EURASIAN JOURNAL OF EMERGENCY MEDICINE
Original Article
DOI: 10.4274/eajem.galenos.2023.82474
Eurasian J Emerg Med. 2023;22(2): 114-20

Comparison of Myocardial Infarction Frequency in Normal and Late Period Populations After Carbon Monoxide Poisoning

Sedat Özbay

Sivas Numune Hospital, Clinic of Emergency Medicine, Sivas, Turkey

Abstract

Aim: Carbon monoxide (CO) poisoning is still an important factor in the rate of emergency visits. For this reason, we aimed to compare the incidence of myocardial infarction (MI) late after discharge of CO poisoning and its types as compared with the normal population.

Materials and Methods: A total of 1369 patients with a diagnosis of CO intoxication and 1617 patients without a history of cardiac disease who were admitted to the emergency department between January 2005 and December 2010 were included in the study. Patients with a COHb level above 10% and the control group was followed up for 60 months for MI. The patients were divided into three groups: inferior, anterior, and non-ST elevation MI.

Results: At the end of sixty months of follow-up, MI was determined in 103 (7.52%) of the CO group and 61 (3.77%) of the control group. When both groups were considered together, a significant relationship was found with gender, mortality, diabetes, hypertension, and use of tobacco products. However, when the CO group was evaluated sequentially, it was seen that it was only associated with gender, mortality, and MI types. MI groups were statistically significant with other variables except gender. In univariate and multivariate linear regression analyses, age, COHb, Tn level, and CO exposure time was found to cause increased mortality and risk of MI. After follow-up, inferior MI and mortality were higher in the patient group, and anterior MI and mortality were higher in the control group.

Conclusion: Acute COHb and Tn levels may be important values in defining the risk of late MI development in patients discharged after CO poisoning.

Keywords: Carbon monoxide poisoning, emergency department, late-period myocardial infarction

Introduction

Carbon monoxide (CO) poisoning, which is the leading cause of toxic deaths, constitutes an importImportantof emergency department (ED) admissions (1,2). Carboxyhemoglobin (COHb), which is formed by binding to hemoglobin with an affinity 240 times higher than oxygen, disrupts the distribution of oxygen to textures and carrying of oxygen Allosteric change occurs when uni of the CO binds to the heme part of the hemoglobin. The binding of the residual three oxygens to Heme increases and the emancipation of oxygen to tissues decreases (3,4). CO has more affinity for cardiac myoglobin than hemoglobin. Therefore, myocardial depression and hypotension may occur due to tissue hypoxia. CO combines with myoglobin and causes a decrease in partial oxygen in muscle tissue and ultimately causes rhabdomyolysis (4-6). Myocardial infarction (MI) can often be associated with CO exposure.

Even 5-10% increases in COHb level in people with coronary disease before can trigger Angina that occurs during exercise. High levels of COHb can lead to myocardial depression even in young and healthy individuals (6). Electrocardiogram (ECG) and cardiac troponin (Tn) should be studied in order not to overlook silent ischemia. Tns are sensitive and specific markers of heart muscle damage. In 2000, they were accepted as standard markers in the diagnosis of acute MI (7-10).

In the study, it was aimed to evaluate the relationship between Tn and COHb levels with the types of MI who presented with ED because of CO poisoning and that could develop in the late period after the patient was discharged.

Corresponding Author: Sedat Özbay MD, Sivas Numune Hospital, Clinic of Emergency Medicine, Sivas, Turkey
Phone: +90 505 355 55 65 **E-mail:** aciltip58@hotmail.com **ORCID ID:** orcid.org/0000-0002-8470-8529

Received: 18.11.2022
Accepted: 02.03.2023

Cite this article as: Özbay S. Comparison of Myocardial Infarction Frequency in Normal and Late Period Populations After Carbon Monoxide Poisoning. Eurasian J Emerg Med. 2023;22(2): 114-20.

Materials and Methods

In this cross-sectional cohort study, two groups above 18 years old who were referred to the ED between January 2005 and December 2010 were included. While the patients diagnosed with CO poisoning formed the patient group, and those who had recently been admitted to the emergency service with CO poisoning and had no history of cardiac disease formed the control group. While determining the control group, attention was paid to the age of the patients and to be close to the age of the cases diagnosed with CO poisoning.

