ORIGINAL REPORT

Comparison of the Results of Cox Proportional Hazards Model and Parametric Models in the Study of Length of Stay in a Tertiary Teaching Hospital in Tehran, Iran

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Abstract- Survival analysis is a set of methods used for analysis of the data which exist until the occurrence of an event. This study aimed to compare the results of the use of the semi-parametric Cox model with parametric models to determine the factors influencing the length of stay of patients in the inpatient units of Women Hospital in Tehran, Iran. In this historical cohort study all 3421 charts of the patients admitted to Obstetrics, Surgery and Oncology units in 2008 were reviewed and the required patient data such as medical insurance coverage types, admission months, days and times, inpatient units, final diagnoses, the number of diagnostic tests, admission types were collected. The patient length of stay in hospital 'leading to recovery' was considered as a survival variable. To compare the semi-parametric Cox model and parametric (including exponential, Weibull, Gompertz, log-normal, log-logistic and gamma) models and find the best model fitted to studied data, Akaike's Information Criterion (AIC) and Cox-Snell residual were used. $P<0.05$ was considered as statistically significant. AIC and Cox-Snell residual graph showed that the gamma model had the lowest AIC (4288.598) and the closest graph to the bisector. The results of the gamma model showed that factors affecting the patient length of stay were admission day, inpatient unit, related physician specialty, emergent admission, final diagnosis and the number of laboratory tests, radiographies and sonographies ($P<0.05$). The results showed that the gamma model provided a better fit to the studied data than the Cox proportional hazards model. Therefore, it is better for researchers of healthcare field to consider this model in their researches about the patient length of stay (LOS) if the assumption of proportional hazards is not fulfilled.

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Introduction

Survival analysis is a set of methods used for analysis of the data which exist until the occurrence of an event and their associated factors. The main variable in these studies is survival time. Survival time is a non-negative random variable which measures the interval between the start of a study and the occurrence of a particular event. This event can be the occurrence of a specific disease, response to a particular treatment, the recurrence of a disease or death. Because of two special specifications in survival data, usual statistical methods cannot be used to analyze them. These specifications are data censoring, as well as, skewing and lack of normality in their distribution. There are various methods to analyze these data such as parametric, semi-parametric and nonparametric (1). Though the semi-parametric Cox proportional hazards model is the most applicable model to analyze the survival data; parametric models can be more suitable in some circumstances.

Most researchers in the health care fields are more inclined to use semi-parametric models such as Cox, because of its ease of use and results interpretations. The use of the Cox model is more flexible than parametric models and does not need to estimate the baseline

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hazard function. In other words, it is not required to specify the distribution of the survival times, but the assumption of proportional hazards should be fulfilled so that the results can be meaningful. Also, when the Cox model is valid for the studied variables, if a suitable distribution can be found, the parametric models are more informative than the Cox model. The main problem in the use of parametric models is the need to determine the most appropriate distribution for the survival time (2-4).

Inpatient length of stay (LOS) is one of the most useful indicators which can be used for various purposes such as managing hospital care, quality control, appropriateness of hospital use, hospital planning, estimating the hospital efficiency and resources consumption (5-7). Logical reduction of hospital LOS provides the opportunity to increase revenue, lower costs, reduce clinical variations, enhance the quality and improve the margins. Also, reducing LOS based on evidence-based guidelines results in increase in admissions, increase in revenue and improvement of the quality by reducing practice variations (8). However, it is essential to note that if some patients leave the hospital without receiving complete services or without full recovery, the use of common statistical methods is not sufficiently accurate and the application of survival analysis methods which consider the patient length of stay leading to recovery' will be preferable.

Poorhoseingholi *et al.* in a retrospective study aimed to compare the efficiency of the Cox regression and parametric models in the survival analysis on patients with gastric cancer treated from January 2003 to December 2006 in Taleghani Hospital, Tehran-Iran. They concluded that the exponential model and Cox model in multivariate analysis were similar. Although in univariate analysis there was no specific model as the more efficient one, the results showed that the Log-normal model was fit to the studied data among the parametric models and could replace Cox model survival analysis in gastric cancer patients (2).

Hosseini *et al.* in a study to compare different models in the study of factors associated with duration of breastfeeding have collected data on women in Mazandaran Province, Iran during 2003-2004. Using Cox-Snell residuals, they concluded that the Cox model was the most appropriate one (among Cox proportional hazard, exponential, Weibull, Gompertz, log-normal, log-logistic and generalized gamma models) to fit to the data (9).

