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Prevalence of Comorbidities and Their Impact on One-year Outcomes in Iranian Patients Hospitalized with ST-segment Elevation Myocardial Infarction

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ABSTRACT

Introduction: Introduction: While it is well-known that comorbidities like hypertension are associated with an increased risk for cardiovascular diseases (CVDs), the risk for death and subsequent CV complications has not been adequately addressed. Therefore, this study was aimed to examine the association between comorbidities and one-year outcomes in patients with STEMI.

Methods: This hospital-based study was a part of the Kermanshah STEMI Registry. After applying inclusion criteria, a total of 2,443 patients were assessed. The data were collected using a standardized case report developed by the European Observational Registry Program (EORP). The outcomes including vital status and major adverse cardiovascular events (MACE) were assessed. We assessed the independent predictors of death and MACE using multivariable logistic regression models .

Results: At first-year follow-up, out of the 2443 patients, 268 (11.06) patients died and 403 (19.0) patients experienced the MACE. On multivariate analysis, patients with hypertension (OR 1.69; 95% CI 1.19-2.38) and diabetes (OR 1.61; 95% CI 1.10-2.34) had a higher risk for death. Patients with hyperlipidemia were at the lowest risk of death (OR 0.63; 95% CI 0.41-0.97).

Conclusion: Diabetes mellitus and hypertension increased the risk of death, however, hyperlipidemia decreased the risk of death. The clinical implications highlight the need for tailoring intervention in all aspects of secondary prevention of CVD especially in patients suffering from comorbidities, managing the common comorbidities, and monitoring diabetics and hypertensive patients.

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Introduction

Acute myocardial infarction (AMI) is a costly condition and the leading cause of mortality and morbidity across the world. ST-segment elevation myocardial infarction (STEMI) is the most deadly sub-class of MI (over 35%) (1). The incidence of AMI and case-mortality rates after AMI are decreasing in most countries (2, 3), this reducing trend of mortality are underpinned by advances in prevention, treatment, and care (4). However, the population growth, aging population, and the increasing prevalence of long-term survivors of AMI justify that the burden of disease is increasingly rising (3). Survivors of MI are at higher risk for a

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recurrent MI, other cardiovascular events, or death (5) .

Comorbidity including diabetes mellitus, high blood pressure levels, hyperlipidemia, and smoking are known as risk factors for CVD (6, 7). On the other hand, comorbidities i.e. diabetes are a significant risk factor for mortality and recurrent cardiovascular events (8, 9). For instance, death rates, both all-cause and CVD-related, for patients with diabetes mellitus are nearly 2-fold higher than those without diabetes, and increasing duration of diabetes is related to increased CVD risk (10, 11). The previous studies showed that the first year following an event of MI represents a critical period for potential secondary prevention of adverse outcomes (8, 12, 13). However, it is important to understand the burden of CVD in the high-risk populations, few studies have described the real-world pattern of mortality and secondary major adverse cardiovascular events by comorbidities status.

Therefore, this study was aimed to examine the association between comorbidities and one-year outcomes in patients with STEMI.

Materials and Methods

Study design and population

This hospital-based study was a part of the Kermanshah STEMI Registry in Imam Ali Cardiovascular Center, Kermanshah University of Medical Sciences (KUMS), western Iran. Imam Ali hospital, as the main cardiovascular center in western Iran, annually provides more than two million population mostly Kurdish with medical services. Between July 1, 2017, and July 1, 2019, all participants who met the inclusion criteria were chosen to participate in the study. The design and foundations of the STEMI registry study were detailed here (14).

Inclusion and exclusion criteria

Inclusion criteria were a definite diagnosis by STEMI, patients aged ≥18 years old, and patients formally signed consent form to participate and complete the study. the diagnosis of STEMI was according to the following criteria: 1) chest pain for more than 20 minutes within the last 24 hours before admission, 2) electrocardiographic changes in accordance with new ST-segment elevations or left bundle branch block, based on the third universal definition of MI described by the European Society of Cardiology/ACCF/AHA/World Heart Federation Task Force for the Universal Definition of MI (15).

In this study, those with incomplete information (n=373), were excluded. Finally, 2443 patients fulfilled the inclusion criteria and were enrolled in the present study.

Data collection and quality control

We used case report forms, which developed by the European Observational Research Program (EORP) to collect data by a nurse and a research assistant, who were trained about the study protocol. All completed questionnaires were checked and verified for errors by a general physician before final analysis. As well as, Data adjudicated by the standards of the EORP.

At the end of one year, all patients were invited and underwent examination (clinical, biochemical, and electrocardiographic exams). The outcomes including vital status and major adverse cardiovascular events (MACE) were assessed. The MACE comprised re-hospitalization due to acute coronary syndrome (including STEMI, non-STEMI, and unstable angina), stroke, heart failure, and arterial fibrillation.

