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Cohort study of the overall survival of patients with pancreatic cancer in a hospital of specialties of Quito-Ecuador in the period 2007–2017

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Abstract

Objectives: Pancreatic cancers in most patients in Ecuador are diagnosed at an advanced stage of the disease, which is associated with lower survival. To determine the characteristics and global survival of pancreatic cancer patients in a social security hospital in Ecuador between 2007 and 2017.

Methods: A retrospective cohort study and a survival analysis were performed using all the available data in the electronic clinical records of patients with a diagnosis of pancreatic cancer in a Hospital of Specialties of Quito-Ecuador between 2007 and 2017. The included patients were those coded according to the ICD 10 between C25.0 and C25.9. Our univariate analysis calculated frequencies, measures of central tendency and dispersion. Through the Kaplan-Meier method we estimated the median time of survival and analyzed the difference in survival time among the different categories of our included variables. These differences were shown through the log rank test.

Results: A total of 357 patients diagnosed with pancreatic cancer between 2007 and 2017 were included in the study. More than two-thirds (69.9%) of the patients were diagnosed in late stages of the disease. The median survival time for all patients was of 4 months (P25: 2, P75: 8).

Conclusions: The statistically significant difference of survival time between types of treatment is the most relevant finding in this study, when comparing to all other types of treatments.

Keywords: Ecuador; pancreatic cancer; survival analysis.

Introduction

Pancreatic neoplasms are associated with one of the higher mortalities around the world [1, 2]. It is the 14th most prevalent neoplasm and the seventh cause of death for neoplasm worldwide [3]. According to GLOBOCAN 2018, the age-standardized incidence rate (ASR) of pancreatic cancer is 5.5 per 100,000 men, and 4.0 per 100,000 women. ASR mortality is 5.1 per 100,000 men and 3.8 per 100,000 women [4]. In Ecuador, there were 373 deaths due to pancreatic neoplasms in 2017, according to the register of Instituto Nacional de Estadísticas y Censos (INEC) [5].

The risk factors for developing pancreatic neoplasms include genetics, tobacco and alcohol consumption, obesity, and diabetes [6]. The time it takes to develop a pancreatic neoplasm is considered to start between 10 and 17 years before the final stages of the disease. Early identification is associated with a better prognosis [7, 8].

The symptoms depend on the localization of the tumor and the stage of the disease. The most common symptoms include abdominal pain, jaundice, nausea, vomit, and steatorrhea [8]. The mean medial survival rate at 5 years is 9% in all stages of the disease according to the American Society of Cancer between 2008 and 2014 [9].

Today, there is no recommendation for routine screenings of pancreatic neoplasms because of its lower incidence in the general population [3]. The stage of the disease at diagnosis is the most important factor associated with survival rates in patients [1]. Less than 20% of the patients can receive surgical treatment considering the diagnosis is usually made in the late stages of the disease [3, 9, 10]. Other types of treatments include chemotherapy, radiotherapy, and others [11].

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Methods

Study design

A retrospective cohort study was conducted. The case records of patients with a histologic diagnosis of pancreatic cancer, treated within the time frame of 2007 and 2017, were reviewed. The included patients were those coded according to the ICD 10 between C25.0 and C25.9.

Data sources

The study uses secondary data from the electronic clinical records of patients with a diagnosis of pancreatic cancer in a Hospital of Specialties in Quito-Ecuador between 2007 and 2017.

Population

Patients with a diagnosis of pancreatic cancer in a Hospital of Specialties were included and were coded according to the ICD 10 between C25.0 and C25.9.

Statistical analysis

The sociodemographic and clinical characteristics of the population are described above. Using the Kaplan–Meier survival curves followed by the logrank tests, the survival time after initial diagnosis among the different categories of included variables were calculated (type of treatment, type of cancer, and stage of diagnosis). An analysis was carried out by performing Cox proportional hazard regression models that compared survival time for each variable in order to determine the variables that had a *p* value of 0.25 or under. Variables that met the criteria or any other variable that was considered clinically relevant into our saturated Cox regression model were included. By backward variable reduction, a final model was obtained. A sensitivity analysis was furtherly performed.

Stata Version 14 and Microsoft Excel were used for the statistical analysis of this study.

Bioethical considerations

All the information came from secondary data. In Ecuador, the use of public databases with secondary data does not require previous approval by any ethics committee. The database was properly anonymized before its use.

