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ORIGINAL RESEARCH

Characteristics of patients with carbon monoxide poisoning due to smoke inhalation and pre-hospital factors related to intensive care unit admission of these patients: a nationwide observational study

Sung Min Lee[1], Dong Hun Lee[1], Jun Ho Han[1], Hyoung Youn Lee[1], Tag Heo[1,2,]*

[1]Department of Emergency Medicine, Chonnam National University Hospital, 61469 Gwangju, Republic of Korea
[2]Department of Emergency Medicine, Chonnam National University Medical School, 61469 Gwangju, Republic of Korea

***Correspondence**
terran034@gmail.com
(Tag Heo)

Abstract

This study aimed to investigate the pre-hospital clinical status of patients with carbon monoxide (CO) poisoning by smoke inhalation and the pre-hospital factors associated with these patients' admission to the intensive care unit (ICU). In this observational study from January 2016 to December 2018, the National Fire Agency's first aid activity log on patients with smoke inhalation was matched with National Emergency Department Information System's patient data with CO poisoning and further analyzed retrospectively. Multiple logistic regression analysis was conducted to identify the relevant pre-hospital associative factors for the decision to admit a patient with CO poisoning to the ICU. Of the 4422 patients with CO poisoning included in the study, 358 (8.09%) were admitted to the ICU. In such patients transported by pre-hospital emergency medical services, age (odds ratio [OR], 1.020; 95% confidence interval [CI], 1.010–1.029), verbal (OR, 3.564; 95% CI, 2.390–5.315), pain (OR, 4.011; 95% CI, 2.661–6.045), unconsciousness (OR, 5.728; 95% CI, 2.708–12.113), SBP (OR, 0.979; 95% CI, 0.969–0.989), HR (OR, 1.011; 95% CI, 1.004–1.018), SpO_2 (OR, 0.965; 95% CI, 0.946–0.985), O_2 supply (OR, 1.725; 95% CI, 1.143–2.603), use of nasal prongs (OR, 0.504; 95% CI, 0.281–0.905), and intentional inhalation (OR, 2.282; 95% CI, 1.659–3.139) were independently associated with ICU admission. Our study demonstrated that age, mental change, SBP, HR, SPO_2, O_2 supply, use of nasal prongs, and intentional inhalation in patients with CO poisoning were associated with their ICU admission.

Keywords

Smoke inhalation; Carbon monoxide poisoning; Pre-hospital emergency medical services; Intensive care unit

1. Introduction

Patients inhaling smoke due to fire, explosion, or other accidents are exposed to various toxic substances. Substances having the most serious influence during smoke inhalation include carbon monoxide (CO) and cyanide (CN) [1, 2]. Most people worldwide die or have sequelae due to CO poisoning following smoke inhalation [3, 4]. Hypoxia is the leading cause of pre-hospital death for accidents such as fires or explosions, by adversely affecting the oxygen transport and utilization systems at the intracellular level owing to toxic substances such as CO or CN, rather than flames or burns [5, 6]. The only similarity between CO and CN is their ability to avidly bind iron ions in the different hemoproteins. The mechanisms of these compounds vary in other aspects. CO impairs the ability of erythrocytes to transfer O_2 while CN does not. Acute CO poisoning primarily alters neurological cognitive function and even consciousness without significant alteration of vital functions, while CN primarily alters consciousness and leads to an early onset of severe alterations of vital functions. O_2 is the only treatment available for CO poisoning, while antidotes in combination with O_2 are more efficient than O_2 alone in the treatment of CN poisoning [7]. In most cases, hypoxia leads to ischemic injury of oxygen-sensitive organs, and in particular, damages the brain and heart [8–11]. In the United States, there are 50,000 carbon monoxide poisoning cases per year and 1000–2000 deaths per year, and a study from Utah in the United States reports that 17.3 per 100,000 cases per year occur [12, 13]. In Europe, 2.24 cases per 100,000 deaths per year were reported [14]. A study from Taiwan, reported 1.13 deaths per 10,000 people per year due to CO poisoning [15]. In the Republic of Korea, according to a report published in 2019 by the Ministry of Health and Welfare, the number of CO poisoning cases increased from 5300 in 2016 to 7152 in 2018, with 1.25 incidences per 10,000 cases. The mortality rate from CO poisoning was declared as 1.3% [16].

Early removal of carboxyhemoglobin (COHb) from the body improves prognosis in CO poisoning [8]. The half-life of CO by spontaneous respiration, normobaric oxygen therapy, and hyperbaric oxygen (HBO_2) therapy are 5–6 h, 74 ± 25 min, and 2–30 min, respectively. The first intervention implemented by rescuers and in-hospital physicians can largely influence the time needed to remove CO from the body [17–19]. Moreover, the protean and non-specific clinical manifestations of CO poisoning can lead to misdiagnosis even experienced medical staff [20]. General guidelines for exposure and poisoning of hazardous substances are available within the standard guidelines for on-site first-aid for 119 emergency personnel of the National Fire Agency (NFA); however, specialized guidelines for smoke inhalation or CO intoxication in patients in the pre-hospital setting are lacking [21]. Previous studies have investigated the clinical characteristics and prognosis of patients with CO poisoning at the in-hospital stage. However, comprehensive research regarding the treatment of patients with CO poisoning by smoke inhalation at the pre-hospital stage and the clinical outcomes of such patients after hospital admission are unavailable [22–24].

