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Literature Review

Correlation between Preoperative and Postoperative Anemia with Disease Outcome in Patients with Gastrointestinal Cancers

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Abstract

It is known that anemia frequently develops in patients with various solid organ cancers such as head and neck cancers, breast cancers, oesophageal cancers, gastric cancers, cervical and bladder cancers. The aim of this study was to search Pubmed in the last 16 years in order to find out correlation between preoperative and postoperative anemia and gastrointestinal cancers. 42 articles were found. The results of this analysis show that preoperative and postoperative anemia indicate poorer disease outcome in patients with gastrointestinal cancers.

Keywords: *Preoperative Anemia; Postoperative Anemia; Gastrointestinal Cancers*

Introduction

It is well known that systemic inflammation and nutritional status play an important role in the prognosis of patients with various cancers. Haemoglobin and albumin are used as a usual indicators for the determination of the nutritional state and their levels are thought to decrease due to the malnutrition and systemic inflammation. Anemia is known to occurr in patients with various solid organ cancers such as head and neck cancers, breast cancers, oesophageal cancers, gastric cancers, cervical and bladder cancers [1-6]. Aproximately 30% of the patients with colorectal cancer are anemic [7]. If anemia is present before the treatment it suggests worse response to the treatment, locoregional control, disease-free period and overall survival [8]. The prevalence of anemia in cancer patients varies, depending on type of malignancy and chosen treatments, but they all have in common reduced survival [9]. It seems that anemia correlates with more agressive tumor behaviour and worse prognosis due to its influence on tissue hipoxia.

Within the tumor tissue, structural and functional disturbances lead to the architectural disarrangement and thus influencing oxygen diffusion into cells which leads to the hypoxia. Low oxygen level in the cells leads to the more agressive cancer behaviour which results in angiogenesis. Oxygen loss within cells decreases free radical development i.e. leads to the treatment resistance. Hypoxia within the tumor tissue leads to the decrease in certain chemotherapy and immunotherapy efficacy which are dependent upon normal oxygen level [10-13].

Large study on 10,218 Chinese patients with cancer showed that anemia was present in 27,5% of these patients. The prevalence of anemia was 64,7% for small bowel cancer, 60,5% for duodenal cancer, 42,6% for colon cancer, 36,6% for cholangiocarcinoma, 33,3% for gastric cancer, 22,6% for pancreatic cancer, 20,4% for rectal cancer, 18,7% for hepatocellular cancer and 10% for esophageal cancer [14].

Materials, Methods and Results

Pubmed was searched regarding publications upon anemia and gastrointestinal cancers with key words: anemia, gastric, colorectal, pancreatic and liver cancer, hepatocellular cancer, decreased haemoglobin, low haemoglobin. 42 articles were included.

Discussion

Anemia and colorectal cancer

Khan., *et al.* [15] analyzed 463 patients with colorectal cancer and found out that haemoglobin values before treatment might be useful marker of the colorectal cancer morphology, response to neoadjuvant chemoirradiation and risk of local recurrence. Haemoglobin values before treatment inversely correlated with cranio-caudal tumour length and T stage before treatment. Patients with colorectal cancer who had haemoglobin values lower than 12 g/dl and moderately differentiated adenocancer, responded worse to the therapy. Local recurrence was more frequent in patients whose haemoglobin values were lower than 12 g/dl during the average follow-up of 12 months. However, that result was not significant.Similar results have been previously reported by Yoon., *et al.* [16] and Rades., *et al* [17]. Yoon *et al.* [16] have shown that pretreatment haemoglobin level is predictor of worse response to preoperative chemoradiotherapy in patients with rectal cancer. Rades., *et al.* [17] have shown worse local control of the disease in patients with recurrent rectal cancer whose haemoglobin values were lower than 12 g/dl, before and during radiotherapy. Patients with haemoglobin values >= 12 g/dl had better local control of the disease and smaller resection range later. In a study including 536 patients with locally advanced colorectal cancer, Jiang., *et al.* [18] developed a novel index HLAN, combined of haemoglobin, lymphocyte, albumin and neutrophil values and found that it was significantly associated with the prognosis. Al-Saeed., *et al.* [19] based on the 154 patients with colorectal cancer reported that anemia before treatment was found in patients who had advanced primary disease and lymph node status. This finding was confirmed also by Kanellos., *et al*. [20], Kandemir., *et al*. [21], Saidi., *et al* [22]. Edna., *et al*. [23] reported on the Norweigan sample that 74.7% patients with colorectal cancer were anemic (out of the total number of 1189 patients). The results of the same study [23] showed that anemia was frequently associated with T stage and not with N or M stage. Mörner., *et al*. [24] proved that preoperative anemia correlated with increased mortality risk, but not with disease recurrence on 496 patients with colorectal cancer. The same authors [24] reported that 50% of patients with colorectal cancer were anemic. Anemia correlates with more advanced stage of colorectal cancer as well as higher mortality [25,26]. Study of Zhen., *et al.* [27] showed that patients with colorectal cancer (stage T3N0M0 and T4N0M0) had shorter disease-free survival which correlated with preoperative anemia. Kulik., *et al.* [28] also reported that preoperative anemia was independently associated with poorer overall outcome in patients with colorectal liver metastases before resection.

