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Obesity and survival in population-based patients with pancreatic cancer in the San Francisco Bay Area

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Abstract

Background—Obesity has been consistently associated with increased risk of pancreatic cancer incidence and mortality. However, studies of obesity and overall survival in patients with pancreatic cancer are notably lacking, especially in population-based studies.

Methods—Active and passive follow-up were used to determine vital status and survival for 510 pancreatic cancer patients diagnosed from 1995–1999 in a large population-based case-control study in the San Francisco Bay Area. Survival rates were computed using Kaplan-Meier methods. Hazard ratios (HR) and 95% confidence intervals (CI) were estimated in multivariable Cox proportional hazards models as measures of the association between pre-diagnostic obesity and pancreatic cancer survival.

Results—An elevated hazard ratio of 1.3 (95% CI, 0.91–1.81) was observed for obese (body mass index [BMI] ≥30) compared with normal range BMI (<25) patients. Associations between overall survival and known pancreatic cancer prognostic and risk factors did not significantly vary by BMI (all *P*-interaction ≥0.18), yet elevated HRs consistently were observed for obese compared with normal BMI patients [localized disease at diagnosis (HR, 3.1), surgical resection (HR, 1.6), ever smokers (HR, 1.6), diabetics (HR, 3.3)]. Poor survival was observed among men, older patients, more recent and current smokers, whereas improved survival was observed for Asian/Pacific Islanders.

Conclusions—Our results in general provide limited support for an association between prediagnostic obesity and decreased survival in patients with pancreatic cancer. Patterns of reduced survival associated with obesity in some patient subgroups could be due to chance and require assessment in larger pooled studies.

Keywords

Pancreatic cancer; obesity; survival; population-based cohort

Introduction

Pancreatic cancer is the fourth leading cause of cancer death in U.S. men and women with a similar number of deaths and new cases diagnosed each year [1]. The prognosis of pancreatic cancer remains extremely poor, with an overall 5-year relative survival rate of 6%

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Conflict of interest
The authors declare that they have no conflict of interest.

[2]. Although the etiology of this deadly disease remains largely unknown, epidemiologic data consistently have indicated that obesity is associated with increased risk of pancreatic cancer [3–6] and pancreatic cancer mortality [7–9]. Few recent observational studies, including two-hospital based studies and one multi-site clinic-based study, reported poorer survival among obese patients, and also found additional effects of smoking, diabetes and age at obesity in their effort to clarify the role of obesity and related biological mechanisms in pancreatic cancer survival [10–12]. In contrast, results have been mixed from clinical studies that evaluated the effect of obesity at time of pancreatic resection on patient outcomes, including survival [13–20]. As current results have largely been limited to clinic- and hospital-based studies or small clinical studies, confirmation and further investigation in population-based studies is needed to clarify the role of obesity in pancreatic cancer survival.

Here we address whether obesity before diagnosis is related to survival in pancreatic cancer patients who participated in our large San Francisco Bay Area population-based pancreatic cancer study that has more than 10 years of patient follow-up with <1% lost to follow-up [21]. Detailed collection of epidemiologic risk factor and clinical data also allowed us to further examine potential confounding or modification of the obesity-survival association by the known clinical prognostic factors (*i.e.* stage) and other risk factors (*i.e.* smoking, and diabetes) that have been reported in previous publications.

Materials and Methods

Study population

Study cases were patients newly diagnosed with adenocarcinoma of the exocrine pancreas identified by the Greater Bay Area Cancer Registry rapid case ascertainment and by Surveillance, Epidemiology and End Results (SEER) registry abstracts, met study eligibility criteria and participated in our population-based, case-control study. Study details have been described previously [22]. Briefly, eligible cases were 21–85 years old at diagnosis, residents of one of six San Francisco Bay Area counties, diagnosed with pancreatic adenocarcinoma from January 1, 1995 to December 31, 1999, alive at first contact, had no physician indicated contraindications to contact and were able to complete an interview in English. Pancreatic cancer diagnoses were confirmed by participants' physicians and by SEER abstracts. Among the 798 eligible cases contacted, 532 completed the interview for a participation rate of 67%. There were 8 patients excluded after additional vital status update due to unconfirmed cancer diagnosis or diagnosis of cancer "in situ". Fourteen out-of-area study patients were not included in the vital status update, leaving 510 patients for these survival analyses. The study was reviewed and approved by the University of California San Francisco Committee on Human Research.

