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Full Length Article

Gastric carcinoma at Tanta Cancer Center: A comparative retrospective clinico-pathological study of the elderly versus the non-elderly

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KEYWORDS

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Abstract *Background and aims:* To study the clinico-pathological features, treatments and outcomes of gastric carcinoma (GC) in the elderly (⩾65 years) and the non-elderly Egyptian patients.
Methods: This retrospective cohort study included 168 patients with histologically confirmed GC treated at Tanta Cancer Center between 2003 and 2007.
Results: Compared to the non-elderly, elderly patients had significantly higher proportion of tumors involving the cardia ($p = 0.034$) and of adenocarcinoma NOS histology ($p = 0.032$). Treatments were largely comparable in the two groups. Response to palliative chemotherapy was achieved in 44.4% of the elderly and 25.5% of the non-elderly patients ($p = 0.417$). The median overall survival (OS), disease-free survival (DFS) and progression-free survival (PFS) were 6, 17 and 3 months, respectively. The median OS was 4 months in the elderly compared to 9 months in the non-elderly ($p = 0.005$). The median DFS was 4 months in the elderly compared to 20 months in the non-elderly ($p = 0.004$). The median PFS was 2 months in the elderly compared to 3 months in the non-elderly ($p = 0.685$). In multivariate analysis, poor performance status was an independent predictor of poor OS, DFS and PFS. Non-curative or no surgery and lack of chemotherapy use were independent predictors of poor OS. Age was an independent predictor of poor DFS.
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.

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Introduction

The peak age for gastric cancer (GC) is 60–80 years [1]. GC in the elderly represents a distinct entity with specific clinical and pathological characteristics and the majority of affected patients belong to this age group [2]. Worldwide, GC is the 5th most common malignancy in both sexes representing 6.8% of their total with an estimated 950,000 cases in 2012. It is the 3rd leading cause of cancer death representing 8.8% of the total cancer mortality with an estimated 725,000 deaths in 2012. Incidence rates are about twice as high in men as in women and mortality rates are high in both sexes [3]. The best established risk factors are Helicobacter pylori infection, male sex, a family history of GC, and smoking. Dietary risk factors are related to diet type and food preservation, such as high intake of salt-preserved foods and dietary nitrite or low intake of fruit and vegetables [4]. More than 70% of GCs occur in developing countries particularly in Eastern Asia [3].

In Egypt, GC is the 12th most common cancer in both sexes representing 1.6% of the total cancers [3,5]. It is the 12th leading cause of cancer death representing 2.2% of the total cancer mortality [3]. This is shown in many Egyptian population-based cancer registries [6]. At the Egyptian National Cancer Institute (ENCI), GC is the 14th most common cancer representing 1.8% of cases in both sexes [7]. The median age of GC in the Egyptians is 56 years [5]. The incidence rises with age and 55% of cases occur between 50 and 70 years of age [8].

When treating patients with GCs, factors related to the patient (comorbidities, performance status [PS], and age), to the tumor (location, histology, and stage) and to the treatment (surgical experience, adjuvant treatment risk-benefit ratio) should be considered [9]. 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 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 [9]. Postoperative decisions about adjuvant chemotherapy and radiotherapy can reduce recurrence and mortality and the decision is based on pathologic staging, the extent of surgery (D0/D1 vs. D2/D3) and the risk–benefit ratio [9].

Adjuvant therapies differ in various regions of the world [10]. In the USA, the Intergroup 0116 trial established the use of postoperative chemo-radiotherapy using fluorouracil/leucovorin as a standard for patients who had upfront surgery [11]. In Europe, the MAGIC trial demonstrated the benefits of perioperative ECF chemotherapy [12]. In Asia, the ACTS-GC [13] and CLASSIC trials [14] established postoperative chemotherapy using S-1 or capecitabine/oxaliplatin as the standard of care after primary surgery that included D2 dissection. In metastatic GC, chemotherapy is the mainstay treatment with capecitabine and oxaliplatin being as effective as fluorouracil and cisplatin [15]. Added to chemotherapy in HER-2 positive metastatic GC, trastuzumab significantly prolonged survival [16]. Studies showed that elderly patients with non-metastatic GCs, curative gastrectomy with lymph node dissection [17] and adjuvant fluoropyrimidine-based chemotherapy [18] are reasonably tolerated and produce benefits comparable to those in the non-elderly.

It is not clearly known whether treatments of GCs in elderly Egyptian patients (aged 65 years or more) are as tolerable and effective as that in the non-elderly patients. The aim of the study was to evaluate safety and efficacy of GC therapy in elderly Egyptian patients and compare this to the non-elderly.

Methods

This is a retrospective study. Patients with histologically proven GC presenting to Tanta Cancer Center (TCC) between the years 2003 and 2007 were included. Data on age, sex, clinical presentation, comorbidities, tumor location, histology, grade and stage, treatment modalities, response, tolerance, relapse/progression, dates of diagnosis, surgery and relapse/progression, and last follow up were extracted from the medical records. The study was approved by the IRB of the Egyptian National Cancer Institute. Overall survival (OS) is defined as the time between diagnosis and death or last follow-up. Disease-free survival (DFS) is the time between curative surgery and recurrence or death. Progression-free survival (PFS) is the time between the start of palliative therapy and progression or death.