In this study, the initial clinical status of the patients, the status of first aid by NFA personnel, and the clinical status and prognosis of patients at the hospital stage were analyzed. This study is aimed at identifying the major pre-hospital prognostic factors in CO poisoning which are associated to the need for admission to the Intensive Care Unit (ICU). Such analysis could provide guidance in developing new specialized first-aid guidelines for optimizing classification, treatment, and transfer of CO-poisoned patients, thereby improving their prognosis.

2. Materials and methods

2.1 Study design and setting

This study was conducted retrospectively based on the matched data among adults (≥18 years) who were transported to the emergency department (ED) after being checked for smoke inhalation in the first-aid activity log of the NFA from January 1, 2016 to December 31, 2018, and from the NEDIS data on patients diagnosed with CO poisoning [code (T58)] in the ED. The present study has been approved by the Chonnam National University Hospital Institutional Review Board (CNUH-EXP-2019-147). We examined the data covering anonymous patient visits; hence, no informed consent was required.

2.2 Data collection and analysis

The NFA first-aid activity log data has been collected nationwide since 1998. The NEDIS, which currently registers nationwide emergency medical information, has been in place in the EDs since June 2003. However, there is no official linkage between these data. In this study, we merged 10791 cases of NFA first-aid activity log data (No. 5901565) and 18802 cases of NEDIS data (N20191720715). The variables used in the merge were the date and time of ED visit, sex, and age of the patients, and the date and time of transfer to the hospital, sex, and age in the NFA first-aid activity log. The following pre-hospital data were analyzed: age, sex, location of smoke inhalation, reasons for smoke inhalation, medical history, mental state of the scene, systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), respiration rate, arterial O_2 saturation by pulse oximetry (SpO_2), body temperature, blood sugar, NFA first-aid, distance from the scene to the ED, time from call to scene arrival, time from patient contact to scene departure, time from scene departure to ED arrival, the total time from call to ED arrival, the result of a patient transfer by NFA following smoke inhalation, and the need for multiplace hyperbaric chamber [10, 25–27]. The following hospital data were analyzed: age, sex, initial mental state in the ED, initial vital sign in the ED, Korea Triage Acuity Score (KTAS) (KTAS was implemented in our ED in May 2016; it is based on the Canadian Triage and Acuity Scale with modifications to adapt it to the Korean emergency medical environment. The KTAS consists of a five-level system [level 1, resuscitation; level 2, emergent; level 3, urgent; level 4, less urgent; and level 5, non-urgent] that classifies patients using a combination of variables, including vital signs and chief complaints), HBO_2 therapy in the ED, HBO_2 therapy after hospital admission, and the result of ED admission. First, we analyzed the epidemiological and clinical status of patients following smoke inhalation in the pre-hospital stage, and the status of first-aid treatment, along with the status in the ED and patient prognosis in the hospital stage. Second, we analyzed the factors related to ICU admission by comparing the ICU admission group and combined group of patients admitted to the general ward and those discharged as a result of ED prognosis.

2.3 Statistical analysis

Continuous variables were presented as means with standard deviations as all continuous variables had a normal distribution. Categorical variables were presented as frequencies with percentages. Continuous variables between independent groups were compared using the two-sample *t*-test with unequal variances, while categorical variables were compared using the chi-square or Fisher's exact tests as appropriate. To determine the relevant pre-hospital factors for the decision to admit a patient with smoke inhalation to the ICU, we constructed a series of multiple logistic regression models. In the first of these, we included variables that were univariately predictive of the ICU admission at the 0.05 significance level. Multicollinearity was assessed, and none of the variables had a variance inflation factor of >5. The results of the logistic regression analyses were reported as odds ratios (ORs) with its corresponding 95% confidence intervals (CIs). Data were analyzed using Stata/SE version 16.1 software for Windows (StataCorp, College Station, Texas, USA). A two-sided *p*-value of 0.05 was considered significant.

3. Results

A total of 5011 adult patients aged >18 years were diagnosed with CO poisoning after being transferred to the ED by NFA Emergency Medical Service (EMS) in the Republic of Korea following smoke inhalation for three years from January 2016 to December 31, 2018. A total of 3355 patients were discharged following ED treatment, 709 patients were admitted to the general ward, 358 patients were admitted to the ICU, 38 were dead on arrival, and 551 patients were transferred to other hospitals. The last two cases (patients who were transferred to other hospitals and patients who died) were excluded, and finally, 4422 patients were included in this study (Fig. 1).

