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Trends in management and outcome of acute coronary syndrome in women ≥80 years versus those <80 years in Israel from 2000–2016☆,☆☆

Roy Rubinstein [a,c], Shlomi Matetzky [a,c], Roy Beigel [a,c], Zaza Iakobishvili [b,c], Ilan Goldenberg [a,c], Michael Shechter [a,c,*,1], on behalf of the Acute Coronary Syndrome Israel Survey (ACSIS)

[a] Leviev Heart Center, Chaim Sheba Medical Center, Tel Hashomer, Israel
[b] Cardiology Department, Rabin Medical Center, Petah Tiqva, Israel
[c] Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

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ABSTRACT

Background: While women ≥80 years old have a high prevalence of coronary artery disease (CAD), little data exist regarding their outcome following acute coronary syndrome (ACS).
Methods: In a retrospective study based on data of 3518 ACS women patients who were enrolled in the ACS Israel Survey (ACSIS), we first evaluated and compared the clinical outcomes of 858 ACS women ≥80 years with 2660 ACS women <80 years, hospitalized during 2000–2016. Secondly, we evaluated the clinical outcome of 450 women ≥80 years hospitalized during 2000–2006 ('early period') and compared them with 408 ACS women of the same age group hospitalized during 2008–2016 ('late period').
Results: Implementation of the ACS AHA/ACC/ESC therapeutic guidelines was lower in ACS women ≥80 years compared with women <80 years. Multivariate Cox regression analysis demonstrated a worse 1-year survival rate in the ACS women ≥80 years compared with those <80 years. During the late period women ≥80 years were treated more frequently with guideline-recommended therapies compared with patients from the same age group who were hospitalized in the early period. A significant decline in in-hospital mortality rates in ACS women ≥80 years hospitalized in the late compared with the early period was demonstrated. However, 7-day, 30-day and 1-year mortality rates were not significantly changed.
Conclusion: Adverse outcome rates of ACS women ≥80 years were significantly higher compared with those <80 years. In-hospital survival rates of ACS women patients ≥80 years improved during the 2000–2016 period; however, long-term survival rates were not significantly changed.

1. Introduction

Patients ≥80 years old constitute the fastest growing segment of the population and have a high prevalence of coronary artery disease (CAD). While studies show lower rates of guideline-recommended therapies and worse prognoses in the >80 compared with the <80 year old patients [1–3], an improvement has been detected in recent years [3–5]. Despite the fact that the number of women among the acute coronary syndrome (ACS) patient population increases with age, there is still a lack of data regarding the impact of ACS therapies among elderly women patients, who are under-represented in clinical trials [6,7].

We believe this study will contribute to the understanding of age- and sex-related differences in the treatment and outcome of ACS patients, as well as recognize the effect of changes in the use of guideline-recommended therapies on the outcome of elderly ACS women patients, a trend enhanced by the current literature [8,9].

2. Methods

2.1. Study design and population

The ACS Israel Survey (ACSIS) registry is a biannual prospective national survey of all patients with ACS hospitalized in 25 coronary care units and cardiology wards in all general hospitals throughout Israel over a 2-month period (March–April) [10,11]. Demographic, historical, and clinical data were recorded on pre-specified forms for all admitted patients diagnosed with ACS. Admission and discharge diagnoses were recorded by the attending physicians based on clinical, electrocardiographic, and biochemical criteria. Patient management was at the discretion of the attending physicians. All patients signed informed consent for the ACSIS trial participation in each medical center and each institution received a priori approval from its human research committee.

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* Corresponding author at: Leviev Heart Center, Chaim Sheba Medical Center, Tel Hashomer 5265601, Israel.
E-mail address: shechtes@netvision.net.il (M. Shechter).
[1] This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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The current study is retrospective, based on data obtained from 3518 ACS women patients who were enrolled in the ACSIS during the years 2000–2016.

