



Cachexia index and its relationship with resection operability in patients with gastric adenocarcinoma

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Abstract

Introduction: Gastric cancer is one of the relatively common malignancies all over the world, and is one of major problems of health care system. Nowadays, importance of cachexia is demonstrated in prognosis of various malignancies. The aim of the present study was to evaluate frequency of cachexia index and its relationship with resection operability in patients with gastric adenocarcinoma.

Methods: In a descriptive-analytical study, 36 patients with gastric adenocarcinoma who referred to Imam Reza and Sina educational medical centers of Tabriz University of Medical Sciences, Tabriz, Iran, for surgery procedures, were included and evaluated in the study. Skeletal muscle index (SMI) was calculated using computed tomography (CT)-scan before performing surgery, patients' cachexia index was calculated by the following formula:

$$\frac{\text{SMI} \times \text{Albumin (ALB)}}{\text{neutrophil to lymphocyte ratio (NLR)}}$$
 Cachexia syndrome, patients' weight loss, resection operability, and cachexia index were evaluated in patients.

Results: Among 36 patients whom were studied, 25 patients (69.4%) were men, and 11 patients (30.6%) were women. Cachexia was seen in 5 patients (13.9%). In terms of gastrotomy operability, 26 patients (72.2%) were operable, and 10 patients (27.8%) were non-operable. Gastrotomy operability in patients with cachexia were significantly less than patients without cachexia syndrome ($P = 0.001$). No significant differences were seen in cachexia index of operable and non-operable patients ($P = 0.105$).

Conclusion: Based on the findings of the present study, gastrotomy operability in patients with cachexia was significantly less than patients without cachexia syndrome; but operable and non-operable patients do not have significant differences in cachexia in comparison to each other.

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Introduction

Gastric cancer is one of the most common malignancies worldwide. Although there has been a considerable advance in its treatment, the five-year survival is low.¹ Gastric cancer is the most common and second most common malignancy in men and women, respectively in Iran.^{2,3} The signs and symptoms of this malignancy are unexplained weight loss, anorexia, dyspepsia, fullness feeling in the

epigastrium, early satiety, nausea and vomiting. Early attention to these signs and symptoms leads to early diagnosis of the disease.⁴

In spite of outstanding advances in the surgical techniques and use of adjuvant chemotherapy, the long-term survival of the disease is not good.⁵ Considering all these, gastric cancer is considered a major health-care associated issue worldwide. Besides

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surgery, which is the mainstay therapy for gastric cancer, the nutritional state of the patient before surgery has an important impact on the general condition and post-surgical long-term outcomes of the patient.^{6,7} Cachexia is a clinical syndrome;⁸ a patient with advanced cachexia experiences, severe weight loss, significant anorexia, fatigue, anaemia and oedema.⁹ The mentioned presentation and its severity may change in the early-onset forms of cachexia.¹⁰

There has been no single definition of cachexia that all scientists would agree upon, but generally an unexplained weight loss more than 10% in a 6-month period is equivalent to cachexia happening in 30%-50% of gastrointestinal (GI) problems.¹¹ Anorexia and poor nutrition which happen during cachexia stem from the changes in the GI system, and protein as well as fat metabolism leads to the muscle volume and adipose tissue loss.^{12,13} The mentioned volume loss is also seen in the respiratory muscles which finally causes pulmonary failure and dyspnea.¹⁴

Cachexia syndrome is usually considered to be a one-way, irreversible road. However, in some inoperable cases of malignancies, nutritional interventions have been shown to have promising effects on their weight gain.¹⁵ This study aimed to evaluate the frequency of severe weight loss and the possibility of surgical resection in patients with gastric adenocarcinoma.

Methods

Gastric cancer is one of the most common malignancies worldwide. Although there has been a considerable advance in its treatment, the five-year survival is low.¹ Gastric cancer is the most common and second most common malignancy in men and women, respectively in Iran.^{2,3} The signs and symptoms of this malignancy are unexplained weight loss, anorexia, dyspepsia, fullness feeling in the epigastrium, early satiety, nausea and vomiting. Early attention to these signs and symptoms leads to early diagnosis of the disease.⁴

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Results

Out of 36 patients enrolled into the study, 25 (69.4%) patients were men and 11 (30.6%) patients were women, who aged between 46 and 85 years with a mean of 61.10 ± 12.37 years. The average time in which the patients had a final diagnosis of gastric adenocarcinoma was 4.47 ± 3.11 months ranging from 1 to 13 months. Table 1 shows

the signs and symptoms of gastric cancer in studied patients.

