



Analysis of the Behavior of Stomach Adenocarcinomas in Asian and Non-Asian Patients

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Introduction

The patterns of incidence, mortality, biological, and gastric cancer location are not uniform among ethnicities around the world [1-6]. Notably, there is a disparity in such characteristics between Asians and non-Asians.⁷ The location of neoplasms in non-Asians has shown an increase in proximal and cardia cancers, while in Asians, they are neoplasms of non-cardia location - tumors that are generally associated with risk factors such as H. pylori, smoking and dietary aspects [1,8]. Geographical and hereditary factors also seem to be involved, since it has been shown that, despite much lower incidence, Asian immigrants (first generation) in the United States have the same pattern of incidence distribution as native Asians [7,9]. Other aspects seem worth noting. Patients of Asian origin have a younger age and a higher proportion of cases with signet ring cell histology [10].

This study aimed to make a comparison to verify whether clinical and epidemiological aspects differ between Asians and non-Asians in Brazil. This may provide tools to individualize treatment in the future.

Methods

Retrospective analysis of data acquired in a prospective data collection registration protocol was carried out. All patients (non-miscegenated), descendants of Japanese, Korean, Chinese and other East Asian countries were defined as Asians. Epidemiological, clinical, surgical and oncological data of all patients were analyzed and compared. Inclusion criteria: all patients with stomach cancer

treated at the service from 1997 to 2018. For histological analysis, Lauren's classification was used: diffuse or intestinal. Global mortality included patients who died from cancer or not, and post-operative deaths (30 days) were excluded. The maximum period of survival was not defined, and the minimum period was one year. Cases considered inoperable included: inextricability, carcinomatosis, metastatic disease, poor general condition or patient refusal. For staging, the 7th edition of the Classification of Malignant Tumors of the International Union Against Cancer (UICC) was used [11]. The tumor sites were based on the Japanese Classification of gastric carcinomas and are classified into three basic regions: [12] U (upper third), M (middle third) and L (lower third); in cases of esophageal invasion, the letter E is placed, and in the case of duodenal invasion, the letter D. For tumors of the gastric esophageal junction, the word cardia (II or III) was associated with the letter U. The acronyms II or III refer to the Siewert classification for neoplasms of the gastric esophageal junction [13] Finally, in neoplasms of the remaining stomach after previous gastrostomies, the site was defined only as a stump. In these cases, only patients previously operated on the stomach for benign disease and those operated for malignant disease more than 5 years after the previous gastrectomy were considered (thus excluding stump recurrences).

Exclusion criteria

patients with non-adenocarcinoma stomach cancer and patients with non-available data. The study did not involve any risk for the patients, and, at no time, there was or will be exposure of

them. For the statistical analysis, the Mann-Whitney test was used to verify differences in age and survival time between different ethnicities: Asian and non-Asian. The Chi-square or Fisher's Exact test was used.

Results

There were no significant age differences between ethnicities. The average age of Asians was 61.7 years \pm 9.25; while non-Asians had an average of 61.4 years \pm 13.23 ($p = 0.89$). Regarding sex, among Asians, 75.6% of them were male, while among non-Asians we had 61.5% of male patients ($p = 0.097$). As for the histological type, the diffuse type predominated widely in both ethnicities. In Asians, we had 63.4% of patients with this histological type, while the intestinal type was 36.6% of cases. In non-Asians, the diffuse type predominated with 62.5% of cases. In Asians the unrespectability was 14.6%, while among non-Asians, this percentage was 32.8%.

Discussion

The differences between the findings regarding gastric adenocarcinomas between populations of Asian and non-Asian origin have long been discussed. Asian countries traditionally, especially Japan and South Korea, have high rates of early diagnosis and consequently better survival rates [14]. Those countries, due to their high incidence rates, perform routine screening, in Japan using contrast radiographs and in Korea using endoscopy upper digestive [15,16]. It is known that as immigrants settle in the countries, the incidence rates gradually approach those of the country in which they live and from the third generation onwards, they generally equal. Apparently, the cause is the change in eating habits, which are responsible for carcinogenesis in those groups [7]. Chen et al. [17] demonstrated in 160 patients operated in Australia that Asians were diagnosed at a younger age than non-Asians, an average of 60 years for the former and 70 for the latter. We did not observe, however, this difference in the studied population, in which age was just over 60 years for both groups. A basic difference between Chen's study and the present study is the fact that we evaluated all patients, including those who were not operated. It is noted that the Asians in our study are similar in age to those studied in Australia, but the native Brazilians were younger than the native Australians. This could be explained by the differences in quality of life and especially food between a developed country and ours, in the process of development. The patients evaluated by us, originate in a large part of the north and northeast regions, where eating habits predisposing to carcinogenesis predominate [18]. Regarding to survival, we have a very broad analysis that includes patients at all stages and also non-operated patients. There is a tendency for better survival rates in Asians (Table 1), which also occurs in the literature in general [17]. In this study, the authors revealed a surprising difference in survival in five years (68% x 31% in five years) despite the groups being similar with regard to stadiums. We

