Iran J Public Health, Vol. 51, No.9, Sep 2022, pp.2108-2116

Original Article

The Evaluation of Survival Rate in Patients with Prostate Cancer by Bayesian Weibull Parametric Accelerated Failure-Time Model

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(Received 15 Apr 2021; accepted 17 Jun 2021)

Abstract

Background: Prostate cancer is the most prevalent malignancy in men. This study was carried out to determine effective factors on the survival rate of patients diagnosed with prostate cancer in Kerman, Iran.

Methods: The present study was conducted as a retrospective cohort of 238 patients diagnosed with prostate cancer from 2011 to 2019 in Kerman, Iran. First, the demographic and clinical information of patients were collected. Then, the information on patient survival up to June 2019 was tracked, and their latest statuses of death or survival were recorded. Kaplan-Meier method, log-rank test, and Bayesian Weibull parametric accelerated failure- time model were used for data analysis. Data analysis was carried out by Stata and SAS.

Results: The mean age of patients in the diagnosis was 73.28±10.08 year. The patient's 1, 2, 3 and 5-years of overall survival rates were equal to 78.54%, 65.97%, 56.64% and 49.30, respectively. Patients under surgical therapy relatively held longer survival times compared to the rest of the therapies. Patients under chemotherapy had shorter survival times. Age at diagnosis, occupation, chemotherapy, surgery, education, and smoking variables significantly affected patients' survival (P<0.05).

Conclusion: Patients' survival duration increases if the disease is diagnosed at younger ages and its preliminary development stages. Smoking cessation is strongly recommended after diagnosis, as it is associated with a lower survival rate. Patients who underwent radical prostatectomy surgery showed higher survival rates than radiotherapy, hormone ablation, or chemotherapy. Moreover, patients with higher education had more prolonged survival.

Keywords: Survival; Therapy type; Kaplan-Meier; Bayesian; Prostate cancer

Introduction

Cancer is a critical threat to individuals' health, which it bears an increasing and constant progression. It is the third global reason for death (1, 2). About 18.1 million new cases and 9.6 million deaths were estimated worldwide in 2018 (3).

The anticipations showed that the number of new cancer cases would increase from 84800 in 2012 to 129700 in 2025 (4). Moreover, the cancer incidence rate in Kerman increased from 2838 in 2007 to 5884 in 2014 (4, 5). An estimation was made on patients diagnosed with 36 different cancer types in 185 countries in 2018. The estimation showed around 1,276,106 new cases and 358,989 deaths due to prostate cancer (3).

Prostate cancer is the most common reason for death among men. Its prevalence directly relates to aging, which means about three-fourth of cases in the world occurred in men above 65 years (6).

A proper therapy depends on several factors. For instance, it depends on PSA rate, disease stage, tumor size, age, and symptoms at diagnosis (physical and mental). The most common therapies for prostate cancer are radiotherapy, chemotherapy, hormone therapy, pharmacotherapy, surgery, or a combination of more than one therapy (7). The therapies' purpose is to identify the best practices for cancer treatment, increased survival, and enhanced life quality of patients diagnosed with cancer (8).

In many patients with prostate cancer, the disease may be alongside metastasis to osseous locations with complications such as pain, spinal fractures. It may disturb the life quality of the patients (9). Radiotherapy and surgery are two standard therapeutic techniques, whereas hormonal therapy and chemotherapy are reserved for advanced cases (10). During recent years, advancements were made in prostate cancer diagnosis and treatment, which led to improved survival in the patients diagnosed with the disease (11).

Further studies are necessary to study the factors which affect the survival rate in patients diagnosed with prostate cancer. In Iran, some studies were carried out on prostate cancer survival to enhance and improve therapeutic methods and reviewing the factors influential on the patients' survival, which has high significance in life quality (7, 12-14).

Prostate cancer is one of the most common malignant types of cancer among men. Moreover, it is the second reason of death in men due to cancer after lung cancer, with a critical role in individual health status. Therefore, reviewing the factors affecting survival and controlling them would make us understand disease fatality and prevent death in patients with prostate cancer.

No study is conducted in Kerman as the biggest South-Eastern city of Iran, to address prostate cancer survival. Therefore, this study surveys the factors affecting patients' survival diagnosed with prostate cancer in Kerman.