Cox *et al.* in a study aimed to compare the survival models (Cox regression and generalized gamma models) in two large groups of patients (1504 males and 461 females) after their clinical diagnosis of AIDS which were followed up in four different time periods and in four different treatment groups. It was shown that generalized gamma model was better than Cox model because the assumption of proportional hazards was not fulfilled (10).

Austin *et al.* in a study to evaluate and compare the relative performance of seven different statistical strategies (linear regression; linear regression with log-transformed length of stay; generalized linear models with the following distributions: Poisson, negative binomial, normal, and gamma; and semi-parametric survival models) for analyzing LOS in a cohort of patients undergoing CABG surgery from April 1998 to February 1999 in Ontario, Canada found that the Cox regression model and generalized linear model with gamma distributions, Poisson and negative binomial, showed the greatest consistency. Excluding Cox regression model, all the models had a similar ability to predict the patients' LOS in the real data but the generalized linear models had less prediction error than linear models and the Cox regression had the most prediction error. Monte Carlo simulation results also showed that generalized linear models had the most ability to predict the length of stay of patients after CABG surgery (11).

Marazzi *et al.* in a study to determine the adequacy of three common models including Log-normal, gamma and Weibull in order to describe the distribution of the patient length of stay in a sample of 3279 patients selected from five million hospitalization cases classified based on DRG in five European countries during the years 1990 to 1998 found that none of the above-mentioned models could fit to data alone; they proposed that other models should be examined (12).

The authors did not find any study of comparing Cox regression model and parametric models (exponential, log normal, log logistic, gamma, Weibull and Gompertz) on the factors affecting the patient length of stay in Iran. Therefore, with regard to this issue, this survey aimed to compare these models to determine the factors influencing the length of stay of patients admitted in the inpatient units of Women Hospital in Tehran, Iran in order to help other researchers in their studies on the length of stay.

Materials and Methods

This study is a historical cohort, descriptive-analytical study aiming to compare the results of the use of the

semi-parametric Cox proportional hazards model and parametric models to determine clinical and non-clinical factors associated with LOS in Women Hospital in Tehran, Iran. This hospital is a teaching hospital affiliated with Tehran University of Medical Sciences (TUMS) which has several units such as Obstetrics, surgery, Oncology, high risk infants, NICU, phototherapy and Obstetrics Emergency. In this study, we only studied the units related to women including Obstetrics, Surgery and Oncology units. These units have 20, 33 and 12 available beds, respectively. We reviewed all 3421 charts of patients admitted to these three units and discharged from them in 2008. Using a data collection sheet, the required patient data such as marital status, age, distance from living area, medical insurance coverage types, admission and discharge months, days and times, inpatient units, related physician specialty and degree, final diagnoses, admission types, patients' status at discharge time, the number of previous hospitalization, the number of laboratory tests, radiographies and sonographies and hospital costs were collected. In order to collect the other data which were not recorded in the patients' charts (such as the patients' and their spouse job, educational levels, and the family income), we conducted interviews with all inpatients for three months which exceeded 951 interviews. The related analyses were done only for these patients. In order to categorize the final diagnoses, we used ICD-10.

Of 3421 reviewed patient charts, 2632 patients (76.9%) had been discharged from the hospital with recovery (full or relative recovery) and the rest of the 789 patients (23.1%) with no recovery (inadequate treatment in the hospital or leaving against medical advice). In this study, the patient length of stay in hospital 'leading to recovery' (hour) was considered as a survival variable. The patients discharged from the hospital without recovery, those who had been left against medical advice, and those about whose disease status we did not have any information were determined as the right-censored data.

Since it is common to use the Cox proportional hazards model for studying multiple interactions among the studied factors, there is a risk that if the assumption of proportional hazards is not fulfilled, the results are not reliable enough. Although due to the ease of the use of Cox's model and its interpretations some researchers ignore this defect in their researches, it is essential to use alternative models with more reliability such as parametric models for more precise investigations in such cases. However, it should be noted that their results are not necessarily the same and with similar reliability. To compare the results of parametric models, using Akaike's Information Criterion (AIC) and Cox-Snell residual has been proposed.