Statistical analysis

All analyses were done using SPSS® software program version 21 (Chicago, USA). The Chi squared or Fisher's exact test was used to compare nominal or categorical variables. Medians were compared using the Mann–Whitney's *U* test. Survival was calculated using the Kaplan Meyer method and groups were compared using the log-rank test. A probability (p) of less than 0.05 (two sided) was considered statistically significant. Stepwise Cox-regression Hazard Model was used to assess the independent impact on survival of parameters with a p-value of $\leqslant$0.0.05 in the log-rank test.

Results

Patients' characteristics

Between 2003 and 2007, 168 cases of GCs presented to TCC. All were histologically confirmed and subtyped. The median age was 54 years (range 21–82 years) with male predominance (Table 1). 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. Most patients had performance status (PS) of 1 or 2. The cardia, pylorus and overlapping sites were the most common tumor locations within the stomach. Adenocarcinoma not otherwise specified (NOS) was the commonest histological subtype (Table 2). Most patients presented at an advanced stage i.e. TNM stage III or IV and peritoneal and liver metastases were the commonest sites of metastases.

Elderly constituted 22.6% of the cases. 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,

Table 1 Clinical characteristics of 168 patients with gastric carcinoma according to age at diagnosis.

	Total *N* (%)	< 65 years *N* (%)	⩾65 years *N* (%)	*P*
	168 (100.0)	130 (77.4)	38 (22.6)	
Age				
Mean ± SD	54.1 ± 12.3	49.3 ± 9.6	70.2 ± 4.6	–
Sex				
Male	95 (56.5)	72 (55.4)	23 (60.5)	
Female	73 (43.5)	58 (44.6)	15 (39.5)	0.574
Clinical presentation				
Abdominal pains	75 (44.6)	60 (46.2)	15 (39.5)	
Vomiting	63 (37.5)	53 (40.8)	10 (26.3)	
Hematemesis/melena	26 (15.5)	14 (10.8)	12 (31.6)	
Dysphagia	20 (11.9)	14 (10.8)	6 (15.8)	
Mass/distension	15 (8.9)	14 (10.8)	1 (2.6)	
Fatigue/weight loss	11 (6.5)	9 (6.9)	2 (5.3)	
Intestinal obstruction	5 (3.0)	4 (3.1)	1 (2.6)	–
Comorbidities				
Yes	24 (14.3)	18 (13.8)	6 (15.8)	
No	144 (85.7)	112 (86.2)	32 (84.2)	0.794
Performance Status	166	128	38	
1–2	142 (84.5)	110 (85.9)	32 (84.2)	
3–4	24 (15.5)	18 (14.1)	6 (15.8)	0.795
Site				
Cardia	32 (19.0)	20 (15.4)	12 (31.6)	
Fundus, body, curves	37 (22.0)	33 (25.4)	4 (10.5)	
Antrum and pylorus	45 (26.8)	37 (28.5)	8 (21.1)	
Overlap/unspecified	54 (32.1)	40 (30.8)	14 (36.8)	0.047

SD: standard deviation.

Table 2 Pathological characteristics of 168 patients with gastric carcinoma according to age at diagnosis.

Characteristic	Total *N* (%)	Age < 65 years *N* (%)	Age ⩾65 years *N* (%)	*P*
Histologic subtype				
Adenocarcinoma (AC) NOS	80 (47.6)	56 (43.1)	24 (63.2)	
Signet ring AC	52 (31.0)	44 (33.8)	8 (21.1)	
Mucinous AC	7 (4.2)	6 (4.6)	1 (2.6)	
Anaplastic carcinoma	23 (13.7)	19 (14.6)	4 (10.5)	
Other carcinomas	6 (3.6)	5 (3.8)	1 (2.6)	–
Histology grouping	162	125	37	
Adenocarcinoma (AC) NOS	80 (49.4)	56 (44.8)	24 (64.9)	
Signet-ring, mucinous, anaplastic	82 (50.6)	69 (55.2)	13 (35.1)	0.032
Grade	167	129	38	
G1–2	70 (41.9)	50 (38.8)	20 (52.6)	
G3–4	97 (58.1)	79 (61.2)	18 (47.4)	0.128
TNM stage	162	126	36	
I	13 (8.0)	11 (8.7)	2 (5.6)	
II	35 (21.6)	27 (21.4)	8 (22.2)	
III	56 (34.6)	42 (33.3)	14 (38.9)	
IV	58 (35.8)	46 (36.5)	12 (33.3)	0.876
Site of mets	58	46	12	
Omental/peritoneal	36 (62.1)	31 (67.4)	5 (41.7)	
Liver	30 (51.7)	24 (52.2)	6 (50)	
PALN LN	14 (24.1)	10 (21.7)	4 (33.3)	
Lung/mediastinal LN/effusion	7 (12.1)	4 (8.7)	3 (25.0)	
Bone/bone marrow	4 (6.9)	4 (8.7)	0 (0)	
Skin	1 (1.7)	1 (2.2)	0 (0)	
Supraclav LN	3 (5.2)	2 (4.3)	1 (8.3)	
Pelvic LN	2 (3.4)	1 (2.2)	1 (8.3)	–

NOS: not otherwise specified, LN: lymph node metastasis.

there were no significant differences in the clinical/pathological characteristics between the two groups (Tables 1 and 2).

