Role of HALP score in predicting short term outcomes after surgery in esophago-gastric cancers.

Ashish Kharel[1], Binay Thakur[1], Shashank Shrestha[1], Mahesh Mani Adhikari[1], Sandeep Sapkota[1], Sagar Khatiwada[1], Manoj Tiwari[1], Shachee Bhattarai[1], Srijana Thapa[1]

[1]Department of Surgical Oncology, thoracic surgery unit BP Koirala Memorial Cancer Hospital, Bharatpur, Nepal

Abstract:

Background: Esophago-gastric cancers are common cancers with poor prognosis. Radical surgery offers the best hope for long term survival but is associated with increased short-term morbidity and mortality. There is a need for a simple scoring system that helps in estimating the short-term prognosis of the patient after undergoing surgery for these cancers. Hemoglobin, Albumin, Lymphocytes, Platelets (HALP) score is such a scoring system that has recently been developed. The aim of this study was to evaluate the role of HALP score in predicting short term outcomes after surgery in esophago- gastric cancers.

Methods: We conducted a prospective study of all patients with esophago-gastric cancers undergoing curative intent surgery in the surgical oncology department. The optimal HALP cut-off point was evaluated using Receiver operating characteristics (ROC) analysis and the cohort was divided into Low and High HALP groups, which were then further analyzed.

Results: The mean age was 61.52 ± 9.07 years. Of these 17 (54.8%) were male and 14 (45.2%) were female. Squamous cell carcinoma was the more common histology. The optimal cut-off value of HALP was 38.0 with a sensitivity of 86.7% and specificity of 87.5%. Low HALP was significantly associated with Anastomotic leak, SSI, overall mortality and prolonged hospital stay.

Conclusion: HALP score can be a good prognostic indicator for patients with esophago-gastric cancers undergoing curative resection.

Keywords: Esophageal cancer, Esophagectomy, HALP score

Introduction

Esophago-gastric cancers are common cancers worldwide with an incidence of 8.7% and 13.2% of deaths among all cancers.[1] Esophageal cancers, including GEJ cancers are the 12th most common cancers in Nepal.[2] Prognosis for these cancers are poor because they are usually diagnosed in advanced stages. Early detection and multimodality treatment, which consists of surgery combined with chemotherapy/ radiotherapy, may most likely help attain long-term survival.[3]

Nutritional and inflammatory status have long been identified as important prognostic factors for survival. Therefore, a variety of Nutritional and/or inflammatory related indices have

Corresponding author:

Dr. Ashish Kharel, Department of Surgical Oncology (Thoracic Unit), BP Koirala Memorial Cancer Hospital, Bharatpur, Nepal. Email: drashkharel@gmail.com, Phone: +9779857088210.

been developed for prognostication in various cancers. The Platelet to lymphocyte ratio (PLR), Prognostic Nutritional Index (PNI), Neutrophil to Lympocyte ratio (NLR), Systemic Immune Inflammation Index (SII) and various other indicators have been developed and validated in various cancers including gastric and esophageal adenocarcinomas.[4–7]

The Hemoglobin, Albumin, Lymphocytes and Platelets (HALP) score is a novel immune-nutritional prognostic marker for several types of malignancies. It was first used to predict the poor clinicopathological outcomes and long term survival in gastric cancer after gastrectomy.[8] Further studies have validated its value in predicting long term prognosis in other gastro-intestinal cancers including esophageal cancer.[9,10]

HALP has also been used to predict short-term outcomes in various diseases including acute pancreatitis[11] although this has not been done in post operative settings. The aim of this study was to evaluate the role of HALP in predicting the short-term outcomes after surgery for esophago-gastric cancers.

Material and Methods

Patients: This was a prospective evaluation of all patients undergoing surgery for esophageal and Esophago-gastric junction cancers in the surgical oncology department of BP Koirala Memorial Cancer Hospital over a 1-year period from January 2024 to January 2025. Patients with benign disease and those with unresectable tumors were excluded from the study. Patients with incomplete HALP parameters were also excluded from the study. Informed consent was obtained from all the study participants and IRC approval was obtained prior to data collection (Proposal reg no. 65/2080-03-26).

