Proceedings of the 2nd International Conference on Biological Engineering and Medical Science (ICBioMed 2022), Part II
DOI: 10.54254/2753-8818/4/20220668

Prognostic and Diagnostic Value of Biomarkers in Gastric Cancer

Jingyu Jiang

University of Technology Sydney, Ultimo NSW 2007 Sydney, NSW 2007 Australia

751300540@qq.com

Abstract. The fifth most prevalent cancer in the world is gastric cancer, which is aggressive illness with a low 5-year survival rate. Even though stomach cancer is becoming less frequent, patients still have a poor prognosis. Thus, early discovery using relevant screening methods, selection of an acceptable treatment strategy, and good monitoring are critical to reducing gastric cancer mortality. Biomarker identification based on clinical data and extensive genomic analysis might enhance diagnosis, prognosis, recurrence prediction, and therapy response. These biomarkers can also enable more specialized treatment strategies. This study provided an overview of the present state and methods in gastric cancer biomarkers, which may be applied for accurate treatment approach prediction, early diagnosis, and future perspectives.

Keywords: gastric cancer, biomarkers, HER2, CEA, CA19-9

1. Introduction

Cancer staging is presently recognized as a credible standard prognosticator that does not take into account prognostic factors other than tumor, node, and metastasis (TNM) stage. Nevertheless, because of variances in biochemical and clinical features, survival of gastric cancer at the same stage varies. Hence, the specific prognosis of patients may be better estimated by including additional key prognostic indicators, such as biomarkers. Gastric cancer has more than 1 million cases, and caused over 76,8000 deaths in 2020, which constitutes a major global health issue [1]. Since gastric cancer is frequently discovered in an advanced stage, the prognosis is generally poor. Therefore, any progress made in gastric cancer for diagnosis or prognosis may have global implications [2]. The purpose of this study was to discuss the prognostic and diagnostic value of known biomarkers used in clinical practice by investigating the previous studies.

2. Gastric cancer

The prevalence of gastric cancer exhibits large geographic differences worldwide. South and Central America, Northeast Asia, and Eastern Europe appeared higher prevalence of gastric cancer [3,4]. Especially in Japan and Korea, gastric cancer is the most commonly diagnosed cancer in men, while in China it is the leading cause of cancer-related death [3-6]. Conversely, Gastric cancer is one of the rarest cancers in Australia, Western Europe, North America and sub-Saharan Africa [3,5]. Biological differences between tumors from different countries increased complexity in determining standard therapy based on international researches. Multidisciplinary care is crucial for treatment selection as surgery, systemic chemotherapy, radiotherapy, targeted therapy, and immunotherapy have all been

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proved effective in in gastric adenocarcinoma [2]. For patients with metastatic or locally advanced cancer, systemic therapy can offer remission, improved quality of life, and improved survival [1]. In clinical studies, targeted treatments including trastuzumab, nivolumab, and pembrolizumab have shown promising outcomes in treating patients with locally advanced or metastatic illness [2].

3. Biomarkers

Chemotherapy for resectable gastric cancer has been widely acknowledged and may constitute a peak for routine cytotoxic chemotherapy for localized illness. The classification of stomach cancer based on molecular subtypes opens the door to individualized therapy [2].

Systemic therapy approaches are becoming more and more driven by biomarkers. Some biomarkers enable the identification of populations most likely to benefit from immunotherapy and targeted therapy [2].

Biomarkers have been used in gastric cancer diagnosis, clinical stage determination, treatment response assessment, relapse monitoring following effective treatments. A number of biomarkers for gastric cancer have been identified. However, the most often employed biomarkers in medical practice for gastric cancer are carcinoembryonic antigen (CEA) and CA19-9.

4. HER2

The first biomarker applied in clinical practice for gastric cancer patients is HER2. It is a receptor tyrosine kinase that is attached to the cell membrane surface and is encoded by ERBB2 on chromosome 17. About 17–20% of people with gastric cancer have HER2 oncogene amplification and overexpression, which is more prevalent in intestinal-type gastric cancer and tumors that are situate at the gastroesophageal junction or in the proximal stomach.

Trastuzumab, a HER2-targeted medicine, is the first molecularly targeted medication to be authorized as a standard treatment for gastric cancer. It can prevent dissociation of the extracellular domain of HER2 via inhibiting HER2-mediated signaling. Gastric cancer with HER2 overexpressing has various distinguishing features, including HER2 expression heterogeneity and a lack of reliance on HER2 signaling following trastuzumab therapy. Patients with gastric cancer that overexpresses HER2 benefit from treatment with trastuzumab. Patients who received trastuzumab in addition to cisplatin and fluoropyrimidine revealed a higher median overall survival rate than those who just received chemotherapy. in the randomised controlled ToGA trial [16]. Trastuzumab should be added to chemotherapy for patients with HER2 overexpression gastric cancer, followed by trastuzumab alone as maintenance.

