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Gastric cancer in young adults: a worse prognosis group?

Câncer gástrico em adultos jovens: um grupo de pior prognóstico?

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A B S T R A C T

Objective: to evaluate the clinical and pathological characteristics and survival of young patients with gastric cancer, regardless of the intention of treatment. **Methods:** we conducted a retrospective analysis of all gastric cancer patients undergoing any surgical treatment between 2008 and 2017. We considered patients under 45 years old as young adults and those over 45 years old, as of advanced age. **Results:** of the 875 patients evaluated, 84 (9.6%) were young adults and 791 (90.4%) were older. Younger patients were associated with female gender (p<0.001), lower *Charlson* score (p=0.002), ASA I/II (p<0.001), diffuse *Lauren* type (p<0.001) and poorly differentiated tumors (p<0.001). There was no difference between groups regarding treatment intention (palliative *versus* curative) (p=0.267) and cTNM clinical stage (p=0.120). Disease-free survival was worse in younger individuals (p=0.049), but overall survival was similar between groups (p=0.578). Multivariate analysis identified total gastrectomy, pT3/T4, pN+, and diffuse *Lauren* type as prognostic factors associated with worse disease-free survival and overall survival. Age was not an independent factor associated with worse prognosis. **Conclusion:** although younger patients had lower disease-free survival, overall survival was similar between groups, and age was not a significant independent prognostic factor.

Keywords: Stomach Neoplasms. Age of Onset. Young Adult. Survival Analysis.

INTRODUCTION

The incidence of gastric cancer (GC) has been decreasing worldwide. However, it remains the fifth most common cancer in the world and still causes significant morbidity and mortality throughout several countries in Europe, Asia, and South America[1]. The main GC carcinogenesis model involves several molecular alterations induced by environmental factors including: 1) high salt intake diets (mostly with high sodium concentrations); 2) poor food conservation; 3) increase in *N*-nitroso compounds in the gastric mucosa; 4) antioxidants/ vitamin deficiencies (e.g. vitamin C); 5) *Helicobacter pylori* infection; 6) proinflammatory cytokine gene polymorphisms; 7) prolonged alcohol and tobacco consumption[2,3]. The cumulative effect of these aggressions on the gastric epithelium over the years leads to the development of neoplasia. Thus, GC usually has its high incidence in the sixth decade of life, in patients with chronic atrophic gastritis and intestinal metaplasia[2].

At the same time, GC may also occur without chronic gastric inflammation as a prerequisite, especially in young adults[4]. These tumors are often associated with changes in the CDH1 gene and exhibit *Lauren*'s diffuse histological type. Therefore, the challenge of early diagnosis and treatment of GC also extends to young patients. Recent data have revealed that young adults gastric cancer (YAGC) accounts for 2-8% of all cancers[5,6]. Besides the obvious social impact, YAGC calls for more and more interest due to the growing importance attached to the genetic causes of the disease. A mechanism of genetic inheritance has already been discovered and proven in a subgroup of 1-3% of cases. These syndromes include Hereditary Diffuse Gastric Cancer (HDGC), *Li-Fraumeni*, Familial Adenomatous Polyposis, *Lynch* and *Peutz-Jeghers*[7-9].

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Concerns about the prognosis and better approach of YAGC remain open to discussion[5,10,11]. Thus, the objective of the present study was to evaluate the clinicopathological characteristics and survival of YAGC submitted to any surgical procedure, regardless of the intention of treatment, with further emphasis on patients undergoing surgery with curative intent surgery.

METHODS

We reviewed all consecutive patients who underwent any surgical or endoscopic procedure due to gastric cancer from 2009 to 2017 at our Institution. We excluded from the analysis tumors not originated in the stomach, non-adenocarcinoma histological types, and gastric surgical procedures related to benign conditions (such as for peptic ulcer and gastrostomies).

We defined YAGC as GC diagnosed at 45 years of age or younger. Patients with more than 45 years were labeled as in the "older adult gastric cancer (OGC) group" for comparison. We carried out preoperative staging by upper gastrointestinal endoscopy with biopsy, computerized tomography and laboratory tests. We performed diagnostic laparoscopy in selected cases with suspected peritoneal carcinomatosis or intended neoadjuvant treatment. Surgical risk assessment used the American Society of Anesthesiologists (ASA) classification[12] and the *Charlson-Deyo* comorbidity index (CCI)[13]. All patients underwent preoperative clinical and laboratory exams. A multidisciplinary meeting discussed complex cases.