In this study, to compare the results of the use of the semi-parametric and parametric models, first of all, qualitative variables (such as marital status, distance from the living area, patients and their spouse job, educational levels, medical insurance coverage types, admission and discharge months, days and times, inpatient units, related physician specialty and degree, and final diagnoses) and quantitative variables (such as age, family size, number of previous hospitalizations, the number of laboratory tests, radiographies and sonographies and percentage share of total insurance cost) were put in the univariate Cox proportional hazards model and were analyzed using stepwise (Backward) method to determine the variables affecting LOS 'leading to recovery'. Then, significant variables in univariate Cox regression models such as marital status, distance from the living area, spouse job, educational levels, seasons and days of admission, inpatient units, related physician's specialty and degree, final diagnoses, admission type (elective or emergency), age, family size, the number of previous hospitalization and laboratory tests, radiographies, and sonographies (P-value<0.05) were put into the multiple Cox and parametric models (including exponential, log normal, log logistic, gamma, Weibull and Gompertz). To compare the efficiency and performance of parametric and semi-parametric models and finding the best model fitted to studied data, Akaike's Information Criterion (AIC) and Cox-Snell residual were used. P<0.05 was considered as statistically significant. The study protocol and ethical aspects were approved by the Ethics Committee of Tehran University of Medical Sciences.

Results

The median length of hospital stay 'leading to recovery' was 50.8 hours and in the studied Obstetrics, Surgery and Oncology units were 48.5, 54.4 and 94.2 hours, respectively. As it can be seen in Table 1 which represents the results of the Cox proportional hazards multiple regression model, the factors associated with the patient length of stay 'leading to recovery' include distance away from the living area, admission day, admission unit, related physician specialty, admission type, final diagnoses and total number of laboratory tests, radiographies, and sonographies performed for patients. In other words, according to the hazard ratio

(HR), the patients who were admitted from an area more than 200 kilometers away from the patients' living area to hospital compared with those who were admitted from the distance of less than that (HR=0.514, *P*<0.001), the patients who were admitted on Thursdays compared with those admitted on Saturdays (HR=0.688, *P*=0.025), the patients who were admitted in Surgery and Oncology units compared with those admitted in Obstetrics unit (respectively, HR=0.592, *P*<0.001 and HR=0.386, *P*<0.001), the patients who were admitted by Internists compared with those admitted by Gynecologists (HR=0.544, *P*=0.028) and the patients who were admitted due to neoplastic diseases, endocrine, nutritional and metabolic diseases and genitourinary system diseases compared with pregnancy, childbirth and peurperium diseases (respectively, HR=0.634, *P*=0.020 & HR=0.075, *P*<0.001 & HR=0.697, *P*=0.023) had longer stays. Also, the more the number of laboratory tests, radiographies and sonographies performed for patients, the longer their LOS (HR=0.791, *P*<0.001 and HR=0.742, *P*<0.001, respectively,). But the patients who had emergent admissions compared with those who had elective ones had shorter length of stays (HR=1.372, *P*<0.001).

Table 2 shows Akaike's Information Criterion (AIC) for the different considered models. According to this criterion, among the desired models, a model that has the lowest AIC. is the best and the most efficient one Therefore, in our study the gamma model was the best fitted model to the length of stay data among other semi-parametric and parametric models.

Table 1. Factors associated with the patient length of stay 'leading to recovery' using the Cox multiple regression model

Factor		Frequency	Wald Test	*P*-value	Hazard Ratio
Distance away from Living Area more than 200 Km		213	13.510	<0.001	0.514
Admission Day					
	Saturday	721	22.176	0.001	1
	Sunday	538	0.196	0.658	1.061
	Monday	623	2.508	0.113	1.232
	Tuesday	551	4.695	0.030	1.351
	Wednesday	409	0.051	0.821	0.968
	Thursday	341	5.049	0.025	0.688
	Friday	238	5.102	0.024	1.527
Inpatient Unit					
	Obstetrics	1704	28.474	<0.001	1
	Surgery	1360	16.726	<0.001	0.592
	Oncology	357	24.889	<0.001	0.386
Related Physician Specialty					
	Gynecologists	1704	7.418	<0.001	1
	Internists	147	4.808	0.028	0.544
	General Surgeons	43	1.545	0.214	1.531
Emergent Admission		1639	10.878	0.001	1.372
Final Diagnoses Categories					
	Pregnancy, Childbirth and Peurperium Diseases	1994	33.513	<0.001	1
	Neoplasms	323	5.414	0.020	0.634
	Endocrine, Nutritional and Metabolic Diseases	106	28.725	<0.001	0.075
	Digestive System Diseases	100	0.160	0.689	0.882
	Genitourinary System Diseases	707	5.180	0.023	0.697
	Other Diseases	191	0.010	0.920	1.025
The Number of Laboratory Tests			148.621	<0.001	0.791
The Number of Radiographies and Sonographies			106.008	<0.001	0.743