Materials and Methods

This study was conducted in Kerman, the biggest South-Eastern city of Iran, as a retrospective cohort. The study sample was composed of medical data of 238 patients diagnosed with prostate cancer in the hospitals of Kerman from 2011 to 2019. The patients' information was collected by their medical profile as well as phone numbers. The patients were tracked up to June 2019, and their latest survival status was recorded. This study's variables were age at diagnosis, education, occupation, family history of the type of cancer, opium abuse, smoking, type of therapy, and diagnosis symptoms. The occupations were divided into the following subgroups: farmers, employees (e.g., retired from administrative offices, teachers, and army personnel), self-employed (e.g., shopkeepers), and others. The therapeutic method adopted to treat patients diagnosed with prostate cancer included five therapies: radiotherapy, chemotherapy, hormone therapy, pharmacotherapy, radical prostatectomy surgery, or a combination of these therapies.

Moreover, disease symptoms at diagnosis were divided into the following subgroups: no symptoms, dysuria, urethral obstruction and frequent urination, and others (including hematuria, body pain, and nausea). Patients surviving until the end of the study (June 2019) were considered as censored observations. The response variable included interval between prostate cancer diagnosis and death or censor time are monthly calculated. If a patient died due to any other cause than cancer, he was excluded from the sample.

Statistical analysis

Kaplan-Meier, log-rank test, and Bayesian Weibull parametric accelerated failure-time model were used for data analysis. In our data, the graph of ln (-ln(s(t)) with ln(t) was linear so, the Weibull distribution adequately fitted the data.

In this study, the results of the classical and Bayesian models were compared with each other.

However, because the results of the Bayesian model were more accurate and had a narrow confidence interval, the Bayesian model was finally selected. Therefore, only the results are given in this article.

In Bayesian Weibull parametric accelerated failure-time model, accelerated factor and 95% credible interval were reported. The modeling process was such that a univariate analysis was first carried out, and variables with p-values smaller than or equal to 0.2 were incorporated into the multivariate model as critical variables. The final model was yielded by the backward method. Data analysis was carried out by Stata ver. 16.0 and SAS ver. 9.4 software, and the significance level was set as 0.05.

Ethics approval

Verbal consent was received from every participant through phone calls, whereby the general objectives were communicated. The study protocol with Reg. No. 97000701 was approved by ethical committee of Kerman University of Medical Sciences (ethical code number: IR.KMU.REC.1397.601).

Results

One hundred patients diagnosed with prostate cancer out of 238 (42.02%) died. The mean age of patients at diagnosis was 73.28±10.08, and variation range was 59 years. The mean follow-up time was eight years, and the shortest and longest survival time during which patients stayed in the study was 0.16 months (2 day) and 92.16 months (2764 day), respectively. The overall average survival duration of patients was 53.76±2.84 months. The data relating to age and overall survival time are shown in Table 1.

Table 1: Age and overall survival time (n=238) of patients diagnosed with prostate cancer Kerman, Iran, 2011–2019

Characteristic	*Mean*	*St. dv*	*Range*	*Min*	*Max*	$Q_{1(\%25)}$	$Q_{2(\%50)}$	$Q_{3(\%75)}$
Age(yr)	73.28	10.08	59	41	100	67	72	81
Survival time(month)	53.76	2.84	92	0.16	92.16	12.86	65.63	a

a- Less than 75% of deaths occur in this study, so we do not have Q3 for survival time variable.

Table 2 indicates the numbers and percentages of alive and dead patients and their 1, 2, 3 and 5-year survival rates due to the characteristics of patients. Fig. 1 shows the overall survival time of prostate cancer patients during 96 months of study.

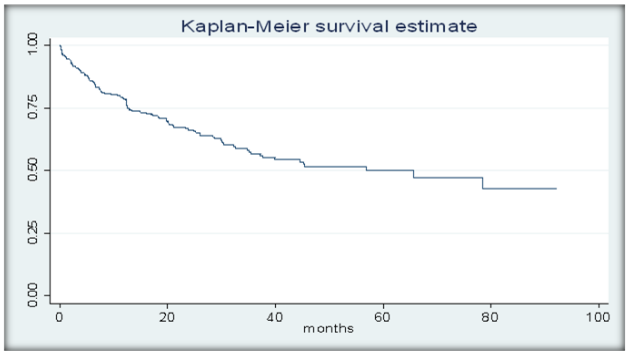

Fig. 1: The overall survival rate among patients diagnosed with prostate cancer, Kerman 2011-2019

The mean survival time was 53.76±2.84, and the median was 65.63 months. The patients' one, two, three and five-year overall survival rates were 78.54, 65.97, 56.64, and 49.30%, respectively.

