International Journal of
Medical Toxicology & Forensic Medicine

Spring 2022, Volume 12, Number 2

Research Paper

Using the Extended Cox Model to Determine Factors Affecting the Length of Hospitalization in Patients with Drug Poisoning

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Citation Sabbaghian Tousi S, Jabbari R, Dadpour B, Roghangaran Khiabani H, Salari R, Golpour P. Using the Extended Cox Model to Determine Factors Affecting the Length of Hospitalization in Patients with Drug Poisoning. International Journal of Medical Toxicology and Forensic Medicine. 2022; 12(2):36738. https://doi.org/10.32598/ijmtfm.vi.36738

https://doi.org/10.32598/ijmtfm.vi.36738

Article info:
Received: 14 Nov 2021
First Revision: 19 Dec 2021
Accepted: 04 Jan 2022
Published: 26 Jun 2022

Keywords:
Length of hospitalization, Drug poisoning, Extended Cox Model

ABSTRACT

Background: Poisoning is a medical emergency, and is considered as a common cause of morbidity and mortality worldwide. In this study, the extended Cox model was used to determine the factors affecting the length of hospitalization in those with drug poisoning.

Methods: The sample size included 2408 patients with opioids poisoning referring to the Emergency Department of Imam Reza Hospital in Mashhad, Iran from March 21, 2018 to March 20, 2019. Extended Cox model was fitted to determine the effect of five covariates (age, gender, marital status, type of poisoning, and type of opioids). In survival analysis, the length of hospitalization was considered as a time covariate (T). Patients' recovery was also regarded as an event.

Results: Of 2408 patients, 399 (16.6%) were censored and 2009 (83.4%) were uncensored. The risk of failure in complete recovery from poisoning in males was 1.189 times more compared to females. The risk of failure in complete recovery for the 15-24, 25-44, 45-64, and >65 years age groups were 0.277, 0.241, 0.289, and 0.481 times lower, respectively compared to the <2 years age group. For the married patients, the risk was 0.291 times lower compared to the divorced patients. For those poisoned accidentally, the risk was 0.490 times lower than compared to those poisoned intentionally. For those used methadone, morphine, opium, and tramadol, the risk was 1.195, 1.243, 1.193, and 1.147 times more, respectively compared to those used marijuana. By increasing the time (day) of hospital stay, the risk of failure for the 25-44, 45-64, and >65 years age groups were 1.024, 1.028, and 1.040 times more, respectively compared to the <2 years age group. Moreover, for those poisoned accidentally, the risk was 1.197 times more compared to those poisoned intentionally by the time (day) of hospital stay.

Conclusion: The factors affecting the length of hospitalization in those poisoned by drugs are gender, marital status, and type of opioids covariate as time-independent covariate, and age and type of poisoning as time-dependent covariates. Since the complications of drug poisoning impose many costs on the health system, knowledge of these covariates can help take some measures for complete recovery of poisoned patients in a shorter length of hospital stay.

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1. Introduction

Poisoning is the potential of a substance causing toxicity in the body due to its chemical activities that leads to lethal and dangerous effects. Poisoning can be accidental (e.g. in children out of curiosity) or intentional (e.g., due to suicide or substance abuse) [1]. Poisoning is a medical emergency and a common cause of morbidity and mortality worldwide. However, the prevalence of poisoning can be reduced by awareness and timely intervention [2]. In the United States, the mortality rate of poisoning has increased considerably since the 1970s; the majority of which is related to unintentional poisoning [3]. The annual number of poisonings is about 5 million [3, 4]. In Iran, about half of the poisoning cases are male, and the most of them (38%) are at the age of 21-30 years. The majority of poisonings (79%) are intentional [5].

