Research Square

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Can Indices of Myocardial Damage Predict Carbon Monoxide Poisoning Outcomes?

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Abstract

Background: Carbon monoxide causes electrical, functional, and morphological changes in the heart. It is not clear, however, whether the indices of myocardial damage can predict the patient's prognosis after carbon monoxide poisoning. This retrospective study aimed to investigate the relation between the carboxyhemoglobin level and electrocardiographic (ECG) changes and whether the ECG changes and troponin I levels are related to the patient's prognosis after carbon monoxide poisoning.

Results: Carboxyhemoglobin, troponin I, and ECG parameters were measured in 70 patients with carbon monoxide poisoning. The QT and RR intervals were measured for each ECG lead in all patients, and the corrected QT interval and corrected QT dispersion were calculated. The correlation between the maximum corrected QT interval and the carboxyhemoglobin level was significant (P=0.0072, R^2=0.1017), as were the relationships between QT dispersion and carboxyhemoglobin (P<0.001, R^2=0.2358) and the corrected QT dispersion and carboxyhemoglobin (P<0.001, R^2=0.2613). The multivariate logistic analysis showed that the significant predictors of sequential disability were hyperbaric oxygen therapy (P=0.0182), corrected QT dispersion (P=0.0062), and troponin I level (P=0.0002).

Conclusions: Patients' prognosis following carbon monoxide poisoning can be predicted based on corrected QT dispersion and the troponin I level. Patients with myocardial damage should be monitored not only for their cardiovascular outcome but also for their neurological outcome and their prognosis.

Background

Carbon monoxide is a colorless, odorless, non-irritating gas. It is produced endogenously in small amounts as a byproduct of the catabolism of heme molecules[1]. It can also be inhaled when hydrocarbon-containing fuels are not completely burned [1, 2]. Survivors of carbon monoxide poisoning may suffer neurological and psychiatric sequelae[1]. Carbon monoxide causes electrical, functional, and morphological changes in the heart[3]. The QT interval has long been known to vary significantly among the individual leads of a surface 12-lead electrocardiogram [3].

A potential clinical application of this inter-lead difference was proposed in 1990 by Day et al., who suggested that the inter-lead difference in the QT interval might provide a measure of repolarization inhomogeneity, which they called "QT dispersion" [3,4]. Although it has been established that carbon monoxide induces electrocardiographic (ECG) changes and alterations of cardiac biomarkers [3, 5], it is not clear whether the indices of myocardial damage can predict the patient's prognosis after carbon monoxide toxicity. Hence, this study aimed to investigate the relation between carboxyhemoglobin and ECG changes and whether the ECG changes and troponin I levels are related to the prognosis of patients with carbon monoxide poisoning.

Methods

The study group of this retrospective study included 70 consecutive patients with carbon monoxide poisoning (42 men, 28 women; age 52±18 years) who had been admitted to St. Mary's Hospital, Kurume, Japan for treatment between June 2013 and September 2019. Clear electrocardiograms were available for each patient. Patients' carbon monoxide poisoning had been confirmed by arterial blood analysis. Carboxyhemoglobin measurements were performed in the ambulance and/or at admission. The highest values were adopted. Encephalopathy was defined as the development or the recurrence of symptoms such as difficulty concentrating, dementia, psychomotor retardation, Parkinsonism, and amnesia or the diagnose from magnetic resonance imaging at discharge or until 6 weeks after admission.

QT interval measures and cardiac enzymes

All 12-lead electrocardiograms were obtained at a paper speed of 25mm/sec with standard lead positions. QT and RR intervals were measured on each electrocardiogram in all patients. The QT interval was measured from the beginning of the QRS complex to the end of the T wave. The QT intervals for each lead were measured and corrected for heart rate (QTc) using Bazett's formula ($QT/\sqrt{RR}$) [6]. The QTc dispersion was the difference between the leads with the shortest and longest QTc intervals [4]. QT intervals were measured upon admission to the emergency department. Additionally, blood samples were obtained and the troponin I level was determined.

Statistical analysis

Retrospective statistical analyses were performed using JMP and SAS university edition software (SAS Institute Inc., Cary, NC, USA). Results are presented as means ± SDs. Independent samples t-test was used to compare continuous variables and Chi-square test or Fisher's exact test was used for categorical variables. Spearman correlation analysis and logistic analysis were used to examine the relationships between carboxyhemoglobin levels and clinical variables. A value of $P<0.05$ was considered to indicate statistical significance.

Results

Patients

Altogether, 70 patients were included in the study. Clinical characteristics of the patients are presented in Table 1. Two patients died after admission. In all, 12 patients were diagnosed with encephalopathy at or after discharge, whereas no patients exhibited cardiomyopathy at or after discharge.

