Correlation of tumor size and survival in pancreatic cancer

Caitlin Takahashi[1], Ravi Shridhar[2], Jamie Huston[3], Kenneth Meredith[3,4]

[1]Department of Surgery, Naval Medical Center Portsmouth, Portsmouth, VA, USA; [2]Department of Radiation Oncology, Florida Hospital Cancer Institute, Orlando, FL, USA; [3]Department of Gastrointestinal Oncology, Sarasota Memorial Healthcare System, Sarasota, FL, USA; [4]Department of Gastrointestinal Oncology, Florida State University College of Medicine, Tallahassee, FL, USA

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Correspondence to: Kenneth Meredith, MD, FACS. Professor, Florida State University College of Medicine; Director, Gastrointestinal Oncology, Sarasota Memorial Institute for Cancer Care, 941-504-5672, 1950 Arlington Suite 101, Sarasota, FL, USA. Email: Kenneth-Meredith@smh.com; kensurg@hotmail.com.

Background: Neoadjuvant therapy (NT) for resectable pancreatic adenocarcinoma (PAC) continues to be debated. We sought to establish the relationship between pancreatic tumor size, neoadjuvant chemotherapy (NCT), neoadjuvant chemoradiation (NCRT), and definitive surgery (DS) on survival.

Methods: Utilizing the National Cancer Database we identified patients with PAC who underwent NT and DS. Patient characteristics and survival were compared with Mann-Whitney U, Pearson's Chi-square, and the Kaplan-Meier method. Multivariable analysis (MVA) was developed to identify predictors of survival. All tests were two-sided and α <0.05 was significant.

Results: We identified 11,707 patients: 9,722 patients with tumors >2 cm and 1,985 with tumors ≤2 cm. There were 523 patients treated with NCT, 559 treated with NCRT, and 10,625 DS. Patients with tumors >2 cm were more likely to have higher T-stage, P<0.001, positive lymph nodes, P<0.001, poor histologic grade, P<0.001, and R1 resections, P<0.001. The median survival for patients with tumors ≤2 cm was 30.6 months compared to 20.5 months for those whose tumors were >2 cm, P<0.001. In the >2 cm groups the median survival for NCT, NCRT, and DS was 22.9, 25.8 and 21.3 months, P=0.01. MVA revealed that age, Charlson/Deyo score, N-stage, grade, tumor size >2 cm, R0 resection, and NT were predictors of survival. Ninety-day mortality was worse in both the NCT and NCRT compared to DS, P<0.001.

Conclusions: The size of pancreatic cancer correlates to pathologic stage and overall survival. Tumors >2 and <2 cm benefited from a NT. However, the 90-operative mortality was significantly worse in those patients receiving NT.

Keywords: Pancreatic cancer; tumor size; neoadjuvant therapy (NT)

Introduction

Pancreatic cancer is the 4th leading cause of cancer mortality in the United States, with overall survival of <5% upon diagnosis (1-3). Surgery has been proven to increase overall survival and with the addition of adjuvant chemotherapy and chemoradiation overall survival can be increased to 28–37% (3-5). Neoadjuvant therapy (NT) has shown to further increase 5-year survival in some series (6) however this approach has not been uniformly adopted.

At diagnosis, the TNM staging system by the American Joint Cancer Committee (AJCC) is used to determine prognosis of pancreatic cancer as well as guide multimodal therapy. The 7th edition of the AJCC TNM staging system includes extra-pancreatic extension as a more important prognostic factor than tumor size (7). However, there is

extensive evidence demonstrating size is an independent risk factor for prognosis of pancreatic cancer patients regardless of extra-pancreatic extension (8-10). Therefore, the 8th edition of the TNM staging [2018] has been updated to exclude whether the tumor has extrapancreatic extension and focus directly on tumor size (11).

Now that tumor size has been identified as fundamental to pancreatic cancer staging and survival, it will have a role in guiding multimodality therapy. One area of evidential weakness in multimodality therapy is the effectiveness of NT. Approximately 38% of patients who have resected pancreatic cancer will have recurrence most commonly as distant metastases suggesting possible unidentified micrometastasis preoperatively (12,13). Current recommendation by the National Comprehensive Cancer Network (NCCN) for resectable and borderline resectable pancreatic cancer is to do definitive surgery followed by adjuvant therapy (14). Adjuvant therapy will be recommended for most patients following pancreatic resection. However, not all resected patients will end up receiving adjuvant therapy due to postoperative complications (15,16).