Currently, the global drug usage rate is high; therefore, poisoning due to these drugs is observed. In Australia, a study showed the increasing rate of opiate overdose deaths during 15 years [6]. Poisoning by drug use is observed in all age groups; children are not immune to the negative effects of drugs. A study in Iran showed that the minimum and the maximum ages of children poisoned by drugs were 7 days and 3.5 years, respectively [7]. In a study on methadone poisoning in children admitted to Imam Reza Hospital in Mashhad city in Iran (mean age=5±3.25 years), more than half of children (60%) were accidentally poisoned with methadone [8]. A study in Gorgan city in Iran about tramadol poisoning showed that 75.6% of the poisoned cases were male, of whom 64.3% were single. The highest rate of poisoning was related to the 21-30 years age group, of which 65.5% used tramadol due to suicidal attempt [9]. Considering that the complications of drug poisoning impose many costs on the health system, in this study, the extended Cox model [10] was used for determining factors affecting the length of hospitalization in those poisoned by drugs.

2. Materials and Methods

Data collection

The sample size included 2408 patients referred to the emergency department of Imam Reza Hospital in Mashhad, Iran due to opioids poisoning from March 21, 2018 to March 20, 2019. This hospital is the only main center for treating the poisoned people in Mashhad. Relevant medical records were obtained from the Hospital Information System (HIS) online. Demographic data including age, gender, marital status, type of poisoning (intentional, accidental), duration of hospitalization, and the treatment outcome (recovered, referred to another health center, death), and type of opioids (Marijuana, Heroin, Methadone, Morphine, Opium, Methamphetamine, Tramadol) were collected. Data were analyzed using survival analysis. In this analysis, the length of hospital stay is considered as a time variable (T). This research consists of censored (16.6%) and uncensored (83.4%) data. Patients' recovery was also regarded as an event. Dying or not completing the treatment due to discharge with personal consent, transferring to other hospitals, or escaping from the hospital were considered as censorship. Based on the principles of research ethics, the patients' privacy and confidentiality were observed. Descriptive statistics were used in SPSS v.16 software for describing the data, and data analysis was conducted in R software. The significance level was set at 0.05.

Survival analysis

Survival analysis is a statistical technique to find the factors that affect an event from the beginning to the end. This duration is regarded as survival time (day, week, month, year). Events may include death, recovery, etc. The survival time (T) can be a nonnegative random variable. The survival function is the chance that an individual can survive till time t. The survival function is then defined as (Equation 1):

$$1)\ S(t)=P(T>t)=\int_x^{\infty} f(t)dt \ And\ f(t)=-\ \frac{dS(t)}{dt}$$

, where F(x)=P(X≤x) is a cumulative distribution function. The life function S(t) is a function that does not rise or monotone down with properties:

1. S(t)=1 for t=0, it means individual chance to live at the moment t=0 is 1.

2. S(t)=0 for t=∞, it means individual chance to live at the moment t=∞ is 0.

Hazard function is another function relevant to the survival function. The hazard function is defined as the conditional failure rate; i.e., the limit of the probability of an individual failing to persist in very short intervals of time t to t+Δt, if the individual has survived until time t. This function is defined as (Equation 2):

$$2)\ h(t)=\lim_{\Delta t\to 0} \frac{(P[T\leq X<t+\Delta t|T\geq t])}{\Delta t}$$

, where the density function is probability [10] (Equation 3):

$$3)\ f(t)=h(t).S(t)$$

Cox proportional hazard model

This model was first proposed by D. Cox, a well-known English statistician, in 1972 to study the effects of explanatory (independent) variables on survival time. The general Proportional Hazard (PH) model is defined as (Equation 4):

4) $h_i(t,X)=h_0(t)exp(\sum^{p}_{(i=1)}\beta_i X_i)$

, where $X=(X_1,X_2,\ldots,X_p)$ is a set of predictive variables. This model can be specified for an individual risk, which has a set of predictive variables of X, at time t; h_0 (t) is a hazard function for an individual that all vector explanatory variables x has a value of zero, which is called baseline hazard function; and $exp^{p}(_{\sum i=1}\beta_i X_i)$ is a PH function, where p is the number of predictor variables. An important feature of the Cox PH model is that h_0 (t) is a time function and independent of predictive variables. This feature is called Cox PH assumption. In case of not meeting this assumption, is just a function of Xs. In this case, Xs are called time-independent variables. but since the PH assumption is no longer valid, the Extended Cox model should be used [10].