Patients diagnosed with CO poisoning were divided into two groups at late-period (1-60 months) as acute coronary syndrome (ACS) development and non-development after discharge. Patients with ACS were divided into three groups inferior MI group (inferior, right ventricular, inferolateral, inferoposterior and posterior MI), anterior MI group (septal, anterior, lateral, high lateral and diffuse anterior MI), and non-ST elevated MI group.

Patients with previous diagnosis of infectious or inflammatory disease or malignancy, previous treatment for severe anemia or other hematological diseases or anemia, and those given erythrocyte suspension in the last six months were excluded from the search. After the patients were discharged from CO poisoning, they were followed up retrospectively for 60 months with an annual automation system.

Statistical Analysis

Data obtained in the study were analyzed using IBM Statistical Package for the Social Sciences Statistics for Windows 20.0 (IBM Corp., Armonk, NY, USA). The Shapiro-Wilk test was used to analyze the normal distribution of the variables. The Student's t-test was used for the variables with normal distribution, and the Mann-Whitney U test was used when examining the differences between the groups for those with non-normal distribution. Chi-square analysis was performed to examine the relationships between the nominal variable groups. Correlation analysis was performed using CO poisoning patient and control groups variables. In addition, univariate linear regression analysis was performed with all the variables in the CO poisoning patient and control groups variables. Predictive values were determined by multivariate linear regression analysis for the significant parameters in the univariate analysis. When interpreting the results, $p<0.05$ was considered statistically significant.

Results

The mean age of the patients was 51.71±17.62 years (52% male, 45.8% patients), and the mean follow-up period was 60 months (range 19 to 88). After sixty months of follow-up, MI was observed in 103 (7.52%) of 1369 patients in the CO group and in 61 (3.7%) of 1617 patients in the control group. The clinical and demographic characteristics of the patients are noted in Table 1.

After sixty months of follow-up, CO poisoning and control groups were found to be statistically significant with developing ACS and diabetes mellitus, hypertension, tobacco use, gender, mortality, and MI types (p=0.001, Table 2).

In the chi-square analysis between ACS and variables that developed after CO poisoning, diabetes mellitus (p=0.091), hypertension (p=0.954), and tobacco use (p=0.621). Were found to be statistically significant with gender, mortality, and MI types (p=0.001, Table 3).

As a result of sixty months of follow-up, in the chi-square analysis of MI types with variables, it was found to be statistically significant with gender (p=0.061), mortality, control and patient groups, hypertension, diabetes mellitus, and use of tobacco products (p=0.001, Table 4).

In univariate analysis, age, emergency admission time, mortality, aspartate amino transferase, alanine aminotransferase (ALT), alkaline phosphatase, C-reactive protein (CRP), Tn, and COHb levels were found to be prognostic indicators. However, in multivariate linear regression analysis, factors including age, the duration of emergency admission, mortality, ALT, CRP, Tn, and COHb were associated with increased MI risk (Table 5).

The correlation between Tn, COHb, mortality, exposure time to CO, and MI types with 60-month cardiac follow-up after CO poisoning was statistically significant (p=0.001, Table 6).

Discussion

In this study, we tried to determine MI types and prognosis after CO poisoning. CO poisoning can be acute or chronic. Since CO has a higher affinity to hemoglobin than oxygen, oxygen is delivered to tissues in fewer amounts. Thus cardiac toxicity may cause myocardial hypoxia. However, the direct toxic effect on myocardial mitochondria plays a more important role (11-14).

In the case of CO poisoning, the cause of cardiac damage is based on 2 mechanisms. The first is ischemic devastation provoked by COHb binding to heme proteins in lieu of oxygen, and the second is toxic damage directly induced by CO (2,15-19). While the cell undergoes direct toxic damage at the mitochondrial level with CO, cytochrome c oxidase inhibition and decreased glutathione levels occur (20,21). This results in anaerobic metabolism in cardiac myocytes, resulting in hypoxia, lactic acidosis, and apoptosis. The cause of endothelial damage is the induction

of the enzyme that occurs during apoptosis formation (22). In contrast, CO stimulates the oxidation of low-density lipoproteins and this increases the free radical formation by inducing peroxynitrite nascency in plasma (23,24). It has been shown that CO exposure triggers venous, arterial, and even stent thrombosis and has a prothrombotic effect (25-30).