Log-rank test results showed that age (P=0.007), education (P=0.004), occupation (P=0.01), chemotherapy (P<0.001), smoking (P=0.04), radical prostatectomy surgery (P=0.0001), and symptoms at diagnosis (P=0.006) were in significant relationship with patients' survival. The family history of cancer (P=0.4), hormone therapy (P=0.98), radiotherapy (P=0.43), opium abuse (P=0.06), and pharmacotherapy (P=0.4) did not have any significant relationship with patients' survival. The univariate model results showed a significant relationship between study variables (age, occupation, education, smoking, chemotherapy, radical prostatectomy surgery, opium

abuse, symptoms)) and survival rate. The results of the univariate model are shown in Table 3.

Table 2: Results of the socio-demographic and clinical variables of patients diagnosed with Prostate cancer and their 1, 2, 3 and 5-year overall survival rates, Kerman, Iran, 2011-2019

Characteristics	*Alive n (%)[a]*	*Dead n (%)[a]*	*Total n (%)[b]*	*1-Year OS (%)*	*2-Year OS (%)*	*3-Year OS (%)*	*5-Year OS (%)*
Age(yr)							
≤72	70(70)	30(30)	100(42)	85.57	78.02	67.00	53.93
>72	68(49.3)	70(50.7)	138(58)	73.53	57.97	49.75	45.09
Education level							
Illiterate	56(47.9)	61(52.1)	117(49.2)	74.68	58.29	45.21	36.80
Under diploma	45(59.2)	31(40.8)	76(31.9)	78.81	67.24	61.79	55.76
Diploma	19(76)	6(24)	25(10.5)	78.72	78.72	78.72	59.04
University degree	18(90)	2(10)	20(8.4)	100.00	94.12	86.27	86.27
Occupation							
Farmer	44(45.4)	53(54.6)	97(40.7)	69.79	57.10	43.17	38.51
Employee	52(66.7)	26(33.3)	78(32.8)	85.53	73.63	67.74	58.06
Self-employed	28(71.8)	11(28.2)	39(16.4)	81.58	72.99	72.99	64.88
Other	14(58.3)	10(41.7)	24(10.1)	86.96	65.22	48.91	36.68
Signs							
No sign	31(60.8)	20(39.2)	51(21.4)	78.00	69.09	66.48	53.61
Dysuria, frequent urination	87(63.5)	50(36.5)	137(57.6)	81.34	71.01	59.47	55.50
Other	20(40)	30(60)	50(21)	71.43	49.78	38.72	27.66
Family history of cancer							
NO	112(60.9)	72(39.1)	184(77.3)	78.83	62.29	57.86	50.35
Yes	26(48.1)	28(51.9)	54(22.7)	77.57	61.86	52.86	46.04
Smoking status							
No	106(62.7)	63(37.3)	169(71)	80.61	68.99	61.87	55.53
Yes (only before diagnosis)	15(45.5)	18(54.5)	33(13.9)	75.38	62.55	44.68	39.10
Yes (before and after diagnosis)	17(47.2)	19(52.8)	36(15.1)	71.83	54.73	44.78	28.49
Opium abuse status							
No	92(61.7)	57(38.3)	149(62.6)	78.08	68.03	61.08	55.92
Yes (only before diagnosis)	9(45)	11(55)	20(8.4)	78.95	55.56	42.48	33.99
Yes (before and after diagnosis)	32(61.5)	20(38.5)	52(21.9)	82.35	70.92	61.24	43.75
Yes (only after diagnosis)	5(29.4)	12(20.6)	17(7.1)	70.59	47.06	26.89	26.89
Radiotherapy							
No	105(60)	70(40)	175(73.5)	78.43	67.75	57.26	52.61
Yes	33(52.4)	30(47.6)	63(26.5)	78.86	61.34	54.88	40.72
Chemotherapy							
No	117(72.2)	45(27.8)	162(68.1)	87.26	78.39	70.45	63.13
Yes	21(27.6)	55(72.4)	76(31.9)	60.53	41.48	30.73	29.14
Radical prostatectomy surgery No							
Yes	98(50.3)	97(49.7)	195(81.9)	75.00	61.11	51.36	43.54
	40(93)	3(7)	43(18.1)	95.12	91.66	91.66	91.66
Hormone-therapy							
No	76(55.9)	60(44.1)	136(57.1)	78.52	66.31	57.20	49.79
Yes	62(60.8)	40(39.2)	102(42.9)	78.57	65.48	55.78	49.75
pharmacotherapy							
No	64(53.8)	55(46.2)	119(50)	76.27	62.15	53.94	48.45
Yes	74(62.1)	45(37.8)	119(50)	80.87	69.95	59.40	49.07