Procedure: All surgeries were performed by experienced surgeons from the thoracic surgery unit of surgical oncology department of BP Koirala Memorial Cancer Hospital. The type of surgery was determined by the unit chief according to the location of the tumor and characteristic of the patient. After surgery, patients were followed up to 30 days and all relevant data were recorded in a proforma. Anastomotic leak was identified according to endoscopic features or intervention required.[12] RLN palsy was identified by laryngoscopy, if suspected. Surgical site infection was defined according to CDC criteria.13 The HALP score was calculated using the following formula:

HALP = Hemoglobin (g/L) * Albumin (g/L) * Lymphocyte (/L) ÷ Platelet (/L)8

Statistical Analysis: Data entry and analysis was done in Statistical Package for the Social Sciences (SPSS) software (Version 26, IBM). Receiver Operating Characteristics (ROC) analysis and curve was used to identify the optimal cut-off point following which the study population was divided into Low HALP and High HALP group for further analysis. Fischer exact test or chi square test for categorial variables and t-tests for continuous variables were used to compare the two groups.

Results

Patient characteristics

A total of 31 patients were included in the study. The mean age was 61.52 ± 9.07 years. Of these 17 (54.8%) were male and 14 (45.2%) were female. The average Body Mass index was 21.1 ± 3.4. Dysphagia was the most common symptom, present in 100% of patients. The mean duration of dysphagia prior to medical consultation was 6.19 ± 3.12 months. Squamous cell carcinoma was the more common histology accounting for 18 patients (58%). The remaining [13] cases were of adenocarcinoma (41.9%). The mean Hemoglobin, albumin, lymphocyte count and

Table 1: Demographic and clinical characteristics of patients

		Low HALP (N=15)	High HALP (N=16)	P- Value
Age		64.67 ± 8.85	58.56 ± 8.52	0.833
Sex	Male	10	7	0.285
	Female	5	9	
BMI		19.66 ± 3.46	22.75 ± 2.64	0.488
Dysphagia Duration (months)		5.93 ± 2.52	6.44 ± 3.66	0.243
Hemoglobin		10.74 ± 1.61	12.15 ± 1.75	0.303
Albumin		3.65 ± 0.48	3.97 ± 0.37	0.683
Lymphocytes		1.84 ± 0.51	2.37 ± 0.81	0.028
Platelet		275 ± 92	195 ± 53	0.165
Histology	Squamous	7	11	0.213
	Adeno	8	5	
Tumor length		5.5 ± 2.4	4.2 ± 1.9	0.140
Tumor location	U/M/L/G1/G2	1/5/2/2/5	1/5/5/1/4	
Neoadjuvant Therapy received		10	10	0.809
Surgical approach	MIS	8	11	0.305
	Open	7	5	
Surgery Type	McKeown	8	11	0.349
	THE	6	2	
	Left Thoracotomy	1	1	
	Ivor Lewis	0	1	
	Extended Total Gastrectomy	0	1	
Hospital Stay		20.27 ± 9.86	11.38 ± 2.53	0.002
OT Duration		278 ± 90	260 ± 65	0.526
Anastomotic Leak	Grade I	3	0	0.018
	Grade II	0	0	
	Grade III	2	0	
RLN Palsy		1	1	1.000
SSI		6	1	0.033
Pneumonia		1	1	1.000
Chylothorax		1	0	0.484
Mortality		4	0	0.043
Overall Morbidity		13	2	<0.001

platelet count were 114.6 ± 18.0 g/L, 38.1 ± 4.5 g/L, 2.11 ± 0.72 x 109/L and 233 ± 83 x 109/L respectively. The mean value of HALP was 44.0 ± 23.5. The most common surgical approach was McKeown's Esophagectomy accounting for 19 cases (61.3%). Other approaches were

Transhiatal esophagectomy (25.8%), Left Thoracotomy approach (6.5%), Ivor Lewis (3.2%) and Extended Total Gastrectomy (3.2%). The mean hospital stay was 15 days (range 8 to 35 days). There were no intraoperative complications, and the mean surgical time was 268 minutes (range 150 to 490 minutes). Post Operative complications were present in 15 cases (48.39%). Surgical Site Infection (SSI) was present in seven cases. Anastomotic leak was present in five cases of which three were clinically insignificant (grade I) while two cases required re-surgery (Grade III). Both these cases had mortality because of the complications. Other complications included Recurrent laryngeal nerve palsy in two cases, pneumonia in two cases and chylothorax in one case. There were overall four deaths due to post operative complications. There were no re-admissions within the 30-day period.

