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Survival improvement in patients with pancreatic cancer by decade: A period analysis of the SEER database, 1981–2010

Huanhuan Sun[1]*, Haiqing Ma[1]*, Guobin Hong[2]*, Hongliu Sun[3] & Jin Wang[4]

[1]Department of Oncology, The Fifth Affiliated Hospital of Sun Yat-sen University, Zhuhai, Guangdong 519000, China, [2]Department of Radiology, The Fifth Affiliated Hospital of Sun Yat-sen University, Zhuhai, Guangdong 519000, China, [3]Department of Pathology, University of Toledo Medical Center, Toledo, OH 43614, United States, [4]Department of Translational Molecular Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX 77030, United States.

Correspondence and requests for materials should be addressed to H.M. (haiqing_ma@163.com) or J.W. (JWang4@mdanderson.org)

* These authors contributed equally to this work.

Pancreatic cancer (PaCa) is an aggressive malignancy with a high mortality rate and a poor prognosis. To evaluate treatment outcomes of patients with pancreatic cancer over the past three decades, data from the Surveillance, Epidemiology, and End Results (SEER) registries were used to assess the survival of patients with PaCa. A total of 63,530 patients diagnosed with pancreatic cancer between 1981 and 2010 were identified from nine original SEER registries. The 1-year relative survival rates (RSRs) improved each decade, from 17.0% to 19.9% to 28.2% ($p < 0.0001$), with a larger increase during the third decade than during the second decade. However, the long-term survival rates have remained very low. The 5-year RSRs increased from 3.1% to 4.4% to 6.9% over these three decades—i.e., still only few patients with PaCa survive more than 5 years. Furthermore, our analysis demonstrated that the survival rates for all the patients with pancreatic cancer were lower in patients of lower socioeconomic status and black race. These results will help predict future trends in PaCa incidence and survival, contribute to better-designed clinical trials by eliminating disparities that may affect the results, and thereby improve the clinical management and outcomes of PaCa.

Pancreatic cancer (PaCa) is one of the major causes of cancer-related deaths worldwide, ranking fourth among causes of cancer-related deaths in both sexes in 2014, and is estimated to become the second-leading cause of cancer death in the United States by 2020[1]. The overall 5-year relative survival rate for PaCa is approximately 6%, and the median survival time is only 3–6 months[2]. Thus, there is an urgent need to not only understand the molecular mechanisms underlying this disease but also analyze data from clinical PaCa, which could aid in improving the clinical management of PaCa and therapeutic outcomes for PaCa patients[3].

The American Cancer Society estimates that a total of 46,420 new PaCa cases were diagnosed and that about 39,590 deaths from PaCa occurred in the United States in 2014, although PaCa accounts for only 2.8% of all new cancer cases in the United States[1]. Moreover, although survival has notably improved over the past several decades for most cancers, the survival associated with PaCa has shown very little improvement. Although previous studies have investigated PaCa outcomes, they tend to evaluate subgroups of patients who come from certain areas[4] or who have received surgery or other treatment[5–7] or to focus on the effects of race, socioeconomic status (SES), or marital status on survival[4,8–10].

To date, three population-based survival datasets on PaCa survival are available, for PaCa patients diagnosed between 1977 and 2001[11], between 1994 and 2000[12], and between 1988 and 2002[13]; these are scant data on survival in PaCa over a longer period and do not include the most recent decade. And recently, the issue of significant racial and SES disparities in US health care has been increasingly emphasized because of increasing evidence of these disparities in various aspects of the US health care system. Therefore, the present study used period analysis to examine changes in 10-year relative survival rates for patients with PaCa diagnosed between 1981 and 2010 and to analyze the potential impacts of age, sex, race, and SES on relative survival rates using the latest data from the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute.

Results

Trends in PaCa incidence at the nine original SEER sites over three decades. We identified 63,530 patients who were diagnosed with PaCa between 1981 and 2010 in the SEER program of the National Cancer Institute at the nine original registry sites. As shown in Fig. 1 and Suppl. Table S1, the incidence of PaCa during 1991–2000 was lower (8.6 per 100,000) than that during 1981–1990 (9.7 per 100,000). The PaCa incidence per 100,000 decreased substantially in the subgroup of patients over 80 years of age, from 69.0 in 1981–1990 to 55.1 in 1991–2000 to 52.2 in 2001–2010 (Suppl. Table S1, Fig. 1[a]). The incidence in 2001–2010 was relatively stable (8.8 per 100,000). However, the number of PaCa cases continually increased in all subgroups over time with the increase in the size of the general population (Suppl. Table S1, Fig. 1[b]). Males showed a substantially higher incidence of PaCa per 100,000 than did females (11.3 vs. 8.4 in 1981–1990, 9.7 vs. 7.6 in 1991–2000, and 9.8 vs. 7.9 in 2001–2010; Suppl. Table S1, Fig. 1[c]).