Table 1. Signs and symptoms of patients

Variables	Rate
Feeling fullness in the epigastrium	31 (86.1)
Persistent heartburn	25 (69.4)
Anorexia	17 (47.2)
	7.53 ± 6.44 months (2-24)
Unexplained vomiting	16 (44.4)
Blood in the stool	10 (27.8)
Weight loss	16 (41.7)
	4.42 ± 2.04 kg (2-9)
Clinical cachexia	5 (13.9)

Data were shown as frequency (%) and mean ± standard deviation (SD).

Table 2 illustrates the clinical, laboratory and CT-scan findings of the included patients.

Table 2. Clinical, laboratory and computed tomography (CT)-scan findings of patients

Variables	Mean ± SD
Weight (kg)	67.83 ± 15.86 (38-87)
Height (cm)	170.03 ± 15.86 (150-183)
BMI (kg/m ²)	23.14 ± 3.89 (17.84-29.75)
Serum ALB (g/dl)	3.59 ± 0.21 (3.3-3.9)
Serum neutrophils (%)	73.91 ± 15.88 (42.20-90.80)
Serum lymphocytes (%)	17.76 ± 11.60 (6.00-43.80)
NLR	6.50 ± 4.63 (0.97-15.00)
SMI	55.44 ± 8.01 (40-65)
Cachexia index	56.85 ± 49.52 (12-169)

SD: Standard deviation; BMI: Body mass index; ALB: Albumin; NLR: Neutrophil to lymphocyte ratio; SMI: Skeletal muscle index

26 (72.2%) patients were considered to be operable and 10 (27.8%) patients were inoperable. Table 3 shows the frequency of the operability of the patients according to the presence of clinical cachexia syndrome.

Based on table 3, rate of operability in patients with clinical cachexia was significantly lower than patients without clinical cachexia (P = 0.001). Mean of cachexia index in operable and inoperable patients were 53.78 ± 19.35 and 59.84 ± 18.98, respectively. There were no significant

differences in mean cachexia index between operable and inoperable patients (P = 0.105).

Discussion

Loss of body mass (either adipose or non-adipose) is associated with the increased risk of chronic diseases and their related disabilities. Further, body adipose mass is directly correlated with the survival of patients with malignancies or severe ailments.^{17,18} Due to the importance of gastric cancer in our region, we evaluated the frequency of severe weight loss and the possibility of surgical resection in patients with gastric adenocarcinoma. In a group of 36 patients with gastric adenocarcinoma, those with clinical cachexia syndrome had significantly higher rate of non-operability. However, the operable and non-operable groups had no significant difference in their cachexia index.

In a study by Kim et al., 250 patients with renal cell carcinoma who underwent radical nephrectomy, were followed up for an average of 33 to 43 months. 37 patients (14.8%) who had at least one sign/symptom indicating cachexia, were considered cachectic. This was associated with a low survival rate in these patients.¹⁹ In another study by Davidson et al., the survival rate of patients with pancreas cancer was assessed in two groups. Patients who had lost more than 1 kg in eight weeks were grouped in the weight losing category. This study showed that this group had a lower survival rate compared to the other one.²⁰ In line with the above-mentioned studies, we showed that the operability rate of cachectic patients was lower than that of non-cachectic ones, indicating a lower survival rate in the former.

In another study by Capuano et al., the effect of weight loss on the prognosis of patients with head and neck malignancies was evaluated in 40 patients.

Table 3. Frequency of the operability and presence of clinical cachexia

	Cachexia syndrome	Patients with cachexia syndrome (n = 5) [n (%)]	Patients without clinical cachexia (n = 31) [n (%)]
Operability			
Operable		0 (0)	26 (83.9)
Inoperable		5 (100)	5 (16.1)
P		0.001	

The authors showed that weight loss more than 20% before the initiation of treatment is directly associated with early death, higher mortality, higher infection rate, higher admission to the hospital, and lower survival rate.²¹ The results of this study showed that the patients who were suffering from cachexia syndrome had a lower operability and survival rates compared to the others.

In a study by Sebastiano et al., the impact of cachexia syndrome on the prognosis of 50 patients with pancreas cancer was assessed. The authors evaluated the body adipose and muscular mass changes using CT-scan, and showed that in average the patients had lost 1.72 kg of muscular and 1.04 kg of adipose tissue mass. They concluded that the higher weight loss rate is linked to the lower survival period.²² However, in this study, we could not show a statistically significant link between cachexia index and operability/non-operability of the patients.

