

Knowing Cancer Diagnosis is a Protective Factor for the Survival of Patients With Breast Cancer : A Retrospective Cohort Study

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Abstract

Background: The health burden of breast cancer is rising in China. The effect of informed diagnosis on long-term survival has not been fully understood. This retrospective cohort study aims at exploring the association between early informed diagnosis and survival time in breast cancer patients.

Methods: 12,327 breast cancer patients were enrolled between October 2002 and December 2016. Potential factors including knowing cancer diagnosis status, gender, age, clinical-stage, surgical history, the grade of reporting hospital and diagnostic year were registered. We followed up all participants every 6 months until June 2017.

Results: By June 2017, 18.04% of the participants died of breast cancer. Both the 3-year and 5-year survival rate of whom knew cancer diagnosis were longer ($P<0.001$). By stratified analysis, except subgroups of male patients and patients in stage III, patients knowing diagnosis showed a better prognosis in all the other subgroups ($P<0.05$). By Cox regression analysis, it was showed that not knowing cancer diagnosis was an independent risk factor for survival in breast cancer patients ($P<0.001$).

Conclusions: Being aware of their cancer diagnosis plays a protective role in extending the survival time in breast cancer patients, which suggests medical staff and patients' families disclose cancer diagnosis to patients timely.

Background

Breast cancer, lung cancer, and colon cancer are the three most common cancers worldwide. One in eight to ten women will get breast cancer during their lifetime [1]. Depending on the National Cancer Institute (NCI)'s Surveillance, Epidemiology, and End Results (SEER) program, the incidence of breast cancer among women aged 20 to 39 years increased from 24.6/1000,000 to 31.7/100,000 from 1975–2015. The 5-year survival increased from 74.0–88.5% [2]. However, breast cancer continues to be the most common cause of female death in developing countries and second to lung cancer in developed countries. Especially in South America, Africa, and Asia, the incidence of breast cancer is increasing instead of decreasing [3].

Since the 1990s, China's incidence of breast cancer has increased more than twice as fast as has global rates, particularly in urban areas [4]. By 2008, China accounted for 12.2% of global cases of invasive breast cancer and 9.6% of related death [5]. It is anticipated that China's cases of breast cancer will rise from less than 60 cases per 100,000 women aged 55–69 years to more than 100 cases per 100,000 women, reaching 2.5 million cases overall by 2021 [6].

Patterns of breast cancer risk for Chinese women are partly aligned with known risk factors for women in developed countries [7]. Reproductive and hormonal factors like nulliparity, increased age at first live birth, limited breastfeeding and so on are associated with an increased risk of breast cancer in the Chinese population which is similar to western women [8–10]. Because of the one-child policy in China, it might

have affected breast cancer risk by reducing the lifetime duration of breastfeeding[8]. Obesity and low levels of physical activity are both known as risk factors for breast cancer in western countries. With the rapid growth of finance in China, these may also play as a risk factor for breast cancer in China [11]. Other factors such as height, hormone replacement therapy, and family history have also been regarded as risk factors of breast cancer for Chinese women [11, 12]. However, few studies paid attention to psychological factors such as the association between cancer diagnosis disclosure and survival time of patients with breast cancer.

People display different attitudes towards life with their age grows. Some studies found that patients of different ages may display different emotional experience. Although the incidence of breast cancer is increased with the growth of age, younger patients may be the most likely to suffer emotional distress compared to older ones. This relationship can be observed in patients ranging from 30 to over 80 years old [13, 14]. Also, there was another study claimed a non-significant correlation between age and affective distress by examining the above association 10 months after diagnosis [15]. However, unrealistic optimism may be more prevalent among older patients [16]. Most studies had a limited sample size, which may affect the effectiveness of the conclusions.

It has traditionally been a controversial topic that whether or not to fully inform patients of their cancer diagnosis. Advocates of concealing the condition to patients argue that patients who know their cancer diagnosis are liable to experience significant distress, which may lead to a worse prognosis [17]. Studies in Iran and Turkey showed that patients knowing their diagnosis were more likely to undergo depression, psychiatric morbidity and other negative emotion [18, 19]. On the other hand, patients who lack the awareness of their condition may undergo unrealistic optimism, which may lead to unfavorable behaviors and finally result in adverse health outcomes [20]. Previous researches showed that having an appropriate perspective of cancer status improved patients' participation in the treatment, as well as reduced their distress level, which helped them meet their psychological needs with self-esteem and respect [21]. On the contrary, without knowing their cancer condition results in an uncompleted understanding of their diagnosis, which would hurt the trust relationship between patients and physicians[22]. Depending on a study of a total of 127 cancer patients and their caregivers, no significant difference was found before and after disclosing the cancer diagnosis to patients, while the quality of life could be improved with psychological care intervention [23]. We have found that knowing their cancer status would carry a better survival rate in patients with lung cancer, while there were few studies about this issue in breast cancer patients [24].

