CHEMOTHERAPY FOR ELDERLY PATIENTS WITH GASTRIC CANCER: EXPERIENCE OF A BRAZILIAN CENTER

Quimioterapia para pacientes idosos com câncer gástrico: a experiência de um centro brasileiro

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ABSTRACT

OBJECTIVE: Gastric cancer (GC) is one of the most common cancers, and its incidence increases with age. The objective of the study was to evaluate the response rate (RR), overall survival (OS), and toxicity in patients aged over 60 years, with metastatic GC and who were undergoing chemotherapy. **METHODS**: This is a retrospective study developed in a university hospital. Medical records of patients treated in the last 4 years were analyzed. **RESULTS**: Twenty-one patients were included; the average age was 69.6 ± 7.6 years, 76.2% men, 61.9% Karnofsky Performance Status (KPS) ≥ 70, 85.7% had weight loss > 10% in 6 months, 28.6% had at least 2 sites of metastasis, and 42.9% had unfavorable histology (diffuse). Most of the patients (85.7%) were treated with combination regimens (4.6 cycles on average). Patients with better nutritional status had a non-statistically significant better tolerance to the treatment (p = 0.17). The median progression-free survival (PFS) was 9.0 months and the median OS was 13.8 months. Toxicity grade 1-2 was observed in 61.9%, and grade 3-4, in 14.3%. Less than two sites of metastasis (hazard ratio [HR] = 0.15; CI95% 0.02 – 0.93), absence of metastasis to non-regional lymph nodes (HR = 0.04; CI95% < 0.01 – 0.44), higher number of chemotherapy cycles (HR = 0.72; CI95% 0.53 – 0.97), objective response (HR = 0.06; CI95% 0.01 – 0.69) were associated with higher OS. Higher body mass index (BMI) was related with a not statistically significant better OS (HR = 0.84; CI95% 0.64 – 1.10). **CONCLUSIONS:** Patients treated in our hospital showed results compatible with literature. The doublet chemotherapy is feasible in elderly individuals with manageable toxicity.

KEYWORDS: stomach neoplasms; drug therapy; palliative care; cachexia; drug-related side effects and adverse reactions.

RESUMO

OBJETIVO: O câncer gástrico (CG) é um dos mais comuns e sua incidência aumenta com a idade. O objetivo deste estudo foi avaliar a taxa de resposta (TR), a sobrevida global (SG) e toxicidade em doentes com idade superior a 60 anos, com GC metastático e tratados com quimioterapia. **MÉTODOS**: Este é um estudo retrospectivo, desenvolvido em Hospital Universitário. Foram revisados prontuários de pacientes tratados nos últimos 4 anos. **RESULTADOS**: Foram incluídos 21 pacientes; a idade média foi de 69,6 ± 7,6 anos; 76,2% eram homens; 61,9% tinham *Karnofsky Performance Status* (KPS) ≥ 70; 85,7% tiveram perda de peso > 10% em 6 meses; 28,6% tinham 2 ou mais sítios de metástase; e 42,9% tinham histologia desfavorável (difuso). A maioria dos pacientes (85,7%) foram tratados com regimes de combinação de agentes, com média de 4,6 ciclos. Melhor estado nutricional mostrou uma tendência de melhor tolerância ao tratamento (p = 0,17). A sobrevida livre de progressão mediana foi de 9,0 meses e a SG mediana foi de 13,8 meses. Toxicidade de grau 1-2 foi observada em 61,9% e grau 3-4 em 14,3%. Menos de 2 sítios de metástases (*hazard ratio* [HR] = 0,15; IC95% 0,02 – 0,93), ausência de metástase para os linfonodos não-regionais (HR = 0,04; IC95% < 0,01 – 0,44), maior número de ciclos de quimioterapia (HR = 0,72; IC95% 0,53 – 0,97) e resposta objetiva (HR = 0,06; IC95% 0,01 – 0,69) foram associados com maior SG. IMC maior esteve relacionado com uma melhor SG, mas a diferença não foi estatisticamente significativa (HR = 0,84; IC95% 0,64 – 1,10). **CONCLUSÕES**: Os pacientes tratados em nosso hospital apresentaram desfechos compatíveis com a literatura. A quimioterapia com agentes combinados foi viável em idosos e teve toxicidade manejável.

