Temporal trends in all-cause mortality of smokers versus non-smokers hospitalized with ST-segment elevation myocardial infarction ☆

Yaron Arbel [a,*], Shlomi Matetzky [b], Natalie Gavrielov-Yusim [b], Meital Shlezinger [b], Gad Keren [a], Arie Roth [a], Eran Kopel [b], Ariel Finkelstein [a], Shmuel Banai [a], Robert Klempfner [b], Ilan Goldenberg [b]

[a] Department of Cardiology, Tel Aviv Medical Center, affiliated to the Sackler School of Medicine, Tel Aviv, Tel Aviv University, Israel
[b] Department of Cardiology, Sheba Medical Center, affiliated to the Sackler School of Medicine, Tel Aviv, Tel Aviv University, Israel

ARTICLE INFO

ABSTRACT

Background/objectives: Over the past decade, the development of novel management strategies has resulted in improved outcomes among patients hospitalized with ST-segment myocardial infarction (STEMI). The aim of the present study was to compare temporal trends in the mortality of smokers versus non-smokers admitted with STEMI in a real world setting between 2000 and 2010.

Methods: We evaluated time-dependent changes in the clinical characteristics, management strategies, and one year all-cause mortality of STEMI patients who were enrolled in the biannual Acute Coronary Syndrome Israeli Survey (ACSIS) between 2000 and 2010, categorized as smokers (n = 2399) and non-smokers (n = 3069). We divided the survey periods into early (2000–2004) and late (2006–2010). The primary endpoint of the study was the occurrence of one-year all-cause mortality.

Results: A total of 4564 STEMI patients were enrolled in the study. Compared with non-smokers, smokers were significantly younger and displayed a significantly lower rate of all-cause mortality at 30 days and 1-year. Both smokers and non-smokers who were enrolled in the late survey period received more evidence-based therapies (primary PCI and guideline-based medications) (p < 0.001 for all). There was a significant reduction in the risk of 1-year all-cause mortality only among non-smokers (HR = 0.664 CI 95% 0.52–0.85, p = 0.0009), whereas smokers who were enrolled in more recent survey periods did not display a significant risk reduction (HR = 1.08 CI 95% 0.77–1.51, p = 0.67).

Conclusion: Survival following STEMI among smokers has not improved over the past decade despite corresponding changes in management strategies. Future trials should focus on reducing the risk in smokers.

1. Introduction

1.1. Background/objectives

Our approach to ST-segment myocardial infarction (STEMI) has evolved rapidly over the past decade with major advances in management techniques. Percutaneous coronary intervention (PCI) gradually became the preferred method of primary reperfusion in patients presenting with STEMI in many centers. Evidence based medical treatments including aspirin, P2Y12 inhibitors, angiotensin converting enzyme inhibitors (ACEI)/angiotensin receptor blockers (ARBs), statins, anticoagulants and beta blockers have been incorporated into management guidelines and are the standard of care [1,2].

In parallel to this progress, the awareness of the hazards of smoking has increased as well as the therapies available to help smokers quit [3,4]. However, success rates of smoking cessation are still low even in randomized trials [3,5]. The incidence of smoking in the Israeli population has decreased over the past decade by 25% (31% versus 24%) [6].

Historically, smokers have a paradoxically lower mortality after STEMI compared with non-smokers, coined the smoker's paradox [7]. Smokers have less conventional risk factors and are younger compared to non-smokers. Currently, however, there are limited data regarding temporal trends in outcomes of smokers hospitalized with a STEMI. Specifically, it is possible that changes in management strategies over the last decade were associated with a differential effect between smokers and non-smokers hospitalized with STEMI.

In the present study, we evaluated the temporal trends in the clinical characteristics and outcomes of smokers and non-smokers presenting with STEMI in a real world setting of patients enrolled in the Acute Coronary Syndrome Israeli Survey (ACSIS) 2000–2010.

---

2. Methods

2.1. Study population

The ACSIS (acute coronary syndrome Israeli survey) registry is a biannual prospective national survey of all patients with ACS hospitalized in all 25 coronary care units and cardiology wards in all general hospitals in Israel during a 2 month period (March–April) [8–10]. ACSIS recruits only patients from Israel in order to allow proper follow up. Demographic, historic, and clinical data are recorded on pre-specified forms for all patients admitted with a diagnosis of acute coronary syndrome (ACS). Admission and discharge diagnoses are recorded as determined by the attending physicians based on clinical, electrocardiographic, and biochemical [elevated creatine kinase (CK)-MB and/or troponin levels] criteria. Patient management is at the discretion of the attending physicians.

The current analysis is based on all patients presenting with ACS who were enrolled in ACSIS from 2000 through 2010. Included in the analysis were patients who had a diagnosis of STEMI at discharge and were treated with primary PCI. We excluded from the analysis past smokers since we did not have credible data on when they stopped smoking. We chose to focus on STEMI patients in order to evaluate a homogenous group that had the most improvement in outcomes after the introduction of evidence-based therapies in the past decade. Smokers were defined as patients that smoked during the past month. Non smokers included patients that never smoked.

The primary analysis focused on temporal trends in the clinical characteristics of smokers and non-smokers with STEMI over the past decade. Comparisons and trend calculations were made using data from all 6 surveys separately (2000, 2002, 2004, 2006, 2008, and 2010), and by dichotomizing the survey period into 2 pre-specified time-intervals defined as early (surveys 2000 through 2004) and late (surveys 2006 through 2010). In a secondary analysis (presented in the Supplementary Appendix), we compared the clinical characteristics and outcomes of smokers and non-smokers.

2.2. Endpoints

The primary endpoint of the study was the occurrence of one-year all-cause mortality. Secondary endpoint included 30-day all-cause mortality and the occurrence of in-hospital complications.