PaCa occurrence by SES and by race. The medium-poverty group showed a slightly higher incidence of PaCa than the low-poverty group, and the high-poverty group showed the lowest PaCa incidence. PaCa incidences per 100,000 in all SES subgroups were lower in the second decade than in the first decade (from 9.5 to 8.5 in the low-poverty group, from 9.9 to 8.8 in the medium-poverty group, and from 9.2 to 7.4 in the high-poverty group). In the third decade, the PaCa incidences in the low- and medium-poverty groups were similar to those in the second decade with a slight increase; however, the PaCa incidence decreased in the high-poverty group (by 6.5 per 100,000; Suppl. Table S1, Fig. 1[d]). As illustrated in Suppl. Table S1 and Fig. 1[e], Blacks had a higher PaCa incidence during the three

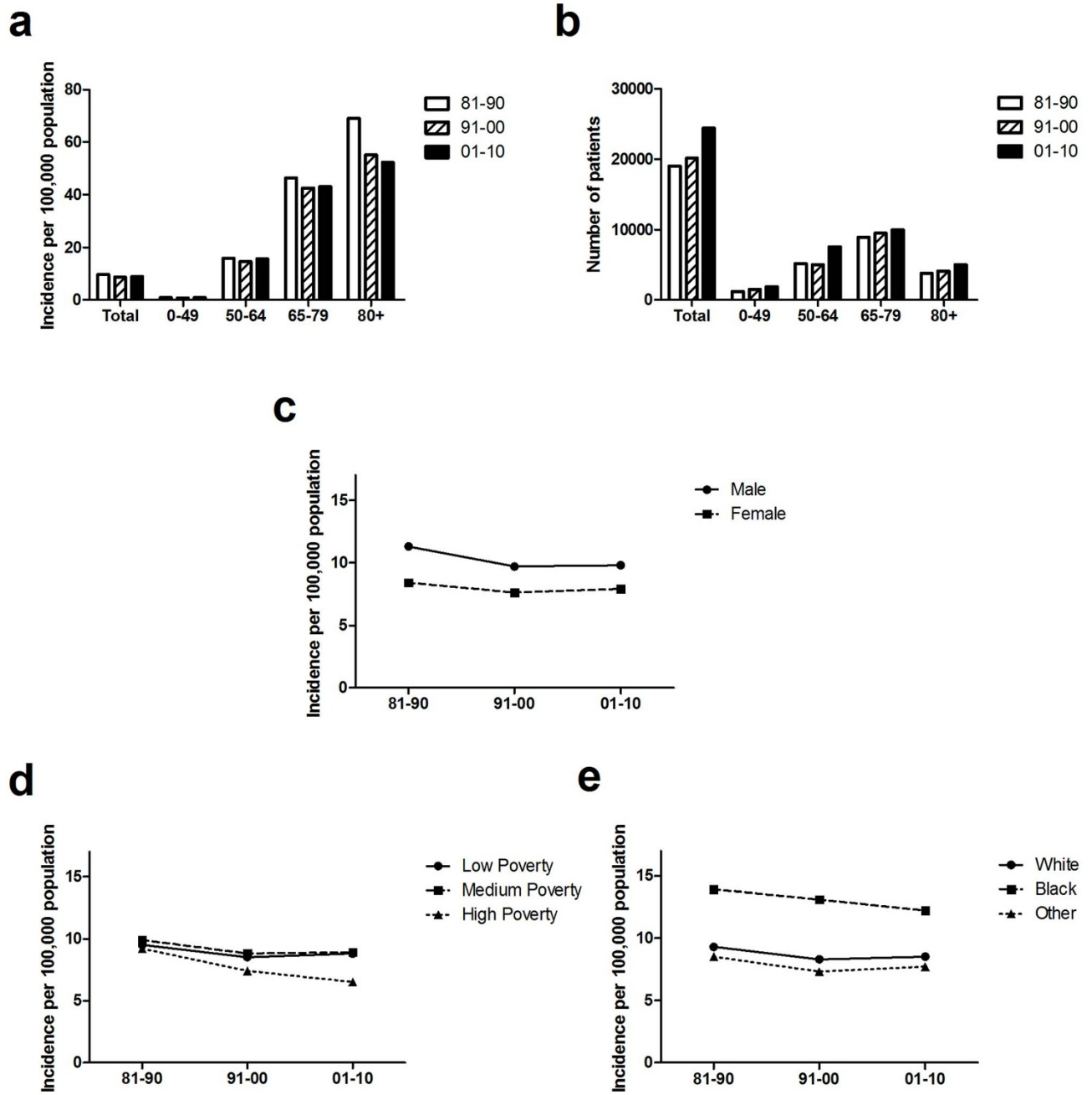

Figure 1 | Summary incidences of patients diagnosed with PaCa between 1981 and 2010 at the original nine SEER sites. Incidence (a) and number (b) of PaCa cases are shown by age group (total and ages 0–49, 50–64, 65–79, and 80+ years) and calendar period. Incidence (c, d, e) of PaCa cases are grouped by sex, SES, and race, respectively.

