Indian Journal of Basic and Applied Medical Research; December 2019: Vol.-9, Issue- 1, P. 417 - 422

Original Article:

Esophageal Squamous Cell Carcinoma: ABO blood group is Non prognostic

Malik Tariq Rasool[1*], Ashfaq Hafiz[2], Saquib Zaffar Banday[3], Bhat Ishtiyaq Ahmad[2], Abid Maqbool Lone[4], Dar Nazir Ahmad[5], Ganai Farooq Ahmad[6] Mohammad Maqbool Lone[7], Fir Afroz[8]

1. Associate Professor, Radiation Oncology, State Cancer Institute, Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar, India.Email: drmaliktariq@gmail.com
2. Ashfaq Hafiz:Senior Residents, Department of Radiation Oncology, State Cancer Institute, Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar, India.
   Email: ashfaq315@gmail.com; Bhat Ishtiyaq Ahmad: Senior Residents, Department of Radiation Oncology, State Cancer Institute, Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar, India. farhan1067@gmail.com
3. Assistant Professor, Department of Medical Oncology, State Cancer Institute, Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar, India. Email: msaquibzb@gmail.comAdditional
4. Postgraduate, Department of Radiation Oncology, State Cancer Institute, Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar, India.
5. Statistician, Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar, India. Email: johnnazirahmad@@gmail.com
6. Assistant Professor, Department of Cardiovascular and thoracic surgery, Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar, India. Email: malikshareefa@gmail.com
7. Professor& Head, Department of Radiation Oncology, State Cancer Institute, Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar, India.
   Email: drlone.m@gmail.com
8. Professor, Department of Radiation Oncology, State Cancer Institute, Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar, India.firafroz@gmail.com

***Corresponding Author: Dr. Malik Tariq Rasool ,** Associate Professor, Radiation Oncology, State Cancer Institute, Sher-i-Kashmir Institute of Medical Sciences, Soura, Srinagar.

Abstract

Background: Esophageal cancer is a global health issue and long term survival rates are dismal. ABO blood group has been reported as a prognostic marker in esophageal squamous cell carcinoma (ESCC) but the results are conflicting. The aim of this study was to study the relationship of ABO blood group with survival in these patients. **Methods:** A hospital-based prospective observational study was conducted at our centre, and newly diagnosed patients with ESCC were screened for ABO and Rh blood group. Common disease and host and treatment related prognostic factors were recorded. The results were compared based on blood group (O versus non-O).

Results: From January 2015 to December 2016, a total of 138 patients with pathologically proven diagnosis of ESCC were prospectively recruited into this analysis. Blood group O was the most common blood group in 50 patients (36.2%) and majority of patients (92%) were Rh positive. In patients with blood group O, the median survival in months was 17 months and in patients with non-O blood group, it was 14 months with a p-value of 0.288. No statistically significant difference in the survival existed

between blood group O and non-O. **Interpretation:** The results of the present study show that ABO blood group does not predict survival in patients with ESCC.

Introduction

Esophageal cancer is one of the major health challenges in the world. In 2018, an estimated 572,000 patients were diagnosed with esophageal cancer worldwide. It is the 7th most frequently diagnosed cancer and 6th leading cause of cancer related deaths globally. (1) Pertinently, esophageal cancer is one of the most common cancers in our region. (2) Most common histology is esophageal squamous cell carcinoma (ESCC). (3) Despite several advances in currently applied combined modality therapies, the prognosis for patients with carcinoma of the esophagus remains poor. Long term survival rates are less than 15%.

A number of factors have been observed to impact survival in patients with esophageal cancer. Stage of disease is the principle tumor related factor which portends survival. Depth of tumor invasion, nodal involvement, histological grade, and presence of distant metastasis have been found to independently predict survival. (4, 5) Perineural invasion (6), tumor length, and size of primary tumor impact outcome. (7) Host factors such as age (8), performance status, and gender (9) also have an influence on survival. There have been efforts to look for molecular markers that may have a bearing on patient outcome, especially in similar stages of disease. Identification of biomarkers could improve the prognosis of patients and help oncologists in providing personalized treatment to patients.

Published data shows that ABO blood group has association with incidence and risk for various cancers, including cancer of stomach (10), ovary (11), pancreas (12), gall bladder (13), nasopharynx (14), and kidney. (15) In addition to this association, ABO blood system has been reported to be associated with prognosis in many cancers including patients with ESCC. However, the results of published studies (16, 17, 18) are inconsistent and accurate clinical consequences are unknown. The aim of this prospective analysis was to assess the relationship between ABO and Rh blood group with survival in patients with ESCC.