If two people i and j have different values of X and their predictions are linear and as follows (Equations 5, 6):

5) $\eta_i=exp(\sum^{p}_{i=1}\beta_i X_i)$

6) $\eta_i=exp(\sum^{p}_{i=1}\beta_i X_i)$

then, the hazard function for them is as follows (Equation 7):

7) $\frac{h_i(t)}{h_i(t)}=\frac{h_0(t)\,e^{\eta i}}{h_0(t)e^{\eta i'}}=e^{\eta i-\eta i'}$

This hazard function is constant at all times. In other words, it does not depend on time.

Examining the validity of Cox proportional hazard model

The Cox PH model consisted of several assumptions. Thus, it is important to assess whether a fitted Cox model adequately describes the data. There are three types of diagnostics for the Cox model: (a) Testing the PH assumption using Schoenfeld residuals [11], (b) Examining influential observations or outliers using deviance residual (symmetric transformation of the Martingale residuals) [12, 13], and (c) Detecting nonlinearity in relationship between the log hazard and the covariates using Martingale residual [14].

Testing the proportional hazard assumption

This assumption can be checked using statistical tests and graphical diagnostics based on the scaled Schoenfeld residuals. In principle, the Schoenfeld residuals are independent of time. A plot that shows a non-random pattern against time is evidence of violation of the PH assumption. The function related to the Schoenfeld residuals provides a convenient solution to test the PH assumption for each covariate included in a Cox regression model fit. For each covariate, this test correlates the corresponding set of scaled Schoenfeld residuals with time, to test for independence between residuals and time. Additionally, it performs a global test for the model as a whole. The PH assumption is supported by a non-significant relationship between residuals and time, and refuted by a significant relationship [11]

Examining influential observations or outliers

We can visualize the deviance residuals or the dfbeta values to test influential observations or outliers. Using the dfbeta values, the estimated changes in the regression coefficients caused by deleting each observation in turn can be plotted; similarly, these values produce the estimated changes in the coefficients divided by their standard errors. The deviance residual is another way to check outliers, it is a normalized transform of the martingale residual. These residuals should be roughly symmetrically distributed about zero with a standard deviation of 1. Positive values correspond to individuals that "died too soon" compared to expected survival times. Negative values correspond to individual that "lived too long". Very large or small values are outliers, which are poorly predicted by the model. In the diagrams of both methods, the x-axis represents the number of observations and the y-axis represents residuals (the dfbeta values or the deviance) [12, 13].

Detecting nonlinearity

assumption should be checked that continuous covariates have a linear form. Nonlinearity is not an issue for categorical variables, so we only examine plots of martingale residuals and partial residuals against a continuous variable. Plotting the Martingale residuals against continuous covariates is a common approach used to detect nonlinearity or, in other words, to assess the functional form of a covariate. This might help to properly choose the functional form of a continuous variable in the Cox model. Fitted lines with LOWESS function should be linear to satisfy the Cox PH assumptions. For a given continuous covariate, patterns in the plot may

suggest that the variable is not properly fit. Martingale residuals may present any value in the range (-∞,1). A value of martingale residuals near 1 represents individuals that "died too soon", and large negative values correspond to individuals that "lived too long" [14].

Extended Cox model

If the survival analysis includes both time-dependent and time-independent predictor variables, we can use the extended Cox model, which includes both types of variables. This semi-parametric model is defined as follows (Equation 8):

8) $h(t,X(t))=h_0(t)exp[\sum_{i=1}^{p1}\beta_i X_i+\sum_{i=1}^{p2}\delta_j X_j(t)]$

where is a covariate that has time independency, because it meets the PH assumptions and is a covariate that has time dependency, because it does not meet PH assumption; therefore, it should interact with the time function. Hence, the time-dependent covariate is , where the time function for covariate j is defined as . The time function can be used in the following form (Equation 9):

9) $X_j(t)=0$ and $X_j(t)=t$ and $X_j(t)=ln(t)$

If all p covariate does not meet the PH assumption, then the number of p covariates should be interacted with time [10].