PALAVRAS-CHAVE: neoplasias gástricas; quimioterapia; cuidados paliativos; caquexia; efeitos colaterais e reações adversas relacionados a medicamentos.

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INTRODUCTION

Gastric cancer (GC) is one of the most common malignancies in the world population, mainly in Asia and in developing countries.[1] Despite a decreasing incidence worldwide, gastric cancer increases with age and reaches its peak around the sixth and seventh decades of life.[2] In Brazil, more than 20 thousand new cases are expected in 2016 and almost 15 thousand deaths occurred in 2013.[3]

The world population has shown a progressive aging in recent decades, and, in Brazil, Brazilian Institute of Geography and Statistics (IBGE) data indicate a life expectancy of 74.6 years, which can lead to an increase in the number of elderly patients with cancer in the country. Factors related to the elderly patient such as decreased functional status, multiple comorbidities, often advanced stage, and limited social support may restrict access and adherence to treatment of neoplasia and, consequently, decrease the survival of these patients.[4] Moreover, weight loss and cachexia in cancer patients are common and associate with reduced tolerance to anticancer therapy[5] and shorter survival.[6]

Clinical conditions and comorbidities of elderly patients can directly affect survival or impair the tolerance to treatment, although most studies evaluated patients with other cancer sites.[7-16]

The cytotoxic treatment of metastatic GC demonstrated benefit in terms of overall survival (OS) and quality of life when compared with best supportive care.[17] Several drugs were tested as single agents for the treatment of metastatic GC, but were considered ineffective or poorly tolerated (response rates ranging between 6% and 30%).[18]

Systematic review and meta-analysis published in 2010 showed benefit in terms of OS for the combination of chemotherapeutic agents (platinum and fluoropyrimidine).[19] The agents classically combined were 5-FU and cisplatin. The 5-FU should be administered preferably by continuous infusion; therefore, it depends on long-term intravenous device and on an infuser that is not available in most of the Brazilian public health system services. Cisplatin has a number of toxicities such as nausea and nephrotoxicity, which may limit the treatment mainly in older patients. Capecitabine is an oral fluoropyrimidine that after metabolism is converted to 5-fluorouracil may be an option to infusional 5-FU.[20,21] Oxaliplatin demonstrated synergistic activity with 5-FU; however, neurotoxicity shows cumulative dose-limiting treatment.[22] REAL-2 trial compared capecitabine with infusional 5-FU and oxaliplatin to cisplatin for patients with advanced gastric adenocarcinoma and showed no inferiority between these drugs.[23]

The treatment of metastatic GC is still a challenge for clinicians. Although new drugs were developed, little benefit in terms of OS was observed. Moreover, the best combination of drugs in the first line setting and the best order of exposure on subsequent lines are not established.[24]

Few studies have been conducted exclusively in elderly patients. In large clinical trials, elderly patients were excluded or underrepresented mainly because they have other diseases that are exclusion factors.[25] Furthermore, elderly patients are seldom referred to the oncologist after cancer diagnosis and, once sent, have lower chance of being treated with chemotherapy.[26]

OBJECTIVE

The aims of this study were to present the experience of the service in the treatment of metastatic GC in patients aged over 60 years old and to discuss the results considering the existing literature on the subject.

METHODS

Type of study

This study is a retrospective examination with a quantitative approach.

Patients

Patients aged 60 years or more were enrolled. The age cutoff was defined based on the socioeconomic characteristics of the Brazilian population and the value most used by the United Nations (UN). All patients had a confirmed histopathological diagnosis of gastric adenocarcinoma and radiologic documentation of metastatic disease. The patients were treated in the Oncology Department of the *Universidade Federal de São Paulo* (UNIFESP) between January 2011 and January 2015. Patients who received at least one complete cycle of chemotherapy, without prior history of chemotherapy, had been included. Individuals with other neoplasms concomitant with GC or patients who were unfit to receive at least one cycle of chemotherapy were excluded. All patients signed the Informed Consent Form (ICF).