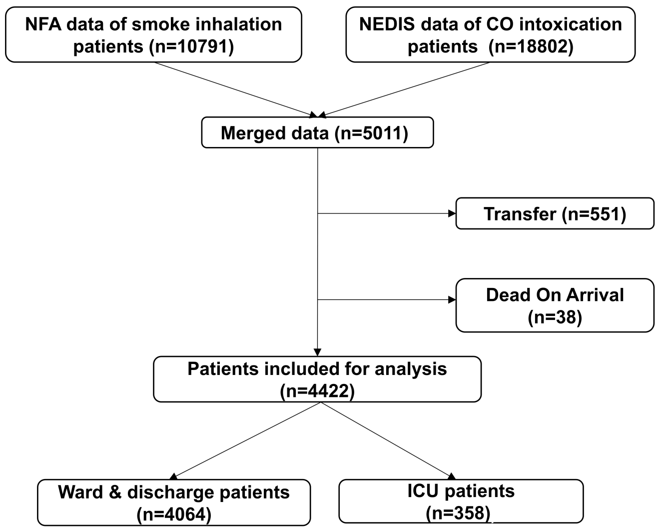

FIGURE 1. Patients with smoke inhalation between January 2016 and December 2018. NFA, National fire agency; NEDIS, National emergency department information system; ICU, intensive care unit.

3.1 Pre-hospital stage characteristics of patients with CO poisoning due to smoke inhalation

The average age of patients following smoke inhalation was 39.49 (±18.42) years, and that of the ICU patients was 43.83 (±16.67) years (Table 1). Overall, 2474 (55.95%) were males, and 1948 (44.05%) were females, while in the ICU-admitted group, 62.57% were males. The main places where smoke inhalation took place were private houses, roads, commercial facilities, and gathering facilities (military, dormitory, and prison). In addition, the proportion of patients who inhaled smoke from homes, roads, and sea/river/mountains in the ICU admission group was relatively higher than in the other groups. Smoke inhalation was intentional in 1232 (31.79%) patients and unintentional in 2463 (68.21%) patients. However, in the ICU group, 198 (63.26%) patients experienced intentional smoke inhalation, almost twice as high as that of the unintentional group, 115 (36.74%). The proportion of patients with cerebrovascular disease was higher in the ICU admission group. The mental status at the scene was alert, verbal, in pain, and unconscious for 3736 (84.52%), 296 (6.7%), 290 (6.56%), and 98 (2.22%), respectively. The vital signs showed that both SBP and DBP were lower, and HR was higher in the ICU group. SpO_2 was also found to be lower in the ICU group. In the first-aid by NFA paramedics, the need for airway manual manipulation and the use of the oropharyngeal device were more frequent in the ICU group. The frequency of O_2-supply implementation and the average provided flow rate of O_2 were also higher in this group. The use of nasal prongs was less common in the ICU group, while the use of a non-rebreather mask and bag valve mask was more frequent. The rate of supraglottic airway and intubation was also higher in this group. The need for ECG check and for intravenous fluid supply were also more frequent in the ICU group, as were the rate of cases receiving medical direction in the field, and CPR.

Regarding the NFA rescue missions, the transfer distance from the scene to the hospital was, overall, of 9.56 (±11.94) km, while it was longer for the ICU group (11.24 (±12.25) km). Overall, the total time from dispatch call to the arrival on the scene was 15.34 (±18.48) min, whereas the ICU group's arrival time on the scene was shorter (10.51 (±9.32) min). The total time to the departure from the scene was, overall, of 8.97 (±10.82) min, while it was shorter, in the ICU group (7.95 (±8.23) min). The overall time from departure to the ED was 14.18 (±12.95) min, while it was longer in the ICU group (15.96 (±17.65) min). The total transfer time from reporting of the patient following smoke inhalation to the arrival at the ED was 45.84 (±27.77) min, while the ICU admitted group took a shorter transfer time of 38.12 (±21.92) min; 909 patients with smoke inhalation were immediately transferred to HBO_2-therapy capable hospitals, corresponding to the 20.56% of the patients; this quote was slightly higher in the ICU group (29.05%). In addition, among the total patients with smoke inhalation transferred, 609 patients (13.77%) required multiplace hyperbaric chamber at the scene, while the proportion of patients requiring multiplace hyperbaric chamber in the ICU group was far higher (44.69%) (Table 1).

3.2 Hospital stage characteristics of patients with carbon monoxide poisoning due to smoke inhalation

At the ED visit, the mental status was alert in 84.57% of the patients, verbal in 8.85%, pain in 5.5%, and unconscious in 1.08%, and the proportion of patients showing mental change was lower than in the pre-hospital stage (Table 2). As for the vital signs assessed in the ED, both SBP and DBP, were found to be lower in the ICU group; the HR and respiration rate were higher, and SpO_2 was lower in this group. The results of KTAS showed: first, second, third, fourth, and fifth-grade classification in 99 (2.38%), 709 (17.08%), 2795 (67.33%), 490 (11.8%), and 55 (1.32%) patients, respectively. HBO_2 therapy was performed in 227 (5.13%) patients in the ED and in 210 (4.75%) after admission. Finally, the outcomes of discharge after hospitalization through the ED were: standard discharge in 720 (68.25%) cases, discharge against medical advice in 211 (20.0%), transfer in 98 (9.29%), death in 18 (1.71%), and "other" in 8 (0.76%) (Table 2).