3. Results

Of 2408 patients, 399 (16.6%) were censored due to dying or being referred to another health center, and 2009 (83.4%) were uncensored because of recovery. The median of survival time (the length of hospitalization) was 14 for 2408 patients. The demographic and positioning-related characteristics (covariates) and the mean length of hospital stay are shown in Table 1 and 2, respectively. All covariates were categorical data; hence, there was no need to examine the nonlinearity assumption.

We detected influential observations or outliers using the martingale residuals. Six observations had the least deviance residuals that were excluded from the data. The Cox PH model was used to determine the relationship between survival time and the covariates suspected to influence survival time. Estimates of Cox PH model parameters is shown in Table 3. The Cox PH model was formulated as (Equation 10):

10) $h_i(t,X)=h_0(t)exp(-0.110X_{12}-0.173X_{22}-0.781X_{23}-0.861X_{24}-0.953X_{25}-1.217X_{26}+0.102X_{32}+0.020X_{33}+0.306X_{34}-0.064X_{42}-0.388X_{52}+0.044X_{53}+0.208X_{54}-0.130X_{55}-0.050X_{56}+0.305X_{57})$

Furthermore, based on the model, the likelihood ratio was tested. Hypothesis : against . The likelihood ratio was 204.5 with a p-value lower than 0.001. Then was rejected and we concluded that there was at least one influential variable in the model established.

The PH assumption was tested by using Schoenfeld residuals (Table 4). Results showed that gender, marital status, and type of opioids covariates met PH assumptions (P>0.05). However, age and type of poisoning covariates had p value lower than 0.001; hence, they did not meet the PH assumption. Consequently, the extended cox model was used. Therefore, the time function of g(t)=t was added to age and type of poisoning covariates. Hence, the new model could estimate parameters. Based on Table 5, the extended Cox model was defined as (Equation 11):

11) $h_i(t,X)=h_0(t)exp(0.172X_{12}-0.323X_{23}-0.275X_{24}-0.340X_{25}-0.655X_{26}-0.345X_{32}+-0.667X_{42}0.178X_{53}+0.217X_{54}+0.176X_{55}+0.129X_{56}+0.137X_{57}-0.323X_{t-23}-0.275X_{t-24}-0.340X_{t-25}-0.655X_{t-26}+0.179X_{t-42}$

Time-dependent explanatory variables that had no significant effect were removed from the model. The value of likelihood ratio was 6776 with a p value <0.001. This indicates that explanatory variables have an influence on the dependent variable (response). The extended Cox model can be interpreted as following:

Gender variable (female as a reference) had a hazard ratio of 1.189. This shows that the risk of failure in complete recovery from poisoning in males is 1.189 times more compared to females;

Age variable (<2 years as a reference) had a hazard ratio of 0.723 for 15-24 years, 0.759 for 25-44 years, 0.711 for 45-64 years, and 0.519 for >65 years. This indicates that the risks of failure in complete recovery from poisoning for those aged 15-24, 25-44, 45-64, and >65 years are 0.277, 0.241, 0.289, and 0.481 times lower, respectively compared to those aged <2 years;

Marital status (divorced as a reference) had a hazard ratio of 0.709 for married patients. This indicates that the risk of failure in complete recovery from poisoning in married patients is 0.291 times lower compared to the divorced patients;

Type of poisoning (Intentional as a reference) had a hazard ratio of 0.510. This shows that the risk of failure in complete recovery from poisoning for those poisoned