In many studies conducted so far, gender and age vary. There were 1441 (48.2%) men in our study and the average age were 51.72 years. In the control group, there were 630 (38.9%) males and their mean age was 63.33 years, and in the patient group, 810 (59%) males and their mean age was 36.2 years. Türkmen and Akgöz (31) found 61.62% males and an average age of 37.73 years in their study; in the Durak (32) study, 71.83% males and 33.39 years of average age were determined. However, Hosseininejad et al. (33) in the meta-analysis study found that of the 4620 people included in the study, 40.12% were male and the average age was 31.68 years. The average age in our study was slightly higher. This may be due to the family and social structure and the other to the general increase in the age average of society. Cardiac involvement can occur immediately after exposure to CO or a few days later. Arrhythmias such as palpitations, sinus tachycardia, atrial fibrillation, and ventricular extrasystole may be observed. In severe cases, bradycardia and complete atrioventricular block may be seen (34). In those with ischemic heart disease, angina pectoris and MI can be triggered. ECG ST segment and T wave changes are common. Transient right and/or left ventricular wall motion disorders may be present (35). In the study published by Lippi et al. (36), the damage caused by CO to the cell; it has been reported that it may cause various cardiac clinical pictures such as cardiomyopathy, angina, MI, arrhythmia, heart failure, pulmonary edema, cardiogenic shock and sudden death. Cases of silent MI caused by acute CO poisoning without chest pain have been reported in the literature. CO cardiotoxicity may be clinically latent and often remain undiagnosed due to specific ischemic changes in ECG and inadequate symptoms (37,38).

There are many studies on ACSs. However, there is no clear information about MI frequency in studies. Sanchis-Gomar et al. (39) found the frequency of MI to be 1.1% in women and 1.7% in men. However, Turkey Cardiovascular Diseases

Table 1. Baseline characteristics of study patients

		Five-year follow-up patients with			Troponin level after carbon monoxide patients with		
	All patients n=2986 Mean±SD	**Control group n=1617 Mean±SD**	**CO patients group n=1369 Mean±SD**	**p value**	**(+) Troponin n=103 Mean±SD**	**(-) Troponin n=1266 Mean±SD**	**p value**
Age (y)	51.72±17.62	63.22±10.51	36.24±15.62	**0.001**	65.44±13.25	33.51±13.20	**0.001**
Female	1545 (51.8%)	987 (61.04%)	559 (40.83%)	**0.001**	64 (62.13%)	752 (59.39%)	**0.024**
Male	1441 (48.2%)	630 (38.96%)	810 (59.17%)		39 (37.87%)	521 (40.61%)	
CRP (mg/L)	4.15±6.23	4.13±6.17	4.19±6.29	0.876	6.26±5.04	3.86±5.99	**0.001**
CO ET (h)	-	-	3.12±2.06	**0.014**	7.10±2.97	2.76±1.61	**0.001**
WBC (10^3/uL)	10.23±3.82	10.22±3.80	10.23±3.83	0.954	11.41±3.29	10.14±3.90	**0.001**
RDW (%)	14.67±1.83	14.67±1.83	14.66±1.81	0.895	14.82±2.00	14.68±1.79	0.327
MPV (fL)	8.43±1.01	8.43±1.03	8.42±0.99	0.797	8.44±0.97	8.42±0.98	0.989
MCHC (g/dL)	33.35±3.59	33.33±3.50	33.38±3.69	0.899	33.34±4.19	33.34±3.38	0.295
MCV (fL)	87.45±7.64	87.31±7.60	87.68±7.71	0.129	87.42±7.60	87.50±7.67	0.829
MCH (pg)	29.28±2.25	29.29±2.24	29.46±2.24	**0.015**	29.38±2.77	29.45±2.19	0.492
BS (mg/dL)	120.82±45.78	120.86±45.82	120.71±45.84	0.521	133.32±44.28	119.89±45.97	**0.004**
AST (U/L)	31.31±23.61	31.21±23.94	31.35±23.21	0.376	45.34±17.32	30.27±22.41	**0.001**
ALT (U/L)	29.40±24.08	29.32±24.31	29.40±23.81	0.587	45.64±20.14	27.91±22.58	**0.001**
ALP (U/L)	107.21±55.25	106.69±55.86	107.59±54.36	0.377	154.85±52.94	102.94±51.41	**0.001**
COHb (%)	-	-	31.63±10.11	**0.001**	55.08±6.23	28.83±6.86	**0.001**
Tn (ng/dL)	-	-	0.92±1.24	**0.001**	1.52±1.39	0.24±0.08	**0.001**

