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Determinants and prognostic value of quality of life in patients with pancreatic ductal adenocarcinoma

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Abstract

Background: Quality of life (QOL) is impaired in pancreatic cancer patients. Our aim was to investigate the determinants and prognostic value of QOL after diagnosis in a hospital-based cohort of racially/ethnically diverse patients with pancreatic ductal adenocarcinoma (PDAC).

Patients and methods: QOL was prospectively assessed using the Short Form-12 in 2478 PDAC patients. The Physical Component Summary (PCS) and Mental Component Summary (MCS) were categorised into tertiles based on their distribution. Ordered logistic regression was adopted to compare the risk of having lower PCS and MCS by patient sociodemographic and

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[1]These authors jointly supervised this work.

Conflict of interest statement

None declared.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.ejca.2017.12.023.

clinical characteristics. The association of PCS and MCS with mortality was assessed by Cox regression.

Results: Compared with non-Hispanic whites, Hispanics were at significantly higher risk of having lower PCS (odds ratio [95% CI], 1.69 [1.26–2.26]; $P < 0.001$) and lower MCS (1.66 [1.24–2.23]; $P < 0.001$). Patients diagnosed with stage III (1.80 [1.10–2.94]; $P = 0.02$) and stage IV (2.32 [1.50–3.59]; $P < 0.001$) PDAC were more likely to have lower PCS than stage I patients. Other determinants of QOL included sex, age, drinking, smoking, education level, comorbidities and time since diagnosis. The low tertile of PCS (hazard ratio [95% CI], 1.94 [1.72–2.18]; $P < 0.001$) and MCS (1.42 [1.26–1.59]; $P < 0.001$) were each related to poor prognosis. Similar results were found for non-Hispanic whites as compared with African-Americans/Hispanics/others.

Conclusion: QOL after diagnosis is a significant prognostic indicator for patients with PDAC. Multiple factors determine QOL, suggesting possible means of intervention to improve QOL and outcomes of PDAC patients.

Keywords

Quality of life; Pancreatic ductal adenocarcinoma; Overall survival; Prognostic indicator; Short Form-12

1. Introduction

Pancreatic cancer (PC) is the third leading cause of cancer mortality in the United States [1] and the seventh globally [2]. In the United States, projections estimate that there will be 53,670 new cases of PC and 43,090 PC deaths in 2017 [1]. Pancreatic ductal adenocarcinoma (PDAC) accounts for 90% of all pancreatic cancers. The prognosis for patients with PDAC remains poor. The 5-year relative survival rate is 8% for all stages combined, 29% for local disease, and 3% for distant stage, respectively [3].

PDAC is known for its debilitating symptom burden and has a profound negative effect on patient quality of life (QOL) [4]. Consequently, QOL has become a subject of paramount importance for PDAC patients. Several studies of patients with PC have shown that higher baseline/pretreatment QOL is associated with longer overall survival [5–13], whereas another study showed no association [14]. However, these studies were limited by small sample sizes (ranging from 50 to 569), and most studies focused on metastatic or advanced-stage cancer without considering early-stage patients.

Identifying the determinants of QOL in PC patients could be important for clinicians to identify patients with poor QOL who need enhanced monitoring or improved care management. Previous studies have found some demographic (age) and clinical (clinical stage, operation type, and weight stabilisation) factors affect QOL in PC patients [15–17]. However, the sample sizes of these studies were also small and did not investigate the difference in determinants of QOL by race/ethnicity. Therefore, we assessed the prognostic value and the determinants of QOL after diagnosis in a large prospective cohort of racially/ethnically diverse patients with PDAC which encompassed all stages.

2. Methods

2.1. Patients

Participants were patients with histologically confirmed PDAC between August 1999 and October 2012 as part of The MD Anderson Cancer Patients and Survivors Cohort Study (MDA-CPSC) [18], a prospective hospital-based cohort study in the United States. At their initial visit, all participants completed a patient history form that collected epidemiologic, sociodemographic, and risk factor information. The patient history form also assessed QOL employing the generic, validated Short Form-12 vision 1 (SF-12v1) questionnaire [19]. Clinical information was abstracted from the institutional Tumour Registry. This study was approved by the institutional review board.

2.2. Eligibility and exclusion criteria

A total of 3725 PC patients completed the patient history form and SF-12v1 questionnaire within 1 year of diagnosis. We excluded patients who were younger than 18 years(N = 12), those who had been diagnosed with non-ductal adenocarcinoma (N = 789), those who had been diagnosed with multiple primary tumours (N = 442), and those who did not give the consents (N = 4). The final number of patients included in this study was 2478.

2.3. SF-12v1 questionnaire

The SF-12v1 questionnaire is a multipurpose generic QOL questionnaire evolved from the Short Form-36 questionnaire. The SF-12v1 questionnaire consists of 12 questions that measure 4 domains (physical, functional, emotional and social) and 8 subscales (physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional and mental health). The 8 subscales of this tool can be summarised into 2 indices: the Physical Component Summary (PCS) and the Mental Component Summary (MCS), which describe the patient's physical and mental well-being respectively [19]. Higher PCS and MCS scores indicated better QOL.

2.4. Statistical analysis

The PCS (high: ≥45.7, medium: 32.7–45.7, low: <32.7) and MCS (high: ≥52.3, medium: 40.3–52.3, low: <40.3) scores were categorised into tertiles based on the scores distribution. Ordered logistic regression was adopted to estimate the associations between patient characteristics and categorical PCS or MCS scores. First, each sociodemographic and clinical variable was independently assessed using a univariate model, with statistical significance set at $P < 0.05$. Next, variables found to be significant in the univariate analysis were included in a multivariate model, and forward selection was used to eliminate variables with a P value > 0.05. Because 1466 patients had missing stage data, we conducted a sensitivity analysis and found similar results when utilising the full data set and the reduced data set (only among those with stage information). Therefore, we presented the results from the full data set below.

Survival time was defined as the period from diagnosis to death or last follow-up. Cox proportional hazards models were adjusted for potential confounders (sex, age, marital status, race, education level, occupation, smoking, alcohol use, tumour size, cancer stage,

comorbidity, treatment before survey, time since diagnosis and years of diagnosis). Survival estimates for the low, medium and high PCS and MCS groups were determined using the Kaplan–Meier method and compared using the log-rank test. All statistical tests were 2 sided, and *P* values < 0.05 were considered statistically significant. Statistical analyses were conducted using Stata 14.2 (StataCorp LP, College Station, Texas).

3. Results

3.1. Study population

The characteristics of the PDAC patients in this study are shown in Table 1. The study population, with a median age of 62.0 years (range: 28.0–90.0 years), consisted of 1489 (60.1%) males and 1966 (79.3%) non-Hispanic whites. Among the 1013 patients with stage information available, 533 (52.6%) were diagnosed with stage IV PDAC. Among the 577 (27.8%) patients who received treatment, 191 (33.1%) patients were treated by curative therapy (pancreatectomy with or without adjuvant treatment), 15 (2.6%) patients were treated by neoadjuvant therapy, 371 (64.3%) patients were treated by palliative treatment, and 56 (9.7%) patients were currently undergoing systemic therapy while surveyed. The mean of PCS and MCS was 38.9 (standard deviation: 11.6) and 45.3 (standard deviation: 10.7), respectively.

