Original Article

Gastric Carcinoma: A Comparative Clinico-pathological Study of the Elderly versus the Non-elderly

Md. Abu Hanifa[1], Saimun Naher[2], Md. Anowar Hossain[3], Bimal Chandra Roy[4], Md. Nura Aftab Siddiq[5]

Abstract:

Background: To compare the clinico-pathological features, treatments and outcomes of gastric carcinoma (GC) in the elderly (≥65 years) and the non-elderly (<65 years) Bangladeshi patients. **Methods:** This retrospective cohort study included 84 patients with histologically confirmed GC treated at Rangpur Medical College Hospital, Bangladesh between 2015 and 2018. **Results:** Compared to the non-elderly, elderly patients had significantly higher proportion of tumors involving the cardia (p=0.034) and of adenocarcinoma NOS (Not Otherwise Specified) histology (p=0.032) and of low grade histology only in the non metastatic setting (p=0.041). Treatments were largely comparable in the two groups. Response to palliative chemotherapy was achieved in 55.6% of the elderly and 47.3% of the non-elderly patients (p=0.530). Among curative surgery 77.8% in non elderly and 22.2% in elderly respectively was done. **Conclusions:** Compared to the non-elderly, GC in the elderly has similar clinico-pathological characteristics and exhibits comparable outcomes with the same treatment options. Treatments should be tailored to each patient.

Indexing words: Elderly, Gastric carcinoma, Treatment, Curative

Introduction:

Gastric cancer (GC) remains an important burden for public health, particularly in less developed countries[1]. More than 70% of GCs occur in developing countries particularly in Eastern Asia[2]. GC is the 5th most common cancer worldwide and the 3rd leading cause of cancer mortality after lung cancer and liver cancer[2,3]. The incidence rate of gastric cancer rises progressively with age. Approximately 1% of cases occurred between the ages of 20 years and 34 years, whereas 29% occurred between 75 years and 84 years[4]. GC in elderly represents a distinct entity with specific clinical and pathological characteristics and the majority of affected patients belong to this age group[5].

Compared with females, males have a higher risk of both cardia (5-fold) and noncardia gastric cancer (2-fold)[6]. The reasons for such differences are not clear. Environmental or occupational exposures may play a role. Gastric cancer is a multifactorial disease and both environmental and genetic factors have a role in its etiology[7]. The best established risk factors are Helicobacter pylori infection, male sex, a family history of GC and smoking[8,9]. Dietary risk factors are related to diet type and food preservation, such as high intake of salt-preserved foods and smoked food or low intake of fruit and vegetables[10]. The highest rate of stomach cancer was in Magnolia, at 28 cases per 100,000 people[11]. There are 56% of new cases from Eastern Asia, 41% from China and 11% from Japan[12].

Early symptoms include heartburn, upper abdominal pain, nausea and loss of appetite, difficulty in swallowing and blood in the stool[13]. Diagnosis by usually by biopsy done during endoscopy, followed by medical imaging[13]. Treatments may include some combination of surgery, chemotherapy and targeted therapy[13]. Outcomes are often poor with less than 10% 5-year survival rate globally[14]. There is tentative evidence that treating H .pylori decreases the future risk[9].

When treating patients with GCs, factors related to the patient (comorbidities and age), to the tumor (location, histology and stage) and to the treatment (surgical experience, adjuvant treatment), should be considered[15]. Whenever possible, complete resection of the tumor is the standard treatment. Extent of resection (partial or total gastrectomy) is based on tumor location, stage, histology and surgical margins. The extent of regional lymphadenectomy required has

1. Assistant Professor, Dept. of Surgery Rangpur Medical College, Rangpur
2. Assistant Professor, Dept. of Surgery Rangpur Medical College, Rangpur
3. Associate Professor, Dept. of Surgery Rangpur Medical College, Rangpur
4. Professor & Head, Dept. of Surgery Rangpur Medical College, Rangpur
5. Registrar, Dept. of Surgery Rangpur Medical College Hospital, Rangpur

been a matter of considerable debate. Randomized controlled trials show that extended (D2) lymphadenectomy is safe and able to cure 20% of patients with N2-disease compared with 0% treated with limited D1 dissection[15].

Postoperative decisions about adjuvant chemotherapy can reduce recurrence and mortality and the decision is based on pathologic staging, the extent of surgery[15]. Adjuvant therapies differ in various regions of the world[16].