OS: Overall Survival; (%)[a] Row Percentage; (%)[b] Column Percentage;

Table 3: The relation between study variables and survival rate among the patients diagnosed with prostate cancer using univariate and multiple Bayesian Weibull regression accelerated failure-time model in Kerman, Iran, 2011-2019

Characteristic	*Univariate*			*Multiple*		
	Accelerated factor	*95% CI*	*P-value*	*Accelerated factor*	*95% CI*	*P-value*
Age(year)						
≤72*	--	--	--	--	--	--
>72	0.46	(0.21, 0.80)	0.01	0.53	(0.28,0.93)	0.007
Education level						
Illiterate*	--	--	--	--	--	--
Under diploma	1.86	(0.93, 0.80)	0.09	2.37	(1.27,4.10)	0.11
Diploma	4.27	(1.00,14.45)	0.08	2.62	(0.56,8.58)	0.53
University degree	96.78	(3.69,14.52)	0.007	12.48	(2.65,39.98)	<0.0001
Occupation						
Farmer *	--	--	--	--	--	--
Employee	2.95	(1.37,5.97)	0.007	1.17	(0.53,2.28)	0.31
Self-employed	4.12	(1.37,10.76)	0.02	3.50	(1.56,6.69)	0.003
Other	1.73	(0.56,4.52)	0.45	2.06	(0.98,3.99)	0.02
Signs				a		
No sign*	--	--	--			
Dysuria, frequent urination	1.13	(0.47,2.25)	0.91			
Other	0.385	(0.14,0.81)	0.02			
Family history of cancer				a		
No*	--	--	--			
Yes	0.83	(0.40,1.54)	0.45			
Smoking status						
No*	--	--	--	--	--	--
Yes (only before diagnosis)	0.62	(0.23,1.31)	0.17	1.17	(0.61,2.15)	0.89
Yes (before and after diagnosis)	0.45	(0.19,0.93)	0.03	0.32	(0.17,0.54)	0.009
Opium abuse status				a		
No*	--	--	--			
Yes (only Before diagnosis)	0.64	(0.21,1.60)	0.26			
Yes (before and after diagnosis)	0.10	(0.43,2.09)	0.84			
Yes (only after diagnosis)	0.35	(0.12,0.84)	0.02			
Radiotherapy				a		
No*	--	--	--			
Yes	0.82	(0.40,1.50)	0.45			
Chemotherapy						
No*	--	--	--	--	--	--
Yes	0.18	(0.09,0.31)	<0.0001	0.18	(0.09,0.31)	<0.0001
Radical prostatectomy surgery						
No*	--	--	--	--	--	--
Yes	56.08	(5.12, 278.80)	0.001	10.81	(2.58,32.18)	0.009
Hormone-therapy				a		
No*	--	--	--			
Yes	1.14	(0.54,1.86)	0.98			
pharmacotherapy				a		
No*	--	--	--			
Yes	1.33	(0.07,2.37)	0.45			

CI: Credible interval, *: Reference category a: These variables were not significant in the multiple model and removed from the model by backward method.

Bayesian Weibull multivariable model showed that age, smoking, radical prostatectomy surgery, chemotherapy, occupation, and education were effective in the patients' survival. These results are indicated in Table 3. Due to Bayesian multi-variable analysis, it is observed that the survival time in patients with ages above 72 was reduced 47% compared to patients with ages below or equal to 72. The survival time for patients with a smoking history before and after diagnosis was reduced by 68% compared to patients with no smoking history. The survival time for patients

with chemotherapy was reduced by 83% compared to patients with no chemotherapy. The survival time for patients who have undergone radical prostatectomy surgery was 10.81 times more than those who did not undergo surgery. The survival time for patients with self-employment is 3.50 times more than patients whose occupation is farming. The survival time for patients with other occupations is 2.06 times more than patients whose occupation is farming. The survival time for patients with university education is 12.48 times more than illiterate patients.

