# Multimodality Therapy for Pancreatic Cancer in the U.S.

## *Utilization, Outcomes, and the Effect of Hospital Volume*

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**BACKGROUND.** Despite decreased perioperative morbidity and mortality and clinical trials suggesting improved outcomes with adjuvant therapy, national practice patterns in the management of pancreatic cancer remain poorly defined. The purpose of the current study was to evaluate multimodality therapy utilization and outcomes relative to hospital type and volume.

**METHODS.** Using the National Cancer Data Base, stage-specific treatment patterns were analyzed for 301,033 patients with pancreatic adenocarcinoma. Logistic regression was used to evaluate treatment utilization. Cox proportional hazards modeling was utilized to evaluate the effect of multimodality therapy on survival.

**RESULTS.** Stage at presentation did not differ from 1985–1994 to 1995–2003; however, the percentage of patients receiving cancer-directed treatment increased from 45.1% to 51.8% ($P < .001$). Pancreatectomy for localized disease (AJCC 6th edition stages I and II) increased from 36.9% to 49.3% ($P < .001$). After resection, the use of adjuvant chemotherapy alone increased from 4.1% to 5.7% ($P < .001$), but the use of adjuvant radiation alone decreased from 7.0% to 4.6% ($P < .001$). Adjuvant chemoradiation use increased from 26.8% to 38.7% ($P < .001$). The use of surgery alone decreased from 62.1% (5213 of 8400 cases) to 49.9% (10,807 of 21,679 cases) ($P < .001$). Patients with localized pancreatic cancer were more likely to receive pancreatectomy and adjuvant chemoradiation at academic and high-volume centers ($P < .001$). Survival for localized disease was better after surgery with adjuvant therapy (hazards ratio [HR], 0.44; 95% confidence interval [95% CI], 0.42–0.47) and surgical resection alone (HR, 0.54; 95% CI, 0.52–0.57) compared with no treatment.

**CONCLUSIONS.** To the authors' knowledge, the current study is the largest study regarding pancreatic cancer performed to date, and the first to investigate national practice patterns for multimodality therapy utilization. Multimodality therapy utilization has increased over time and appears to have a beneficial impact on survival. ***Cancer* 2007;110:1227–34.** © *2007 American Cancer Society.*

**KEYWORDS: pancreatic neoplasms, surgery, chemotherapy, radiation therapy, multimodality therapy, National Cancer Data Base.**

Pancreatic cancer is the fourth leading cause of cancer deaths in the U.S. For 2007, the American Cancer Society estimates that nearly 34,000 patients will be diagnosed with pancreatic cancer, and over 32,000 will die of the disease.[1] Patients with pancreatic cancer have a particularly dismal prognosis due to multiple factors including insidious presentation, aggressive tumor biology, technically challenging surgical management, and lack of effective systemic therapies.


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However, over the last 20 years, significant advances in preoperative evaluation, surgical techniques, and postoperative care have reduced the perioperative morbidity and mortality associated with pancreatic surgery.[2–6] Mortality after pancreaticoduodenectomy has dropped from approximately 25% in the 1960s to < 3% in some high-volume centers [4,5,7–10] Surgery remains the only potentially curative treatment for localized pancreatic cancer.[6] Furthermore, several multiinstitutional randomized clinical trials have demonstrated the efficacy of multimodality therapy.[11–14]

Despite improved morbidity and mortality after pancreatectomy and clinical trials demonstrating increased survival with adjuvant therapy, national practice patterns in the management of pancreatic cancer remain poorly defined and may vary widely. The objectives of this study were to 1) evaluate treatment trends in pancreatic adenocarcinoma over the last 20 years, 2) identify hospital characteristics that predicted whether patients received surgery with or without adjuvant therapy, and 3) assess the impact of surgery and adjuvant therapy on survival.