Surgeons with extensive experience in the surgical management of GC operated all cases according to the Japanese Gastric Cancer Association guidelines[14]. A curative-intent D2 lymphadenectomy took place whenever feasible, according to suspected preoperative and/or intraoperative GC staging and the patient's medical conditions. We treated upper GC, as defined as per the Japanese Gastric Cancer Association Classification, by total gastrectomy, and GC of the middle and lower thirds, by subtotal (4/5) gastrectomy. The lymph node chains removed defined the extent of nodal dissection (D1 or D2 lymphadenectomy)[14]. Residual tumor classification was as follows: R0, no residual tumor; R1, microscopic residual tumor; R2, macroscopic residual tumor. TNM staging was performed according to the eighth edition[15].

We graded postoperative complications (POC) according to the *Clavien-Dindo's* classification[16]. We classified major complications as *Clavien* III-IV-V. We considered postoperative mortality when death occurred in the first 30 days after surgery or during hospital stay after the procedure.

We conducted the postoperative follow-up on a quarterly basis in the first year after surgery, and every six months in the following years. We performed follow-up studies for relapse detection based on the presence of symptoms. We considered loss of follow-up when patients missed their postoperative outpatient clinical appointments for more than 12 consecutive months.

Descriptive statistics included frequencies with percentages for nominal variables and means for continuous variables. We used the Chi-square test to evaluate the differences between categorical variables, and the *t* test for continuous ones. We estimated disease-free survival (DFS) and overall survival (OS) using the *Kaplan-Meier* method, and differences in survival using the Log Rank Test.

We built Cox proportional hazard regression models for analysis of risk factors for survival outcomes in GC. We included variables that were significant on the univariate analysis and covariates in the multivariable analysis to determine which ones independently affected prognosis. We calculated survival time from the date of surgery until the date of death/recurrence. We censored the patients who were alive at the date of last personal contact. All tests were two-sided and statistical significance was defined as $p<0.05$. We performed the analyses using the SPSS software, version 18.0 (SPSS Inc, Chicago, IL).

This study was approved by the Hospital Ethics in Research Committee (document NP 993/16) and registered online (www.plataformabrasil.saude.gov.br).

RESULTS

During the period studied, 934 patients underwent surgical or endoscopic procedures due to GC. From these, 875 (93.7%) were diagnosed as gastric adenocarcinoma and were included in this study. There were 550 males (62.9%) and 325 females (37.1%), with a mean age of 65 years (range 22-94 years) (Figure 1). There were 84 (9.6%) patients who were 45-years old or younger (YAGC group), and 791 (90.4%) were older (OGC age group).

Table 1 shows the clinical and surgical characteristics of gastric adenocarcinoma patients.

The number of female patients was higher in the YAGC group (56% vs 35.1%, $p<0.001$). Patients in the OGC group had higher CCI and ASA scores when compared to the YAGC group (10.8% vs 0%, $p=0.002$ and 29.2% vs 7.1%, $p<0.001$; respectively). YAGC patients had more poorly differentiated tumors (81.8% vs 45.7%. $p<0.001$) and *Lauren´s* diffuse type (86.9% vs 35.9%, $p<0.001$).

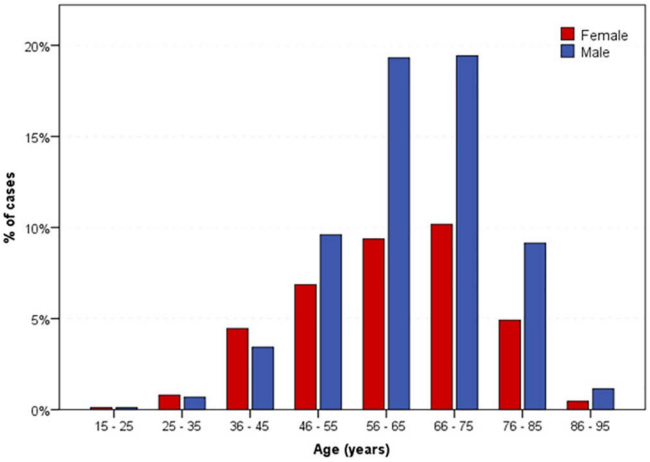

Figure 1. *Distribution of gastric cancer according to age groups and gender.*

Considering the type of surgical procedures, there was no difference regarding curative and palliative procedures between the groups ($p=0.267$). However, endoscopic resection was uncommon in the YAGC group (1.2% vs 5.2%)**.** Although the frequency of curative intent resection was the same, D2 lymphadenectomy was more common in the YAGC group (63.1% vs 47.8%, $p=0.027$).