The association between diagnosis disclosure of breast cancer and the prognosis of patients was detected in this retrospective cohort study based on the baseline and long-term follow-up information of a large sample. The results may provide valuable evidence for clinical practice.

Methods

The study was designed to find out the role that knowing cancer diagnosis plays in the survival rate of patients with breast cancer by collecting information of patients with different backgrounds.

Participants

12327 patients were included in this study who were diagnosed with breast cancer between October 2002 and December 2016. All participants were registered at the certified hospitals in Pudong New Area, Shanghai, China. This study was following the Helsinki Declaration of 1975 and was approved by the Ethics Committee of Second Military Medical University. The informed consent was obtained from participants or their families.

Data collection

Knowledge status of cancer diagnosis of participants was collected at the time of study enrollment by Shanghai Cancer Registry. Information on demographics, breast cancer diagnosis, clinical stage and other relevant data were collected at the same time. The survival data of patients with breast cancer were collected through the Center for Disease Control and Prevention of the Pudong New Area, Shanghai. Community doctors followed up patients by telephone or household survey every 6 months, and regarding death as the primary outcome event. The follow-up ended in June 2017.

Statistical analysis

χ^2 tests are used to explore all categorical variables. One-way analysis of variance (ANOVA) was conducted to compare continuous variables. Life table was used to calculate the 3-year survival rate and 5-year survival rate, and to compare the differences between subgroups in survival curve. The Cox proportional hazard regression model (Forward Stepwise, Likelihood Ratio test) with hazard ratios (HR) and 95% confidence intervals (CI) calculated was used to conduct multivariate analysis of factors influencing survival time. Statistical Package for Social Sciences software (version 23.0, SPSS, Inc., Chicago, IL) was used to conduct all statistical analyses which were two-sided. $P < 0.05$ was defined as statistically significant.

Results

Baseline characteristics

A total of 12327 patients with breast cancer were enrolled in this study. Table 1 shows the baseline characteristics of the participants. Among all 12327 participants, 9466 (76.79%) patients were aware of their cancer, 2756 (22.36%) patients had no idea of their situation. There were 105 (0.85%) patients' knowledge of their diagnosis was unclear. As shown in Table 1, there was no difference in gender composition between participants who knew their diagnosis and those who didn't know (women accounted for 99.26% vs. 99.24%, $P = 0.904$). Significant differences could be found in age, clinical stage, surgical history and reporting hospital-grade between patients who knew their diagnosis and those who didn't know ($P < 0.05$). A trend of telling patients of their cancer diagnosis was found also by noticing the

difference between different phases of diagnostic time (when participants were diagnosed with breast cancer, 1: before 2006, 2: 2007–2011, 3: 2012–2016, Linear-by-Linear Association: value = 4.232, $P = 0.040$). Patients who knew their diagnosis had younger average age (55.97 ± 11.94 vs. 60.49 ± 14.20 , $P < 0.001$), earlier clinical stage (stage 0–I: 31.94% vs. 22.28%, $P < 0.001$), higher surgery rate (56.20% vs. 49.24%, $P < 0.001$), and more recent diagnostic year (being diagnosed from 2012 to 2017: 40.78% vs. 40.50%, $P = 0.001$). Besides, patients registered and reported in higher grade hospitals were more likely to be informed of their diagnosis (high-grade hospital: 57.91% vs. 55.70%, $P < 0.05$).