Correlation between carboxyhemoglobin and QT intervals

The correlation between maximum QT intervals and the carboxyhemoglobin levels was not significant. Conversely, the correlation between the maximum QTc interval and the carboxyhemoglobin level was significant ($P=0.0072$, $R^2=0.1017$; Fig. 1), as were the relationships between QT dispersion and carboxyhemoglobin (P<0.001, R^2=0.2358; Fig. 1) and the QTc dispersion and carboxyhemoglobin (P<0.001, R^2=0.2613; Fig. 1).

The comparison between the patients with and without sequential disability.

There are not difference in sex and age between the patients with and without sequential disability. The frequencies of the patients taking minor tranquilizers, major tranquilizers, antidepressants, and other drugs did not change with or without sequential disability (Table 2). Maximum QT interval (p=0.0269), corrected maximum QT interval (p=0.0002), QT dispersion (p=0.0003) and corrected QT dispersion (p=0.0001) in the patients with sequential disability were significantly longer than them without it (Table 2). There was no difference in the carboxyhemoglobin level between the patients with and without sequential disability (Table 2).

Logistic analyses

Death, carbon monoxide encephalopathy, and cardiomyopathy at or after discharge were defined as sequential disabilities. However, none of the patients in this study had cardiomyopathy. The reference values for the maximum QTc interval, QTc dispersion, carboxyhemoglobin level, and troponin I level were established based on the Classification and Regression Tree. Univariate logistic analysis showed that the significant predictors of sequential disability were smoking (P=0.0361), consciousness disorder on admission (P=0.0072), maximum QTc interval time (>484 ms; P=0.0009), QTc dispersion (>46 ms; P=0.0003), high concentration of carboxyhemoglobin (>44%; P=0.0044), and high troponin I level (>0.36 ng/ml; P<0.001; Table 3). The multivariate logistic analysis indicated that the significant predictors of sequential disability were hyperbaric oxygen therapy (P=0.0182), QTc dispersion (P=0.0062), and troponin I level (P=0.0002; Table 3).

Discussion

Carbon monoxide poisoning, a serious health problem, is associated with a high incidence of severe morbidity and mortality. It causes myocardial toxicity and life-threatening arrhythmias. Carbon monoxide reduces the oxygen-carrying capacity of blood and binds with cardiac myoglobin, causing a rapid decrease in myocardial oxygen reserves [6]. Several studies have shown that carbon monoxide intoxication causes increased QT intervals and QT dispersions [6-8]. This study showed that QTc dispersion and carboxyhemoglobin are significantly related. Furthermore, QTc dispersion and troponin I are predictors of sequential disability.

Correlation between carboxyhemoglobin and QT intervals

The *QT interval* is an indicator of ventricular repolarization on the electrocardiogram. A *prolonged QT interval* reflects impaired myocardial refractoriness. *QT dispersion* reflects the physiological variability of regional ventricular repolarization. *Increased QT* dispersion is related to the heterogeneity of regional ventricular repolarization and is accepted as a marker for arrhythmia and sudden death [9]. In this study, the QTc interval and QTc dispersion correlated with the carboxyhemoglobin level. Hanci et al. also reported that the QTc interval and QTc dispersion show good correlations with carboxyhemoglobin [10]. Increased QTc dispersion and interval in carbon monoxide toxicity might be caused by carbon monoxide on the myocardium, which causes homogeneous impulse formation in the ventricles.

The relation between the prognosis of patients with carbon monoxide toxicity and cardiac markers

The univariate logistic analysis indicated that the predictors of sequential disability in patients with carbon monoxide toxicity were smoking, consciousness disorder, maximum QTc interval, QTc dispersion, carboxyhemoglobin, and troponin I. The multivariate analysis revealed that the significant predictors of sequential disability were hyperbaric oxygen therapy, QTc dispersion, and troponin I. Note that the multivariate analysis did not find that carboxyhemoglobin was related to a poor outcome. The prognosis of patients with carbon monoxide toxicity could be predicted by the duration of carbon monoxide exposure and its concentration. Conversely, carboxyhemoglobin was not necessarily related to the exposure time or the concentration of the carbon monoxide. Because patients with carbon monoxide toxicity usually receive treatment immediately after the rescue, carboxyhemoglobin was not measured at its peak concentration.