3.2. Risk factors for lower PCS and MCS

We assessed the association between patient characteristics and PCS (Table 1) or MCS (Table 2) scores which were categorised into tertiles. In multivariate analysis, Hispanic ethnicity, low education level, presence of comorbidity were all significantly associated with poorer PCS and MCS. Specially, individuals reporting Hispanic ethnicity had a 1.69-fold (odds ratio [OR] 95% confidence interval [95% CI], 1.69 [1.26–2.26]; $P < 0.001$) increased risk of lower PCS and a 1.66-fold (1.66 [1.24–2.23]; $P < 0.001$) increased risk of lower MCS than did non-Hispanic whites. Patients with college degree or above were more likely to have higher PCS (0.59 [0.42–0.83]; $P < 0.001$) and MCS (0.71 [0.51–0.98]; $P = 0.04$) than were patients with less than high school attainment. Patients with comorbidities were more likely to have lower PCS (1.39 [1.17–1.65]; $P < 0.001$) and MCS (1.22 [1.03–1.44]; $P = 0.02$) than were patients with no comorbidities.

Smoking, alcohol use, tumour stage and time since diagnosis were significantly associated with PCS. Specially, current smokers carried a 1.59-fold (1.59 [1.23–2.06]; $P < 0.001$) increased risk of lower PCS than did never-smokers. Current alcohol drinkers were more likely to have higher PCS (0.46 [0.38–0.55]; $P < 0.001$) than were patients who never consumed alcohol. Patients diagnosed with stage III (1.80 [1.10–2.94]; $P = 0.02$) and stage IV (2.32 [1.50–3.59]; $P < 0.001$) were more likely to have lower PCS than were patients diagnosed with stage I (P for trend < 0.001). Compared to patients diagnosed within one month, those diagnosed from one to three months carried an increased risk of low PCS (1.27 [1.07–1.52]; $P = 0.007$).

Sex and age at diagnosis were significantly associated with MCS. Specially, female patients had a significantly elevated risk of lower MCS than did male patients (1.37 [1.16–1.64]; $P <$

0.001). Patients aged from 65 to 74 years (0.66 [0.47–0.93]; $P = 0.02$) and 75 years and over (0.56 [0.37–0.84]; $P = 0.005$) carried reduced risk of lower MCS. Our study also showed a trend for improved PCS and MCS by years of diagnosis (all ORs < 1.0, P for trend $_{PCS} = 0.03$; P for trend $_{MCS} = 0.02$) in univariate analysis. However, the association was not statistically significant in multivariate analysis. Similar results were found across different race/ethnicity strata (Supplemental Tables 1 and 2).

3.3. Association of PCS and MCS with survival

The median follow-up time was 60.2 months (95% CI: 52.5–64.1 months). The median survival time for all patients was 12.5 months (95% CI: 12.0–13.0 months). The overall 1-year and 5-year relative survival rates for all patients were 52.1% and 8.1%, respectively.

Differences in the overall survival by PCS or MCS scores are shown in Table 3, Figs. 1 and 2. We found that patients with low-PCS and medium-PCS had a significantly reduced survival rate than did patients in the high-PCS group (log-rank $P < 0.001$; Fig. 1A). After adjustment for sex, age, marital status, race, education level, occupation, smoking, alcohol use, tumour size, cancer stage, comorbidity, treatment before survey, time since diagnosis and years of diagnosis, patients in the low-PCS (hazard ratio [95% CI], 1.94 [1.72–2.18]; $P < 0.001$) and medium-PCS (1.37 [1.22–1.53]; $P < 0.001$) groups had significantly increased risk of death than did patients in the high-PCS group. Similarly, patients in the low-MCS and medium-MCS groups had significantly reduced survival rate (log-rank $P < 0.001$; Fig. 2A) and carried a 1.42-fold (1.42 [1.26–1.59]; $P < 0.001$) and a 1.26-fold (1.26 [1.12–1.41]; $P < 0.001$) increased risk of dying than did patients in the high-MCS group. To assess any possible bias stemming from the effects of missing disease stage, we repeated the analysis for the 1013 patients with stage information available, and we observed similar results (Figs. 1B and 2B). When further stratified by stage, this effect of PCS on overall survival was consistent between early- and late-stage patients (Fig. 1C and D). However, no significant association of MCS with survival was found in stage I, II PDAC (Fig. 2C). We also repeated the analysis stratified by race/ethnicity and treatment before survey history, the impact of lower PCS and MCS on survival was consistent for non-Hispanic whites as compared with African-Americans/Hispanics/others and patients without treatment before survey comparing to those with treatment before survey (Supplemental Figures 1, 2, 3, and 4).

4. Discussion

In this study, we evaluated the association of QOL after diagnosis with survival and explored the determinants of QOL in PDAC patients. Two main findings were obtained. First, QOL after diagnosis was a significant prognostic factor for overall survival. Second, multiple sociodemographic and clinical factors affected QOL. To the best of our knowledge, this is the first study using the SF-12v1 questionnaire to probe the prognostic value and the determinants of QOL in a large cohort of racially/ ethnically diverse patients with PDAC.

Consistent with results from previous studies [5–13], our study demonstrated that better QOL was significantly associated with longer survival time in patients with PDAC. Furthermore, this effect on survival was consistent across different racial/ethnic groups. The mechanism by which QOL affects survival is not completely understood. The first possible

mechanism is related to elevated inflammatory activation. Elevated inflammatory activation is observed in patients who have poor QOL [20,21] and also has been found in PDAC patients with poor survival [22,23]. Therefore, dysregulation of some pro-inflammatory cytokines, such as tumour necrosis factor-α (TNF-α) and interleukin-6 (IL-6) may explain the relationship between QOL and survival in PDAC patients. The second possible mechanism is associated with the patient's stress [24]. A review of studies of animal models and humans indicated chronic stress and depression impair the immune response and may promote the initiation and progression of some types of cancer [25]. In addition, another animal study also shows under chronic stress, dopamine (DA) levels in brain are lower as a consequence of decreased release of DA [26], which has been demonstrated to inhibit tumour growth via the activation of dopamine receptor D2 (DRD2) [27]. Therefore, poor QOL with weaken immune responses and low level of DA may contribute to tumour progression and ultimately influence PDAC patients' overall survival. The third possible mechanism is related to the patient's physical ability to tolerate treatment. A clinical trial demonstrated that a lower physical well-being score was related to worse response to treatment and shorter survival duration in patients with lung cancer [28]. In addition, QOL could influence the treatment decision-making for PDAC patients [16]. Interestingly, we found no significant prognostic value of low MCS for stage I, II PDAC. Although we have adjusted many potential confounding factors and performed stratified analysis by cancer stage, race/ethnicity, and treatment before survey to minimise the impact from these factors, we could not exclude the possibility of residual confounding from unmeasured common factors. Further studies need to explore the underlying mechanisms. Our findings suggest QOL measures may provide clinicians with helpful information on the monitoring and treatment of PDAC patients.