$p<0.05$.
Statistical data were obtained with the Mann-Whitney U test. $p<0.05$ value was considered statistically significant.
(+): Positive, (-): Negative, CRP: C-reactive protein, CO ET: Carbon monoxide exposure time, WBC: White blood cell, RDW: Red cell distribution width, MPV: Mean platelet volume, MCHC: Mean corpuscular hemoglobin concentration, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, BS: Blood sugar, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, ALP: Alkaline phosphatase, CK: Creatine kinase, CK-MB: Creatine kinase-muscle brain, COHb: Carboxyhemoglobin, Tn: Troponin, SD: Standard deviation

Prevention and Control Program Action Plan (40) women in the study 1.33%, 3.03% in men was found to be acute MI. In our study, patients discharged after CO poisoning was followed for 60 months. These data were retrospectively recorded annually. After CO poisoning, MI types that were not previously detected in the literature were examined. At the end of this 60-month follow-up, it was observed that MI developed in 103 (7.52%) patients in the CO group. In spite of the higher mean age of the control group 61 (3.7%) cases had MI. The 2-fold higher MI frequency may be a predictive indicator of MI that may develop CO intoxication. Tn and COHb values in all patients of the Co patient group were significantly higher than those without MI at the 60-month follow-up. Inferior MI in the CO patient group and anterior MI in the control group was more common. While most MI cases in the control group were diagnosed with hypertension, most cases developing MI after intoxication was normotensive patients. This could be due to two reasons. First, the inferior group MI is generally hypotensive and bradycardic. Second, the sinus node is close to the right coronary artery. It was most common in mortality in MI with ST elevation, especially in the inferior MI group.

Henry et al. (41) found that acute myocardial damage in patients with CO poisoning, followed for an average of 7.6 years, is a long-term risk of death. In another study with 10.6 years follow-up after CO poisoning, it was found to be a neutral predictor of all long-term mortal situations. Huang et al. (42) found that CO intoxication increases the risk of death in the long term. Lee et al. (43) showed that CO intoxication increases the risk of CAD and heart failure in the long term.

In our study, during the 60-month follow-up, mortality was detected as 31 (2.2%) in the CO patient group and 19 (1.1%) in the control group. In all cases with mortality in the CO patient group, it was determined that the COHb level was above 40 and the accompanying Tn elevation. Mortality in the CO patient group was common in the inferior MI group, and in the control

Table 2. Analysis of patient and control groups according to variables after five years of follow-up

	Five-year follow-up		χ^2	p value
	The CO patient group n (%)	Control group n (%)		
Gender				
Male	559 (18.7)	987 (51.8)	**121.228**	**<0.001**
Female	810 (27.1)	630 (21.1)		
Mortality				
No	1338 (44.8)	1598 (53.5)	**5.344**	**<0.021**
Yes	31 (1.0)	19 (0.6)		
HT				
No	1152 (38.6)	842 (28.2)	**343.844**	**<0.001**
Yes	217 (7.3)	775 (26.0)		
DM				
No	1026 (34.4)	1009 (33.8)	**53.759**	**<0.001**
Yes	343 (11.5)	608 (20.4)		
Tobacco				
No	379 (12.7)	1137 (38.1)	**539.060**	**<0.001**
Yes	990 (33.2)	480 (16.1)		
MI				
No	1266 (42.4)	1556 (52.1)	**40.054**	**<0.001**
Inferior	64 (2.1)	16 (0.5)		
Anterior	30 (1.0)	39 (1.3)		
NSTEMI	9 (0.3)	6 (0.2)		