Clinical outcomes included 30-day major adverse cardiac events (MACE), including death, myocardial infarction (MI), stroke, unstable angina, stent thrombosis, urgent revascularization, and 1-year mortality. Data of 30-day MACE were ascertained by hospital chart review, telephone contact, and clinical follow-up. Mortality rates at 30 days were determined for all patients from hospital charts and by matching identification numbers of patients with the Israeli National Population Register. One-year mortality rates were ascertained from the Israeli National Population Registry.

The study was performed in two stages. First, we evaluated the clinical outcomes of 858 ACS women ≥80 years and compared them with those of 2660 ACS women <80 years, hospitalized during 2000–2016. Second, we evaluated clinical outcomes of 450 ACS women ≥80 years hospitalized during 2000–2006, known as the early period, and compared them with 408 ACS women of the same age hospitalized during 2008–2016, known as the late period.

Hypertension was defined by documented medical chart diagnosis and/or when the patient was chronically prescribed antihypertensive medications, and/or for patients with blood pressure >140/90 mm Hg registered twice. Diabetes mellitus (DM) was defined by documented medical chart diagnosis or when the patient was chronically prescribed insulin or oral hypoglycemic medications. Chronic renal failure (CRF) was defined by documented medical chart diagnosis or when the calculated glomerular filtration rate was <60 mL/min/1.75 m^2. Congestive heart failure (CHF) was defined by documented medical chart diagnosis or when the left ventricular ejection fraction (LVEF) before hospitalization was <40%. Dyslipidemia was defined by documented medical chart diagnosis, chronically prescribed lipid-lowering therapy or blood test on admission demonstrating one or more of the following: total cholesterol ≥200 mg/dL, calculated-LDL ≥130 mg/dL, calculated-HDL ≤40 mg/dL, triglycerides ≥150 mg/dL.

2.2. Statistical analysis

Characteristics of study participants were compared using χ^2 test for categorical variables and Student's *t*-test or Wilcoxon rank tests for continuous variables. The Wilcoxon test was used for comparison of non-normally distributed continuous variables. Survival curves were graphically displayed using the Kaplan-Meier method for the main outcomes: all-cause mortality during 30 days and 1 year, following Log rank test to compare survival between the study groups. Multivariable analysis was performed using Cox proportional hazard models in order to evaluate the effect of the study group on the risk for main outcomes, adjusted for potential confounders.

The following factors were pre-specified as covariates in the multivariate Cox models: hospitalization period; age; history of premature familial cardiovascular disease; prior cardiovascular comorbidities and procedures: dyslipidemia, hypertension, DM, MI, angina pectoris, percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), CHF, CRF, cerebrovascular accident (CVA)/transient ischemic attack (TIA), peripheral vascular disease (PVD), smoking and KILLIP class at admission. R software was used for all analyses. A *p*-value of <0.05 was considered statistically significant for all tests.

3. Results

Baseline characteristics by age groups (< and ≥80 years) are presented in Table 1a. While ACS women ≥80 years had lower rates of traditional cardiovascular risk factors, except for hypertension, they had higher cardiovascular comorbidities. Concomitant cardiovascular medications were usually more common in women ≥80 compared with those <80 years, with the exception of statins (used at a slightly lower rate by the older women), and also clopidogrel and angiotensin receptor blockers (ARB), which showed no significant difference between the groups.

More ACS women ≥80 arrived at the hospital in mobile intensive cardiac care units (ICCUs) or via regular ambulance services compared with those <80 years. No significant difference was found between the 2 age groups regarding the amount of time from symptom onset to emergency room (ER) admission, whereas the time from ER admission to 1st ward and door-to-balloon time were longer in the older group (the latter with a trend toward a significant difference, $p = 0.052$). ACS women ≥80 presented more frequently to the ER with a higher degree of heart failure (Killip class ≥2), and had a higher incidence of LVEF <50% on echocardiography.

Post-admission therapy rates are presented in Table 1b.

At hospitalization, ACS women ≥80 years were less likely to receive reperfusion therapy, including primary PCI in STEMI (ST-elevation MI), compared with patients <80 years, (33% vs. 43.8%, $p < 0.001$; respectively).

