RESEARCH COMMUNICATION

Prevalence and Characteristics of Anemia in Patients with Solid Cancers at Diagnosis in Southwest China

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Abstract

Purpose: Cancer-related anemia is common and may have myriad causes, but the physiological consequences of a low hemoglobin level are similar. Besides chemotherapy-induced anemia, it is also important to understand the anemia in treatment-naïve patients, which may represent a consequence of cancer itself and/or cancer complications, and this may help assess anemia risk and facilitate appropriate treatment. The purpose of this study was to analyze the prevalence and characteristics of anemia in solid cancer patients at diagnosis in a Chinese population. Methods: 1133 patients with newly diagnosed cancers who were admitted to West China Hospital of Sichuan University during January 2010 to May 2011 met the inclusion criteria. Data on age, gender, change of food intake, the diagnosis and the stage of the tumor, bleeding history, the locations of metastasis, and blood cell analysis were searched and analyzed. Results: Prevalence of anemia at diagnosis of cancers was 18.98% in unclassified cancers. Gastric cancers, colorectal cancers, and hepatopancreatobiliary cancers occupied the first three ranks in the cohort. Age, decreased food intake, and bleeding history were identified as independent risk factors for anemia occurrence. Furthermore, decreased food intake was found to be also associated with the severity of anemia. Conclusion: Our analysis described the prevalence and risk factors of anemia in new diagnosed solid cancer patients in China. To deal with cancer-related anemia, we suggest that it should be important to improve food intake and nutrition, while controlling bleeding, especially in elderly patients.

Keywords: Cancer-related anemia - decreased food intake - bleeding - elderly - China

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Introduction

Anemia is common in cancer patients, and may have myriad causes, including myelotoxicity from antineoplastic drugs, cytokine-mediated inhibition of erythropoiesis, bleeding, renal injury, nutrient deficiency, and so on (Steensma, 2008; Spivak et al., 2009). Cancer-related anemia is defined as a consequence of tumor itself or its therapy (Abdel-Razeq, 2004). Accumulating data has indicated that anemia has the negative impact on the cancer patients such as impaired organ function, reduced quality of life, aggressive tumor behavior, lower sensitivity to chemotherapy, even shorter survival (Blohmer et al., 2005; Bohlius et al., 2006; Spivak et al., 2009). Thus, the treatment for cancer-related anemia attracted attention of clinicians and researchers. Chemotherapy is one of the most important causes of anemia in cancer patients. Recently, the treatment of chemotherapy-induced anemia has been considered important in the management of patients with cancers, especially the erythropoiesis stimulating agents (ESAs), which were verified to improve erythropoiesis and reduce transfusion needs in anemic cancer patients receiving chemotherapy (Corwin et al., 2002; Spivak et al., 2009). Actually, it is also very important to understand the anemia in treatment-naïve patients, which may represent the consequence of cancer themselves and/or cancer complications, and may help assess anemia risks and treat anemia in the following treatment. However, limited data described the anemic status in cancer patients at diagnosis, and the data in Chinese patients is absent. Here, we reported the prevalence and characteristics of anemia in solid cancer patients at diagnosis in southwest China.

Materials and Methods

Study Population

Data on patients with cancers who admitted in West China Hospital of Sichuan University during January 2010 to May 2011 were searched. Inclusion criteria were: male or female aged 18 years or over; histologic or cytologic confirmation of malignant tumors; the cancers were firstly diagnosed with no prior antitumor therapy; had complete data of medical history and examinations. Patients were excluded for the following reasons: a history of diseases of hematological system (including hematological

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malignancies) or bone marrow, or anemia of all causes, or chronic renal diseases; those received blood transfusion, ESAs, or iron supplementation < 3 months before the cancer diagnosis.