Table 1 | Relative survival rates of PaCa patients during the periods 1981–1990, 1991–2000, and 2001–2010 at nine SEER sites. Data are means ± standard error of the mean, with number of patients in parentheses

	Decade		
Age Group	1981–1990	1991–2000	2001–2010
6-mo RSR			
All	34.7 ± 0.4 (19024)	38.7 ± 0.3 (20101)***	47.7 ± 0.3 (24405)***
0–49	49.3 ± 1.5 (1176)	56.5 ± 1.3 (1484)**	66.4 ± 1.1 (1884)***
50–64	42.0 ± 0.7 (5128)	45.9 ± 0.7 (5006)***	56.0 ± 0.6 (7555)***
65–79	33.2 ± 0.5 (8931)	37.7 ± 0.5 (9498)***	46.7 ± 0.5 (9946)***
80+	23.4 ± 0.7 (3789)	25.3 ± 0.7 (4113)	30.1 ± 0.7 (5020)***
12-mo RSR			
All	17.0 ± 0.3	19.9 ± 0.3***	28.2 ± 0.3***
0–49	28.8 ± 1.3	34.8 ± 1.2**	44.0 ± 1.2***
50–64	21.4 ± 0.6	24.3 ± 0.6**	34.7 ± 0.6***
65–79	15.5 ± 0.4	18.7 ± 0.4***	26.3 ± 0.5***
80+	11.0 ± 0.5	11.9 ± 0.5	15.7 ± 0.5***
18-mo RSR			
All	9.7 ± 0.2	12.9 ± 0.2***	18.9 ± 0.3***
0–49	19.4 ± 1.2	24.6 ± 1.1*	34.2 ± 1.1***
50–64	12.1 ± 0.5	16.1 ± 0.5***	23.4 ± 0.5***
65–79	8.5 ± 0.3	11.6 ± 0.3***	17.3 ± 0.4***
80+	6.5 ± 0.4	7.6 ± 0.5	9.5 ± 0.5*
24-mo RSR			
All	6.7 ± 0.2	9.4 ± 0.2***	14.0 ± 0.2***
0–49	15.0 ± 1.0	20.6 ± 1.1**	27.0 ± 1.1***
50–64	8.4 ± 0.4	12.0 ± 0.5***	17.1 ± 0.5***
65–79	5.5 ± 0.3	8.0 ± 0.3***	12.5 ± 0.4***
80+	4.3 ± 0.4	5.1 ± 0.4	7.0 ± 0.4**
36-mo RSR			
All	4.5 ± 0.2	6.2 ± 0.2***	9.6 ± 0.2***
0–49	11.9 ± 1.0	16.1 ± 1.0*	20.9 ± 1.0**
50–64	5.5 ± 0.3	7.9 ± 0.4***	11.7 ± 0.4***
65–79	3.5 ± 0.2	5.0 ± 0.2***	8.3 ± 0.3***
80+	3.0 ± 0.3	3.2 ± 0.3	4.4 ± 0.4
48-mo RSR			
All	3.6 ± 0.1	5.1 ± 0.2***	7.8 ± 0.2***
0–49	9.9 ± 0.9	13.8 ± 0.9*	18.0 ± 1.0*
50–64	4.3 ± 0.3	6.3 ± 0.4***	9.3 ± 0.4***
65–79	2.7 ± 0.2	3.9 ± 0.2***	6.6 ± 0.3***
80+	2.6 ± 0.3	2.8 ± 0.3	3.6 ± 0.4
60-mo RSR			
All	3.1 ± 0.1	4.4 ± 0.2***	6.9 ± 0.2***
0–49	9.2 ± 0.9	12.7 ± 0.9*	16.5 ± 1.0*
50–64	3.7 ± 0.3	5.5 ± 0.3***	8.0 ± 0.4***
65–79	2.2 ± 0.2	3.4 ± 0.2***	5.8 ± 0.3***
80+	2.3 ± 0.3	2.3 ± 0.3	3.3 ± 0.4
120-mo RSR			
All	2.0 ± 0.1	3.2 ± 0.1***	4.9 ± 0.3***
0–49	6.2 ± 0.7	9.1 ± 0.8*	13.5 ± 1.1*
50–64	2.4 ± 0.2	3.9 ± 0.3***	5.8 ± 0.5*
65–79	1.4 ± 0.2	2.4 ± 0.2**	3.6 ± 0.4*
80+	1.3 ± 0.4	1.7 ± 0.4	2.0 ± 08

Abbreviations: mo, month; RSR, relative survival rate; SEM, standard error of the mean.
*$p < 0.01$, **$p < 0.001$, and ***$p < 0.0001$ for comparisons with the preceding decade.

decades than Whites and people of other races. However, this incidence gap between Blacks and the other groups started to shrink between the second and third decades.