Statistical data were obtained with the chi-square test. p<0.05 value was considered statistically significant.
DM: Diabetes mellitus, HT: Hypertension, MI: Myocardial infarction, NSTEMI: Non-ST elevation MI, CO: Carbon monoxide

Table 3. Analysis of variables with AMI according to 5-year follow-up in the CO patient group

	Troponin		χ^2	p value
	Negative n (%)	Positive n (%)		
Gender				
Male	514 (40.6)	38 (38.8)	**8.893**	**<0.002**
Female	756 (59.4)	60 (61.2)		
Mortality				
No	1338 (97.7)	31 (2.3)	**140.923**	**<0.001**
Yes	80 (81.6)	18 (18.4)		
DM				
No	850 (93.6)	58 (6.4)	4.799	>0.091
Yes	421 (91.3)	40 (8.7)		
HT				
No	849 (92.9)	64 (7.1)	0.095	>0.954
Yes	422 (92.5)	34 (7.5)		
Tobacco				
No	763 (92.5)	61 (7.5)	0.953	>0.621
Yes	508 (93.2)	37 (6.8)		
MI				
No	1266 (99.7)	3 (0.3)	**1315.788**	**<0.001**
Inferior	1 (1.7)	61 (98.3)		
Anterior	0 (0)	29 (100)		
NSTEMI	2 (22.2)	7 (77.8)		

Statistical data were obtained with the chi-square test. p<0.05 value was considered statistically significant.
DM: Diabetes mellitus, HT: Hypertension, MI: Myocardial infarction, NSTEMI: Non-ST elevation MI, CO: Carbon monoxide

Table 4. Analysis of patients who developed AMI after five years of follow-up with variables						
Acute myocardial infarction						
	No n (%)	**Inferior n (%)**	**Anterior n (%)**	**NSTEMI n (%)**	**χ^2**	**p value**
Gender						
Male	1476 (49.4)	38 (1.3)	27 (0.9)	5 (0.2)	7.363	0.061
Female	1346 (45.1)	42 (1.4)	42 (1.4)	10 (0.3)		
Mortality						
No	2796 (93.6)	69 (2.3)	58 (1.9)	13 (0.4)	**178.269**	**0.001**
Yes	26 (0.9)	11 (0.4)	11 (0.4)	2 (0.1)		
Five-year CO						
Follow-up	1266 (42.4)	64 (2.1)	30 (1.0)	9 (0.3)	**40.054**	**0.001**
Cont	1556 (52.1)	16 (0.5)	39 (1.3)	6 (0.2)		
HT						
No	1928 (64.6)	27 (0.9)	31 (1.0)	8 (0.3)	**58.434**	**0.001**
Yes	894 (29.9)	53 (1.8)	38 (1.3)	7 (0.2)		
DM						
No	1960 (65.6)	39 (1.3)	30 (1.0)	6 (0.2)	**40.910**	**0.001**
Yes	862 (28.9)	41 (1.4)	39 (1.3)	9 (0.3)		
Tobacco						
No	1390 (46.6)	57 (1.9)	54 (1.8)	15 (0.5)	**51.422**	**0.001**
Yes	1432 (48.0)	23 (0.8)	15 (0.5)	0 (0.0)		

Statistical data were obtained with the chi-square test. P<0.05 value was considered statistically significant.
NSTEMI: Non-ST elevation myocardial infarction, CO: Carbon monoxide, AMI: Acute myocardial infarction