## MATERIALS AND METHODS

### Patients and Data Acquisition

The National Cancer Data Base (NCDB) is a program of the American College of Surgeons and is recognized as the world's largest clinical registry.[15] The NCDB captures newly diagnosed malignancies from more than 1440 hospitals in the U.S., all of which are approved by the Commission on Cancer (CoC). These hospitals account for approximately 75% of all new cancers in the U.S. each year. The NCDB collects data regarding patient demographics, socioeconomic status, tumor variables, preoperative and postoperative staging, treatment details, recurrence, survival, and health systems/
provider information. Currently, there are more than 1440 hospitals reporting to the NCDB, which account for approximately 73% of all new pancreatic cancers diagnosed in the U.S.[1] This study was approved by the Institutional Review Board of Northwestern University. Results reported are in compliance with the privacy requirements of the Health Insurance Portability and Accountability Act of 1996 as reported in the Standards for Privacy of Individually Identifiable Health Information; Final Rule (45 CFR Parts 160 and 164).

Patients admitted between 1985 and 2003 with 2nd and 3rd edition International Classification of Disease – Oncology (ICD-O-2 and ICD-O-3) codes specific for the pancreas were selected (C25.0, C25.1, C25.2, C25.3, C25.7, C25.8, and C25.9).[5,16] Patients were limited by ICD-O codes for histologies consistent with pancreatic adenocarcinoma, yielding 301,033 patients from 1667 institutions. Patients were divided into 2 groups (1985–1994 and 1995–2003) for comparison. These intervals were selected based on preliminary data demonstrating a change in pancreatic cancer treatment in 1995 (Fig. 1). Patients were grouped by treatment combination received: surgery alone, surgery and radiation, surgery and chemotherapy, surgery and chemoradiation, radiation alone, chemotherapy alone, and chemoradiation alone. Surgery is defined as a cancer-directed resection including pancreaticoduodenectomy (with or without pylorus preservation), distal pancreatectomy, total pancreatectomy, and pancreatectomy not otherwise specified.[17,18] Palliative procedures and exploratory surgery without a cancer-directed resection are not included in our analysis. If a patient is reported by more than 1 hospital, the less complete of the duplicate records is eliminated to ensure that patients are not represented twice in the dataset.

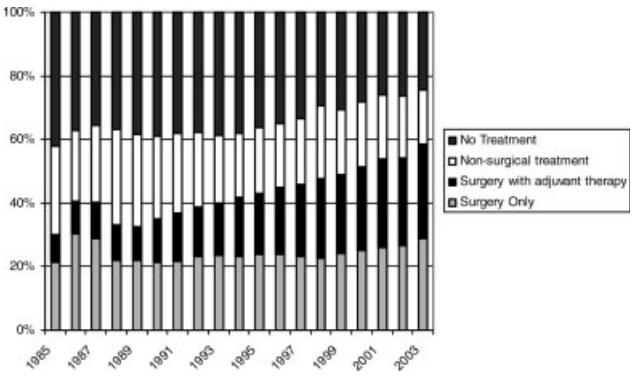


**FIGURE 1.** Treatment trends by modality in the management of localized (stages I and II) pancreatic adenocarcinoma from the National Cancer Data Base, 1985–2003 (n = 66,663).

### Hospital Classification

Hospitals in the NCDB are classified into academic and community cancer centers based on case volume and services offered.[19] Academic hospitals must be affiliated with teaching and research institutions, meet annual case-volume requirements, and fulfill criteria regarding the ability to provide a wide range of cancer-specific services. For analysis, Community and Comprehensive Community Cancer Centers were grouped together and compared with Teaching/Research/Academic Hospitals. The National Comprehensive Cancer Network (NCCN) is a consortium of 19 major adult comprehensive cancer centers in the U.S. One of their primary goals is to develop treat-

ment guidelines for all body sites including pancreatic cancer.[20] The NCDB contains 17 of the 19 NCCN hospitals. In addition, the National Cancer Institute (NCI) designates cancer centers, and the NCDB contains 33 of the 61 NCI centers. NCCN and NCI hospitals were combined for the analysis. Hospitals were characterized as being in metropolitan versus urban/rural locations. Urban and rural were combined due to the small number of rural hospitals that report to the NCDB. Metropolitan, urban, and rural were defined by county population and proximity to major cities per the 2003 Urban-Rural Continuum Codes.[21]