Table 2. Results of the Cox and parametric models in the multiple analysis of LOS 'leading to recovery' in the studied hospital

Models	Cox	Exponential	Weibull	Log-logistic	Log-normal	Gamma	Gompertz
AIC	35728	6960.194	5044.177	4305.736	4307.352	4288.598	6465.407

Table 3. The comparison results of the significant factors of the univariate Cox multiple regression model between the Cox and gamma models

Factors	Frequency	Cox model			Gamma model		
		Coefficient	SE	*P*-value	Coefficient	SE	*P*-value
Distance of more than 200 kilometers from patients' living area to hospital	213	-0.1380	0.0880	0.117	0.0641	0.0373	0.086
Admission Days							
Saturday	721						
Sunday	538	-0.1307	0.0667	0.050	0.0566	0.0291	0.052
Monday	623	-0.0331	0.0649	0.610	0.0542	0.0280	0.053
Tuesday	551	0.0098	0.0662	0.882	0.0154	0.0289	0.594
Wednesday	409	-0.2527	0.0722	<0.001	0.0988	0.0316	0.002
Thursday	341	-0.2982	0.0755	<0.001	0.1204	0.0333	<0.001
Friday	238	0.0934	0.0853	0.273	-0.0384	0.0376	0.308
Inpatient Units							
Obstetrics	1704						
Surgery	1360	-0.2800	0.0626	<0.001	0.090	0.0271	0.001
Oncology	357	-0.6021	0.0967	<0.001	0.2356	0.0398	<0.001
Related Physician Specialty							
Gynecologists	1704						
Internists	147	-0.5369	0.1487	<0.001	0.267	0.0612	<0.001
General Surgeons	43	0.0080	0.2177	0.971	0.1552	0.0892	0.082
Emergent Admissions	1693	0.1800	0.0430	<0.001	-0.1028	0.0194	<0.001
Final Diagnoses Categories							
Pregnancy, Childbirth and Peurperium Diseases	1994						
Neoplasms	323	-0.7599	0.0970	<0.001	0.4139	0.0404	<0.001
Endocrine, Nutritional and Metabolic Diseases	106	-1.5360	0.1988	<0.001	0.5941	0.0671	<0.001
Digestive System diseases	100	-0.2917	0.1651	0.077	0.2104	0.0717	0.003
Genitourinary System Diseases	707	-0.4318	0.0750	<0.001	0.2193	0.0327	<0.001
Other Diseases	191	-0.5010	0.1097	<0.001	0.1605	0.0449	<0.001
The Number of Laboratory Tests		-0.1978	0.0095	<0.001	0.1161	0.0038	<0.001
The Number of Radiographies and Sonographies		-0.1963	0.0133	<0.001	0.1013	0.0060	<0.001

Afterwards, we evaluated and compared the considered models (Cox, exponential, Weibull, log-normal, log logistic, gamma and Gomprtz) using the Cox-Snell residuals. For each model, we calculated the Cox-Snell residuals, estimated their survival functions using Kaplan-Meier method and, then, calculated the cumulative hazard functions for these estimations. Finally, according to Cox-Snell residuals, the hazard function graphs were drawn. Considering that the closer the graph to the bisector the better fitted model to the data, we saw that in our study the gamma model was the best fitted model to the studied LOS data of all (Figure 1).