Final TNM stage was similar between the two groups ($p=0.120$), but stage I patients were more frequent in the OGC group (26.7% vs 21.4%) and stage IV, in the YAGC group (32.1% vs 25.4%). The mean postoperative length of hospital stay was longer in the OGC group (11.9 vs 9.6 days, $p=0.039$), with a median of eight (range 1-49) and nine days (range 1-73) for the YAGC and OGC groups, respectively.

With a mean follow-up duration of 26.4 months (median of 19.5 months, SD±24.4), 397 patients had residual disease or recurrence, and 395 died. Regarding age groups, there were no differences in OS between YAGC and OGC patients. Median OS was 33.3 and 40.9 months, respectively ($p=0.578$) (Figure 2). DFS rate was significantly poorer in the YAGC group than in the OGC (47% vs 55.6%, $p=0.049$), with a median DFS of 12.9 and 49.6 months, respectively.

Table 1. *Clinicopathologic characteristics of Young adults GC and Older adults GC groups. All gastric adenocarcinoma cases (n=875).*

Variables	≤45 years YAGC n=84 (%)	>45 years OGC n=791 (%)	*p*
Gender			<0.001
Male	37 (44)	513 (64.9)	
Female	47 (56)	278 (35.1)	
BMI (Kg/m^2)			0.198
Mean (SD)	22.9 (4.1)	23.8 (5.0)	
Neutrophil-to-lymphocyte ratio (NLR)			0.841
Mean (SD)	2.78 (4.1)	2.67 (2.1)	
Charlson-Deyo comorbidity index (CCI)			0.002
0-1	84 (100)	687 (89.2)	
>1	0 (0)	81 (10.8)	
ASA (American Society of Anesthesiologists)			<0.001
I-II	78 (92.9)	560 (70.8)	
III-IV	6 (7.1)	231 (29.2)	
Histological differentiation*			<0.001
Well/Moderately	12 (18.2)	350 (54.3)	
Poorly	54 (81.8)	294 (45.7)	
Lauren's type*			<0.001
Intestinal	9 (13.6)	366 (56.7)	
Diffuse/Mixed	57 (86.9)	255 (35.9)	
Undetermined	0 (0)	25 (3.9)	
Type of surgery			0.267
Curative intent (D1 or D2)	56 (66.7)	500 (63.2)	
Palliative/Diagnostic	27 (32.1)	250 (31.6)	
Endoscopic	1 (1.2)	41 (5.2)	
Type of lymphadenectomy			0.027
D2	53 (63.1)	378 (47.8)	
D1	8 (9.5)	121 (15.3)	
Not applicable	23 (27.4)	292 (36.9)	
TNM stage			0.120
I	18 (21.4)	211 (26.7)	
II	11 (13.1)	125 (15.8)	
III	28 (33.3)	254 (32.1)	
IV	27 (32.1)	201 (25.4)	
Hospital stay (days)			0.039
Mean (SD)	9.6 (7.4)	11.9 (9.6)	
Median (range)	8 (1-49)	9 (1-73)	