Statistical analysis

Data were analyzed using descriptive statistics including mean ± standard deviation (SD), median, frequencies and percentages wherever applicable. Differences between subgroups were assessed using independent t-tests for continuous and normally distributed variables and chi-square (or Fisher exact tests) for other variables. We assessed the independent predictors of death and MACE using multivariable logistic regression models. Odds ratios (ORs) and 95% Confidence Intervals (CIs) were calculated. A test was considered statistically significant if the probability value (P-value) was less than 0.05. All analyses were carried out using Stata software (version 14.1) (Stata Corp, College Station, TX, USA).

Results

During 24 months, a total of 2443 patients met the inclusion criteria for this study. At one year follow-up, out of the 2443 patients, 268 (11.06) patients died and 403 (19.0) patients experienced the MACE. Table 1 indicates baseline characteristics. Those with age more than 65 years, illiterate, BMI less than 18.5, prior PCI, prior MI, and prior stroke were more likely to experience MACE. Those with age more than 65 years, female, illiterate, diabetic, hypertensive, non-smoker, BMI more than 30, prior stroke, and those with cancer were more likely to die.

Table 2 provides the results of the odds ratio (ORs) and 95% CI of death and MACE according to comorbidities. After adjusting model 1 for sex, age, and level of education, diabetics (OR: 1.76; 95% CI: 1.26 to 2.46), hypertensive (OR: 1.37; 95% CI: 1.00 to 1.87), and those with cancer (OR: 2.33; 95% CI: 1.28 to 4.26) had a higher risk for death. However, a significant association and negative relationship appeared between hyperlipidemia and death in model 1(OR: 0.60; 95% CI: 0.41 to 0.89).

Table 1. Baseline characteristics of participants.

Characteristic		Total	Outcomes			
			MACE	p-value	death	p-value
N (%)		2443(100)	403(19.0)		268(11.06)	
Gender	Male	1886(77.2)	316(78.41)	0.624	167(62.31)	0.001>
	Female	557(22.8)	87(21.59)		101(37.69)	
Age group	18-45	263(10.77)	36(8.93)	0.001>	11(4.10)	0.001>
	46-65	1384(56.65)	217 (53.85)		95(35.45)	
	65<	796(32.58)	150 (37.22)		162(60.45)	
Educational level	Illiterate	738(32.21)	137(35.49)	0.001>	132(60.0)	0.001>
	1-5 year	582(25.40)	118(30.57)		46(20.91)	
	6-12 year	341(14.88)	53(13.73)		15(6.82)	
	Diploma	358(15.63)	43(11.14)		20(9.09)	
	College	272(11.87)	35(9.07)		7(3.18)	
Diabetes mellitus	No	1941(79.65)	315(78.16)	0.141	181(69.08)	0.001>
	Yes	496(20.35)	88(21.84)		81 (30.92)	
Hypertension	No	1420(58.17)	233(57.82)	0.206	108(40.60)	0.001>
	Yes	1021(41.83)	170(42.18)		158(59.40)	
Hyperlipidemia	No	1875 (77.07)	303(75.19)	0.436	208(80.62)	0.145
	Yes	558(22.93)	100(24.81)		50(19.38)	
Current smoker	No	1247(51.25)	215(53.35)	0.107	158(61.24)	0.001
	Yes	1186(48.75)	188(46.65)		100(38.76)	
Cancer	No	2406(98.89)	399(99.01)	0.726	248(96.12)	0.001>
	Yes	27(1.11)	4(0.99)		10(3.88)	
BMI (kg/m^2)	Below 18.5	47 (1.92)	12(2.98)	0.001	7(2.61)	0.001>
	18.5 – 24.9	930(38.07)	174(43.18)		103(38.43)	
	25.0 – 29.9	1038(42.49)	172(42.68)		88(32.84)	
	30.0 and Above	428(17.52)	45(11.17)		70(26.12)	
Prior CABG	No	2357(96.80)	385(95.53)	0.059	248(95.38)	0.180
	Yes	78(3.20)	18(4.47)		12(4.62)	
Prior PCI	No	2276(93.51)	363(90.07)	0.001	236(91.12)	0.107
	Yes	158(6.49)	40(9.93)		23(8.88)	
Prior MI	No	2059(87.65)	310(78.88)	0.001>	211(58.08)	0.194
	Yes	290(12.35)	83(21.12)		37(14.92)	
Prior stroke	No	2299(94.80)	377(93.55)	0.009	222(86.38)	0.001>
	Yes	126(5.20)	26(6.45)		35(13.62)	
LDL	-	104.9631±0.64	104.62±32.09	0.331	102.06±35.27	0.063
HDL	-	41.35±0.19	41.46±9.75	0.619	41.20±11.11	0.343
Total cholesterol	-	176.34±0.87	177.35±43.0	0.596	173.17±45.01	0.095

Table 2. The univariate and multiple logistic regression for evaluation of association between MACC and death, and comorbidity by adjusted important predictors.

