The impact of indirect notification of cancer diagnosis on postoperative esophageal cancer patients in stage T3: A propensity score matching analysis

Minhao Yu (503071468@qq.com)
Chengdu BOE Hospital https://orcid.org/0000-0003-2536-4196

Research Article

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Abstract

Background: Chinese doctors are required to inform cancer diagnosis to patients' direct relatives rather than patients themselves. Patients may be hidden disease from their family members, and it may cause some serious results. Therefore, we carried out a retrospective study to evaluate whether indirect notification of cancer diagnosis can impact the prognosis of postoperative esophageal cancer patients in stage T3.

Methods: We selected postoperative T3 esophageal cancer patients hospitalized from June 2015 to December 2016 as research subjects, and divided them into a direct-notification group and an indirect-notification group. Several variables are allowed for evaluating 36-month progress-free survival of the two groups. Propensity score matching analysis were used to adjust selection bias.

Results: There were 72 patients enrolled in the study. Sex and indirect notification of cancer diagnosis were significantly predicted poor survival while stage, pathological differentiation, education background and age were not after propensity score matching analysis (P=0.02, 0.02, 0.30, 0.18, 0.07, 0.05, respectively). Cox multivariate regression analysis shows male and indirect notification of cancer diagnosis independentlly predict poor survival of progress-free survival of esophageal cancer at postoperative T3 stage (harzard ratio = 0.264, 95% confidence interval: 0.099-0.703, P=0.01; harzard ratio =2.823, 95% confidence interval: 1.360-5.861, P=0.01, respectively).

Conclusions: Indirect notification of cancer diagnosis is an important negative predictors of postoperative esophageal cancer patients' progress-free survival.

Introduction

Esophageal cancer (EsC) is one of the most fatal malignancies in the world. It is the 4th leading cause of death from cancer and the 6th most common cancer in China in 2014[1], and is likely to hit 4th in mortality and 3rd in incidence with a total of 188044 death and 245651 new cases estimated in 2015[2,3]. The two main subtypes are esophageal squamous cell carcinoma (ESCC) and adenocarcinoma, which account for more than 95% of EsC, and ESCC is the major histology in Asian countries[4]. The risk factors for ESCC include sex, smoking and achalasia[5]. A prevalence study indicated that ESCC is 2–4 fold more common in males than females[6]. It has been reported that current smokers have an increased risk of ESCC, as compared to nonsmokers (odds ratio (OR) = 2.9; 95% confidence interval (CI), 2.1-4.1)[7]. Besides, some studies referred to alcohol found the average weekly alcohol intake exceeded 170g, and the OR was significantly increased in ESCC patients but not in esophageal adenocarcinoma patients[8]. Furthermore, dietary factors can also contribute to EsC.

EsC has a poor prognosis and high mortality rate. Despite development in diagnosis and treatment, the overall five-year survival rate is 15% to 20% worldwide[9], may be because it is often diagnosed during its advanced stages, the main reason being the lack of early clinical symptoms[10]. Besides, some social and

psychological factors are also relevant to the prognosis of patients with EsC, such as cancer concealment. Researches in other disciplines have showed that patients who gain truth telling of cancer diagnosis experience more favorable survival than those who do not. Li et al. compared 10 030 colorectal cancer patients and found that cancer concealment was an independent predictor associated significantly with poor survival[11]. Jiang et al. enrolled 865 non-small cell lung cancer patients and found that cancer-specific and all-cause survival was poorer in the cancer concealment group[12]. In fact, doctors in China can not conceal cancer diagnosis but prefer informing cancer diagnosis to patients' direct relatives rather than patients themselves. It is bescuse that most Chinese people believe hiding the actual situation of patients can reduce patients' psychological burden and protect them to keep a happy life. If a doctor directly tell the truth of cancer diagnosis to a patient, he may be prosecuted by the family members. However, if inform indirectly, patients may be hidden disease from their family members, and it may cause some serious results. Therefore, we carried out a retrospective study to evaluate whether indirect notification of cancer diagnosis can impact the prognosis of postoperative EsC patients in stage T3. As far as we know, there are no study have referred to it.