Data collection

Detailed data including age, race, education, medical history, history of smoking, physical activity, and anthropometric measures were collected during in-person interviews by trained interviewers. No proxy interviews were conducted. Patient prognostic clinical information was obtained from SEER abstracts/registry data and from in-person interviews. For these analyses, age at diagnosis was grouped as <50, 50–59, 60–69, 70–79, 80+ years and race/ethnicity as non-Hispanic white, Hispanic white, black/African American, Asian/Pacific Islander/other. Usual adult body mass index (BMI: kg/m^2) was classified into normal weight (BMI <25 kg/m^2), overweight (BMI 25-<30 kg/m^2), and obese (BMI ≥30 kg/m^2) categories. Stage at diagnosis was determined by SEER registry abstractors using pathological and clinical data, and was classified as localized (confined to the pancreas), regional (extension to surrounding organs/or regional lymph nodes), or distant disease (metastases). Initial

treatment data were obtained from SEER abstracts and in-person interviews and were coded as surgical resection (Whipple or local resection), chemotherapy/radiation therapy, bypass/stent, other treatment and therapy unknown.

Vital status

Patient vital status was determined using multiple passive and active methods as previously described [21]. In brief, date of death was actively ascertained as part of the patient recruitment process. In the years after the parent case-control study had ended, vital status and date of death were updated using SEER abstract and registry data, the Social Security Death Index and the California Death Records databases. When patient vital status was not available from the aforementioned sources, patients, their relatives, their treating physicians and/or the treating hospitals were contacted to determine patient vital status. Using these methods, vital status and survival-related data were completed for all patients through December 31, 2008. Survival time was defined as the time from diagnosis to death or to date of last contact for patients who remained alive or who were lost to follow-up.

Statistical analysis

We examined means and frequency distributions of demographic and clinical characteristics across BMI categories and tested for statistically significant associations using one-way ANOVA and chi-square tests. Kaplan-Meier methods and log-rank tests were used to estimate the mortality-free survival by categorical variables of interest. Multivariable Cox proportional hazards models were used to estimate the hazard ratios (HR) and 95% confidence intervals (CI) for associations among BMI, demographic, tumor and treatment factors and overall survival from pancreatic cancer [23]. An unknown category was created for variables of stage at diagnosis, tumor grade, site of tumor, and initial treatment when they were included in the model.

Statistical tests were two-sided and considered statistically significant for $p < 0.05$. Statistical analyses were conducted using SAS software v9.2 (SAS Institute, Inc., Cary, NC).

Results

Study patients' demographic and clinical characteristics by BMI categories are provided in Table 1. BMI was not associated with clinical prognostic factors, including cancer stage (P=0.92) and tumor grade (P=0.23). BMI also was not related to the tumor location (P=0.11) or to the initial treatment modalities (P=0.35). However, compared with patients whose BMI was in the normal range, obese patients were more likely to be younger, men, African American, never smokers, and diabetic (all $P \leq 0.02$).