NT allows for tumor biology to declare itself and may improve the rate of resectable patients undergoing multimodal therapy despite surgical outcomes. Counter arguments that some patients will develop disease progression who would have been otherwise been potentially curable with an upfront surgery approach given the poor response rates to a neoadjuvant approach. It has been reported that neoadjuvant treatment improves median and overall survival in resectable and borderline resectable pancreatic cancer (17-20). However, there has never been a study on the survival of patients receiving NT stratified by size of the tumor. Our goal is to identify the significance of NT on survival as it pertains to tumor size and whether tumor size can influence the decision to utilize NT.

Methods

Patients

This retrospective study was approved and deemed exempt by the institutional review board at Sarasota Memorial Hospital as it did not involve patient identifiers. The National Cancer Database (NCDB) is a dataset maintained by the American College of Surgeons and the American Cancer Society and collects patient data from >1,500 centers across the United States. Our patient population

was obtained from the Pancreatic Participant Use Data File (PUF). Data represents more than 70 percent of newly diagnosed cancer cases nationwide. PUF's are entirely de-identified data files available to selected investigators at CoC-approved institutions for the advancement of patient care. We queried the NCDB for patients with a diagnosis of pancreatic adenocarcinoma (PAC) who underwent surgery between 2006 and 2013. Patients were compared by therapy, definitive surgery (DS), neoadjuvant chemotherapy only (NCT), or neoadjuvant chemoradiation (NCRT), and stratified by size of tumor, ≤2 or >2 cm.

Statistics

Baseline univariate comparisons of patient characteristics between the >2 and ≤2 cm patients were made for continuous variables using the Mann-Whitney U and Kruskal Wallis tests as appropriate. Pearson's Chi-square test and Fisher's exact test was used to compare categorical variables when appropriate. Overall survival was defined from the time of diagnosis to death or last contact. Survival time was censored for patients alive at the end of the study period. Kaplan-Meier survival analysis was used to generate overall survival curves and estimate median survival with 95% confidence intervals for each group. Survival distributions were compared across groups using the log-rank test.

Multivariable Cox proportional hazard models were developed comparing treatment methods (definitive surgery, NCT, NCRT). Predictors of long-term survival included in the models were age, sex, pathologic T-stage, pathologic N-stage, tumor grade, tumor size, lymph nodes harvested, number of lymph of positive lymph nodes, surgical margins, institution volume, adjuvant therapy and use of induction therapy. Facility volume was calculated as the total number of cases within a facility for a given year.

To correct for baseline differences among treatment groups, propensity score matching (PSM) was used to match for age, Charlson/Deyo comorbidity score, facility volume, and NT. Matching occurred on a 1:1 basis and only exact matches were allowed. PSM creates treatment groups in a way that approximates the effect of randomization, and therefore partially removes the bias that typically accompanies treatment assignment in nonrandomized studies. All statistical tests were two-sided and α (type I) error <0.05 was considered statistically significant. Statistical analysis was performed using SPSS® version 24.0 (IBM®, Chicago, IL, USA). This study was approved as exempt by

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the Institutional Review Board.

Results

We identified 11,707 patients in the NCDB with PAC; 9,722 with tumors >2 cm and 1,985 with tumors ≤2 cm. The median age of both groups of patients was 67 [22–90], P=0.70 and the majority of the patients were male; 4,968 (51.1%) in >2 cm, and 989 (49.8%) in ≤2 cm (*Table 1*).

NT was received in 916 (9.4%) patients in the >2 cm group and in 166 (8.4%) in the ≤2 cm group. In the >2 cm group, NT was chemotherapy in 448 (4.6%) and chemoradiation in 468 (4.8%). The ≤2 cm group NT was chemotherapy in 75 (3.8%) and chemoradiation in 91 (4.6%). There were more lymph nodes removed in the >2 cm group versus ≤2 cm group; 16 [0–90] and 14 [0–63] removed respectively, P<0.001. Histologic grade was found to be high in 3,851 (39.6%) of the >2 cm group and 635 (32.0%) in the ≤2 cm group, P<0.001. T-stage, clinical stage and pathologic stage also was found to be higher in the >2 cm group than ≤2 cm group, P<0.001 (*Table 1*).

R0 resection was achieved in 7,313 (75.2%) of the >2 cm group and 1,708 (86.0%) in the ≤2 cm group, P<0.001. In all there were 3,653 node negative patients and 8,054 node positive patients. Node status was negative in 2,748 (28.3%) and positive in 6,974 (71.7%) of the >2 cm group. There were more node positive patients found in the >2 cm group, P<0.001. Whereas the nodal status was negative in 905 (45.6%) and positive in 1,080 (54.4%) of the ≤2 cm group, P<0.001 (*Table 1*).

Median survival demonstrated improvement in all patients who received NT versus definitive surgery with adjuvant therapy (DS); 25.9 *vs.* 22.5 months respectively, P=0.03. Neoadjuvant chemoradiation (NCRT) demonstrated slightly better median survival versus NCT; 25.9 *vs.* 25.5 months, P=0.03 respectively (*Figure 1*).

