International Surgery Journal
Gupta A et al. Int Surg J. 2019 Dec;6(12):4435-4439
http://www.ijsurgery.com
pISSN 2349-3305 | eISSN 2349-2902

DOI: http://dx.doi.org/10.18203/2349-2902.isj20195408

Original Research Article

Prognostic role of serum C-reactive protein in carcinoma oesophagus

Arun Gupta, Tejinder Singh Dall*, Darpan Bansal

Department of Surgery, Sri Guru Ram Das Institute of Medical Sciences and Research, Vallah, Sri Amritsar, Punjab, India

Received: 05 November 2019
Revised: 21 November 2019
Accepted: 22 November 2019

***Correspondence:**
Dr. Tejinder Singh Dall,
E-mail: drtejindersinghdall@gmail.com

ABSTRACT

Background: Oesophageal cancer (EC) is the eighth most common cancer around the world. EC incidence and mortality are affected by geography. Eastern Asia, eastern and southern Africa has the highest rates, whereas Europe and North America show lower rates.
Methods: The study was conducted on 30 cases of EC diagnosed in Sri Guru Ram Das Institute of Medical Sciences and Research, Sri Amritsar. The study was carried during period starting from January 2017 to June 2018. Serum C - reactive protein levels measurement was made in addition to the other routine investigations.
Results: The sample consisted of 30 patients presenting with EC. Total number of males was 7 (23.33%) and there were 23 (76.66%) females. It was found in present study that the most common age group presenting with oesophageal cancer was 41-60 years followed by 61-80 years. It was also observed in the present study that majority of patients 15 (50%) were housewives. It was also observed that 17 (56.67%) of patients had more than 6 mg/l level of preoperative C-reactive proteins. Among the poorly differentiated histological grade patients 14 (73.68%) had high level of C-reactive proteins. Moreover hospital stay was also more among the patients having high pre-operative levels of C-reactive proteins (CRPs).
Conclusions: The prognosis for patients with preoperative serum elevation of CRP was significantly more unfavourable than that for patients without serum CRP elevation.

Keywords: Carcinoma oesophagus, C-reactive proteins, Dysphagia

INTRODUCTION

Oesophageal cancer (EC) is the eighth most common cancer around the world.[1] EC incidence and mortality are affected by geography. Eastern Asia, eastern and southern Africa have the highest rates, whereas Europe and North America show lower rates.

In India at state level, extremely high incidence rates, reaching endemic proportions, have been reported from Jammu and Kashmir. In Punjab the incidence rates calculated were however lowest in the country.[2]

In the US and Europe 85% of cases of oesophageal cancers are attributed to alcohol and tobacco use.[3] In India, etiopathogenesis of EC is attributed to multiple factors including malnutrition (vitamin A, E, C, riboflavin and niacin along with deficiency of micronutrients such as molybdenum and zinc) and betel quid chewing (relative risk 1.5 to 3.5).[4-8]

Prognostication in cancer can be either subjective or objective. In the former, dependent on clinician skill and experience, it is often inaccurate and usually overly optimistic.[2] Despite advances in medical technology and biology, it is still an inexact science even with extensive

and expensive investigations.[2,3] Objective determination of prognosis can be based on a combination of tumor, patient, and environmental factors. The use of biological tumor markers to help prognostication (alone or combined with other parameters) has an appeal. An ideal potential tumor marker should have a long half-life, be measured accurately and precisely by a simple and inexpensive blood test. It is also important that it should be sensitive to change so that it can be followed over time through serial measurements. A few biologic markers meet these criteria.[4] C-reactive protein (CRP) is one.

CRP secretion by hepatocytes appears controlled by interleukin 6 (IL-6). Interleukin-1 (IL-1) and tumor necrosis factor (TNF) also stimulate CRP synthesis.[9] CRP is a stable downstream marker of inflammation, unlike the pro-inflammatory cytokines, which have short half-lives (minutes). In chronic inflammatory diseases, serial CRP levels have been correlated with disease severity, and response to therapy.[10]

Chronic inflammation has been linked to cancer at tumor initiation, but may also be associated with invasive potential and disease progression. A relationship has been proposed between systemic inflammation and various cancer symptoms.[11-13] A strong positive correlation between high CRP and high IL-6 levels was shown in advanced esophageal cancer.[14-16]

However, there has been no definitive conclusion about the relation between serum CRP level and prognosis of esophageal cancer. Some researchers showed that the overall survival (OS) was significantly shorter in the EC patients with elevated serum CRP level.[17,18] However some researches showed that the correlation between elevated serum CRP level and shorter OS was not statistically significant.[19] Due to the small sample size of the individual studies, the current opinion is still controversial. So, this study was conducted to assess the correlation of elevated serum CRP level with the overall prognosis of esophageal cancer patients.