Mortality data during hospitalization and at 30 days and 1 year were determined for all patients from hospital charts and by matching identification numbers of patients with the Israeli National Population Register. All parameters captured by the registry were defined by protocol.

2.3. Statistical analysis

Characteristics of study participants were compared using χ^2 test for categorical variables and Student's t-test or Wilcoxon rank tests, as appropriate for continuous variables. The Kruskal–Wallis test was used for comparison of non-normally distributed continuous variables. The probability of all-cause mortality during 30-day and 1-year interval was graphically displayed using the Kaplan–Meier method. Cox proportional hazards multivariate- adjusted survival models were used to evaluate the independent effects of smoking and survey period on 30-days and 1-year all-cause mortality.

In order to assess the specific contribution of treatment period on all-cause mortality, we created several Cox proportional hazard models with all-cause mortality as the dependent variable and potential confounders as independent variables. The following factors were prespecified as covariates in the multivariate survival models: gender, age >74 years, history of diabetes, history of renal failure, systolic blood pressure <100 mm Hg, admission Killip >1, and survey period (categorized as early [years: 2000–2004] vs. late [years: 2006–2010]).

The effect of the survey period on outcome among smokers and non-smokers was assessed by including a smoking-by-survey period interaction-term in the multivariate models. All data analysis was performed using SAS program version 9.3. A 2-sided value of p < 0.05 was used for declaring statistical significance.

3. Results

The study population comprised a total of 4564 STEMI patients who were enrolled in the 6 surveys composing the ACSIS 2000–2010. In the 2000–2004 surveys (early period), 2616 patients were enrolled, of whom 1253 (48%) were smokers and 1363 (52%) were non-smokers. In the 2006–2010 surveys (late period), 1948 patients were enrolled, of whom 1146 (59%) were smokers and 802 (41%) non-smokers. The rate of smokers presenting with STEMI has increased over the past decade from 42% to 47% (p for trend ≤ 0.001). Compared with non-smokers, smokers were significantly younger and had a significantly lower frequency of baseline clinical risk factors, including hypertension, diabetes mellitus and obesity (Supplementary Appendix Table 1). At baseline, smokers were treated by less medication compared to non-smokers (Supplementary Appendix Table 2). Nevertheless, smokers had lower rates of mortality (Supplementary Fig. 1).

Table 1
Baseline characteristics by smoking status in early versus late survey periods.

	Smokers			Non-Smokers		
	Early N = 1253	Late N = 1146	p-Value	Early N = 1363	Late N = 802	p-Value
Age (±SD)	56 ± 11	56 ± 11	0.71	68 ± 13	67 ± 13	0.26
Female Gender	150 (12%)	126 (11%)	0.25	504 (337%)	321 (40%)	0.15
BMI (±SD)	27 ± 4	27 ± 5	<0.001	27 ± 4.4	27 ± 4	0.029
Diabetes mellitus	263 (21%)	275 (24%)	0.09	475 (35%)	271 (34%)	0.65
Hypertension	388 (31%)	458 (40%)	<0.001	752 (55%)	484 (60%)	0.019
Dyslipidemia	551 (44%)	711 (62%)	<0.001	593 (44%)	500 (63%)	<0.001
Family history of coronary artery disease	301 (24%)	378 (33%)	<0.001	196 (14%)	162 (21%)	<0.001
Chronic Renal failure	38 (3%)	46 (4%)	0.33	101 (7%)	78 (10%)	0.06
History of Congestive heart failure	25 (2%)	23 (2%)	0.37	69 (5%)	39 (5%)	0.83
History of myocardial infarction	238 (19%)	206 (18%)	0.59	256 (19%)	148 (18.5%)	0.85
History of angina	288 (23%)	298 (26%)	0.07	330 (24%)	208 (26%)	0.36
History of PCI	150 (12%)	218 (19%)	<0.001	137 (10%)	135 (17%)	<0.001
History of CABG	25 (2%)	23 (2%)	0.15	56 (4%)	35 (4%)	0.77
History of stroke/TIA	75 (6%)	46 (4%)	0.037	119 (9%)	66 (8%)	0.69
PVD	88 (7%)	80 (7%)	0.64	73 (5%)	46 (6%)	0.70
Medications at admission						
Aspirin	451 (36%)	332 (29%)	0.057	435 (32%)	297 (37%)	0.025
Beta-blockers	200 (16%)	218 (19%)	0.06	349 (26%)	252 (31%)	0.007
Statins	213 (17%)	355 (31%)	<0.001	290 (21%)	305 (38%)	<0.001
Clopidogrel	13 (1%)	46 (4%)	<0.001	23 (2%)	36 (5%)	<0.001
Anticoagulants	13 (1%)	11 (1%)	0.37	28 (2%)	32 (4%)	0.020
Nitrates	88 (7%)	23 (2%)	<0.001	151 (11%)	45 (6%)	<0.001
ACEI/ARB	188 (15%)	241 (21%)	0.001	338 (25%)	273 (34%)	<0.001
Time from symptom onset to Reperfusion (min)	305 ± 640	295 ± 520	p = 0.76	320 ± 757	376 ± 604	p = 0.18
Laboratory results						
Peak CPK IU	1650 ± 2208	1413 ± 2950	0.02	1519 ± 2298	1270 ± 1389	p = 0.007
Admission glucose mg/dl	158 ± 78	142 ± 64	p < 0.001	167 ± 89	189 ± 101	p < 0.001

BMI — body mass index, PCI — percutaneous coronary intervention, CABG — coronary artery bypass grafting, TIA — transient ischemic attack, PVD — peripheral vascular disease, ACEI — angiotensin converting enzyme inhibitors; ARB — angiotensin receptor blocker.