Throughout hospitalization, ACS women ≥80 compared with those <80 years were significantly less likely to receive guideline-recommended pharmacotherapies, such as dual anti-platelet therapy, beta-blockers and statins. Nevertheless, diuretics, calcium channel blockers (CCB) and nitrates were administered more frequently to women ≥80 compared with those <80 years.

No significant difference was found between the 2 groups regarding secondary prevention, with most of the pharmacological guideline-recommended treatments, including statins, angiotensin converting enzyme inhibitors (ACE-I)/ARB and beta-blockers. However, differences were found in the prevalence of anti-platelet administration, with higher rates of clopidogrel and slightly lower rates of aspirin use in the older compared with the younger group of women.

Referral to and participation in cardiac rehabilitation programs were lower in women ≥80 compared with those <80 years.

Clinical outcomes by age groups are presented in Table 1c. ACS women ≥80 compared with those <80 years had higher rates of in-hospital MACE, as well as 2–3 fold higher mortality rates. Fig. 1 demonstrates Kaplan-Meier survival curve, adjusted to the traditional CAD risk

Table 1a
Characteristics by age groups.

Variable	< 80 years (n = 2660)	≥ 80 years (n = 858)	*p* value
Baseline characteristics			
Age, years (mean ± SD)	65.5 ± 9.9	84.9 ± 4.3	<0.001
Dyslipidemia	69.6%	60.5%	<0.001
Hypertension	69.5%	84.4%	<0.001
Current smokers	23.0%	4.0%	<0.001
Diabetes mellitus	46.1%	34.6%	<0.001
Family history of CAD	22.7%	6.9%	<0.001
BMI (kg/m^2), (mean ± SD)	28.7 ± 9.4	26.6 ± 4.9	<0.001
Prior MI	23.7%	31%	<0.0001
Prior CABG	7.5%	7.5%	1.000
Prior PCI	21.2%	18.6%	0.109
Chronic renal failure	9.2%	18.9%	<0.001
PVD	7.2%	7.6%	0.739
s/p CVA/TIA	9.0%	15%	<0.001
History of CHF	8.3%	16.3%	<0.001
Prior medications			
Aspirin	47.7%	55.2%	<0.001
Clopidogrel	8.0%	8.8%	0.520
ACEI/ARB	27.0%	35.9%	<0.001
Beta blockers	41.5%	51.4%	<0.001
Statins	51.8%	47.5%	0.048
CCB	25.6%	38.0%	<0.001
Nitrates	12.3%	22.2%	<0.001
Angiotensin receptor antagonist	2.6%	3.4%	0.631
Hypoglycemic agents	30.1%	20.3%	<0.001
Diuretics	23.4%	36.6%	<0.001
Means of arrival to hospital and time to treatment			
Mobile ICCU	33.4%	43.9%	<0.001
Regular ambulance	14.8%	18.5%	0.013
Private car	45.1%	30.4%	<0.001
Time from symptoms onset to ER (median, IQR) (min)	195 [95, 590]	201 [100, 464]	0.952
Time from ER to 1st ward (median, IQR) (min)	113 [54, 203]	124 [60, 220]	0.015
Door to balloon time (median, IQR) (min)	67 [36, 130]	83 [45, 143]	0.052
Killip class on admission			
1	80.8%	64.2%	<0.001
2	11.0%	19.3%	<0.001
3	6.4%	13.6%	<0.001
4	1.8%	3.0%	0.044
LVEF <50% rates			
LVEF<50%	47.9%	58.2%	0.003

ACEI-Angiotensin converting enzyme inhibitors, ARB-Angiotensin receptor blockers, BMI-Body mass index, CABG-Coronary artery bypass grafting, CAD-Coronary artery disease, CCB-Calcium channel blockers, CHF-Congestive heart failure, CVA-Cerebrovascular accident, ER-Emergency room, ICCU-Intensive cardiac care unit, IQR-Interquartile range, LVEF-Left ventricle ejection fraction, MI-Myocardial infarction, PCI-Percutaneous coronary intervention, PVD-Peripheral vascular disease, SD-Standard deviation, TIA-Transient ischemic attack.