Table 1. Demographic and poisoning-related characteristics of participants

Variables		No.(%)		
		Censored	Uncensored	Total
Gender	Female	130(32.6)	726(36.1)	856(35.5)
	Male	269(67.4)	1283(63.9)	1552(64.5)
Age (Y)	0-2	24(6.0)	200(9.9)	224(9.3)
	3-14	14(3.5)	213(10.6)	227(9.4)
	15-24	121(30.3)	528(26.3)	649(26.9)
	25-44	142(35.6)	692(34.6)	834(34.6)
	45-64	65(16.3)	293(14.5)	358(14.9)
	65≤	33(8.3)	83(4.1)	116(4.8)
Marital Status	Divorced	14(3.5)	84(4.2)	98(4.0)
	Married	209(52.4)	883(43.9)	1092(45.4)
	Single	167(41.8)	1005(50)	1172(48.7)
	Widow/Widower	9(2.3)	37(1.9)	46(1.9)
Type of poisoning	Intentional	350(87.7)	1604(79.8)	1954(81.2)
	Accidental	49(12.3)	405(20.2)	454(18.8)
Type of opioids	Marijuana	7(1.7)	26(1.3)	33(1.4)
	Heroin	2(0.5)	8(0.4)	10(0.4)
	Methadone	130(32.6)	724(36)	854(35.5)
	Morphine	19(4.8)	108(5.4)	127(5.3)
	Opium	96(24.1)	464(23.1)	560(23.2)
	Crystal	26(6.5)	133(6.6)	159(6.6)
	Tramadol	119(29.8)	546(27.2)	665(27.6)

accidentally is 0.490 times lower compared to those poisoned intentionally;

Type of opioids (Marijuana as a reference) had a hazard ratio of 1.195 for methadone, 1.243 for morphine, 1.193 for opium, and 1.147 for tramadol. This indicates that the risks of failure in complete recovery from poisoning for those used methadone, morphine, opium, and tramadol are 1.195, 1.243, 1.193, and 1.147 times more, respectively compared to those used marijuana;

Time-dependent age variable (<2 years as a reference) had a hazard ratio of 1.024 for 25-44 years, 1.028 for 45-64 years, and 1.040 for >65 years. This indicates the risks of failure in complete recovery from poisoning for patients aged 25-44, 45-64, and >65 years are 1.024, 1.028, and 1.040 times more, respectively compared to patients aged <2 years by increasing the time (day) of hospital stay.

Time-dependent type of poisoning (Intentional as a reference) had a hazard ratio of 1.197. This indicates that the risk of failure in complete recovery from poisoning for those poisoned accidentally is 1.197 times more compared to those poisoned intentionally by increasing the time (day) of hospital stay.

Table 2. The mean length of hospital stay (day) in participants

Variables		Mean (day)
Gender	Female	3.18
	Male	4.4
Age (y)	0-2	2.3
	3-14	2.61
	15-24	3.21
	25-44	4.69
	45-64	4.97
	65≤	5.72
Marital Status	Divorced	4.73
	Married	4.45
	Single	3.42
	Widow/Widower	4.54
Type of poisoning	Intentional	2.87
	Accidental	4.22
Type of opioids	Marijuana	3.85
	Heroin	4
	Methadone	3.9
	Morphine	3.81
	Opium	5.19
	Crystal	5
	Tramadol	2.79

4. Discussion

With identified time-dependent variables (age and the type of poisoning), the extended Cox model was fitted with five factors (gender, marital status, type of opioids, age, and type of poisoning) that affect the length of hospitalization for those poisoned by drugs. Many studies have been carried out to determine the factors affecting the length of hospitalization for the poisoned people. Satar et al. analyzed these factors for adult patients with acute poisoning referred to an emergency department. They reported the mortality rate of poisoning as 3.9%. The mean length of hospital stay in their study was 2.9±1.8 days and the percentage of patients who stayed for longer than 2 days was 44.3%. Their study indicated that the length of hospital stay was affected by many variables. Of these variables, gender, age, reason (intentional or unintentional), and type of agent were also reported in our study. The mean length of hospital stay was longer in males, patients >30 years of age, and those poisoned unintentionally [15]. In the present study, the length of hospital stay was longer in men, those aged >65 years, and those poisoned intentionally. Thomas et al. conducted a study on factors affecting hospital admission and length of stay of poisoned patients in the North East of England. Prolonged stay was affected by factors such as age, potential hazard and past history. Longer length of hospital stay (>2 nights) was more common in patients over 65 years, and those with intentional poisoning [16]. Their results are consistent with the present study. Chien et al. carried out a study on the related factors of hospitalization caused by unintentional poisoning in Taiwan. The