Materials And Methods

1 Patients

We began to visualize the study on June 2020 and selected postoperative T3 EsC patients who treated in the same medical group at Sichuan Science City Hospital from June 2015 to December 2016 as the research subjects, and divided them into a direct-notification group and an indirect-notification group. The inclusion criteria were who underwent surgical treatment, preoperative neoadjuvant chemotherapy and postoperative chemotherapy, and persisted in regular follow-up. Exclusion criteria were as follows: non-surgical treatment patients, loss to follow-up, patients did not write consent or power of attorney, death because of operation related complication and other non-tumor specific factors. Follow-up deadline was December 2019. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of the Chengdu BOE Hospital (NO.: 2021001), and informed consent for this retrospective analysis was obtained from all patients and their legal guardians for the purpose of publication.

2 Trial design

The grouping criteria via reviewing medical records. Patients would be placed in the direct-notification group if they have written a consent that doctors could not tell the disease to anyone else except for the patients themselves. On the contrary, a patient would be placed in the indirect-notification group if he has appointed a direct relative as bailee and both the patient and relative have signed a power of attorney, and doctors had the right to tell the truth of cancer diagnosis to the bailee rather than the patients. 36-month progress-free survival (PFS) is the major observation target. Social variables, such as sex, age, education background, tumor stage and tumor differentiation, were used to evaluate it.

3 Statistical analysis

SPSS 22.0 (IBM Corp., Armonk, NY, USA) software was used for the statistical analysis. Survival curves were analyzed by Kaplan–Meier method. Continuous data were expressed as the mean ±standard deviation or the median. A t-test was used to compare normally distributed data according to whether the variance was equal or not. The Mann-Whitney U test was used to compare non-normally distributed data sets. Categorical data were expressed as counts and percentages, and comparisons between groups were performed using the chi-square test or the Fisher exact probability method. Indicators with statistically significant results were incorporated into a Cox regression analysis for multivariate analysis of risk factors of PFS. We used propensity score matching (PSM) to adjust selection bias. The difference was statistically significant at $P<0.05$.

Results

1 Patients characteristics

There were 72 patients enrolled in the study, including 55 men and 17 women. The youngest was 45 and the oldest was 77 years old. The sex, age, education background, and location, histopathology, differentiation and stage of tumor between the two groups were not significantly different. The clinical characteristics of the two groups before and after PSM are shown in table 1.

2 PFS and risk variables of esophageal cancer progression

Before PSM analysis, sex, stage and pathological differentiation were significant predictors of poor survival, on 36-month PFS Kaplan-Meier curves, while age, education background and indirect notification of cancer diagnosis were not (Figure 1). After PSM analysis, sex and indirect notification of cancer diagnosis were significantly predicted poor survival, and both of them were independent predictors of PFS of EsC patients at postoperative T3 stage when using cox multivariate regression analysis (Fig 2, Table 2).

Discussion

Locally advanced EsC is associated with poor survival, as a result of several factors such as age, sex, malnutrition, body mass index (BMI), comorbidity, location of tumor, socioeconomic factors, histological type, tumor stage, et al[13]. A review form Vellayappan showed that five-year overall survival (OS) of locally advanced disease was 18.4%[14]. Even though the treatment technique of locally advanced EsC have improved a lot, inclouding adjuvant and neoadjuvant treatment, minimally invasive esophagectomy (MIE), and three-field lymph node dissection (3FLD), it is hard to say we won the game. Therefore, we should transfer our attentions to other directions.

Some researchers believe successful cancer treatment relies on effective communication, informed decision making, treatment adherence, and the use of effective coping strategies[15]. It means having

enough communication with patients plays an important role in the treatment of EsC and whether implementing it may fluctuate patients' treatment compliance. However, in some cultures, it is general to hide the actual situation of patients to reduce their psychological burden and to protect them to keep a happy life[11,16]. So, most family members in China require doctors not to tell the truth of cancer to patients, but to them instead. In this situation, the family members may select or not to transmit the cancer diagnosis to patients, and doctors do not know whether the patient have cleared about his disease. Therefore, we carried out the study to assess whether informing cancer diagnosis indirectly can influence the survival of postoperative EsC patients.