Table 5. Univariate and multivariate linear regression analysis for predicting the development of acute myocardial infarction in the CO patient group										
Acute myocardial infarction										
	Univariate					**Multivariate**				
	R square	**F**	**β**	**t**	**p value**	**R square**	**F**	**β**	**t**	**p value**
Age	**0.112**	**172.753**	**-0.214**	**-6.510**	**<0.001**			**0.002**	**59.675**	**<0.001**
CO ET (h)	**0.105**	**159.865**	**-0.067**	**-2.836**	**<0.005**			**0.011**	**3.697**	**<0.001**
Mortality	**0.303**	**6.081**	**0.249**	**4.881**	**<0.001**			**-0.678**	**9.925**	**<0.001**
ALT	**0.014**	**19.179**	**0.109**	**4.983**	**<0.001**			**0.000**	**0.798**	**<0.029**
CRP	**0.016**	**12.169**	**0.140**	**8.496**	**<0.001**	**0.883**	**359.259**	**0.004**	**4.986**	**<0.001**
Tn	**0.223**	**391.213**	**0.114**	**9.005**	**<0.001**			**0.051**	**5.529**	**<0.001**
COHb	**0.386**	**859.500**	**-0.810**	**-22.78**	**<0.001**			**0.007**	**10.259**	**<0.001**
BS	0.001	0.685	0.153	3.925	>0.408					
AST	**0.006**	**7.840**	**0.131**	**5.643**	**<0.005**					
ALP	**0.029**	**40.904**	**0.010**	**0.347**	**<0.001**					

Statistical data were obtained with uni/multivariate regression analysis. P<0.05 value was considered statistically significant.
CO ET: Carbon monoxide exposure time, COHb: Carboxyhemoglobin

Table 6. Correlation coefficients for 5-year cardiac follow-up		
Acute myocardial infarction		
	R	**p value**
Mortality	**0.234**	**<0.001**
COHb	**0.621**	**<0.001**
Tn	**0.472**	**<0.001**
CO ET(h)	**0.234**	**<0.001**
AMI	**0.384**	**<0.001**

Statistical data were obtained by correlation analysis. p<0.05 value was considered statistically significant.
CO ET: Carbon monoxide exposure time, COHb: Carboxyhemoglobin, AMI: Acute myocardial infarction

group, anterior MI was common. The correlation between MI and mortality was positively correlated.

This is the first study to establish whether high co levels are a long-term detached risk factor for MI types. Kalay et al. (44) emphasized that increased CO levels in blood and extended duration of exposure to CO poisoning are risk factors for MI development. In our study, the exposure time and rate of cardiac damage were similar.

As a result, the high COHb and Tn values in the acute period of the patients who applied to the ED with CO poisoning and the MI frequency in the late period after discharge were more than two times higher than the normal population. In addition, while anterior MI and mortality were common in the normal population, inferior MI and mortality were found to be higher in the CO patient group. These data show that patients are in a higher risk group after CO discharge.

Study Limitations

The major limitation of the study is that it is not multi-centered and retrospective. Therefore, it was difficult to reach some data.

Conclusion

Cardiac disorders that may develop in the future can be easily overlooked in CO poisoning, especially if the patients are asymptomatic. Considering the COHb and Tn levels evaluated in our study by physicians may guide the prevention of future cardiac problems and early diagnosis.

Ethics

Ethics Committee Approval: The study was approved by the Cumhuriyet University Faculty of Medicine of Local Ethics Committee (decision no: 2012/12-09, date: 04.12.2012).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Financial Disclosure: The author declared that this study received no financial support.