Table 1b
Post admission therapy by age group.

Variable	<80 years (n = 2660)	≥80 years (n = 858)	*p* value
Reperfusion therapy			
STEMI n.	1111 (41.8%)	370 (43.1%)	0.52
Thrombolysis	27.1%	24.0%	0.466
Angio without PCI	0.5%	0.7%	0.740
Primary PCI in STEMI	43.8%	33.0%	<0.001
Any PCI in STEMI	69.4%	47.3%	<0.001
Any PCI in all patients	56.7%	41.7%	<0.001
CABG	4.6%	3.6%	0.275
Use of IIb/IIIa antagonists	33.8%	17.2%	<0.001
In-hospital medical therapy			
Aspirin	94.1%	91.7%	0.018
Clopidogrel	63.3%	58.7%	0.020
Warfarin/oral anticoagulation	6.1%	8.0%	0.063
UF heparin	45.4%	42.3%	0.121
LMW heparin	48.4%	48.8%	0.903
ACE-I/ARB	49.2%	47.1%	0.297
Beta blockers	79.1%	70.3%	<0.001
Diuretics	33.7%	55.9%	<0.001
Statins	79.2%	72.6%	<0.001
CCB	19.8%	25.3%	0.002
Nitrates	37.3%	41.9%	0.031
Hypoglycemic agents	19.3%	11.7%	<0.001
Therapy at 30-day follow-up			
Aspirin	92.8%	87.7%	0.007
Clopidogrel	61.7%	71.4%	0.003
Statins	93.2%	90.1%	0.094
ACE-I/ARB	27.4%	27.3%	0.957
Beta blockers	82.1%	77.9%	0.128
Referral to rehabilitation program	23.2%	14.0%	<0.001
Participation in rehabilitation program	6.9%	3.0%	<0.001

ACEI-Angiotensin converting enzyme inhibitors, ARB-Angiotensin receptor blockers, CABG-Coronary artery bypass grafting, CCB-Calcium channel blockers, LMW-Low molecular weight, PCI- Percutaneous coronary intervention, STEMI-ST elevation myocardial infarction, UF- Unfractionated.

factors and comorbidities which appear in Table 1a, with a significantly lower survival probability during the 1st year after hospitalization in ACS women ≥80 compared with those <80 years.

Baseline characteristics of ACS women ≥80 by the 2 study periods are presented in Table 2a. Women ≥80 hospitalized during the late period were older, had a higher prevalence of traditional CAD risk factors, as well as a higher prevalence of prior PCI, whereas no significant difference was found between the 2 time periods regarding the prevalence of cardiovascular comorbidities. Women ≥80 years in the late period

Table 1c
Clinical outcomes by age group.

Variable	<80 years (n = 2660)	≥80 years (n = 858)	*p* value
In-hospital complications			
Killip 3	8.9%	16.5%	<0.001
Killip 4	4.1%	8.1%	<0.001
Re MI	1.4%	1.9%	0.356
Post MI angina	6.2%	7.1%	0.403
Stent thrombosis	1.1%	1.0%	0.4125
Free wall rupture	0.4%	2.0%	<0.001
High degree AV block	2.8%	5.3%	0.001
TIA/CVA	0.8%	2.3%	0.001
Acute renal failure	6.0%	14.7%	<0.001
Major bleeding	1.8%	3.5%	0.006
Death rates			
In-hospital death	121 (4.5%)	112 (13.1%)	<0.001
7-day mortality	83 (3.1%)	82 (9.6%)	<0.001
30-day mortality	145 (5.5%)	134 (15.6%)	<0.001
1-year mortality	262 (9.9%)	241 (28.3%)	<0.001

AV - Atrioventricular, CVA - Cerebrovascular accident, MI - Myocardial infarction, TIA - Transient ischemic attack.