Hospital volume was based on the annual volume of all pancreatic cancer cases (analytic cases) reported to the NCDB annually, including surgical and nonsurgical patients. Quartiles were determined based on having equal numbers of hospitals within each quartile. However, this led to 49.9% of the pancreatic cancer cases being seen at institutions in the top quartile, with case volume ranging from 13 to 300 patients per year within that top quartile. Thus, quartiles were recalculated based on having equal numbers of cases per quartile. This led to a more even distribution where the top quartile consisted of 38 hospitals that saw 25% of cases annually and volume ranged from 82 to 300 patients per year in this top quartile. All analyses were performed with both quartile determinations, but as the results were similar, only the latter method is presented. We define 'high-volume' centers as the top quartile hospitals with patients are evenly distributed within quartiles.

### Statistical Analysis

Categorical variables were compared with the chi-square test. The Bonferroni correction was used for multiple comparisons. Graphs and tables were used as needed to examine the distribution of each variable. Binary logistic regression models were used to identify hospital factors predicting treatment type while adjusting for gender, age (<55 years, 55–64 years, 65–74 years, and ≥75 years), race (white, black, Asian, Hispanic, and other), extent of surgery (pancreaticoduodenectomy, distal pancreatectomy, and total pancreatectomy), AJCC 6th edition stage (I vs II), and year of diagnosis (1985–1989, 1990–1995, 1996–1999, and 2000–2003). Five-year overall survival was estimated by the Kaplan-Meier method and modalities were compared using the log-rank test.[22] Cox proportional hazards modeling was utilized to assess the impact of surgery and adjuvant therapy on survival while controlling for gender, age (<55 years, 55–64 years, 65–74 years, and ≥75 years), race (white, black, Asian, Hispanic, an other), extent of surgery (pancreaticoduodenectomy, distal pancreatectomy, and total pancreatectomy), stage (I vs II), and year of diagnosis (1985–1989, 1990–1995, 1996–1999, and 2000–2003).[23] The proportional hazards assumptions were confirmed graphically. The level of statistical significance was set to $P < .001$. All $P$ values reported are 2-tailed. Statistical analyses were performed using SPSS software (version 14; SPSS Inc, Chicago, Ill).

**TABLE 1**
**Patient Characteristics for All Patients and the Comparison Groups: 1985–1994 and 1995–2003**

| | All patients | 1985–1994 | 1995–2003 |
|---|---|---|---|
| No. of patients | 301,033 | 126,891 | 174,172 |
| Sex | | | |
| Men | 49.8% (149,990) | 49.3% (62,657) | 49.8% (86,659) |
| Women | 50.2% (150,922) | 50.7% (64,263) | 50.2% (87,423) |
| Age, y | | | |
| <55 | 13.6% (41,041) | 12.4% (15,679) | 14.6% (25,362) |
| 56–65 | 20.9% (63,021) | 21.8% (27,689) | 20.3% (35,332) |
| 66–75 | 32.6% (98,156) | 34.2% (43,449) | 31.4% (54,707) |
| 76–85 | 25.6% (77,175) | 24.8% (31,529) | 26.2% (45,646) |
| >85 | 7.2% (21,640) | 6.7% (8545) | 7.5% (13,095) |
| Race | | | |
| White | 81.8% (245,392) | 82.7% (104,586) | 81.2% (140,806) |
| Black | 11.1% (33,309) | 10.8% (13,581) | 11.4% (19,728) |
| Hispanic | 3.8% (11,536) | 3.6% (4562) | 4.0% (6974) |
| Asian | 1.2% (3700) | 1.1% (1355) | 1.4% (2345) |
| Other | 2.0% (6046) | 1.9% (2388) | 2.1% (3658) |
| Stage | | | |
| I | 9.7% (20,247) | 10.0% (7296) | 9.4% (12,951) |
| II | 22.1% (46,416) | 21.3% (15,461) | 22.6% (30,955) |
| III | 12.8% (116,307) | 12.7% (40,604) | 12.8% (75,503) |
| IV | 55.4% (209,813) | 55.9% (72,619) | 55.2% (137,194) |
| Hospital type | | | |
| Academic | 38.8% (10,5842) | 36.8% (40,959) | 40.2% (64,883) |
| Community | 61.2% (166,967) | 63.2% (70,389) | 59.8% (96,578) |
| Cancer center designation | | | |
| NCCN/NCI | 8.7% (26,077) | 6.7% (8559) | 10.1% (17,518) |
| Non-NCCN/NCI | 91.3% (274,956) | 93.3% (118,332) | 89.9% (156,624) |