Setting

This study was performed in a university hospital which is funded by the Brazilian public health system.

Procedures

Patient records were accessed, and the epidemiological, clinical and therapeutic data were evaluated. The study was approved by the institutional ethics committee and was

conducted in accordance with the provisions of Resolution no. 466/12 of the Brazilian Ministry of Health.

The physicians have chosen the chemotherapy agent according to clinical characteristics of the patients. There was no an institutional guideline for the regimen choice. Epirubicin, oxaliplatin, and capecitabine (EOX) protocol consisted of intravenous bolus of epirubicin 50 mg/m^2 and oxaliplatin 130 mg/m^2 on day 1 every three weeks, combined with oral capecitabine 625 mg/m^2 taken continuously twice daily. The protocol described as Fluoropyrimidine plus Platinum (FP) was composed preferably and predominantly by intravenous oxaliplatin 130 mg/m^2 on day 1 followed by oral capecitabine 1,000 mg/m^2 given twice a day for 14 days every three weeks. If capecitabine was not available, the regimen was modified to oxaliplatin 85 mg/m^2 on day 1, followed by an intravenous bolus of 5-fluouracil 500 mg/m^2 and folinic acid 60 mg/m^2 on days 1 and 2 of every two-week cycle. The Cisplatin plus 5-Fluouracil (CF) protocol consisted of intravenous bolus of cisplatin 70 mg/m^2 and 5-fluouracil 1,000 mg/m^2 on the first five days of every four-week cycle. The single-agents 5-Fluouracil (5-FU) or Capecitabine (C) protocol consisted of a 2-hour intravenous infusion of folinic acid 500 mg/m^2 and a bolus infusion of 5-fluouracil 500 mg/m^2 weekly for six weeks followed by two weeks with no chemotherapy. The other single-agent protocol consisted of oral capecitabine 1,000 mg/m^2 twice a day for 14 days every three weeks.

Main measurements

The end point was the OS, defined as the interval (in months) between diagnosis of the disease and the death from any cause. The result was compared with the international literature. Secondary end points were response rate (RR), progression-free survival (PFS) and toxicity.

The imaging studies were evaluated by UNIFESP Radiology Department according to the Response Evaluation Criteria in Solid Tumors (RECIST).[27] The frequency of imaging was done in accordance with the respective protocol. The PFS was defined as the time interval (in months) between the first day of treatment and the first documentation of progression by RECIST or death from any cause, whichever occurred first.[28] Toxicities were graded by Common Terminology Criteria for Adverse Events (CTCAE) of the National Cancer Institute (NCI),[29] and laboratory tests were performed in the Central Laboratory of UNIFESP.

The performance status was evaluated according to the Eastern Cooperative Oncology Group (ECOG), which is a scale from 0 to 5.[30]

Patients were assessed by a nutritionist at a random time for measure of body mass index (BMI), cachexia status, bioimpedance phase angle and patient-generated subjective global assessment (PG-SGA).

BMI may mask the true nutritional status since that does not consider body composition or recent weight loss. Fearon et al. classified cachexia in four stages: without cachexia, pre-cachexia, cachexia and refractory cachexia (the most severe stage, considered a non-responsive patient to antineoplastic therapy and low expectancy of life).[31]

The PG-SGA is an easy and inexpensive method that classifies patients into three categories of nutritional status: SGA-A "well-nourished," SGA-B "moderately malnourished," or SGA-C "severely malnourished." The test result indicates whether the patient is at risk for complications caused by an inadequate nutritional status and nutritional intervention to promote patient benefits. The PG-SGA also reviews weight loss, food intake, nutritional impact symptoms, and functional capacity and physical examination.[32]

Statistical analysis

The demographic aspects of the population were evaluated with descriptive statistics. The analysis of OS and PFS were made using the Kaplan-Meier method. Potential influence of epidemiological, clinical, and therapeutic characteristics in the OS of patients was explored using the stratified log-rank test[33] and univariate Cox regression model[34] for each subgroup evaluated. No multivariate tests were performed because of the relatively small sample size. It was considered a p less than 0.05 as statistically significant. Two decimal places were used.