** data not available in some cases; BMI: body mass index; SD: standard deviation.*

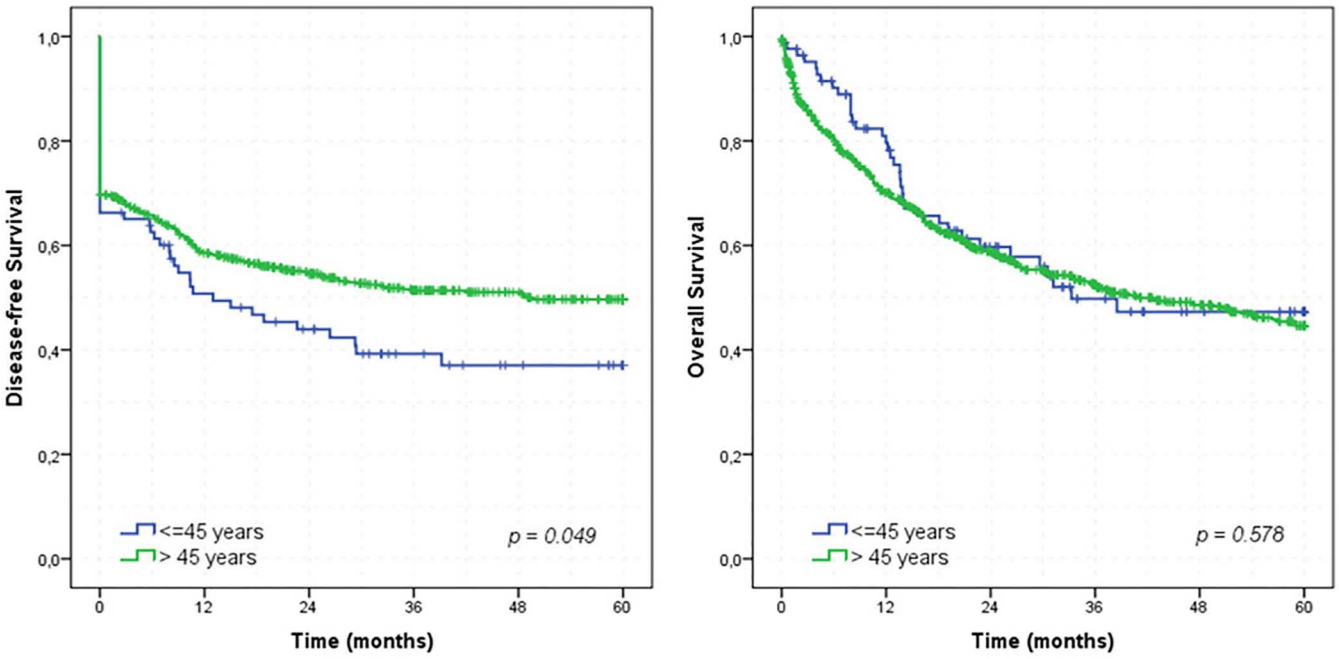

Figure 2. *Kaplan-Meier curves for DFS and OS of the entire population.*

We performed curative intent D2 lymphadenectomy in 425 patients. Fifty-two (12.2%) were 45 years old or younger and the remaining 373 (87.8%) patients were older. Considering the clinicopathological characteristics (Table 2), there was no difference in relation to gender between the groups (p=0.094). Type of resection and the use of neoadjuvant chemotherapy were also similar. YAGC patients were more likely to have poorly differentiated tumors (82.7% vs 49.3%, p<0.001) and diffuse/mixed *Lauren* histological type (88.5% vs 41.8%, p<0.001). We observed no difference between the two groups with respect to pTNM stage (p=0.206). POC were more frequent in the OGC group (p=0.049). The YAGC group received more adjuvant therapy (51.9% vs 36.2%, p=0.029).

Tumor location and size, body mass index (BMI), number of harvested lymph nodes, lymphatic/venous/perineural invasion and length of hospital stay were similar between the groups (Table 3).

At the completion of this study, 107 patients had presented disease recurrence and 119 patients had died**.** DFS and OS rates for the patients submitted to D2 were 74% and 72%, respectively. Considering the age groups, the *Kaplan-Meier* survival analysis showed worse DFS for the YAGC group (p=0.012) than for the OGC. There was no difference in OS (p=0.805) between YAGC and OGC (Figure 3).

We performed univariate and multivariate analyses to evaluate the prognostic factors affecting DFS and OS in the group of patients submitted to D2 lymphadenectomy (Table 4). Multivariate analysis identified the extension of surgery (total gastrectomy), pT and pN categories as independent prognostic factors associated with worse DFS and OS. Additionally, *Lauren's* diffuse histological type was also associated with worse OS. There was no significant association between the patient's age and survival.