NCCN indicates National Comprehensive Cancer Network; NCI, National Cancer Institute.

## RESULTS

For the diagnoses years 1985 through 2003, the NCDB contained data regading 306,796 pancreatic cancer patients, of whom 301,033 had histologies that were consistent with adenocarcinoma. Patients were divided into 2 groups for statistical comparison: 1985 through 1994 (n = 126,891 patients) and 1995 through 2003 (n = 174,142 patients). Patient demographics and tumor variables did not change significantly between the 2 time periods (Table 1). Moreover, the stage of presentation did not differ considerably over time.

**TABLE 2**
**Treatment Trends in the Management of Localized Pancreatic Adenocarcinoma From 1985–2003**

| All patients with localized disease | 1985–1994 Percent (no.) | 1995–2003 Percent (no.) | *P* |
|---|---|---|---|
| All patients (stage I and II) | 22,757 | 43,906 | |
| Total surgery | 37.2% (8474) | 49.7% (21,802) | <.001 |
| Total chemotherapy | 31.0% (7062) | 40.4% (17,754) | <.001 |
| Total radiation therapy | 32.5% (7395) | 36.4% (15,967) | <.001 |

**TABLE 3**
**Facility Characteristics Predicting Pancreatectomy Utilization Patients With Localized Pancreatic Adenocarcinoma**

| | Unadjusted rate of surgery utilization | *P* | Adjusted OR (95% CI) |
|---|---|---|---|
| Facility type | | | |
| Academic | 54.5% | <.001 | 1.70 (1.64–1.76) |
| Community | 39.5% | | 1.00* |
| Cancer center designation | | | |
| NCCN/NCI | 60.6% | <.001 | 1.77 (1.67–1.88) |
| Non-NCCN/NCI | 43.7% | | 1.00* |
| Facility case volume | | | |
| 75–99th percentile | 49.8% | <.001 | 1.45 (1.35–1.55) |
| 50–74th percentile | 41.4% | | 1.07 (1.00–1.15) |
| 25–49th percentile | 39.5% | | 1.02 (0.94–1.10) |
| 0–25th percentile | 39.8% | | 1.00* |
| Location | | | |
| Metropolitan | 45.8% | <.001 | 1.26 (1.17–1.36) |
| Urban/rural | 38.2% | | 1.00* |
| Census region | | <.001 | |
| Northeast | 49.1% | | 1.35 (1.19–1.55) |
| Atlantic | 46.1% | | 1.39 (1.29–1.51) |
| Southeast | 45.6% | | 1.26 (1.19–1.34) |
| Great Lakes | 49.5% | | 1.21 (1.14–1.28) |
| South | 42.3% | | 1.37 (1.29–1.45) |
| Midwest | 43.3% | | 1.10 (1.03–1.19) |
| West | 43.9% | | 1.09 (1.01–1.17) |
| Mountain | 41.0% | | 0.94 (0.85–1.04) |
| Pacific | 41.5% | | 1.00* |

OR indicates odds ratio; 95% CI, 95% confidence interval; NCCN, National Comprehensive Cancer Network; NCI, National Cancer Institute.

* Denotes reference categories. Controlled for gender, age, race, stage, and extent of surgery.