Treatments

Surgery and chemotherapy were used in 71.4% and 54.8% patients, respectively, while chemo-radiotherapy was used in 7.1% (Table 3). Surgery was of curative intent in 44.8% of cases. Total gastrectomy was the commonest procedure and R0 resection was achieved in the majority of cases with no significant differences between elderly and non-elderly patients. Chemotherapy was used in 55.8% of patients with almost equal distribution between the adjuvant and palliative settings for a median of 3 cycles (range, 1–8). Cisplatin/Fluorouracil and Fluorouracil/calcium leucovorin were the two regimens used. In the palliative setting, the overall response rate was 30.2%. There were no significant differences regarding chemotherapy use, intent, regimens, cycle numbers or response between the elderly and the non-elderly patients (Table 3). Chemotherapy was tolerated comparably in both groups. Adjuvant chemo-radiotherapy was used occasionally and almost exclusively in the non-elderly patients. Radiotherapy or concomitant chemo-radiotherapy was given adjuvant to surgery in 4 and 8 non-elderly patients, respectively with positive surgical margin and nodal involvement.

Overall survival

After a median follow up of 29 months (95% confidence interval [CI], 9.7–48.3), 111 patients were dead. For the whole group, the median OS was 6 months (95% CI, 3.3–8.7). The median OS was 4 months in the elderly patients compared to 9 months in the non-elderly ($p = 0.005$) (Fig. 1). Compared to the other counterparts (Table 4), OS was significantly lower in patients who had advanced stage ($p = 0.001$), poor PS ($p < 0.001$), did not undergo curative surgery ($p < 0.001$) or

Table 3 Treatments used in 168 gastric carcinoma patients according to age at diagnosis.

	All years *n* (%)	Age <65 years *n* (%)	Age ⩾65 years *n* (%)	*P*
Treatments	168	130	38	–
None	5 (3.0)	3 (2.3)	2 (5.3)	
Surgery	120 (71.4)	92 (70.8)	28 (73.7)	
Chemotherapy	92 (54.8)	74 (56.9)	18 (47.4)	
Concomitant CRT (FU)	12 (7.1)	11 (8.5)	1 (2.6)	–
Surgery	163	127	36	0.316
No	43 (26.4)	35 (27.6)	8 (22.2)	
Exploration/palliative	47 (28.8)	35 (27.6)	12 (33.3)	
Curative	73 (44.8)	57 (44.9)	16 (44.4)	0.730
Curative surgical procedure	73	57	16	
Total gastrectomy	63 (86.3)	49 (86.0)	14 (87.5)	
Partial gastrectomy	10 (13.7)	8 (14.0)	2 (12.5)	0.100
Surgical residual after curative	73	57	16	
R0	63 (86.3)	49 (86.0)	14 (87.5)	
R1	10 (13.7)	8 (14.0)	2 (12.5)	1.000
90-day postoperative mortality	73	57	16	
Yes	5 (6.8)	4 (7.0)	1 (6.3)	
No	69 (93.2)	53 (93.0)	16 (93.7)	0.699
Chemotherapy	165	128	37	
Yes	92 (55.8)	74 (57.8)	18 (48.6)	
No	73 (44.2)	54 (42.2)	19 (51.4)	0.249
Chemotherapy mode	92	74	18	
Adjuvant	47 (51.1)	39 (52.7)	8 (44.4)	
Palliative	45 (48.9)	35 (47.3)	10 (55.6)	0.530
Chemotherapy regimen	92	74	18	
FL	53 (57.6)	43 (58.0)	10 (55.5)	
CF	39 (42.6)	31 (42.0)	8 (44.5)	1.000
Chemotherapy cycles	92	74	18	
Median (range)	3 (1–8)	3 (1–8)	2 (2–6)	0.249
Response to palliative chemotherapy	45	35	10	
CR	2 (4.4)	2 (5.7)	–	
PR	11 (24.4)	7 (20)	4 (40)	
SD	11 (24.4)	10 (28.9)	1 (10)	
PD	19 (42.8)	15 (43.5)	4 (40)	
Unknown	2 (4.4)	1 (2.9)	1 (10)	–
Response group	43	34	9	
Response	13 (30.2)	9 (26.5)	4 (44.4)	
No response	30 (69.8)	25 (73.4)	5 (55.6)	0.417

CRT: concomitant chemo-radiotherapy, FU: fluorouracil, CF: cisplatin/fluorouracil, FL: fluorouracil/calcium leucovorin, CR: complete response, PR: partial response, SD, stable disease, PD: progressive disease.

did not receive chemotherapy ($p = 0.005$). Patients who received chemotherapy had superior survival to those who did not receive such therapy ($p = 0.024$).