3.3 Pre-hospital factors associated with intensive care unit admission of patients with carbon monoxide poisoning due to smoke inhalation transported by NFA

Table 3 shows the results of the multiple logistic regression analysis of the ICU admission. In patients who underwent

TABLE 1. A comparative analysis of factors related to pre-hospital demographic and clinical status between the combined general ward admission and discharged group, and ICU group in patients with carbon monoxide poisoning due to smoke inhalation.

	Carbon monoxide poisoning due to smoke inhalation			*p*-value
	Total (n = 4422)	Ward + Discharge (n = 4064)	Intensive care unit (n = 358)	
Age, mean (SD), y	39.49 (18.42)	39.10 (18.52)	43.83 (16.67)	<0.001
Sex, n (%)				0.008
Male	2474 (55.95)	2250 (55.36)	224 (62.57)	
Female	1948 (44.05)	1814 (44.64)	134 (37.43)	
Location of smoke inhalation, n (%)				<0.001
House	2694 (60.92)	2467 (60.7)	227 (63.41)	
Commercial facility	487 (11.01)	457 (11.25)	30 (8.38)	
Road	230 (5.2)	194 (4.77)	36 (10.06)	
Factory/industry/construction facility	193 (4.36)	185 (4.55)	8 (2.23)	
Dormitory/military/prison facility	187 (4.23)	175 (4.31)	12 (3.35)	
Medical facility	85 (1.92)	80 (1.97)	5 (1.4)	
Sea/river/mountain	54 (1.22)	46 (1.13)	8 (2.23)	
Others	492 (11.13)	460 (11.32)	32 (8.94)	
Reasons for smoke inhalation, n (%)	3875	3562	313	<0.001
Unintentional	2643 (68.21)	2528 (70.97)	115 (36.74)	
Intentional	1232 (31.79)	1034 (29.03)	198 (63.26)	
Medical History, n (%)				
Hypertension	298 (6.74)	268 (6.59)	30 (8.38)	0.196
Diabetes mellitus	142 (3.21)	132 (3.25)	10 (2.79)	0.640
Cerebrovascular accident	37 (0.84)	30 (0.74)	7(1.96)	0.015
Cardiovascular disease	61 (1.38)	58 (1.43)	3 (0.84)	0.360
Malignancy	41 (0.93)	36 (0.89)	5 (1.4)	0.334
Chronic lung disease	22 (0.5)	22 (0.54)	0 (0.0)	0.163
Chronic liver disease	4 (0.09)	4 (0.1)	0 (0.0)	0.553
Chronic renal disease	2 (0.05)	1 (0.2)	1 (0.28)	0.03
Allergy	1 (0.02)	1 (0.02)	0 (0.0)	0.767
Mental state, n (%)				<0.001
Alert	3736 (84.52)	3597 (88.55)	139 (38.83)	
Verbal	296 (6.7)	224 (5.51)	72 (20.11)	
Pain	290 (6.56)	196 (4.83)	94 (26.26)	
Unconsciousness	98 (2.22)	45 (1.11)	53 (14.8)	
Vital signs				
Systolic blood pressure, mean (SD), mmHg, n	127.10 (19.45), 3750	127.83 (18.94), 3434	119.48 (23.00), 316	<0.001
Diastolic blood pressure, mean (SD), mmHg, n	81.20 (13.78), 3672	81.70 (13.84), 3361	75.70 (15.73), 311	<0.001
Heart rate, mean (SD), min^{-1}, n	96.95 (19.69), 4026	96.45 (19.19), 3698	102.60 (23.98), 328	<0.001
Respiration rate, mean (SD), frequency/min, n	18.47 (4.38), 3952	18.44 (4.34), 3631	18.7 (4.82), 321	0.300
O_2 saturation, mean (SD), (%), n	96.53 (5.00), 4051	96.93 (4.50), 3719	91.99 (7.53), 332	<0.001
Temperature, mean (SD), °C, n	36.60 (0.50), 3799	36.61 (0.48), 3492	36.60 (0.71), 307	0.775
Blood sugar, mean (SD), mg/dL, n	144.45 (76.32), 296	145.24 (79.26), 82	141.19 (63.36), 58	0.680
NFA personnel for first aid				
Manual airway maneuver, n (%)	1498 (33.88)	1321 (32.5)	177 (49.44)	<0.001

TABLE 1. Continued.

