In Defense of the Whipple: An Argument for Aggressive Surgical Management of Pancreatic Cancer

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INTRODUCTION

In 1898, Allesandro Codivilla performed the first pancreaticoduodenectomy; however, it was Kausch who first described the surgical technique in 1912. More than two decades later (1935), Allen O. Whipple performed a two-staged pancreaticoduodenectomy that involved a biliary diversion and gastrojejunostomy followed by resection of the duodenum and head of the pancreas. In 1941, Whipple modified the operation into a one-stage pancreaticoduodenectomy, which would situate his name into the history of pancreatic surgery. Despite this technical achievement, the procedure lacked rapid adoption because of its difficulty, and came to be associated with high hospital morbidity, and mortality rates approaching 30%. More than a century since the first Whipple procedure, pancreatic cancer continues to affect 200,000 people worldwide and claim 34,200 American lives each year, with an additional 37,680 new diagnoses expected in 2008. The lifetime risk for developing pancreatic cancer is now 1 in 79 for both men and women, and it remains the fourth leading cause of cancer death in the U.S. [1]. Whereas death rates for cancers of the stomach, lung, colon, and prostate have decreased over the past 20 years, death rates from pancreatic cancer have remained stable, with a slow increase in those aged >70 years. Although some of this may be a result of an increased overall life expectancy, the natural history of pancreatic cancer, lack of early detection strategies, inability to adequately identify at-risk populations, and aggressive biology play important roles in the disease’s lethality, and remain a challenge to its treatment.

PANCREATIC CANCER: A STRUGGLE AGAINST NIHILISM

The nihilistic approach to the surgical treatment of pancreatic cancer and the negativity surrounding the Whipple procedure that dominated much of the mid-to-late 20th century were codified in a manuscript by Tendler and Livermore (1959) that evaluated the role of radical surgery for carcinoma of the pancreas and ampullary region. These authors describe a medical community with an overwhelmingly pessimistic perspective toward the surgical treatment of pancreatic cancer [2]. But that was then and this is now, so why revisit that surgical history? Although certainly much has changed, naysayers abound and arguments against aggressive surgery for pancreatic cancer continue to dominate the thinking.
ARGUMENTS FOR SURGICAL NIHILISM IN PANCREATIC CANCER CARE: “DESPITE HEROIC SURGICAL EFFORTS, THE COSTS IN PATIENT MORBIDITY AND MORTALITY ARE GREAT, AND THERE IS LITTLE CHANGE IN SURVIVAL”

Beginning in the early 1980s, surgical attitudes toward pancreatic cancer and the Whipple procedure changed as high-volume surgical centers of excellence emerged. In experienced surgical hands, hospital mortality following a Whipple procedure fell to approximately 5%, operative times decreased, blood loss was minimized, and severe morbidity was minimized (though the overall morbidity rate remains near 40%) [3–5] (Table 1). Even more important, superior long-term survival rates for early-stage pancreatic cancer patients were achieved [6–9]. Winter et al. [10] published a series of 1,423 pancreaticoduodenectomies for pancreatic ductal adenocarcinoma performed at the Johns Hopkins University between 1970 and 2006. Those authors reported 1-year, 2-year, and 5-year survival rates of 65%, 37%, and 18%, respectively. Additionally, the median postoperative stay declined over time, from 16 days to 8 days during the study period, and the perioperative mortality rate declined from 30% to 1%. Equally importantly, a Gastrointestinal Quality of Life Index administered postoperatively found that most patients reported an excellent quality of life after a Whipple procedure [6, 8]. With such improvements in surgical technique, superior long-term survival for early-stage patients managed surgically, and an increase in post-surgical quality of life, surgical attitudes toward the Whipple procedure changed, but are our nonsurgical colleagues equally convinced?