Material and Methods

A hospital-based prospective observational study was conducted at our centre, which is the largest tertiary care cancer centre in the region. Patients with newly diagnosed, histopathologically proven ESCC were screened for ABO and Rh blood group typing. Patients who were treated at our center, from January 2015 to December 2016 were enrolled into this study.

Following patient details were recorded: age, gender, performance status as per Eastern Cooperative Oncology Group (ECOG), height, weight, BMI, BSA, associated co-morbidities, and smoking status. Disease and laboratory parameters such as, stage of disease (as per AJCC 7th Edition), metastatic site/s, tumor site (upper, middle and lower), histological type and grade of tumor, complete blood count, liver and kidney functions, ABO and Rh blood group status, were documented. Treatment related factors related to radiation therapy, chemotherapy, surgery or a combination of these was also recorded.

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

Statistical Analysis

All the data was recorded and maintained in both hard and/or soft format patient files at State Cancer Institute (SCI). All the quantitative data was expressed using range, mean & standard deviation while qualitative data was expressed in frequency & percentage. The patients were divided into two groups. One group comprised of patients with blood group A, B or AB and the second group included patients with blood group O. These two groups of interest were compared with the help of standard statistical tests like Independent T-Test. Survival rates were plotted by the Kaplan–Meier method and all events of death were analyzed by Cox regression model. All the data was analyzed using SPSS statistical software package, version 22.0. We hypothesized that there is a difference between survival in patients with ESCC based on O or non-O blood group. Therefore, we analyzed if blood type A/B/AB or O predicted survival in patients with ESCC.

Results

From January 2015 to December 2016, a total of 138 patients with pathologically proven diagnosis of ESCC were prospectively recruited into this analysis. All patients with previous history of malignancy, major surgery, radiotherapy or chemotherapy were excluded from this study. Blood group O was the most common blood group in 50 patients (36.2%) and majority of patients (92%) were Rh positive. Table No. 1 shows the distribution of ABO and Rh blood groups in all patients.

For analyzing the impact of blood group on survival, the patients were divided into two groups, based on principle variable of blood group (A/B/AB and O). There was marginal trend towards better survival for blood group O, however, no statistically significant difference existed between the two groups. In patients with blood group O, the median survival in months was 17 months and in patients with non-O blood group, it was 14 months with a p-value of 0.288.

Most commonly reported prognostic factors in patients with ESCC were analyzed for their correlation with blood group O versus blood group non-O. The analysis was done for age, gender, performance score, BMI, stage of disease, grade of tumor, location of primary tumor, co-morbidities, smoking status, and treatment received. Both the groups were comparable for all studied clinical and pathological characteristics and no correlation was found between blood group and any of the studied parameter (Table No. 2). Although, we have not analyzed long term follow up of patients, but we can see in Kaplan-Meier curves of overall survival between patients with blood group O and blood group non-O (Figure 1), the curved are separating after 18 months which may suggest that, the difference in survival may reach significant levels for longer follow up.

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

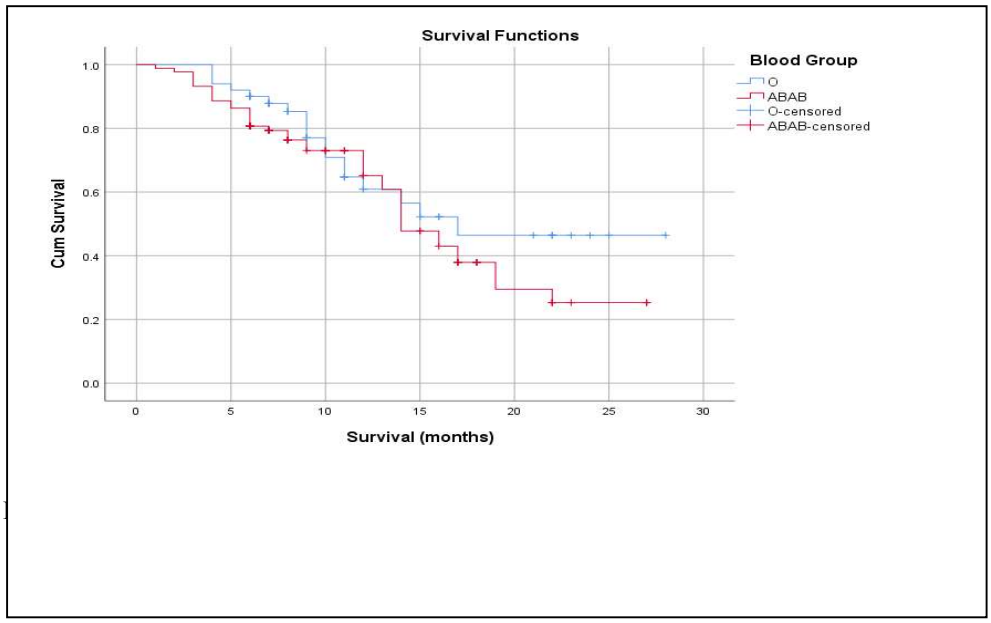

Figure 1. Kaplan-Meier curves of overall survival between patients with blood group O and blood group non-O (P=0.288)