RESULTS

Patients

Twenty-one elderly patients were included in the study. At the time of evaluation, eight patients remained on treatment and one participant lost follow-up after seven months of treatment. The average age was 69.6 years, and the standard deviation was 7.6 years. The majority of the patients were male (76.2%), Caucasian (57.1%) and born in the Southeast/South regions of Brazil (66.7%). There was a higher prevalence of smoking compared to alcoholism (71.4 *versus* 47.6%, respectively). Almost nine out of ten patients had a weight loss higher than 10% of body mass during the six months before the neoplasm diagnosis. There was a high prevalence of diffuse type of cancer (42.9%) as well as primary tumors located at the body of the stomach (42.9%). The majority of patients had some comorbidity (52.4%), and the most prevalent was hypertension (28.6%), followed by

diabetes mellitus (19%), and congestive heart failure (19%). Table 1 summarizes the demographic and clinical characteristics of the patients.

Treatment

The average days to start chemotherapy were 107.5 days (11–216 days). Patients with better ECOG (scores 0-1)

Table 1 Baseline clinical, nutritional and demographic characteristics.

Age	Mean	SD	Age	Mean	SD
	69	7.6		69	7.6
	N	%		N	%
Gender			Site of metastasis		
Female	5	23.8	Peritoneum	8	38.1
Male	16	76.2	Liver	7	33.3
Region			Nonregional lymph node	3	14.3
North/Northeast	6	28.6	Bone	2	9.6
South/Southeast	14	66.7	Other	2	9.6
NA	1	4.8	Lauren classification		
Ethnic group			Intestinal	9	42.9
Caucasian	12	57.1	Diffuse	9	42.9
Afrodescendant	6	28.6	NA	3	14.3
Asiatic	1	4.8	Tumor location		
NA	2	9.5	Antrum/Pylorus	6	28.6
ECOG			Body	9	42.9
0	3	14.3	EGJ	3	14.3
1	10	47.6	Fundus/Cardia	3	14.3
2	8	38.1	CEA		
Smoking			Normal	3	19.0
Yes	15	71.4	Elevated	6	28.6
No	6	28.6	NA	12	52.4
Alcoholism			Comorbidities		
Yes	10	47.6	Hypertension	6	28.6
No	11	52.4	Diabetes	3	19.0
Weight Loss >10% 6 months			Heart failure	3	19.0
Yes	18	85.7	Dementia	1	4.8
No	3	14.3	None	10	47.6
Number of metastasis sites			Days to start chemotherapy		
1	15	71.4	Mean	Median	SD
2 or more	6	28.6	107.5	92	54.4

SD: standard deviation; NA: not available; ECOG: performance was evaluated according to guidelines of the Eastern Cooperative Oncology Group, with a score of 0 indicating normal performance status, 1 mildly symptomatic, 2 symptomatic but in bed less than half the day, 3 symptomatic and in bed more than half the day, and 4 in bed the whole day; CEA: carcinoembryonic antigen; EGJ: esophagogastric junction.

initiated chemotherapy earlier (p = 0.04). The chemotherapy protocols used were 5-Fluouracil (F) or capecitabine (C) single-agent for three patients, FP for 16 patients, and EOX for two patients. The choice of chemotherapy protocol single-agent rather than the combined therapy was correlated with ECOG (p = 0.04). An average of 4.6 cycles of chemotherapy in first line was realized (3.7 cycles for single-agent, 4.8 cycles for FP, and 4.5 cycles for EOX [p = 0.61]). Higher BMI was related with higher number of cycles of chemotherapy, however this relationship was not statistically significant (p = 0.17). Other nutritional aspects were not related with the number of cycles of chemotherapy. The main reasons for first line treatment discontinuation were: progression of disease (33.3% for single-agent chemotherapy, 18.8% for FP, and 0% for EOX [p = 0.65]), performance status drop (0% for single-agent, 31.3% for FP, and 50% for EOX [p = 0.43]), and adverse events (33.3% for single-agent, 6.3% for FP, and 0% for EOX [p = 0.57]).