Table 1
Demographic and clinical characteristics of participants, n(%)

VVariable	Total sample (N = 12327)	Knowing status of cancer diagnosis			
		Did Know (n = 9466)	Did not know (n = 2756)	Unclear (n = 105)	P*
Gender					
Male	93(0.74)	70(0.74)	21(0.76)	2 (1.9)	0.904
Female	12234(99.26)	9396 (99.26)	2735(99.24)	103(98.1)	
Average age	57.10 ± 12.70	55.97 ± 11.94	60.49 ± 14.20	69.52 ± 15.10	< 0.001
< 35	380(3.08)	305(3.22)	74(2.68)	1(9.52)	< 0.001
35-	1564(12.69)	1258(13.29)	298(10.81)	8(6.6)	
45-	3821(31.00)	3137(33.14)	672(24.38)	12(7.62)	
55-	3488(28.30)	2762(29.18)	709(25.72)	17(16.19)	
65-	1789(14.51)	1289(13.62)	482(17.49)	18(17.14)	
≥ 75	1285(10.42)	715(7.55)	521(18.90)	49(46.67)	
Clinical stage					
Stage 0- I	3641(29.54)	3024(31.94)	614(22.28)	3(2.86)	
Stage II	3700(30.02)	3037(32.08)	657(23.84)	6(5.71)	
Stage III	1135(9.21)	908(9.59)	220(7.98)	7(6.67)	
Stage IV	517(4.19)	358(3.78)	149(5.41)	10(9.52)	
Unclassified	3334(27.05)	2139(22.60)	1116(40.49)	79(75.24)	
Surgery history					< 0.001
Yes	6697(54.33)	5320(56.20)	1357(49.24)	20(19.05)	
No	5630(45.67)	4146(43.80)	1399(50.76)	85(80.95)	

* patients who knew diagnosis vs. patients who did not know diagnosis.

^a Diagnostic year 1 means those being diagnosed before 2006, 2 means those being diagnosed from 2007 to 2011, 3 mean those being diagnosed from 2012 to 2016.

VVariable	Total sample (N = 12327)	Knowing status of cancer diagnosis			
		Did Know (n = 9466)	Did not know (n = 2756)	Unclear (n = 105)	p*
Diagnostic year ^a					
1: before 2006	3268(26.51)	2442(25.80)	802(29.10)	24(22.86)	0.001
2: 2007–2011	4074(32.83)	3163(33.41)	838(30.41)	73(69.52)	
3: 2012–2016	4985(40.44)	3861(40.78)	1116(40.50)	8(7.62)	
Hospital grade					< 0.05
Primary grade hospital	166(1.35)	103(1.09)	45(1.63)	18(17.14)	
Middle grade hospital	5088(41.28)	3881(41.00)	1176(42.67)	31(29.52)	
High grade hospital	7073(57.38)	5482(57.91)	1535(55.70)	56(53.33)	
* patients who knew diagnosis vs. patients who did not know diagnosis.					
^a Diagnostic year 1 means those being diagnosed before 2006, 2 means those being diagnosed from 2007 to 2011, 3 mean those being diagnosed from 2012 to 2016.					

Univariate analysis of factors influencing the survival time of patients with breast cancer

Altogether 2152 (17.24%) death occurred among the 12327 registered patients during this 14-year median follow-up. The 3-year survival rate and 5-year survival rate of our participants were 0.86 and 0.81 respectively. As shown in Table 2, participants with different characteristics had significant differences in prognosis. The 3-year survival rate and 5-year survival rate of patients who knew their diagnosis were both longer than those who didn't know (0.89 vs. 0.79, 0.85 vs. 0.73, $P < 0.001$). Besides, it was found that female ($P = 0.011$), younger age ($< 35: P < 0.001$), earlier clinical stage ($P < 0.001$), higher rate of surgery ($P < 0.001$), being diagnosed more recently ($P < 0.001$) and reported from higher grade hospitals ($P < 0.001$) contributed to better survival rate.

Table 2
Survival of breast cancer patients with different characteristics

Variable	Death number/ Total number	3-year survival rate	5-year survival rate	p*
Knowing status of cancer diagnosis ^a				< 0.001
Did know	1446/9466	0.89	0.85	
Did not know	778/2756	0.79	0.73	
Gender				0.011
Male	29/93	0.78	0.70	
Female	2123/12234	0.86	0.81	
Age(years)				< 0.001
< 35	248/1944	0.90	0.87	
45-	521/3821	0.90	0.86	
55-	443/3488	0.89	0.86	
65-	360/1789	0.85	0.78	
≥ 75	580/1285	0.62	0.51	
Clinical stage ^b				< 0.001
Stage 0- I	184/3641	0.97	0.95	
Stage II	440/3700	0.92	0.88	
Stage III	296/1135	0.78	0.70	
Stage IV	340/517	0.44	0.33	
Surgery history				< 0.001

* overall comparison of survival curves in subgroups;

^a patients with unclear knowing status of cancer diagnosis were not included;

^b patients with unclassified clinical stage were not included;

^c Diagnostic year 1 means those being diagnosed before 2006, 2 means those being diagnosed from 2007 to 2011, 3 mean those being diagnosed from 2012 to 2016.