Our study also identified multiple determinants of physical and mental QOL and most of these determinants similarly influenced QOL across the different racial/ethnic groups. We found Hispanic patients had lower mean PCS and MCS scores than non-Hispanic whites. Previous studies also indicated Hispanic cancer patients experience lower QOL [29]. Socioeconomic status (SES) appears to be the main reason for this disparity. SES has been shown to be related to race/ethnicity. More minority than white residents of the United States are in low SES categories [30]. Low SES can influence access to medical care and is related to higher rates of comorbidities and later disease stage at diagnosis in minority populations [30,31]. Our findings suggest that Hispanic PDAC patients are at increased risk of lower QOL and appropriate supportive interventions should be formulated for this group of patients.

We found women and younger patients were more likely to report poor mental QOL than were men and elderly patients, which suggests sex and age should be considered in clinical practice. One recent study showed sex is an important predictive factor for QOL and women with cancer had poorer QOL than men [32]. One possible reason is that somatic symptoms influence quality of life more deleteriously among women than men [33]. One recent study showed that some QOL components (social functioning and financial problems) improve with age, whereas other components (physical functioning and constipation) deteriorate with age in cancer patients [34]. Interestingly, our study showed elderly patients had better mental

QOL than younger patients. This may be due to older adults having more adaptive experience of severe illness [35] and bearing less of a financial burden [34].

Our results showed tumour stage is an independent factor that predicts physical QOL in PDAC patients. This finding was consistent with the results from one recent study of pancreatic cancer [36]. Advanced tumours tend to infiltrate the retroperitoneal nerve plexus, bile duct, stomach, and duodenum, causing abdominal and mid-back pain, obstructive jaundice, vomiting, mal-digestion, and cachexia [37]. All of these symptoms negatively affect the QOL of PDAC patients. This study indicates clinicians should focus on interventions to alleviate the symptom burden of advanced PDAC patients.

A notable finding of our study is that the time period of one to three months from diagnosis was a risk factor of low PCS. Longitudinal assessment of QOL during diagnosis and treatment of PC is of great interest. Previous studies on surgery showed that pancreatectomy had a short-term negative impact on patient's QOL within 3 months [38–40], whereas QOL recovered from surgery after 6 months [15,39,40]. Several studies among patients on chemotherapy reported an improvement of QOL after chemotherapy compared with baseline [11,41,42]. Specifically, a previous study found that QOL improved at the end of treatment (6 months) among patients on the FOLFIRINOX chemotherapy regimen [11]. In another study among patients treated by gemcitabine or gemcitabine combined with capecitabine, an improvement in mood and coping effort was noted in both groups within 2–5 months after starting treatment [41]. In a third study, global QOL was significantly improved after receiving fluorouracil combined with mitomycin for 6 months [42]. Two studies also found that the improvement in QOL of cognitive function within 3 months [9] and physical function at 2 months [12] predicted improved survival. Another concern of researchers during the longitudinal assessment of QOL is response shift of cancer patients. Cancer patients are faced with the necessity to adapt to their illness. Response shift is an important mediator of this adaption, which involves the change of internal standards, values and conceptualisation of QOL [43]. Integrating response shift into QOL assessment allows researchers to better understand the longitudinal change of QOL in cancer patients, which requires more extensive research.

The 5-year survival of PC patients has improved over the past several decades, from 3.0% in 1975 to 8.5% now [44]. Our study showed a trend of increasing PCS and MCS from 1999 to 2012, which we hypothesised was representative of the advancement in the treatment and medical care of PDAC. Given the potential positive impact of favourable QOL on improving survival of PDAC patients and understanding the determinants of QOL, we can expect further improvement of survival of PDAC by targeting the determinants of QOL in the future.

A major strength of our study is the large, diverse PDAC patient population. Our findings can be generalised to both non-Hispanic whites and other racial/ethnic groups. Second, patients with localised (I, II) disease were included, whereas other studies only focused on patients with metastatic or advanced stage [6,9–12]. Third, the SF-12v1 questionnaire is easy and reliable to use in routine clinical practice [45] and can assess physical and mental QOL separately. The main limitation to our study is that tumour stage information was

missing for 1465 of the 2478 patients, however, our sensitivity analysis showed similar results when limiting the analysis to patients with tumour stage information. In addition, education and occupation were used as indicators of social class, but information on other social class indicators (e.g. family income) was not available. Finally, we did not perform the longitudinal assessment of QOL and could not investigate whether changes in QOL during treatment could predict survival of patients with PC.

In summary, this study highlighted that QOL after diagnosis is an independent prognostic indicator for PDAC. QOL measurement could help clinicians identify subpopulations of PDAC patients who are at risk of poor survival, which may be helpful in monitoring patients or formulating interventions. We also identified multiple sociodemographic and clinical factors that can influence the QOL of PDAC patients. Clinicians could use these factors to tailor individualised interventions aimed at improving QOL and survival in PDAC patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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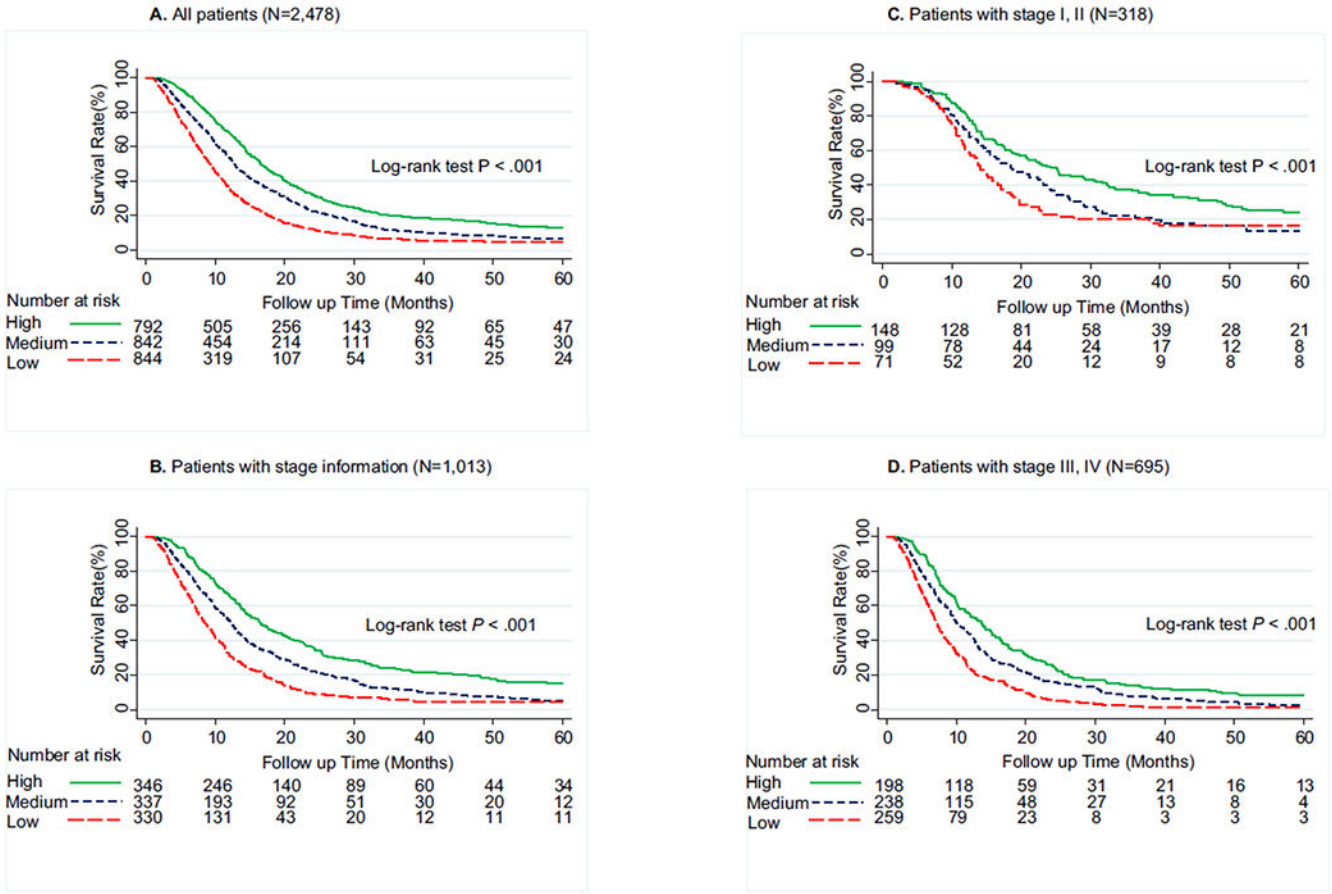