	Carbon monoxide poisoning due to smoke inhalation			*p*-value
Oral airway, n (%)	144 (3.26)	84 (2.07)	60 (16.76)	<0.001
O_2 supply, n (%)	2955 (66.82)	2657 (65.38)	298 (83.2)	<0.001
	Total (n = 4422)	Ward + Discharge (n = 4064)	Intensive care unit (n = 358)	
O_2 flow, mean (SD), L/min, n	10.33 (5.07), 2955	10.04 (5.12), 2657	12.84 (3.77), 298	<0.001
Nasal prongs, n (%)	690 (15.6)	670 (16.49)	20 (5.59)	<0.001
Facial mask, n (%)	693 (15.67)	637 (15.67)	56 (15.64)	0.987
Non-rebreathing mask, n (%)	1721 (38.92)	1485 (36.54)	236 (65.92)	<0.001
Bag valve mask, n (%)	68 (1.54)	34 (0.84)	34 (9.5)	<0.001
Supraglottic airway device, n (%)	18 (0.41)	8 (0.2)	10 (2.79)	<0.001
Tracheal intubation, n (%)	6 (0.14)	3 (0.07)	3 (0.84)	<0.001
ECG check (AED), n (%)	1055 (23.86)	857 (21.09)	198 (55.31)	<0.001
Fluid supply, n (%)	82 (1.85)	51 (1.25)	31 (8.66)	<0.001
Fluid dose, mean (SD), mL, n	464.21 (398.68), 82	513.53 (387.53), 51	383.06 (409.77), 31	0.152
Drug supply, n (%)	6 (0.14)	5 (0.12)	1 (0.28)	0.441
AED monitoring, n (%)	285 (6.45)	204 (5.02)	81 (22.63)	<0.001
AED shock, n (%)	5 (0.11)	4 (0.1)	1 (0.28)	0.329
Medical direction	579 (13.09)	455 (11.2)	124 (34.64)	<0.001
CPR, n (%)	26 (0.59)	10 (0.25)	16 (4.47)	<0.001
Stop CPR, n (%)	3 (0.07)	1 (0.02)	2 (0.56)	<0.001
Distance and time related to smoke inhalation patient transfer				
Distance from scene to ED, mean (SD), km	9.56 (11.94)	9.42 (11.91)	11.24 (12.25)	0.006
Time from call to scene arrival, mean (SD), min	15.34 (18.48)	15.77 (19.01)	10.51 (9.32)	<0.001
Time from patient contact to scene departure, mean (SD), min	8.97 (10.82)	9.06 (11.01)	7.95 (8.23)	0.017
Time from scene departure to ED arrival, mean (SD), min	14. 17 (12.95)	14.01 (12.44)	15.96 (17.65)	0.041
Total time from call to ED arrival, mean (SD), min	45.84 (27.77)	46.52 (28.13)	38.12 (21.92)	<0.001
Smoke inhalation patient hospital transfer result				
First transfer HBO_2 available hospital, (%)	909 (20.56)	805 (19.81)	104 (29.05)	<0.001
Retransfer, (%)	47 (1.06)	42 (1.03)	5 (1.4)	0.521
Retransfer HBO_2 available hospital, (%)	9 (19.15)	8 (19.05)	1 (20)	0.959
Critical patients with smoke inhalation requiring multiplace hyperbaric chamber, (%)	609 (13.77)	449 (11.05)	160 (44.69)	<0.001
Transfer of critical patients with smoke inhalation for multiplace hyperbaric chamber, (%)	158 (25.94)	108 (24.05)	50 (31.25)	0.075

ICU, Intensive Care Unit; NFA, National Fire Agency; ECG, electrocardiogram; AED, automated external defibrillator; IV, Intravenous; CPR, Cardiopulmonary resuscitation; ED, Emergency department; HBO_2, Hyperbaric oxygenation.

smoke inhalation, and were transported by the 119 NFA ambulance, age (OR, 1.020; 95% CI, 1.010–1.029), verbal (OR, 3.564; 95% CI, 2.390–5.315), pain (OR, 4.011; 95% CI, 2.661–6.045), unconsciousness (OR, 5.728; 95% CI, 2.708–12.113), SBP (OR, 0.979; 95% CI, 0.969–0.989), HR (OR, 1.011; 95% CI, 1.004–1.018), SpO_2 (OR, 0.965; 95% CI, 0.946–0.985), O_2 supply (OR, 1.725; 95% CI, 1.143–2.603), use of nasal prongs (OR, 0.504; 95% CI, 0.281–0.905), and intentional inhalation (OR, 2.282; 95% CI, 1.659–3.139) were independently associated with ICU admission.

4. Discussion

Through this study, we were able to identify the pre-hospital epidemiology, vital signs, emergency treatment, hospital transfer status, and clinical outcomes of patients with CO poisoning after smoke inhalation. We further showed that the age, mental change, SBP, HR, SpO_2, O_2 supply, use of nasal prongs, and intentional inhalation were associated with ICU admission for patients with smoke inhalation. The relative affinities of CO and O_2 for hemoglobin, myoglobin, and cytochrome p450 proteins are very different. The CO/O_2 affinity ratio is 200–

TABLE 2. A comparative analysis of hospital factors between the combined general ward admission and discharged group, and ICU group in patients with carbon monoxide poisoning due to smoke inhalation.