References

1. Ernst A, Zibrak JD. Carbon monoxide poisoning. N Engl J Med. 1998;339:1603-8.
2. Weaver LK. Clinical practice. Carbon monoxide poisoning. N Engl J Med. 2009;360:1217-25.
3. No authors listed. Health effects of outdoor air pollution. Part 2. Committee of the Environmental and Occupational Health Assembly of the American Thoracic Society. Am J Respir Crit Care Med. 1996;153:477-98.
4. Kandis H, Katırcı Y, Çakır Z, Aslan Ş, Uzkeser M, Bilir Ö. Retrospective Analysis of Embolic Carbon Monoxide Intoxication Cases. Academic Emergency Med J. 2007;5:21-5.
5. Koruk S, Tuncel İ, Mızrak A, Akçalı AH, Ganidağlı S. Cerebrovascular Changes and EEG Findings in Carbon Monoxide Intoxication: Case Report. AKATOS. 2010;1:23-6.
6. Stanley T. Omaye, Metabolic Modulation of Carbon Monoxide Toxicity. Toxicology. 2002;180:139-50.
7. Katırcı Y. The frequency and associated factors of neuropsychiatric disorders in patients poisoned with carbon monoxide. Master thesis; Erzurum-Turkey 2005.
8. Kavsak PA, MacRae AR, Lustig V, Bhargava R, Vandersluis R, Palomaki GE, et al. The impact of the ESC/ACC redefinition of myocardial infarction and new sensitive troponin assays on the frequency of acute myocardial infarction. Am Heart J. 2006;152:118-25.
9. Braunwald E, Antman EM, Beasley JW, Califf RM, Cheitlin MD, Hochman JS, et al. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction-summary article: a report of the American College of Cardiology/American Heart Association task force on practice guidelines (Committee on the Management of Patients With Unstable Angina). J Am Coll Cardiol. 2002;40:1366-74.
10. Task Force for Diagnosis and Treatment of Non-ST-Segment Elevation Acute Coronary Syndromes of European Society of Cardiology; Bassand JP, Hamm CW, Ardissino D, Boersma E, Budaj A, et al. Guidelines for the diagnosis and treatment of non-ST-segment elevation acute coronary syndromes. Eur Heart J. 2007;28:1598-660.
11. Panteghini M, Pagani F, Yeo KT, Apple FS, Christenson RH, Dati F, et al. Evaluation of imprecision for cardiac troponin assays at low-range concentrations. Clin Chem. 2004;50:327-32.
12. Penney DG. Hemodynamic response to carbon monoxide. Environ Health Perspect. 1988;77:121-30.
13. McMeekin JD, Finegan BA. Reversible myocardial dysfunction following carbon monoxide poisoning. Can J Cardiol. 1987;3:118-21.
14. Gandini C, Castoldi AF, Candura SM, Locatelli C, Butera R, Priori S, et al. Carbon monoxide cardiotoxicity. J Toxicol Clin Toxicol. 2001;39:35-44.
15. Teksam O, Gumus P, Bayrakci B, Erdogan I, Kale G. Acute cardiac effects of carbon monoxide poisoning in children. Eur J Emerg Med. 2010;17:192-6.
16. Horner JM. Anthropogenic emissions of carbon monoxide. Rev Environ Health. 2000;15:289-98.
17. Boehning D, Moon C, Sharma S, Hurt KJ, Hester LD, Ronnett GV, et al. Carbon monoxide neurotransmission activated by CK2 phosphorylation of heme oxygenase-2. Neuron. 2003;40:129-37.
18. Schmidt R, Ryan H, Hoetzel A. Carbon monoxide--toxicity of low-dose application. Curr Pharm Biotechnol. 2012;13:837-50.
19. Hampson NB. Emergency department visits for carbon monoxide poisoning in the Pacific Northwest. J Emerg Med. 1998;16:695-8.