Patients with tumors >2 cm did demonstrate statistically significant improved median survival with NT *vs.* DS + adjuvant therapy; 25.4 *vs.* 21.3 months, P=0.002. The median survival in the >2 cm group for NCT, NCRT and DS with adjuvant were 22.9, 25.8, and 21.3 months respectively, P=0.01 (*Figure 2*). However, the NCT and NCRT had significantly worse 90-day mortality compared to the DS with adjuvant therapy 5.1%, 6.9%, and 0.7%, respectively, P<0.001. In patients with ≤2 cm who received NT, median survival was improved; NCT 43.1 months, NCRT 26.3 months and DS + adjuvant therapy 31.1 months, P=0.03 (*Figure 3*). NCT, NCRT

similarly demonstrated significantly worse 90-day mortality for ≤2 cm group compared to the DS with adjuvant therapy; 2.2%, 4.2%, and 0%, P<0.001.

Multivariate analysis revealed that age, Charlson/Deyo score, pathologic T-stage, pathologic N-stage, grade, tumor size (>2 cm), surgical margins, facility volume, and NT were predictors of survival, P<0.001 (*Table 2*). For R1/R2 resections, hazard ratio (HR) was 1.39 (1.3–1.5), P<0.001. The HR for >2 cm was 1.35 (1.22–1.49), P<0.001.

Propensity score matched analysis for age, Charlson/Deyo comorbidity score, facility volume, and NT demonstrated that tumor size significantly influenced nodal positivity (P<0.001), T-stage (P<0.001), N-stage (P<0.001), grade (P<0.001), and surgical margins (*Table 1*). Median survival stratified by size for >2 cm was 20.2 months and for ≤2 cm was 31 months, P<0.001 (*Figure 4*). In the >2 cm group, median survival for NCT, NCRT, and definitive surgery with adjuvant therapy were 32.1, 22.2, and 20.8 months respectively, P=0.04 (*Figure 5*). The ≤2 cm group demonstrated significant difference between median survival of NCT, NCRT, and definitive surgery with addition of adjuvant therapy; 43.6, 28.3, and 31.1 months respectively, P=0.03 (*Figure 6*). Overall median survival by therapy was best with NCT versus NCRT or definitive surgery with adjuvant therapy; 38.5, 24.2, and 24.4 months, P=0.002 (*Figure 7*). Similar to the non-propensity score cohort, NCT and NCRT demonstrated significantly worse 90-day mortality compared to DS in patients with tumors >2 and <2 cm (<2 cm 2.6%, 4.9%, and 0%, P<0.001), and (>2 cm, 2.9%, 9.2%, and 0.5%, P<0.001).

Discussion

Between the 7ᵗʰ edition and 8ᵗʰ edition of the AJCC TNM staging guidelines, many studies have reported the significance of pancreatic tumor size on survival, influencing the 8ᵗʰ edition to base T-staging solely off tumor size (11). However, there has been little advancement in the use of tumor size for guiding multimodality therapy, specifically NT. Our study is among the first to compare NT amongst pancreatic tumor size. Multivariate analysis demonstrates that NT is an independent predictor of prognosis, as is tumor size. NCT showed the most improved survival as compared to neoadjuvant chemoradiation and definitive surgery. Furthermore, this study identifies the significance of utilizing NT in patients with pancreatic cancer tumors >2 and <2 cm to significantly improve survival however the 90-day mortality in these patients are also increased.

