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Review

Vimentin immunohistochemical expression as a prognostic factor in gastric cancer: A meta-analysis

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ABSTRACT

Objective: The prognostic value of vimentin expression in Gastric Cancer (GC) has been assessed for years while the results are still in dispute. Thus, we performed a meta-analysis to determine the effect of vimentin immunohistochemical (IHC) expression on the prognosis of GC.

Methods: Literature searches were performed in PubMed and Embase. The meta-analysis examined the association of vimentin IHC expression with prognosis and clinicopathological characteristics of GC patients.

Results: In total, ten studies involving 1598 cases were enrolled in this meta-analysis. Vimentin positive expression was significantly correlated with poor overall survival (OS) in GC patients (HR = 2.05, 95% CI: 1.29–3.24) but there was a significant degree of heterogeneity (I^2 = 77%, P = 0.0006). Subgroup analysis indicated that vimentin expression had an unfavorable impact on OS in Chinese patients (HR = 2.43, 95% CI: 1.30–4.55). Moreover, vimentin positive expression rates was significantly associated with age, tumor location, TNM stage and lymph node metastasis. However, vimentin positive expression rates did not correlate with gender, grade of differentiation, vascular invasion, the depth of invasion, hepatic metastasis or peritoneal metastasis.

Conclusions: Positive vimentin expression could serve as a poor prognostic marker in GC.

1. Introduction

Although the incidence of gastric cancer(GC)is decreasing, it still remains the fifth most common cancer and the third leading cause of cancer-related death in the world. [1] Although there has been significant progress in the treatment of GC, the prognosis of patients with gastric cancer is still poor due to the advanced stage of the disease when diagnosed and the treatment options at the advanced stage are limited [2]. As a result, it is important to find a prognostic marker for the potentially curable group of patients.

Epithelial-mesenchymal transition (EMT), a developmental process in which epithelial cells acquire a mesenchymal cell phenotype, may promote tumor development, invasion or metastasis. In the EMT, cells gradually lose the epithelial characteristic of intercellular adhesion, thereby acquiring migratory fibroblastoid properties, and become resistant to apoptosis [3,4]. EMT is associated with downregulation of epithelial markers such as E-cadherin and an abnormal upregulation of mesenchymal markers such as vimentin [5,6]. Vimentin, which is a 57 kDa intermediate filament protein, forms a part of the cytoskeleton and plays a significant role in the transformations in adhesion and motility that occur during the EMT [7]. Generally, vimentin is expressed in mesenchymal cells, such as fibroblasts, chondrocytes, macrophages and endothelial cells, but not in epithelial cells [8]. However, the expression of vimentin has been detected in various carcinomas such as lung cancer, colon cancer, cervical carcinoma and prostatic cancer. And the aberrant expression of vimentin has been linked to a more aggressive status in these tumors [9–12]. Meanwhile, a number of studies have demonstrated that vimentin is also expressed in gastric cancer, and it has been shown to be an predictive factor of prognosis in patients with GC [13–15]. However, the relationship between vimentin expression and clinicopathological features and prognosis remains controversial. So far several studies have demonstrated that vimentin positive expression may be a predictive factor of poor prognosis in patients with GC [16–18]. However, Hou et al. [19] showed that there was no association between vimentin expression and prgnosis of patients with GC. Therefore, we conducted a meta-analysis to investigate the correlation between vimentin expression and prognosis of GC and to consider if vimentin-positive expression could act as a predictive factor