Table 3. Parameter estimation of the Cox proportional hazard model

Explanatory Variables		Variable	Coefficient	Exp (β_j)	SE (β_j)
Gender (Female)	Male	X_{12}	-0.110	0.895	0.050
Age (0-2) (y)	3-14	X_{22}	-0.173	0.841	0.102
	15-24	X_{23}	-0.781	0.457	0.135
	25-44	X_{24}	-0.861	0.422	0.137
	45-64	X_{25}	-0.953	0.385	0.148
	65≤	X_{26}	-1.217	0.295	0.181
Marital status (Divorced)	Married	X_{32}	0.102	1.108	0.115
	Single	X_{33}	0.020	1.020	0.120
	Widow	X_{34}	0.306	1.359	0.211
Type of poisoning (Intentional)	Accidental	X_{42}	-0.064	0.937	0.108
Type of opioids (Marijuana)	Heroin	X_{52}	-0.388	0.677	0.406
	Methadone	X_{53}	0.044	1.045	0.200
	Morphine	X_{54}	0.208	1.232	0.219
	Opium	X_{55}	-0.130	0.878	0.203
	Crystal	X_{56}	-0.050	0.951	0.215
	Tramadol	X_{57}	0.305	1.357	0.202

hospitalization rate in men was higher than that in women. The age group of 45–64 years had the highest hospitalization rate [17]. In the present study, although those poisoned both unintentionally and intentionally were considered, the length of hospital stay in men and those with higher age were longer. Mehrpour et al. conducted a study on clinical and epidemiological characters of acute poisoning in patients admitted to intensive care units in eastern Iran during 2010-2017. Among the poisoning agents, exposure to opioids and pesticides were reported higher. The mortality rate of the poisoned patients in the intensive care unit was relatively high. Opioid poisoning had the highest mortality rate and was the most important cause of death. The highest length of hospital stay belonged to those poisoned by pesticide [18]. In our study, those with opium poisoning had the highest length of hospital stay. Abdelhamid conducted for assessing the severity of poisoning exposures among patients in 2019. Many variables affecting the length of hospital stay were evaluated including age, type of poisoning, mode of poi-

Table 4. Testing proportional hazard assumption by using Schoenfeld residuals

Variables	χ^2	P
Gender	0.345	0.56
Age	35.228	0 < 0.001
Marital Status	5.911	0.12
Type of poisoning	23.596	0 < 0.001
Type of opioids	8.277	0.22
Total	54.182	0 < 0.001

Table 5. Parameter estimation of the extended cox model

Explanatory Variables		Variable	Coefficient	Exp (β_j)	SE (β_j)	P
Gender (Female)	Male	X_{12}	0.172	1.189	0.052	<0.001
Age (0-2)	3-14	X_{22}	0.071	1.074	0.075	0.331
	15-24	X_{23}	-0.323	0.723	0.051	<0.001
	25-44	X_{24}	-0.275	0.759	0.047	<0.001
	45-64	X_{25}	-0.340	0.711	0.064	<0.001
	65≤	X_{26}	-0.655	0.519	0.115	<0.001
Marital status (Divorced)	Married	X_{32}	-0.345	0.709	0.062	<0.001
	Single	X_{33}	-0.022	0.977	0.045	0.616
	Widow	X_{34}	0.071	1.074	0.168	0.673
Type of poisoning (Intentional)	Accidental	X_{42}	-0.667	0.510	0.112	<0.001
Type of opioids (Marijuana)	Heroin	X_{52}	-0.072	0.929	0.356	0.838
	Methadone	X_{53}	0.178	1.195	0.047	<0.001
	Morphine	X_{54}	0.217	1.243	0.100	0.029
	Opium	X_{55}	0.176	1.193	0.053	0.001
	Crystal	X_{56}	0.129	1.139	0.091	0.156
	Tramadol	X_{57}	0.137	1.147	0.050	0.007
Time-dependent age (0-2)	(3-14) × t	Xt_{-22}	0.016	1.016	0.019	0.396
	(15-24) × t	Xt_{-23}	0.017	1.018	0.011	0.139
	(25-44) × t	Xt_{-24}	0.023	1.024	0.009	0.009
	(45-64) × t	Xt_{-25}	0.028	1.028	0.011	0.014
	(65≤) × t	Xt_{-26}	0.039	1.040	0.017	0.024
Time-dependent type of poisoning (Intentional)	Accidental × t	Xt_{-42}	0.179	1.197	0.049	<0.001