Table 2. *Clinicopathologic characteristics of patients treated with curative intent D2 resection (n=425).*

Variables	≤45 years YAGC n=52 (%)	>45 years OGC n=373 (%)	*p*
Gender			0.094
Male	24 (46.2)	218 (58.4)	
Female	28 (53.8)	155 (41.6)	
Neoadjuvant chemotherapy (NACT)			0.077
No	49 (94.2)	318 (84.3)	
Yes	3 (5.8)	55 (14.7)	
Type of resection			0.278
Subtotal gastrectomy	29 (55.8)	237 (63.5)	
Total gastrectomy	23 (44.2)	136 (36.5)	
Lauren's type			<0.001
Intestinal	6 (11.5)	198 (53.4)	
Diffuse/mixed	46 (88.5)	155 (41.8)	
Undetermined	0 (0)	18 (4.9)	
Histological differentiation			<0.001
Well/Moderately	9 (17.3)	188 (50.7)	
Poorly	43 (82.7)	183 (49.3)	
pT category			0.209
pT1/T2	17 (32.7)	156 (41.8)	
pT3/T4	25 (67.3)	217 (58.2)	
pN category			0.247
pN negative	19 (36.5)	168 (45)	
pN positive	33 (63.5)	205 (55)	
TNM stage			0.206
I-II	25 (48.1)	214 (57.4)	
III-IV	27 (51.9)	159 (42.6)	
Postoperative complication (Clavien-Dindo classification)			0.049
None/Grade I-II	50 (96.2)	323 (86.6)	
Grade III-IV-V	2 (3.8)	50 (13.4)	
Adjuvant therapy			0.029
No	25 (48.1)	238 (63.8)	
Yes	27 (51.9)	135 (36.2)	

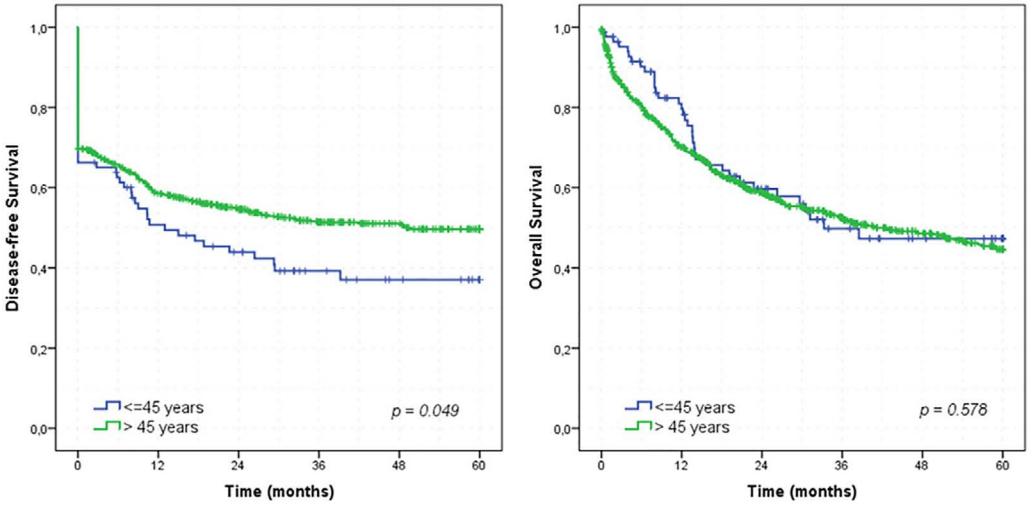

Figure 3. *Kaplan-Meier curves for DFS and OS of curative intent D2 lymphadenectomy patients.*

Table 3. *Clinicopathologic characteristics of patients treated with curative intent D2 resection (n=425).*