Worldwide, ESCC is the leading histological type of esophageal cancer (3). Neoadjuvant chemoradiation therapy followed by surgery remains the most important curative modality for ESCC. However, majority of patients will not be fit to receive this treatment due to various patient or disease related factors, and will receive definitive chemoradiation or will end up with palliative therapy. Various prognostic factors have been studied in different treatment modalities and have proven beneficial in predicting survival. However, it is debatable if all of these factors are relevant in differing treatment settings. There have been many efforts to identify prognostic markers for ESCC. Prognostic value of various proteins detected with immunohistochemistry, expression profiles of genes is also being extensively studied in ESCC. Blood group has also been proposed to have prognostic importance. However, no conclusive data has emerged so far in this regard.

In this study, we prospectively collected the data about 138 patients with esophageal squamous cell cancer, who reported at our center. This analysis was done irrespective of stage at presentation or treatment received. Most common blood group that we found in patients with ESCC was blood group O (36.2%), followed by B and A (Table No. 1). Majority of the patients (92%) had Rh positive blood group. The prevalence of ABO and Rh blood groups was consistent with donor population from the same ethnic background (19). We did not find any statistically significant difference in patient survival between O and non-O blood groups. There was no association with studied clinical and pathological factors in our analysis. The results from Wang W et al also failed to suggest an association between ABO blood group and disease-free or overall survival in patients with ESCC (20). No correlation between ABO blood group and prognosis was found in another study. (16) However, various studies have shown certain blood types to predict survival in ESCC. Patients with blood group O in one study were observed to have

www.ijbamr.com P ISSN: 2250-284X , E ISSN : 2250-2858

significantly worse overall survival than non-O blood groups (18). Blood types B and O have been observed to negatively affect survival in patients having a history of smoking. (17) Overall, more than 60% (59.1 in Non-O and 66% in O) of patients in our patient population were chronic smokers and ABO blood group did not influence survival in smokers. Therefore, prognostic role of ABO blood group in ESCC remains largely obscure.

Even in other malignancies, the role of blood group as a prognostic marker remains indefinable. For example, in pancreatic cancer there are some authors have observed prognostic value of ABO blood group (21), while others have not. (22) ABO blood group was found to be non prognostic in patients with non-small cell lung cancer (23), but in other analysis, blood group A and AB were found to have a shorter overall survival (24). ABO blood typing did not predict outcome in patients with gastric (25), and breast cancer (26)

The impact of blood group on disease outcome is not well understood and it remains largely elusive why the ABO blood group antigens affect the survival of patients with ESCC. ABO blood group may alter the biological behavior of tumors. The expression of blood group antigens on cancer cells may be modified by hypermethylation of the ABO promoter, which may have a role in tumor invasion and metastasis. (27)

There are some limitations of the present study. First, the sample size in this study was only 138, and we included all patients irrespective of stage of disease or treatment received. Therefore some of the patients received palliative treatment only. In conclusion, the results of the present study show that ABO blood group does not predict survival in patients with ESCC. More research is needed to elucidate the prognostic value of ABO blood group in patients with ESCC.

References:

1. World Health Organization. International Agency for research on Cancer. GLOBOCAN 2018: Oesophagus cancer fact sheet. 2018.
2. Rasool MT, Lone MM, Wani ML, Afroz F, Zaffar S, Mohib-ulHaq M. Cancer in Kashmir, India: Burden and pattern of disease. J Can Res Ther2012;8:243-6.
3. Rustgi AK, El-Serag HB. Esophageal carcinoma. N Engl J Med 2014;371(26):2499-509.
4. Nomura M, Shitara K, Kodaira T, et al. Prognostic impact of the 6th and 7thAmerican Joint Committee on Cancer TNM staging systems on esophageal cancer patients treated with chemoradiotherapy. Int J Radiat Oncol Biol Phys 2012;82:946-952.
5. Yueguan J, Shifeng C, Bing Z. Prognostic factors and family history for survival of esophageal squamous cell carcinoma patients after surgery. Ann Thorac Surg 2010;90(3):908-913.
6. Gao A, Wang L, Li J, et al. Prognostic Value of Perineural Invasion in Esophageal and Esophagogastric Junction Carcinoma: A Meta-Analysis. Dis Markers. 2016;2016:7340180. doi:10.1155/2016/7340180
7. Wang BY, Goan YG, Hsu PK, et al. Tumor length as a prognostic factor in esophageal squamous cell carcinoma. Ann ThoracSurg2011;91:887-893.
8. Gertler R, Stein HJ, Langer R, et al. Long-term outcome of 2920 patients with cancers of the esophagus and esophagogastric junction: evaluation of the New Union InternationaleContre le Cancer/American Joint Cancer Committee staging system. Ann Surg 2011;253:689-698.
9. Kauppila JH, Wahlin K, Lagergren P, Lagergren J. Sex differences in the prognosis after surgery for esophageal squamous cell carcinoma and adenocarcinoma.Int J Cancer 2019;144(6):1284-91.