noticed in our sample, a certain predominance of stage I in Asians and stage IV in non-Asians (Table 2). The presence of metastases (M1) was also significantly higher in westerners (Table 3). Our remarkably low survival (median of 26 and 13 months) is explained by the fact that we included patients at a very advanced stage, so they were often submitted only to palliative treatments or even no type of treatment. It should be noted that survival was higher in Asians and this can be attributed to the greater number of Eastern patients in whom resection can be performed when compared to Westerners, since it is known that one of the greatest healing factors is gastrectomy. In Westerners the already known predominance of males, although noted, is less pronounced than among Orientals. This gender difference is not always noticed in other studies. In this regard, we wonder whether women of the second and third generations of Asian descent would not have improved their eating habits earlier than their male counterparts. It should also be highlighted here several aspects of male nutrition, especially in our environment, where the routine use of alcohol is much more noticeable in males [19]. It is known to be an aggressive factor that exposes the mucosa to more mutations. The same can be said about smoking, which is still prevalent among men [20]. The benzopyrene present in cigarettes has been known as a type I carcinogen for decades [21]. Another aspect worth mentioning is the incidence of the diffuse type, which was twice the intestinal type of Laurén in both groups (Table 4). According to the literature, the intestinal type is the most common one of adenocarcinoma, occurring in approximately 54% of cases of adenocarcinomas, while the diffuse type would occur in approximately 30% [22]. What surprised us was the fact that there was a high rate of diffuse type tumors in a developing country, since it is known that in these countries *H. pylori* infection is high and eating conditions are favorable to the intestinal type.

Table 1: Survival time (in months).

Asians	Non-asians
N = 39*	N = 958**
Minimum = 0.0	Minimum = 0.0
Maximum = 197	Maximum = 244
Median = 26.0	Median = 13.0
Mean = 45.5	Mean = 31.2
Standard Deviation = 53.4	Standard Deviation = 41.7
Mann-Whitney test	calculated Z = 1.6145 p = 0.05
There was significant statistical difference in survival time between the studied groups.	
*2 patients with non-available data	
**108 patients with non-available data	

Table 2: Final stage.

Stage	Ethnicity				Total	
	Asians		Non-Asians			
	N	%	N	%	N	%
Tumor absence	0	0	4	0.4	4	0.4
IA	8	19.5	144	13.5	152	13.7
IB	2	4.9	72	6.8	74	6.7
IIA	3	7.3	46	4.3	49	4.4
IIB	2	4.9	85	7.9	87	7.8
IIIA	5	12.2	70	6.6	75	6.8
IIIB	3	7.3	111	10.4	114	10.3
IIIC	11	26.8	163	15.3	174	15.7
IV	7	17.1	371	34.8	378	34.2
Total	41	100	1066	100	1107	100

Fisher's exact test $p=0.1568$ (N.S.) There was no relevant statistical difference in stage between both groups.

Table 3: Presence of metastases.

M Stage	Ethnicity				Total	
	Asians		Non-Asians			
	N	%	N	%	N	%
0	34	82.9	374	35.1	408	36.8
1	7	17.1	692	64.9	699	63.2
Total	41	100	1066	100	1107	100

*5 without data
Chi-square test $X^2= 38.831$ $p<0.0001$ *
M0 stage was predominant in Asian patients
M1 stage was predominant in Non-Asian patients

Table 4: Lauren's histological type.

Histological Type	Ethnicity				Total	
	Asians		Non-Asians			
	N	%	N	%	N	%
Diffuse	26	63.4	657	62.5	683	62.5
Intestinal	15	36.6	349	33.2	364	33.4
Mixed	0	0	7	0.7	7	0.6
Non-identifiable	0	0	38	3.6	38	3.5
Total	41	100	1051	100	1095	100

*15 without data
Fisher's exact test $p=0.5943$
There was no notable difference in histological type between the groups.

Inoperability was doubled in Western patients in our patients. In the literature, there is a tendency towards greater inoperability in non-Asian patients, this difference is even more noticeable when we look at our series of cases in which the incidence of inoperable patients is twice greater in Westerners when compared to Asians. 10 We think that this fact may be related to the socio-cultural level of Asians, who in our country are, in general, more privileged in that aspect. There are reports, for example, that black populations have less access to treatment than Caucasians and Asians [23]. Regarding

location, Strong et al. [24] demonstrated that both ethnicities, Asian and non-Asian, have more distal tumors (Table 5) than proximal tumors (Table 5). However, in the literature, it is customary to find that Asians have, in their population, a much higher proportion of distal tumors than non-Asians. In our sample, both ethnicities have a predominance of distal gastric adenocarcinomas, as expected, however, for us, the proportion among non-Asians was 65.85% of distal neoplasms to 15.85% of proximal neoplasms (almost the quadruple). On the other hand, in the group of Asians the proportion

went from 60.97% to 12.19% (almost 5 times), respectively. This finding differs from what is found in the literature in general, since the difference in the distal-proximal proportion between both ethnicities was not as large as one could expect [25]. This is probably due to the fact that the Asians we studied, most of them, are Brazilian descendants of Asians. In this way, it is possible that the different dietary patterns and the epigenetic influence of the environment in these patients may influence this finding. Finally, in relation to the stage of the patients, since the survival rates are noticeably more favorable in patients of oriental descent, it is easy to conclude that they must have a less advanced stage. Strong et al. [24], as expected, reports in their results a higher incidence of stage IA in Asian patients. In our study, we could see something similar, Asian patients tend to have a better degree of staging with a tendency for a greater number of patients in stage I compared to western patients, while the latter have higher numbers for stage IV. We then return to the clear fact that the diagnosis in non-Asian patients in our country happens later.

Table 5: Tumor location.

Location	Ethnicity				Total	
	Asians		Non-asians			
	N	%	N	%	N	%
Distal	25	60.97	702	65.85	727	65.67
Proximal	5	12.19	169	15.85	174	15.71
Excluded	11*	26.84	195*	18.3	206*	18.62
Total	41	100	1066	100	1107	100

*(Non specified, stump e affecting all portions)

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