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Survival Prediction for Romanian Patients with Pancreatic Cancer

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Abstract

Pancreatic cancer is one of the most lethal malignancies worldwide and in some of the latest statistics ranks fourth in the total number of deaths related to cancer in patients of both genders. Currently, curative treatment is only possible in cases of resectable disease and during the initial stages. Still, although complete surgical resection is the only potential curative approach of this disease, it can only be performed in 10 to 20% of patients, since most individuals present with advanced disease upon diagnosis. Moreover, in the recent decades the development and improvement of surgical techniques have only improved postoperative mortality, without having any significant impact on the survival, with specialized pancreatic surgery centres reporting mortality below 5%. In this way, in the present study conducted on 188 patients from the "St. Spiridon" Clinical Emergency Hospital Iasi, we were interested in determining the survival rates in pancreatic cancer, as well as looking at the staging criteria for adenocarcinoma of the pancreas that follows the tumor/node/metastasis (TNM) system and the correlations between any of these stages and the overall survival. Weibull distribution was used to estimate the overall survival. Reduced survival in pancreatic cancer was found to be within the limits found in the published literature: 41.7% at 1 year, 8.7% at 3 years and 1.9% at 5 years. Still, no significant correlation was found between any of the disease stages and the overall survival.

Keywords: Pancreatic cancer; Pancreatectomy; Survival

Introduction

Pancreatic cancer is one of the most lethal malignancies worldwide, and ranks fourth in the total number of deaths related to cancer in patients of both genders. Moreover, in 2013 the United States registered about 45,000 new cases, and reported that the number of expected deaths was very similar to the number of new cases. Also, the median overall survival at 5 years is between 2 and 6% [1].

Also, adenocarcinoma of the pancreas is the most common type of pancreatic neoplasm, with all of its subtypes accounting for 85% of cases [1,2].

Currently, curative treatment is only possible in cases of resectable disease and during the initial stages [3]. Still, although complete surgical resection is the only potential curative approach of this disease, it can only be performed in 10 to 20% of patients, since most individuals present with advanced disease upon diagnosis [3,4]. Moreover, after surgical resection, 7 to 25% of patients have a 5-year survival rate [5], with better results in individuals which undergo curative resection (R0) [6].

The prognosis for the patients with pancreatic cancer and which have indication for the resection with curative intent is determined by the lymphatic metastasis, the invasion of vascular walls and the peripancreatic nerve plexus or also by the degree of the micrometastases in nearby tissues and organs.

As we mentioned before, unfortunately 95% of patients come to the doctor when the cancer is advanced and unresectable [7-9]. Moreover, in the recent decades the development of surgical techniques have only improved postoperative mortality, without having any significant impact on the survival, with specialized pancreatic surgery centres reporting a mortality below 5% [10,11].

Approximately 60% of pancreatic cancers have cephalic location. With the reduction of operative mortality after duodenopancreatectomies, improved survival rates of 30% were reported [12], which is three times higher than previously published results [13,14].

However, early results improvement (decreased mortality, increase resectability rate) and the long-term survival are different aspects and it seems that sometimes there is no causal relationship between them.

Moreover, some surgeons are not fully confident in these sudden improvements of the survival parameters, as it was suggested by several authors, an increase need for the anatomopathological reconfirmation of the original diagnosis, while other authors have proposed standardized methods of evaluation and reporting systems of survival data and a clear delimitation for the subgroups of patients [15].

For now, surgical resection is still the best chance to prolong the disease-free interval. In addition, with all the development in perioperative management and despite the reduction in operative mortality corresponding to more aggressive resections, the literature showed no appreciable improvement for this disease over the past 20 years [16].

In this way, in the present study conducted on 188 patients from the local Clinical Emergency Hospital "Sf. Spiridon" Iasi, Romania, we were interested in determining the survival rates in pancreatic cancer, as well as looking at the staging criteria for adenocarcinoma of the pancreas that follows the tumor/node/metastasis (TNM) system and the correlations between any of these stages and the overall survival.