	Carbon monoxide poisoning due to smoke inhalation			*p*-value
	Total (n = 4422)	Ward + Discharge (n = 4064)	ICU (n = 358)	
ED mental state, n (%)	4090	3744	346	<0.001
Alert	3459 (84.57)	3344 (89.32)	115 (33.24)	
Verbal	362 (8.85)	281 (7.51)	81 (23.41)	
Pain	225 (5.5)	106 (2.83)	119 (34.39)	
Unconsciousness	44 (1.08)	13 (0.35)	31 (8.96)	
Vital signs				
Systolic blood pressure, mean (SD), mmHg, n	131.15 (22.23), 3887	132.10 (21.77), 3559	120.89 (24.44), 328	<0.001
Diastolic blood pressure, mean (SD), mmHg, n	80.43 (14.95), 3884	80.83 (14.58), 3559	76.05 (17.95), 325	<0.001
Heart rate, mean (SD), (min^{-1}), n	94.56 (18.71), 4029	93.88 (18.24), 3697	102.15 (21.97), 332	<0.001
Respiration rate, mean (SD), frequency/min, n	20.48 (4.18), 4020	20.37 (3.92), 3700	21.75 (6.31), 320	<0.001
O_2 saturation, mean (SD), %, n	97.63 (3.01), 3769	93.08 (21.16), 3615	93.42 (15.30), 337	0.706
Temperature, mean (SD), °C, n	36.66 (0.51), 4065	36.67 (0.49), 3727	36.53 (0.73), 338	<0.001
KTAS	4151	3803	348	<0.001
1, n (%)	99 (2.38)	27 (0.71)	72 (20.69)	
2, n (%)	709 (17.08)	534 (14.04)	175 (50.29)	
3, n (%)	2795 (67.33)	2705 (71.13)	90 (25.86)	
4, n (%)	490 (11.8)	485 (12.75)	5 (1.44)	
5, n (%)	55 (1.32)	49 (1.29)	6 (1.72)	
8, n (%)	3 (0.07)	3 (0.08)	0 (0.0)	
HBO_2 result, n (%)				
HBO_2 therapy in ED	227 (5.13)	182 (4.48)	45 (12.57)	<0.001
HBO_2 therapy in hospital admission	210 (4.75)	153 (3.76)	57 (15.92)	<0.001
Result of hospital admission, n (%)	1055	702	353	<0.001
Normal discharge	720 (68.25)	526 (74.93)	194 (54.96)	
Discharge against medical advice	211 (20.0)	135 (19.23)	76 (21.53)	
Transfer	98 (9.29)	34 (4.84)	64 (18.13)	
Death	18 (1.71)	1 (0.14)	17 (4.82)	
Others	8 (0.76)	6 (0.85)	2 (0.57)	

ICU, Intensive Care Unit; ED, Emergency department; KTAS, Korea Triage Acuity Score; HBO_2, Hyperbaric oxygenation.

250 for hemoglobin, 20–25 for myoglobin, and <1 for the cytochrome system [28]. In case of CO poisoning due to smoke inhalation, CO gets strongly bound to hemoglobin, making pulse oximetry unreliable in estimating O_2Hb saturation in CO-exposed patients. Hence, it is necessary to carefully observe the clinical symptoms of the patient. In addition, it is difficult to accurately measure the COHb level in the field, and the measured value does not reliably reflect the patient's severity [29]. Thus, overall observations, including mental status, SpO_2, and ECG of the patient, are required.

In this study, the first-aid results by NFA personnel at the pre-hospital stage revealed oxygen administration performed in 66.82% of all patients, and 83.2% in the ICU group ($p < 0.001$). In addition, the average oxygen dose was 10.33 (±5.07) L/min in all patients, and 12.84 (±3.77) L/min in the ICU group ($p < 0.001$). Previous studies on suspected CO poisoning recommended 100% oxygen supply by a tight-fitting face mask at normal atmospheric pressure at the scene or during transport [29, 30]. In addition, administration of 100% O_2 as early as possible is recommended for all patients with a relevant suspected diagnosis (in alert patients, for example, using non-invasive continuous airway pressure, respiration using a mask with a demand valve, or administration of 15 L/min O_2 through a reservoir mask) [31]. However, in our study, 33.18% of patients with smoke inhalation did not even receive oxygen supply, and 15.6% of them were treated with nasal prongs as the only oxygen supply method. These results suggest that medical recommendations were less strongly enforced in the pre-hospital setting. In addition, the ECG check rates were quite low (23.86% overall, and 55.31% in the ICU group). In case of suspected CO poisoning by smoke inhalation the heart may be affected, and if an ECG abnormality is observed, it may

TABLE 3. Multiple logistic regression analyses demonstrating pre-hospital factors associated with intensive care unit (ICU) admission in patients with carbon monoxide poisoning due to smoke inhalation.