10. Aird I, Bentall HH, Roberts JA. A relationship between cancer of stomach and the ABO blood groups. Br. Med. J1953;1(4814),799-801.
11. Yuzhalin AE, Kutikhin AG. ABO and Rh Blood Groups in Relation to Ovarian, Endometrial and Cervical Cancer Risk among the Population of South-East Siberia. Asian Pacific Journal of Cancer Prevention 2012;13(10):5091-6.
12. Wolpin BM, Chan AT, Hartge P, Chanock SJ, Kraft P, Hunter DJ, Giovannucci EL, Fuchs CS. ABO blood group and the risk of pancreatic cancer. J Natl Cancer Inst 2009;101:424-431.
13. Pandey M, Gautam A, Shukla VK. ABO and Rh blood groups in patients with cholelithiasis and carcinoma of the gall bladder. BMJ. 1995;310(6995):1639. doi:10.1136/bmj.310.6995.1639.
14. Sheng L, Sun X, Zhang L, Su D. ABO blood group and nasopharyngeal carcinoma risk in a population of Southeast China. International J cancer 2013;133(4):893-7.
15. Joh HK, Cho E, Choueiri TK. ABO blood group and risk of renal cell cancer. Cancer Epidemiol. 2012;36(6):528–532. doi:10.1016/j.canep.2012.07.001
16. Nozoe T, Ezaki T, Baba H, Kakeji Y, Maehara Y. Correlation of ABO blood group with clinicopathologic characteristics of patients with esophageal squamous cell carcinoma. Dis Esophagus 2004;17(2):146-149.
17. Sun P, Chen C, Zhang F, et al. The ABO blood group predicts survival in esophageal squamous cell carcinoma in patients who ever smoked: a retrospective study from China. TumourBiol 2014;35(7):7201-7208.
18. Yang X, Huang Y, Feng JF. Is there an association between ABO blood group and overall survival in patients with esophageal squamous cell carcinoma? Int J ClinExp Med 2014;7(8):2214-2218
19. Ali I, Parveen S, Kadla SA, Shah NA. Prevalence of ABO and Rhesus Blood Groups in various blood donors in Kashmir. Eur Acad Res 2015;3(3),3647-56.
20. Wang W, Liu L, Wang Z, et al. Impact of ABO blood group on the prognosis of patients undergoing surgery for esophageal cancer. BMC Surg. 2015;15:106. Published 2015 Sep 29. doi:10.1186/s12893-015-0094-1.
21. Rahbari NN, Bork U, Hinz U, Leo A, Kirchberg J, Koch M, et al. AB0 blood group and prognosis in patients with pancreatic cancer. BMC Cancer2012;12:319.
22. Wang DS, Wang ZQ, Zhang L, Qiu MZ, Luo HY, Ren C, et al. Are risk factors associated with outcomes in pancreatic cancer? PLoS ONE. 2012;7,e41984.
23. Unal D, Eroglu C, Kurtul N, Oguz A, Tasdemir A, Kaplan B. ABO blood groups are not associated with treatment response and prognosis in patients with local advanced non- small cell lung cancer. Asian Pac J Cancer Prev2013;14:3945-8.
24. Fukumoto K, Taniguchi T, Usami N, et al. The ABO blood group is an independent prognostic factor in patients with resected non-small cell lung cancer. J Epidemiol. 2015;25(2):110–116. doi:10.2188/jea.JE20140102.
25. Qiu MZ, Zhang DS, Ruan DY, Luo HY, Wang ZQ, Zhou ZW, et al. A relationship between ABO blood groups and clinicopathologic characteristics of patients with gastric adenocarcinoma in China. Med Oncol 2011;28 Suppl1:S268-73.
26. Gates MA, Xu M, Chen WY, Kraft P, Hankinson SE, Wolpin BM. ABO blood group and breast cancer incidence and survival. Int J Cancer 2012;130:2129-3.
27. Gao S, Worm J, Guldberg P, et al. Genetic and epigenetic alterations of the blood group ABO gene in oral squamous cell carcinoma. Br J Cancer 1996;73(4):420-423.