From 1985 through 1994 to 1995 through 2003, the percentage of all patients receiving treatment for pancreatic cancer increased from 45.1% to 51.8% ($P < .001$). Cancer-directed therapy was evaluated for patients presenting with localized disease (stage I and stage II). Pancreatectomy for localized disease increased from 37.2% to 49.7% ($P < .001$) (Fig. 1, Table 2). This increase was observed in conjunction with adjuvant therapy as the use of surgery alone decreased from 62.1% to 49.9% ($P < .001$) of resected patients. Of those patients who underwent curative resection, the use of adjuvant chemotherapy alone increased from 4.1% to 5.7% ($P < .001$). However, the use of adjuvant radiation alone decreased from 7.0% to 4.6% ($P < .001$). Adjuvant chemoradiation use increased from 26.8% to 38.7% ($P < .001$).

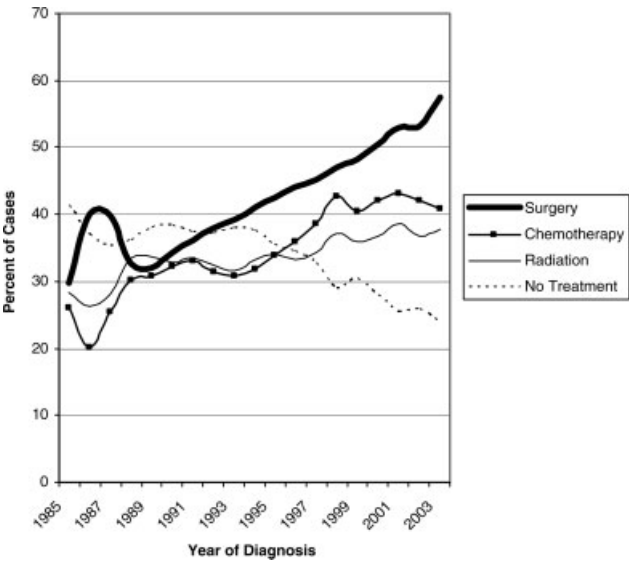


**FIGURE 2.** Total treatment trends in the management of localized (stages I and II) pancreatic adenocarcinoma from the National Cancer Data Base, 1985–2003 (n = 66,663). *The percentages of treatment type do not add up to 100% because those patients who received multiple treatment modalities are counted in the trend lines for each of the individual treatments received.

In all patients with localized pancreatic cancer (n = 66,663), the total proportion of patients receiving adjuvant therapy in any combination increased from 1985 through 1994 to 1995 through 2003; the use of chemotherapy increased from 31.0% to 40.4% ($P < .001$) and the use of radiation therapy increased from 32.5% to 36.4% ($P < .001$) (Fig. 2).

The impact of hospital type and volume on utilization was analyzed separately for surgery and adjuvant therapy. Patients with localized pancreatic cancer were more likely to undergo pancreatectomy at academic compared with community institutions (54.5% vs 39.5%; $P < .001$) (Table 3). Patients with localized pancreatic cancer were also more likely to receive adjuvant chemoradiation at academic compared with community institutions (18.4% vs 15.3%; $P < .001$) (Table 4). Multimodality therapy was employed more often at higher-volume centers ($P < .001$). Patients treated at NCCN/NCI hospitals underwent surgery and received adjuvant therapy more often than patients treated at other academic or community centers ($P < .001$). Facilities in metropolitan areas were more likely to utilize surgery and

**TABLE 4**
**Facility Characteristics Predicting Adjuvant Chemoradiation Utilization in Patients With Localized Pancreatic Adenocarcinoma (Stage I and II)**