The main aim of the study was to evaluate raised preoperative serum CRP level and prognosis of EC.

The study was done with the objective to study preoperative serum CRP levels, histological grade of early-stage EC in the study patient and to study preoperative serum CRP levels in the context of post-operative ICU stay in patients of EC.

METHODS

The study was conducted on 30 cases of EC diagnosed in Sri Guru Ramdas Institute Of Medical Sciences and Research, Amritsar during the study period starting from January 2017 to June 2018. The patients were to undergo serum CRP levels measurement in addition to the other routine investigations.

Inclusion criteria

Inclusion criteria were histopathological proven cases (both squamous as well as adenocarcinoma) of carcinoma esophagus presenting to the hospital, cases fit to undergo surgery, age 18 years to 70 years.

Exclusion criteria

Exclusion criteria were patients with locally advanced carcinoma (unresectable growth), patients who have already undergone surgery for EC.

Measurement of serum CRP

Serum was collected 1 day prior to the operation to measure the CRP level, which was determined once for each patient. Serum CRP was measured using CRP ELISA (enzyme-linked immunosorbent assay) kit. The normal serum CRP range is 0-6 mg/l. Hence, a serum CRP concentration of >6 mg/l was considered positive.

Follow-up

Patients were followed-up weekly, fortnightly, monthly then according to condition of patient. Each patient's history, physical examination, thoracic CT scans and blood investigations were recorded at each follow -up session. Survival time was recorded from the day of operation to last follow-up visit.

The data collected was analysed with SPSS 19 Software.

RESULTS

The present study was conducted on 30 patients above 18 years of age of either sex, scheduled for elective esophagectomy in our institute after an informed consent. Primary outcomes of the study was the prognosis of carcinoma oesophagus with respect to preoperative levels of serum CRP and post-operative ICU stay.

Table 1: Age wise distribution.

Age group (years)	N	%
20-40	4	13.33
41-60	15	50.0
61-80	11	36.66
Total	30	100.0
Mean±SD	55.33±13.62	

As shown in the Table1 it was found that the maximum number of patients (15, 50%) with carcinoma oesophagus who presented with dysphagia was in the age group 41-60 years. The second most common age group was 61-80 years with 11 (36.66%) patients. The incidence was less in younger group i.e. below 40 years.

Table 2: Gender wise distribution.

Sex	N	%
Female	23	76.66
Male	7	23.33
Total	30	100.0

As shown in Table 2 out of 30 patients, 7 (23.33%) were male and 23 (76.66 %) were female. X^2=8.53, df=1, p≤0.05. Therefore the difference between males and females is statistically significant. Hence it was found that in present research there is female preponderance.

Table 3: Occupation wise distribution.

Occupation	N	%
Daily wager	2	6.66
Farmer	10	33.33
Housewives	15	50.0
Shopkeeper	1	3.33
Tailor	1	3.33
Teacher	1	3.33
Total	30	100.0

As shown in Table 3 maximum number of patients were housewives i.e. (15, 50%), followed by 10 (33.33%) were farmers, 2 (6.66%) were daily wagers.

Table 4: Distribution of patients according to pre-operative CRP Level.

CRP	N	%
≤6.0	13	43.33
>6.0	17	56.66
Total	30	100.0
Mean±SD	8.73±9.52	

As shown in the Table 4, CRP levels were found to be greater than 6 mg/l (that is the cut-off value taken in present study) in 17 (56.66%) of the patients & was lesser than 6 mg/l in 13 (43.33%) patients.

Table 5: Distribution of patients according to histological grade.

Histological grade	Low CRP (≤6 mg/l) (n=11)		High CRP (>6 mg/l) (n=19)	
	N	%	N	%
Well and moderately differentiated	8	72.72	5	26.31
Poorly differentiated	3	27.27	14	73.68

Table 6: Distribution of patients according to CRP levels and postoperative ICU stay.

