164 (95 %)	45/47 (95.7 %)
Urgent angiography	3357/5646 (59.5 %)	208/622 (33.4 %)	41/198 (20.7 %)
PCI	4461/5646 (79.0 %)	413/622 (66.4 %)	123/198 (62.1 %)
Early period (2000–2010)	2743/3803 (72 %)	273/458 (59.6 %)	83/151 (55 %)
Late period (2013–2021)	1718/1843 (93.2 %)	140/164 (85.4 %)	40/47 (85.1 %)
Primary PCI	3275/5646 (58 %)	202/622 (32 %)	39/198 (19.7 %)
Early period (2000–2010)	1721/3803 (45 %)	91/458 (20 %)	17/151 (11 %)
Late period (2013–2021)	1554/1843 (84 %)	111/164 (68 %)	22/47 (47 %)
Time from arrival to PPCI (minutes)	59 [30–93]	77 [38–144]	65 [40–163]
Time from arrival to angiography in late PCI (hours)	29 [12–66]	23 [8–51]	36 [15–70]

STEMI = ST-elevation MI, PCI = percutaneous coronary intervention, PPCI = primary PCI.
The number of patients in the headline refer to the entire study groups. The number of patients in the early and late periods appear in the denominator in the corresponding rows.

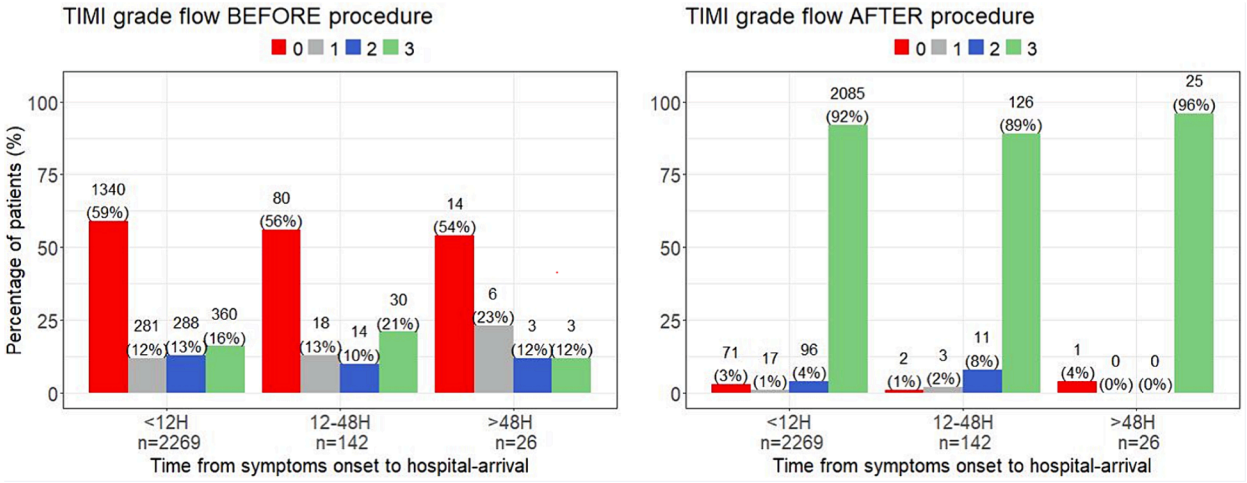

Fig. 2. TIMI flow Before and after primary PCI. PCI = percutaneous coronary intervention.

Table 3
Outcome of late arrival STEMI by management strategy.

		<12 h (n = 5,646)			12–48 h (n = 622)			>48 h (n = 198)		
Angiography		**No** (n = 697)	**Yes** (n = 4,949)	**P value**	**No** (n = 123)	**Yes** (n = 499)	**P value**	**No** (n = 37)	**Yes** (n = 161)	**P value**
	MACE 30 days	194 (27.8)	582 (11.8)	<0.001	38 (30.9)	69 (13.9)	<0.001	12 (32.4)	39 (24.2)	0.41
	1-year mortality	177 (25.6)	304 (6.3)	<0.001	31 (25.2)	36 (7.3)	<0.001	9 (24.3)	14 (8.7)	0.018
PCI		**No** (n = 1185)	**Yes** (n = 4,461)		**No** (n = 209)	**Yes** (n = 413)		**No** (n = 75)	**Yes** (n = 123)	
	MACE 30 days	276 (23.3)	500 (11.2)	<0.001	53 (25.5)	54 (13.1)	<0.001	23 (30.7)	28 (22.8)	0.29
	1-year mortality	223 (19.1)	258 (5.9)	<0.001	39 (18.8)	28 (6.9)	<0.001	12 (16.2)	11 (8.9)	0.5

PCI = percutaneous coronary intervention
"**No**" refers to patient who did not undergo coronary angiography or PCI, and "**Yes**" to patients who did.