| | Unadjusted rate of adjuvant therapy utilization | *P* | Adjusted OR (95% CI) |
|---|---|---|---|
| Facility type | | <.001 | |
| Academic | 18.4% | | 1.08 (1.00–1.73) |
| Community | 15.3% | | 1.00* |
| Cancer center designation | | | |
| NCCN/NCI | 21.5% | <.001 | 1.27 (1.18–1.36) |
| Non-NCCN/NCI | 15.8% | | 1.00* |
| Location | | | |
| Metropolitan | 16.5% | NS | 0.89 (0.79–1.01) |
| Urban/rural | 16.6% | | 1.00* |
| Facility case volume† | | <.001 | |
| 75–99th percentile | 18.1% | | 1.20 (1.10–1.32) |
| 50–74th percentile | 15.8% | | 1.10 (0.99–1.21) |
| 25–49th percentile | 14.0% | | 0.98 (0.87–1.09) |
| 0–25th percentile | 14.6% | | 1.00* |
| Census region | | <.001 | |
| Northeast | 20.7% | | 1.67 (1.50–1.83) |
| Atlantic | 16.0% | | 1.22 (1.12–1.33) |
| Southeast | 16.2% | | 1.22 (1.12–1.32) |
| Great Lakes | 20.4% | | 1.55 (1.43–1.68) |
| South | 13.4% | | 0.95 (0.85–1.06) |
| West | 17.0% | | 1.30 (1.18–1.43) |
| Mountain | 14.4% | | 1.02 (0.93–1.13) |
| Midwest | 14.7% | | 1.03 (0.89–1.19) |
| Pacific | 13.9% | | 1.00* |

OR indicates odds ratio; 95% CI, 95% confidence interval; NCCN, National Comprehensive Cancer Network; NCI, National Cancer Institute; NS, not significant.

* Denotes reference categories.

† Volume quartiles by number of analytic cases reported annually.

Controlled for gender, age, race, stage, and extent of surgery.

adjuvant therapy than those hospitals in urban/rural settings ($P < .001$). Geographic location demonstrated significant differences in the utilization of surgery and adjuvant therapy. Patients in the Great Lakes and Northeast census regions were more likely to receive multimodality therapy for localized pancreatic cancer ($P < .001$). Multivariate analysis controlling for stage and age demonstrated that facility type and volume (academic centers, NCCN/NCI centers, high-volume hospitals) were independent predictors of increased utilization of surgery and adjuvant therapy ($P < .001$).

Finally, we sought to investigate the impact of surgery and adjuvant therapy on survival. The unadjusted 5-year survival rate was 16.3% for patients who underwent surgery alone (median survival, 13.1 months) (Fig. 3) (Table 5). The 5-year survival rate for patients treated with surgery combined with adjuvant chemotherapy and radiation therapy was

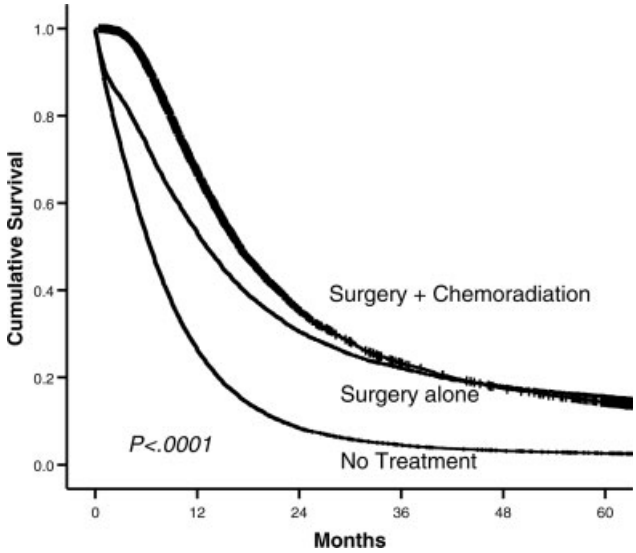


**FIGURE 3.** Five-year overall survival for stages I and II pancreatic cancer patients by whether they received surgery and adjuvant therapy, surgery alone, or no treatment. Survival between all 3 groups is highly significant ($P < .0001$ for all pairwise comparisons).

18.8% (median survival, 17.0 months). For patients who did not undergo surgery, the 5-year survival was 3.5% (median survival, 6.5 months). Cox proportional hazards modeling controlling for patient, tumor, and hospital characteristics demonstrated that survival was better with surgery and adjuvant therapy (hazards ratio [HR], 0.44; 95% confidence interval [95% CI], 0.42–0.47) and surgery alone (HR, 0.54; 95% CI, 0.52–0.57) compared with those who were not selected to undergo surgical treatment. Moreover, patients who underwent surgery with adjuvant therapy had better adjusted survival than patients who underwent surgery alone (HR, 0.83; 95% CI, 0.79–0.88 [$P < 0.001$]).