soning, etc. Among these variables, poisoning severity (mild, moderate, and severe) had the highest effect on the length of hospital stay [19]. In our study, the effect of poison severity score was not evaluated. A study by Doak et al. on self-poisoning in older adults for determining the agents ingested by people over the age of 60 years admitted to hospital after overdose compared to those age <60 years, showed that patients over 60 years of age were more likely to stay at hospital more than one night and had higher mortality rate [20]. In our study, both intentional and unintentional poisonings were considered. Those with older age (> 65 years) stayed at hospital longer and had higher mortality rate. A study by Chen et al. on assessing opioid poisoning in New York, showed that opioid poisoning rate increased by 741.5% in patients >65 years compared to 364.6% increase in the general opioid poisoning rate, which is consistent with our results [21]. Lamminpaa carried out a study concerning hospitalization due to poisoning in Finland. Drugs and technochemical products accounted for 73.9% and 26.1% of poisonings, respectively. The average length of hospital stay was 5 days per patient for drug poisoning and 3.3 days for other poisonings. Cigarettes caused 53 cases of hospital admissions annually; the median duration of hospitalization was 1.3 days [22]. In the present study, the median of hospitalization length stay was 14 days. Poisoning caused by cigarette was not considered in our study. Karbakhsh et al. carried out a study on acute

opiate overdose as one of the most considerate complications of drug abuse. Drug poisoning was more common among men. Opium was the most frequent poisoning agent (56.5%) followed by heroin. The mean length of stay in hospital was 2.68±5.06 days with a median of one day [23]. In the present study, the median of hospitalization stay was 14 days, and opium was determined as an important agent causing a hospitalization length of 5.19 days. Gupta in a study in the United States on the predictors of mortality from opioid overdose (race, gender, age, and region), found that the statistically significant independent predictors were male gender and age <60 years [24]. However, in our study, men and those above 65 years of age stayed longer at hospital.

Strengths and limitations

The main strength of the present study was testing both assumptions of PH for the observed observations or outliers and the nonlinearity of covariates. In others studies, only one of these assumptions have been tested. In survival studies, it is better not to censor more than 40% of people [25]. In this regard, another strength of this study was that only 16.6% of patients were censored (right-censoring). The main limitation of this study was the lack of similar studies using survival analysis and opioid poisoning simultaneously.

5. Conclusion

In this study, the extended Cox model was fitted for determining the factors affecting the length of hospitalization in those poisoned by drugs. According to findings, age, gender, marital status, and type of opioids are time-independent factors, and age and type of poisoning are time-dependent factors affecting the length of hospitalization. Since the complications of drug poisoning impose many costs on the health system, knowledge of these factors can help take some measures for complete recovery of patients in a shorter length of hospital stay.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

Funding

This study was approved by the Ethics Committee of Mashhad University of Medical Sciences (Ethics code: IR.MUMS.REC.1400.362) (Code: 4000580).

Authors' contributions

Conceptualization, Methodology, Data collection, and Data analysis: Parastoo Golpour and Sara Sabbaghian Tousi; Writing – original draft: Roya Jabbari and Bita Dadpour; Writing – review & editing: Roya Jabbari, Bita Dadpour.

Conflict of interest

The authors declare no competing interests.

Acknowledgments

The authors would like to thank the Vice-Chancellor for Research of Mashhad University of Medical Sciences for the financial support.

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