5. CEA

CEA, a glycoprotein that is linked to the surface of enterocytes and has a function in both cell adhesion and programmed cell death. Non-smokers have a normal value of 3 ng/mL, whereas smokers have a value of 5 ng/mL. Since it has an average half-life of three days, the marking can be repeated every seven days. High pre-therapeutic CEA levels are associated with disease stage, with individuals who have peritoneal serous carcinoma in particular [7].

CEA is the most commonly employed marker for digestive tract cancer in clinical practice [7]. For the purpose of predicting liver metastases recurrence, CEA has been identified as an independent risk factor. Raised CEA levels are detected in a fraction of all gastric cancer patients in advanced stages; hence, CEA levels can not be considered as a useful technique of screening. The inclusion of immunohistochemistry CEA testing to standard cytology enhanced sensitivity. RT-PCR analysis of CEA mRNA is beneficial for identifying micrometastasis in the peritoneal cavity [8].

In the peritoneal fluid, elevated CEA levels statistically associate much better than normal cytology with the diagnosis of peritoneal relapse of gastric cancer, according to Xiao's meta-analysis [9]. According to researches [7,10], the association between CEA and locoregional recurrence is statistically significant and acts as a marker for gastric cancer prognosis. In the event of a liver metastatic recurrence, the CEA level may rise around three months before the illness is detected

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radiologically. Normal pre-therapeutic levels of CEA, particularly in patients undergoing perioperative chemotherapy, could be a positive predictive feature associated with improved survival [11]. At least at the peritoneal level, a rise in its level often denotes relapse [12]. For different cancer metastatic locations, it is less sensitive [13].

6. CA19-9

A glycolipid antigen called CA19-9 is involved in cell adhesion, and CA19-9 has been found to be present in colorectal cancer. In addition, it is a ligand for the endothelial cell-surface protein E-selectin [7]. Although it is prevalent in many cancer types, including pancreatic and gastric cancer, CA19-9 has historically been a frequently utilized marker in gastric cancer. The test of CA19-9 is performed on peripheral blood.

When determining the illness stage prior to surgery, evaluating the amount of CA 19-9 in peritoneal fluid appeared to be more accurate [7]. CA 19-9 levels should return to normal within two months after the surgical therapy. Past two months, increased CA19-9 levels indicate a watchful prognosis [12]. The early stage of the disease and the preoperative level are related [11]. CA 19-9 was examined as an evaluation prior to surgery in individuals with gastric cancer. Although it was statistically linked to lymph node involvement, it was less effective than CEA at identifying patients who could undergo surgery [14]. Regular measurement of CA 19-9 blood levels in gastric cancer patients confirms recurrence roughly 2 months prior than the radiological approach [7].

7. Comparison study of CEA and CA19-9

Bagaria looked at these biomarkers in three separate sites: the esophagus, the stomach, and the colon. CEA has a sensitivity of 30% and a negative predictive value (NPV) of 58.82 % in gastric cancer. In colorectal cancer, it has a sensitivity of 74% and an NPV of 79.36 % [15]. CA 19-9 has a greater sensitivity in gastric cancer than CEA, at 42%, with an NPV of 63.29%. In comparison, CA 19-9 is less efficient in colorectal cancer, with a sensitivity for only 26% and an NPV of 57.47% [15]. When cases are evaluated via CEA/CA19-9 combined, the sensitivity rises to 58% [15]. Combined research revealed that diagnostic sensitivity in esophageal and gastric cancer was higher than in colon cancer [15]. In colorectal cancer, CEA tends to be the preferable marker, while CA 19-9 shows to be more responsive in gastric cancer.

8. Conclusion

Although a high level of a tumor marker may suggest malignancy, this finding is insufficient to make a diagnosis. As a result, further procedures, such biopsies, are commonly added to measures of tumor markers. A combination of biomarkers, is of certain sense for enhancing sensitivity and/or specificity in the diagnosis of gastro-intestinal cancer [15]. Biological scientists have published many results about gastric cancer biomarkers, but just traditional biomarkers including HER2, CEA, CA19-9 are still used in clinical practice.

Traditional cancer biomarkers has been well acknowledged in the diagnosis and prediction of relapse in gastric cancer. However, because to the lack of specificity and sensitivity, these biomarkers are unable to identify early gastric cancer. As a result, innovative and trustworthy tumor biomarkers are desperately needed.

Many additional potential genes were discovered during a genome-wide analysis of cancer transcriptomes. It is critical to identify the important roles that might be studied for the creation of biomarkers and leads for improved cancer management. The identification of exact biomarkers associated with GC development can potentially be used in therapy. We expect that this paper will aid in the construction of strong biomarkers for clinical care of patients as well as being useful for the eventual prevention and treatment of GC.