Fig. 1.

Five-year survival of pancreatic ductal adenocarcinoma cancer patients by Physical Component Summary (PCS) scores categorised into tertiles. (A) Overall population (N = 2478), (B) patients with available tumour stage information (N = 1013), (C) patients with stage I & II (N = 318), (D) patients with stage III & IV (N = 695). Higher PCS scores indicate better physical quality of life. High, ≥45.7; medium, 32.7–45.7; low, <32.7.

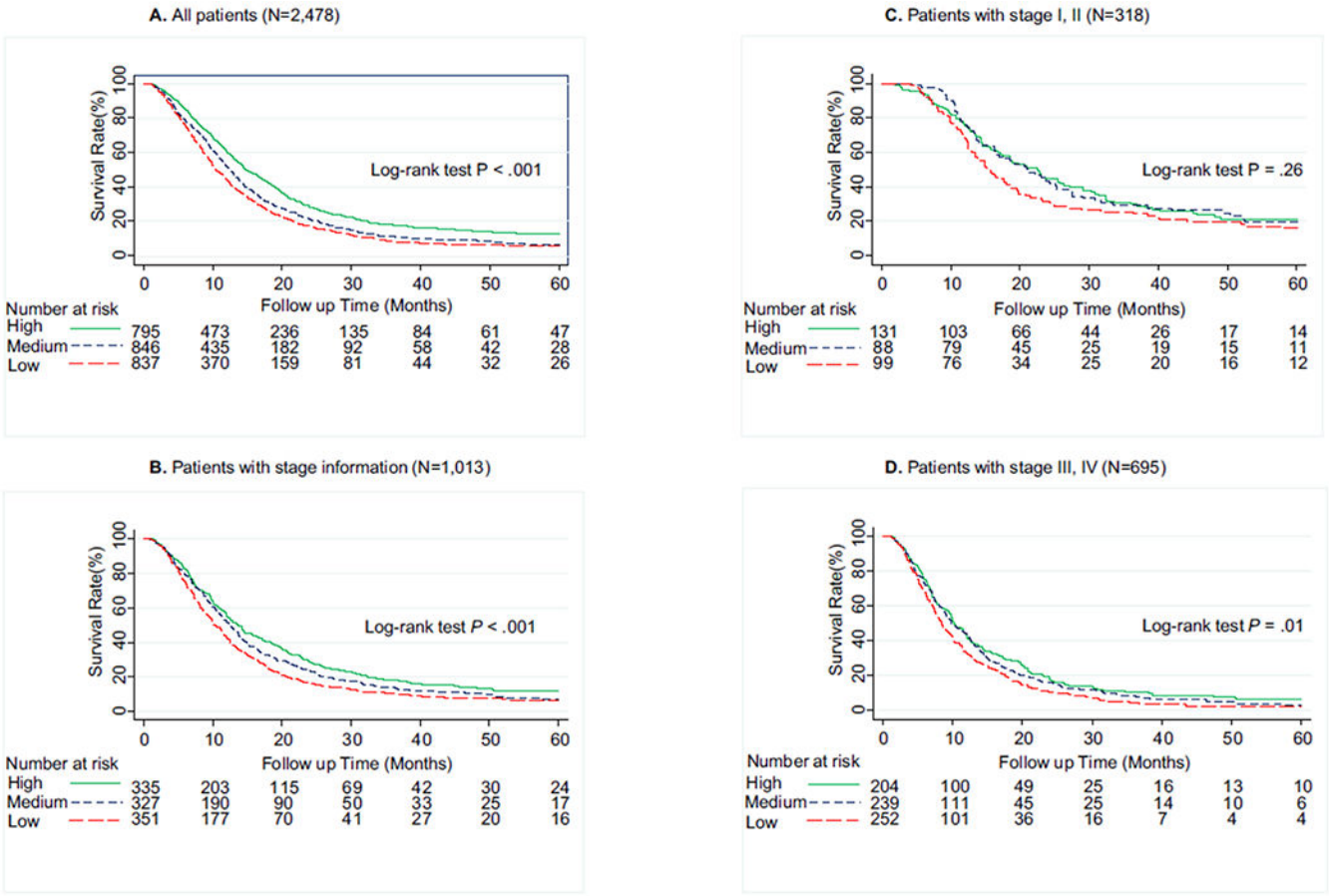

Fig. 2.

Five-year survival of pancreatic ductal adenocarcinoma cancer patients by Mental Component Summary (MCS) scores categorised into tertiles. (A) Overall population (N = 2478), (B) patients with available tumour stage information (N = 1013), (C) patients with stage I & II (N = 318), (D) patients with stage III & IV (N = 695). Higher MCS scores indicate better mental quality of life. High, ≥52.3; medium, 40.3–52.3; low, <40.3.

Table 1

Association of patient characteristics with lower PCS score.