Relative survival estimates for the nine SEER sites over three decades. The median survival of patients with PaCa remained less than 1 year, however, it improved each decade from 4 months to 5 months to 7 months. Relative survival rates (Table 1 and Fig. 2[a]) and survival times improved over the course of the three decades for patients with PaCa in each of the age groups analyzed. The 1-year relative survival rate during 1991–2000 was higher than that during 1981–1990 (19.9% vs. 17.7%, $p < 0.0001$), and the 1-year relative survival rate during 2001–2010 was even higher (28.2% vs. 19.9%, $p < 0.0001$). The 1-year survival rate in the third decade was 42% higher than that of the second decade, which was substantially larger than the 17% increase from the first decade to the second decade. This trend of increases in survival over time was noted with a follow-up of up to 5 years. Kaplan-Meier survival analysis also showed incremental increases in survival time over the three decades for all age groups (Fig. 2[b]). But the long-term survival rates are still very low; the 5-year RSRs increased from 3.1% to 4.4% to 6.9% over these three decades—i.e., still only few patients with PaCa survive more than 5 years (decades ago and today).

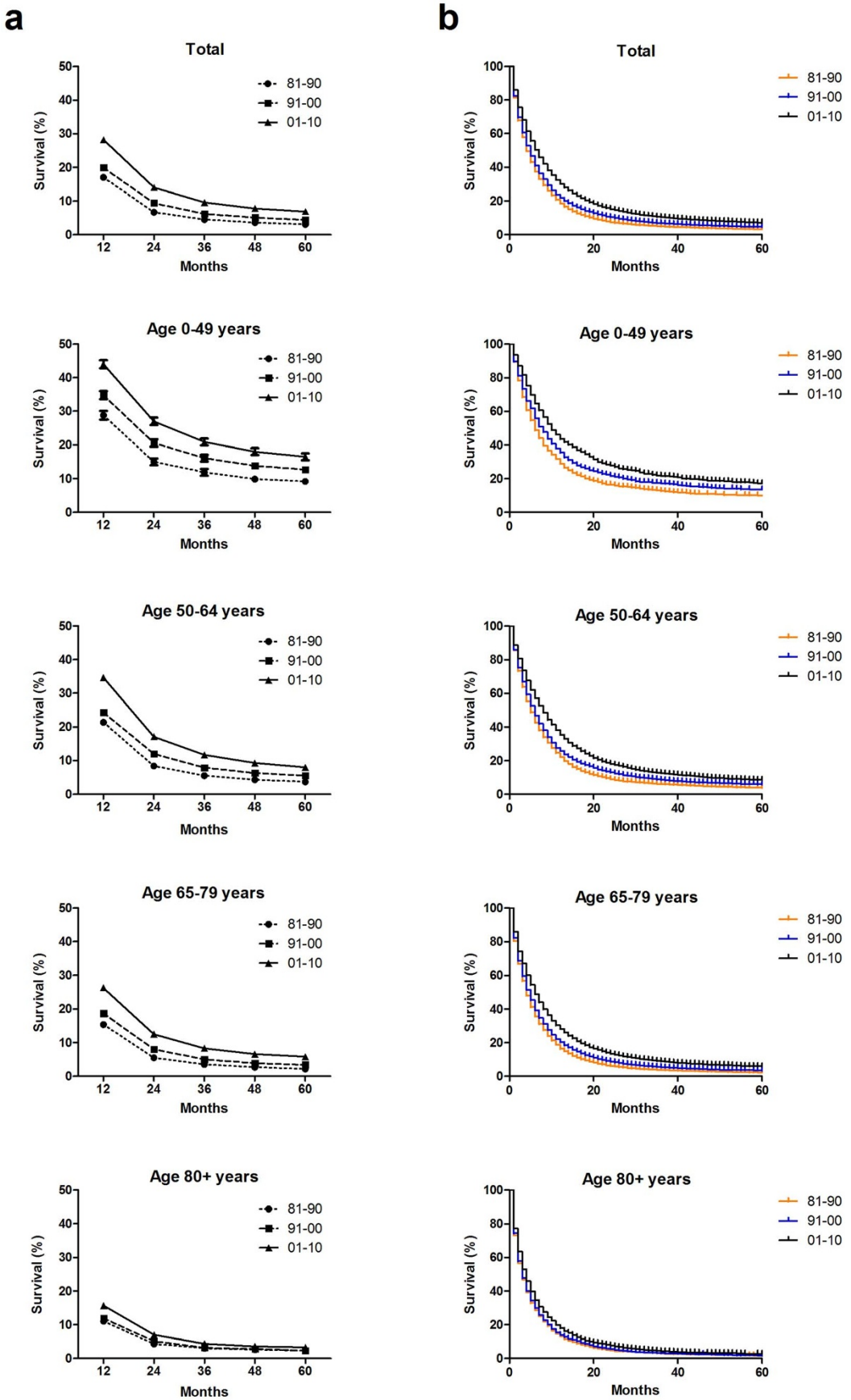

Figure 2 | **Trends in 10-year relative survival rates (a) and Kaplan-Meier survival analysis (b) for patients with PaCa at nine SEER sites between 1981 and 2010 according to age group (total and ages 0–49, 50–64, 65–79, and 80+ years) and calendar period.**

Table 2 | Six-month relative survival rates of PaCa patients according to sex, age group, and calendar period from 1981 to 2010 at nine SEER sites. Data are means ± standard error of the mean, with number of patients in parentheses

		Sex	
Decade	Age Group	Male	Female
81–90	6-mo RSR		
	All	33.9 ± 0.5 (9432)	35.4 ± 0.5 (9592)
	0–49	43.9 ± 1.9 (685)	56.9 ± 2.2 (491)***
	50–64	40.2 ± 0.9 (2986)	44.6 ± 1.1 (2142)*
	65–79	31.9 ± 0.7 (4391)	34.5 ± 0.7 (4540)*
	80+	21.5 ± 1.2 (1370)	24.5 ± 0.9 (2419)
91–00	6-mo RSR		
	All	38.2 ± 0.5 (9811)	39.0 ± 0.5 (10290)
	0–49	50.5 ± 1.7 (898)	65.7 ± 2.0 (586)***
	50–64	43.0 ± 0.9 (2936)	49.9 ± 1.1 (2070)***
	65–79	36.6 ± 0.7 (4577)	38.8 ± 0.7 (4921)
	80+	25.5 ± 1.2 (1400)	25.2 ± 0.9 (2713)
01–10	6-mo RSR		
	All	47.8 ± 0.5 (12232)	47.6 ± 0.5 (12173)