Table 1 Patient characteristics

Variable	Non-PSM			PSM		
	≤2 cm, N=1,985, N (%)	>2 cm, N=9,722, N (%)	P	≤2 cm, N=1,941, N (%)	>2 cm, N=1,941, N (%)	P
Median age [range]	67 [34–90]	67 [22–90]	0.7	67 [34–90]	67 [34–90]	1.0
Gender			0.3			0.35
Male	989 (49.8)	4,968 (51.1)		967 (49.8)	996 (51.3)	
Female	996 (50.2)	4,754 (48.9)		974 (50.2)	945 (48.7)	
Charlson/Deyo			0.006			1.0
0	1,344 (67.7)	6,320 (65.0)		1,331 (68.6)	1,331 (68.6)	
1	532 (26.8)	2,691 (27.7)		517 (26.6)	517 (26.6)	
2	109 (5.5)	711 (7.3)		93 (4.8)	93 (4.8)	
Grade			<0.001			<0.001
Low	270 (13.6)	840 (8.6)		264 (13.6)	192 (9.9)	
Intermediate	1,080 (54.4)	5,031 (51.7)		1,056 (54.4)	1,027 (52.9)	
High	635 (32.0)	3,851 (39.6)		621 (32.0)	722 (37.2)	
Clinical T-stage			<0.001			<0.001
T0	12 (0.6)	35 (0.4)		12 (0.6)	11 (0.6)	
T1	843 (42.5)	953 (9.8)		826 (42.6)	178 (9.2)	
T2	402 (20.3)	3,965 (40.8)		393 (20.2)	805 (41.5)	
T3	728 (36.7)	4,760 (49.0)		710 (36.6)	943 (48.6)	
T4	0	9 (0.1)		0	4 (0.2)	
Clinical N-stage			<0.001			<0.001
N0	1,489 (75.0)	6,610 (68.0)		1,458 (75.1)	1,243 (64.0)	
N1	496 (25.0)	3,112 (32.0)		483 (24.9)	698 (36.0)	
Path T-stage			<0.001			<0.001
T0	12 (0.6)	34 (0.3)		12 (0.6)	12 (0.6)	
T1	621 (31.3)	69 (0.7)		606 (31.2)	5 (0.3)	
T2	49 (2.5)	1,523 (15.7)		48 (2.5)	318 (16.4)	
T3	1,293 (65.1)	7,962 (81.9)		1,266 (65.2)	1,573 (81.0)	
T4	10 (0.5)	134 (1.4)		9 (0.5)	33 (1.7)	
Path N-stage			<0.001			<0.001
N0	905 (45.6)	2,748 (28.3)		883 (45.5)	544 (28.0)	
N1	1,080 (54.4)	6,974 (71.7)		1,058 (54.5)	1,397 (72.0)	
Path stage group			<0.001			<0.001
0	11 (0.6)	34 (0.3)		11 (0.6)	11 (0.6)	
I	430 (21.7)	746 (7.7)		416 (21.4)	142 (7.3)	
IIA	469 (23.6)	1,939 (19.9)		461 (23.8)	382 (19.7)	
IIB	1,045 (52.6)	6,741 (69.3)		1,024 (52.8)	1,346 (69.3)	
III	13 (0.7)	150 (1.5)		12 (0.6)	39 (2.0)	
IV	17 (0.9)	112 (1.2)		17 (0.9)	21 (1.1)	

Table 1 (*continued*)

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Table 1 (*continued*)

Variable	Non-PSM			PSM		
	≤2 cm, N=1,985, N (%)	>2 cm, N=9,722, N (%)	P	≤2 cm, N=1,941, N (%)	>2 cm, N=1,941, N (%)	P
Median lymph nodes removed [range]	14 [0–63]	16 [0–90]	<0.001	14 [0–63]	15 [0–73]	0.03
Median lymph nodes positive [range]	1 [0–23]	2 [0–32]	<0.001	1 [0–23]	2 [0–32]	<0.001
Surgical margins			<0.001			<0.001
R0	1,708 (86.0)	7,313 (75.2)		1,671 (86.1)	1,439 (74.1)	
R1/R2	277 (14.0)	2,409 (24.8)		270 (13.9)	502 (25.9)	
Neoadjuvant status			0.14			1.0
Neoadjuvant	166 (8.4)	916 (9.4)		141 (7.3)	141 (7.3)	
Def Surgery	1,819 (91.6)	8,806 (90.6)		1,800 (92.7)	1,800 (92.7)	
Neo treatment			0.23			0.94
Neo chemo	75 (3.8)	448 (4.6)		62 (3.2)	59 (3.0)	
Neo chemo/rad	91 (4.6)	468 (4.8)		79 (4.1)	82 (4.2)	
Def surgery	1,819 (91.6)	8,806 (90.6)		1,800 (92.7)	1,800 (92.7)	
Adjuvant status			0.01			<0.001
No	829 (41.8)	3,771 (38.8)		803 (41.4)	652 (33.6)	
Yes	1,156 (58.2)	5,951 (61.2)		1,138 (58.6)	1,289 (66.4)	
Adjuvant treatment			0.1			<0.001
Chemo only	654 (32.9)	3,333 (34.3)		641 (33.0)	671 (34.6)	
Rad only	23 (1.2)	129 (1.3)		21 (1.1)	24 (1.2)	
Chemo/rad	479 (24.1)	2,489 (25.6)		476 (24.5)	594 (30.6)	
None	829 (41.8)	3,771 (38.8)		803 (41.4)	652 (33.6)	
Overall treatment			0.1			<0.001
Neo chemo	75 (3.8)	448 (4.6)		62 (3.2)	59 (3.0)	
Neo chemo/rad	91 (4.6)	468 (4.8)		79 (4.1)	82 (4.2)	
Def surgery, adjv	1,110 (55.9)	5,571 (57.3)		1,100 (56.7)	1,223 (63.0)	
Def surgery, no adjv	709 (35.7)	3,235 (33.3)		700 (36.1)	577 (29.7)	
Facility volume			0.11			1.0
Low (≤10/yr)	955 (48.1)	4,849 (49.9)		940 (48.4)	940 (48.4)	
Med (11–19/yr)	589 (29.7)	2,659 (27.4)		572 (29.5)	572 (29.5)	
High (≥20/yr)	441 (22.2)	2,214 (22.8)		429 (22.1)	429 (22.1)	