The results from us showed that the PFS in the indirect-notification group was shorter than the direct-notification group, and indirect notification was an independent risk factor associating with poor survival (Fig 2, table 2). It means patients in the indirect-notification group have higher risk on tumor progression than those in the direct-notification group 36-month after surgery, and indicates that notifying cancer diagnosis indirectly does harm to patients' 36-month PFS independently. The reason may be that the patients could be hidden the truth from their family members, because of worrying about increasing patients' psychological burden. However, if patients do not clear about their conditions, they may not follow doctors' advices well, which may cause adverse result. Besides, there is no evidence that cancer concealment significantly increase patients' psychological stress, even so, it can be remitted via psychotherapy and communication. A study showed communication with patients with serious and life-threatening illness, including tumor, had no increased depression, anxiety and hopelessness for them[17]. Otherwise, some patients prefer to obtain information about the disease and its treatment because they want to receive psychological support from other patients or staff, learn more about other patients' experiences, learn how to manage daily problems, and provide support to other patients[18]. Moreover, some scholars believe that patients' positive poor-prognosis disclosure preference was associated with patients' better quality of life and caregivers' reduced perceived stress levels[19]. Therefore, notifying cancer diagnosis directly is indispensable and contributes to a longer survival for postoperative T3 stage EsC.

Our study also manifested that tumor stage were not independent predictors of PFS of EsC patients at postoperative T3 stage, which was opposite to the find of Cao et al.[20] that larger tumor size, advanced grade, depth of invasion and increased number of metastasized lymph nodes were independent prognostic factors of EsC. This is because the cases are limited and its representation is weak. Besides, even if we used PSM to adjust selection bias, this is a retrospective study and the clinical persuasiveness is feeble. Therefore, a long-term research and more cases can be involved to evaluate the relation between cancer notification and overall survival for future prospective research.

Conclusions

Indirect notification of cancer diagnosis is an important negative predictors of postoperative EsC patients' PFS. We should persist the principle that it is patients themselves have the right to know cancer

diagnosis, and the patients have the right to decide who can be informed, not the other way around.

Declarations

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Data availability statement: The data that support the findings of this study are openly available in *Harvard Dataverse* at https://doi.org/10.7910/DVN/LNDOMK.

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Abbreviations

EsC: esophageal cancer

ESCC: esophageal squamous cell carcinoma

OR: odds ratio

CI: confidence interval

PFS: progress-free survival

PSM: propensity score matching

BMI: body mass index

OS: overall survival

MIE: minimally invasive esophagectomy

3FLD: three-field lymph node dissection

Tables

Table 1

Clinical characteristics of the 72 patients enrolled in the study pre- and post-PSM

Items	Pre-PSM				Post-PSM		
	Cancer awareness	Cancer concealment	P value		Cancer awareness	Cancer concealment	P value
Sex			0.587				0.488
Male	25	30			18	15	
Female	6	11			4	7	
Age (year)	63.57 ± 8.093	65.71 ± 7.696	0.257		64.59 ± 7.738	66.32 ± 7.200	0.448
Education background			0.305				1.000
Under middle school	18	31			17	16	
Above middle school	12	11			5	6	
Location of tumor			0.455				0.547
Upper thoracic	2	6			1	1	
Middle thoracic	18	27			15	17	
Lower thoracic	4	2			2	0	
Cardia	6	7			4	4	
Histopathology			0.662				0.835
Squamous	24	33			18	19	
Adenocarcinoma	5	4			2	2	
Others	2	4			2	1	
Pathological differentiation			0.926				0.479
Poorly	11	15			8	8	
Moderately	13	17			8	11	
Well	6	10			6	3	

Abbreviations: PSM, propensity scores matching.

Items	Pre-PSM				Post-PSM		
	Cancer awareness	Cancer concealment	P value		Cancer awareness	Cancer concealment	P value
TNM stage			0.841				0.729
IIA	9	10			5	6	
IIB	8	12			5	3	
IIIB	13	20			12	13	
Abbreviations: PSM, propensity scores matching.							