Results

For the period of time of the study, 357 clinical records of patients with pancreatic cancer were found. The mean age in pancreatic cancer patients was 62.7 years old (SD 14.3), with the predominance of females (55.74%). The most frequent personal history was smoking and alcohol consumption (12 and 51.8%, respectively), and 60% of patients had a history

Table 1: Sociodemographic and clinical characteristics of the population.

Variable	n, %
Mean Age (Range, years)	62.75 (19–92)
Gender	
Female	199 (55.74%)
Male	158 (44.26%)
Education	
Primary	157 (43.98%)
Secondary	110 (30.81%)
Higher education	90 (25.21%)
Alcohol history	
Yes	129 (36.1%)
No	228 (63.9%)
Smoking history	
Yes	43 (12%)
No	314 (88%)
Diabetes history	
Yes	216 (60.5%)
No	141 (39.5%)
Clinical sign of admission	
Abdominal pain	182 (50.98%)
Jaundice	104 (29.13%)
Abdominal mass	39 (10.92%)
Vomit	19 (5.32%)
Weight loss	13 (3.64%)
Ca 19-9	
Positive	254 (68.63%)
Negative	104 (29.13%)
No data	8 (2.24%)
Type of cancer	
Endocrino	39 (10.2%)
Exocrino	318 (89.8%)
Anatomical location	
Head	211 (59.10%)
Tail	35 (9.80%)
Body	70 (19.61%)
Others	41 (11.49%)
Stage of cancer	
0	1 (0.28%)
I	63 (17.65%)
II	46 (12.89%)
III	54 (15.13%)
IV	193 (54.06%)
Type of treatment*	
Combined	40 (11.20%)
Palliative	155 (43.42%)
None	38 (10.64%)
Chemotherapy	27 (7.56%)
Surgical	97 (27.17%)

of diabetes. The main sign of admission was abdominal pain (50.98%). Sixty-eight percent% of patients had a positive antigen Ca 19-9. Adenocarcinoma was the most frequent type of cancer (56.86%), the most frequent location was the head of the pancreas (59.10%). More than two-thirds (69.19%) of

the patients were diagnosed in the late stages of the disease, we account for stages III and IV that represented 15.13 and 54.06%, respectively, as of late stages for pancreatic neoplasm. Of these 38.3% ($n=137$) patients received surgical treatment, in this group 27.17% had surgery alone and 11.2% had surgery plus another treatment (Table 1).

Kaplan–Meier survival curves were created and then followed by a logrank test to compare survival functions. These tests showed a statistically significant difference in survival between groups of treatment ($p<0.001$). Survival time from the moment of diagnosis was highest among the group that received surgical treatment at 1, 2, 5 years, and at the end of follow-up (Table 2). The lowest survival proportion for this group was of 0.51 at 3 years of follow up, compared to zero when receiving no treatment or palliative care, 0.16 when receiving chemotherapy, and 0.29 when receiving combined treatment.

The overall survival rate based on treatment modality is shown in Figure 1. The median survival time from the moment of diagnosis for no treatment was 2 months, for

chemotherapy 5 months, for surgical treatment 17 months, for combined therapy 7 months, and for palliative care 2 months.

The overall survival rates based on the type of cancer are shown in Figure 2. There is no statistically significant difference in survival rates if the patient was diagnosed with exocrine cancer compared to endocrine cancer ($p=0.605$).

The stage at which the cancer was detected clearly marks a difference in survival rate. The median survival time was 14 months for stage II, 5 months for stage III, and 2 months for stage IV.

An unadjusted Cox Regression model that analyzed the relationship between survival time and age, gender, stage at diagnosis, type of cancer, and type of treatment was done to determine the variables that had a p value of 0.25 or under. A saturated model which included stage of diagnosis and type of treatment was performed with variables that met the inclusion criteria. We also included the type of cancer due to its clinical relevance. By backward

Table 2: Survival time according to type of treatment.