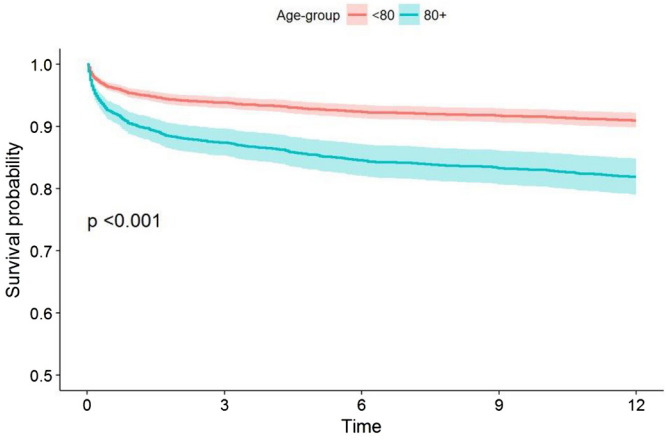

Fig. 1. A Kaplan-Meier 1-year survival curve of acute coronary syndrome women patients ≥80 years old (blue line, n = 858) vs. patients <80 years (red line, n = 2660), adjusted for cardiovascular risk factors, co-morbidities and hospitalization period ($p < 0.0001$). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

received more concomitant medical cardiovascular treatments at home, prior to hospitalization. Means of transportation to hospital as well as duration of time to treatment did not change significantly during the 2 study periods. ACS women ≥80 years in the late period had a significantly lower incidence of high Killip class on hospital admission compared with those in the early period, although the rate of patients admitted with LVEF <50% was similar during the 2 study periods.

Post admission therapy rates of women ≥80 by the 2 study periods are presented in Table 2b. Primary PCI in STEMI and any PCI in ACS women ≥80 years were significantly more common in the late compared with the early period. However, thrombolytic therapy declined significantly during the late study period according to trends in the guideline recommendations [8,9]. Accordingly, there was a marked increment in the use of mainstay guideline-recommended medications throughout the study periods. However, there was a decline in the use of diuretics, nitrates and digoxin. While an increase in referrals to cardiac rehabilitation programs was seen throughout the study periods, rates of participation were unchanged.

Clinical outcomes of women ≥80 by study period are presented in Table 2c. Most of the evaluated in-hospital complications were unchanged during the 2 study periods, except for 3 which improved over the study period (Killip class to 3rd degree, post-MI angina and acute renal failure).

There was a significant decline in in-hospital mortality rates in ACS women ≥80 years hospitalized during the 2 study periods. However, 7-day, 30-day and 1-year mortality rates were not significantly changed (although there was a trend toward a significant reduction in 1-year mortality rates in the late compared with the early period). Fig. 2 shows a 1-year survival curve, adjusted to the traditional CAD risk factors and prior comorbidities as presented in Table 2a, indicating no significant change between the 2 study periods.

4. Discussion

Our study demonstrated lower rates of in-hospital guideline-recommended therapies and cardiac rehabilitation programs, as well as worse in-hospital and post-discharge prognosis of ACS women above and below 80 years of age. However, this study also showed raised invasive and medical in-hospital guideline-recommended therapy rates in the older women during the years 2000–2016, with matching improved in-hospital mortality rates. Nevertheless, there was no significant improvement in 7-day, 30-day and 1-year mortality rates.

Cardiovascular co-morbidity rates were higher in the older patients consistent with previous reports [12,13], which correspond with higher

Table 2a
Characteristics of women ≥80 years by early and late study periods.