NT in pancreatic cancer continues to be controversial. Its use in pancreatic cancer has previously demonstrated higher likelihood of achieving R0 margins in borderline resectable disease (18,21-25). Achieving an R0 resection over R1 has demonstrated a significant improvement in median survival by 6 months (26). NT in resectable pancreatic cancer has also proven to have a higher R0 resection rate. A few prospective studies have demonstrated up to 100% R0 resection rates with the use of NT in resectable pancreatic cancer (6,20). These studies are limited by their small sample sizes. However, our study corroborates these findings in a much larger series.

Treatment	Median OS (months)	30-day mortality (%)	P	90-day mortality (%)	P
Neo chemo	25.6	4 (1.1)		17 (4.8)	
Neo chemo/rad	25.9	15 (3.2)	<0.001	30 (6.5)	<0.001
Def surgery, adjv	22.5	1 (0.1)		30 (0.5)	
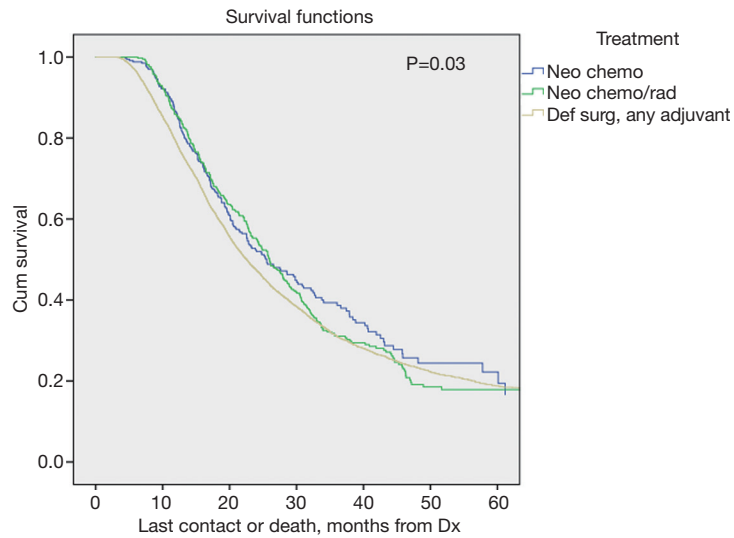
Figure 1 Overall survival by treatment.

Treatment	Median OS (months)	30-day mortality (%)	P	90-day mortality (%)	P
Neo chemo	22.9	4 (1.3)		16 (5.1)	
Neo chemo/rad	25.8	15 (3.8)	<0.001	27 (6.9)	<0.001
Def surgery, adjv	21.3	1 (0.1)		30 (0.7)	
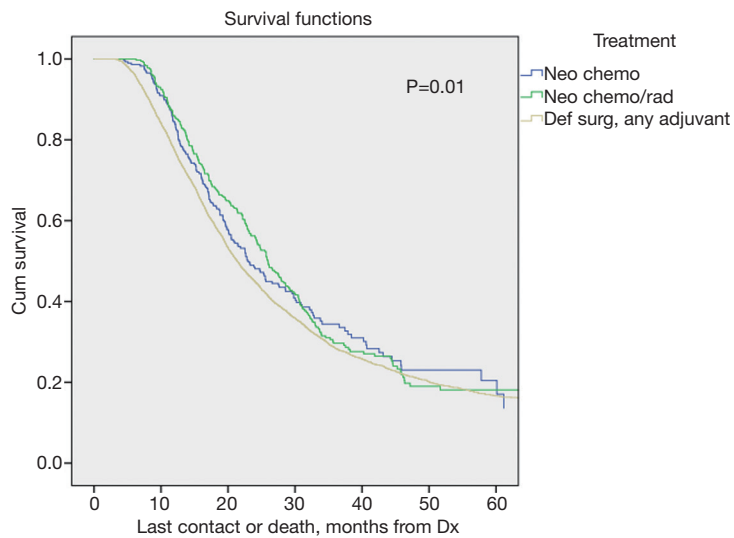
Figure 2 Tumor >2 cm overall survival by treatment.