Propensity score matching was performed to reduce bias between late-arrival patients who had PCI with those who didn't, using a caliper of 0.04 and 2:1 matching (PCI Vs. no PCI). The following covariates were used to match groups: Age, gender, chronic renal failure, diabetes and study period (2000–2010 Vs. 2013–2021).

Missing values in the included covariates were sparse and were imputed with baseline values. All tests were conducted at a two sided overall 5 % significance level (a = 0.05). All analyses were performed using R (R-studio, V.4.3.2, Vienna, Austria).

3. Results

The ACSIS registry included 18,739 patients enrolled between 2,000–2,021, of which 7,866 presented with STEMI (Fig. 1). Data regarding the time from symptom onset to hospital admission was available in 6,466 patients with STEMI. Of these, 622 (9.6 %) arrived 12–48 h and 198 (3 %) > 48 h from symptom onset. Over the years, STEMI patients were less likely to arrive late: 12–48 h (458/4412 [10.4 %] in 2000–2010 and 164/2054 [8 %] in 2013–2021, p = 0.003. In > 48 h (151/4412 [3.4 %] and 47/2054 [2.3 %]), accordingly, p = 0.017. Overall, 10.3 % of STEMI patients arrive > 12 h from symptom onset in recent years.

Baseline characteristics are summarized in Table 1. Patients presenting late were older, more likely to be females and have diabetes mellitus and hypertension, and less likely to have a history of MI or previous PCI. Late-arrival patients were more likely to arrive to the hospital by a private car and have a higher GRACE score and heart rate, but they had similar Killip class and blood pressure on arrival. Typical angina was present in 493 (79 %) of the patients presenting after 12–48 h and 145 (73 %) in those > 48 h.

Coronary angiography was performed in 80 % of the patients presenting between 12–48 h and 81 % presenting > 48 h, compared to 88 % presenting < 12 h (p for trend < 0.001), Table 2. In the 12–48 h group, PCI was performed in 66 % of the patients, and in 83 % of those who had coronary angiography. In the > 48 h group 62 % had PCI (76 % of those with coronary angiography), compared to 79 % and 90 %, respectively, in the < 12 h group (p for trend < 0.001).

In patients presenting 12–48 h after symptom onset, compared to patients who did not undergo coronary angiography, those who underwent coronary angiography were younger (61 [52–71] Vs. 71 [60–79] years old, p < 0.001), more likely to be males (77.4 % Vs. 67.5 %, p = 0.03), and less likely to have chronic renal failure (4.8 % Vs. 13 %, p = 0.002) and a GRACE score > 140 (4.5 % Vs. 41.4 %, p < 0.001).

The rate of coronary angiography in the 12–48 h group increased over the years from 75 % to 95 % (p = 0.001), and in the > 48 h group from 77 to 96 % (p < 0.007). Similarly, PCI rate increased from 60 % in the 12–48 h group and 55 % in the > 48 h group to 85 % in both groups in later years (p ≤ 0.001), Table 2.

Urgent coronary angiography was performed in 33 % of the patients arriving 12–48 h and in 21 % of the patients arriving > 48 h. Primary PCI was performed in 32 % of the patients arriving in 12–48 h and in 20 % of those arriving > 48 h. The chance of undergoing primary PCI increased over the years from 20 % in the early period to 68 % in the late period in patients arriving 12–48 h, and from 11 % to 47 % in those arriving > 48 h. Of note, the rate of primary PCI in early-arrivals (<12 h) increased over the years as well, from 45 % to 84 %, with the abandonment of thrombolytic therapy.

Data regarding TIMI flow was available since 2008 for patients who had primary PCI (n = 2553), in 2437 (95 %) of those patients (Fig. 1). Preprocedural TIMI-0 flow in the infarct related artery was present in

Table 4
Propensity score matching for late-arrival STEMI 12–48 h.