Median survival duration and overall patient survival associated with demographic characteristics, clinical factors and other covariates assessed using Cox proportional hazards regression are presented in Table 2. With a median follow-up of 10.1 years, 495 (97.0%) patients were confirmed dead, 11(2.2%) were alive at last contact, and vital status was unknown for 4 (0.8%) patients. The median overall survival was 10.1 months. The association of BMI with overall survival in pancreatic cancer patients was estimated in a model adjusted for age, sex, race/ethnicity, education level, and for smoking status, diabetes and clinical prognostic factors. An elevated hazard ratio of 1.28 (95% CI, 0.91–1.81, P=0.16) was observed for obese compared with normal BMI patients. Risk of dying was highest, as expected, among older patients (80+ years old, HR=2.65) and among patients who were diagnosed with distant disease (HR= 1.93) or poorly differentiated tumor (HR= 1.73). In contrast, the lowest HRs were observed among patients whose initial treatment was surgical resection and other active treatment modalities (HRs from 0.40 to 0.74) relative to

those with unknown initial treatment. Better overall survival also was observed among Asians or Pacific Islanders when compared with non-Hispanic whites, and among women when compared with men.

The association of BMI with overall survival in pancreatic cancer patients stratified by stage, by smoking status and by diabetes was determined using multivariable Cox proportional hazards models adjusted for age, sex, race/ethnicity, education level, and for smoking status, diabetes and clinical prognostic factors as appropriate (Table 3). Obesity was associated with reduced overall survival among patients with localized stage at diagnosis (HR= 3.08) or who had received surgical resection (HR= 1.58), although confidence intervals were wide and included unity. Results also suggested that association between obesity and overall survival differed by smoking status (non-smokers vs. smokers) and by history of diabetes. In stratified analyses, risk of dying was greater for smokers (HR= 1.58; 95% CI, 0.86–2.90) and for diabetics (HR= 3.31; 95% CI, 1.16–9.44), although formal tests of statistical interaction were not statistically significant (all $P \geq 0.18$).

Discussion

Pre-diagnostic obesity (BMI ≥30) based on usual adult weight was not statistically significantly associated with overall survival for pancreatic cancer in our study population. The association between known pancreatic cancer prognostic and risk factors did not significantly vary by BMI. Relatively few obese patients may have constrained our analyses. Chance could not be eliminated as the reason for the observed pattern of elevated HRs between obesity and overall survival by cancer stage at diagnosis, initial therapy, smoking status and diabetes.

Most published studies of obesity and pancreatic cancer survival are small clinical studies that investigated the relationship between BMI and various patient outcomes, including survival, after pancreatic resection. The association between obesity and survival from these studies has been mixed [13, 17, 19, 20] and may be explained by a variety of factors including small study size, assessment of outcomes unrelated to obesity, and heterogeneity in criteria for study enrollment and in BMI measures [24]. Additionally, many of these studies were designed to determine how obesity at time of surgery affected patient surgical outcome(s), rather than to assess the relationship between usual adult obesity (or obesity at a specific age) and survival duration in pancreatic cancer patients. Further, results from these studies are generalizable only to the approximate 20% of patients who received surgical resections (most of whom have localized disease), thus preventing an overall conclusion about the association between obesity and survival in pancreatic cancer patients.

Few epidemiological studies have evaluated the effect of obesity on pancreatic cancer survival after accounting for known risk factors, grade, stage and treatment. Our results are consistent in magnitude and direction of obesity-related effects reported in these few studies [10–12]. Our observation that obesity was associated with poorer survival in certain subgroups of patients, including those diagnosed with localized disease or who had received surgical resection, was similar to results from recent studies conducted at MD Anderson Cancer Center (MDACC) [10] and at Memorial Sloan Kettering Cancer Center (MSKCC) [11]. Both the MDACC and MSKCC studies reported that obesity was associated with decreased overall survival, particularly in the resected group (MDACC HR=3.4; MSKCC: HR=1.6), although results from MSKCC, 9 similar to our study, were not statistically significant. Results from a large clinic-based study at the Mayo Clinic also showed decreased survival with increased BMI in the total cohort of patients (BMI ≥30: HR=1.3; BMI ≥40: HR=1.6, p for trend <0.001) but found no differences by cancer stage [12]. Data from clinical studies suggest that obese patients may have had higher complication rates

following their surgery, thus leading to shorter survival and a greater likelihood of dying [13, 15, 16]. However, it should be noted that a relatively small proportion of patients in our study population were obese (10%) compared with these other studies (23% to 36%), thus limiting the power of our study to detect a statistically significant effect. It also is possible that underlying differences in patients recruited from clinic- and hospital-based studies that tend to be conducted in single tertiary care institutions such as MSKCC, MDACC and the Mayo Clinic, and from population-based studies such as ours, may further explain some of the variation in results across observational studies. Additional large population-based studies are needed to examine this association further, particularly given the growing prevalence of obesity among U.S. adults over the past decade.

