
Early pancreatic cancer: Are we doing enough?

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SUMMARY

Surgery remains the only modality with the potential to cure pancreatic cancer, which has an overall dismal prognosis due to late presentation,

aggressive tumour biology, complex surgical management, and the lack of effective systemic therapies. Overall 5-year survival rates have remained at 5%, although it is clear that resection of localized disease would enable survival rates of up to 30% at 5 years. Further, improvements in preoperative evaluation, surgical techniques and perioperative care have brought mortality rates following pancreaticoduodenectomy from around 25% in the 1960s to <3% in high-volume centres.

Against this background, the authors of this paper hypothesized that an air of therapeutic nihilism still existed among clinicians treating pancreatic cancer and sought to verify this by examining (i) the utilization rate of surgery in pancreatic adenocarcinoma, (ii) the reasons for failing to apply surgery in localized disease, and (iii) the effect of surgical resection on survival.

The source of data was the National Cancer Data Base (NCDB) of the American College of Surgeons and the Commission on Cancer, which accounted for over 75% of all cancers treated in the USA with over 19 million patients from 1440 hospitals. This database is unique because it requires both clinical and pathological staging information

in patients who undergo surgical resection. Only those patients with pancreatic cancer who had complete staging information and were clinically stage I (T1N0M0, T2N0M0) were included in the analysis. Thus, out of 192 565 patients with pancreatic cancer, 9559 with pretreatment clinical stage I disease who were potentially resectable were selected for analysis. The study made some important observations:

1. Over 60% of patients had Medicare or private insurance.
2. About 70% of tumours were in the pancreatic head.
3. Academic hospitals treated only around 45% of patients, and the remaining were treated at community hospitals.
4. Overall, 2736 patients (28.6%) underwent surgery, of which 96% had resectable tumours.
5. The reasons for not subjecting patients to surgery included co-morbid conditions (6.4%), patient refusal (4.2%), advanced age (9.1%), 'not offered surgery' (38.2%) and unknown reasons (13.5%).
6. On comparing the data of operated patients with those who were not, the following observations were made:
 - a. Operated patients were younger (65.1 v. 71.7 years)
 - b. Failure to operate occurred more among patients who had the following characteristics
 - i. Older
 - ii. Black race
 - iii. Lower annual incomes
 - iv. Lower education
 - v. Medicare/Medicaid beneficiaries
 - vi. Three-fold less likelihood in head/body tumours as opposed to tumours of the pancreatic tail
 - vii. Low-volume centres
 - viii. Community hospitals (the best operation rate was at National Cancer Institute Cancer centres, followed by other academic centres, with community hospitals having the least operation rates)
 - c. Refusal of surgery also occurred more often in (i) older patients, (ii) blacks, (iii) Medicaid beneficiaries, (iv) those with lesions of the head/body of pancreas, (v) low-volume and community hospitals. Surprisingly, annual income and level of education did not affect patients' refusal of surgery.
7. 5-year survival rates for clinical stage I disease among patients who underwent pancreatectomy were better (19.3%) than those for patients with clinical stage III/IV disease (0.8%). The corresponding median survival was 19.1 and 4.2 months, respectively.
8. Stage I patients not offered surgery had a median survival of only 8.4 months which was only marginally better than that for stage IV patients.
9. Pancreatectomy was an independent predictor of a greater than 2-fold increase in the likelihood of survival.
10. During 1995–2004, the utilization of pancreatectomy in stage I patients increased from 21.8% to 35.7%.

COMMENT

This remarkable paper underlines the importance of documentation. Despite the inherent difficulties in achieving completeness of data entry into registries, the paper has thrown up some serious issues.

First, this paper provides one more evidence that surgical resection is the treatment of choice for localized pancreatic cancer, a fact highlighted in previous papers.^{1–3} The study did not include T3 and N1 tumours, both of which are also benefited by surgery; had they been included, the power of this study would have been enhanced.

Second, the paper underlines the fact that even in 2004, only 35.7% of patients with stage I disease underwent surgical resection. This indicates that 2 of every 3 patients who were candidates for surgical therapy did not actually undergo surgical resection. In

over half these patients there was no documented reason for not offering surgery, and in 38%, it appeared that they were simply not offered surgery. This reflects a persistent therapeutic nihilism that still ails medical practice, with many physicians believing that pancreatic cancer is untreatable, and that surgical treatment has a high risk and doubtful benefit. Although not evaluated in this study, it is clear that pancreatic resection currently has a low operative mortality,^{4–6} and is the only therapy that currently has the potential to cure.

Third, disparities in care were identified in the analyses. The lower rates of surgery in the elderly is understandable given that they may have greater co-morbid illnesses; but racial disparity was difficult to explain, as was the fact that malignancies of the pancreatic tail were resected more often than those in the head. Cancer of the tail of the pancreas is usually advanced at presentation, and stage I cancers are few. The higher number of resections of pancreatic tail tumours can only be explained on the basis that distal pancreatectomy for tail cancer may be technically easier than the Whipple operation; this reflects nihilism among surgeons as well. The higher rate of surgery in academic institutions reflects a greater willingness among surgeons in such institutions to operate on pancreatic cancer. Further, one may argue that patients not offered surgery might have had co-morbid conditions which were not reported, but the data showed that patients not operated had in fact a lower Charlson score than those who were. It is possible that data entry was more complete for those patients who were surgically treated than those who were not; this is a limitation of data from registries.

The stated weakness of the paper; namely, that stage II patients were not included, is actually its strength; if those had been included, the figures might have been even more startling. The paper emphasizes 3 important facts: (i) surgery is superior to non-operative treatment for localized pancreatic cancer, (ii) surgery must be offered to all patients with localized pancreatic cancer regardless of age, race, hospital setting or tumour location, and (iii) therapeutic nihilism must be eradicated from the minds of physicians and surgeons treating pancreatic cancer.

This is only a first step, and I feel that the principle must be carried forward to application of a multimodality approach to localized pancreatic cancer, so that survival can be improved further.

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