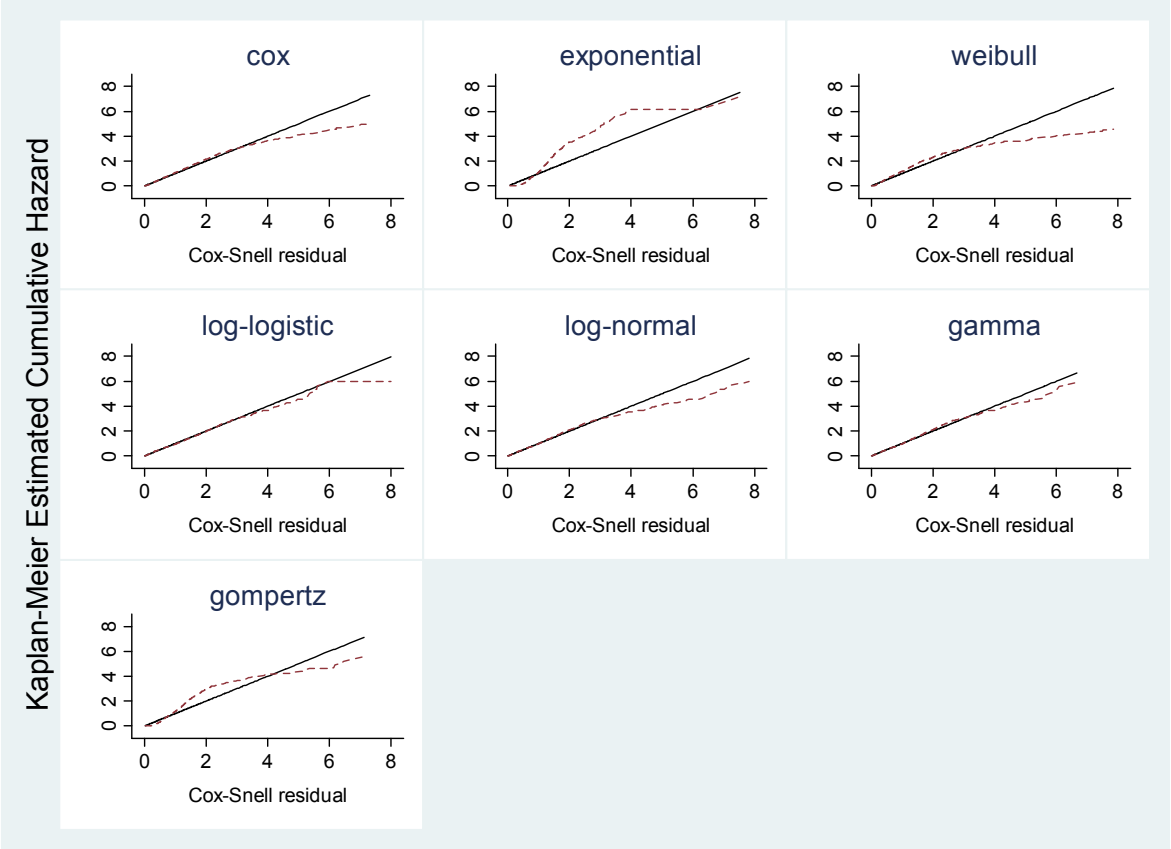

Figure 1. The Cox-Snell residuals in the considered semi-parametric and parametric models

Then, we studied the factors associated with LOS using gamma model and compared the results with those of the Cox model. As shown in Table 3, the results of these two models are similar in most cases except for patients who were admitted on Mondays (P=0.053 vs. P=0.610), patients admitted by general surgeons (P=0.082 vs. P=0.971),and those admitted and hospitalized due to the digestive system diseases (P=0.003 vs. P=0.077).

Discussion

Health care services and outcomes research are frequently interested in determining the association between hospital LOS and its associated factors in different diseases. However, there is no agreement on analytic strategy for determining the association between them (11).

In this study, 23.1% of the cases had been discharged from the hospital with no recovery considered as right censored data. Therefore, specific statistical methods (survival analysis methods) should be used in order to reduce the risk of potential loss of data.

This study aimed to compare the semi-parametric Cox proportional hazards model and parametric models to determine the factors associated with the patient's length of admission into the units of Women Hospital in Tehran, Iran. Using the Akaike's Information Criterion (AIC), we found that among the seven considered models used for fitting to LOS data, gamma model which had the lowest AIC was the best model (Table 2).

Also, the Cox-Snell residual graphs of seven models showed that the gamma model graph was closer to the bisector than the others; therefore, it was the best fit to the studied LOS data (Figure 1).

Comparison of the Cox proportional hazards model and gamma model showed that although the results of the two models are similar in most cases, there were considerable differences between them in some cases. For example, the results of the gamma model (unlike the Cox model) showed that the length of stay of patients with digestive system diseases was more than that of patients hospitalized due to pregnancy, childbirth and puerperium diseases and statistically significant. It is logical because of performing various diagnostic tests required for diagnosis, as well as, length of hospital stay

needed to make a full recovery from these diseases. Although the differences between the results of the two models of longer LOS of patients admitted on Mondays compared to those admitted on Saturdays and patients admitted by general surgeons compared to those admitted by gynecologists were remarkable, they were not statistically significant.