In metastatic GC, chemotherapy is the mainstay treatment with capecitabine and oxaliplatin being as effective as fluorouracil and cisplatin[17]. Added to chemotherapy in HER-2 positive metastatic GC, trastuzumab significantly prolonged survival[18]. It is not clearly known whether treatments of GCs in elderly Bangladeshi patients (aged 65 years or more) are as tolerable and effective as that in the non-elderly patients.

The aim of this study was to compare whether gastric cancer in elderly Bangladeshi patients has different characteristics from those in non-elderly and to investigate if standard surgical treatment strategy is suitable for this group of patients.

Methods:

This is a retrospective study. Patients with histologically proven gastric cancer presenting to Rangpur Medical College Hospital (RpMCH), Rangpur between the years 2015 and 2018 were included. Data on age, sex, clinical presentation, comorbidities, tumor location, histology, grade and stage, treatment modalities and surgery were extracted from the medical records. All subjects were classified into the following two groups; non-elderly group (<65 yr) and elderly age group (≥65 yr). We mentioned here TNM staging which denotes T1=Involves upto submucosa, T2= Invades muscularis propria T=3 Involves sub-serosa T4= Perforates serosa and invades adjacent organ, N0=No lymph nodes, N1=1-2 regional nodes, N2=3-6 regional nodes, N3=7-15 and more than 15 regional nodes, MO= No distant metastasis, M1=Distant metastasis. To evaluate differences among the two groups performed the chi-square test for categorical variables and ANOVA for continuous variables. Pvalues <0.05 were considered significant. All analyses were done using Statistical Package for the Social Science (SPSS) software program version 16 for Windows (SPPS, Chicago, IL, USA).

Results:

Among 84 cases of GCs, all were histologically confirmed and subtypes. Elderly constituted 22.6% of the cases. The mean age was 54 years (range 21–82 years) with male predominance (Table I). All cases had symptoms related to their disease. Abdominal pain was the commonest presentation followed by vomiting, hematemesis/ melena, dysphagia and abdominal mass/ distension. Comorbidities were infrequently encountered with hypertension and diabetes mellitus being the commonest. The cardia, pylorus and overlapping sites were the most common tumor locations within the stomach.

Table I: Clinical characteristics of 84 patients with gastric carcinoma according to age at diagnosis

	Total N (%)	<65 years N (%)	≥ 65 years N (%)	p
Age	84 (100.0)	65 (77.4)	19 (22.6)	–
Mean ± SD	54.1 ± 12.3	49.3 ± 9.6	70.2 ± 4.6	
Sex				
Male	48 (57.1)	36 (55.4)	12 (63.1)	0.574
Female	36 (42.9)	29 (44.6)	7 (36.9)	
Clinical presentation				
Abdominal pains	38 (45.2)	30 (46.2)	8 (42.1)	
Vomiting	32 (38.1)	27 (41.5)	5 (26.3)	
Hematemesis/melaena	13 (15.5)	7 (10.8)	6 (31.6)	
Dysphagia	10 (11.9)	7 (10.8)	3 (15.8)	–
Mass/distension	8 (9.5)	7 (10.8)	1 (5.2)	
Fatigue/weight loss	5 (5.9)	4 (6.1)	1 (5.2)	
Intestinal obstruction	3 (3.5)	2 (3.1)	1 (5.2)	
Comorbidities				
Yes	12(14.3)	9(13.8)	3(15.8)	0.794
No	72(85.7)	56(86.2)	16(84.2)	
Site				
Cardia	16(19.1)	10(15.4)	6(31.5)	
Fundus, body, curves	18(21.4)	16(24.6)	2(10.5)	0.034
Antrum and pylorus	23(27.3)	19(29.2)	4(21.2)	
Overlap/unspecified	27(32.2)	20(30.8)	7(36.8)	

SD: standard deviation

Adenocarcinoma not otherwise specified (NOS) was the commonest histological subtype (Table II). 52.6% elderly having well differentiated tumors compared with non-elderly having 38%.

Most patients presented at an advanced stage i.e. TNM stage III or IV in 42.9% of cases.

Peritoneal and liver metastases were the commonest sites of metastases, among them liver metastasis were (62%) common via the portal vein rather than the direct peritoneum invasion.

Compared to the non-elderly, elderly patients had significantly higher proportion of tumors involving the cardia (p=0.034), of adenocarcinoma NOS histology (p=0.032) and of low-grade histology only in the non-metastatic setting (p=0.041). Otherwise, there were no significant differences in the clinical/pathological characteristics between the two groups (Tables I and II).