Variable	Death number/ Total number	3-year survival rate	5-year survival rate	P*
Yes	1100/6696	0.91	0.87	
No	1052/5630	0.80	0.75	
Diagnostic year ^c				
1: before 2006	1051/3268	0.82	0.76	< 0.001
2: 2007–2011	761/4074	0.86	0.82	
3: 2012–2016	340/4985	0.91	0.89	
Hospital grade				< 0.001
Primary grade hospital	34/166	0.47	0.41	
Middle grade hospital	903/5085	0.86	0.82	
High grade hospital	1215/7073	0.87	0.82	
*overall comparison of survival curves in subgroups;				
^a patients with unclear knowing status of cancer diagnosis were not included;				
^b patients with unclassified clinical stage were not included;				
^c Diagnostic year 1 means those being diagnosed before 2006, 2 means those being diagnosed from 2007 to 2011, 3 mean those being diagnosed from 2012 to 2016.				

Stratified analysis of the impact of cancer diagnosis knowledge on survival time in patients with breast cancer

As shown in Table 3, participants were stratified by gender, age, clinical stage, surgery history, diagnostic time and grade of reporting hospital to explore the relationship between awareness of cancer diagnosis and prognosis. Except in male patients ($P=0.103$) and in the subgroup of patients in stage III ($P=0.265$), patients who knew their cancer diagnosis displayed a better survival rate than those who didn't know ($P<0.05$).

Table 3

Relationship between cancer awareness and survival time of breast cancer patients by stratified analysis

Stratified factors	3-year survival rate		5-year survival rate		P*
	Did know cancer diagnosis	Did not know cancer diagnosis	Did know cancer diagnosis	Did not know cancer diagnosis	
Gender					
Male	0.85	0.66	0.76	0.58	0.103
Female	0.89	0.79	0.85	0.73	< 0.001
Age (years)					
< 45	0.92	0.87	0.88	0.82	< 0.001
45-	0.91	0.86	0.87	0.82	< 0.001
55-	0.91	0.85	0.87	0.81	< 0.001
65-	0.89	0.79	0.82	0.73	< 0.001
≥ 75	0.70	0.56	0.60	0.45	< 0.001
Clinical stage ^a					
Stage 0- I	0.97	0.95	0.96	0.91	< 0.001
Stage II	0.93	0.89	0.89	0.85	0.001
Stage III	0.79	0.76	0.71	0.69	0.265
Stage IV	0.47	0.40	0.34	0.31	0.005
Unclassified	0.84	0.70	0.79	0.63	< 0.001

* overall comparison of survival curves in subgroups;

^a patients with unclear knowing status of cancer diagnosis were not included;^b Diagnostic year 1 means those being diagnosed before 2006, 2 means those being diagnosed from 2007 to 2011, 3 mean those being diagnosed from 2012 to 2016.

Stratified factors	3-year survival rate		5-year survival rate		P*
	Did know cancer diagnosis	Did not know cancer diagnosis	Did know cancer diagnosis	Did not know cancer diagnosis	
Surgery history					
Yes	0.92	0.87	0.88	0.82	< 0.001
No	0.85	0.70	0.81	0.63	< 0.001
Diagnostic year ^b					
1: before 2006	0.85	0.73	0.80	0.67	< 0.001
2: 2007–2011	0.90	0.80	0.86	0.75	< 0.001
3: 2012–2016	0.93	0.84	0.92	0.81	< 0.001
Hospital grade					
Primary grade hospital	0.60	0.36	0.52	0.36	0.034
Middle grade hospital	0.89	0.78	0.86	0.71	< 0.001
High grade hospital	0.89	0.81	0.85	0.75	< 0.001
* overall comparison of survival curves in subgroups;					
^a patients with unclear knowing status of cancer diagnosis were not included;					
^b Diagnostic year 1 means those being diagnosed before 2006, 2 means those being diagnosed from 2007 to 2011, 3 mean those being diagnosed from 2012 to 2016.					