Materials and Methods

This study was conducted on 188 patients from Clinical Emergency Hospital "Sf. Spiridon" Iasi, Romania, all with solid form of pancreatic

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cancer. 97 of the patients were females, 91 males. The median age was 65 years old. 53% of the patients were rural areas and 47% from urban areas. All the patients included in this group were diagnosed with solid pancreatic tumors, all malignant (largely represented pancreatic adenocarcinoma). Exclusion criteria were represented by cystic forms (pancreatic pseudocyst, pancreatic cystadenocarcinoma) and benign forms (chronic pancreatitis - pseudo tumoral form).

Weibull distribution was used to estimate the overall survival. This method is the most popular method for measuring statistical events involving data with timeframes [17]. Alpha is an interpretation of probability of 63.2% that the event will occur. Beta is the interpretation of probability that hazard to grow (beta>1) to decrease (beta<1) while beta = 1 is an exponential distribution with constant hazard. If beta factor is nearly 1, we can conclude that the distribution is exponential and it has a constant hazard rate.

In addition, we also used Cox Proportional Hazard method for assessing the correlation between tumor/node/metastasis (TNM) cancer staging system [18,19] and the overall survival. The Cox proportional hazards model has been the most widely used procedure over many years of experience in medical research, especially considering its applicability to a wide variety of clinical studies [20,21].

Results

In this way, as it can be seen in Figure 1, by using the Weibull distribution we observed that in our 188 patients with pancreatic cancer from Clinical Emergency Hospital "Sf. Spiridon" Iasi, the estimates of survival results were the following: 41.7% at 1 year, 8.7% at 3 years and 1.9 at 5 years.

Moreover, as mentioned before, Weibull distribution was used to estimate the overall survival (Figure 2). In this way, in our case we obtained a β of 0.93. As it is indicated by the plot, Weibull distributions with β<1 have a failure rate that decreases with time, also known as infantile or early-life failures. This could suggest that our general survival estimation accuracy increases with time. Also, with β being relatively close to 1, we can conclude that this is an exponential distribution with fairly constant hazard.

In addition, when we performed the statistical correlations between the general survival and the tumor/node/metastasis (TNM) system by using Cox Proportional Hazard method, we could not find any significant correlation between the selected factors as follows:

- The tumor size and/or amount of spread into nearby structures (T) vs. overall survival: Probability>Chi sq; 0.1836;

- Whether the cancer has spread into nearby lymph nodes (N) vs. overall survival: Probability>Chi sq; 0.1700;

- Whether the cancer has spread (metastasized) to distant parts of body (M) vs. overall survival: Probability>Chi sq; 0.7611.

Discussion

Over the past decades significant progress was made regarding surgical management of patients with pancreatic cancer. It is now well known that in specialized centres for pancreatic resection the reported mortality is up to 5%. This is due to both the improvement and standardization of surgical techniques and also to the postoperative care progress. But despite these facts minimal progress was made in achieving better rates of survival for patients with resectable tumours [7-9]. The chances for long-term survival are still small. A survival at 5 years reported in the literature varies between 13% and 25% for the subgroup of patients which received resection with curative intent [10].

On the other hand, long-term survival at 5 years after R0 resection is reported in the literature as being below 10% on series of selected patients with no evidence of recurrence during this period. These results are inconsistent with other studies reporting values of actuarial survival at 5 years 20% - 40% of resected patients. One explanation consists in the very fact that the statistical method of Kaplan-Meier for the survival appreciation excludes from calculations both in hospital deceased patients and those who were lost from under observation. In this way, other methods and criteria should be used in order to properly judge the results of resection, such as the actual survival [5].

Also, the reduced survival for pancreatic cancer in the present study falls within the limits found in the previously published literature: 41.7% at 1 year, 8.7% at 3 years and 1.9% at 5 years. In this way, we can cite here the previous studies of Grace et al. from UCLA reporting a 5-year survival of 3% on 37 patients or the report of Connolly group from the Chicago University describing a 3.4% survival at 5 years on 89 patients [10]. Still, there are studies reporting a 30% 5-years survival on 103 patients in Japan or 25.4% in Mannheim on 122 patients, as in study conducted by Trede et al. group [10].