Adverse events

There was a higher rate of adverse events in patients treated with FP regimen; however, the difference was not statistically significant (p = 0.87). Among the 21 patients, the main adverse events observed were grade 1 or 2: anemia (28.6%), nausea (23.8%), neuropathy (23.8%), and thrombocytopenia (19%). Neutropenia grade 3 or 4 was observed in one patient (4.8%). In five cases (23.8%), the chemotherapy dose had been reduced, and in two cases (9.5%) the treatment had to be suspended. Table 2 summarizes the adverse events.

In the population of the study, a relationship between adverse events and baseline characteristics as performance status (p = 0.75), number of metastatic sites (p = 1.00), comorbidities (p = 0.76), or cardiac failure (p = 0.44) was not observed. Nutritional aspects as BMI (p = 0.47), PG-GSA (p = 0.78), bioimpedance phase angle (p = 0.78) and cachexia (p = 0.77) were not related with treatment toxicities. There was a trend toward hematologic toxicity of any grade and performance status (p = 0.08).

Efficacy

Objective response rate

Among 21 patients, 15 were evaluated for treatment response. A total 46.7% of objective response rate was observed, 33.3% of patients had stable disease and 20% had disease

Table 2 Adverse events for fluoropirimidine and platinum (FP) doublet chemotherapy protocol.

	EOX (N=2) N (%)		FP (N=16) N (%)		F (N=3) N (%)	
Adverse event	Grade 1-2	Grade 3-4	Grade 1-2	Grade 3-4	Grade 1-2	Grade 3-4
Anemia	1 (50.0)	0 (0)	6 (37.5)	0 (0)	0 (0)	0 (0)
Neutropenia	0 (0)	0 (0)	2 (12.5)	1 (6.3)	0 (0)	0 (0)
Febrile neutropenia	0 (0)		0 (0)		0 (0)	
Thrombocytopenia	0 (0)	0 (0)	3 (18.8)	0 (0)	0 (0)	0 (0)
Neuropathy	1 (50.0)	0 (0)	3 (18.8)	0 (0)	0 (0)	0 (0)
"Hand-Foot"	0 (0)	0 (0)	2 (12.5)	0 (0)	0 (0)	0 (0)
Mucositis	0 (0)	0 (0)	1 (6.3)	0 (0)	0 (0)	(0)
Diarrhea	0 (0)	0 (0)	2 (12.5)	0 (0)	0 (0)	0 (0)
Nausea	0 (0)	0 (0)	4 (25.0)	0 (0)	1 (33.3)	1 (33.3)
Asthenia	0 (0)	0 (0)	3 (18.8)	0 (0)	1 (33.3)	0 (0)
Dose reduction	0 (0)		5 (31.3)		0 (0)	
Treatment suspension	0 (0)		1 (6.3)		1 (50.0)	
Cycles	Mean	Total	Mean	Total	Mean	Total
	4.5	9	4.8	77	3.7	11

EOX: epirubicin, oxaliplatin and capecitabine; FP: fluoropyrimidine and platinum; F: fluoropyrimidine monodrug; N: number.

progression. There was no difference statistically significant between the treatment protocols (p = 0.70) (Table 3).

Progression-free and overall survival

The median PFS was nine months. The median OS was 13.8 months (Figure 1).