Variables	MACE				Death			
	Crude OR (95%CI)	Model 1OR (95%CI)	Model 2 OR (95%CI)	Model 3 OR (95%CI)	Crude OR (95%CI)	Model 1 OR (95%CI)	Model 2 OR (95%CI)	Model 3 OR (95%CI)
Diabetes mellitus	1.22(0.93, 1.59)	1.25(0.94, 1.66)	1.28(0.96,1.70)	1.24(0.93,1.65)	1.89(1.42, 2.51)	1.76(1.26, 2.46)	1.68(1.16,2.43)	1.61(1.10,2.34)
Hyperlipidemia	1.10(0.85, 1.42)	1.09(0.83, 1.43)	1.14(0.87,1.49)	1.04(0.78, 1.37)	0.78(0.56, 1.08)	0.60(0.41, 0.89)	0.66(0.43, 1.00)	0.63(0.41,0.97)
Hypertension	1.15(0.92, 1.43)	0.99(0.78, 1.26)	1.04(0.81,1.33)	0.99(0.77,1.27)	2.22(1.71, 2.88)	1.37(1.00, 1.87)	1.75(1.23, 2.47)	1.69(1.19,2.38)
Cancer	0.92(0.37,2.29)	0.78(0.30, 2.04)	0.73(0.28, 1.92)	0.71(0.27,1.90)	3.08(1.79, 5.32)	2.33(1.28,4.26)	1.38(0.55, 3.42)	1.36(0.55, 3.40)
Current Smoking	0.83(0.67, 1.03)	0.88(0.68, 1.13)	0.85(0.66, 1.09)	0.87(0.67, 1.13)	0.63(0.48, 0.82)	0.94(0.67, 1.32)	1.05(0.73, 1.52)	1.00(0.68, 1.46)

Model 1= Adjusted by sex, age, and level of education.
Model 2= Model 1+adjusted by BMI.
Model 3= Model 1+ Model 2+adjusted by prior MI, Prior CABG, Prior stroke, and prior PCI.

Adjusted model 2 for model 1 plus BMI indicated the dual effects of BMI on the relationship between comorbidities and death. BMI had a reducing effect on the increased OR of death by diabetes mellitus and decreased the risk of death by diabetes mellitus (OR: 1.68; 95% CI: 1.16 to 2.43). However, BMI increased the influence of hypertension on death (OR: 1.75; 95% CI: 1.23 to 2.47). Adjusted model 3 for model 1 plus model 2 plus prior MI, prior CABG, prior stroke, and prior PCI, showing a reducing trend in the OR of death across the comorbidities.

The association between comorbidities and the OR of death and MACE (model 3) is illustrated in Figure 1.

Discussion

While it is well-known that comorbidities including hypertension, hyperlipidemia, smoking, cancer, and diabetes are associated with an increased risk for mortality, the remaining magnitude of risk for subsequent CV complications has not been adequately addressed. In this study of the relationship between comorbidities and CV outcomes in 2443 patients with STEMI, we found that the prevalence of comorbidities including hypertension (41.83%), hyperlipidemia (22.93%), smoking (48.75%), and diabetes (20.35%), was high in the study population. Athar et al. involved 28 771 patients to predict outcomes following MI by a history of diabetes, they found the prevalence of diabetes was 26% (16). Nguyen et al. assessed 302 patients hospitalized with a first AMI, showed that among the CVD comorbidities, hypertension was the most common comorbidity (59%) (17). Given the aging Iranian population, increasing westernized diet, and sedentary lifestyle, it is expected that the prevalence of patients with multiple comorbidities will continue to increase in Iran.

Our results demonstrated that the risk of MACE and death during the first year after the index STEMI was 19.0% and 11.06%, respectively. A large Swedish registry study involved 97,254 patients discharged after MI, reported that the risk of non-fatal MI, non-fatal stroke, or CV death at one-year follow-up was 18.3% (8). Likewise, a large Swedish registry study that comprised of the four-country analysis, included 114 364 survivors of MI, found that death, stroke, and MI at one-year follow up occurred in about one-third of patients (13). Suying Li et al. showed that one-third of patients died within one-year post-MI or ischemic stroke in 2019 (12). The high prevalence of CV events after one-year post-STEMI proposes that prolonged control, surveillance, and management of more than 12 months is needed in STEMI patients.