Variables	No PCI (n = 125)	PCI (n = 250)	P Value
Age (y)	62.00 [53–74]	63 [54–72]	0.545
Gender (male)	93 (74.4)	197 (78.8)	0.407
Diabetes mellitus	40 (32.0)	75 (30.0)	0.782
Current smokers	59 (47.6)	112 (45.0)	0.715
Family history of CAD	22 (18.3)	51 (21.0)	0.650
Prior MI	21 (16.8)	35 (14.0)	0.573
Prior PCI	8 (6.4)	29 (11.6)	0.159
Chronic renal failure	7 (5.6)	16 (6.4)	0.939
s/p CVA/TIA	8 (6.4)	15 (6.0)	1.000
GRACE score > 140	5 (12.5)	5 (3.1)	0.044
Self-evacuation	67 (54.0)	111 (44.8)	0.029
Time from CP onset to admission (hours)	21.50 [15.67–31.00]	19.87 [15.05–26.56]	0.084
Vital signs on FMC			
Admission Killip ≥ 2	16 (12.8)	28 (11.3)	0.797
Heart rate	80.00 [67–95]	80.00 [68–90.50]	0.694
Systolic blood pressure	135.00 [118–155]	135.00 [116–152]	0.931
EF class (%)			
NORMAL (EF > 50 %)	23 (24.2)	57 (26.1)	0.533
MILD (EF 40–50 %)	34 (35.8)	88 (40.4)	0.533
MODERATE (EF 30–40 %)	26 (27.4)	56 (25.7)	0.533
In-hospital complications			
CHF mild-moderate (Killip-2)	19 (15.4)	21 (8.4)	0.059
Pulmonary edema (Killip-3)	9 (7.2)	17 (6.8)	1.000
Post MI angina/re-ischemia	9 (7.3)	15 (6.0)	0.815
New atrial fibrillation	11 (8.8)	19 (7.6)	0.840
High degree (2-3o) AVB	5 (4.0)	16 (6.4)	0.480
30-Day clinical outcomes			
Re-hospitalization	32 (27.4)	29 (12.3)	0.001
MACE	24 (19.4)	36 (14.4)	0.280
Death rates			
30-day mortality	11 (8.9)	12 (4.8)	0.189
1-year mortality	17 (13.8)	16 (6.5)	0.032

AVB = atrioventricular block, CAD = coronary artery disease, CHF = congestive heart failure, CP = chest pain, CVA = cerebrovascular accident, EF = ejection fraction, FMC = first medical contact, MACE = Major adverse cardiac events, MI = myocardial infarction, PCI = percutaneous coronary intervention, STEMI = ST-elevation myocardial infarction, TIA = transient ischemic attack.

54–59 % of patients, irrespective of time of presentation, p = 0.4 (Fig. 2). Similarly, there was no statistically significant difference between groups in the rate of TIMI-3 flow following primary PCI (89 % in patients arriving after 12–48 h, 96 % in those arriving > 48 h and 92 % in patients presenting within 12 h (p = 0.6).

In patients arriving 12–48 h, coronary angiography and PCI (early or late) were associated with significantly lower 30-day MACE and 1-year all-cause mortality, similar to patients arriving < 12 h (Table 3). In patients arriving > 48 h, coronary angiography was associated with better 1-year mortality but not associated with MACE, and PCI was not associated with outcomes, but the number of patients with outcomes in this category was relatively small.

After adjustment for age, gender, study period (2000–2010 Vs. 2013–2021), chronic renal failure, diabetes and left ventricular ejection fraction, PCI (early or late) in patients arriving 12–48 h after symptom onset was associated with a lower 1-year all-cause mortality, HR 0.49 (95 % CI 0.29–0.82), p = 0.01, and 30-day MACE, OR 0.64 (0.40–1.01), p = 0.06 (the later with borderline statistical significance). We repeated this analysis for patients arriving 24–48 h after symptom onset. PCI in this group was associated with a lower 1-year all-cause mortality, HR 0.28 (95 % CI 0.10–0.77), p = 0.02, and 30-day MACE, OR 0.33 (0.15–0.73), p = 0.01, similar to patients arriving 12–48 h after symptom onset.

To further assess the effect of PCI on outcomes in patients arriving 12–48 h after symptom onset we used propensity score matching. Baseline characteristics after propensity score matching of patients who had PCI (n = 250) and those who didn't (n = 125) are presented in Table 4. The two groups were well matched except for a high GRACE score which was less prevalent in the PCI group. After propensity score matching, patients who had PCI (early or late) had a lower 1-year all-cause mortality, (6.5 % Vs 13.8 %), p = 0.03, lower 30-day rehospitalization rate (12.3 % Vs. 27.4 %), p = 0.001, but similar 30-day MACE, (14.4 % Vs. 19.4 %), p = 0.3.

In a logistic regression model adjusted for age, gender, study period (2000–2010 Vs. 2013–2021), chronic renal failure and performance of PCI, late-arrival (>48 h Vs. < 12 h) was associated with worse 30-day MACE, OR 1.78 (95 % CI 1.25–2.49), but similar 1-year mortality, HR 0.98 (95 % CI 0.64–1.49). Late arrival 12–48 h was not associated with worse adjusted outcomes.

4. Discussion

Data regarding the management of patients presenting late after the onset of STEMI is conflicting [15–19]. Our data, derived from a large Israeli database, show that patients with late-arrival STEMI are more likely to be older, females, and have diabetes, in concordance with previous data [20,21]. According to our data, the use of invasive strategy in late-arrival patients increased during the last 20 years. The rate of coronary angiography increased from 75-77 % in the early period to 95–96 % in the later. PCI rate increased from 60 % and 55 % in patients arriving 12–48 h and > 48 h to 85 % in both groups, as did the rate of primary PCI. The association of coronary angiography with better outcomes in late-arrival patients may be, at least partly, the result of selection bias. Patients with comorbidities and poor prognosis were probably less likely to be selected for an invasive approach.

