International Journal of Surgery 53 (2018) 304–311

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.elsevier.com/locate/ijsu

Review

# The pretreatment thrombocytosis as one of prognostic factors for gastric cancer: A systematic review and meta-analysis

Yong-Hong Wang[a,b], Jin-Ke Kang[a,*], Yong-Fa Zhi[a], Yi Zhang[a], Zhi-Qiang Wang[a], Qing Zhou[a], Wen-Yu Niu[a], Ming-Jie Ma[a]

[a] Department of Gastrointestinal Surgery, Qinghai Red Cross Hospital, Xi'ning 810000, China
[b] The First Clinical Medical College of Lanzhou University, Lanzhou 730000, China

ARTICLE INFO

*Keywords:*
Thrombocytosis
Prognosis
Gastric cancer
Meta-analysis

ABSTRACT

*Background & aims:* At present, increasing reports have shown that pretreatment platelet count was associated with the prognosis of many types of cancer. We performed rounded analysis to comprehensively analyze and evaluate the prognostic significance of pretreatment thrombocytosis for patients with gastric cancer.

*Methods:* We identified relevant studies by searching database including PubMed, Embase, Cochrane Library and Web of Science. The relative risk (RR) with its 95% confidence interval (CI) was used to assess the correlation between thrombocytosis and overall survival (OS) of gastric cancer patients. We also conducted subgroup analysis and sensitivity analysis for the prognostic effect of thrombocytosis on OS. The analysis was performed and assessed using Review Manager 5.2.

*Results:* A total of nine studies including 7158 participants were included in this systematic review. Analysis results showed that pretreatment thrombocytosis had a close relationship with 1, 3 and 5 years survival of gastric cancer, with the pooled RRs being 0.80 (95% CI 0.71–0.90; $P = 0.0004$), 0.65 (95% CI 0.45–0.92; $P = 0.02$) and 0.64 (95% CI 0.47–0.87; $P = 0.004$) respectively.

*Conclusions:* The present rounded analysis suggests that pretreatment thrombocytosis may have significant association with poor survival of patients with gastric cancer.

## 1. Introduction

Gastric cancer, as one of the increasingly common malignancies, is raging throughout many countries at present. It was estimated that gastric cancer is the fifth most frequently diagnosed cancer and the third leading cause of death from cancer worldwide [1]. Gastric cancer is often diagnosed at an advanced stage and surgical resection is the optimal option at present. However, the survival of gastric cancer after operation is not satisfied and at least approximately 50% patients receiving curative resection die within 5 years of diagnosis [2]. At present, one of the most useful indicators for predicting prognosis of tumors is clinical stage after operation. However, clinical stage could be identified accurately after operation and depend on the diagnosis of pathologist and the integrity of specimens, which may lead to some bias. Up to now, none of prognostic biomarkers prior to operation is found.

Recently, the association between inflammation and malignant tumor has been explored extensively in many studies [3–5]. Many studies have shown that inflammatory response, including neutrophil lymphocyte ratio and platelet lymphocyte ratio, are associated with a poor prognosis in patients with various types of cancer [6–9]. It is universally acknowledged that lymphopenia serves as a surrogate of impaired cell-mediated immunity, meanwhile neutrophilia acts as a response to systemic inflammation. Thus, the neutrophil lymphocyte ratio, which is calculated as the neutrophilia count divided by the lymphocyte count, has been suggested as a marker of the immune response to systemic inflammation in patients with various malignancies [7,9,10].

In addition, the platelet count was also explored expecting the same prognostic role like neutrophil lymphocyte ratio and platelet lymphocyte ratio. Many studies have reported that elevated platelet counts or pretreatment thrombocytosis may be associated with the poor prognosis of colorectal cancer [11–14]. Therefore, we designed a meta-analysis based on relevant studies to comprehensively analyze and evaluate the prognostic role of pretreatment thrombocytosis in patients with gastric cancer. Besides, to identify whether the incidence of thrombocytosis in gastric cancer was influenced by many clinicopathologic characteristics, we also analyzed the association between

* Corresponding author. Department of Gastrointestinal Surgery, Qinghai Red Cross Hospital, No. 55, South Street, Cheng Zhong District, Xi'ning 810000, Qinghai, China.
*E-mail address:* wandx1026@126.com (J.-K. Kang).

https://doi.org/10.1016/j.ijsu.2018.03.084
Received 14 March 2018; Accepted 31 March 2018
Available online 11 April 2018

incidence of thrombocytosis and 12 clinicopathologic characteristics including 36 comparing subgroups of gastric cancer patients.

## 2. Methods and materials

### 2.1. Including and excluding criteria

#### 2.1.1. Including criteria

(1) Prospective and observational retrospective studies; (2) The patients included in studies were pathologically diagnosed with gastric cancer; (3) Circulating platelet counts of patients prior to receiving therapies were reported; (4) Prognostic indicators such as overall survival and response rate after treatment could be obtained; (5) The number of participants in both control and experimental groups was reported; (6) The cut-off value of thrombocytosis was reported or can be obtained.