Characteristic	N (%)[a]	PCS score			Unadjusted	*P* value	Adjusted[b]	*P* value
		≥45.7	32.7–45.7	<32.7	OR (95% CI)		OR (95% CI)	
Sex								
Male	1,489 (60.1)	498	517	474	1.00 (Ref)		1.00 (Ref)	
Female	989 (39.9)	294	325	370	1.23 (1.06–1.43)	0.005	1.10 (0.93–1.30)	0.29
Age at diagnosis, yrs								
18–44	162 (6.5)	45	56	61	1.00 (Ref)		1.00 (Ref)	
45–54	534 (21.5)	165	197	172	0.82 (0.60–1.14)	0.24	0.83 (0.59–1.17)	0.29
55–64	888 (35.8)	306	303	279	0.75 (0.55–1.02)	0.06	0.76 (0.54–1.05)	0.10
65–74	651 (26.3)	207	214	230	0.87 (0.63–1.19)	0.38	0.91 (0.65–1.29)	0.60
≥75	243 (9.8)	69	72	102	1.10 (0.76–1.59)	0.61	1.06 (0.71–1.60)	0.77
***P* for trend**						0.29		0.35
Marital status								
Married	1952 (78.8)	640	684	628	1.00 (Ref)		1.00 (Ref)	
Never married	203 (8.2)	61	66	76	1.20 (0.92–1.57)	0.18	1.10 (0.83–1.46)	0.50
Divorced	138 (5.6)	44	38	56	1.25 (0.90–1.73)	0.18	1.11 (0.79–1.56)	0.55
Widowed	167 (6.7)	42	51	74	1.58 (1.18–2.13)	0.002	1.10 (0.79–1.54)	0.58
Others	18 (0.7)	5	3	10	2.09 (0.83–5.29)	0.12	2.91 (1.13–7.51)	0.03
Race								
Non-Hispanic whites	1966 (79.3)	678	655	633	1.00 (Ref)		1.00 (Ref)	
African-Americans	166 (6.7)	34	54	78	1.94 (1.44–2.61)	<0.001	1.33 (0.97–1.83)	0.07
Hispanics	186 (7.5)	34	72	80	1.81 (1.38–2.39)	<0.001	1.69 (1.26–2.26)	<0.001
Others	160 (6.5)	46	61	53	1.16 (0.87–1.55)	0.32	1.01 (0.74–1.39)	0.93
Education								
< High school	171 (6.9)	29	55	87	1.00 (Ref)		1.00 (Ref)	
High school/vocational	681 (27.5)	190	199	292	0.65 (0.47–0.89)	0.008	0.80 (0.57–1.12)	0.19
≥ College degree	1508 (60.9)	540	545	423	0.38 (0.28–0.52)	<0.001	0.59 (0.42–0.83)	<0.001
Unknown	118 (4.8)	33	43	42	0.54 (0.35–0.84)	0.006	0.69 (0.43–1.10)	0.12
***P* for trend**						<0.001		<0.001

Characteristic	N (%)[a]	PCS score			Unadjusted	*P* value	Adjusted[b]	*P* value
		≥45.7	32.7–45.7	<32.7	OR (95% CI)		OR (95% CI)	
Occupation								
White collar	914 (36.9)	307	339	268	1.00 (Ref)		1(reference)	
Blue collar	311 (12.6)	81	114	116	1.41 (1.12–1.78)	0.004	1.12 (0.86–1.45)	0.40
Others	164 (6.6)	55	56	53	1.07 (0.79–1.45)	0.67	0.83 (0.60–1.15)	0.26
Unknown	1089 (43.9)	349	333	407	1.24 (1.06–1.46)	0.008	1.10 (0.92–1.31)	0.30
Smoking status								
Never	1122 (45.6)	373	382	367	1.00 (Ref)		1.00 (Ref)	
Former	1056 (42.9)	345	367	344	1.01 (0.87–1.18)	0.90	1.07 (0.91–1.26)	0.43
Current	282 (11.5)	72	83	127	1.60 (1.25–2.04)	<0.001	1.59 (1.23–2.06)	<0.001
***P* for trend**						0.004		0.003
Alcohol use								
Never	1030 (41.8)	275	329	426	1.00 (Ref)		1.00 (Ref)	
Former	671 (27.3)	171	248	252	0.93 (0.78–1.11)	0.44	0.93 (0.77–1.13)	0.47
Current	761 (30.9)	344	255	162	0.41 (0.34–0.49)	<0.001	0.46 (0.38–0.55)	<0.001
***P* for trend**						<0.001		<0.001
Tumour size								
0–20 mm	105 (4.2)	44	35	26	1.00 (Ref)		1.00 (Ref)	
21–30 mm	233 (9.4)	94	81	58	1.04 (0.68–1.60)	0.85	1.20 (0.77–1.88)	0.42
>30 mm	526 (21.2)	173	174	179	1.52 (1.03–2.24)	0.04	1.40 (0.92–2.13)	0.11
Unknown	1614 (65.1)	481	552	581	1.70 (1.18–2.45)	0.004	1.49 (0.99–2.25)	0.06
***P* for trend**						<0.001		0.04
AJCC cancer stage								
I	97 (3.9)	45	33	19	1.00 (Ref)		1.00 (Ref)	
II	221 (8.9)	103	66	52	1.07 (0.69–1.67)	0.77	1.08 (0.68–1.72)	0.75
III	162 (6.5)	58	54	50	1.64 (1.03–2.62)	0.04	1.80 (1.10–2.94)	0.02
IV	533 (21.5)	140	184	209	2.47 (1.65–3.69)	<0.001	2.32 (1.50–3.59)	<0.001
Unknown	1465 (59.1)	446	505	514	2.05 (1.40–3.00)	<0.001	1.72 (1.12–2.65)	0.01
***P* for trend**						<0.001		<0.001
Metastatic site(s)								
1	239 (44.8)	64	76	99	1.00 (Ref)			

Characteristic	N (%)[a]	PCS score			Unadjusted	*P* value	Adjusted[b]	*P* value
		≥45.7	32.7–45.7	<32.7	OR (95% CI)		OR (95% CI)	
≥2	294 (55.2)	76	108	110	0.92 (0.67–1.26)	0.61	0.89 (0.64–1.25)	0.52
Comorbidity								
No	721 (29.1)	268	255	198	1.00 (Ref)		1.00 (Ref)	
Yes	1757 (70.9)	524	587	646	1.46 (1.24–1.71)	<0.001	1.39 (1.17–1.65)	<0.001
Heart disease								
No	2003 (80.8)	666	679	658	1.00 (Ref)		1.00 (Ref)	
Yes	475 (19.2)	126	163	186	1.30 (1.06–1.60)	0.002	1.30 (1.06–1.60)	0.01
Lung disease								
No	2281 (92.1)	751	783	747	1.00 (Ref)		1.00 (Ref)	
Yes	197 (7.9)	41	59	97	1.95 (1.48–2.57)	<0.001	1.86 (1.39–2.48)	<0.001
Diabetes								
No	1825 (73.6)	635	625	565	1.00 (Ref)		1.00 (Ref)	
Yes	653 (26.4)	157	217	279	1.67 (1.42–1.97)	<0.001	1.43 (1.19–1.72)	<0.001
Hypertension								
No	1343 (54.2)	470	449	424	1.00 (Ref)		1.00 (Ref)	
Yes	1135 (45.8)	322	393	420	1.31 (1.14–1.52)	<0.001	1.11 (0.92–1.34)	0.27
Liver disease								
No	2343 (94.6)	759	796	788	1.00 (Ref)		1.00 (Ref)	
Yes	135 (5.4)	33	46	56	1.43 (1.04–1.97)	0.03	1.06 (0.76–1.49)	0.72
Renal disease								
No	2210 (89.0)	729	756	725	1.00 (Ref)		1.00 (Ref)	
Yes	268 (10.8)	63	86	119	1.62 (1.28–2.06)	<0.001	1.48 (1.14–1.91)	<0.001
Infectious disease								
No	2439 (98.4)	786	829	824	1.00 (Ref)		1.00 (Ref)	
Yes	39 (1.6)	6	13	20	2.19 (1.21–3.97)	0.01	1.85 (0.99–3.43)	0.05
Stroke								
No	2397 (96.7)	786	812	799	1.00 (Ref)		1.00 (Ref)	
Yes	81 (3.3)	6	30	45	2.89 (1.90–4.39)	<0.001	2.57 (1.65–3.99)	<0.001
Digestive tract bleeding								
No	2420 (97.7)	780	825	815	1.00 (Ref)		1.00 (Ref)	