Our results showed that subjects with diabetes and hypertension had 1.61 and 1.69-fold higher risk for death after adjustment for important confounders. In the Hoorn cohort study, the incidence rate of a recurrent cardiovascular event per 100 person-years during approximately 4.1 years of follow-up was 12.5 (8.5–17.6) for individuals with diabetes. In other words, the incidence rate was 60% higher in diabetics compared with non-diabetics. (18). In 2017, Johansson et al. conducted a systematic review of patients who survived for at least 1 year following MI, found that comorbidities, including diabetes and hypertension, were associated with a greater risk of recurrent cardiovascular events or death (19). Suying Li et al. found a 1.5-fold increase in long-term death risk after MI for patients with diabetes compared with non-diabetics (12). Donahoe et al. assessed 62036 patients with ACS, diabetics were associated with significantly higher mortality one-year after UA/NSTEMI (adjusted HR 1.65) or STEMI (adjusted HR 1.22) (20). Athar et al. indicated that diabetes was strongly associated with an increased risk for all-cause death (adjusted hazard ratio (HR) 1.37), CV death (adjusted HR 1.38), fatal re-infarction (adjusted HR 1.78), HF hospitalization (adjusted HR 1.50), and composite outcomes (adjusted HR 1.48) during a mean follow-up of ~2 years (16). Mehlum et al. included 13 803 patients, reported that a 5 mmHg increase in SD of systolic blood pressure was related to a 10% increase in the risk of death (HR 1.10), and also higher visit-to-visit systolic blood pressure variation is related to increased risk of cardiovascular events in 2018.(21)

Our findings showed the decreased OR for death among patients with hyperlipidemia at one-year follow-up. Although the possibility of inverse causality cannot be ruled out, our analyses show that the decreased OR for death among patients with hyperlipidemia persists despite adjusting for important confounders. Thus, “protective” effects that have been attributed to hyperlipidemia in STEMI patients should be addressed in future studies. Van Der Heijden et al. reported that cholesterol levels were not a predictor for recurrent CV events.(18)

Strengths and limitations of the study

Our study has several limitations. First, the nature of the study design (observational registry) may not be able to control for the effects of cofactors due to non-randomized design, however, the researchers measured and controlled for the effects of main confounding factors. Second, differences in post-discharge care/treatment may have influenced the outcomes.

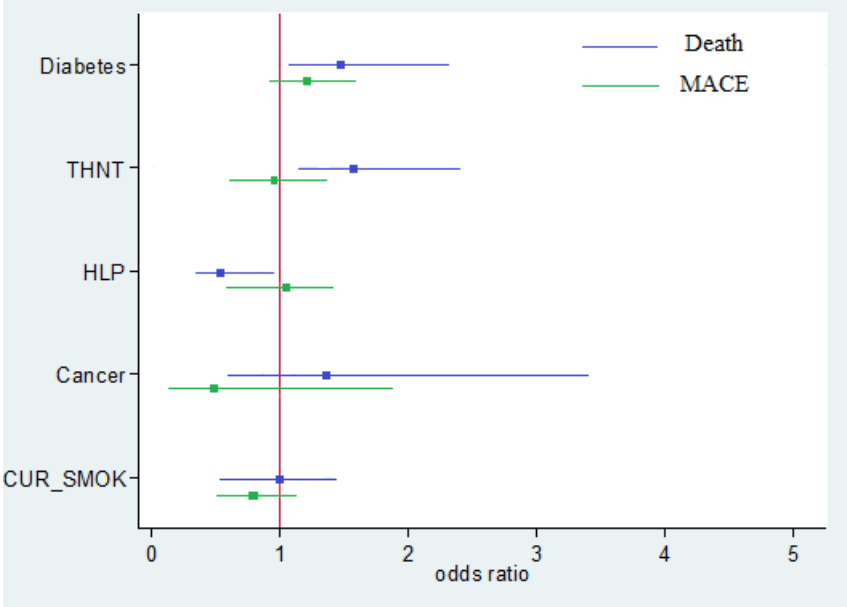

Figure 1.Forest plot of ORs (95% CIs) of death and MACE according to comorbidities.

Third, our data were derived from a single-center registry; thus, our findings may not be generalizable to other racial/ethnic populations. Data reported here can only determine the association between comorbidities and one-year outcomes; no long-term follow-up data are available. This study has some strengths for example this was the first population-based registry with a large sample done in the west of Iran. Furthermore, patients were evaluated by trained and experienced experts.

Conclusion

The prevalence of comorbidities such as hypertension, hyperlipidemia, smoking, and diabetes, was high in the study population. This sample of patients who survived an event of STEMI experienced high rates of MACE (19.0%) and high death rates (11.06%) at the one-year follow-up. Diabetes mellitus and hypertension increased the risk of death, however, hyperlipidemia decreased the risk of death. This protective effect that has been attributed to hyperlipidemia in STEMI patients should be addressed in future studies. The clinical implications highlight the need for tailoring intervention in all aspects of secondary prevention of CVD especially in patients suffering from comorbidities, managing the common comorbidities, and monitoring diabetics and hypertensive patients.

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