Interval, months	Beg. Total	Deaths	Lost	Survival	Standard error	[95% Conf. Int.]
No treatment						
0–12	38	38	0	0.0000	-	-
Chemotherapy						
0–12	27	20	1	0.2453	0.0836	0.1043 0.4174
12–24	6	2	0	0.1635	0.0730	0.0531 0.3274
24–36	4	0	1	0.1635	0.0730	0.0531 0.3274
36–48	3	0	2	0.1635	0.0730	0.0531 0.3274
60–72	1	0	1	0.1635	0.0730	0.0531 0.3274
Surgical treatment						
0–12	97	23	29	0.7212	0.0494	0.6110 0.8051
12–24	45	10	11	0.5386	0.0620	0.4102 0.6508
24–36	24	1	4	0.5141	0.0639	0.3832 0.6304
36–48	19	0	5	0.5141	0.0639	0.3832 0.6304
48–60	14	0	5	0.5141	0.0639	0.3832 0.6304
72–84	9	0	5	0.5141	0.0639	0.3832 0.6304
84–96	4	0	1	0.5141	0.0639	0.3832 0.6304
108–120	3	0	1	0.5141	0.0639	0.3832 0.6304
132–144	2	0	1	0.5141	0.0639	0.3832 0.6304
144–156	1	0	1	0.5141	0.0639	0.3832 0.6304
Combined treatment						
0–12	40	24	5	0.3600	0.0784	0.2120 0.5103
12–24	11	2	1	0.2914	0.0770	0.1531 0.4448
24–36	8	0	1	0.2914	0.0770	0.1531 0.4448
36–48	7	1	2	0.2429	0.0780	0.1099 0.4037
48–60	4	0	1	0.2429	0.0780	0.1099 0.4037
60–72	3	0	3	0.2429	0.0780	0.1099 0.4037
Palliative care						
0–12	155	151	3	0.0163	0.0102	0.0039 0.0471
12–24	1	1	0	0.0000	-	-

Figure 1: Kaplan–Meier estimates by type of cancer.

Figure 2: Kaplan–Meier estimates by type of treatment.

Figure 3: Kaplan–Meier estimates by stage of diagnosis.

variable reduction, a final model which included stage of diagnosis and type of treatment was chosen. The researchers furtherly performed a sensitivity analysis by

Table 3: Final Cox regression model.

Stage at diagnosis	Hazard ratio	p-Value	95% Confidence interval	
Stage 1	1			
Stage 2	7.288759	0.000	2.77248	19.16191
Stage 3	25.36602	0.000	9.354024	68.78695
Stage 4	44.48086	0.000	16.30272	121.363
Type of treatment	1			
No treatment	1			
Chemotherapy	0.5537656	0.036	0.31873	0.9621194
Surgery	0.4945155	0.013	0.2837633	0.8617942
Combined	0.3400392	0.000	0.2015927	0.5735658
Palliative care	0.780844	0.177	0.5454472	1.11783

eliminating all patients diagnosed at stage 0, which significantly changed our results, leading us to exclude stage 0 patients. It was found that when adjusting for stage of cancer, there is a 0.49 Hazard Ratio when patients are treated with surgery compared to no treatment ($p=0.013$) and of 0.34 when patients are treated with both surgery and chemotherapy ($p<0.001$) as described in Table 3.

Discussion

New diagnosis techniques and treatments have been discovered for pancreatic neoplasms in the last decade. Despite all these advantages, the survival rates have not improved [3, 12].

In our study, 69.9% of the patients were diagnosed in the late stages of the disease. This could be compared with McGuigan's review of patients, who noted that this was a result of the unspecific symptoms and the rapid invasion of blood vessels [3].

The mean survival rate of patients at 5 years was 2–9% in a study performed in Shanghai [12], comparable to a 14% survival rate in our study [13].

The study results show a survival time of 14 months from the moment of diagnosis for patients at stage III compared with only two months in patients at stage IV [14], this data could be compared to the results of Cancer Research UK in which the mean survival time for patients at stage III was 6–11 months and 2–6 months for patients at stage IV [13]. Other studies have found similar results [15–17].

Surgery was associated with the best survival time in patients with pancreatic neoplasms. The mean survival time for patients who underwent surgery was 17 months compared with 5 months for those patients who received chemotherapy. Similar results have been described by Nakeeb [18], Kardosh [16], Nakagawa [19], Brooks [20], and Cancer Research UK [13].

A limitation of the study was the exclusion of some patients because their clinical records were incomplete. There were fewer registered patients with pancreatic neoplasms in the years previous to 2010 and some of the patients did not continue with follow-up treatment due to a lack of subsequent appointments at the hospital.

Conclusion

The statistically significant difference of survival time from the moment of diagnosis between types of treatment is the most relevant finding in this study. When compared to all other types of treatments, surgery yields the best results. An early diagnosis increases the possibility of receiving surgery and having a better survival time in patients.

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Competing interests: Andrés Moreno Roca, Luciana Armijos Acurio, Ruth Jimbo Sotomayor, Carlos Céspedes Rivadeneira, Carlos Rosero Reyes, Carlos López Ayala, declares no conflict of interest.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (Hospital Carlos Andrade Marín) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by hospital authorities and the Human Research Ethics Committee.

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