Variables	ICU admission		
	Odds Ratio	95% CI	*p*-value
Epidemiology factor			
Sex	1.113	0.824–1.503	0.485
Age	1.020	1.011–1.029	<0.001
Distance from scene to ED, km	0.985	0.971–1.000	0.055
Time from call to scene arrival, min	0.997	0.986–1.009	0.660
Time from patient contact to scene departure, min	1.003	0.986–1.020	0.733
Time from scene departure to ED arrival, min	1.010	0.997–1.023	0.124
Smoke inhalation region			
House	Reference		
Sea/river/mountain	1.827	0.731–4.563	0.197
Medical facility	1.806	0.594–5.487	0.297
Road	1.212	0.741–1.984	0.444
Factory/Industry/Construction facility	1.727	0.743–4.014	0.204
Commercial facility	1.201	0.727–1.984	0.475
Dormitory/military/Prison facility	1.087	0.508–2.323	0.830
Others	1.038	0.642–1.678	0.879
Past history			
Cerebrovascular disease	1.457	0.420–5.057	0.554
Scene mental state			
Alert	Reference		
Verbal	3.564	2.390–5.315	<0.001
Pain	4.011	2.662–6.046	<0.001
Unconsciousness	5.728	2.708–12.114	<0.001
Scene vital sign			
Systolic blood pressure	0.979	0.969–0.989	<0.001
Heart rate	1.011	1.004–1.018	0.002
Oxygen saturation	0.965	0.946–0.985	0.001
NFA personnel first aid			
Manual airway maneuver	0.991	0.738–1.330	0.951
Oral airway	1.201	0.712–2.0267	0.492
Tracheal intubation	1.376	0.092–20.660	0.818
O_2 supply	1.724	1.143–2.603	0.009
Nasal prongs	0.504	0.281–0.905	0.022
Non-rebreathing mask	1.038	0.716–1.505	0.842
Bag valve mask	1.372	0.557–3.382	0.492
ECG(AED) check	1.170	0.848–1.615	0.339
AED monitoring	1.422	0.945–2.138	0.091
Medical direction	1.269	0.897–1.793	0.178
Reasons for smoke inhalation			
Unintentional	Reference		
Intentional	2.282	1.659–3.139	<0.001

The multiple logistic regression model included all variables with a p-value of <0.05 in the univariate analyses except variables presumed to have interactions with other variables. ICU, intensive care unit; CI, confidence interval; ECG, electrocardiogram; AED, automated external defibrillator; NFA, National fire agency; ED, Emergency department.

represent an indication for HBO_2 therapy; therefore, it should be checked at the scene [32].

Patients suspected of CO poisoning should be transferred to a hospital capable of HBO_2 therapy in case of a possible neurological change, which mandates for HBO_2 therapy [33, 34]. HBO_2 should be critically considered and initiated within 6 h in patients with neurologic deficits, cardiac ischemia, pregnancy, and/or a very high COHb concentration. If HBO_2 therapy is administered, it should be initiated within 6 h, but under no circumstances, it should be initiated after more than 24 h [31]. Although it is not directly related to the outcomes of this study, some important considerations must be made for pregnant women suspected of CO poisoning, especially with respect to indications for HBO_2 therapy. The elimination COHb half-life is 2 h for the mother and 7 h for the fetus. In the fetal system, saturation and elimination, possibly occurs at a slower rate than those in the maternal system. Therefore, some researchers regard pregnancy as a strict indication for HBO_2, especially in the presence of neurological symptoms, signs of fetal distress, syncope, or high COHb levels [35, 36].

In this study, the evaluation of consciousness status was investigated through the alert, verbal, pain, unresponsive score alone, and not the Glasgow Coma Scale score. We considered consciousness below verbal as a relevant threshold for mental-status change, and logistic regression analysis showed a positive correlation between the need for intensive care and mental-status change, with the strength of this correlation being proportional to the severity of that change (unconsciousness > pain > verbal). Some studies have shown that consciousness changes are associated with aspiration pneumonia and poor prognosis in patients with CO poisoning. In addition, in patients with CO poisoning undergoing major changes in consciousness and aspiration pneumonia, the rate of ventilator use was found to be higher, and the duration of ventilator use and hospital stay longer [37]. If a patient with initial smoke inhalation shows an altered mental status in the field, it will be helpful for the patient's prognosis to be transferred to a hospital where HBO_2 therapy and intensive care are available.

In previous studies, patients with intentional smoke inhalation had higher mortality rates and higher ICU admission rates [38–40]. Similarly, in our study, intentional smoke inhalation was highly related to ICU admission. In the last years, the suicide rate in the Republic of Korea has decreased slightly until 2017, the highest level being 31.7 incidents per 100,000 population in 2011. However, in 2018, the value increased again to a level of 26.6 per 100,000 population. In addition, within the Organization for Economic Co-operation and Development member countries, referring to the most recent record of 2016, the Republic of Korea has the world's second-highest suicide rate of 24.6 per 100,000 population (beaten only by Lithuania, with a 26.7 per 100,000 rate). As of 2018, the most common means of suicide in the Republic of Korea were: hanging (52.1%), fall (16.6%), and gas poisoning (15.7%). There is a consistent number of CO-poisoning cases in the Republic of Korea caused by intentional smoke inhalation [41]. According to our findings, patients with CO poisoning caused by intentional smoke inhalation are more likely to have a poor prognosis; hence, it appears to be crucial to assess intentionality at the scene.