Hospital stay	LOW CRP (≤6 mg/l) n=14	Percentage of patients (%)	High CRP (>6 mg/l) n=16	Percentage of patients (%)
Less than 7 days	11	78.57	3	18.75
More than 7 days	3	21.42	13	81.25

As shown in the Table 5 poorly differentiated carcinoma oesophagus is associated with high levels of CRP in 14 (73.68%) of the patients and hence poor outcome. X^2=7.11, df=1, p≤0.05. Therefore the difference between CRP levels of patients with poorly differentiated histological grade is statistically significant.

It can be inferred from table 6 that patients (13, 81.25%) having CRP level more than 6 mg/l had more than 7 days stay at hospital compared to the lower levels of CRP. X^2=6.25, df=1, p≤0.05. The difference between patients with low CRP level and High CRP level who stayed for more than 7 days was statistically significant.

DISCUSSION

The results demonstrate that the preoperative elevation of serum CRP can be an indicator for malignant potential of tumours and unfavourable prognosis of the patients with oesophageal carcinoma. Patients with oesophageal carcinoma are usually in poor nutritional condition and in a state of impaired immunity. Moreover the surgical treatment for carcinoma of the oesophagus is more invasive compared with that for other organs. In present study it was found that poorly differentiated carcinoma oesophagus is associated with high levels of CRP and hence poor outcome. The results of present research is in line with study conducted by Huang.[20]

Age incidence

In present study it was found that the most common age group presenting with dysphagia was 41-60 years followed by 61-80 years which was the second most common. Hence the incidence of dysphagia was most common in the middle to elderly age group in present study. These findings are similar to a study conducted by Datta et al.[21] The most likely factors contributing to this finding can be malnutrition, obesity, poor oral health, low intake of fresh fruits and vegetables, alcohol and tobacco consumption, smoking, red meat, hot tea drinking.

Gender wise incidence

It was also found from present study that dysphagia was more common in females as compared to males. Our

finding was supported by Bhattacharyya.[22] Women were more likely than men to report a swallowing problem. However more prevalence in males was seen by Yang et al contrary to our results.[23]

Hospital and ICU stay

The patients with growth oesophagus had much prolonged hospital and ICU stay of at least 7 days or more. On comparing the finding of present research of hospital stay with study conducted by Altman et al which says that patient with dysphagia had more median number of hospital and ICU stay length i.e. 4.04 days compared with 2.4 days for those patients without dysphagia.[24]

CONCLUSION

As a result we can conclude that dysphagia has significant impact on hospital and ICU stay length and is a bad prognostic indicator. Early recognition of dysphagia and intervention in the hospitalized patient is advised to reduce morbidity and length of hospital stay. It was also found that patients with higher levels of preoperative CRP were associated with prolonged hospital stay.