Subgroup analysis

The subgroup analysis was performed according to the demographic, clinical and therapeutic characteristics of patients (Figure 2). As factors of better prognosis for OS were identified: < 2 sites of metastasis (HR = 0.15; CI95% 0.02 – 0.93), absence of metastasis to nonregional lymph nodes (HR = 0.04; CI95% < 0.01 – 0.44), higher number of chemotherapy cycles (HR = 0.72; CI95% 0.53 – 0.97), and objective response (HR = 0.06; CI95% 0.01 – 0.69). Patients with comorbidities had a worst prognostic; however, it was not statistically significant (HR = 2.13; CI95% 0.53 – 8.61; p = 0.29). Higher BMI was related with a not statistically significant better prognosis (HR = 0.84; CI95% 0.64 – 1.10; p = 0.20).

Second-line treatment

Among the 21 patients, 10 had progression of disease, and three (30%) were treated with second-line chemotherapy. Each patient was treated with a different chemotherapy agent (fluoropirimidine, taxane and irinotecan). An average of 3.3 cycles in second-line treatment was observed. Two patients were evaluated for response to treatment and all had progression of disease (100%) in a median PFS of 3.7 months.

Table 3 Response to therapy according to chemotherapy protocol.

	EOX (N = 2)	FP (N = 16)	F (N = 3)
Evaluated	2 (100%)	11 (100%)	2 (100%)
Objective response	1 (50.0)	5 (45.5)	1 (50.0)
Complete response	0 (0)	0 (0)	0 (0)
Partial response	1 (50.0)	5 (45.5)	1 (50.0)
Stable disease	1 (50.0)	4 (36.4)	0 (0)
Progressive disease	0 (0)	2 (18.1)	1 (50.0)

These differences were not statistically significant (p = 0.70); EOX: epirubicin, oxaliplatin and capecitabine; FP: fluoropyrimidine and platinum; F: fluoropyrimidine monodrug; N: number.

DISCUSSION

Elderly patients treated with chemotherapy for metastatic GC in our institution had good outcomes, with almost 50% of response and more than one year of median OS. These results were similar compared with literature. Moreover, protocols with more than one agent were well tolerated.

Liu et al. reported the results of treating 44 patients aged 65 years or more with bolus oxaliplatin plus infusional 5-fluouracil (mFOLFOX-4). Of the 40 patients assessed for response, 52.5% had objective response. The median time to progression (TTP) was 6.5 months, and the median OS was 10 months. No grade 4 hematologic toxicities were described, and the major observed toxicity was neuropathy (34.1%).[25]

Similar results were presented by Dong et al. using capecitabine and oxaliplatin to treat 44 individuals aged over 70 years. Of the 41 patients evaluated for response, 51.2% had objective response. The median TTP was 5.6 months, and the median OS was 9.8. Grade 3-4 hematologic toxicity was observed in 13.6% of patients and two had febrile neutropenia. Neuropathy 1-2 degrees was observed in 43.1% of patients.[35]

In our study, 16 patients were treated with doblet FP. Among the 11 patients assessed for response, 45.4% had objective response. The median PFS was nine months, and the median OS was 13.8 months. Regarding adverse events, 31.3% of the patients had anemia grade 1-2, 25% had

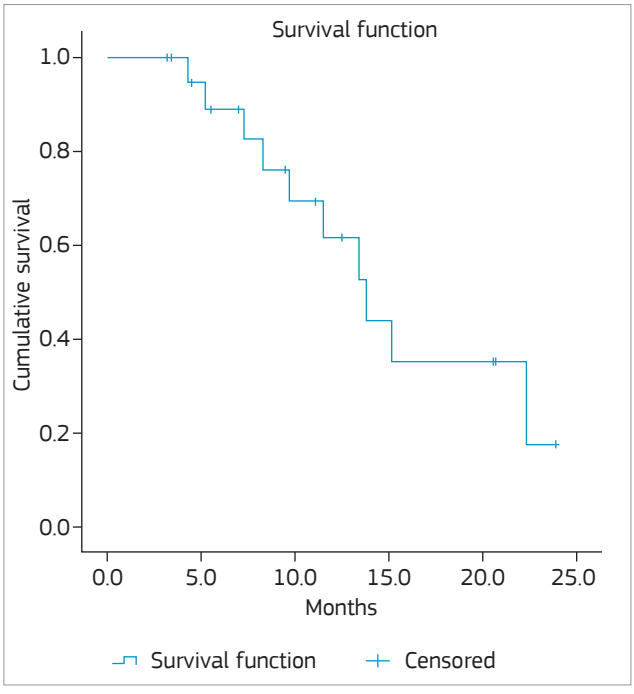


Figure 1 Kaplan-Meier method estimates of elderly patients overall survival. All included patients (N = 21).

thrombocytopenia grade 1-2, and 25% had neuropathy grade 1-2. Grade 3-4 hematologic toxicity was observed in 6.3%.