Table 2

Multivariate analysis on risk variables of patients in postoperative stage T3 esophageal cancer progression pre- and post-PSM

	Pre-PSM			Post-PSM	
	HR (95% CI)	P value		HR (95% CI)	P value
Cancer concealment (Yes vs. No)	1.993 (1.117–3.556)	0.020		2.823 (1.360–5.861)	0.005
Sex (Female vs. Male)	0.490 (0.233–1.034)	0.061		0.264 (0.099–0.703)	0.008
Stage (IIIB vs. IIA + IIB)	1.829 (1.027–3.258)	0.040			
Pathological differentiation (moderately + well vs. poorly)	0.457 (0.259–0.805)	0.007			
Abbreviations: HR, harzard ratio; CI, confidence interval. PSM, propensity scores matching.					

Figures

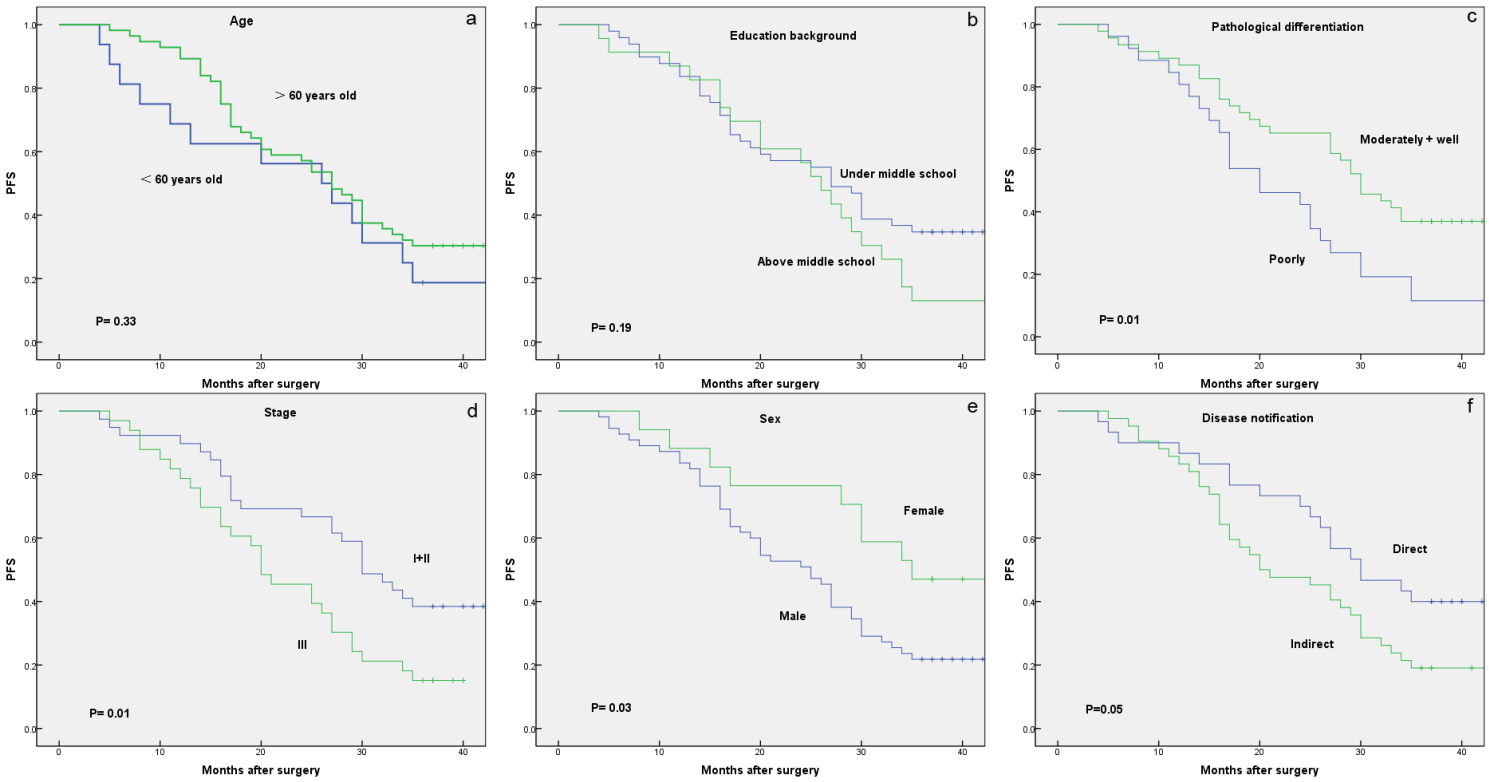

Figure 1

Progress-free survival of age (a), education background (b), pathological differentiation (c), stage (d), sex (e) and (f) pre-PSM.