Multivariate analysis of factors influencing the survival time of patients with breast cancer

We included knowledge of cancer diagnosis status, gender, age, clinical stage, surgical history, diagnostic time and reporting hospital grade in the Cox proportional hazard regression model (Forward Stepwise, Likelihood Ratio test). Knowledge of cancer diagnosis status, age, surgery history, reporting hospital

grade, diagnostic year and clinical stage were independent influencing factors of survival time of patients with breast cancer ($P < 0.001$, Table 4). It showed that not having knowledge of cancer diagnosis was significantly associated with a poor prognosis compared to those knowing (HR, 1.405, 95% CI, 1.285–1.537, $P < 0.001$). Having surgery contributed to a better survival (HR, 0.647, 95% CI, 0.594–0.706; $P < 0.001$), while age was a risk factor of survival time (HR, 1.434, 95% CI, 1.285–1.537; $P < 0.001$). Compared to patients from primary grade hospital, patients from higher grade hospital had a better survival rate (HR, 0.457, and 0.478, respectively; $P < 0.001$). The more recently the patients were diagnosed, the longer they would survive (HR, 0.802, and 0.649, respectively; $P < 0.001$, Table 4). In addition, compared to patients in Stage 0- I, the more advanced stage patients in, the poorer prognosis they would have (HR, 2.085, 4.988, and 13.953, respectively; $P < 0.001$, Table 4).

Table 4

Factors influencing survival time of breast cancer patients by Cox proportional hazard regression model
(n = 16456)

Variable	B	SE	HR (95%CI)	P
Knowing status of cancer diagnosis				
Did know			1.00	< 0.001
Didn't know	0.340	0.046	1.405(1.285–1.537)	< 0.001
Unclear	1.613	0.110	5.017(4.047–6.220)	< 0.001
Age	0.361	0.017	1.434(1.387–1.484)	< 0.001
Surgery history	-0.435	0.044	0.647(0.594–0.706)	< 0.001
Hospital grade				
Primary grade hospital			1.00	< 0.001
Middle grade hospital	-0.783	0.112	0.457(0.367–0.569)	< 0.001
High grade hospital	-0.737	0.111	0.478(0.385–0.595)	< 0.001
Diagnostic year ^a				
1: before 2006			1.00	< 0.001
2: 2007–2011	-0.220	0.048	0.802(0.730–0.882)	< 0.001
3: 2012–2016	-0.433	0.066	0.649(0.594–0.706)	< 0.001
Clinical Stage				
Stage 0- I			1.00	< 0.001
Stage II	0.735	0.085	2.085(1.766–2.462)	< 0.001
Stage III	1.607	0.091	4.988(4.173–5.962)	< 0.001
Stage IV	2.636	0.090	13.953(11.699–16.642)	< 0.001
Unclassified	1.371	0.080	3.938(3.369–4.603)	< 0.001
<i>HR hazard ratio, CI confidence interval</i>				
^a Diagnostic year 1 means those being diagnosed before 2006, 2 means those being diagnosed from 2007 to 2011, 3 mean those being diagnosed from 2012 to 2016.				

Discussion

According to our long-term follow-up research of a large size sample, disclosure of patients' diagnosis was found to be a protective factor for the longer survival time of patients with breast cancer through

univariate and multivariate analyses. Age, clinical-stage, surgical history and diagnosis year were also associated with patients' survival time.

The disclosure of cancer diagnosis to patients with breast cancer has always been a contentious topic all over the world. Owing to the different cultural backgrounds of different countries, opinions on this topic are varied. There was a survey indicated that in the United Kingdom, almost all patients wanted to be aware of their diagnosis while in Asian culture, physicians and family members may worry more about whether to inform[25]. What's more, there is a change of attitude when the hypothetical diagnosis changed from the initial stage to the terminal stage. The percentage of those who wanted to reveal the diagnosis to patients decrease significantly (from 87.5%-40.5%) [26]. The reasons for physicians and family members hesitating to disclose the real to patients may include psychological impact and pain of treatment needed to undergo, especially the loss of physical integrity. It has been proved that losing a breast by mastectomy could bring about severe mental impairments resulted from body image, female identity, self-worth, social interactions and so on [27].

In this study, we found that the popularization of making patients know the diagnosis is increasing year by year, and the disclosure of patients' diagnosis is an independent protective factor for patients with breast cancer to prolong their survival time. Patients without knowing their real condition may form unrealistic optimism which may lead to an unhealthy lifestyle making their condition worse. In contrast, having a clear perspective of their cancer status will lead to a healthier way of life. Informing patients of their breast cancer as early as possible assists them to have a precise knowledge of themselves. What's more, there are many strategies to help patients cope with their emotional distress such as psychological care and breast reconstruction, which have had some effectiveness already [28, 29].