It should be noted that if the assumption of proportional hazards is not fulfilled, the reliability of the results of the Cox proportional hazards model is low and it would be preferred to use parametric models (in this study, the gamma model).

Previous studies revealed different results as compared to those of the current study (2,9-12). Austin *et al.* concluded that the generalized linear models were better than the linear models for predicting the length of stay (11); however, these models have not been studied in the current study. Marazzi *et al*. in their study showed that none of considered parametric models (including lognormal, Weibull, and gamma) appeared to fit satisfactorily across a variety of samples to describe the LOS distribution (12).

Perhaps, the reason of the discrepancy observed in the results of studies may be using different types of data and model they have used. In other words, the findings of a study cannot necessarily be generalized to other studies due to the differences in the types of the considered data by virtue of the selected types of models and distribution for them**.**

In this study, the results of the parametric gamma model showed that the patient LOS in the hospital was associated with the following factors:

The length of stay of patients admitted on Wednesdays and Thursdays was longer than that of patients admitted on Saturdays probably because in the next days (weekends in Iran) less diagnostic and curative procedures had been performed and they usually were delayed until the first day of the next week. Cannoodt and McMullan *et al.* in their studies concluded that patients admitted on Fridays and Saturdays have longer LOS than others. Thus, considering that Fridays and Saturdays are the last days of the weeks in their countries, their results confirm our results (13,14).

The patients who were admitted in the Oncology and Surgery units had longer LOS compared with those who were admitted in Obstetrics unit because of the type and severity of their illnesses, requiring more diagnostic tests as well as more length of stay to recover from their diseases.

The patients who were admitted by internists had longer LOS than those who were admitted by Gynecologists because of the type of the illnesses they treat and the need to more diagnostic and curative procedures to diagnose and treat these patients. Moloney *et al.* found that the LOS of patients who were admitted by GPs was shorter than that of those admitted by the specialists. However, they did not compare the patients' LOS among those admitted by different specialists (15).

Elective patients had longer LOS than emergent ones probably because of suffering from chronic diseases which need longer care and stay in hospital to recover. Faraji Khiavi in a study on the patients undergoing heart bypass surgery in a Heart Hospital, Tehran-Iran concluded that elective patient LOS was 5.38 days shorter than that of emergent patients (16). These results contrast with ours probably because of the difference between the types of patients studied in these two studies. Because coronary-artery patients admitted through Emergency Department should be usually hospitalized in CCU, ICU and Surgery units (if they need surgery) and stay there for a long time. Therefore, they will stay longer than elective patients in hospital.

The patients admitted due to diseases other than pregnancy, childbirth and puerperium diseases had longer LOS because of they need for numerous examinations, laboratory tests and radiographies to diagnose the diseases and longer time of their treatment courses. Aguirre-Gas *et al.* concluded that malignant tumors increased the patients' LOS (17). Ramezanpoor's study also found that suffering from genitourinary system diseases and pregnancy, childbirth and puerperium diseases resulted in longer and shorter LOS, respectively (18). Both of these results confirmed our findings.

Finally, our results showed that increasing the number of diagnostic laboratory tests, radiographies and sonographies performed for patients lengthens their LOS in the hospital. It was probably because of the large number of primary routine tests and examinations done in order to diagnose the patients' diseases and the delay in delivering their results from laboratory and radiography units to inpatient units in order to start and continue the curative procedures.

The current study had two limitations. This study has been conducted only in a women's hospital and the results probably cannot be generalized to other hospitals, especially general hospitals. Moreover, for collecting data which were not recorded in the patients' charts (such as patients' and their spouse job and educational levels, family income), we conducted 951 interviews with all the patients admitted in the units in the last three months of the year, because this survey began from the

last days of autumn, and related analyses had been carried out only for these patients.

In conclusion, the results of this study showed that, according to our LOS data, the parametric gamma model could better determine the factors associated with the patients' LOS than the semi-parametric Cox proportional hazards model. In other words, in the present study, the gamma model provided a better fit to the studied data than the Cox proportional hazards model. Therefore, it would be better for researchers of health care field to consider this model in their researches about the patients' LOS, if the assumption of proportional hazards is not fulfilled. The results of the parametric gamma model showed that the factors affecting the patient length of stay 'leading to recovery' were admission day, inpatient unit, related physician's specialty, emergent admission, final diagnosis and the number of laboratory tests, radiographies and sonographies.

The authors declare that they have no conflicts of interest.

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