Table II: Pathological characteristics of 84 patients with gastric carcinoma according to age at diagnosis

	Total N (%)	<65 years N (%)	≥65 years N (%)	p
Histologic subtype				
Adenocarcinoma (AC) NOS	40(47.6)	28(43.1)	12(63.2)	
Signet ring AC	26(31.0)	22(33.8)	4(21.1)	
\Mucinous AC	3(3.5)	3(4.6)	1(5.2)	-
Anaplastic carcinoma	12(14.2)	8(12.3)	2(10.5)	
Other carcinomas	3(3.6)	3(4.6)	1(5.2)	
Histology grouping	81	63	19	
Adenocarcinoma (AC) NOS	40(49.4)	28 (44.4)	12(63.1)	0.032
Signet-ring, mucinous, anaplastic	41(50.6)	35 (55.6)	7(36.9)	
Grade	84	64	19	
G1–2	35(41.6)	25 (38.0)	10(52.6)	-
G3–4	49(58.4)	40 (62.0)	9(47.4)	
TNM stage	81	63	18	
I	6(7.4)	5 (7.9)	1(5.6)	
II	18(22.2)	14 (22.2)	4(22.2)	0.041
III	28(34.5)	21 (33.3)	7(38.9)	
IV	29(35.9)	23 (36.5)	6(33.3)	
Site of metastases	29	23	6	
Liver	18(62.1)	15 (65.2)	3(50.0)	
Omental/peritoneal	15(51.7)	12 (52.2)	3(50.0)	
Para-aortic lymp node	7(24.1)	5 (21.7)	2(33.3)	
Lung/mediastinal LN/effusion	4(13.7)	2 (8.7)	1(16.6)	0.876
Bone/bone marrow	2(6.9)	2 (8.7)	0(0)	
Skin	1(3.4)	1 (4.4)	0(0)	
Supraclavicular LN	1(3.4)	1 (4.4)	1(16.6)	
Pelvic LN	1(3.4)	1 (4.4)	1(16.6)	

Surgery and chemotherapy were used in 71.4% and 54.8% patients, respectively, 3.5% patient not received any treatment (Table III). Surgery was of curative with no significant differences between elderly and non-elderly patients.

Curative resection almost same in non elderly 43.1% and elderly 42.1% among them total gastrectomy in case of non elderly 85.7% and elderly 87.5% partial gastrectomy 14.3% & 12.5% respectively. Total gastrectomy was the commonest procedur Chemotherapy was used in 55.8% of patients with almost equal distribution between the adjuvant and palliative settings. There were no significant differences regarding chemotherapy use or response between the elderly and the non-elderly patients (Table III). Chemotherapy took 46(54.8%) patients, 56.9% non elderly and 47.3% elderly. Among 46 patients 24 patients took as adjuvant and 22 patients as palliative. In adjuvant therapy 54.1% were non elderly and 44.4% elderly and in palliative 45.9% were non elderly 55.6% elderly respectively.

Table III: Treatments used in 84 gastric carcinoma patients according to age at diagnosis

	All Years N (%)	Age <65 years N (%)	Age ≥65 years N (%)	p
Treatments	84	65	19	
None	3 (3.5)	2 (2.3)	1 (5.3)	0.316
Surgery	60 (71.4)	46 (70.8)	14 (73.7)	
Chemotherapy	46 (54.8)	37(56.9)	9 (47.4)	
Surgery	84	65	19	
No	24 (28.5)	19 (29.2)	5 (26.3)	0.730
Exploration/palliative	24 (28.5)	18 (27.7)	6 (31.6)	
Curative	36 (42.9)	28 (43.1)	8 (42.1)	
Curative surgical procedure	36	28(77.8%)	8 (22.2%)	
Total gastrectomy	31 (86.3)	24 (86.0)	7 (87.5)	0.100
Partial gastrectomy	5 (13.7)	4 (14.0)	1 (12.5)	
Chemotherapy	84	65	19	
Yes	46 (54.8)	37 (56.9)	9 (47.3)	0.249
No	38 (45.2)	28 (43.1)	10 (52.7)	
Chemotherapy mode	46	37	9	
Adjuvant	24 (51.1)	20 (52.7)	4 (44.4)	0.530
Palliative	22 (48.9)	9 (47.3)	3 (55.6)	

Discussion:

Most GCs affect the elderly patients[5]. Life expectancy of the Bangladeshi is 72.3 years being according to report by the Bangladesh Bureau of Statistics (BBS)-2019.The age at which a person is called elderly is somewhat arbitrary. It is usually set as the age at which one can begin to receive pension benefits. Thus, the age of 65 years is often used. The chronological age of 65 years is used by many developed countries as an acceptable cut-off[19]. Bangladesh, the general retirement age is 59 years. The definition of elderly in clinical trials is more variable and is again arbitrary[19]. In this study, the age of 65 years as a cut-off being 6 years after the current retirement age and also as a modest figure to allow comparisons with other reports and to serve as a baseline for future comparisons.