Variables	≤45 years YAGC n=52 (%)	>45 years OGC n=373 (%)	*p*
BMI (Kg/m^2)			0.122
Mean (SD)	23.5 (2.6)	24.9 (5.2)	
ASA (American Society of Anesthesiologists)			0.009
I-II	51 (98.1)	314 (84.2)	
III-IV	1 (1.9)	59 (15.8)	
Charlson-Deyo comorbidity index (CCI)			0.023
0-1	52 (100)	332 (91)	
>1	0 (0)	33 (9)	
Tumor location			0.144
Upper	1 (1.9)	32 (8.6)	
Middle	7 (13.5)	83 (22.3)	
Lower	37 (71.2)	224 (60.1)	
All stomach	1 (1.9)	9 (2.4)	
Others	6 (11.5)	25 (6.7)	
Tumor size (cm)			0.910
Mean (SD)	4.6 (2.6)	5.0 (3.5)	
Harvested lymph nodes			0.453
Mean (SD)	40.3 (17.5)	42.1 (17.5)	
Lymphatic invasion*			0.443
Absent	23 (46)	189 (51.8)	
Present	27 (54)	176 (48.2)	
Venous invasion*			0.201
Absent	29 (58)	245 (67.1)	
Present	21 (42)	120 (32.9)	
Perineural invasion*			0.276
Absent	22 (44)	189 (52.2)	
Present	28 (56)	173 (47.8)	
pT			0.184
T1	14 (26.9)	106 (28.4)	
T2	3 (5.8)	50 (13.4)	
T3	16 (30.8)	120 (32.2)	
T4	19 (36.5)	97 (26)	
pTNM			0.173
I	15 (28.8)	125 (33.5)	
II	10 (19.2)	89 (23.9)	
III	24 (46.2)	156 (41.8)	
IV	3 (5.8)	3 (0.8)	
Hospital stay (days)			0.288
Mean (SD)	10.0 (5.6)	11.4 (8.1)	
Median (range)	9 (4-30)	9 (4-59)	

** data not available in some cases.*

Table 4. *Univariate and multivariate analyses for disease-free survival and overall survival – D2-gastrectomy with curative intent (n=425).*

Disease-free Survival	Univariate			Multivariate		
Variables*	HR	95% CI	p	HR	95% CI	*p*
Age >45 vs ≤45	1.83	1.13-2.95	0.013	1.33	0.80-2.20	0.267
Female vs Male	0.99	0.68-1.45	0.964	-	-	-
Charlson 0-1 vs *Charlson* >1	0.54	0.20-1.46	0.225	-	-	-
ASA I-II vs ASA III-IV	0.67	0.34-1.33	0.256	-	-	-
Subtotal vs Total gastrectomy	2.11	1.44-3.09	<0.001	1.77	1.21-2.60	0.003
Intestinal vs Diffuse/Mixed type	1.80	1.22-2.65	0.003	2.21	0.80-1.83	0.354
pT1/T2 vs pT3/T4	9.44	4.77-18.69	<0.001	3.55	1.56-8.04	0.002
pN0 vs pN1/2/3	7.89	4.32-14.40	<0.001	3.27	1.83-5.83	<0.001
Adjuvant therapy: present vs absent	1.46	0.99-2.13	0.052	-	-	-
Overall Survival	Univariate			Multivariate		
Variables*	HR	95% CI	p	HR	95% CI	*p*
Age > 45 vs ≤45	0.96	0.55-1.68	0.963	-	-	-
Female vs Male	1.02	0.71-1.47	0.896	-	-	-
Charlson 0-1 vs *Charlson* >1	1.61	0.88-2.92	0.119	-	-	-
ASA I/II vs ASA III/IV	1.52	0.94-2.45	0.090	-	-	-
Subtotal vs Total gastrectomy	2.18	1.52-3.12	<0.001	1.85	1.29-2.66	0.001
Intestinal vs Diffuse/mixed type	1.75	1.21-2.52	0.003	1.45	1.01-2.10	0.049
pT1/T2 vs pT3/T4	3.84	2.39-6.16	<0.001	2.27	1.33-3.86	0.003
pN0 vs pN1/2/3	3.73	2.38-5.84	<0.001	2.20	1.32-3.65	0.002
Adjuvant therapy: present vs absent	1.14	0.80-1.65	0.466	-	-	-

** the first serve as reference category.*

DISCUSSION

Up to now, a common concept has persisted in expert GC treatment centers that patients 45 years-old or younger present a biologically more aggressive GC and, therefore, have a poorer prognosis. They are considered more prone to relapse, despite aggressive surgical treatment and neoadjuvant strategies[6,17,18]. Our data partially corroborate this concept.

YAGC patients were predominantly female and, as expected, had a lower number of comorbidities. Tumors with *Lauren's* diffuse and poorly differentiated histological types also occurred more frequently in the YAGC group. However, the clinical/pathological stage and treatment intent did not differ between the age groups. Survival analysis showed that young adults did not present a worse OS, despite having worse DFS compared with the rest of the population.