Data Collection

Data on age, gender, the change of food intake, the diagnosis and stage of the tumor (clinic stage and TNM stage), bleeding history (including hemoptysis, haematemesis, hematochezia, epistaxis, hematuria, etc.), the locations of metastasis, and blood cell analysis were searched. Metastasis in liver or bone was identified by computed tomography (CT) and whole-body bone scan. Anemia and its grades were regarded according to National Cancer Institute (NCI) anemia scale from Common Terminology Criteria for Adverse Events (CTCAE) Version 3.0. Anemia was defined as hemoglobin (HB) concentration < 120 g/L for male and < 110 g/L for female. The grades of anemia were divided into grade 1 to 4: 100 g/L ≤ HB < lower limit of normal (LLN) was considered as degree 1, 80 g/L ≤ HB < 100 g/L as degree 2, 65 g/L ≤ HB < 80 g/L as degree 3, and HB < 65 g/L as degree 4.

Statistics Analysis

Chi-square statistics were used to examine differences in anemia occurrence between dichotomous variables as mentioned above. It was considered statistically significant when the p-value was less than 0.05. As the quote above says, gender, age, diet, stage, bleeding, bone and liver metastasis were analyzed separately. Stratified analysis was added to explain some factor we suspect to be confounding factors. Binary logistic regression analysis was used to determine whether any of these variables were jointly associated with being "positive" or "negative" for prevalence of anemia or severity of anemia. SPSS statistics 13.0 was the tool software.

Results

The Prevalence Rate of Anemia

Totally 1242 cancer inpatients, who were firstly diagnosed at West China Hospital of Sichuan University during January 2010 to May 2011, were searched. And finally 1133 patients with complete data met the inclusion criteria and were enrolled for analysis. The types of cancer included lung cancers (235 cases), colorectal carcinomas (147 cases), hepatopancreatobiliary cancers (136 cases), gastric cancers (121 cases), esophageal carcinomas (109 cases), head and neck carcinomas (94 cases), breast cancer (93 cases), urological malignancies (84 cases) and others (114 cases), as Figure 1 showed. Anemia was diagnosed in 215 of the 1133 patients (18.98%) and mean concentration (± SD) of HB was 135.34 g/L ± 13.56 g/L in 918 non-anemic patients while that was 98.02 g/L ± 16.18 g/L in 215 anemic patients. Majority of anemia (68.64%) was normocytic anemia, and others were microcytic anemia (13.02%), microcytic hypochromic anemia (11.63%), normocytic hypochromic anemia (4.65%) and macrocytic anemia (1.86%). The prevalence rate of anemia varied in those carcinomas: gastric cancer 38.02%, colorectal cancer 23.13%, hepatopancreatobiliary cancers 22.06%, urological malignancies 21.43%, lung cancers 19.15%, and so on, as shown in Figure 2.

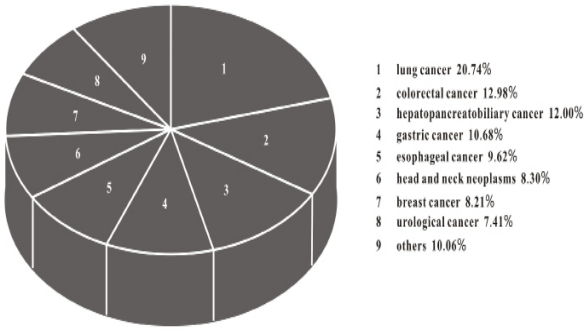

Figure 1. The Types of Cancers Involved

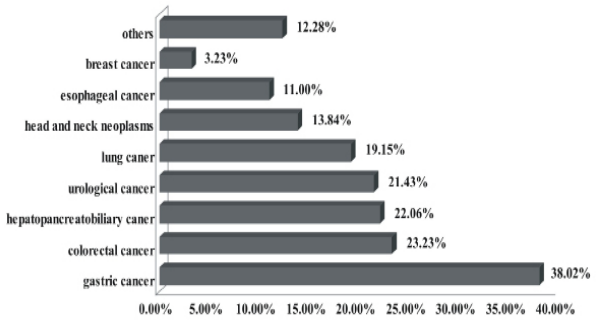

Figure 2. Prevalence of Anemia in Different Type of Cancers

Risk Factors for Anemia Occurrence

To analyze the possible risk factors for anemia, the patients were divided into anemia group and non-anemia group according to NCI anemia scale as described above. We found the patients aged 65 years or older got more probabilities for anemia than those aged below 65, and the prevalence rate was 29.08% and 14.70% respectively (P < 0.01, OR = 2.38, 95%CI 1.75-3.23). The decreased