Characteristic	N (%)[a]	PCS score			Unadjusted	*P* value	Adjusted[b]	*P* value
		≥45.7	32.7–45.7	<32.7	OR (95% CI)		OR (95% CI)	
Yes	58 (2.3)	12	17	29	1.93 (1.17–3.16)	0.01	1.55 (0.93–2.60)	0.09
Seizure								
No	2449 (98.8)	786	835	828	1.00 (Ref)		1.00 (Ref)	
Yes	29 (1.2)	6	7	16	2.24 (1.09–4.57)	0.03	1.83 (0.87–3.83)	0.11
Time since diagnosis[c]								
< 1 month	1174 (47.4)	429	375	370	1.00 (Ref)		1.00 (Ref)	
1–3 months	890 (35.9)	226	326	338	1.49 (1.27–1.74)	<0.001	1.27 (1.07–1.52)	0.007
3–6 months	218 (8.8)	64	72	82	1.36 (1.04–1.77)	0.03	1.10 (0.79–1.52)	0.58
≥ 6 months	196 (7.9)	73	69	54	0.90 (0.68–1.19)	0.47	0.83 (0.59–1.16)	0.28
***P* for trend**						0.17		0.99
Years of diagnosis								
1999–2001	218 (8.8)	59	79	80	1.00 (Ref)		1.00 (Ref)	
2002–2004	355 (14.3)	109	110	136	0.96 (0.71–1.31)	0.81	0.97 (0.70–1.34)	0.86
2005–2007	632 (25.5)	204	215	213	0.83 (0.63–1.10)	0.20	0.87 (0.64–1.17)	0.35
2008–2010	820 (33.1)	269	275	276	0.82 (0.63–1.08)	0.16	0.89 (0.66–1.18)	0.41
2011–2012	453 (18.3)	151	163	139	0.76 (0.57–1.02)	0.07	0.87 (0.64–1.20)	0.40
***P* for trend**						0.03		0.34

Abbreviations: AJCC, American Joint Committee on Cancer; CI, confidence interval; OR, odds ratio; PCS, Physical Component Summary.

[a]Missing values not included: smoking status (N = 18); alcohol status (N = 16), percentages may not add up to 100% due to rounding.

[b]Adjusted for sex, age, marital status, race, education level, occupation, smoking, alcohol use, tumour size, cancer stage, comorbidity, treatment before survey, time since diagnosis and years of diagnosis if appropriate.

[c]The interval between initial diagnosis and quality-of-life survey.

Table 2

Association of patient characteristics with lower MCS score.

Characteristic	N (%)[a]	MCS score			Unadjusted	*P* value	Adjusted[b]	*P* value
		≥52.3	40.3–52.3	<40.3	OR (95% CI)		OR (95% CI)	
Sex								
Male	1489 (60.1)	517	512	460	1.00 (Ref)		1.00 (Ref)	
Female	989 (39.9)	278	334	377	1.37 (1.18–1.59)	<0.001	1.37 (1.16–1.64)	<0.001
Age at diagnosis, yrs								
18–44	162 (6.5)	42	59	61	1.00 (Ref)		1.00 (Ref)	
45–54	534 (21.5)	168	179	187	0.83 (0.61–1.15)	0.27	0.81 (0.58–1.13)	0.21
55–64	888 (35.8)	257	332	299	0.85 (0.63–1.16)	0.31	0.82 (0.59–1.13)	0.23
65–74	651 (26.3)	232	208	211	0.71 (0.52–0.98)	0.04	0.66 (0.47–0.93)	0.02
≥75	243 (9.8)	96	68	79	0.65 (0.45–0.94)	0.02	0.56 (0.37–0.84)	0.005
***P* for trend**						0.006		0.001
Marital status								
Married	1952 (78.8)	637	691	624	1.00 (Ref)		1.00 (Ref)	
Never married	203 (8.2)	62	65	76	1.19 (0.91–1.56)	0.20	1.03 (0.78–1.36)	0.82
Divorced	138 (5.6)	40	36	62	1.49 (1.07–2.07)	0.02	1.37 (0.97–1.92)	0.07
Widowed	167 (6.7)	52	48	67	1.26 (0.93–1.69)	0.13	1.11 (0.79–1.54)	0.55
Others	18 (0.7)	4	6	8	1.69 (0.71–3.99)	0.24	1.81 (0.75–4.39)	0.19
Race								
Non-Hispanic whites	1966 (79.3)	656	670	640	1.00 (Ref)		1.00 (Ref)	
African-Americans	166 (6.7)	43	52	71	1.51 (1.12–2.02)	0.007	1.24 (0.91–1.68)	0.18
Hispanics	186 (7.5)	40	62	84	1.75 (1.32–2.31)	<0.001	1.66 (1.24–2.23)	<0.001
Others	160 (6.5)	56	62	42	0.84 (0.63–1.13)	0.24	0.82 (0.60–1.12)	0.22
Education								
< High school	171 (6.9)	43	47	81	1.00 (Ref)		1.00 (Ref)	
High school/vocational	681 (27.5)	205	218	258	0.70 (0.51–0.97)	0.03	0.81 (0.58–1.13)	0.22
≥ College degree	1508 (60.9)	509	545	454	0.54 (0.40–0.73)	<0.001	0.71 (0.51–0.98)	0.04
Unknown	118 (4.8)	38	36	44	0.66 (0.43–1.03)	0.07	0.79 (0.50–1.26)	0.32
***P* for trend**						<0.001		0.06