In patients who underwent curative surgery, the median OS was 35 months with adjuvant therapy significantly compared to 11 months without adjuvant therapy ($p = 0.02$). This was also demonstrated in the non-elderly (36 months vs. 11 months; $p = 0.011$) but not in the elderly (6 months vs. 5 months; $p = 0.459$). With adjuvant therapy, the median OS was 36 months in the non-elderly compared to 6 months in the elderly ($p < 0.001$).

In patients who did not undergo curative surgery, palliative chemotherapy produced a median OS of 6 months compared to 2 months in patients who did not receive chemotherapy at all ($p = 0.144$) with no significant difference between the elderly and non-elderly ($p = 0.963$).

In the multivariate analysis, poor performance status, non-curative or no surgery at all, and not receiving chemotherapy were independent predictors for poor survival. The hazard of death in patients with PS 3–4 was 2.69 times that of patients with PS 1–2 ($p < 0.001$). The hazard of death in patients who had no curative surgery or no surgery at all was 2.55 times that of patients who had curative surgery ($p < 0.001$). The hazard of death in patients who did not receive chemotherapy was 1.71 times that of patients who received chemotherapy ($p = 0.007$). Age was not an independent predictor of poor survival (Table 7).

Disease-free survival

For the 73 patients who underwent curative surgery, the median DFS was 17 months (95% CI, 5.4–28.6; Table 4). The median DFS was 4 months in the elderly patients compared to 20 months in the non-elderly ($p = 0.004$) (Fig. 2). The median DFS in patients with PS 0–2 was 17 months compared to 0.3 months in patients with PS 3 ($p < 0.001$). The median DFS was 23 months with adjuvant therapy compared to 5 months without adjuvant therapy ($p = 0.026$; Table 5). This trend was also shown in the non-elderly (27 months vs. 9 months; $p = 0.006$) but not in the elderly (3 months vs. 4 months; $p = 0.327$). Adjuvant therapy was associated with a median DFS of 27 months in the non-elderly compared to 3 months in the elderly ($p < 0.001$).

In the multivariate analysis, elderly age and poor PS were predictors of poor DFS. The hazard of death in patients $\geqslant$65 years was 2.61 times that of patients $<$65 years ($p = 0.015$). The hazard of death in patients with PS 3–4 was 4.49 times that of patients with PS 1–2 ($p = 0.004$; Table 7).

Table 4 Overall survival (OS) in 168 patients with gastric carcinoma.

Group	Number	2YOSR (SE)	5YOSR (SE)	*P*
All	168	20 (3.8)		–
Age				
$<$65 years	130	23.1 (4.6)	14.2 (4.2)	
$\geqslant$65 years	38	8.4 (5.6)	0 (0)	0.005
Sex				
Male	95	21.7 (5.5)	13.8 (5.1)	
Female	73	18.3 (5.3)	8.0 (4.2)	0.624
Site				
Cardia	32	18.5 (9.2)	0 (0)	
Fundus, body, curves	37	20.6 (8.1)	15.4 (7.5)	
Antrum, pylorus	45	22.8 (7.7)	15.2 (6.7)	
Overlapping, unspecified	54	17.5 (6.2)	7.0 (5.8)	0.657
Histology				
Adenocarcinoma NOS	80	19.1 (5.5)	3.2 (3.0)	
Other	82	19.6 (5.4)	14.7 (5.0)	0.841
Grade				
Low (1–2)	70	21.4 (6.1)	9.2 (5.5)	
High (3–4)	97	18.5 (4.9)	11.1 (4.1)	0.234
TNM stage group				
I–III	104	30.2 (5.7)	17.9 (5.4)	
IV	58	4.7 (3.2)	2.3 (2.3)	0.001
Performance status				
Good (1,2)	142	23.3 (4.4)	12.5 (3.8)	
Poor (3,4)	42	0 (0)	0 (0)	$<$0.001
Surgery				
No	43	6.2 (4.2)	3.1 (3.0)	
Non-curative	47	5.7 (3.9)	0 (0)	
Curative	73	43.4 (7.4)	28.0 (7.9)	$<$0.001
Adjuvant treatment				
Yes	47	55.0 (8.8)	41.2 (10.7)	
No	26	22.3 (11.0)	7.4 (7.1)	0.024
Chemotherapy				
Yes	92	25.1 (5.5)	16.3 (5.5)	
No	46	11.1 (5.1)	2.8 (2.7)	0.005

SE: standard error, 2YOSR: 2-year OS rates, 5YOSR: 5-year OS rates, AC NOS: adenocarcinoma not otherwise specified.

Table 5 Disease-free survival (DFS) in 73 patients with gastric carcinoma who had curative surgery.