In 2007, Bilimoria et al. [11] reviewed data on 9,559 patients with clinical stage I pancreatic cancer. Amazingly, those authors found that nearly 40% (38.2%) of patients with clinical stage I disease lacking any identifiable contraindication to surgery were not offered operative care (Table 2). Among this cohort, only 28.6% of the group underwent surgical resection, whereas 71.4% did not have surgery. This is despite the fact that complete surgical resection was achieved in 96.1% of all patients upon whom it was attempted. Among the group of patients who did not undergo surgery, extensive comorbidities, advanced age, and patient refusal accounted for 19.7% of the reason patients did not undergo surgery. In 13.5% of the patients, the reason surgery was not offered was unknown, and most strikingly, in 38.2% of the patients, the reason patients did not undergo surgery was because they were “not offered surgery.” This latter fact is made all the more glaring (and sad), when one compares 1-year, 5-year, and median survival rates between those who underwent surgery and those who did not. In the surgery group, the 1-year and 5-year survival rates were 69.8% and 24.6%, respectively, whereas the median survival duration was 19.3 months. Among those not of-

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### Table 1. Improvements in intraoperative and postoperative benefits associated with the Whipple procedure

<table>
<thead>
<tr>
<th>Study</th>
<th>Years</th>
<th>n of patients</th>
<th>Operative time (hours)</th>
<th>Estimated blood loss (ml)</th>
<th>Intraoperative blood transfusion (ml)</th>
<th>Postoperative length of stay (days)</th>
<th>Perioperative mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crist et al. (1987)</td>
<td>1969–1986</td>
<td>88</td>
<td>8.4 ± 0.24</td>
<td>2,519 ± 263</td>
<td>4,900 ± 390</td>
<td>NA</td>
<td>12.5</td>
</tr>
<tr>
<td>Yeo et al. (1997)</td>
<td>1990–1996</td>
<td>650</td>
<td>7</td>
<td>625</td>
<td>0</td>
<td>13</td>
<td>1.6</td>
</tr>
<tr>
<td>Tseng et al. (2007)</td>
<td>1990–2004</td>
<td>650</td>
<td>9.2</td>
<td>900</td>
<td>NA</td>
<td>14</td>
<td>1.4</td>
</tr>
<tr>
<td>Mullen et al. (2005)</td>
<td>2001–2004</td>
<td>272</td>
<td>7.3</td>
<td>650</td>
<td>NA</td>
<td>10</td>
<td>1.1</td>
</tr>
<tr>
<td>Winter et al. (2006)</td>
<td>1970–2006</td>
<td>1,423</td>
<td>6.3</td>
<td>800</td>
<td>0–27 units</td>
<td>9</td>
<td>2</td>
</tr>
</tbody>
</table>

Improvements in intraoperative and postoperative benefits associated with the Whipple procedure over the past 35 years are demonstrated by the studies listed. Of major importance are the significant reductions in intraoperative blood loss and perioperative mortality.

**Abbreviation:** NA, not available.

### Table 2. 1-year, 5-year, and median survival rates of stage I pancreatic cancer patients

<table>
<thead>
<tr>
<th>Treatment and disease</th>
<th>1-yr survival (%)</th>
<th>5-yr survival (%)</th>
<th>Median survival (mos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreatectomy (clinical stage I)</td>
<td>69.8</td>
<td>24.6</td>
<td>19.3</td>
</tr>
<tr>
<td>Not offered surgery (clinical stage I)</td>
<td>26.8</td>
<td>2.9</td>
<td>8.4</td>
</tr>
<tr>
<td>No surgery (clinical stage III/IV)</td>
<td>7.8</td>
<td>0.8</td>
<td>4.2</td>
</tr>
</tbody>
</table>

The 1-year, 5-year, and median survival rates of stage I pancreatic cancer patients who underwent surgery and were not offered surgery, and those with advanced disease (stage III or IV) who did not undergo surgery in the study published by Bilimoria et al. [11].
fered surgery, the 1-year and 5-year survival rates were 26.8% and 2.9%, respectively, with a median survival time of 8.4 months. As detailed in Table 2, Figure 1, and Figure 2, survival among the clinical stage I patients who were not offered surgery was little to no better than that for patients presenting with stage III or IV disease. Although the reason many patients were not offered surgery was not made clear in this study, the lack of uniformity is striking. For example, patients with clinical stage I pancreatic cancers were far more likely to be offered surgical treatment combined with chemoradiation if they were cared for at an “academic” hospital versus a community medical center. It seems evident that the nihilistic approach toward the surgical treatment of pancreatic cancer persists and creates an environment where objectivity is absent and inaction is deemed appropriate.