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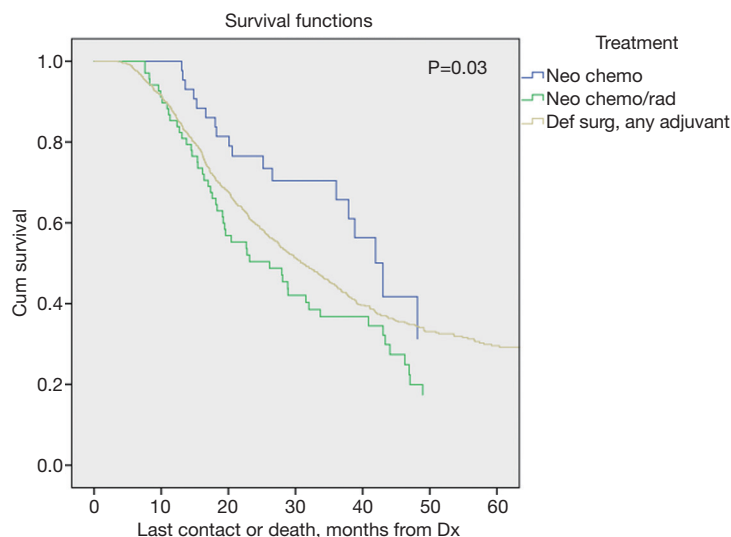| Treatment	Median OS (months)	30-day mortality (%)	P	90-day mortality (%)	P
Neo chemo	43.1	0		1 (2.2)	
Neo chemo/rad	26.3	0	–	3 (4.2)	<0.001
Def surgery, adjv	31.1	0		0	

Figure 3 Tumor ≤2 cm overall survival by treatment.

Another advantage to utilizing NT is to ensure that all patients receive adequate multimodal therapy. The NCCN recommends as of April 2017, to utilize definitive surgery in all resectable and borderline resectable pancreatic cancer followed by adjuvant therapy (14). Many previous studies that supported definitive surgery then adjuvant therapy were found to have selection bias by excluding patients who were not able to receive all adjuvant therapy (up to 60% in some cases) due to post-operative complications (3,4,27,28). A study by Tzeng *et al.* of 167 patients, 115 who underwent NT and 52 who underwent definitive surgery and adjuvant therapy, discovered that 83% of the NT group completed all multimodality therapy, whereas only 58% of the definitive surgery group was able to complete adjuvant therapy (29). The utilization of NT will allow more patients to receive all necessary multimodality therapy upfront thereby obviating post-operative complications as an impact on adjuvant therapies administered.

Several authors have reported that NT improves median and overall survival of pancreatic cancer patients with resectable or borderline resectable disease (30-32). A retrospective study by Artinyan *et al.* of 458 patients demonstrated improved median and overall 5-year survival in patients receiving NT versus definitive surgery (31). Our study similarly identifies NT as an independent predictor of survival. We also found improved survival with NCT over NCRT. With more studies geared towards NT, this finding has potential to influence the decision between chemotherapy and chemoradiation for neoadjuvant treatment.

Tumor size has been an integral part of staging pancreatic cancer according to the AJCC guidelines. However, only recently did tumor size come under scrutiny as a prognostic factor for survival. A retrospective study by Park *et al.* of 6,145 patients from the Surveillance Epidemiology and End Result database sought to identify whether the 7th edition of AJCC TNM staging accurately represented tumor size versus extrapancreatic extension. What they demonstrated was that tumor size was more determinant of prognosis than extrapancreatic extension (8). Other studies, including our own, also show that tumor size is an independent risk factor of survival in patients with pancreatic cancer (9,10). Therefore, the 8th edition of the AJCC TNM staging guidelines to be used starting January 1st 2018 will solely utilizes tumor size in its T-stage system (11).