We have shown that procedural success in late-arrival patients undergoing primary PCI, as depicted by TIMI-3 flow after PCI, was excellent (Fig. 2) similar to patients presenting early. These findings are in accordance with our main finding, that patients who arrive 24–48 h after symptom onset and have PCI have better outcome: better adjusted 1-year survival, and lower 30-day MACE, although the later finding had a borderline statistical significance. Interestingly, only 32 % of these

patients underwent primary PCI and the rest had late PCI, although in recent years this number increased to 68 %. Our real-life data is in agreement with previous publications. In the BARVE 2 study patients presenting 12–48 h from symptom onset had better outcome with PCI [10,11]. Similarly, the FAST-MI registry reported better outcome with PCI in patients presenting with STEMI 12–48 h from symptom onset, but patients presenting > 48 h from symptom onset were not included in this study [12]. These data resulted in a IIa recommendation for primary PCI in the 2023 ESC ACS guidelines in patients presenting 12–48 h from symptom onset [8].

We have also shown, that in patients presenting 24–48 h after symptom onset, PCI was associated with lower adjusted 1-year survival and better adjusted 30-day MACE, supporting the ESC guidelines, but not the ACC guidelines which limit their recommendation for PCI to patients presenting within 24 h [7,8].

The correlation between ischemic time and infarct size was first demonstrated in animal models in the 1970 s [22]. These animal studies suggested myocardial survival time of only 6 h, but later, clinical studies in the thrombolysis era demonstrated benefit from revascularization by thrombolysis for up to twelve hours [23,24]. While in animal models the infarct related artery was completely occluded, partial or fluctuating occlusion of the infarct related artery may be present in real life, extending myocardial survival time and accounting for the discrepancy in myocardial survival between studies.

Our results in patients presenting > 48 h stand in concordance with the OAT trial in which the primary outcome at 4 years, death MI or heart failure, did not differ significantly [17.2 % vs 15.6 %, (p = 0.20)] between the PCI and the conservative group [9]. In the OAT study the median time from symptom onset to PCI was 8 days, representing very late revascularization. Steg et al in DECOPI, a small randomized study, reported similar results at 34 months in patients presenting 2–15 days after symptom onset [25]. In contrast, median time from symptom onset to PCI in the > 48 h group in our study was 4 days. The number of patients arriving > 48 h who had outcome events in our study was small, and the analysis therefore was statistically underpowered. Interestingly, despite the results of the OAT trial and current guidelines, rate of coronary angiography and PCI in patients presenting > 48 h increased over the years according to our study. It remains to be seen which patients benefit from such an invasive approach. It is possible that earlier intervention would result in better outcomes, but larger studies are needed to test this hypothesis.

4.1. Study limitations

Our study has several limitations. First, this study is an observational retrospective study with its inherent weaknesses. The indication for primary PCI in late-arrival patients (such as on-going chest pain), especially those presenting > 48 h was unavailable. The number of patients presenting > 48 h was small rendering statistical analysis underpowered for the effect of PCI on outcome. Data regarding cause of death, cardiac versus non-cardiac, was also not available. Finally, TIMI flow data for patients with late (and not primary) PCI was unavailable. Follow up in the ACSIS registry was limited to 1 year, and long-term effect of PCI on survival in our study is unknown.

5. Conclusions

Our real-life data show that Late-arrival STEMI patients have higher risk characteristics, and STEMI patients arriving > 48 h have worse 30-day MACE but similar 1-year mortality, compared to early arrivals. In recent years, late arrival > 12 h decreased to 10 % of all STEMI patients, and most patients, even those arriving later than 48 h, undergo coronary angiography and PCI. TIMI-3 flow after primary PCI is achievable in most late-arrival STEMI patients, similar to early arrivals. Most importantly, PCI performed 12–48 h after symptom onset is associated with lower adjusted 1-year all-cause mortality.

CRediT authorship contribution statement

Moataz Tarabih: Writing – original draft, Investigation. **Tal Ovdat:** Formal analysis. **Basheer Karkabi:** Writing – review & editing. **Maguli S. Barel:** Writing – review & editing. **Mahamid Muhamad:** Writing – review & editing. **Roy Beigel:** Writing – review & editing, Resources, Funding acquisition. **Katia Orvin:** Writing – review & editing, Project administration, Funding acquisition. **Avinoam Shiran:** Writing – review & editing, Validation, Supervision, Resources, Project administration, Methodology, Conceptualization. **Amnon Eitan:** Writing – review & editing, Writing – original draft.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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