**ARGUMENTS FOR SURGICAL NIHILISM IN PANCREATIC CANCER CARE: “DESPITE LIMITED SURVIVAL ADVANTAGES, THE COSTS OF AGGRESSIVE SURGICAL THERAPY ARE TOO GREAT FOR THE LITTLE GAINS ACHIEVED”**

Despite the technical and survival advantages outlined above, there are those who argue that radical, aggressive, and expensive care for pancreatic cancer patients is irrational and inappropriate. Indeed, we too are not oblivious to many grim features uniquely associated with a diagnosis of pancreatic cancer. Pancreatic cancer is best treated as a systemic disease. Less than 25% of all patients are candidates for “curative” resection, and even when an R0 resection is achieved, local or systemic recurrence is the norm for >80% of all such patients. The quick lethality of the malignancy and rapid decline in performance status of the afflicted patient have limited the development and testing of systemic therapies that are so desperately needed if we are to make real progress. Yet despite these sad facts concerning pancreatic cancer, those who question the appropriateness of aggressive treatment of this disease are in essence asking the question “Is the 19.3-month median survival time worth the cost?” Although clinicians and ethicists far

**Figure 1.** Flowchart recounts the management of 9,559 clinical stage I pancreatic cancer patients as assessed by Bilimoria et al. [11]. Of note is the rate of complete surgical resection achieved (96.1%, 2,630 of 2,736 patients) in patients who underwent an attempt (red box). The percentage of patients not offered surgery is encircled in red. From Bilimoria KY, Bentrem DJ, Ko CY et al. National failure to operate on early stage pancreatic cancer. Ann Surg 2007;246:173–180, with permission.

**Figure 2.** Cumulative survival duration difference (red double arrow) is demonstrated by Bilimoria et al. [11] with operative versus nonoperative management of clinical stage I pancreatic cancers. From Bilimoria KY, Bentrem DJ, Ko CY et al. National failure to operate on early stage pancreatic cancer. Ann Surg 2007;246:173–180, with permission.

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smarter than us will debate this issue on many levels, we do believe that these questions are worth considering. So as to not bias against the patient with early-stage pancreatic cancer, and in order to appropriately contextualize this question, we think it is more appropriate to consider how all that is required to achieve a 19.3-month median survival time for stage I pancreatic cancer patients compares with what we do (often in an obligatory way) in the treatment of patients with other "terminal illnesses." Figure 3 represents a plot of 1-year, 3-year, and 5-year survival rates for various benign terminal illnesses, including New York Heart Association stage IV congestive heart failure, stage IV chronic obstructive pulmonary disease, as well malignant diseases such as gastric, esophageal, non-small cell lung, and pancreatic cancers. Also, represented within the same figure are comparative survival analyses of end-stage renal disease and acute myelogenous leukemia. In all instances, spent resources are vast and costly, and the outcomes generally poor because of the inherent biological behavior of the disease. Though each disease state has its own constituency, it is antithetical to all we hold dear as physicians that we should surrender to a disease merely because the prognosis is poor. In light of these facts, we argue that aggressive surgical management of patients with pancreatic cancer is no worse, albeit no better, than for many other advanced or terminal illnesses. Thus, we believe we can once and for all put to rest the widespread notion that a diagnosis of early-stage pancreatic cancer may somehow warrant less aggressive treatment that continues to dominate much of the medical community. Just as Tendler and Livermore sought to dismantle the myth that pancreatic cancer is an untreatable disease, we stake a similar (and more evidence based) claim on behalf of pancreatic cancer patients who plea to be heard and attended to.

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Manuscript writing: Ronald Scott Chamberlain
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REFERENCES