Table 1. Relationships Between Prevalence of Anemia and Factors

	Anemia	No-anemia	χ^2	P-value
Gender				
Male	142(19.11%)	601(80.89%)		
Female	73(18.71%)	317(81.29%)	0.026	0.936
Age				
<65	117(14.70%)	679(85.30%)		
≥65	98(29.08%)	239(70.92%)	31.85	0.000
Diet				
Normal	130(15.66%)	700(84.34%)		
Less	85(28.05%)	218(71.95%)	22.163	0.000
Metastasis				
No	158(17.79%)	730(82.21%)		
Yes	57(23.27%)	188(76.73%)	3.74	0.065
Bleeding				
No	141(16.59%)	709(83.41%)		
Yes	74(26.15%)	209(73.85%)	12.621	0.001
Bone metastasis				
No	202(18.83%)	871(81.17%)		
Yes	13(21.67%)	47 (78.33%)	0.298	0.611
Liver metastasis				
No	198(18.64%)	864(81.36%)		
Yes	17(23.94%)	54 (76.06%)	1.216	0.275

Table 2. Relationships Between Severity of Anemia and Factors

	Grade 1	Grade 2	Grade 3-4	χ^2	P-value
Gender					
Male	87(61.27%)	38(26.76%)	17(11.97%)		
Female	29(39.73%)	30(41.09%)	14(19.18%)	9.02	0.011
Age					
<65	60(51.28%)	36(30.77%)	21(17.95%)		
≥65	56(57.14%)	32(32.65%)	10(10.20%)	2.62	0.270
Diet					
Normal	74(56.92%)	44(33.85%)	12(9.23%)		
Less	42(49.41%)	24(28.24%)	19(22.35%)	7.19	0.028
Metastasis					
No	93(58.86%)	45(28.48%)	20(12.66%)		
Yes	23(40.35%)	23(40.35%)	11(19.30%)	5.81	0.055
Bleeding					
No	79(56.03%)	46(32.62%)	16(11.35%)		
Yes	37(50.00%)	22(29.73%)	15(20.27%)	3.14	0.209
Bone metastasis					
No	105(51.98%)	66(32.67%)	31(15.35%)		
Yes	11(84.62%)	2(15.38%)	0(0%)	5.56	0.062
Liver metastasis					
No	113(57.07%)	57(28.79%)	28(14.14%)		
Yes	3(17.65%)	11(64.71%)	3(17.65%)	11.03	0.004

Grade 1, 100 g/L ≤ HB < LLN; Grade 2, 80 g/L ≤ HB < 100 g/L; Grade 3-4, HB < 80 g/L

food intake complained by the patients was found to be correlated with higher anemia incidence, compared with the normal food intake patients (28.05% vs. 15.66%, P < 0.01, OR = 2.10, 95%CI 1.54-2.87). The patients with bleeding history were also found to have a higher anemia incidence than those without bleeding history (26.15% vs. 16.59%, P < 0.01, OR = 1.78, 95%CI 1.29-2.45). No statistically significant differences were found in gender, stage of cancers, bone metastasis or liver metastases between anemia group and non-anemia group, as presented in Table 1. All the three risk factors (age, food intake, and bleeding history) were identified as independent risk factors by stepwise logistic regression analysis.

Risk Factors Associated With the Severity of Anemia

To analyze the risk factors associated with the severity of anemia, the anemia patients were divided into 3 groups (grade 1, grade 2, and grade 3-4 according to the NCI anemia scale). The decreased food intake was found to be also associated with the severity of anemia. Furthermore, female patients or patients with liver metastasis suffered more severe anemia. There were no significant differences were found in age, stage of cancers, bleeding history or bone metastasis among the groups of different grades of anemia (Table 2).