Group	Number	2YDFSR (SE)	5YDFSR (SE)	*P*
All	73	39.0 (7.5)	24.3 (7.5)	–
<65 years	57	44.5 (8.5)	30.5 (8.9)	
⩾65 years	16	11.9 (11.1)	0 (0)	0.004
Sex				
Male	48	42.5 (9.7)	26.6 (9.5)	
Female	25	32.0 (11.9)	21.3 (11.8)	0.594
Site				
Cardia	21	28.7 (13.7)	0 (0)	
Fundus, body, curves	17	36.6 (14.2)	36.6 (14.2)	
Antrum, pylorus	17	57.2 (15.6)	34.2 (15.6)	
Overlapping, unspecified	18	31.9 (13.3)	31.9 (13.3)	0.420
Histology				
Adenocarcinoma NOS	38	37.1 (10.6)	16.5 (9.5)	
Other	32	45.7 (10.6)	36.6 (11.8)	0.861
Grade				
Low (1–2)	33	46.3 (12.2)	37.0 (12.8)	
High (3–4)	40	33.3 (9.2)	16.6 (8.2)	0.075
TNM stage group				
I–II	33	39.4 (10.9)	19.7 (11.4)	
III	37	42.0 (10.4)	30.0 (10.3)	0.619
Performance status				
Good (1,2)	1–2: 65	42.5 (8.0)	26.5 (8.1)	
Poor (3,4)	3: 6	0 (0)	0 (0)	<0.001
Surgery				
Total gastrectomy	59	39.2 (8.2)	22.9 (7.9)	
Partial gastrectomy	14	27.0 (20.8)	27.0 (20.8)	0.552
Adjuvant treatment				
Yes	47	45.2 (9.6)	33.0 (10.2)	
No	26	28.3 (11.2)	9.4 (8.6)	0.026

SE: standard error, 2YDFSR: 2-year DFS rates, 5YDFSR: 5-year DFS rates, NOS: not otherwise specified, CTX: chemotherapy.

Progression-free survival

For the 95 patients who did not undergo curative surgery, the median PFS was 3 months (95% CI, 2.2–3.8; Table 6). The median PFS was 2 months in the elderly patients compared to 3 months in the non-elderly ($p = 0.685$) (Fig. 3). The median PFS of patients with PS 0–2 was 3 months compared to one month in patients with PS 3–4 ($p = 0.002$). For the subset of patients who received palliative chemotherapy ($n = 45$), the median PFS was 3 months in the elderly compared to 9 months in the younger patients ($p = 0.890$) and the median OS was 5 months vs. 7 months respectively ($p = 0.963$).

Discussion

Most GCs affect the elderly patients [2]. Life expectancy of the Egyptians is 70–75 years being 5–6 years lower than the American [19]. The growth of elderly people in developing countries, including Egypt, is projected to be faster than any other segment of the population and at a rate higher than that of developed countries [19]. Thus, GCs in the elderly will be an emerging health problem.

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 60–65 years is often used. The chronological age of 65 years is used by many developed countries as an acceptable cut-off [20]. In Egypt, the general retirement age is 60 years but this is proposed to increase to 65 years starting from the year 2012 [21]. The definition of elderly in clinical trials is more variable and is again arbitrary [22]. In the current study, we adopted the age of 65 years as a cut-off being 5 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.

Our GC cohort is largely similar to an older smaller ($n = 55$) cohort treated at the ENCI between 1970 and 1977 [23]. Both cohorts were comparable regarding age at diagnosis, male predominance, clinical presentations, predominant histology and predominance of proximal tumors and pattern of metastases. However, surgery was more frequent and chemotherapy was not reported in the older series. This reflects the pattern of care during that time where surgery was the prevailing treatment option and chemotherapy was not as developed and as effective as it is nowadays. Our study provides more thorough and updated analyses particularly relating to treatments and their outcomes.

GC in the elderly has peculiar clinico-pathological characteristics [2,17,24]. Male predominance is more pronounced in the elderly [2]. This is confirmed in the current study where the M:F ratio was 1.53:1 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 [2].

Lower or distal third tumors were reported to be more common in the elderly (42–63%) than in the non-elderly (31–44%) [2,25]. This may be related to differential impact of risk factors particularly H. pylori in distal tumors and smoking in the

Table 6 Progression-free survival (PFS) in 95 patients with gastric carcinoma.

Group	Number	6MPFS (SE)	12MPFS (SE)	*P*
All	95	33.4 (5.4)	24.7 (5.5)	–
Age				
< 65 years	73	36.4 (6.2)	26.8 (5.8)	
⩾65 years	22	24.5 (10.4)	18.4 (9.4)	0.685
Sex				
Male	47	24.1 (7.1)	18.0 (6.5)	
Female	48	41.9 (7.7)	30.7 (7.4)	0.412
Site				
Cardia	11	10.6 (10.0)	10.6 (10.0)	
Fundus, body, curves	20	42.9 (12.8)	21.5 (10.9)	
Antrum, pylorus	28	29.6 (9.8)	24.7 (9.3)	
Overlapping, unspecified	36	39.1 (8.7)	31.1 (8.9)	0.169
Histology				
Adenocarcinoma NOS	42	32.9 (7.7)	20.9 (6.8)	
Other	50	35.0 (7.6)	29.1 (7.3)	0.969
Grade				
Low (1–2)	35	42.2 (8.5)	29.2 (8.0)	
High (3–4)	54	26.9 (6.8)	21.5 (6.4)	0.408
TNM stage group				
II–III	37	35.5 (9.3)	26.6 (8.8)	
IV	58	32.7 (6.8)	23.3 (6.3)	0.713
Performance status				
Good (1,2)	77	40.0 (6.2)	29.1 (5.9)	
Poor (3,4)	18	6.9 (6.6)	6.9 (6.6)	0.002
Surgery				
No	43	39.4 (8.0)	24.3 (7.3)	
Non-curative	47	28.8 (7.3)	25.9 (7.1)	0.293
Chemotherapy				
Yes	45	42.0 (7.8)	25.2 (7.1)	
No	47	25.5 (7.4)	22.3 (7.1)	0.549

SE: standard error, 6MPFSR: 6-month PFS rate, 12MPFSR: 12-month PFS rate, AC NOS: adenocarcinoma not otherwise specified.