Smoking and diabetes have been consistently associated with increased risk of pancreatic cancer [25–31], and although each has been associated with obesity, little is known about whether they modify the association between obesity and survival from pancreatic cancer. In our analyses by smoking and by diabetes, we found that obese current smokers and obese diabetics had poorer survival than obese patients without these exposures/conditions. These suggestive joint effects require further study but may be partly explained by obesity-related mechanisms that are tumor enhancing. Obesity and diabetes are both associated with insulin resistance and insulin resistance results in higher circulating levels of insulin and insulin-like growth-factor 1 (IGF-1). Higher circulating insulin and IGF-1 have been shown to promote tumor progression 10 and metastasis [32–35] and thus may impact overall survival. Obesity also results in increased levels of leptin and other adipokines that can promote angiogenesis, an important factor in the growth and spread of many cancers [36–39]. Finally, obesity induces a pro-inflammatory environment including increased circulating tumor necrosis factor α and interleukins that also may contribute to tumor progression and metastasis [40–42].

Study patients were identified from a population-based cancer registry and we had extensive epidemiologic data available that allowed us to conduct detailed analyses of obesity and survival including assessment of multiple potential covariates, such as smoking and diabetes. We also had long-term follow-up for a median duration of 10 years for a total of 510 pancreatic cancer patients. Our use of active follow-up methods that included contact of physicians' offices, hospitals, patients' relatives and patients in addition to multiple passive follow-up approaches that included use of SEER data and various vital statistics databases, allowed us to obtain nearly complete vital status and survival assessment (<1% loss to follow-up). Our findings are consistent with published data but several factors should be considered when interpreting our results. Clinical data were obtained mainly from the SEER abstracts and thus tumor-related data were unknown for some patients. However, to diminish the effect of unknown data on our estimates, unknown data were grouped and included in our analyses. Given the high fatality rate of pancreatic cancer, cases who were interviewed and included in our study were healthier and more likely to have had better survival. Our study patients had longer median survival duration (10 months) than pancreatic cancer patients in the California SEER registry (3.5 months) diagnosed during the same time period. If obese patients were more likely to die before contact and thus are under-represented in our study, our results may underestimate the effect of obesity on overall survival. Further, the small number of obese patients limited our ability to adequately test some hypotheses in the stratified analyses, and these results require confirmation and further investigation.

In conclusion, our results in general are consistent with those from previously published studies and provide support for an association between pre-diagnostic obesity and decreased survival in patients with pancreatic cancer. Results that show the risk of dying associated with obesity was greater in some patient subgroups, such as among diabetics, should be

interpreted conservatively and require confirmation. Because obesity is a risk factor for multiple diseases including pancreatic cancer, and is both preventable and amenable to intervention, it is important to continue to stress this message in public health presentations. Given the accumulating but limited research to suggest that obesity may be associated with survival in pancreatic cancer patients, larger pooled studies, especially from population-based projects, are warranted to further address this association.