This difference in 5-year survival in all these studies may be related to many factors. It is known that the treatment outcome in pancreatic cancer does not only depend on the chemotherapy regimen used, but also on the nature of the primary tumour and the surgery performed [3]. In addition, most patients have multiple comorbidities, which are also related to the epidemiology of cancer itself, such as smoking, obesity, diabetes and older age [22,23]. Thus, a better control of these variables, which are also the main known risk factors in all types of cancer could lead of course to closer results.

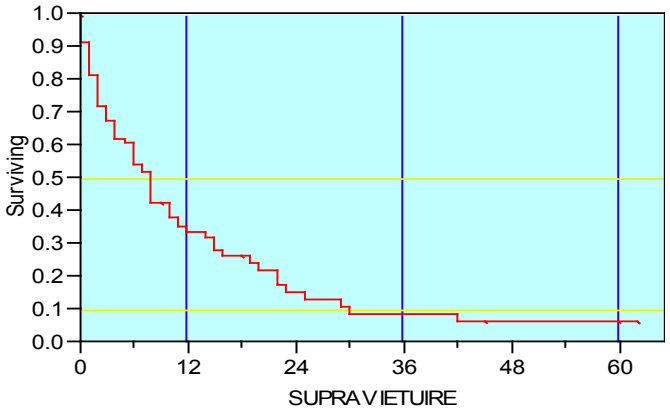

Figure 1: Overall survival in our selected group of patients with pancreatic cancer.

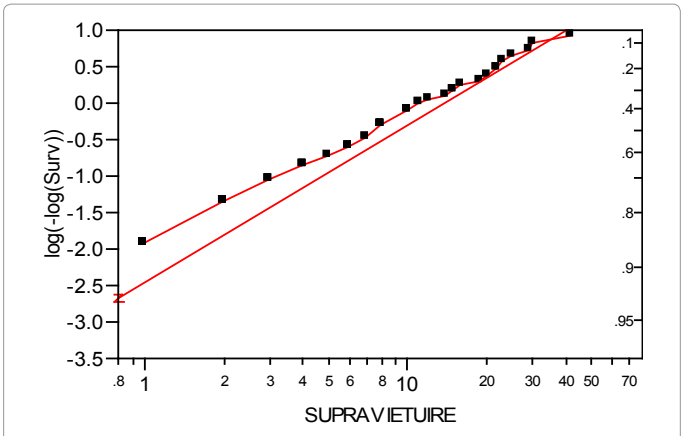

Figure 2: Weibull plot for our selected group of patients with pancreatic cancer.

Moreover, one population based study made on 1,759 patients from The Surveillance Epidemiology and End Results (SEER) database found that early diagnosis using high-resolution multi detector CT and accurate staging are associated with improvement in survival [24]. This fact also supports previous studies that have identified tumour size, lymph node status and degree of differentiation as significant predictors of survival in pancreatic cancer [25]. As mentioned before, in our study none of the cancer stages correlated with overall survival.

In addition, other studies showed that the best survival rates differentiated on stages were obtained after surgical resection. Therefore the resection is desirable when it can be performed with an acceptable rate of postoperative complications. The statistical methods of multivariate analysis showed that for all patients the tumour grading was a significant predictor of survival, while for resected patients the first predictor was the tumour stage followed by grading as predictive factors [26].

Conclusion

In this way, the conclusion for our data would be that until further progress will be made in the strategies for an early diagnosis of pancreatic cancer or new effective chemotherapy drugs will be discovered, survival rate will not increase. Also, the surgical exploration is the method with the highest accuracy in the diagnosis, staging and the resectability of pancreatic tumours.

Conflict of Interest

Authors have no conflict of interest to disclose.

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