Characteristic	N (%)[a]	MCS score			Unadjusted	*P* value	Adjusted[b]	*P* value
		≥52.3	40.3–52.3	<40.3	OR (95% CI)		OR (95% CI)	
Occupation								
White collar	914 (36.9)	302	321	291	1.00 (Ref)		1.00 (Ref)	
Blue collar	311 (12.6)	95	103	113	1.17 (0.93–1.49)	0.19	1.07 (0.83–1.39)	0.58
Others	164 (6.6)	56	52	56	1.03 (0.76–1.40)	0.86	0.89 (0.64–1.24)	0.50
Unknown	1089 (43.9)	342	370	377	1.11 (0.94–1.30)	0.22	1.07 (0.90–1.27)	0.47
Smoking status								
Never	1122 (45.6)	368	398	356	1.00 (Ref)		1.00 (Ref)	
Former	1056 (42.9)	331	372	353	1.07 (0.92–1.25)	0.37	1.09 (0.92–1.28)	0.33
Current	282 (11.5)	90	70	122	1.35 (1.05–1.73)	0.02	1.15 (0.89–1.49)	0.29
***P* for trend**						0.03		0.21
Alcohol use								
Never	1030 (41.8)	326	357	347	1.00 (Ref)		1.00 (Ref)	
Former	671 (27.3)	177	216	278	1.35 (1.13–1.62)	0.001	1.44 (1.18–1.75)	<0.001
Current	761 (30.9)	288	265	208	0.75 (0.63–0.89)	0.001	0.84 (0.70–1.01)	0.07
***P* for trend**						0.005		0.08
Tumour size								
0–20 mm	105 (4.2)	34	34	37	1.00 (Ref)		1.00 (Ref)	
21–30 mm	233 (9.4)	82	80	71	0.84 (0.55–1.29)	0.43	0.92 (0.60–1.43)	0.71
>30 mm	526 (21.2)	165	182	179	0.99 (0.68–1.46)	0.98	1.02 (0.68–1.54)	0.92
Unknown	1614 (65.1)	514	550	550	0.99 (0.68–1.42)	0.94	1.06 (0.71–1.59)	0.77
***P* for trend**						0.53		0.45
AJCC cancer stage								
I	97 (3.9)	36	29	32	1.00 (Ref)		1.00 (Ref)	
II	221 (8.9)	95	59	67	0.81 (0.52–1.27)	0.36	0.80 (0.50–1.27)	0.34
III	162 (6.5)	45	52	65	1.46 (0.92–2.34)	0.11	1.57 (0.96–2.55)	0.07
IV	533 (21.5)	159	187	187	1.24 (0.83–1.86)	0.30	1.16 (0.75–1.78)	0.51
Unknown	1465 (59.1)	460	519	486	1.15 (0.78–1.68)	0.49	1.22 (0.80–1.87)	0.36
***P* for trend**						0.16		0.07
Metastatic site(s)								
1	239 (44.8)	70	83	86	1.00 (Ref)		1.00 (Ref)	

Characteristic	N (%)[a]	MCS score			Unadjusted	*P* value	Adjusted[b]	*P* value
		≥52.3	40.3–52.3	<40.3	OR (95% CI)		OR (95% CI)	
≥2	294 (55.2)	89	104	101	0.94 (0.69–1.29)	0.71	0.98 (0.70–1.36)	0.90
Comorbidity								
No	721 (29.1)	240	262	219	1.00 (Ref)		1.00 (Ref)	
Yes	1757 (70.9)	555	584	618	1.16 (0.99–1.36)	0.07	1.22 (1.03–1.44)	0.02
Heart disease								
No	2003 (80.8)	646	706	651	1.00 (Ref)		1.00 (Ref)	
Yes	475 (19.2)	149	140	186	1.19 (0.99–1.44)	0.06	1.37 (1.11–1.68)	0.003
Lung disease								
No	2281 (92.1)	737	782	762	1.00 (Ref)		1.00 (Ref)	
Yes	197 (7.9)	58	64	75	1.19 (0.91–1.56)	0.21	1.15 (0.87–1.53)	0.31
Diabetes								
No	1825 (73.6)	584	630	611	1.00 (Ref)		1.00 (Ref)	
Yes	653 (26.4)	211	216	226	1.02 (0.86–1.20)	0.82	0.92 (0.77–1.11)	0.40
Hypertension								
No	1343 (54.2)	432	477	434	1.00 (Ref)		1.00 (Ref)	
Yes	1135 (45.8)	363	369	403	1.08 (0.93–1.25)	0.30	1.01 (0.84–1.21)	0.95
Liver disease								
No	2343 (94.6)	762	802	779	1.00 (Ref)		1.00 (Ref)	
Yes	135 (5.4)	33	44	58	1.50 (1.09–2.08)	0.01	1.32 (0.94–1.84)	0.11
Renal disease								
No	2210 (89.0)	710	755	745	1.00 (Ref)		1.00 (Ref)	
Yes	268 (10.8)	85	91	92	1.02 (0.81–1.29)	0.84	1.04 (0.81–1.33)	0.78
Infectious disease								
No	2439 (98.4)	787	835	817	1.00 (Ref)		1.00 (Ref)	
Yes	39 (1.6)	8	11	20	2.02 (1.10–3.69)	0.02	1.75 (0.94–3.25)	0.08
Stroke								
No	2397 (96.7)	775	817	805	1.00 (Ref)		1.00 (Ref)	
Yes	81 (3.3)	20	29	32	1.35 (0.90–2.03)	0.14	1.30 (0.85–1.98)	0.22
Digestive tract bleeding								
No	2420 (97.7)	779	825	816	1.00 (Ref)		1.00 (Ref)	

Characteristic	N (%)[a]	MCS score			Unadjusted	*P* value	Adjusted[b]	*P* value
		≥52.3	40.3–52.3	<40.3	OR (95% CI)		OR (95% CI)	
Yes	58 (2.3)	16	21	21	1.17 (0.73–1.88)	0.52	1.07 (0.66–1.76)	0.77
Seizure								
No	2449 (98.8)	787	835	827	1.00 (Ref)		1.00 (Ref)	
Yes	29 (1.2)	8	11	10	1.12 (0.58–2.18)	0.73	0.98 (0.50–1.93)	0.96
Time since diagnosis[c]								
< 1 month	1174 (47.4)	356	432	386	1.00 (Ref)		1.00 (Ref)	
1–3 months	890 (35.9)	289	276	325	1.04 (0.88–1.22)	0.65	0.99 (0.83–1.18)	0.92
3–6 months	218 (8.8)	83	66	69	0.81 (0.62–1.06)	0.13	0.92 (0.66–1.28)	0.61
≥ 6 months	196 (7.9)	67	72	57	0.84 (0.64–1.11)	0.23	1.05 (0.75–1.46)	0.77
***P* for trend**						0.14		0.94
Years of diagnosis								
1999–2001	218 (8.8)	57	73	88	1.00 (Ref)		1.00 (Ref)	
2002–2004	355 (14.3)	111	132	112	0.73 (0.53–0.99)	0.04	0.72 (0.52–0.99)	0.05
2005–2007	632 (25.5)	204	195	233	0.80 (0.61–1.07)	0.14	0.88 (0.65–1.19)	0.41
2008–2010	820 (33.1)	267	288	265	0.72 (0.55–0.95)	0.02	0.78 (0.59–1.05)	0.10
2011–2012	453 (18.3)	156	158	139	0.66 (0.49–0.90)	0.007	0.75 (0.55–1.03)	0.08
***P* for trend**						0.02		0.24

Abbreviations: AJCC, American Joint Committee on Cancer; CI, confidence interval; MCS, Mental Component Summary; OR, odds ratio.

[a]Missing values not included: smoking status (N = 18); alcohol status (N = 16), percentages may not add up to 100% due to rounding.

[b]Adjusted for sex, age, marital status, race, education level, occupation, smoking, alcohol use, tumour size, cancer stage, comorbidity, treatment before survey, time since diagnosis and years of diagnosis if appropriate.

[c]The interval between initial diagnosis and quality-of-life survey.

Table 3

Association of PCS/MCS score with five-year survival.