Table 7 Multivariate analysis of factors affecting OS and DFS.

Variables in equation	OS (n = 147)		DFS (n = 71)	
	HR (CI)	*P*	HR (CI)	*P*
Performance status (1 and 2 vs. 3 and 4)	2.69 (1.61–4.50)	< 0.001	4.49 (1.61–12.49)	0.004
Curative surgery (No vs. yes)	2.55 (1.66–3.91)	< 0.001	–	–
Chemotherapy (No vs. yes)	1.71 (1.16–2.51)	0.007	–	–
Age (⩾65 years vs. < 65 years)	–	–	2.61 (1.20–5.69)	0.015

OS: overall survival, DFS: disease-free survival, HR = hazard ratio, CI: 95% confidence interval.

proximal ones [26,27]. This is not shown in the current study where distal third tumors were lower in the elderly patients (30.8%) than in the non-elderly (40%) while the cardia was higher. Similar to our findings, Hamzaki et al. reported predominance of proximal tumors in the elderly [28]. 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 30% of tumor locations in the current study were either unspecified (NOS) 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 [2]. Several studies have indicated that GCs in elderly patients, irrespectively of tumor stage, are mainly well differentiated [2]. This is confirmed in the current study where 52.6% of elderly had G1–2 tumors compared to 38.8% in the non-elderly. The difference was most marked in the non-metastatic setting (58% vs. 35%; p = 0.041).

Early studies had indicated that gastric cancer in elderly patients exhibits less metastasizing activity and that its pattern of metastases and recurrence is confined to the area around the primary focus in the upper abdomen including the liver [2,25,29]. Later, Holmes and Hearne did not find a significant positive correlation between age and advanced clinical stage in gastric cancer [29]. Similarly, we did not find significant correlation between age and stage. The early reports did not take the histological type into consideration nor the pathological stage of gastric cancer [2].

In elderly GC patients, the predominant well-differentiated intestinal type adenocarcinoma generally tends to invade

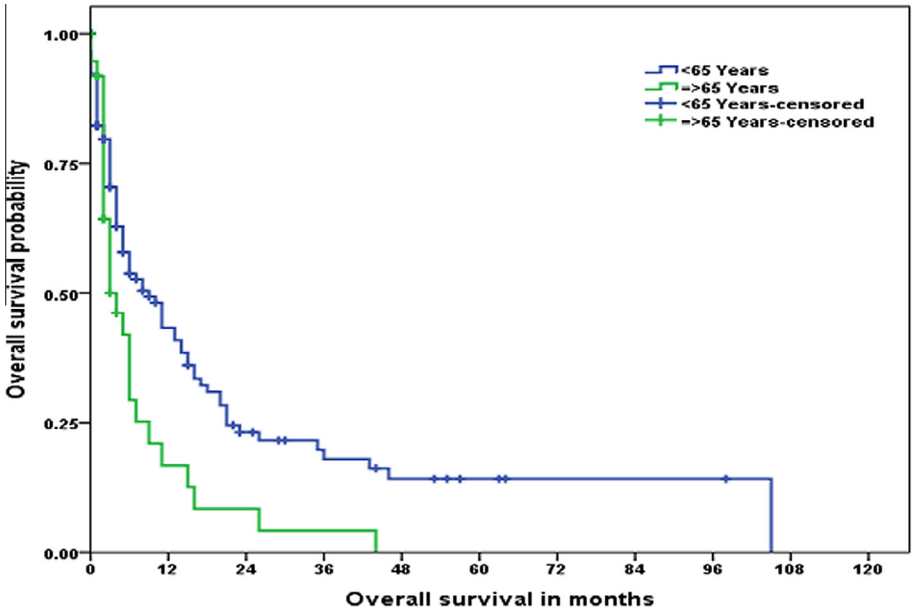

Figure 1 Overall survival in gastric carcinoma according to age groups.