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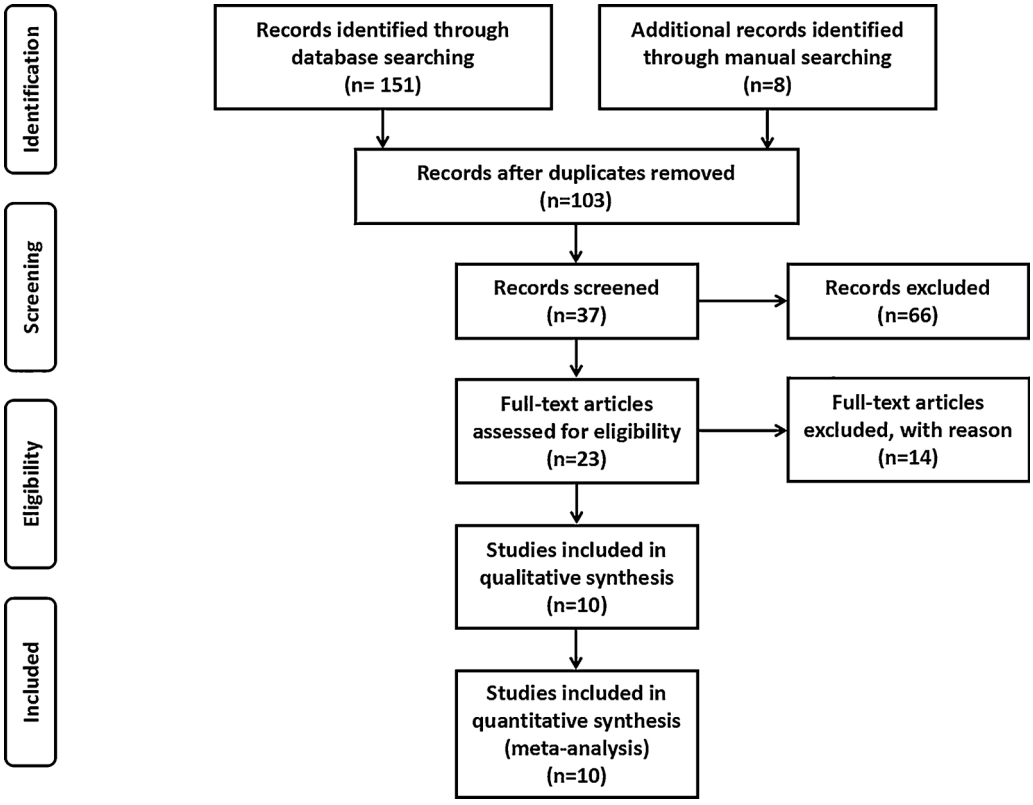

Fig. 1. Flowchart showing selection of studies for inclusion in the meta-analysis. IHC: Immunohistochemistry.

for survival in GC patients.

2. Materials and methods

2.1. Literature search

We searched the PubMed and Embase databases. Key words used were “vimentin”, “Gastric Neoplasms”, “Gastric Cancer”, “Gastric Carcinoma”, “Gastric Tumor”, “Stomach Cancer”, “Stomach Carcinoma”, “prognostic”, “Prognosis” and “survival”. The search ended in February 23, 2017, with no lower date limit. Reference cited in an identified study were also searched manually to triage other appropriate article.

2.2. Inclusion and exclusion criteria

Inclusion criteria included : (1) articles to assess vimentin expression in human GC tissues by IHC; (2) papers to compare vimentin expression with clinicopathological features and prognosis of GC by IHC; (3) articles published in English language; (4) papers with adequate information provided to assess odds ratio (OR), hazard ratio (HR), and their 95% confidence interval (CI).

Excluded criteria included: (1) letters, case reports, reviews, and meetings abstracts without adequate information; (2) studies without sufficient relevant data; (3) experimental specimens as animals or human cells.

2.3. Data extraction and assessment

The data from each eligible study was extracted independently by two investigators (CFF and YS). The main characteristics of articles were listed as follows: (1) first author; (2) Study location; (3) year of publication; (4) gender(male/female); (5) Median age; (6) antibody source; (7) Adequacy of evaluating vimentin expression. The quality of each of the available studies in our analysis was assessed according to the Newcastle–Ottawa quality assessment scale [20].

2.4. Statistical analysis

For the quantitative aggregation of survival outcomes, HRS and their 95% CI were used to assess the relationship between vimentin expression and overall survival. The most accurate method is to obtain the HR estimate and its 95%CI directly from the study, or calculate them through the parameters which is provided in the article: O-E statistic and variance [21]. Otherwise, Kaplan-Meier curves were obtained by Engauge Digitizer version 2.11. Heterogeneity was assessed through the χ2-based Q statistical test or the I^2 statistic. For studies with $p > 0.1$ or $I^2 \leq 50\%$, we considered no heterogeneity in the included studies, and fixed-effects model (the Mantel-Haenszel method) was used. When $p \leq 0.1$ or $I^2 > 50\%$, we chose random-effects model (the DerSimonian and Laird method). For the pooled analysis of the relationship between vimentin expression and clinicopathological features (histologic type, depth of tumor invasion, TNM stage, lymph node metastasis, vascular invasion, hepatic metastasis, peritoneal metastasis), vimentin positive expression rates and their 95% CIs were combined to assess the effect.

Sensitivity analysis was perfomed by continuous omission of individual studies, indicating that eliminating any single study does not significantly influence the pooled HRs. The correlation between vimentin expression and prognosis of GC were conducted by Review Manager 5.3 (RevMan version5.3). The relationship of vimentin positive expression rates with clinicopathological features were performed by the Comprehensive Meta-Analysis software package (Biostat, Englewood, NJ, USA).