	0–49	62.1 ± 1.5 (1063)	72.1 ± 1.6 (821)***
	50–64	53.3 ± 0.8 (4454)	59.9 ± 0.9 (3101)***
	65–79	46.0 ± 0.7 (4856)	47.2 ± 0.7 (5090)
	80+	30.9 ± 1.1 (1859)	29.6 ± 0.8 (3161)

Abbreviations: mo, month; RSR, relative survival rate; SEM, standard error of the mean.
*$p < 0.01$, **$p < 0.001$, and ***$p < 0.0001$ for comparisons with the Male group.

Both sexes showed improved survival over the three decades (Table 2 and Fig. 3[a]). In 1981–1990, females showed a slightly higher 6-month relative survival rate than males (35.4% vs. 33.9%), but in the next two decades, both sexes showed similar 6-month RSR (39.0% for females vs. 38.2% for males in 1991–2000 and 47.6% for females vs. 47.8% for males in 2001–2010; Table 2). The same trend was also observed in 12-month and 18-month relative survival (Suppl. Table S2 and Suppl. Fig. S1). Kaplan-Meier survival analysis indicated that survival times significantly differed between males and females in 1981–1990 only ($p = 0.0044$), not in 1991–2000 ($p = 0.3497$) or in 2001–2010 ($p = 0.2877$; Suppl. Fig. S2).

In some age groups, a difference in survival rates between the sexes was more apparent (Table 2 and Fig. 3[a]). For patients aged 0–49 years, females showed a significantly higher 6-month relative survival rate than males in each decade (56.9% vs. 43.9% in 1981–1990, 65.7% vs. 50.5% in 1991–2000, 72.1% vs. 62.1% in 2001–2010; $p < 0.0001$ for each). Likewise, for patients aged 50–64 years, females showed a higher 6-month relative survival rate than males in each decade (44.6% vs. 40.2% in 1981–1990, $p < 0.01$; 49.9% vs. 43.0% in 1991–2000, $p < 0.0001$; 59.9% vs. 53.3% in 2001–2010, $p < 0.0001$). However, the difference in survival between females and males in the 50–64 age group was less than that in the 0–49 age group, and the difference was even smaller in the 65–79 age group. For patients over 80 years of age, although females showed a slightly higher 6-month relative survival rate than males in the first decade (24.5% vs. 21.5%), their survival rates became similar in the second decade (25.2% in females vs. 25.5% in males) and even reversed in the third decade (29.6% in females vs. 30.9% in males). A similar decrease in the difference between the sexes with age was shown in 12-month and 18-month RSR (Suppl. Table S2 and Suppl. Fig. S3).