#### 2.1.2. Excluding criteria

(1) Non-human researches or trials on animals; (2) Articles belong to abstracts, letters, editorials, expert opinions, reviews, case reports or laboratory studies; (3) Patients having other primary tumors or severe disease which may affect their survival; (4) Studies without sufficient data for analysis; (5) The cut-off value of thrombocytosis was not given or did not meet our criteria; (6) Duplicate articles were excluded.

### 2.2. Search strategy

We identified relevant studies by searching database including PubMed, Embase, Cochrane Library and Web of Science to February 2018. Our searching terms and procedures were as follows: (1) “platelet count” OR “thrombocytosis”; (2) “gastric cancer” OR “stomach cancer” OR “gastric carcinoma” OR “stomach carcinoma” OR “gastric neoplasm”; (3) “prognosis” OR “survival” OR “outcome”. The retrieval formula was as follows: (1) AND (2) AND (3). The databases above were searched with these terms and retrieval formula in English. Two investigators who received normative and unitive training beforehand independently screened the titles and abstracts of each study after duplicate references were excluded. Once potential studies which may meet our including criteria were found, their full texts were obtained for further evaluation.

### 2.3. Quality assessment and data extraction

Two assessors receiving normative training beforehand independently evaluated the quality of all the included studies using the 9-star Newcastle-Ottawa Scale (NOS) [15]. The total NOS scores of each study were displayed in the characteristics table (Table 1). The scores were judged according to the three aspects of NOS of evaluation: selection, comparability, and outcome between the case group and control group. A study with a NOS score $\geq 6$ is considered experiencing good quality. In addition, in order to observe the bias of our included studies better, the risk of bias for each studies and the risk of bias across all studies were evaluated and shown with figures generated by RevMan 5.2 software [16].

Two same reviewers above extracted the data for analysis based on their intensive reading of included articles, and disagreement was resolved by their discussion. In addition, the other contents included study published year, sample size, country, trial design type, incidence of thrombocytosis, primary outcome, follow-up time, cut-off value, age (median and range) and treatment were also extracted using a standardized form (Table 1). Data collected were input into RevMan 5.2 software for analysis [16].

### 2.4. Statistical analysis

In this meta-analysis, the overall survival of gastric cancer patients

**Table 1**
The characteristics of included studies for meta-analysis of the association between thrombocytosis and prognosis of gastric cancer.

| Study (author and year) | Country | Study design | Participants | Age (median and range) | Incidence of thrombocytosis | Cut-off value | Treatment | Follow-up time (month) | NOS score | Primary outcome |
|---|---|---|---|---|---|---|---|---|---|---|
| Hu C et al., 2014 | China | Retro | 1763 | 66 (34–88) | 4% | $400 \times 10^9$/L | Operation | Per 4 week | 8 | OS, RFS |
| Hu C et al., 2014[a] | China | Retro | 1763 | 66 (34–88) | 12.1% | $300 \times 10^9$/L | Operation | Per 4 week | 8 | OS, RFS |
| Hwang SG et al., 2012 | Korea | Pro | 1593 | | 6.4% | $400 \times 10^9$/L | Operation | 104.7 (1.8–194.6) | 7 | OS, RFS |
| Ikeda M et al., 2002 | Japan | Retro | 369 | 63.5 (27–87) | 11.4% | $400 \times 10^9$/L | Oper, Chemo | NR | 6 | OS |
| Ikeda M et al., 2002[a] | Japan | Retro | 369 | 63.5 (27–87) | 18.2% | $340 \times 10^9$/L | Oper, Chemo | NR | 6 | OS |
| Ishizuka M et al., 2014 | Japan | Retro | 544 | 67 | NR | $300 \times 10^9$/L | Operation | 1443 (10–4428) | 7 | OS |
| Li FX et al., 2014 | China | Pro | 1596 | 60 (25–89) | 7.5% | $400 \times 10^9$/L | Oper, Chemo | 3M, until death | 8 | OS |
| Qiu MZ et al., 2010 | China | Retro | 616 | NR | 7.1% | $400 \times 10^9$/L | NR | 31 (3–115) | 6 | OS |
| Shoda K et al., 2015 | Japan | Retro | 306 | NR | NR | $250.9 \times 10^9$/L | Operation | NR | 4 | OS |
| Wang J et al., 2017 | China | Retro | 273 | 57 | NR | $326.5 \times 10^9$/L | Chemotherapy | NR | 7 | RR, OS |
| Wang L et al., 2012 | China | Retro | 98 | 52 (32–73) | 21% | $400 \times 10^9$/L | Operation | At least 5 years | 7 | OS |

[a] They were from the same study above them; NOS, Newcastle-Ottawa Scale; OS, overall survival; RR, response rate; RFS, recurrence free survival; Retro, retrospective; Pro, prospective; Oper, operation; Chemo, chemotherapy; NR, not report.