The new T-stage will invariably alter the way

Table 2 Multivariate analysis

Variable	Non-PSM			PSM		
	HR	95% CI	P	HR	95% CI	P
Age	1.01	1.00–1.01	<0.001	1.01	1.01–1.02	<0.001
Gender						
Male	REF	REF	REF	REF	REF	REF
Female	0.99	0.93–1.05	0.73	0.94	0.84–1.04	0.22
Charlson/Deyo						
0	REF	REF	REF	REF	REF	REF
1	1.07	1.00–1.14	0.06	1.14	1.01–1.28	0.04
2	1.11	0.97–1.25	0.12	1.35	1.03–1.77	0.03
Path T-stage						
T0	REF	REF	REF	REF	REF	REF
T1	0.49	0.20–1.20	0.12	0.46	0.15–1.45	0.19
T2	0.47	0.19–1.13	0.09	0.4	0.13–1.27	0.12
T3	0.52	0.22–1.25	0.15	0.48	0.15–1.50	0.21
T4	0.71	0.28–1.76	0.45	0.55	0.16–1.85	0.33
Path N-stage						
N0	REF	REF	REF	REF	REF	REF
N1	1.59	1.50–1.69	<0.001	1.48	1.31–1.68	<0.001
Grade						
Low	REF	REF	REF	REF	REF	REF
Intermediate	1.22	1.09–1.37	0.001	1.25	1.03–1.51	0.02
High	1.58	1.41–1.77	<0.001	1.76	1.44–2.13	<0.001
Tumor size						
≤2 cm	REF	REF	REF	REF	REF	REF
>2 cm	1.35	1.22–1.49	<0.001	1.45	1.28–1.64	<0.001
Surgical margins						
R0	REF	REF	REF	REF	REF	REF
R1/R2	1.39	1.30–1.50	<0.001	1.54	1.35–1.75	<0.001
Facility volume						
Low (≤10/yr)	REF	REF	REF	REF	REF	REF
Med (11–19/yr)	0.96	0.89–1.03	0.22	1.02	0.91–1.16	0.7
High (≥20/yr)	0.92	0.85–0.99	0.03	0.91	0.79–1.06	0.22
Treatment						
Def surgery, adjv	REF	REF	REF	REF	REF	REF
Neo chemo	0.92	0.80–1.06	0.27	0.69	0.49–0.99	0.04
Neo chemo/rad	1.1	0.98–1.25	0.12	1.35	1.09–1.67	0.006

Tumor size	Median OS (months)	30-day mortality (%)	P	90-day mortality (%)	P
≤2 cm	31.0	43 (2.7)	0.21	83 (5.2)	0.04
>2 cm	20.2	55 (3.5)		110 (6.9)	
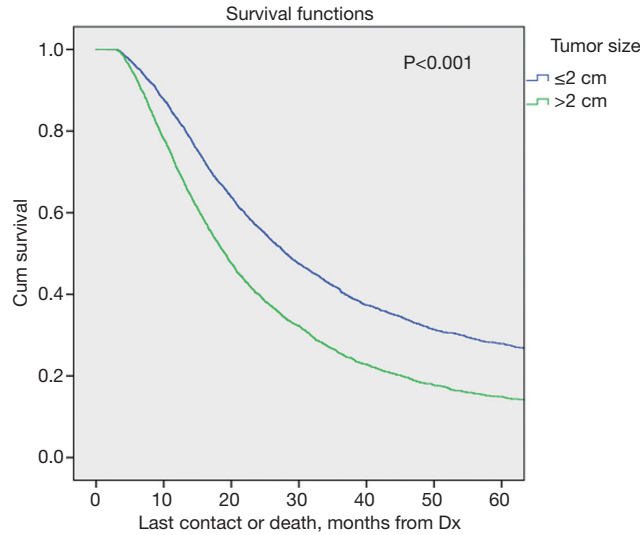
Figure 4 Overall survival by tumor size.

Treatment	Median OS (months)	30-day mortality (%)	P	90-day mortality (%)	P
Neo chemo	32.1	0	<0.001	1 (2.9)	<0.001
Neo chemo/rad	22.2	3 (4.6)		6 (9.2)	
Def surgery, adjv	20.8	0		5 (0.5)	
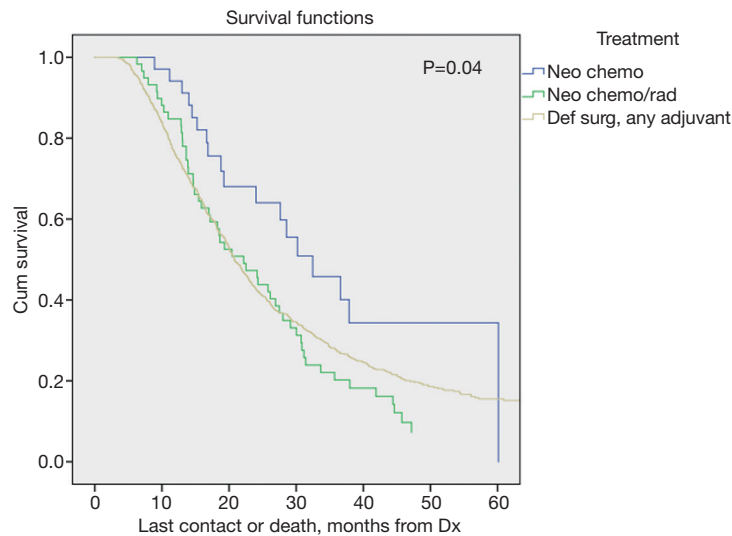
Figure 5 Tumor >2 cm overall survival by treatment.