Hampson et al. found that carboxyhemoglobin measurement was a poor predictor of clinical status in patients with carbon monoxide poisoning [11]. Moreover, mortality was associated with the absolute difference in carboxyhemoglobin [11]. Satran et al., however, reported that moderate-to-severe carbon monoxide poisoning causes myocardial injury when assessed by electrocardiography or biomarkers [5]. Henry et al. reported that patients with myocardial injury (cardiac troponin I >0.7 ng/ml, the creatine kinase-MB level, and/or diagnostic ECG changes) had increased mortality [12].

Carbon monoxide-mediated toxicity results from several factors. Carbon monoxide binds to hemoglobin with an affinity 200–250 times that of oxygen. Thus, exposure to carbon monoxide, even in low concentrations, results in competitive binding to hemoglobin, reduced oxygen delivery, and profound tissue hypoxia [13]. Carbon monoxide also binds to cytochrome-c oxidase, directly interfering with cellular respiration [14]. These mechanisms are believed to cause neurological injury and likely contribute to myocardial injury as well [12]. Although there were no patients with cardiomyopathy at/after discharge in this study, the indices of myocardial injury could lead to neurological injury or even mortality. The mechanisms described influence this result.

Limitations

The primary limitations of this study were the small sample population, single-center design, and retrospective nature. Because our subjects included both intentional and unintentional patients, the beginning time of the carbon monoxide exposure could not be found out in many patients. Therefore the exposure time could not be calculated exactly. Despite these limitations, the study may act as a good basis for further study of the topic. The findings must be confirmed in prospective, multicenter studies with larger populations.

Conclusion

The prognosis for patients with carbon monoxide poisoning may be predicted based on the QTc dispersion value and the troponin I level. Patients with myocardial damage should be monitored not only for their cardiovascular outcome but also for their neurological outcome and their prognosis.

Abbreviations

ECG: electrocardiogram

QTc: corrected QT interval

Declarations

Availability of data and materials

The datasets used in the current study are available from the corresponding author on reasonable request.

DISCLOSURES

The protocol for this research project was approved by a suitably constituted ethics committee of our institution (St. Mary's Hospital; Approval No. 19-0710). The study conforms to the provisions of the Declaration of Helsinki.

Consent for publication

Not applicable

Competing interests

There are no competing interests to declare in this study.

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Contributions

HT, KY, and HK conducted the study design. KY, HK, KM, TI, AO, SU, SS, and KO collected the data. HT performed the statistical analysis and prepared this manuscript. HT, HK, and HY finalized the manuscript. The authors read and approved the final manuscript.

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Tables

Table 1. Patients' characteristics

Male sex (%)	42 patients (60%)
Age (mean ± SD)	51.6 ± 18.2 years
Smoker	26 patients (37.1%)
Hypertension	10 patients (14.3%)
Diabetes mellitus	4 patients (5.7%)
Asymptomatic patients (%)	23 patients (33%)
Consciousness disorder on admission (%)	37 patients (53%)
Cardiopulmonary arrest (%)	3 patients (4%)
Hyperbaric oxygen therapy (%)	49 patients (70%)
Carboxyhemoglobin level (%) (normal range 0.5–1.5)	21.8±14.8
Troponin I (ng/ml) (normal range 0.00–0.09)	0.85±3.36
Mean emergency department arrival time (min)	165±148

Table 2. The comparison between the patients with and without sequential disability.

	Sequential disability (+) n=15	Sequential Disability (-) n=55	p
Sex (Male :%)	67% (n=10)	58% (n=32)	0.5521
Hypokalemia (%)	20% (n=3)	16% (n=9)	0.7405
Minor tranquilizer (%)	13% (n=2)	13% (n=7)	0.9504
Major tranquilizer (%)	7% (n=1)	5% (n=3)	0.8577
Antidepressant (%)	7% (n=4)	7% (n=1)	0.9356
Other drugs (%)	27% (n=4)	29% (n=16)	0.8538
Age (years)	53.9±17.3	51.0±18.5	0.5895
Maximum QT interval (msec)	395.7±54.1	370.6±32.6	0.0269
Maximum QTc interval (msec)	482.6±63.4	435.7±32.1	0.0002
QT dispersion (msec)	54.8±35.6	25.0±23.6	0.0003
QTc dispersion (msec)	64.1±35.4	29.3±27.3	0.0001
Carboxy hemoglobin level (%)	27.1±17.3	20.3±13.7	0.1089