## DISCUSSION

Pancreatic cancer is a formidable disease, and identifying factors that affect outcomes is critical to improving cancer care and the delivery of stage-specific treatments. To our knowledge, the current study is the largest study regarding pancreatic cancer performed to date and the first to investigate the utilization of multimodality therapy by hospital type. This study demonstrates that over the past 20 years there has been an increase in the utilization of surgery and adjuvant therapy for localized pancreatic cancer, particularly at academic centers, high-volume hospitals, and NCCN/NCI-designated cancer centers.

**TABLE 5**
**Unadjusted and Adjusted Survival Analysis for Patients With Stage I and II Pancreatic Cancer by Whether They Received Surgery and Adjuvant Therapy, Surgery Alone, or No Treatment***

| | No of patients | 3-year survival | 5-year survival | Median survival, mo (95% CI) | HR (95% CI) |
|---|---|---|---|---|---|
| Surgery with adjuvant therapy | 6351 | 23.3% | 18.8% | 17.0 (16.5–17.5) | 0.44 (0.42–0.47) |
| Surgery alone | 10,536 | 22.1% | 16.3% | 13.1 (12.7–13.4) | 0.54 (0.52–0.57) |
| No treatment | 24,442 | 4.5% | 3.5% | 6.5 (6.4–6.6) | 1.00 (Referent) |

95% CI indicates 95% confidence interval; HR, hazards ratio.
* Survival between all 3 groups was found to be highly significant ($P < .0001$ for all pairwise comparisons).

### Treatment Utilization

Reports from numerous institutions have demonstrated that pancreatectomy can be performed safely and results in improved outcomes in properly selected patients.[2,4,5,8–10] A previous report from the NCDB examined treatment utilization in patients diagnosed between 1985 and 1995 and found that pancreatectomy was utilized in 21.9%.[24] Recent studies have demonstrated increased utilization of surgery over time.[25,26] Our results also demonstrate a gradual increase in surgery from 1985 to 2003. However, the use of surgery alone has decreased; thus, the increase in utilization of surgery is observed in conjunction with an increase in adjuvant therapy.

Randomized clinical trials have demonstrated the improved efficacy of adjuvant chemotherapy treatment.[11–14] Prior studies utilizing the NCI's Surveillance, Epidemiology, and End Results (SEER) program have not been able to investigate chemotherapy utilization because SEER does not report information regarding systemic therapies.[25,26] We found that adjuvant chemotherapy utilization has increased over time, particularly in conjunction with adjuvant radiation therapy.

Baxter et al.[25] utilized SEER to evaluate adjuvant radiation therapy use and found that utilization increased over time. When examined with information on chemotherapy utilization, we found that use of radiation alone actually decreased over time and that the increase in adjuvant radiation has been considered to be multimodality therapy, in which chemotherapy and radiation are used together.

Together, these results indicate that surgery and multimodality therapy are being used with increasing frequency for localized pancreatic cancer. This may be attributable to the numerous studies demonstrating improved perioperative morbidity and long-term survival after resection.[2–6,8–10] Similarly, the increased utilization of adjuvant therapy may be the result of multiple randomized clinical trials demonstrating a survival benefit.[11–14,27]

### Hospital Type

Numerous studies have demonstrated a volume/outcome relation for perioperative mortality and long-term survival after surgery for pancreatic cancer.[28–32] However, less is known regarding factors contributing to the volume/outcome relationship. To our knowledge, no prior studies have examined pancreatectomy and adjuvant therapy utilization by hospital type. We found that pancreatectomy was used more often at high-volume centers, academic institutions, and NCCN/NCI-designated cancer centers. These findings may suggest that more frequent utilization of surgery and adjuvant treatments at these specialized centers underlie the improved outcomes at these hospitals.