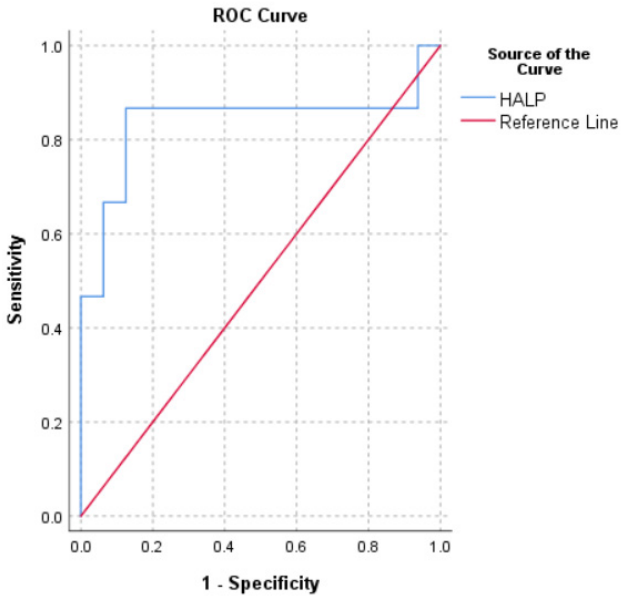
Determination of Cut-Off Value:

To create a cut-off value of HALP, an ROC analysis and ROC curve were created (figure 1). The Youden index was calculated to be 0.742 on basis of sensitivity and specificity tables and the optimal cut-off value was determined to be 38.0 with a sensitivity of 86.7% and specificity of 87.5%. Based on this cut-off value, the patients were divided into Low HALP and High HALP groups.

HALP association with Clinical Characteristics:

HALP was significantly associated with Anastomotic leak, SSI, overall mortality and prolonged hospital stay. The demographic and clinical characteristics of both groups are given in Table 1.

Figure 1. Receiver Operating Characteristics (ROC) for HALP



Discussion

Esophagogastric cancers are common cancers. They are usually detected in advanced stages and therefore have poor prognosis. Although chemotherapy and radiotherapy are useful adjuncts in treatment of these cancers, surgery is the only modality which can offer long term survival in these patients.[14] However, esophageal resections are associated with high postoperative morbidity and mortality rates.[15] The need for a simple, yet effective prognostic tool to determine the early post operative course is imperative to effect decision making. Although various scores exist to ascertain the operative risk of surgery, including ASA, APACHE II, POSSUM, these are general scores used in all types of surgeries. Few scores have been developed for risk prediction in esophagogastric surgeries, one of which is the O-POSSUM score. This score is complicated and difficult to use in daily practice. Other scores have also been developed including the Preoperative Esophagectomy Risk (PER) score[16] and esophagectomy Surgical Apgar Score (eSAS)[17], but these have yet not been widely accepted in clinical practice.

The HALP score was specifically developed to estimate long term survival after surgery in gastric

carcinoma and has been validated in many other cancers, including esophageal cancers. However, its use to predict the short-term outcomes after surgery has not been evaluated. As nutrition and immunological factors play important roles in the outcome after surgery, the HALP score as a surrogate marker of immune-nutritional status of the patient may be useful in predicting the post operative course after surgery. Furthermore, as esophageal cancer patients are prone to poor nutritional status due to prolonged undernutrition as a result of the location of the tumor, the HALP score may be useful to direct the management prior to surgery.

This study explored the association between the preoperative HALP score and clinical characteristics; and short-term morbidity and mortality outcomes in patients undergoing curative intent surgery in esophago-gastric cancers. The results demonstrated that HALP score is a good prognostic indicator for poor post-operative outcomes in this patient cohort. At a cut-off score of 38, HALP demonstrated sensitivity of 86.7% and specificity of 87.5% in detecting post-operative complications.

Chen et al. were the first to evaluate the role of the HALP score in prognostication of gastric cancer. Their findings suggested that HALP was closely associated with clinicopathological features and was an independent prognostic factor in gastric cancer patients. Their cohort of 1332 patients was randomly divided into training and validation sets and subsequent analysis revealed the HALP cut-off point of 56.8.8 In our study, the HALP cut-off point is lower at 38, although other studies have suggested cut-off points as low as 15 for prognostication.[10,18]

In our study, HALP score was significantly associated with post-operative complications. The Low HALP score group had a significantly higher rate of anastomotic leakage. The High HALP score group did not have any anastomotic leakage. Similar findings were present for surgical site infections, with the Low HALP group having significantly higher rates of SSI. This may be explained because anastomosis and wound integrity are highly dependent on patient immune-nutritional status. Malnourished patients would have a poor healing capacity leading to anastomosis breakdown and wound infection, although this relationship with post operative outcomes was not found in their study by Yalav et al.18 Our patient cohort had four mortalities, all of them because of post operative complications. Two patients had complications of anastomotic break-down while two other patients had respiratory complications and sepsis each. All four mortalities occurred in the Low HALP group. Other studies have not found a direct association between early postoperative deaths and Low HALP score, although short term mortality in patients with acute pancreatitis was reliably predicted by HALP.[11]

Our findings suggest the significant role of HALP score in predicting the short-term post operative outcomes in patients with esophago-gastric cancers undergoing curative resection. Although our study is prospective, it has limitations of being single-centered and with a small patient cohort. These findings should be confirmed by multicenter and larger sample size studies.