The preoperative serum elevation of CRP can be a simple and useful marker for the malignant potential of the tumours and an independent prognostic indicator in oesophageal carcinoma.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. CA Cancer J Clin. 2013;63(1):11-30.
2. Zhang HZ, Jin GF, Shen HB. Epidemiologic differences in esophageal cancer between Asian and Western populations. Chinese J Cancer. 2012;31(6):281.
3. Akhtar S. Areca nut chewing and esophageal squamous-cell carcinoma risk in Asians: A meta-analysis of case-control studies. Cancer Causes Control. 2013;24(2):257-65.
4. Terry P, Lagergren J, Ye W, Nyrén O, Wolk A. Antioxidants and cancers of the esophagus and gastric cardia. Int J Cancer. 2000;87(5):750-4.
5. Decarli A, Liati P, Negri E, Franceschi S, La Vecchia C. Vitamin A and other dietary factors in the etiology of esophageal cancer. Nutr Cancer. 1987;10(1-2):29-37.
6. Nomura AM, Ziegler RG, Stemmermann GN, Chyou PH, Craft NE. Serum micronutrients and upper aerodigestive tract cancer. Cancer Epidemiol Biomarkers Prev. 1997;6(6):407-12.
7. La Vecchia C, Altieri A, Tavani A. Vegetables, fruit, antioxidants and cancer: a review of Italian studies. Eur J Nutr. 2001;40(6):261-7.
8. Kabat GC, Ng SK, Wynder EL. Tobacco, alcohol intake, and diet in relation to adenocarcinoma of the esophagus and gastric cardia. Cancer Causes Control. 1993;4(2):123-32.
9. Weinhold B, Rüther U. Interleukin-6-dependent and independent regulation of the human C-reactive protein gene. Biochem J. 1997;327:425-9.
10. Nozoe T, Saeki H, Sugimachi K. Significance of pre-operative elevation of serum C-reactive protein as an indicator of prognosis. Am J Surg. 2001;182(2):197-201.
11. Canna K, McArdle PA, McMillan DC, McNicol AM, Smith GW, McKee RF et al. The relationship between tumour T-lymphocyte infiltration, the systemic inflammatory response and survival in patients undergoing curative resection for colorectal cancer. Br J Cancer. 2005;92(4):651.
12. Chia-SIU Wang, Chien Feng Sun. C-Reactive protein and malignancy: Clinico-pathological association and therapeutic implication. Chang Gung Med J. 2009;32:471-82.
13. Haffty BG, Yang Q, Moran MS, Tan AR, Reiss M. Estrogen-dependent prognostic significance of cyclooxygenase-2 expression in early-stage invasive breast cancers treated with breast-conserving surgery and radiation. Int J Radiation Oncol Biol Physics. 2008;71(4):1006-13.
14. Leu CM, Wong FH, Chang C, Huang SF, Hu CP. Interleukin-6 acts as an antiapoptotic factor in human esophageal carcinoma cells through the activation of both STAT3 and mitogen-activated protein kinase pathways. Oncogene. 2003;22:7809-18.
15. Deans DA, Wigmore SJ, Gilmour H, Paterson-Brown S, Ross JA, Fearon KC. Elevated tumour interleukin-1beta is associated with systemic inflammation: a marker of reduced survival in gastro-oesophageal cancer. Br J Cancer. 2006;95:1568-75.
16. Nozoe T, Korenaga D, Futatsugi M, Saeki H, Maehara Y, Sugimachi K. Immunohistochemical expression of C-reactive protein in squamous cell carcinoma of the esophagus—significance as a tumor marker. Cancer Lett. 2003;192:89-95.
17. Feng JF, Zhao HG, Liu JS, Chen QX. Significance of preoperative C-reactive protein as a parameter in patients with small cell carcinoma of the esophagus. Onco Targets Therap. 2013;6:1147.
18. Song ZB, Lin BC, Li B, He CX, Zhang BB, Shao L et al. Preoperative elevation of serum C-reactive protein as an indicator of poor prognosis for early-stage esophageal squamous cell carcinoma. The Kaohsiung J Med Sci. 2013;29(12):662-6.
19. Miyata H, Yamasaki M, Kurokawa Y, Takiguchi S, Nakajima K, Fujiwara Y, et al. Prognostic value of an inflammation-based score in patients undergoing pre-operative chemotherapy followed by surgery for

esophageal cancer. Experimental Therap Med. 2011;2(5):879-85.
20. Huang W, Wu L, Liu X, Long H, Rong T, Ma G. Preoperative serum C-reactive protein levels and postoperative survival in patients with esophageal squamous cell carcinoma: a propensity score matching analysis. J Cardiothoracic Surg. 2019;14(1).
21. Datta G, Gupta M, Rao N. Clinical profile of cases of dysphagia presenting in ENT department: a study from rural tertiary care centre. Int J Otorhinolaryngol Head Neck Surg. 2017;3(3):639-45.
22. Bhattacharyya N. The prevalence of dysphagia among adults in the United States. Otolaryngol Head Neck Surg. 2014;151(5):765-9.
23. Yang EJ, Kim MH, Lim JY, Paik NJ. Oropharyngeal Dysphagia in a community based elderly cohort: the Korean Longitudional study on health and ageing. J Korean Med Sci. 2013;28(10):1534-9.
24. Altman KW, Yu GP,Schaefer SD. Consequence of dysphagia in the hospitalized patient: impact on prognosis and hospital resources. Arch Otolaryngol Head Neck Surg. 2010;136(8):784-9.

Cite this article as: Gupta A, Dall TS, Bansal D. Prognostic role of serum C-reactive protein in carcinoma oesophagus. Int Surg J 2019;6:4435-9.