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Table 1

Demographic and clinical characteristics of 510 pancreatic cancer patients by body mass index (BMI) from a population-based case-control study in the San Francisco Bay Area, 1995–1999

Characteristics	Body Mass Index (kg/m^2)			*P*-value[a]
	<25 (n=269)	**25-<30 (n=190)**	**≥30 (n=51)**	
Age at diagnosis (yrs), mean (SD)	66.1 (10.2)	63.2 (10.6)	62.0 (11.2)	0.002
	n (%)	**n (%)**	**n (%)**	
Age				0.01
<50	21 (7.8)	15 (7.9)	7 (13.7)	
50–59	45 (16.7)	55 (28.9)	14 (27.5)	
60–69	84 (31.2)	64 (33.7)	15 (29.4)	
70–79	100 (37.2)	42 (22.1)	12 (23.5)	
≥80	19 (7.1)	14 (7.4)	3 (5.9)	
Sex				<0.0001
Men	110 (40.9)	136 (71.6)	32 (62.8)	
Women	159 (59.1)	54 (28.4)	19 (37.2)	
Race/Ethnicity				0.01
Non-Hispanic white	224 (83.2)	148 (77.9)	36 (70.6)	
Hispanic white	5 (1.9)	7 (3.7)	3 (5.9)	
African-American/Black	14 (5.2)	21 (11.0)	10 (18.9)	
Asian/Other	26 (9.7)	14 (7.4)	2 (3.8)	
Education				0.61
Less than high school	28 (10.4)	29 (15.3)	8 (15.7)	
High school graduate	86 (32.0)	56 (29.5)	19 (37.2)	
1–4 years college	106 (39.4)	68 (35.8)	16 (31.4)	
Graduate school	49 (18.2)	37 (19.5)	8 (15.7)	
Smoking status				0.02
Never smokers	83 (30.9)	53 (27.9)	22 (43.1)	
Former smokers, quit>15yrs	58 (21.6)	61 (32.1)	8 (15.7)	
Former smokers, quit 1–15yrs	54 (20.1)	26 (13.7)	5 (9.8)	
Current smokers +quit<1yr	68 (25.2)	44 (23.2)	12 (23.5)	
Cigar smokers	6 (2.2)	6 (3.2)	4 (7.8)	
Diabetes				<0.0001
No	243 (90.7)	163 (85.8)	31 (60.8)	
Yes	25 (9.3)	27 (14.2)	20 (39.2)	
Stage at diagnosis				0.92
Local	31 (11.5)	26 (13.7)	6 (11.8)	
Regional	113 (42.0)	83 (43.7)	25 (49.0)	
Distant	86 (32.0)	53 (27.9)	14 (27.4)	
Unstaged/unknown	39 (14.5)	28 (14.7)	6 (11.8)	

Characteristics	Body Mass Index (kg/m^2)			*P*-value[a]
Tumor grade				0.23
Well differentiated	33 (12.3)	22 (11.6)	2 (3.9)	
Mod-Well differentiated	10 (3.7)	10 (5.2)	4 (7.8)	
Moderate differentiated	61 (22.7)	28 (14.7)	9 (17.6)	
Mod-Poor differentiated	19 (7.1)	15 (7.9)	4 (7.8)	
Poorly differentiated	38 (14.1)	25 (13.2)	12 (23.5)	
Not graded/unknown	108 (40.1)	92 (47.4)	20 (39.2)	
Tumor site				0.11
Head	164 (61.0)	132 (69.5)	35 (68.6)	
body	30 (11.1)	8 (4.2)	3 (5.9)	
Tail	14 (5.2)	15 (7.9)	4 (7.8)	
Head/body/tail	22 (8.2)	8 (4.2)	2 (3.9)	
NOS/Unknown	39 (14.5)	27 (14.2)	7 (13.7)	
Initial treatment				0.35
Whipple or local resection	85 (31.6)	58 (30.5)	15 (29.4)	
Chemo/radiation	71 (26.4)	56 (29.5)	20 (39.2)	
Other treatment	27 (10.0)	15 (7.9)	3 (5.9)	
Bypass/stent	18 (6.7)	20 (10.5)	6 (11.8)	
Treatment unknown	68 (25.3)	41 (21.6)	7 (13.7)	

NOS: not otherwise specified

[a] *P*-value of chi-square test or Fisher's exact test (if more than 25% of cells with an expected value less than 5) for categorical variables or of one-way ANOVA for continuous variables