In another study by Dalal et al., the association between BMI as well as longitudinal body composition alterations with the survival rate of 41 patients with pancreas cancer was assessed. These patients were non-operable, and received chemo-radiation. Body composition was assessed using CT-scan before and after radiation (a 104-day period). In average, the patients had 5% weight loss, 13% adipose tissue loss, and 4% muscle mass loss. Advanced age, underlying obesity, increased weight loss, and adipose and muscle mass loss bore a lower survival rate.²³ In line with that, in this study, the operability of the patients with gastric adenocarcinoma had a reverse link with cachexia syndrome.

Yip et al. assessed sarcopenia (muscle mass loss more than 2 SD) using CT-scan before and after pretreatment with N-acetylcysteine (NAC) in 35 patients with esophageal cancer. These patients underwent esophagectomy and received chemotherapy. The results of this study showed that there was

no significant link between changes in the body mass and patients' survival rate.²⁴ We did not directly assess the survival rate of the patients in this study; thus, we cannot compare the results with that of Yip et al.'s study.

Conclusion

The importance of cachexia syndrome and weight loss in the final outcome of patients with malignancy is undeniable. Our results showed that clinical cachexia significantly lowers the operability rate of patients with gastric adenocarcinoma. Thence, early detection of this syndrome in patients with gastric malignancy will lower the need for unnecessary surgeries.

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Authors' Contribution

Study conception and design: Alireza Barband, Farzad Kakaei, Reza Javadrashid

Acquisition of data: Mehrangiz Ebrahimi-Mameghani, Mohammadreza Mafi

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Critical revision: Alireza Barband, Farzad Kakaei, Reza Javadrashid.

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Conflict of Interest

Authors have no conflict of interest.

Ethical Approval

This study was approved by the Medical Ethics Committee of Tabriz University of Medical Sciences with registration code of 94/3-10/18.

References

1. Ang TL, Fock KM. Clinical epidemiology of gastric cancer. *Singapore Med J* 2014; 55(12): 621-8. DOI: 10.11622/smedj.2014174
2. Sadjadi A, Nouraie M, Mohagheghi MA, Mousavi-Jarrahi A, Malekezadeh R, Parkin DM. Cancer occurrence in Iran in 2002, an international