It is worth noting the difficulty in defining "who is a young adult patient" when it comes to gastric cancer. The cut-off value of age to define YAGC has been predictably controversial. Frequently, it has been defined between the limits of 40 and 50 years, without a clear reason[5,6,10,11,17,19-22]. Takatsu *et al*.[5] defined YAGC as patients within the bottom fifth percentile in the age histogram. Accordingly, less than 40 years old were identified as the younger group. Nakamura *et al*.[22] determined a 34-year cut-off point to define YAGC using the area under ROC curve, based on the death status.

These distinct cut-off values may also reflect different national policies for defining and collecting data on cancer cases in adolescents and young adults, including tumor types other than GC[19,23]. In the present study, we used 45 years, in agreement with most of the papers on YAGC[6,18,20,21,24,25].

YAGC is generally uncommon, and some recent studies have focused on this group of patients. Cancer registries data from 2009-2014 in the State of São Paulo, Brazil, have shown a constant incidence of 5% for GC patients under 40 years of age[26]. Italian and German publications report incidences of GC patients with 50 years old or less of 15.1% and 13.2%, respectively[10,11].

In this study, there were more females than males in the YAGC group. One of the hypotheses for this predominance refers to hormonal differences, which may contribute to women being more susceptible to the development of CG. On the other hand, it has been suggested that male preponderance in older patients derives from a prolonged exposure to carcinogens, leading to a higher incidence of *Lauren's* intestinal type GC[5,17,18,22].

A major questioning that exists when analyzing surgical outcomes of YAGC patients is whether this group is already diagnosed at more advanced stages. Most of the reports are confined to analyzing only those cases that have been resected, which may lead to selection bias, since more advanced cases would not be included in the analysis. To address this issue, our initial analysis included all patients submitted to any surgical or endoscopic procedure. We verified that the initial clinical stage and the frequency of surgeries with curative and palliative intent did not differ between the groups. However, a difference was evident regarding endoscopic treatment, due to the preponderance of *Lauren's* diffuse type cancer in the YAGC group.

Although some authors have proposed that YAGC may be diagnosed at more advanced stages due to protracted endoscopic studies of minor dyspepsia, our data showed similar TNM clinical staging and surgical treatment intent for both groups, which suggests no delay in diagnosis for YAGC[17,22].

D2 lymphadenectomy has the gold standard care for GC[14,27]. The YAGC group had a greater proportion of patients submitted to D2 lymphadenectomy. Since the OGC group had more comorbidities, a greater indication of D1 lymphadenectomy is expected[28]. As the extent of lymphadenectomy influences survival, we decided to perform the survival analysis only including patients submitted to curative intent resection with D2 lymphadenectomy. In this analysis, we verified that clinicopathological characteristics were similar to the total population. The extension of gastrectomy and length of hospital stay did not differ between the two age groups. However, as expected, major POC were more common in the OGC group.

There was no difference in the neoadjuvant therapy rate between the age groups, but YAGC patients received more adjuvant chemotherapy than OGC ones, probably due to their better medical status. Additionally, the higher incidence of POC and lower ability of elderly patients to tolerate adjuvant therapy may have influence on non-adherence to postoperative chemotherapy[29]. Accordingly, this fact may adversely affect long-term survival in OGC patients.

Although YAGC is historically associated with the idea of worse prognosis and survival, the existing data are still insufficient to indicate the need for a more aggressive approach in these cases[6]. A German study showed better survival for younger patients[11]. Conversely, Asian studies have shown that OS is equal in both age populations[5,22,25].

YAGC patients may present better performance, since they allow the adoption of more aggressive multimodal treatment regimes. A meta-analysis including seven Asian and two Western studies showed that younger patients have better prognosis than older ones[20]. Different criteria in the definition of the YAGC group and the use of different control groups for comparison contribute to the occurrence of conflicting results, as well as the variation of survival between different countries.

Regarding prognosis, curative intent cases did not differ in the final pathological staging. Multivariate analysis showed that only type of resection, pT and pN categories were associated to prognosis. DFS was worse for YAGC patients, both in the analysis of the total population and in cases treated with D2 curative intent. Importantly, the majority of YAGC individuals had *Lauren's* diffuse type, in agreement to other reports, which is usually associated to a more aggressive biological behavior[5,6,18]. However, these findings were not enough to impact on a difference in OS. A greater commitment to the diagnosis of relapses in the YAGC group, as well as higher proportion of unrelated cancer deaths in the old age group, may have influenced this result.

