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Pancreatic Cancer 80 Years

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Abstract

Resections for pancreatic adenocarcinoma have now been carried out for 80 yrs. Opinions still differ as to the results. The incidence of pancreatic cancer was estimated to be 48,960 in 2015 in the US. It is projected to increase to 88,000 for both sexes in 2030 and to become the second to third leading cause of cancer-related deaths by 2030. O'Neill and colleagues studied the total direct medical cost of treatment of pancreatic patients 66 years and older who were diagnosed from 2000-2007 in the US. The total direct cost for resectable disease was $134,700, and for unresectable locoregional disease $65,300. Assuming a 2.5% inflation over 10 years, the cost in 2017 could be $172,500 for resections and for unresectable (or bypasses) $83,500.

This author has scrutinized the literature on surgical results over the last 80 years, checking for the number of survivors and the overall survival percentage. Approximately 1230 papers have been found which deal with resections and reveal at least some survival information.

Papers on the surgical aspects of pancreatic cancer differ as to the approach and the composition of the patient group and the method of reporting. Only papers with separate pathologic information on patients were selected for analysis. The search revealed that of these 1230 papers, only 621 papers report 5-year survivors. Special attention has been paid to the time period each study covered, patient composition, the subset of patients used for calculations and the statistical method used.

Reservation, Non-Resected Survivors

The first reservation about the effect of surgery on this disease was expressed by Glenn and Thorbjarnarson [1-5] in 1964, again by Gallitano [6] in 1968 whose only 5-year survivor was "non-resected", and then strongly by Crile in 1970 [7], whose only survivor was also non-resected. Crile's criticism was directed at the then high mortality rate and the survival calculations which might count only those who survived the operation.

The presence of non-resected survivors has been disputed [8], but is a major issue in the debate on survival. In a previous review 41 reports were found from 31 institutions in 12 countries. Non-resected survival is a fact and should be kept in mind in assessing overall therapeutic results.

Initially reports detailed the course of all patients diagnosed at a particular institution, but in recent decades reports have concentrated only on resected patients.

Survival Calculations

The survival percentage depends not only on the number of survivors but not less on the subset from which the number is calculated.

Overall survival success must be based on the original group diagnosed with pancreatic cancer (the TN or total number) and the number of survivors, and not only on a small subgroup. Different methods of calculation have been used to enumerate the results, i.e. actual versus actuarial.

Initially most papers revealed the TN, the number of resections and simply the number of survivors. In the late 1980's the papers started reporting only the number of resections and survival as actuarial percentages, usually calculated with the Kaplan-Meier method, with or without the actual number of survivors being reported [9].

Sir Austin Bradford Hill pointed out in his book in 1937 that when a "large number of patients is lost sight of" the outcome might be erroneously high [10]. In a frequently quoted paper 11 survivors out of 201 are claimed as 22% survival [11,12].

In a previous report the original TN of patients studied was revealed in only 90 or 14.5% of the papers and in these the actual number of survivors was only 66. Detailed information on the original TN group studied, number of resections and actual number of survivors is therefore reported in

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only 66 or 10.6% of all papers on pancreatic cancer. In the remaining 89.4% some form of estimate or calculation is required to assess survival percentage.

In 424 reports with survival calculations by actuarial methods the number of survivors is stated in only 147 or 34.6% but through inquiry the actual number of survivors was known in 205 of the 424 reports or 48.3%. The actuarial and actual percentage figures can therefore be compared, showing that the actuarial percentage is on the average 2.75 higher than the actual percentage. This figure has therefore been used to estimate the number of survivors and the survival percentage in the relevant studies where only the actuarial percentage has been published.

The resection rate has been variable and can only be assessed accurately if the original group is known. Of the studies published in the last 5 years, 156 of 161 or 97% report only the number of resections and the percentages. In a previous study by this author the resection rate was 10.8% [12]. In earlier US studies the rate was, respectively, 8.4% and 12% [13,14]. In 2 European national studies [15,16] the rate was from 8% - 12% over the last 5 years. It is therefore practical to assume that the resection rate is10% in the studies where the original TN of the group is not reported in order to estimate the TN accordingly, and divide the percentage by 2.5 - 3 where only the actuarial percentage has been published.

After totaling the numbers in the 621 studies with survivors with the above correction, the TN comes to 1,731,834, the number of resected patients comes to 162,207, and the number of survivors to 11,300, for an apparent survival percentage of 0.77%.

After totaling the number of patients in all the 1230 reports, the original TN comes to 3,188,543, the number of resected patients to 284,298, and the number of survivors to 11,330. The overall survival percentage would then be only 0.45%.

Repetitions

Repetition of reporting the same survivors in different papers was first pointed out in 1978 [4], and detail in 1995 [17]. It occurs in various ways, though mainly when the patient population and survivors from a certain year are reported several times from the same institution. Repetition has occurred up to 6-8 times in Germany, Italy and Japan, and up to 20 times in the US.

Repetition also occurs when papers include survivors from many different institutions in a specific country or even when a study includes patients from many countries. Thus 92 of the 620 studies with 5-year survivors are from many institutions in a specific country or 14.8%, and 10 of these from many countries or 1.6% [4].

Examination of one or more reports from a single institution which together cover the entire study period and state the number of survivors, and then adding up the number of patients from all the studies, reveals that the total number reported is over 10 times larger.

There is no scientific method to assess the number of repetitions accurately but each reported 5-year survivor and therefore respective resection and the TN seem to be reported 3-5 times. Dividing the number of reported survivors and respective resections and TN by 4, the overall number of 5-year survivors is hardly more than 2,800, the number of resections 40,500, and the original TN number of patients 433,000.

Repetitions occur also in the "no-survivor" group of reports, but not as frequently. It may be assumed that all published reports with or without survivors are drawn from a TN of approx. 1,000,000 patients and with fewer than 3,000 survivors, of whom a significant number were non-resected, meaning that the overall survival rate was no more than approximately 0.3%.

Mortality, Positive Margins and Nodes

Mortality during the first 20 years, 1945-1965, was on average 25.2% with a single report of 62.5%. and during the last 5 years 4%, The overall mortality rate has therefore been greatly reduced.

In the majority of reports in recent decades the number of positive margins and nodes and numbers over 60% - 70% are frequently quoted [18]. It is of great interest that even in the most experienced hands in only 16% of cases were both margins and nodes negative [19].

Discussion and Conclusion

Pancreatic cancer is thus both a costly and devastating disease and has usually spread beyond its boundaries at the time of diagnosis and treatment and is thus a systemic disease.

The use of actuarial calculation methods exaggerates the percentage and thereby the number of presumed survivors in a particular study.

Reporting the same patients repeatedly without any qualification gives a false impression of success.

Life table curves should be accompanied by the actual number of survivors. The course of non-resected patients should be studied.

Surgical skills are imperative for the care and palliation of pancreatic cancer patients, including possible resections, but they have had only a minimal impact on the survival rate.

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