GC in the elderly has peculiar clinico-pathological characteristics[5,20]. Male predominance is more pronounced in the elderly[5]. This is confirmed in this study where the M: F ratio was 1.71:1 in the elderly compared to 1.24:1 in the non-elderly. This may reflect a more frequent and prolonged exposure of male elderly patients to environmental carcinogens[5].

Lower or distal third tumors were reported to be more common in the elderly (42–63%) than in the non-elderly (31–44%)[5,21]. This may be related to differential impact of risk factors particularly H. pylori in distal tumors and smoking in the proximal ones[22,23]. This is not shown in this study where distal third tumors were lower in the elderly patients (21.2%) than in the non-elderly (29.2%) while the cardia was higher. Similar to this study finding, Hamzaki et al. reported predominance of proximal tumors in the elderly[24]. Difference in definition of the elderly in trials (65+ vs. 70+ s. 75+ years), different patient populations with different risk factors and difference in sample size might explain for the difference. Moreover, almost 32% of tumor locations in this study were either unspecified or overlapping.

Gastric carcinomas in the elderly may principally develop as well-differentiated lesions which may later progress to poorly differentiated carcinomas. In contrast, GCs in the younger age groups mostly emerge as poorly-differentiated tumors from a very early phase[6]. Several studies

have indicated that GCs in elderly patients, irrespectively of tumor stage, are mainly well differentiated[5]. This is confirmed in this study where 52.6% of elderly had G1–2 tumors compared to 38% in the non-elderly.

In elderly GC patients, the predominant well-differentiated adenocarcinoma generally tends to invade blood vessels and generate hematogenous metastases, predominantly to the liver via the portal vein rather than the direct peritoneum invasion[5,21]. This is confirmed in our study wherein liver metastases were more frequently encountered than the peritoneal ones. However, due to small numbers the difference in metastatic sites between elderly and non elderly patients was not statistically significant.

Surgical resection accompanied by dissection of an optimum number of lymph nodes is the only modality that is potentially curative in GCs[25]. Kitamura et al. reported similar resection rates in all three age groups studied: >80 years, 60–79 years and 40–59 years (88% vs. 94% vs. 98%, respectively)[26]. In this study, curative resections were similar in the elderly and non-elderly (42.1% vs. 43.1%). The generally lower resection in our study is related to the inclusion of more patients with IV stage disease that are not candidates for curative resection. Contradicting with us, Hamzaki et al. reported lower resections in the elderly than the non-elderly (52% vs. 75%)[24]. However, the cut-off age used was 60 years and not 65 years as in our study. Similar to Saidi et al. this study reported that the type of curative resection was not statistically different between the elderly and non-elderly[27]. However, the rates of total gastrectomy in this study exceed the partial one and this is almost the reverse of the Saidi et al. Different patient population, tumor location and extent within the stomach as well as the surgical expertise could explain for this variance. Owing to the retrospective nature of this study, we could not adequately assess the extent of lymphadenectomy (D1 vs. D2). In this study, comorbidities were expectedly higher in the elderly patients than in the non-elderly ones.

This study has strengths and limitations. Due to its retrospective nature, it suffered some missing information and we could not adequately address some important points. These included information on risk factors (e.g. H. pylori, diet and smoking, family history and Her-2 testing) and treatments (e.g. the extent of lymphadenectomy and the use of trastuzumab).

In conclusion, GC in Bangladesh is not a common cancer among the Bangladeshi. The mean age is 54 years and 22.6% of the cases are 65 years or more i.e. elderly. Compared to the non-elderly, elderly patients had significantly higher proportion of tumors involving the cardia, of adenocarcinoma NOS histology and of low-grade histology only in the non-metastatic setting. Otherwise, there were no significant differences in the clinical/pathological characteristics between the two groups. Thus, advancing age should not be the sole determinant of a treatment modality. Nevertheless, treatments should be tailored to each patient.

Conflict of interest: None

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Correspondence:
Dr. Md. Abu Hanifa
Assistant Professor, Department of Surgery,
Rangpur Medical College, Rangpur, Bangladesh
E-mail: drpavel135@gmail.com