### Survival

Due to the poor prognosis and relative absence of long-term survivors, many have questioned the utility of multimodality therapy for pancreatic cancer.[6,33] However, surgical resection and adjuvant chemoradiation have been shown to be powerful predictors of survival.[6,34] Similarly, we found that survival was significantly better for patients treated with surgery compared with those who were not selected to undergo resection. Moreover, patients selected to undergo multimodality therapy demonstrated better survival than those patients who underwent resection alone. Thus, surgery and adjuvant therapy are effective stage-specific treatments associated with improved outcomes.

### Limitations

Our study has several potential limitations. Underreporting is a systematic bias associated with registry data.[35–38] Underreporting may lead to underestimation of the percentage of patients receiving adjuvant therapies, particularly because these treatments may be administered on an outpatient basis months after surgery.[37] Studies attempting to quantify the reporting disparity by comparing registry data to patient

charts and Medicare claims have shown that the underreporting ranges from 5% to 12% for chemotherapy and radiation depending on the cancer site.[35,37,39,40] However, we excluded unknowns and evaluated proportions of patients receiving surgery and adjuvant treatments to demonstrate trends in treatment over time. Adjuvant therapy may be underreported if a patient receives treatment at multiple hospitals. However, if a patient undergoes surgery at Hospital A and chemotherapy at Hospital B, the Institution A cancer registrar accesses information from Hospital B or the physician's office record. An additional limitation is that the NCDB started collecting data describing secondary diagnoses (comorbidities) in 2003. As a result, we were unable to risk-adjust for specific comorbidities in this study.[41–43] Our logistic regression and Cox proportional hazards models controlled for numerous factors including age, race, stage, and facility type. Prior studies concerning pancreatic cancer using administrative data have reported that high-volume, academic centers are more likely to see patients with worse coexisting illnesses (based on higher Charlson Comorbidity Index scores) than low-volume or community hospitals.[29,44–47] Thus, the finding that patients seen at high-volume, academic institutions receive surgery more frequently would likely be more pronounced with risk adjustment for comorbidities. A further limitation of this study is that we were only able to study cancer-directed surgery (ie, pancreatectomy) because information regarding palliative surgery and exploration without resection is limited in cancer registries. Thus, we focused on patients undergoing cancer-directed surgery for localized disease (stages I and II) with curative intent. In addition, the NCDB collects data from hospitals that are approved by the CoC, which may introduce a patient selection bias because smaller hospitals may not be CoC-approved. Low-volume, community hospitals in the NCDB may have a higher level of specialization compared with hospitals in the U.S. that are not approved by the CoC. This may decrease the differences observed in the current study between high-volume, academic hospitals in comparison to low-volume, community hospitals; however, at the national level, this would only further the findings that there are differences in treatment utilization between hospital types. Furthermore, differences in utilization by facility type may be due in part to regionalization of pancreatic cancer care. Further investigation is needed to evaluate the impact of regionalization on utilization of pancreatectomy in the U.S. Finally, we compared survival in patients who underwent surgery with those who received adjuvant therapy, surgery alone, and no surgery. These comparisons are retrospective and suffer from a selection bias. They offer some insight into the issue, but further evaluation in prospective studies is required.

## Conclusions

As a result of multiple institutional studies over the past 20 years demonstrating the increased safety and efficacy of pancreatic surgery, the utilization of curative resection for localized pancreatic cancer is on the rise. Furthermore, multiple randomized clinical trials have advocated the employment of adjuvant chemoradiation, and the results of the current study demonstrate that multimodality therapy utilization is increasing as well. Patients receiving surgery and adjuvant therapy also had better outcomes. Despite these favorable findings, a large percentage of patients with early-stage disease are not receiving appropriate, stage-specific treatments. Thus, there is an opportunity to improve cancer care by offering stage-specific treatment to appropriate pancreatic cancer patients. Adhering to national consensus guidelines such as those put forth by the NCCN may improve the utilization of treatment for pancreatic cancer.[20] Alternatively, the regionalization of pancreatic cancer care to centers of excellence may be warranted. Further investigation is needed to characterize this underutilization of treatment in the U.S.

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