In male patients' subgroup, diagnosis disclosure was not linked with survival time. Male breast cancer is uncommon, and there were only 93(0.75%) male patients involved in our study. Similarly, there were 2470 (0.98%) men with breast cancer in the USA while 252,710 women with breast cancer in 2017 [30]. Since most data for breast cancer research are from female patients, men tend to be diagnosed with breast cancer at a later age than women since most treatment and diagnostic decisions are made by female patients' data [31]. In addition, breast cancer appeared in female patients more frequently, therefore, male patients may undergo a special perceptual experience. Because of the gender stereotype, male patients knowing their diagnosis were more likely to have a high level of cancer-specific distress and depressive symptoms [32]. More researches may be needed on the psychological state of this particular and rare group.

Our study found that disclosure of cancer status and other factors such as female, younger age, earlier clinical stage, surgical history, and more recent diagnostic year were significantly related to better survival. The more recent diagnostic year predicts a shorter time for cancer to develop and more advanced treatment to receive. In addition, there were more patients being told of their own cancer status in which group was diagnosed currently. Therefore, patients with these conditions may have a better prognosis.

In our study, we use a narrow definition of cancer disclosure, only focusing on informing patients of their cancer diagnosis, but not considering the patient's knowledge of treatment, prognosis, and other relevant information. We didn't obtain detailed information about the treatment that participants were received, which may influence the final result of participants. Because of challenges in data collection and uncertainty, some potential factors such as psychological condition of patients, education level and income were not included. In the following research, patients might be concerned about their own conditions, however, the decision patients' families made at the first time may reflect patients' characteristics to some extent. So we regarded their diagnosis were concealed if they didn't know their own condition when they were enrolled in our study. Despite the above limitations, this retrospective cohort study provides clear evidence to promote the diagnosis disclosure to breast cancer patients through long-term follow-up of a large sample size, which hopefully offer a new direction in clinical practice.

Our study offered consequences that more and more medical staff and patients' families are more and more willing to disclose the truth to patients according to our analysis on diagnostic year, which implies that knowing cancer status predicts a better prognosis and longer survival time than those who don't know. It is positive evidence suggests that disclosing the diagnosis to patients does better to patients' survival with breast cancer. Previous studies showed that most patients were ready to have sufficient knowledge of their diagnosis while the majority of medical staff and families were not [33]. The reason for this phenomenon may be that it is a difficult task of revealing cancer diagnosis to patients, which would make physicians feel uncomfortable and unprepared [34, 35]. With the consent right becomes ever more common, the debate between whether to tell patients their diagnosis would be replaced by how and when to tell. Existing guidelines for breaking bad news based on expert opinion are available [36]. However, some guidelines were found not completely derived from empirical data [37]. Therefore, formal guideline for breaking bad news is necessary to be made. Furthermore, oncological care for patients is also needed to help them keep a positive attitude towards their cancer status and overcome their emotional distress [38].

Conclusions

Based on the long-term follow-up of a large sample, the popularization of disclosure of cancer diagnosis to patients has increased as time go on which may contribute to a longer survival time in patients with breast cancer. Even though it may arouse emotional distress in patients after being told of their cancer status, with more adequate information on their condition and better skills of medical staff to disclose it, patents would benefit from it in the long-term. Our finding provides further evidence to disclose cancer diagnosis to patients. Formal guidelines of medical staff to reveal cancer diagnosis and education for patients' families of psychological care need further complement in clinical practice.

Declarations

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional committee and with the 1964 Helsinki Declaration and its later comparable ethical standards. The study was approved by the Bioethics Committee of Second Military Medical University.

Consent for publication

Written informed consent for publication of their clinical details was obtained from the patient/parent/guardian/ relative of the patient. A copy of the consent form is available for review by the Editor of this journal.

Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Author's contributions

TS and XPL conceived and designed the study. CH, Wen Xi Zhu, YXT, YHB, ZL and XPL collected the data. CH, JFX and TS analyzed the data. The first draft of the manuscript was written by CH. HW, SYX, JZX, LX, RKZ, YJW, JD and YJH commented on designation and modification of the manuscript. All authors read and approved the final manuscript.

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