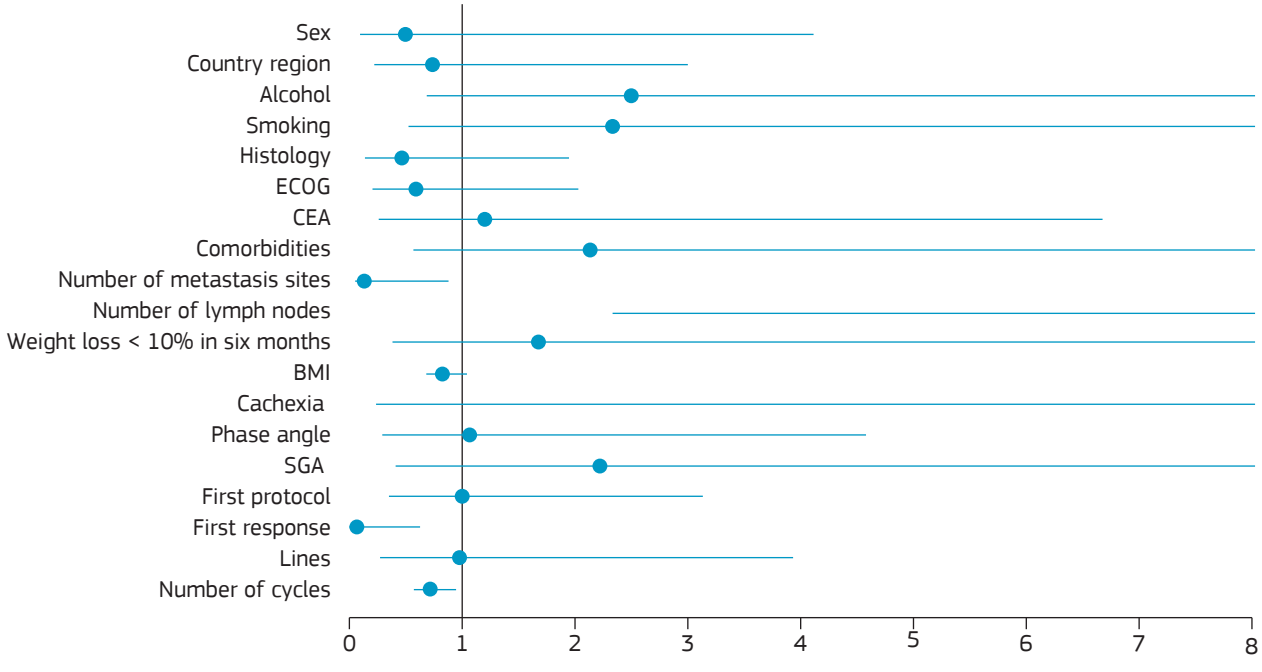
Compared to treatment with single-agent, Sun et al. presented the results of 178 patients older than 70 years treated with single-agent fluoropyrimidine-based (N = 70) to the combination of agents FP (N = 108). The objective response rates were 8.6% and 24%, respectively. The median PFS was 4.4 months and 4.1 months, respectively (p = 0.295), and the median OS were 6.6 and 7.6 months, respectively (p = 0.782). The adverse hematological effects (p < 0.001) and non-hematologic effects (p < 0.001) were lower in patients treated with single-agent.[36]

In our population, only three patients were treated with single-agent regimen and two were evaluated for response to treatment, one had objective response and the other had disease progression. Regarding PFS, two patients showed disease progression (one after 15.9 months and the other after 3.3 months), and analyzing OS, one patient reached 22.3 months and the other 13.4 months. Regarding toxicity, no hematological toxicity was observed in patients treated with single-agent.