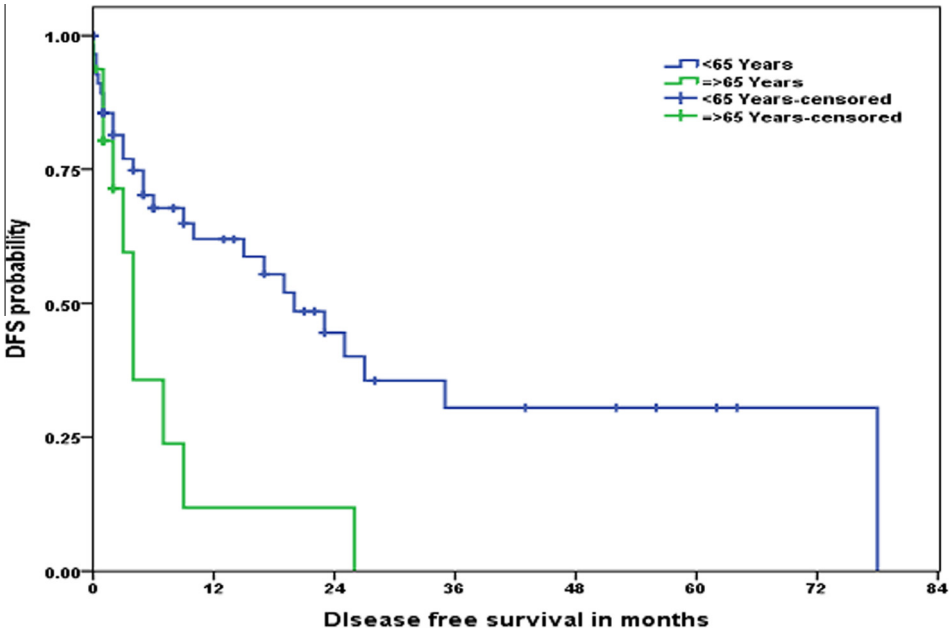

Figure 2 Disease free survival in gastric carcinoma according to age groups.

blood vessels and generate hematogenous metastases, predominantly to the liver via the portal vein rather than the direct peritoneum invasion [2,24,30]. This is confirmed in the current 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 [31]. Earlier studies reported 20%-50% rates of curative resections in the elderly in the 1950's–1980's. This increased to 50%-75% in more recent studies [2]. 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) [32]. In the current study, curative resections were similar in the elderly and non-elderly (44.4% vs. 44.9%). The generally lower resection in the current 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%) [28]. However, the cut-off age used was 60 years and not 65 years as in the current study. Similar to Saidi et al. we reported that the type of curative resection was not

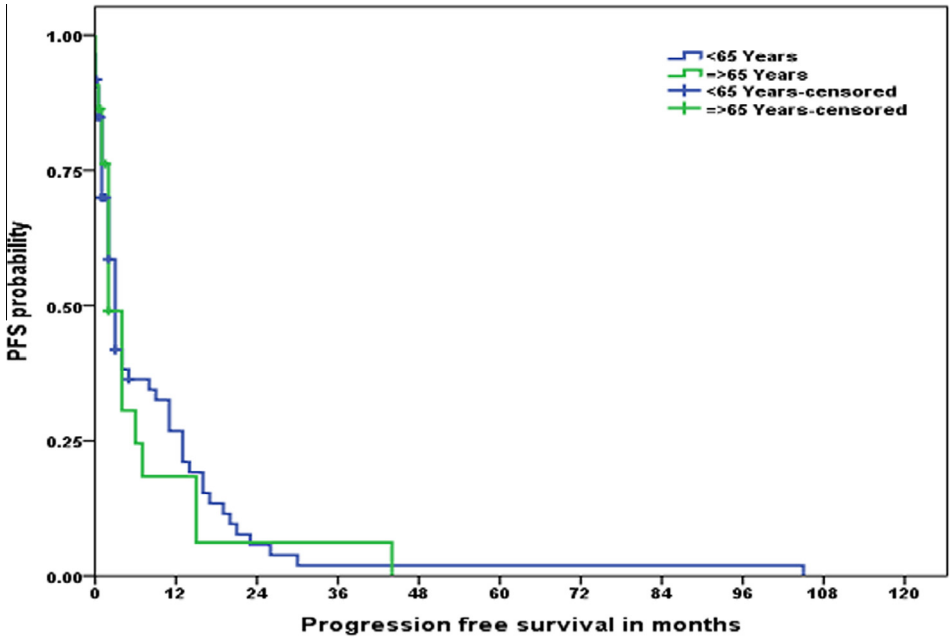

Figure 3 Progression-free survival in gastric carcinoma according to age groups.

statistically different between the elderly and non-elderly [33]. However, the rates of total gastrectomy in the current study surpassed the partial one and this is almost the reverse of the Saidi et al. figures. 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 the study, we could not adequately assess the extent of lymphadenectomy (D1 vs. D2). Surgical risk as determined by the American Society of Anesthesiologists (ASA) score, is significantly higher in the elderly patients owing to higher comorbidities [2]. The correlation between the ASA risk and postoperative mortality and morbidity in elderly patients with GCs is in controversy [34,35]. In the current study, comorbidities were expectedly higher in the elderly patients than in the non-elderly ones. Similar to Orsenigo et al. [35], we reported a similar 90-day mortality between the elderly and non-elderly. This could be attributed to advances in surgical and anesthetic techniques coupled with improved perioperative intensive care [2].