SF-12 score	Dead (N)	Alive (N)	HR (95% CI)[a]	*P* value	MST (month)	Log rank *P*
All patients						
PCS						
≥45.7	562	230	1.00 (Ref)		16.6	
32.7–45.7	685	157	1.37 (1.22–1.53)	<0.001	12.7	
<32.7	694	150	1.94 (1.72–2.18)	<0.001	9.2	<0.001
P for trend			1.39 (1.31–1.48)	<0.001		
MCS						
≥52.3	594	201	1.00 (Ref)		14.8	
40.3–52.3	664	182	1.26 (1.12–1.41)	<0.001	12.4	
<40.3	683	154	1.42 (1.26–1.59)	<0.001	10.4	<0.001
P for trend			1.19 (1.12–1.26)	<0.001		
Patients with stage						
PCS						
≥45.7	282	64	1.00 (Ref)		16.6	
32.7–45.7	305	32	1.32 (1.12–1.57)	0.001	12.5	
<32.7	311	19	2.05 (1.71–2.45)	<0.001	8.5	<0.001
P for trend			1.43 (1.31–1.57)	<0.001		
MCS						
≥52.3	282	53	1.00 (Ref)		13.7	
40.3–52.3	295	32	1.10 (0.92–1.30)	0.30	12.6	
<40.3	321	30	1.40 (1.19–1.66)	<0.001	10.4	<0.001
P for trend			1.19 (1.09–1.29)	<0.001		
Stage (I, II)						
PCS						
≥45.7	107	41	1.00 (Ref)		24.3	
32.7–45.7	82	17	1.56 (1.14–2.12)	0.005	18.6	
<32.7	62	9	1.78 (1.27–2.51)	<0.001	14.0	<0.001
P for trend			1.35 (1.15–1.60)	<0.001		

SF-12 score	Dead (N)	Alive (N)	HR (95% CI)[a]	*P* value	MST (month)	Log rank *P*
MCS						
≥52.3	98	33	1.00 (Ref)		22.6	
40.3–52.3	70	18	0.94 (0.67–1.32)	0.72	21.1	
<40.3	83	16	1.39 (1.00–1.92)	0.049	15.5	0.26
P for trend			1.18 (1.00–1.40)	0.05		
Stage (III, IV)						
PCS						
≥45.7	175	23	1.00 (Ref)		13.7	
32.7–45.7	223	15	1.28 (1.04–1.58)	0.02	10.0	
<32.7	249	10	2.15 (1.72–2.69)	<0.001	7.2	<0.001
P for trend			1.47 (1.32–1.65)	<0.001		
MCS						
≥52.3	184	20	1.00 (Ref)		10.1	
40.3–52.3	225	14	1.14 (0.93–1.40)	0.22	9.9	
<40.3	238	14	1.44 (1.18–1.77)	<0.001	8.4	0.01
P for trend			1.20 (1.09–1.33)	<0.001		
Whites						
PCS						
≥45.7	490	188			16.6	
32.7–45.7	531	124	1.38 (1.21–1.56)	<0.001	12.9	
<32.7	527	106	2.00 (1.75–2.29)	<0.001	9.2	<0.001
P for trend			1.41 (1.32–1.51)	<0.001		
MCS						
≥52.3	496	160			15.1	
40.3–52.3	535	135	1.25 (1.10–1.41)	<0.001	12.8	
<40.3	517	123	1.42 (1.25–1.61)	<0.001	10.3	<0.001
P for trend			1.19 (1.12–1.27)	<0.001		
African-Americans						
PCS						
≥45.7	25	9	1.00 (Ref)		14.4	
32.7–45.7	45	9	2.02 (1.06–3.86)	0.03	12.4	

SF-12 score	Dead (N)	Alive (N)	HR (95% CI)[a]	*P* value	MST (month)	Log rank *P*
<32.7	65	13	3.08 (1.63–5.79)	<0.001	7.9	0.01
P for trend			1.71 (1.27–2.31)	<0.001		
MCS						
≥52.3	35	8	1.00 (Ref)		10.0	
40.3–52.3	41	11	0.80 (0.43–1.49)	0.48	10.2	
<40.3	59	12	1.25 (0.70–2.23)	0.45	8.6	0.45
P for trend			1.15 (0.86–1.55)	0.34		
Hispanics						
PCS						
≥45.7	20	14			17.6	
32.7–45.7	63	9	1.18 (0.65–2.17)	0.58	11.8	
<32.7	66	14	1.77 (0.96–3.26)	0.07	9.3	0.003
P for trend			1.37 (1.03–1.83)	0.03		
MCS						
≥52.3	27	13			13.2	
40.3–52.3	50	12	1.24 (0.70–2.21)	0.46	11.0	
< 40.3	72	12	1.27 (0.72–2.23)	0.41	11.3	0.17
P for trend			1.10 (0.85–1.44)	0.47		
African-American/Hispanics/others						
PCS						
≥45.7	72	42			17.1	
32.7–45.7	154	33	1.47 (1.07–2.03)	0.02	12.4	
<32.7	167	44	2.00 (1.45–2.76)	<0.001	9.4	<0.001
P for trend			1.41 (1.20–1.64)	<0.001		
MCS						
≥52.3	98	41			13.7	
40.3–52.3	129	47	1.27 (0.93–1.72)	0.13	11.0	
<40.3	166	31	1.45 (1.08–1.94)	0.01	11.1	0.007
P for trend			1.20 (1.04–1.38)	0.02		
No treatment before survey						
PCS						

SF-12 score	Dead (N)	Alive (N)	HR (95% CI)[a]	*P* value	MST (month)	Log rank *P*
≥45.7	464	167	1.00 (Ref)		15.7	
32.7–45.7	516	102	1.35 (1.18–1.53)	<0.001	11.6	
<32.7	547	105	1.93 (1.69–2.21)	<0.001	8.3	<0.001
P for trend			1.39 (1.30–1.49)	<0.001		
MCS						
≥52.3	453	130	1.00 (Ref)		13.0	
40.3–52.3	523	131	1.19 (1.04–1.35)	<0.001	11.6	
<40.3	551	113	1.34 (1.18–1.53)	<0.001	9.9	<0.001
P for trend			1.16 (1.09–1.23)	<0.001		
Treatment before survey						
PCS						
≥45.7	98	63	1.00 (Ref)		19.8	
32.7–45.7	169	55	1.53 (1.17–2.00)	0.002	17.0	
<32.7	147	45	2.16 (1.64–2.85)	<0.001	12.7	<0.001
P for trend			1.47 (1.28–1.68)	<0.001		
MCS						
≥52.3	141	71	1.00 (Ref)		19.3	
40.3–52.3	141	51	1.63 (1.26–2.11)	<0.001	15.1	
< 40.3	132	41	1.91 (1.46–2.51)	<0.001	13.5	<0.001
P for trend			1.39 (1.21–1.58)	<0.001		

Abbreviations: CI, confidence interval; HR, hazard ratio; MST, medium survival time; MCS, Mental Component Summary; PCS, Physical Component Summary.

[a]Adjusted for sex, age, marital status, race, education level, occupation, smoking, alcohol use, tumour size, cancer stage, comorbidity, treatment before survey, time since diagnosis and years of diagnosis.