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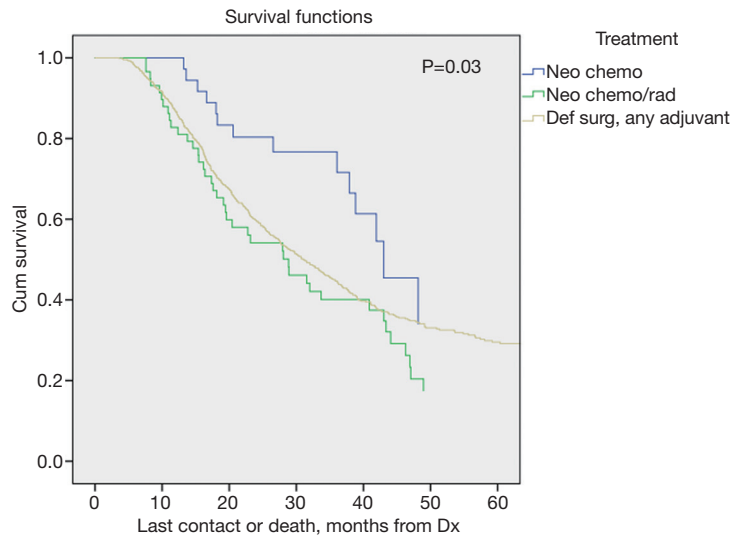| Treatment	Median OS (months)	30-day mortality, (%)	P	90-day mortality, (%)	P
Neo chemo	43.6	0		1 (2.6)	
Neo chemo/rad	28.3	0	–	3 (4.9)	<0.001
Def surgery, adjv	31.1	0		0	

Figure 6 Tumor ≤2 cm overall survival by treatment.

Treatment	Median OS (months)	30-day mortality, (%)	P	90-day mortality, (%)	P
Neo chemo	38.5	0		2 (2.7)	
Neo chemo/rad	24.2	3 (2.4)	<0.001	9 (7.1)	<0.001
Def surgery, adjv	24.4	0		5 (0.3)	
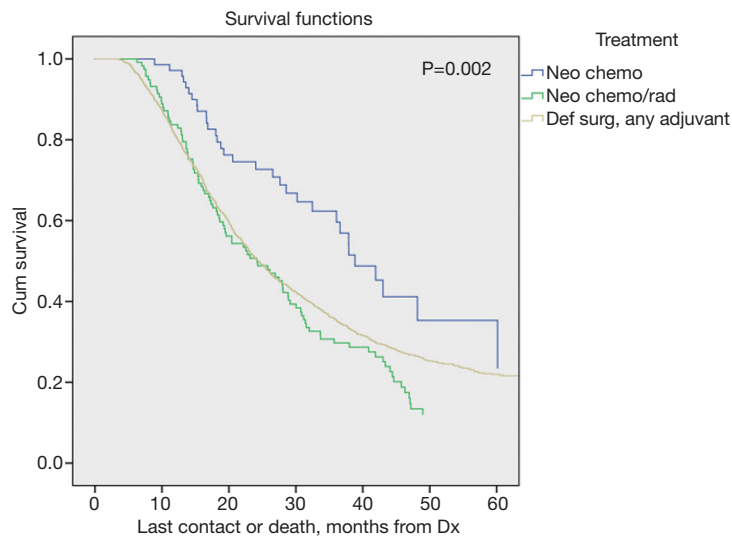
Figure 7 Overall survival by treatment.

multimodality therapy will be guided. Since the current NCCN guidelines recommends surgical therapy followed by adjuvant therapy, most studies are geared towards adjuvant therapy as an independent factor for survival (3,14,27). Aoyama *et al.* retrospectively studied 76 patients, stratified by pancreatic tumor size, who underwent surgical resection of pancreatic cancer and received adjuvant therapy. They discovered that tumor size was the most important prognostic factor for survival specifically in patients receiving adjuvant therapy (33). We similarly found size to be an independent factor of survival and further studied those patients who received NT. Our data demonstrated that NT was a statistically significant predictor of survival in patients with tumor size >2 cm.

Our study is limited by inherent selection bias by being a retrospective analysis, but we attempted to limit this bias by including propensity score matching. We also are unable to standardize data input across institutions and are unable to monitor the guidelines used for collecting data and making diagnosis. Additionally we are unable to account for the accuracy of imaging staging prior to surgery between institutions.

Conclusions

NT demonstrated a survival benefit in all pancreatic cancer patients. NCT demonstrated the most significant improvements in both tumor size >2 and <2 cm. However, in both the NCT and NCRT groups the 30- and 90-day mortality was significantly worse. While pancreatic cancer tumor size is a prognostic factor for survival it should not be used to determine which patients should receive NT. This data supports the use of NT in all pancreatic cancer patients.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: This retrospective study was approved and deemed exempt by the institutional review board at Sarasota Memorial Hospital as it did not involve patient identifiers.

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