Despite R0 GC resections, a significant percentage will develop local–regional and/or distant recurrence [36]. Thus, to improve survival after curative resection in high-risk patients, adjuvant modalities are recommended [31]. Randomized controlled trials (RCTs) showed that DFS/RFS and OS were improved with the use of adjuvant therapy [12,13,37]. The median DFS/RFS increased from 19 to 30 months with CRT and from 13 to 19 months with ECF perioperative chemotherapy. The 36-month DFS rate increased from 60% to 72% with S-1 chemotherapy. The median OS increased from 27 to 36 months with CRT and from 20 to 25 months with ECF perioperative chemotherapy. The 36-month OS rate increased from 70% to 80% with S-1 chemotherapy. The current study showed the same trend both in the whole group as well as in the younger ones. In the whole group, adjuvant therapy significantly improved DFS (23 vs. 5 months, $p = 0.018$) and OS (35 vs. 11 months, $p = 0.02$) compared to no adjuvant treatment. In the non-elderly, adjuvant therapy significantly improved DFS (27 vs. 9 months, $p = 0.006$) and OS (36 vs. 11 months, $p = 0.011$) compared to no adjuvant treatment. However in the current study, the surgery alone arm had lower survival than the control arm in the mentioned trials. Reasons for this might be different patient population, small sample size and may be the poor prognostic features in the surgery only group.

In GC key adjuvant RCTs, elderly patients only represented a fraction of the total study population [12,13,37]. Thus, definitive clear conclusions are not reached regarding the use of various modalities (perioperative chemotherapy, post-operative chemotherapy or post-operative chemo-radiotherapy) in the elderly patients [2]. GC adjuvant RCTs did not find noticeable differences in benefits or toxicities between elderly and non-elderly patients [12,13,37]. This implies that elderly patients receiving adjuvant therapy have better outcomes than elderly patients in the surgery-alone arm and that elderly patients derive comparable benefits to those in the non-elderly. Contrarily, elderly in the current study receiving adjuvant chemotherapy drove no benefits additional to those of curative surgery and their outcomes were significantly inferior to those in the non-elderly.

Compared to no adjuvant treatment, we depicted that adjuvant chemotherapy in the elderly patients did not significantly improve DFS (median of 3 vs. 4 months) or OS (median of 6 vs. 5 months). Despite the absolute numbers are very small to substantiate this finding (adjuvant = 9, no adjuvant = 7), a recent population-based retrospective study of >1000 patients showed that chemotherapy did not improve survival in elderly patients. In fact, it tends to be detrimental [38]. Unfortunately, we also reported that elderly had significantly inferior DFS (median of 3 vs. 27 months) and OS (median of 6 vs. 36 months) compared to the non-elderly patients. While this contradicts with RCTs [12,13,37], it is similar to a big cohort of elderly GC patients [38] where advanced age at diagnosis was associated with poor survival. In that study, each year above 65 increases mortality by 3% [38]. The small

absolute numbers of the elderly patients who received adjuvant therapy ($n = 9$) and the high proportion of deaths among them ($n = 6$) contributed to the lower OS and DFS as death is an event in both endpoints. Moreover, elderly patients in the current study showed poor tolerance to adjuvant chemotherapy as death following the first cycle of adjuvant chemotherapy was encountered in 67% of the elderly (4/6) compared to 25% in the non-elderly patients (3/12). Additionally, living patient received only one cycle of adjuvant chemotherapy in 67% of the elderly (2/3) compared to 15% of the non-elderly (4/26).

Palliative systemic chemotherapy offers survival advantages and better quality of life than best supportive care alone and therefore represents the recommended treatment modality [31]. However, there is no single global standard regimen for the treatment of advanced gastric cancer [31]. Moreover, in elderly patients there is uncertainty regarding the extent of systemic palliative chemotherapy that should be offered [2]. Several trials reported on the use of palliative various chemotherapy regimens in the elderly patients [39–43]. These trials reported response rates between 17%-53% and median PFS/EFS between 3.1–6.4 months and median OS between 5–14 months and [39–43]. In the current study, response rate in the elderly was 44.4% with a median PFS of 6 months and median OS of 7 months. These represent the modest figures that fit within the range of the reported trials [39–43]. The higher figures in the mentioned trials may be related to the use of more efficacious regimens that incorporate oxaliplatin, docetaxel and capecitabine. For example, oxaliplatin-containing regimens (FLFOX4, FLO, and FLOX) produced 41%-53% RRs, 5.4–6.4 month PFS and 7.4–13.9 month OS in the elderly patients [15,40–42]. Similar to Trumper et al. we reported that elderly and non-elderly had comparable benefits (RR, PFS and OS) and toxicities [39].

The current 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). Nevertheless, and to the best of our knowledge, this is the largest Egyptian study on gastric carcinoma that reports on clinico-pathological features, treatments and outcomes.

In conclusion, GC in Egypt is not a common cancer among the Egyptians. The median age is 54 years and 22.6% of the cases are 65 years or more i.e. elderly. Apart from more proximal locations and more differentiated histologies in the elderly, clinical and pathological features were not significantly different in the elderly and non-elderly. Despite treatments were largely comparable, univariate analysis showed that OS and DFS were lower in the elderly compared to the non-elderly. However, age was not an independent predictor of poor OS, DFS or PFS in multivariate analysis. 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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