Discussion

It is important to deal with cancer-related anemia during the treatment of cancers. Although cancer causes anemia in a variety of ways, the physiological consequences of a low hemoglobin level are similar (Steensma, 2008). Thus, it is also important to pay attention to the anemia caused by cancers or their complications, besides the chemotherapy-induced anemia. For this purpose, 1133 treatment-naïve, newly diagnosed, solid cancer patients in our hospital were included for this analysis. Overall, prevalence of anemia at diagnosis of cancers was 18.98% in unclassified cancers, and gastric cancers (38.02%, 46/121), colorectal cancers (23.13%, 34/147), and hepatopancreatobiliary cancers (22.06%, 30/136) occupied the first three ranks in the cohort. In a survey containing 15367 cancer cases in Europe, 39.7% of 1145 non-treatment cancers were observed to anemia occurrence, and gastrointestinal/colorectal cancers were the first common diseases of anemia occurrence in non-hematological malignancies, which was accordant with our results (Ludwig et al., 2004). However, in the European survey, a higher anemia percentage (43%) of patients with untreated gastrointestinal/colorectal cancer was observed, possibly because a longer survey period (6-month) was adopted and the percentage was defined as being anemic at least once during the survey (Ludwig et al., 2004). Otherwise, our data was collected only at diagnosis of cancers.

Our study indicated three factors were associated with the occurrence of anemia, those were age, food intake and bleeding history. The patients over or equal to 65 had a 2.38 times higher risk to develop anemia, compared with those below 65. When grouping patients at 60 or 70 years of age respectively, a higher risk of anemia was also observed in elder patients (data not shown). Generally, in common population, the prevalence of anemia increases with age, anemia prevalence rates rose rapidly after age 50 years, and 11.0% of men and 10.2% of women 65 years and older were anemic (Guralnik et al., 2004; Spivak, 2005). The most common causes of anemia in the elderly are chronic disease and iron deficiency. Also, vitamin B12 deficiency, folate deficiency, gastrointestinal bleeding and myelodysplastic syndrome are among other causes of anemia in the elderly (Smith, 2000). For these reasons, the treatment of cancer-related anemia in elderly become more complex, and should be more active and concerned about. In our analysis, decreased food intake was also found to be related with anemia occurrence. Cancers may lead to decreased food intake by varieties of mechanisms, such as anorexia, maldigestion,nausea, fatigue, pain, obstruction in the digestive tract, diarrhea or constipation, and so on, which eventually lead to poor nutrition absorption and malnutrition. This may be one of mechanisms for developing cancer-related anemia. It is logical that the patients with bleeding history have a higher risk for anemia occurrence and this was also confirmed in our reports. Besides more disorder of digestive function, unperceived and long period bleeding was common in carcinomas of digestive tract, those might be an interpretation for a higher anemia incidence in gastrointestinal/colorectal cancer. In our analysis, age, decreased food intake, and bleeding were independent risk factors for anemia in cancer patients at diagnosis. Thus, to deal with cancer-related anemia, we suggested that it is important to improve food intake and nutrition, control bleeding, especially in elderly patients. However, in this analysis, decreased food intake and chronic bleeding were events for a long time period and it was hard to be quantified accurately in patient history,

which may discount the credit of the analysis, further perspective studies are needed to provide detailed data.

Among the 215 anemic patients, we tried to find the possible correlations factors for severity of anemia. We found gender is not a risk factor for anemia occurrence but severe anemia was more common in women patients. The reasons remained unclear because a small sample of the anemic women patients was included in our study. Another factor associated with the severity of anemia was decreased food intake, that is to say, in our study, not only anemia occurrence but also severity of anemia was found to be affected by the decreased food intake. Thus, nutrition deficiency may play a critical role in developing anemia in cancer patients. Since the treatment modalities, such as chemotherapy and radiotherapy, can cause further disorder of digestive function, which may aggravate the nutrition deficiency, hence our study suggested that improving food intake and nutrition should be more concerned in dealing with cancer-related anemia, especially during and after the antitumor treatment. Additionally, we found that the liver metastasis was related with heavier anemia, the reasons and clinical significance were uncertain since the sample of liver metastasis was small in our study, and further observations are needed to confirm.

Some studies have already demonstrated the prevalence of cancer-related anemia in western population (Knight et al., 2004; Ludwig et al., 2004), however, there may have differences between eastern and western peoples because of cancer spectrum, the stages at diagnosis, food habits, nutritional status, and so on. Our study analyzed the prevalence of anemia in solid cancer patients at diagnosis in Chinese population, which represented the consequence of cancers themselves or their complications in treatment naïve patients. We believe it is clinically significant to cancer treatment in eastern population.

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