Abbreviation: QTc: coorected QT

Table 3. Findings of the univariate and multivariate analyses

	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	p	Odds ratio (95% CI)	p
Sex (M)	1.4375(0.433-4.772)	0.5533		
Age (>30)	1.714(0.190-15.452)	0.6309		
Smoke	0.3478 (0.088-1.374)	0.1319	2.282 (0.317 – 16.411)	0.4125
Consciousness disorder	6.476((1.634-25.669)	0.0078	1.012(0.142– 7.201)	0.9905
Hyperbaric oxygen therapy	0.563 (0.171-1.851)	0.3493	0.1049 (0.013 – 0.871)	0.0368
QTc dispersion (>46msec)	12.375 (3.260-46.970)	0.0002	29.568 (2.542 – 343.854)	0.0068
Carboxyhemoglobin level (>44%)	8.666 (1.779-42.215)	0.0044	2.064 (0.130 – 32.758)	0.6073
Troponin I (>0.36ng/ml)	14.571 (3.463-61.311)	0.0003	59.117 (3.826 – 913.550)	0.0035

Abbreviation: QTc: corrected QT

Figures

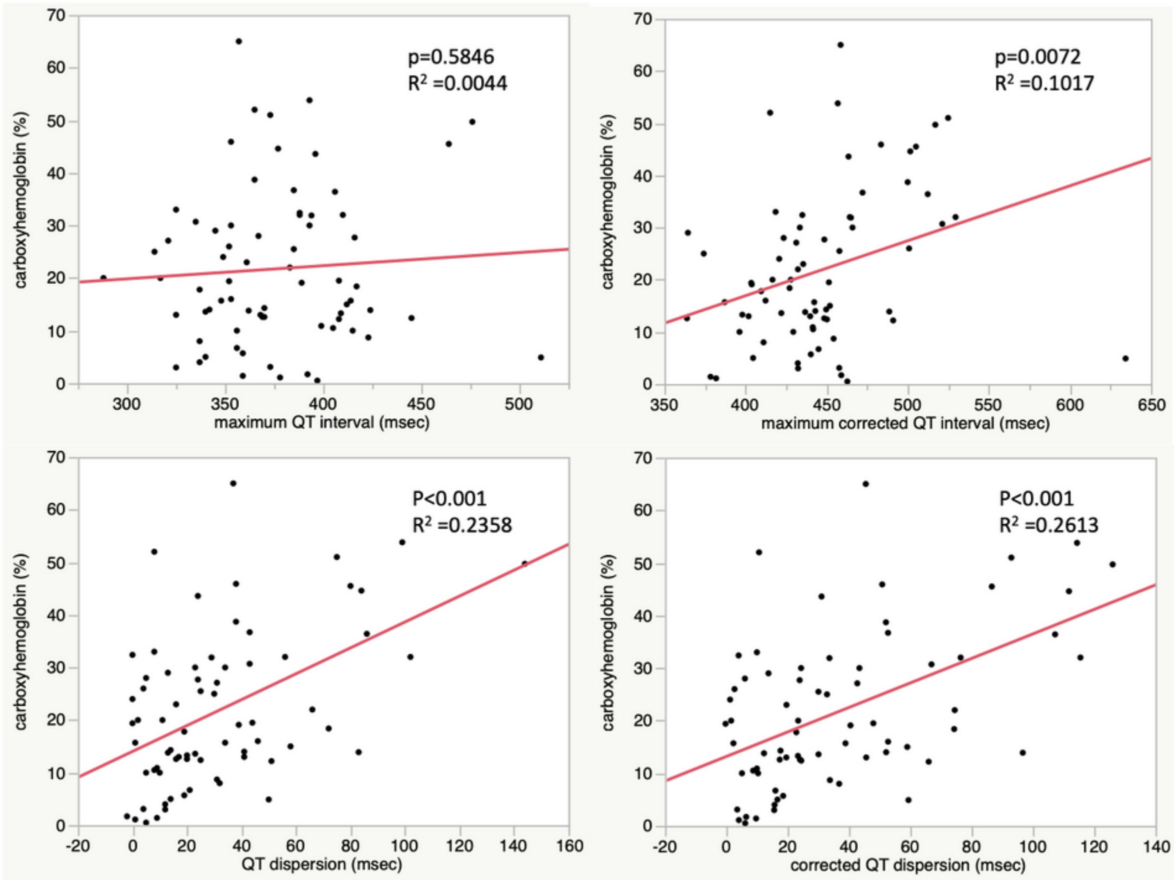

Figure 1

Top left. Relation between the maximum QT interval and the carboxyhemoglobin level. Top right. Relation between the maximum corrected QT interval and the carboxyhemoglobin level. Bottom left. Relation between QT dispersion and the carboxyhemoglobin level. Bottom right. Relation between corrected QT dispersion and the carboxyhemoglobin level. The relationships between the maximum QT interval and carboxyhemoglobin is not significant, whereas the other relationships are all significant.