To the best of our knowledge, this is the first study evaluating role of HALP score in predicting outcomes after surgery in esophageal cancer from Nepal.

Conclusion

HALP score can be a good prognostic indicator for patients with esophago-gastric cancers undergoing curative resection. Larger prospective studies should be done to further

assess the usefulness of this remarkable immune-nutritional index.

References

1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA: A Cancer Journal for Clinicians. 2021;71(3):209-249.
2. Janaki Dotel Uprety BT Sarojini Sharma, Babita Subedi and Durga Khanal. Trends of Oesophageal cancer in Nepalese scenario.
3. Sjoquist KM, Burmeister BH, Smithers BM, et al. Survival after neoadjuvant chemotherapy or chemoradiotherapy for resectable oesophageal carcinoma: an updated meta-analysis. The Lancet Oncology. 2011;12(7):681-692.
4. Pirozzolo G, Gisbertz SS, Castoro C, van Berge Henegouwen MI, Scarpa M. Neutrophil-to-lymphocyte ratio as prognostic marker in esophageal cancer: a systematic review and meta-analysis. Journal of Thoracic Disease. 2019;11(7):3136.
5. Gou M, Zhang Y. Pretreatment platelet-to-lymphocyte ratio (PLR) as a prognosticating indicator for gastric cancer patients receiving immunotherapy. Discover Oncology. 2022;13:118.
6. Kuroda K, Toyokawa T, Miki Y, et al. Prognostic impact of postoperative systemic inflammatory response in patients with stage II/III gastric cancer. Scientific Reports. 2022;12(1).
7. Aoyama T, Ju M, Komori K, et al. The Platelet-to-Lymphocyte Ratio Is an Independent Prognostic Factor for Patients With Esophageal Cancer Who Receive Curative Treatment. In Vivo. 2022;36(4):1916.
8. Chen XL, Xue L, Wang W, et al. Prognostic significance of the combination of preoperative hemoglobin, albumin, lymphocyte and platelet in patients with gastric carcinoma: a retrospective cohort study. Oncotarget. 2015;6(38):41370-41382.
9. Hu SJ, Zhao XK, Song X, et al. Preoperative maximal voluntary ventilation, hemoglobin, albumin, lymphocytes and platelets predict postoperative survival in esophageal squamous cell carcinoma. World journal of gastroenterology. 2021;27(4):321-335.
10. Feng JF, Wang L, Yang X. The preoperative hemoglobin, albumin, lymphocyte and platelet (HALP) score is a useful predictor in patients with resectable esophageal squamous cell carcinoma. Bosnian journal of basic medical sciences. 2021;21(6):773-780.
11. Güler İ, Ustaalioğlu İ. Predictive power of HALP score in estimating short-term mortality in patients with acute pancreatitis. Ulus Travma Acil Cerrahi Derg. 2023;29(10):1098-1102.
12. Low DE, Alderson D, Cecconello I, et al. International Consensus on Standardization of Data Collection for Complications Associated With Esophagectomy: Esophagectomy Complications Consensus Group (ECCG). Ann Surg. 2015;262(2):286-294.
13. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care–associated infection and criteria for specific types of infections in the acute care setting. American Journal of Infection Control. 2008;36(5):309-332.
14. Bausys A, Mazeikaite M, Bickaite K, Bausys B, Bausys R, Strupas K. The Role of Prehabilitation in Modern Esophagogastric Cancer Surgery: A Comprehensive Review. Cancers (Basel). 2022;14(9):2096.
15. Thakur B, Devkota M, Bhandari N, Shrestha S, Kharel A. Minimally invasive esophagectomy/ gastroesophagectomy for cancer - Long term results from a single institution. Nepalese Journal of Cancer. 2022;6(2):7-15.
16. Reeh M, Metze J, Uzunoglu FG, et al. The PER (Preoperative Esophagectomy Risk) Score: A Simple Risk Score to Predict Short-Term and Long-Term Outcome in Patients with Surgically Treated Esophageal Cancer. Medicine. 2016;95(7):e2724.
17. Xing XZ, Wang HJ, Qu SN, et al. The value of esophagectomy surgical apgar score (eSAS) in predicting the risk of major morbidity after open esophagectomy. Journal of Thoracic Disease. 2016;8(7).
18. Yalav O, Topal U, Unal AG, Eray IC. Prognostic significance of preoperative hemoglobin and albumin levels and lymphocyte and platelet counts (HALP) in patients undergoing curative resection for colorectal cancer. Annali italiani di chirurgia. 2021;92:283-292.