Kaplan-Meier survival analysis for the 2001–2010 period further confirmed the age-dependent difference in survival rates between males and females (Fig. 3[b]). Although no significant survival difference was observed between females and males of all ages during 2001–2010 ($p = 0.2877$), females showed significantly higher survival than males in the groups of patients younger than 64 years of age ($p < 0.0001$) but not in those aged 65–79 years ($p = 0.3025$) or older than 80 years ($p = 0.5987$).

Furthermore, Cox regression analyses of overall survival for the 2001–2010 period revealed that age, race, and SES were significantly associated with overall survival, whereas the variable of sex was not. But after the patients were stratified by age group, sex became an independent predictor of overall survival in patients 0–49 years old and 50–65 years old. Only age was an independent predictor in all stratified age groups (Suppl. Table S3).

PaCa survival by race and by SES. White patients showed a slightly higher 6-month relative survival rate than black patients during 1981–1990 (34.8% vs. 32.2%; Fig. 4[a] and Table 3). This survival advantage in white patients became significant in the second decade (38.9% in white patients vs. 35.7% in black patients; $p < 0.01$) and kept widening in the third decade (48.7% in white patients vs. 41.9% in black patients; $p < 0.0001$). A similar widening over time was observed for 12-month and 18-month survival rates (Suppl. Table S4).

When 6-month, 12-month, and 18-month RSR were analyzed, the low-poverty group consistently showed the highest survival rates, and the high poverty group consistently showed the lowest survival rates (Fig. 4[b], Table 4 and Suppl. Table S5). Despite the fact that all SES groups showed improvements in survival over the course of the three decades, the gaps in survival rates between the three SES groups were significantly wider during the third decade than during the previous decade. For example, the 6-month survival rates in the low-, medium-, and high-poverty groups in 1981–1990 were 36.2%, 32.9%, and 29.8%, respectively, with differences of 3.3% between low- and medium-poverty and 3.1% between medium- and high-poverty; however, these differences increased to 5% and 4.8%, respectively, in 2001–2010 (49.8%, 44.8%, and 40.0% in the low-, medium-, and high-poverty groups, respectively; Table 4). A similar widening of the gaps in survival rates was found in the 12-month and 18-month survival rates (Suppl. Table S5). It is worth noting that the distribution of SES groups differed between races: there were more low-poverty individuals among white patients than among black patients (63.1% vs. 26.0%) and more medium-poverty individuals among black patients than among white patients (73.7% vs. 34.6%; Suppl. Fig. S4, Suppl. Table S6). Indeed, the survival dif-