Variable	2000–2006 (n = 450)	2008–2016 (n = 408)	*p* value
Baseline characteristics			
Age, (years) (mean ± SD)	84.5 ± 4.2	85.3 ± 4.5	0.005
Dyslipidemia	45.7%	76.7%	<0.001
Hypertension	79.8%	89.6%	<0.001
Current smokers	3.6%	4.4%	0.689
Diabetes mellitus	31.5%	38.1%	0.050
Family history of CAD	4.8%	9.7%	0.013
BMI (kg/m^2), (mean ± SD)	26.5 ± 4.8	26.7 ± 4.9	0.675
Prior to admission cardiovascular morbidity			
s/p MI	28.7%	33.5%	0.152
s/p CABG	6.2%	8.8%	0.190
s/p PCI	12.7%	25.1%	<0.001
Chronic renal failure	17.2%	20.7%	0.223
PVD	8.7%	6.4%	0.251
s/p CVA/TIA	15.7%	14.3%	0.631
History of CHF	15.8%	16.7%	0.805
Prior concomitant medications (at home)			
Aspirin	55.3%	55.1%	1.000
Clopidogrel	3.9%	13.2%	<0.001
ACE-I/ARB	14.9%	59.1%	<0.001
Beta blockers	46.5%	55.9%	0.013
Statins	35.7%	58.7%	<0.001
CCB	34.4%	41.3%	0.059
Nitrates	29.1%	15.8%	<0.001
Hypoglycemic agents	18.4%	21.9%	0.261
Diuretics	40.4%	34.1%	0.129
Means of arrival at hospital and time to treatment			
Mobile ICCU	43.8%	44.1%	0.972
Regular ambulance	19.0%	17.9%	0.730
Private car	29.9%	30.9%	0.821
Time from symptom onset to ER (min) (median, IQR)	202 [105, 505]	199 [96, 426]	0.278
Time from ER to 1st ward (min) (median, IQR)	120 [62, 195]	132 [59, 239]	0.407
Door to balloon time (min) (median, IQR)	92 [49, 146]	79 [45, 130]	0.453
Killip class on admission			
≥2	43.0%	27.8%	<0.001
≥3	20.1%	12.5%	0.004
LVEF			
LVEF <50%	60.3%	57.6%	0.795

ACEI- Angiotensin converting enzyme inhibitors, ARB- Angiotensin receptor blockers, BMI- Body mass indeed, CABG- Coronary artery bypass grafting, CAD- Coronary artery disease, CCB- Calcium channel blockers, CHF- Congestive heart failure, CVA- Cerebrovascular accident, ER- Emergency room, ICCU - Intensive cardiac care unit, IQR-Interquartile range, LVEF- Left ventricle ejection fraction, MI- Myocardial infarction, PCI- Percutaneous coronary intervention, PVD- Peripheral vascular disease, SD- Standard deviation, TIA- Transient ischemic attack.

rates of most prior concomitant cardiovascular pharmacotherapy found in the older group.

Despite the fact that rates of reperfusion therapies in the older women more than doubled over the years (Table 2b), no significant change was detected in their survival rates (Fig. 2). Nevertheless, the in-hospital mortality rate of the older women was significantly decreased between the 2 study periods, while the decrease in 1-year mortality showed a trend toward significance ($p = 0.054$; Table 2c). These inconsistent results may correspond with the ambiguity in the literature regarding the appropriate treatment for women with ACS of all ages. Some studies demonstrated no benefit from early invasive reperfusion intervention in women, showing higher rates of adverse outcomes among women compared with men [14–17]. However, benefit from early invasive strategy for both sexes, has been previously documented [18,19]. While this uncertainty is even greater among elderly women, who are under-represented in clinical trials [6,7], a recent study found an association between coronary revascularization and lower 1-year mortality in elderly women, as well as similar in-hospital and better

Table 2b
Post admission therapies of women ≥80 years by the early and late study periods.

Variable	2000–2006 (n = 450)	2008–2016 (n = 408)	*p* value
Reperfusion therapy			
STEMI	210 (46.7%)	160 (39.2%)	0.033
Thrombolysis	46.0%	2.3%	<0.001
Angio without PCI	0.0%	1.9%	0.014
Primary PCI in STEMI	20.5%	49.4%	<0.001
Any PCI in STEMI	32.9%	66.2%	<0.001
Any PCI in all patients	28.4%	56.4%	<0.001
CABG	4.9%	2.2%	0.054
Use of IIb/IIIa antagonists	10.6%	27.9%	0.002
In-hospital therapy			
Aspirin	93.3%	90.0%	0.098
Clopidogrel	39.7%	79.6%	<0.001
Warfarin/oral anticoagulation	6.8%	9.3%	0.211
UF heparin	45.4%	38.9%	0.067
LMW heparin	53.6%	43.5%	0.004
ACE-I/ARB	24.7%	71.8%	<0.001
Beta blockers	67.2%	73.8%	0.043
Diuretics	60.1%	51.0%	0.010
Statins	55.9%	91.8%	<0.001
Digoxin	5.6%	2.1%	0.017
Nitrates	54.4%	31.2%	<0.001
Hypoglycemic agents	9.0%	14.7%	0.012
Referral to rehabilitation program	3.1%	26.5%	<0.001
Participation in rehabilitation program	1.9%	4.2%	0.104