Table 2

Hazard ratios (HR) and 95% confidence intervals (CI) as estimates of risk of dying associated with body mass index (BMI), demographic, clinical and other lifestyle factors in 510 pancreatic cancer patients from a population-based case-control study, San Francisco Bay Area, 1995–1999

Characteristics	Patients N (%)	Deaths (N)	Survival in mos. Med. (IQR)	HR (95% CI)[a]	HR (95% CI)[b]	*P*-value[c]
Total patient cohort	510	495	10.1 (6.4–17.9)			
Body mass index (BMI)						0.32
<25	269 (52.8)	261	9.9 (6.3–18.5)	1.00	1.00	
25-<30	190 (37.2)	184	10.7 (6.4–17.2)	1.01 (0.83–1.22)	1.04 (0.83–1.28)	
≥30	51 (10.0)	50	9.1 (6.4–15.7)	1.27 (0.93–1.72)	1.28 (0.91–1.81)	
Age at diagnosis						<0.0001
<50	43 (8.4)	37	9.8 (5.1–26.6)	1.00	1.00	
50–59	114 (22.4)	110	11.5 (7.0–17.2)	1.25 (0.86–1.82)	1.21 (0.80–1.83)	
60–69	163 (32.0)	161	11.0 (6.8–19.3)	1.25 (0.87–1.79)	1.05 (0.70–1.57)	
70–79	154 (30.2)	151	9.2 (6.0–17.0)	1.46 (1.01–2.09)	1.62 (1.07–2.45)	
80+	36 (7.0)	36	7.8 (4.7–9.8)	2.46 (1.54–3.91)	2.65 (1.57–4.49)	
Sex						0.01
Men	278 (54.5)	273	10.0 (6.2–16.2)	1.00	1.00	
Women	232 (45.5)	222	11.0 (6.6–21.0)	0.78 (0.65–0.94)	0.77 (0.62–0.95)	
Race						0.02
Non-Hispanic white	408 (80.0)	399	9.9 (6.2–17.0)	1.00	1.00	
Hispanic white	15 (2.9)	15	19.3 (9.4–26.6)	0.72 (0.42–1.25)	0.80 (0.45–1.42)	
African American/Black	45 (8.8)	44	9.6 (6.8–15.8)	1.07 (0.78–1.46)	0.85 (0.59–1.23)	
Asian/other	42 (8.2)	37	14.9 (7.1–23.5)	0.78 (0.55–1.09)	0.58 (0.40–0.83)	
Education						0.93
Less than high school	65 (12.8)	65	9.2 (6.4–13.2)	1.00	1.00	
High school graduate	161 (31.6)	158	10.2 (6.6–17.8)	0.77 (0.57–1.03)	0.91 (0.66–1.26)	
1–4 years college	190 (37.2)	185	11.3 (6.4–18.8)	0.74 (0.55–0.99)	0.89 (0.65–1.23)	
Graduate school	94 (18.4)	87	9.8 (6.0–23.1)	0.66 (0.47–0.92)	0.91 (0.63–1.32)	
Diabetes status						0.26