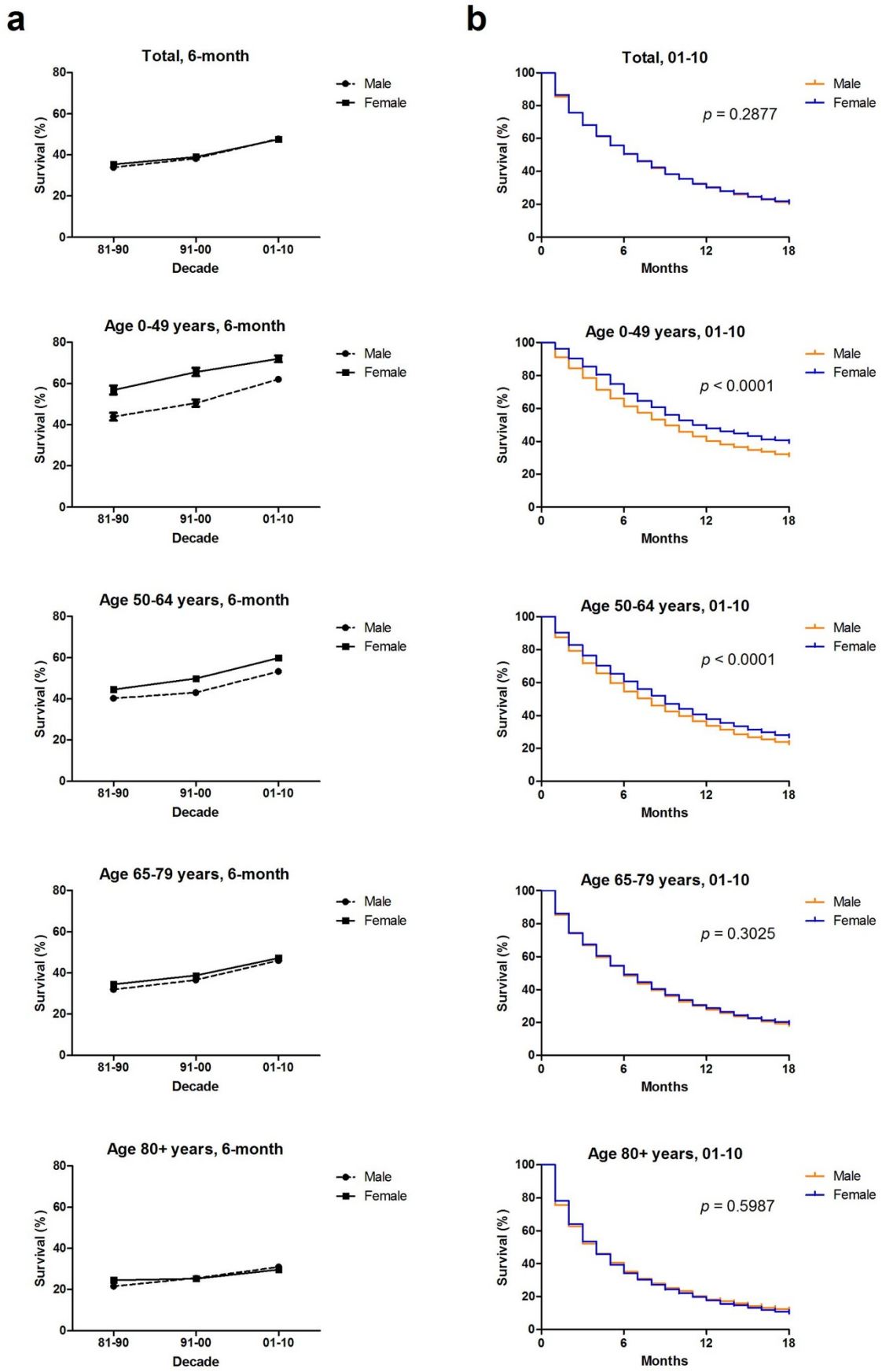

Figure 3 | Six-month relative survival rates from 1981 to 2010 (a) and Kaplan-Meier survival analysis from 2001 to 2010 (b) for patients with PaCa at nine SEER sites according to sex by age group (total and ages 0–49, 50–64, 65–79, and 80+ years).