Finally, HBO_2 therapy to quickly remove CO from the body in patients with CO poisoning caused by smoke inhalation should be adequately provided as soon as possible. However, this study showed that the overall rate of direct transfer from the scene to a hospital capable of HBO_2 was 20.56%, and as low as 29.05% in the ICU group. In addition, 13.77% of the patients required multiplace hyperbaric chamber, and 25.94% of them were transferred to a hospital equipped with a multiplace hyperbaric chamber. Previous studies have shown that monoplace hyperbaric chambers with certified medical equipment in high-pressure environments can provide adequate treatment even for critically ill CO poisoning patients [26, 42]. Therefore, it should be transferred to a hospital that can at least a monoplace hyperbaric chamber treatment, but the total transfer rate to a hospital with a hyperbaric oxygen chamber was only 20.56%. So, there was a problem in the selection of hospitals by paramedics. In addition, the transfer time of the total patients with smoke inhalation was 45.84 ($\pm$27.77) min, 33.16 min being the national average for other general acute conditions. The transfer time was longer than that for cardiovascular disease (25 min) or cerebrovascular disease (27 min) [43]. To date, there is no established cut-off value for the start time of HBO_2 therapy in patients with CO poisoning, although HBO_2 therapy shows great effectiveness in dissociating CO from hemoglobin in the early stages of CO poisoning. In addition, HBO_2 therapy is known to help reduce delayed neurological sequelae and to remove cyanide, thermal burns, or upper airway inhalation burn injuries. Thus, this treatment is particularly important for patients with CO poisoning caused by smoke inhalation [8, 10, 44–46]. In the future, based on such considerations and on the findings of our study, we think that, in the development of future specialized guidelines, clear indications regarding HBO_2 therapy must be deemed as a necessary and critical factor for optimizing the management of patients with smoke inhalation and for guiding their timely transfer to the most suitable hospital.

This study has some limitations. First, this study used retrospective data of patients transferred to the ED by the NFA ambulance at the pre-hospital stage. In the case of patients with clear evidence of death at the site, CPR was not performed and the cases were immediately handed over to the police. Hence, there is a possibility that the mortality rate or severity of the study may be lower than the actual result due to the occurrence of selection bias. In addition, patients who were transferred to non-emergency medical institutions that did not transmit data to NEDIS might have not been included in the study subject and therefore might have affected the study outcomes. Second, in the case of patients with smoke inhalation, there is the possibility of concurrent damage such as airway inhalation injury and superficial burn. However, due to the nature of the data available to us, it was not possible to identify the prognostic impact of these additional factors. Third, due to the nature of NEDIS data in this study, the data for evaluating patient prognosis included only the results of ED discharge, hospital discharge, and patient diagnosis. The patient's COHb level, other blood tests, radiological tests, treatment prescriptions, and consciousness status at hospital discharge were not included; thus, there were limitations in the evaluation of the patient's treatment process and prognosis. Fourth, in the analysis of the transferred patients based on the emergency department results, it was virtually impossible to match the prognosis after transfer to another hospital due to data limitations. Therefore, the group of transferred patients was primarily excluded from the analysis. Fifth, due to the nature of the data, it was not possible to analyze the presence and role of other possibly toxic gases. In emergency medicine, there is a general lack of awareness of the role of other toxic gases that are widely recognized in environmental medicine [7]. This lack of awareness greatly hinders the progress of understanding the mechanisms of toxicity of these poisonous substances, likely resulting in unsatisfactory treatment and enhanced mortality. Therefore, further studies on other toxic gaseous substances are needed. In the future, large-scale prospective and comprehensive studies are needed to better assess the prognostic significance of comorbid injuries, laboratory results, radiologic findings, specific HBO_2-therapy parameters, state of consciousness at discharge, and possible complications during hospital-stay.

5. Conclusions

Our study demonstrated that age, mental change, SBP, HR, SpO_2, O_2 supply, use of nasal prongs, and intentional inhalation were associated with ICU admission in patients with CO poisoning by smoke inhalation. Considering these results, it is necessary to improve the pre-hospital EMS guidelines for CO poisoning patients by smoke inhalation.

AUTHOR CONTRIBUTIONS

Conceptualization—TH. Data curation—JHH. Formal analysis—JHH. Funding acquisition—SML, TH. Investigation—SML, DHL. Methodology—DHL, HYL. Software—DHL. Validation—TH. Writing - original draft—SML, HYL. Writing - review & editing—SML, DHL, JHH, TH.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Approval for data abstraction was obtained from the Institutional Review Board of Chonnam National University Hospital (CNUH-EXP-2019-147). This study is a database study on anonymous patient visits; therefore, no informed consent from patients was required.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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