ACEI - Angiotensin converting enzyme inhibitors, ARB - Angiotensin receptor blockers, CABG - Coronary artery bypass grafting, LMW - Low molecular weight, PCI - Percutaneous coronary intervention, STEMI-ST elevation myocardial infarction, UF - Unfractionated.

1-year outcomes of elderly women compared with men [20], in accord with previous studies which demonstrated no disparity in outcomes between elderly women and elderly men [21–23].

We believe that the remarkable increment in rates of guideline-recommended interventional and medical therapies did have an impact on the outcomes of the older women in this study. Nevertheless, this approach is probably not enough, since elderly women have specific characteristics as demonstrated by Vicent L, et al. who showed an increased risk of hospital readmissions (within 6 months) in octogenarian women presenting with non-ST-segment elevation ACS compared with men [24]. Vicent L, et al. found frailty, a predictor of poor prognosis, to be more common in elderly women than men. Furthermore, a higher proportion of disability and dementia was noted among elderly women, a fact which could also have impacted on clinical decision making and

Table 2c
Clinical outcomes of women ≥80 years by early and late study periods.

	2000–2006 (n = 450)	2008–2016 (n = 408)	*p* value
In-hospital complications			
Killip 3	21.7%	10.8%	<0.001
Killip 4	8.8%	7.4%	0.544
Re MI	2.7%	1.0%	0.110
Post MI angina	10.2%	3.7%	<0.001
Stent thrombosis	0.0%	1.2%	0.509
Free wall rupture	2.0%	2.0%	1.000
High degree AV block	5.2%	5.4%	1.000
TIA/CVA	2.0%	2.7%	0.654
Acute renal failure	17.1%	12.0%	0.048
Major bleeding	2.9%	4.2%	0.416
Mortality rates			
In-hospital death	70 (15.6%)	42 (10.3%)	0.029
7-day mortality	49 (10.9%)	33 (8.1%)	0.206
30-day mortality	78 (17.3%)	56 (13.8%)	0.179
1-year mortality	140 (31.2%)	101 (25.0%)	0.054

AV – Atrioventricular, CVA - Cerebrovascular accident, MI - Myocardial infarction, TIA - Transient ischemic attack.

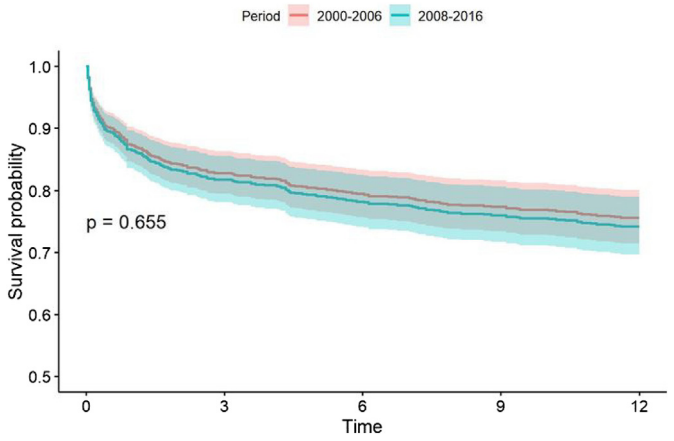

Fig. 2. A Kaplan-Meier 1-year survival curve of all patients ≥80 years stratified to the 2 study periods: patients hospitalized in the early 2000–2006 period (red line) and late 2008–2016 period (blue line), adjusted for cardiovascular risk factors, co-morbidities and hospitalization period ($p = 0.724$).

outcomes. These results may partially explain why no change was demonstrated in the 1-year survival curve among elderly women during the 2 time periods in our study, despite the increment in treatment rates by guideline-recommended therapies. Frailty assessment before choosing appropriate treatment, as well as geriatric monitoring and frequent follow-up during and after hospitalization may be needed in order to improve the outcomes of these patients.