References

[1] Ajani, J.,D., Corvera, C., Das, P., Enzinger, P., Enzler, T., Fanta, P., Farjah, F., Gerdes, H.,

DOI: 10.54254/2753-8818/4/20220668

Gibson, M., Hochwald, S., Hofstetter, W., Ilson, D., Keswani, R., Kim, S., Kleinberg, L., Klempner, S., Lacy, J., Ly, Q., Matkowskyj, K., McNamara, M., Mulcahy, M., Outlaw, D., Park, H., Perry, K., Pimiento, J., Poultsides, G., Reznik, S., Roses, R., Strong, V., Su, S., Wang, H., Wiesner, G., Willett, C., Yakoub, D., Yoon, H., McMillian, N. and Pluchino, L., 2022. Gastric Cancer, Version 2.2022, NCCN Clinical Practice Guidelines in Oncology. Journal of the National Comprehensive Cancer Network, 20(2), pp.167-192.

[2] Joshi, S. and Badgwell, B.(2021). Current treatment and recent progress in gastric cancer. A Cancer Journal for Clinicians.71(3).pp.264-279.

[3] Kim, Y. and Cho, S., 2017. Effectiveness of the Korean National Cancer Screening Program in Reducing Gastric Cancer Mortality. The Korean Journal of Helicobacter and Upper Gastrointestinal Research, 17(2), p.110.

[4] Hamashima, C., Ogoshi,, Okamoto, Shabana, M., Kishimoto, T. and Fukao, A., 2013. A Community-Based, Case-Control Study Evaluating Mortality Reduction from Gastric Cancer by Endoscopic Screening in Japan. Value in Health, 16(7), p.A395.

[5] Bray, Ferlay,Soerjomataram, Siegel, R., Torre, L. and Jemal, A., 2018. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer Journal for Clinicians, 68(6), pp.394-424.

[6] Zhao, J., Wu, M., Kim, C., Jin, Z., Zhou, J., Han, R., Yang, J., Zhang, X., Wang, X., Liu, A., Gu, X., Su, M., Hu, X., Sun, Z., Li, G., Li, L., Mu, L. and Zhang, Z., 2017. Jiangsu Four Cancers Study: a large case–control study of lung, liver, stomach, and esophageal cancers in Jiangsu Province, China. European Journal of Cancer Prevention, 26(4), pp.357-364.

[7] Shimada, H., Noie, T., Ohashi, M., Oba, K. and Takahashi, Y., 2013. Clinical significance of serum tumor markers for gastric cancer: a systematic review of literature by the Task Force of the Japanese Gastric Cancer Association. Gastric Cancer, 17(1), pp.26-33.

[8] Zhang, Y., 2006. Detection of carcinoembryonic antigen mRNA in peritoneal washes from gastric cancer patients and its clinical significance. World Journal of Gastroenterology, 12(9), p.1408.

[9] Li, G., Zhang, Z., Ma, X., Gu, W., Wang, Y. and Li, J., 2011. Are biomarkers correlated with recurrence patterns in patients with resectable gastric adenocarcinoma. Molecular Biology Reports, 39(1), pp.399-405.

[10] Xiao, Y., Zhang, J., He, X., Ji, J. and Wang, G., 2013. Diagnostic values of carcinoembryonic antigen in predicting peritoneal recurrence after curative resection of gastric cancer: a meta-analysis. Irish Journal of Medical Science (1971 -), 183(4), pp.557-564.

[11] Chen, S., 2012. Normal carcinoembryonic antigen indicates benefit from perioperative chemotherapy to gastric carcinoma patients. World Journal of Gastroenterology, 18(29), p.3910.

[12] Nam, D., Lee, Y., Park, J., Lee, H., Shin, S., Lee, S., Lee, Y., Cheong, J., Hyung, W., Noh, S. and Kim, C., 2013. Prognostic Value of Early Postoperative Tumor Marker Response in Gastric Cancer. Annals of Surgical Oncology, 20(12), pp.3905-3911.

[13] Takata, A., Kurokawa, Y., Fujiwara, Y., Nakamura, Y., Takahashi, T., Yamasaki, M., Miyata, H., Nakajima, K., Takiguchi, S., Mori, M. and Doki, Y., 2013. Prognostic Value of CEA and CK20 mRNA in the Peritoneal Lavage Fluid of Patients Undergoing Curative Surgery for Gastric Cancer. World Journal of Surgery, 38(5), pp.1107-1111.

[14] Duraker, N. and Celik, AN., 2001. The prognostic significance of preoperative serum CA 19-9 in patients with resectable gastric carcinoma: comparison with CEA. Journal of Surgical Oncology, 76(4), pp.266-271.

[15] Bagaria B, Sood S, Sharma R, Lalwani S., 2013. Comparative study of CEA and CA19-9 in esophageal, gastric and colon cancers individually and in combination (ROC curve analysis). Cancer Biol Med, 10(3), pp.148–157.