Regarding clinical and pathological factors that may affect the survival of elderly patients with metastatic GC, large retrospective series of 357 patients with 65 years or more was published by Lu et al. After univariate analysis presented as prognostic factors for OS between 220 metastatic patients: LDH levels (p < 0.001), involvement of supraclavicular lymph nodes (p = 0.047), number of metastatic lesions (p < 0.001), number of chemotherapy cycles (p < 0.001), cisplatin-based regimen (p = 0.03) and response to treatment (p < 0.001).[37]

In our population, the LDH dosage was not available for analysis, but no involvement of nonregional lymph nodes (p = 0.009), fewer than two metastatic lesions (p = 0.042), higher number of cycles of chemotherapy (p = 0.028), and achieving objective response (p = 0.025) were also defined as prognostic factors associated with higher OS.

Deans & Wigmore reported that cachexia is a significant cause of morbidity and mortality, affecting more than 85% of patients with gastrointestinal cancer at the time of diagnosis.[38] Of the 12 patients with available data, the index of cachexia reached 75% with 1 case of refractory cachexia. Furthermore, 86% of treated patients had more than 10% of weight loss (in six months). This finding indicates the presence of cachexia and/or nutritional risk. However, because of the small sample, cachexia was not statistically significant related with OS.



ECOG: Eastern Cooperative Oncology Group, with a score of 0 indicating normal performance status, 1 mildly symptomatic, 2 symptomatic but in bed less than half the day, 3 symptomatic and in bed more than half the day, and 4 in bed the whole day; CEA: carcinoembryonic antigen; BMI: body mass index; SGA: patient generated subjective global assessment.

Figure 2 Forest-plot of overall survival prognostic factors. All included patients (N = 21).

Regarding toxicity, low BMI was associated with toxicities of any grade, but this relationship was not statistically significant (p = 0.47), probably due to the small sample size. In severe weight loss there is always depletion of skeletal muscle leading to increased toxicity in chemotherapy, worse prognosis, and quality of life. Ravasco et al., in a study of 271 cancer patients, found that weight loss and lower calorie-protein intake were associated with worse quality of life.[39]

In this study, 33.3% of patients were classified as PG-SGA C, or severely malnourished, at this stage that the food intake is severely reduced and there are clear signs of malnutrition. Thus, nutritional support has to be considered rather as synergetic and neo-adjuvant to oncological treatment than as a separated action. Nutrition is not a routine care and tailor individually prescription is mandatory.[40]

The nutritional assessment and monitoring of the elderly patient with metastatic GC is of great importance, since the control of sarcopenia could prevent the progression of cachexia and consequently control the toxicity, the number of cycles of chemotherapy, and, consequently, the overall patient survival. Prospective studies demonstrating the clinical evolution using well established protocols are required. Furthermore, elderly patients, regardless of disease, have physical and social issues related to the functionality and self-care that can enhance the nutritional risks and hinder the effectiveness of the adopted behaviors.

The main limitation of this study is the small number of participants that restrict some statistical tests. In addition, the retrospective nature of the study makes it impossible to construct conclusions to compare the treatment regimens, especially regarding the PFS. However, we observed similar results to those reported in the literature. Even for patients aged over 60 years, our experience is better with doublet chemotherapy with manageable toxicity; however, instances where the patient is unable to tolerate that combination treatment, single-agent may be an option, and it has activity in the treatment of metastatic GC.

Prospective randomized studies with the inclusion of elderly patients with comorbidities are needed to better understand the most appropriate treatment for this population.

CONCLUSION

Elderly patients treated with doublet chemotherapy achieved almost 50% of response, one year of median OS, and manageable adverse events. Prospective randomized studies are required for further confirmation.

CONFLICT OF INTERESTS

The authors report no conflict of interests.

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