Door-to-balloon time was longer in women ≥80 compared with women <80, with a trend for significance ($p = 0.052$, Table 1a), a fact which corresponds with older age being a predictor of pre-hospital and treatment delays [25–27]. Moreover, no improvement was demonstrated in pre-hospital delay or door-to-balloon time during the 2 time periods among ≥80 year old ACS women. Pre-hospital and door-to-balloon delays in ACS patients have been discussed previously [27–29]. Despite efforts by healthcare providers and patient education programs [8,30], almost no significant improvement was demonstrated in our study. Further investigation, particularly in elderly women, is needed to evaluate the effectiveness of measures taken.

There were no significant changes in the rate of arrival via ICCUs between the 2 study periods. Mobile ICCUs provide, in addition to better treatment facilities, the option for a pre-hospital ECG, which was found to be a predictor for bringing contact-to-device time down to <90 min [26]. The importance of obtaining a pre-hospital ECG should be addressed to the emergency medical service teams, as it may be crucial in hastening time-to-treatment in elderly women who suffer from significant pre-hospital delays anyway.

Although the rate of referral to rehabilitation programs among elderly women patients increased during the study period, participation in rehabilitation programs did not change significantly between the 2 study periods. While cardiac rehabilitation services improve various clinical outcomes in cardiovascular disease patients, demonstrating a reduction in post ACS all-age mortality rates by 20% [31,32], they were found to be under-utilized, particularly in women and elderly patients [32,33]. Physicians should encourage elderly women patients to participate in these programs.

Noteworthy are the differences between the higher rates of prior-to-admission cardiovascular medical guideline-recommended treatments (Table 2a), as well as the higher rates of prior PCI in the late compared with the early time period. On the one hand, these differences may reflect the higher rate of cardiovascular comorbidity (although the higher rates of dyslipidemia, hypertension and diabetes may partially be derived from changes in normal value definitions), while on the other hand, they probably contributed to the lower Killip class levels on admission, with subsequent improved outcomes (Table 2a). This may emphasize the importance of appropriate prior guideline-recommended treatment in this population.

The current study has some limitations. First, it was based on registry data and as such may exhibit some limitations. Secondly, the ACSIS survey is a biannual study, performed during a 2-month period, and thus might not adequately represent an entire year, which could influence morbidity and mortality of ACS. Thirdly, the ACSIS registry includes only patients who were hospitalized in ICCUs. It should be noted that most ACS patients in Israel, especially those presenting with STEMI, are hospitalized in cardiology departments with integrated ICCUs. However, few ACS patients, usually those with non-STEMI, are hospitalized in internal wards and are therefore excluded from the ACSIS registry. This might have some potential limitations on the study results.

In conclusion, ACS women ≥80 have a worse prognosis compared with ACS women <80 years. During the 2000–2016 period decrements were detected in the in-hospital and 1-year mortality rates of the older women (the latter rate with a trend for significance). However, this improvement was not demonstrated in an adjusted survival analysis. We believe that the increase in the use of guideline-recommended therapy in elderly women throughout the years has had a positive impact on their outcome. However, further investigation with special emphasis on the characteristics of elderly women patients (e.g. higher rates of frailty compared with elderly men) is still needed, since the results of this study are ambiguous. In addition, further evaluation is also needed to investigate the rationale behind pre-hospital and door-to-balloon delays, as well as the relatively low participation rates of elderly ACS patients in cardiac rehabilitation programs.

Disclosures

None.

Declarations of interest

None.

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