20. Townsend CL, Maynard RL. Effects on health of prolonged exposure to low concentrations of carbon monoxide. Occup Environ Med. 2002;59;10:708-11.
21. Alonso JR, Cardellach F, López S, Casademont J, Miró O. Carbon monoxide specifically inhibits cytochrome c oxidase of human mitochondrial respiratory chain. Pharmacol Toxicol. 2003;93:142-6.
22. Taskiran D, Nesil T, Alkan K. Mitochondrial oxidative stress in female and male rat brain after ex vivo carbon monoxide treatment. Hum Exp Toxicol. 2007;26:645-51.
23. Thom SR, Fisher D, Xu YA, Notarfrancesco K, Ischiropoulos H. Adaptive responses and apoptosis in endothelial cells exposed to carbon monoxide. Proc Natl Acad Sci U S A. 2000;97:1305-10.
24. Thom SR, Fisher D, Xu YA, Garner S, Ischiropoulos H. Role of nitric oxide-derived oxidants in vascular injury from carbon monoxide in the rat. Am J Physiol. 1999;276;984-92.
25. Wattel F, Favory R, Lancel S, Neviere R, Mathieu D. Monoxyde de carbone et coeur: des effets univoques? [Carbon monoxide and the heart: unequivocal effects?]. Bull Acad Natl Med. 2006;190:1961-74.
26. Franchini M, Mannucci PM. Short-term effects of air pollution on cardiovascular diseases: outcomes and mechanisms. J Thromb Haemost. 2007;5:2169-74.
27. Baccarelli A, Martinelli I, Zanobetti A, Grillo P, Hou LF, Bertazzi PA, et al. Exposure to particulate air pollution and risk of deep vein thrombosis. Arch Intern Med. 2008;168:920-7.
28. Franchini M, Mannucci PM. Particulate air pollution and cardiovascular risk: short-term and long-term effects. Semin Thromb Hemost. 2009;35:665-70.
29. Dileo PA, Tucciarone M, Castro ER, Guerrero M. Late stent thrombosis secondary to carbon monoxide poisoning. Cardiovasc Revasc Med. 2011;12:56-8.
30. Wronska A, Kurkowska-Jastrzebska I, Santulli G. Application of microRNAs in diagnosis and treatment of cardiovascular disease. Acta Physiol (Oxf). 2015;213:60-83.
31. Türkmen N, Akgöz S. Deaths due to carbonmonoxide poisoning autopsied in Bursa. J Forensic Med. 2005;19:20-5.
32. Durak D. Deaths due to carbon monoxide poisoning. Bursa State Hospital Bulletin. 1999;15:131-3.
33. Hosseininejad SM, Aminiahidashti H, Goli Khatir I, Ghasempouri SK, Jabbari A, Khandashpour M. Carbon monoxide poisoning in Iran during 1999-2016: A systematic review and meta-analysis. J Forensic Leg Med. 2018;53:87-96.
34. Lee D, Hsu TL, Chen CH, Wang SP, Chang MS. Myocardial infarction with normal coronary artery after carbon monoxide exposure: a case report. Zhonghua Yi Xue Za Zhi (Taipei). 1996;57:355-9.
35. McMeekin JD, Finegan BA. Reversible myocardial dysfunction following carbon monoxide poisoning. Can J Cardiol. 1987;3:118-21.
36. Lippi G, Rastelli G, Meschi T, Borghi L, Cervellin G. Pathophysiology, clinics, diagnosis and treatment of heart involvement in carbon monoxide poisoning. Clin Biochem. 2012;45:1278-85.
37. Fiorista F, Casazza F, Comolatti G. Silent myocardial infarction caused by acute carbonmonoxide poisoning. G Ital Cardiol. 1993;23:583-7.
38. Marius-Nunez AL. Myocardial infarction with normal coronary arteries after acute exposure to carbonmonoxide. Chest. 1990;97:491-4.
39. Sanchis-Gomar F, Perez-Quilis C, Leischik R, Lucia A. Epidemiology of coronary heart disease and acute coronary syndrome. Ann Transl Med. 2016;4:256.
40. Turkey Cardiovascular Diseases Prevention and Control Program Action Plan 2015-2020. Available from: https://www.tkd.org.tr/TKDData/Uploads/files/Turkiye-kalp-ve-damar-hastaliklari-onleme ve-kontrol-programi.pdf.
41. Henry CR, Satran D, Lindgren B, Adkinson C, Nicholson CI, Henry TD. Myocardial injury and long-term mortality following moderate to severe carbon monoxide poisoning. JAMA. 2006;295:398-402.
42. Huang CC, Chung MH, Weng SF, Chien CC, Lin SJ, Lin HJ, et al. Long-termprognosis of patients with carbon monoxide poisoning: a nationwide cohort study. PLoS One. 2014;9:105503.
43. Lee FY, Chen WK, Lin CL, Kao CH. Carbon monoxide poisoning and subsequent cardiovascular disease risk: a nationwide population-based cohort study. Medicine (Baltimore). 2015;94:624.
44. Kalay N, Ozdogru I, Cetinkaya Y, Eryol NK, Dogan A, Gul I, et al. Cardiovascular effects of carbon monoxide poisoning. Am J Cardiol. 2007;99:322-4.