- perspective. *Asian Pac J Cancer Prev* 2005; 6(3): 359-63.
3. Malekzadeh R, Derakhshan MH, Malekzadeh Z. Gastric cancer in Iran: Epidemiology and risk factors. *Arch Iran Med* 2009; 12(6): 576-83.
 4. Songun I, Putter H, Kranenbarg EM, Sasako M, van de Velde CJ. Surgical treatment of gastric cancer: 15-year follow-up results of the randomised nationwide Dutch D1D2 trial. *Lancet Oncol* 2010; 11(5): 439-49. DOI: 10.1016/S1470-2045(10)70070-X
 5. Sant M, Allemani C, Santaquilani M, Knijn A, Marchesi F, Capocaccia R. EUROCARE-4. Survival of cancer patients diagnosed in 1995-1999. Results and commentary. *Eur J Cancer* 2009; 45(6): 931-91. DOI: 10.1016/j.ejca.2008.11.018
 6. Ray-Coquard I, Cropet C, Van Glabbeke M, Sebban C, Le Cesne A, Judson I, et al. Lymphopenia as a prognostic factor for overall survival in advanced carcinomas, sarcomas, and lymphomas. *Cancer Res* 2009; 69(13): 5383-91. DOI: 10.1158/0008-5472.CAN-08-3845
 7. Schwegler I, von Holzen A, Gutzwiller JP, Schlumpf R, Muhlebach S, Stanga Z. Nutritional risk is a clinical predictor of postoperative mortality and morbidity in surgery for colorectal cancer. *Br J Surg* 2010; 97(1): 92-7. DOI: 10.1002/bjs.6805
 8. Mondello P, Mian M, Aloisi C, Fama F, Mondello S, Pitini V. Cancer cachexia syndrome: Pathogenesis, diagnosis, and new therapeutic options. *Nutr Cancer* 2015; 67(1): 12-26. DOI: 10.1080/01635581.2015.976318
 9. Fearon K, Strasser F, Anker SD, Bosaeus I, Bruera E, Fainsinger RL, et al. Definition and classification of cancer cachexia: An international consensus. *Lancet Oncol* 2011; 12(5): 489-95. DOI: 10.1016/S1470-2045(10)70218-7
 10. Argiles JM, Moore-Carrasco R, Fuster G, Busquets S, Lopez-Soriano FJ. Cancer cachexia: The molecular mechanisms. *Int J Biochem Cell Biol* 2003; 35(4): 405-9.
 11. Fearon KC, Voss AC, Huestad DS. Definition of cancer cachexia: Effect of weight loss, reduced food intake, and systemic inflammation on functional status and prognosis. *Am J Clin Nutr* 2006; 83(6): 1345-50. DOI: 10.1093/ajcn/83.6.1345
 12. Lenk K, Schuler G, Adams V. Skeletal muscle wasting in cachexia and sarcopenia: Molecular pathophysiology and impact of exercise training. *J Cachexia Sarcopenia Muscle* 2010; 1(1): 9-21. DOI: 10.1007/s13539-010-0007-1
 13. Tisdale MJ. Are tumoral factors responsible for host tissue wasting in cancer cachexia? *Future Oncol* 2010; 6(4): 503-13. DOI: 10.2217/fon.10.20
 14. Viola R, Kiteley C, Lloyd NS, Mackay JA, Wilson J, Wong RK. The management of dyspnea in cancer patients: a systematic review. *Support Care Cancer* 2008; 16(4): 329-37. DOI: 10.1007/s00520-007-0389-6
 15. Baldwin C, Spiro A, McGough C, Norman AR, Gillbanks A, Thomas K, et al. Simple nutritional intervention in patients with advanced cancers of the gastrointestinal tract, non-small cell lung cancers or mesothelioma and weight loss receiving chemotherapy: A randomised controlled trial. *J Hum Nutr Diet* 2011; 24(5): 431-40. DOI: 10.1111/j.1365-277X.2011.01189.x
 16. Jafri SH, Prevgigliano C, Khandelwal K, Shi R. cachexia index in advanced non-small-cell lung cancer patients. *Clin Med Insights Oncol* 2015; 9: 87-93. DOI: 10.4137/CMO.S30891
 17. Jeon HG, Choi DK, Sung HH, Jeong BC, Seo SI, Jeon SS, et al. Preoperative prognostic nutritional index is a significant predictor of survival in renal cell carcinoma patients undergoing nephrectomy. *Ann Surg Oncol* 2016; 23(1): 321-7. DOI: 10.1245/s10434-015-4614-0
 18. Martin L, Birdsell L, MacDonald N, Reiman T, Clandinin MT, McCargar LJ, et al. Cancer cachexia in the age of obesity: Skeletal muscle depletion is a powerful prognostic factor, independent of body mass index. *J Clin Oncol* 2013; 31(12): 1539-47. DOI: 10.1200/JCO.2012.45.2722
 19. Kim HL, Han KR, Zisman A, Figlin RA, Beldegrun AS. Cachexia-like symptoms predict a worse prognosis in localized t1 renal cell carcinoma. *J Urol* 2004; 171(5): 1810-3. DOI: 10.1097/01.ju.0000121440.82581.d3
 20. Davidson W, Ash S, Capra S, Bauer J. Weight stabilisation is associated with improved survival duration and quality of life in unresectable pancreatic cancer. *Clin Nutr* 2004; 23(2): 239-47. DOI: 10.1016/j.clnu.2003.07.001
 21. Capuano G, Grosso A, Gentile PC, Battista M, Bianciardi F, Di PA, et al. Influence of weight loss on outcomes in patients with head and neck cancer undergoing concomitant chemoradiotherapy. *Head Neck* 2008; 30(4): 503-8. DOI: 10.1002/hed.20737
 22. Di Sebastiano KM, Yang L, Zbuk K, Wong RK, Chow T, Koff D, et al. Accelerated muscle and adipose tissue loss may predict survival in pancreatic cancer patients: the relationship with diabetes and anaemia. *Br J Nutr* 2013; 109(2): 302-12. DOI: 10.1017/S0007114512001067
 23. Dalal S, Hui D, Bidaut L, Lem K, Del FE, Crane C, et al. Relationships among body mass index, longitudinal body composition alterations, and survival in patients with locally advanced pancreatic cancer receiving chemoradiation: a pilot study. *J Pain Symptom Manage* 2012; 44(2): 181-91. DOI: 10.1016/j.jpainsymman.2011.09.010
 24. Yip C, Goh V, Davies A, Gossage J, Mitchell-Hay R, Hynes O, et al. Assessment of sarcopenia and changes in body composition after neoadjuvant chemotherapy and associations with clinical outcomes in oesophageal cancer. *Eur Radiol* 2014; 24(5): 998-1005. DOI: 10.1007/s00330-014-3110-4