Importantly, the presence of neoplasia in young adults always raises suspicion of some inherited genetic alteration. There are different hereditary cancer syndromes associated with the development of GC, including Hereditary Diffuse Gastric Cancer (HDGC), *Li-Fraumeni*, Familial Adenomatous Polyposis, *Lynch* and *Peutz-Jeghers*. HDGC is an inherited condition associated with mutation of the CDH1 gene germline, responsible for the coding of E-cadherin. Most of the mutation carriers will have GC before the age of 40 and the lifetime risk for diffuse GC is estimated in 67% to 70% for men and 56% to 83% for women by the age of 80[8,9,24]. Women with HDGC also have an increased risk of lobular breast cancer[7]. Recently, revised clinical diagnostic criteria were proposed based on 1) families with two or more patients with GC at any age, one confirmed diffuse GC; 2) individuals with diffuse GC before the age of 40; and 3) families with diagnoses of both diffuse GC and lobular breast cancer, one diagnosis before the age of 50[8,9]. CDH1 germline mutations are observed in about 20% of cases that meet the clinical criteria for HDGC[7-9]. However, only 5% of patients younger than 40 years without other clinical criteria for HDGC have a mutation in the CDH1 gene[7]. In Brazil, it has been reported a frequency of 40% to 50% of CDH1 germline mutation in patients that met the clinical criteria for HDGC[30,31].

Due to the retrospective nature of the study, medical records poorly documented the background information on neoplasia in family members, especially in the OGC group. Thus, we did not include this information in the present study. Indeed, we had one patient in the YAGC group that showed clinical criteria for HDGC. As the test for CDH1 gene mutation was not performed in the YAGC group, it is possible that we have included some patients with HDGC in the analysis. When assessing the influence of genetic components on GC in young adults, it is important to note that the characteristics of the comparison group composed of older patients are not similar between studies. Countries with high incidence of GC will have control populations with different characteristics from countries with low incidences, being much

more influenced by environmental factors related to exposure to carcinogens and *H. pylori* infection.

Our study showed that YAGC was predominant in females, patients with better clinical conditions, diffuse histological type and poorly differentiated tumors. Nonetheless, there was no difference in the TNM stage, and YAGC patients underwent the same type of surgical treatment as the older ones. YAGC had worse disease-free survival, but overall survival OS was similar between the age groups, and age was not an independent factor associated with worse prognosis in GC.

R E S U M O

Objetivo: *avaliar as características clínico-patológicas e sobrevivência de pacientes jovens, portadores de câncer gástrico, independentemente da intenção de tratamento.* **Métodos:** *análise retrospectiva de todos os pacientes com câncer gástrico submetidos a qualquer tratamento cirúrgico entre 2008 e 2017. Pacientes com idade inferior a 45 anos foram considerados adultos jovens, e aqueles com mais de 45 anos foram definidos como grupo com idade avançada.* **Resultados:** *dos 875 pacientes avaliados, 84 (9,6%) eram adultos jovens e 791 (90,4%) tinham idade avançada. Jovens associaram-se ao sexo feminino (p<0,001), menor escore de Charlson (p=0,002), ASA I/II (p<0,001), tipo difuso de Lauren (p<0,001) e tumores pouco diferenciados (p<0,001). Não houve diferença entre os grupos quanto à intenção de tratamento (paliativo versus curativo) (p=0,267) e estádio clínico cTNM (p=0,120). A sobrevida livre de doença foi pior nos jovens (p=0,049), mas a sobrevida global foi semelhante entre os grupos (p=0,578). A análise multivariada identificou gastrectomia total, pT3/T4, pN+ e tipo difuso de Lauren como fatores prognósticos associados a pior sobrevida livre de doença e sobrevida global. A idade não foi um fator independente associado a pior prognóstico.* **Conclusão:** *apesar de os jovens apresentarem uma menor sobrevida livre de doença, a sobrevida global foi semelhante entre os grupos, e a idade não demonstrou ser um fator prognóstico independente significativo.*

Descritores: *Neoplasias Gástricas. Idade de Início. Adulto Jovem. Análise de Sobrevida.*

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