Characteristics	Patients N (%)	Deaths (N)	Survival in mos. Med. (IQR)	HR (95% CI)[a]	HR (95% CI)[b]	*P*-value[c]
No	437 (85.8)	422	10.2 (6.4–18.1)	1.00	1.00	
Yes	72 (14.2)	72	9.9 (6.2–16.1)	1.16 (0.90–1.50)	0.85 (0.64–1.13)	
Smoking						0.03
Never smokers	158 (31.0)	150	11.3 (6.7–21.8)	1.00	1.00	
Former smokers, quit>15yrs	127 (24.9)	123	10.4 (6.4–20.3)	1.01 (0.79–1.29)	0.98 (0.74–1.28)	
Former smokers, quit 1–15yrs	85 (16.7)	85	9.4 (6.2–14.6)	1.60 (1.22–2.10)	1.46 (1.09–1.96)	
Current smokers +quit<1yr	124 (24.3)	121	9.7 (6.0–17.8)	1.24 (0.97–1.58)	1.22 (0.94–1.58)	
Cigar/pipe smokers	16 (3.1)	16	9.8 (7.2–17.3)	1.14 (0.68–1.92)	0.81 (0.47–1.42)	
Stage at diagnosis						<0.0001
Local	63 (12.4)	56	14.6 (7.3–32.9)	1.00	1.00	
Regional	221 (43.3)	215	12.8 (7.7–21.5)	1.44 (1.06–1.94)	1.21 (0.88–1.66)	
Distant	153 (30.0)	152	7.0 (4.8–11.2)	3.02 (2.20–4.14)	1.93 (1.35–2.77)	
Unstaged/Unknown	72 (14.3)	72	9.7 (7.3–18.9)	1.72 (1.20–2.46)	0.99 (0.65–1.51)	
Tumor grade						0.09
Well differentiated	57 (11.2)	54	13.4 (9.0–32.9)	1.00	1.00	
Moderately-well differentiated	24 (4.7)	21	12.0 (7.9–21.0)	1.17 (0.70–1.95)	1.32 (0.78–2.23)	
Moderately differentiated	98 (19.2)	92	13.6 (7.0–21.9)	1.32 (0.94–1.86)	1.36 (0.95–1.93)	
Moderately-poor differentiated	38 (7.4)	36	10.6 (4.6–23.4)	1.25 (0.82–1.92)	1.32 (0.85–2.05)	
Poor differentiated	75 (14.7)	75	8.6 (5.4–14.9)	2.23 (1.56–3.19)	1.73 (1.16–2.58)	
Not graded/unknown	218 (42.8)	217	9.1 (6.1–14.3)	2.02 (1.49–2.74)	1.42 (1.02–1.99)	
Tumor site						
Head	331 (64.9)	317	10.5 (6.6–19.1)	1.00	1.00	0.30
Body	41 (8.0)	41	8.9 (6.1–11.2)	1.95 (1.40–2.72)	1.49 (1.04–2.14)	
Tail	33 (6.5)	33	11.5 (9.1–17.9)	1.05 (0.73–1.50)	1.01 (0.69–1.47)	
Head/body/tail	32 (6.3)	32	7.5 (5.8–11.3)	1.46 (1.01–2.11)	1.15 (0.77–1.73)	
NOS/unknown	73 (14.3)	72	11.1 (5.2–18.9)	1.11 (0.86–1.44)	1.05 (0.79–1.38)	
Initial treatment						
Treatment unknown	158 (31.0)	144	8.5 (5.5–12.9)	1.00	1.00	<0.0001
Whipple or local resection	147 (28.8)	147	17.9 (9.9–34.4)	0.37 (0.29–0.48)	0.40 (0.29–0.56)	

Characteristics	Patients N (%)	Deaths (N)	Survival in mos. Med. (IQR)	HR (95% CI)[a]	HR (95% CI)[b]	*P*-value[c]
Chemo/radiation therapy	45 (8.8)	45	10.1 (6.3–14.6)	0.87 (0.69–1.11)	0.74 (0.56–0.98)	
Other treatment	44 (8.6)	44	8.5 (5.1–13.2)	0.98 (0.70–1.39)	0.70 (0.48–1.02)	
Bypass/stent	116 (22.8)	115	8.0 (6.1–11.8)	1.10 (0.78–1.56)	1.02 (0.69–1.51)	

Med.: Median; IQR: interquartile range; HR: hazard ratio; 95% CI: 95% confidence interval, NOS: not otherwise specified

[a] Results were from age-adjusted analysis

[b] Results were from multivariable-adjusted model including age, sex, race, education, body mass index, smoking status, diabetes, stage, tumor grade, tumor site, and primary treatment

[c] *P*-value is from Wald Chi-Square test in multivariable-adjusted models

Table 3

Hazard rations (HR) and 95% confidence intervals (CI) for body mass index (BMI) associated with overall survival in stratified analyses among 510 pancreatic cancer patients from a population-based case-control study, San Francisco Bay Area, 1995–1999