The variables of the family history of cancer, opium abuse, radiotherapy, hormone therapy, pharmacotherapy, and symptoms at diagnosis did not have significant effects on patients' survival ($P>0.05$)

Fig. 2 shows the graph of ln (-ln(s (t)) with ln (t) was linear so, the Weibull distribution adequately fitted the data.

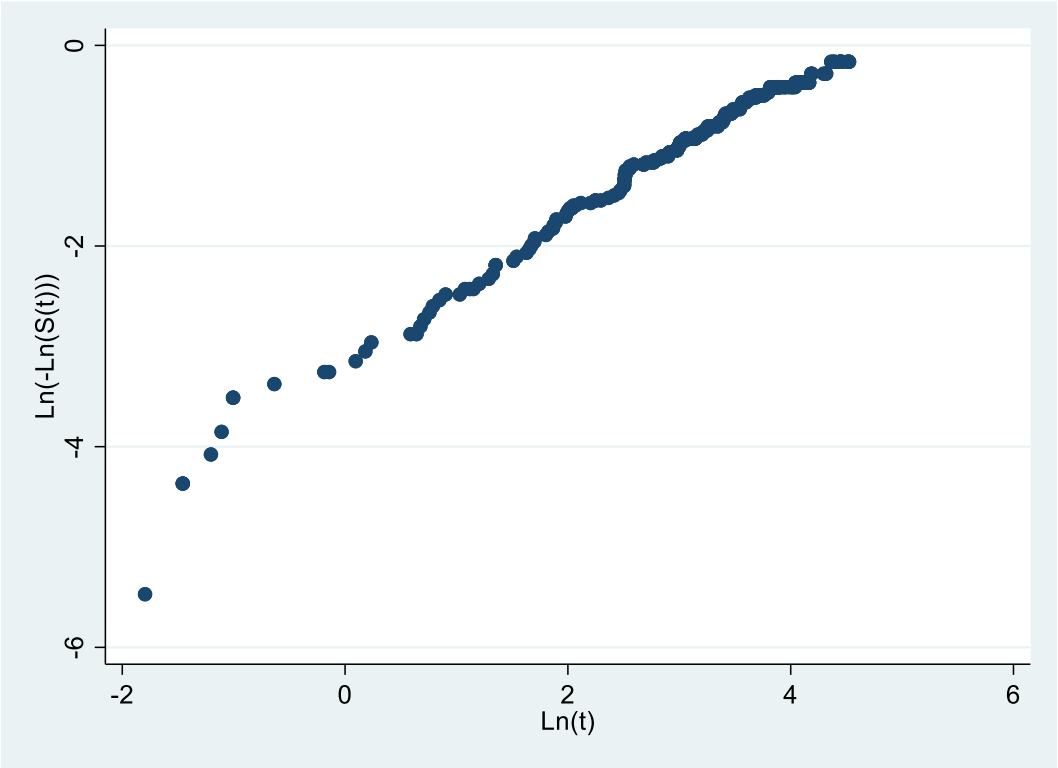

Fig. 2: ln (-ln(s (t)) plotted against ln (t) among patients diagnosed with prostate cancer, Kerman 2011-2019

Discussion

This study investigated factors associated with patients' survival rate with prostate cancer in Kerman City; using Bayesian parametric accelerated failure time models.

The mean age of patients with prostate cancer at diagnosis was equal to 73.28 yrs. old. In Iran, the mean age at diagnosis was 71.85 (2). Two studies conducted in the United States (US) reveal that the mean age at diagnosis was 66.19 and 66 yrs (15). Therefore, prostate cancer incidence directly relates to age, taking place at older ages around the age of 70 on average.

Although prostate cancer often occurs in older men, a third of men in their 30s and 40s have prostate adenocarcinoma (16). In Victoria, men between 45 to 54 yrs have better survival status compared to those between 55 to 64 years. Therefore, 5-years survival rate in the age group

of 45 to 54 yrs, 55 to 64 yrs, and 65 yrs and above were 97.7%, 96.9%, and 94.5%, respectively (17). In the US, 50-years-old or younger men had a lower recurrence rate than older men (18). Therefore, due to the present study supported by other studies' results, the survival rate is higher among younger patients; hence, screening and detecting the disease at a younger age is recommended.