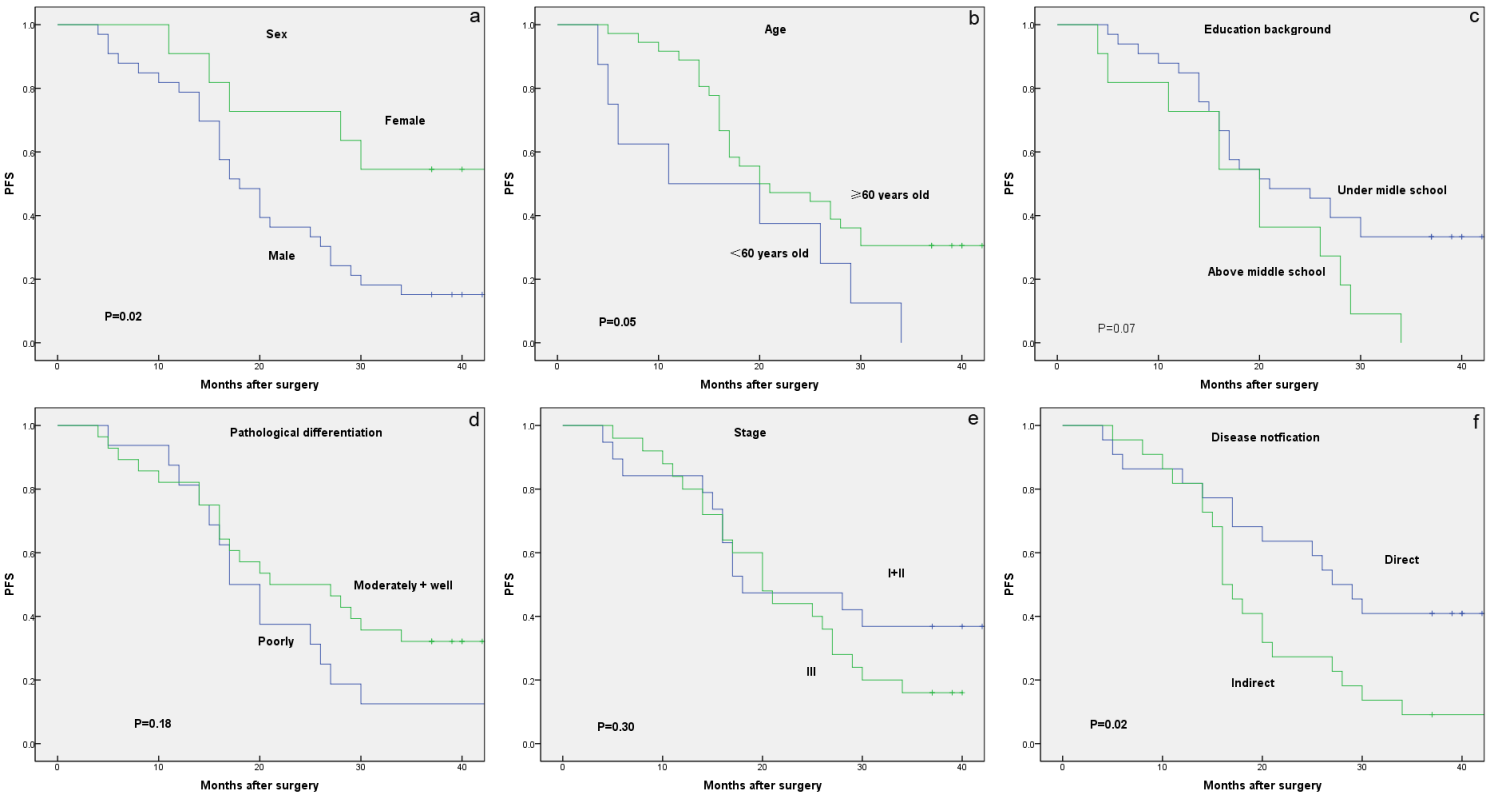

Figure 2

Progress-free survival of sex (a), age (b), education background (c), pathological differentiation (d), stage (e) and disease notification (f) post-PSM.