Anemia and gastric cancer

Cancer-related anemia is common clinical manifestation in patients with gastrointestinal cancers and it seems that anemia occurs more frequently in the elderly patients. Yu., *et al*. [29] reported that preoperative morbidity of cancer-related anemia was 36,6% in 131 patients with gastric cancer and the morbidity of iron deficiency anemia was 52,1%. Li., *et al*. [30] reported that among other conditions, preoperative anemia was independent factor for complications in the elderly patients with gastric cancer. Liu., *et al*. [31] performed study on 2163 patients with gastric cancer and stated that anemic patients had poorer overal survival when compared to the nonanemic patients after resection for TNM stage III but not stage I or II. The same authors [31] concluded that preoperative anemia, even mild anemia is an important predictor of postoperative survival for TNM stage III in gastric cancer patients. The same finding was also supported by the results of Kim., *et al*. [32] who found that overall survival rate was significantly lower in the patients with gastric cancer who were anemic when compared to the patients with gastric cancer who were not anemic after gastrectomy. They [32] further added that anemia might be associated with nutritional problems and a poor prognosis which was also confirmed by the findings of Lim., *et al* [33].

Anemia and liver cancer

Only limited data are available in the literature regarding correlation of decreased serum iron status and prognosis of hepatocellular carcinoma patients. Finkelmeier., *et al*. [34] based on a study including 199 of patients with hepatocellular carcinoma (HCC) reported that low haemoglobin values (≤ 13 g/dl) indicate higher mortality in these patients, independently of tumor stage. Wei., *et al*. [35] in a retrospective study including 586 patients with hepatitis B related HCC have determined a cut-off value of serum iron level at 15.1 μmol/l, by ROC curve analysis. Serum iron values lower than 15.1 μmol/l correlated with progression of chronic HBV infection, greater tumor size and worse overall survival rate. Patients with tumor size greater than 10 cm by subgroup analysis had the lowest serum iron levels. The same authors [35] concluded that serum iron value lower than 15.1 μmol/l is independent risk factor for the survival of HCC. Qiu., *et al.* [36] confirmed these findings as they found out that anemia was independent prognostic factor in patients with HCC.

Blood iron status does not only affect the prognosis of cancer, but also the onset of complications after treatment. Chen., *et al*. [37] studied risk factors for postoperative delirium in patients who have underwent hepatectomy for the treatment of HCC. Their results have shown that low postoperative haemoglobin values (lower than 10.16 g/dL), among other conditions, is independent risk factor for the development of postoperative delirium after hepatectomy. Anemia was also identified as risk factor for surgical site infection after liver resection, in a study of Kokudo., *et al*. [38] including 226 patients. Kai Nie., *et al*. [39] reported that anemia is independent risk factor for intra-abdominal infections after liver transplantation in patients with hepatocellular carcinoma.

Anemia and pancreatic cancer

The results of Ludwig., *et al*. [40] in a study including 1528 patients with different types of cancer have shown that iron defficiency was most prominent in patients with pancreatic cancer, and then in patients with colorectal and lung cancer. The same authors [40] have shown that iron defficiency and anemia is associated with tumor stage, anticancer therapy within 12 weeks before testing and poor performance status in patients. Anemic patients have greater risk for complications after pancreaticoduodenectomy, as shown in a study of Hughes., *et al* [41].

Anemia and esophageal cancer

Qiu., *et al*. [36] confirmed that anemia was independent prognostic factor in patients with esophageal cancer which was previously found by Rades., *et al* [42].

Conclusion

Anemia in cancer patients is an important prognostic factor of cancer and cancer related complications. Cancer patients should routinely have their haemoglobin level determined.

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