The mean survival time for patients diagnosed with prostate cancer was 53.76 months, and the patients' 5-year survival rate was found to be 49.30%. In Iran, the patients' 5-year survival rate was 54.6%, which is almost coherent with the results of this study (2). It is while in the studies conducted outside of Iran, the 5-year survival rates were higher, 5-year survival rate was calculated in Italy, the US, and the UK as being 93.6%, 71%, and 56%, respectively (11, 19, 20). The survival rate of different studies varies. The reason may be due to different methods adopted for study design; disease diagnosis occurs at its preliminary stages in some countries and their therapeutic methods.

Bayesian Weibull parametric accelerated failure-time model showed that age at diagnosis, smoking, occupation, radical prostatectomy surgery, chemotherapy, and education were effective on patients diagnosed with prostate cancer. Regarding the studies carried out in Iran and elsewhere, age is one of the critical risk factors for prostate cancer survival (9, 15-18). Hence, it seems to be reasonable that as age increases, the patients' survival goes down. Consequently, older patients should receive more care.

Numerous studies were conducted to investigate the therapeutic method's effect on prostate cancer survival rate. Those patients undergone radical prostatectomy showed more prolonged survival compared to others with different therapeutic methods. Patients undergoing radical prostatectomy had longer survival compared to other patients with other therapies (8). Radical prostatectomy surgery is addressed and recommended as a standard and primary therapy for prostate cancer patients, which increases their survival rate. However, one of the concerns patients deal with is post-surgery complications, including urinary incontinence, bleeding, rectum injury, infection, which reduces the life quality of patients (21, 22).

Five-year survival rate for patients treated by chemotherapy was lower than other therapies. The 5-year survival rate for chemotherapy patients was less than those who did not (23). Therefore, other therapies showed better performance in prostate cancer survival rate compared to chemotherapy. Perhaps the reason is that chemotherapy is reserved for hormone-resistant cancers that are more aggressive tumors. In general, therapy is one of the critical and effective factors for the patients' survival, and various researches yet have to be done in this context to improve the therapies.

Smoking was effective on prostate cancer patients' survival. However, those patients who keep smoking before and after diagnosis have shorter survival than those with no smoking history or who quit smoking. Therefore, we strictly recommend smoking cessation after their cancer diagnosis to have more prolonged survival. In other studies, smoking was not among the factors affecting patients' survival. The reason may be that the smoking grouping in our study was different from others (24-26).

The patients with agricultural occupations have a lower survival rate than other occupations (employees, self-employed). Perhaps, their exposure to insecticides and agricultural pesticides or other agricultural exposures may reduce the survival rate (27). Another possible cause is that this group has lower education levels and therefore does not come for routine PSA screening. We observed that those patients with university education, diploma, and under diploma education have higher survival rates compared to illiterate patients. Patients with lower education levels went through less screening and therapy than those with higher education levels; consequently, their survival rate was lower (28). Therefore, the level of education is among predicting primary treatments that may positively affect patients' understanding of the risks and advantages of thera-

peutic interventions and survival. More studies seem to be required in this regard (29).

Limitations

In this study, the data was used related to 2011 until June 2018. Unfortunately, the information on the stage and grade of disease, tumor size, and PSA value were not accurately recorded for most of patients from 2011 to 2019. Consequently, due to flawed medical profiles and patients' information, mentioned factors were excluded from this study.

Conclusion

Age, smoking, surgery, chemotherapy, occupation, and education variables significantly affected the survival rate of patients. Diagnosis in Older age was associated with a lower survival rate. Smoking cessation is strongly recommended after the diagnosis, as smokers showed a lower survival rate. Patients who underwent radical prostatectomy surgery showed higher survival rates than radiotherapy, hormone ablation, or chemotherapy. Education level improves attitude and increases the patients' survival.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Acknowledgements

This study was the output of an MSc thesis. We want to express our gratitude to all personnel and patients of teaching hospitals in Kerman, and Kerman University of Medical Sciences. They helped to handle the present study.

Conflict of interests

The authors declare they have no conflicts of interest.

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