Characteristics	BMI (kg/m^2)	Cases N (%)	HR (95% CI)[a]	HR (95% CI)[b]
Stage				
Local				
	<25	31 (49.2)	1.00	1.00
	25-<30	26 (41.3)	1.09 (0.62–1.93)	0.53 (0.19–1.46)
	≥30	6 (9.5)	2.37 (0.92– 6.11)	3.08 (0.46–20.73)
Regional				
	<25	113 (51.1)	1.00	1.00
	25-<30	83 (37.6)	1.04 (0.77–1.40)	0.96 (0.67–1.38)
	≥30	25 (11.3)	1.28 (0.83–1.99)	1.03 (0.56–1.88)
Distant				
	<25	86 (56.2)	1.00	1.00
	25-<30	53 (34.6)	1.01 (0.71–1.44)	0.87 (0.55–1.38)
	≥30	14 (9.2)	1.28 (0.71–2.31)	1.06 (0.53–2.11)
Unstaged/Unknown				
	<25	39 (53.4)	1.00	1.00
	25-<30	28 (37.5)	1.02 (0.60–1.75)	0.84 (0.41–1.70)
	≥30	6 (8.2)	1.67 (0.50–5.58)	0.91 (0.21–3.91)
$P_{BMI\times Stage}$	0.89			
Surgery (initial treatment)				
No				
	<25	184 (52.3)	1.00	1.00
	25-<30	132 (37.5)	0.98 (0.78–1.23)	1.04 (0.80–1.35)
	≥30	36 (10.2)	1.05 (0.73–1.52)	1.22 (0.82–1.83)
Yes				
	<25	85 (53.8)	1.00	1.00
	25-<30	58 (36.7)	0.92 (0.64–1.34)	0.64 (0.42–0.99)

Characteristics	BMI (kg/m^2)	Cases N (%)	HR (95% CI)[a]	HR (95% CI)[b]
	≥30	15 (9.5)	1.75 (1.00–3.06)	1.58 (0.76–3.32)
$P_{BMI\times Surgery}$	0.54			
Smoking status[c]				
Non-smoker				
	<25	147 (48.8)	1.00	1.00
	25-<30	120 (39.9)	1.08 (0.85–1.39)	0.90 (0.67–1.20)
	≥30	34 (11.3)	1.37 (0.93–2.01)	1.05 (0.67–1.65)
Ever smoker				
	<25	122 (58.4)	1.00	1.00
	25-<30	70 (33.5)	0.92 (0.66–1.27)	1.14 (0.79–1.66)
	≥30	17 (8.1)	1.25 (0.74–2.11)	1.58 (0.86–2.90)
$P_{BMI\times Smoking}$	0.26			
Diabetes				
No				
	<25	243 (55.6)	1.00	1.00
	25-<30	163 (37.3)	1.00 (0.81–1.22)	0.94 (0.74–1.19)
	≥30	31 (7.1)	1.32 (0.90–1.94)	1.21 (0.80–1.82)
Yes				
	<25	25 (34.7)	1.00	1.00
	25-<30	27 (37.5)	1.08 (0.62–1.88)	1.20 (0.50–2.88)
	≥30	20 (27.8)	1.08 (0.59–1.97)	3.31 (1.16–9.44)
$P_{BMI\times Diabetes}$	0.18			

HR: hazard ratio; 95% CI: 95% confidence interval

[a]Results were from age-adjusted analysis

[b]Estimates were from multivariable Cox proportional hazards models that included adjustment for age, sex, race, education, smoking status, diabetes, stage, tumor grade, tumor site, and primary treatment, but excluded the specific stratified variable from the model (i.e., stage, surgical status, smoking status, and diabetes status)

[c]Non-smokers: never smokers and former smokers who had quit >15 years ago; Smokers: current smokers and former smokers who had quit <1 to 15 years ago