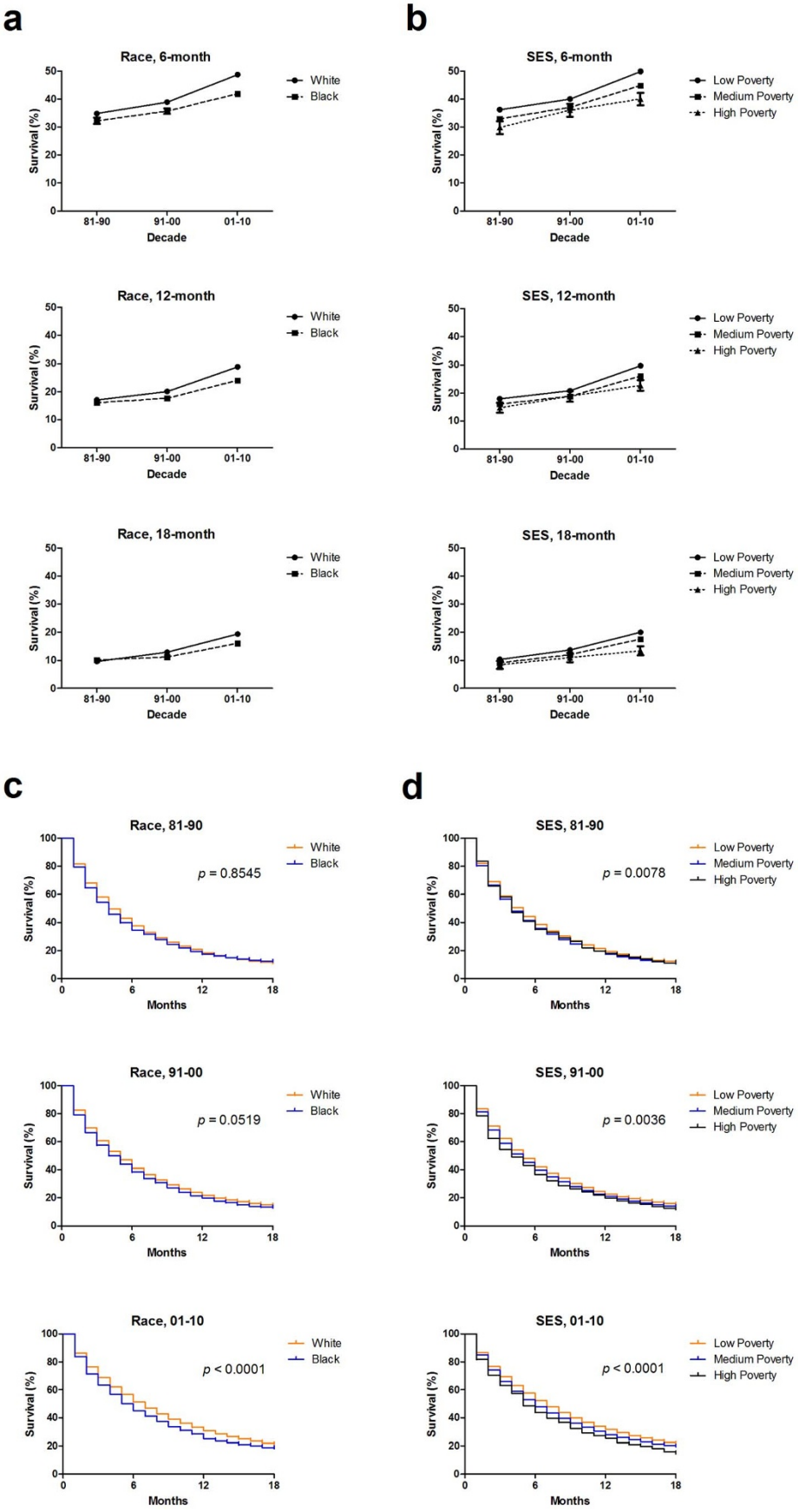

Figure 4 | **Six-month, 12-month, and 18-month relative survival rates according to race (a) and SES/county-level poverty rates (b) and Kaplan-Meier survival analysis according to race (c) and SES/county-level poverty rates (d) for patients with PaCa at nine SEER sites from 1981 to 2010.**

Table 3 | Six-month relative survival rates of PaCa patients according to race, age group, and calendar period from 1981 to 2010 at nine SEER sites. Data are means ± standard error of the mean, with number of patients in parentheses

		Race		
Decade	Age Group	White	Black	Other
81–90	6-mo RSR			
	All	34.8 ± 0.4 (15977)	32.2 ± 1.1 (2029)	37.8 ± 1.5 (1005)
	0–49	48.9 ± 1.7 (893)	50.7 ± 3.6 (192)	50.0 ± 5.3 (88)
	50–64	42.7 ± 0.8 (4118)	36.8 ± 1.8 (712)*	45.9 ± 2.9 (291)
	65–79	33.9 ± 0.6 (7585)	26.5 ± 1.5 (862)***	35.0 ± 2.2 (481)
	80+	23.3 ± 0.8 (3381)	24.9 ± 2.8 (263)	23.0 ± 3.6 (145)
91–00	6-mo RSR			
	All	38.9 ± 0.4 (16311)	35.7 ± 1.0 (2377)*	40.7 ± 1.3 (1394)
	0–49	58.0 ± 1.5 (1102)	48.7 ± 3.1 (263)*	58.3 ± 4.6 (115)
	50–64	46.8 ± 0.8 (3909)	39.3 ± 1.8 (745)**	49.4 ± 2.7 (345)
	65–79	38.1 ± 0.6 (7782)	33.7 ± 1.5 (1021)	39.7 ± 1.9 (688)
	80+	25.6 ± 0.8 (3518)	23.9 ± 2.4 (348)	22.9 ± 2.7 (246)
01–10	6-mo RSR			
	All	48.7 ± 0.4 (19149)	41.9 ± 0.9 (2950)***	46.7 ± 1.1 (2236)
	0–49	67.4 ± 1.3 (1379)	64.1 ± 2.7 (315)	61.7 ± 3.7 (180)
	50–64	57.6 ± 0.7 (5760)	46.9 ± 1.5 (1118)***	56.9 ± 1.9 (654)
	65–79	48.1 ± 0.6 (7889)	38.3 ± 1.5 (1076)***	44.1 ± 1.6 (949)
	80+	30.8 ± 0.7 (4121)	21.9 ± 2.0 (441)***	31.7 ± 2.2 (453)

Abbreviations: mo, month; RSR, relative survival rate; SEM, standard error of the mean.
*$p < 0.01$, **$p < 0.001$, and ***$p < 0.0001$ for comparisons with the White group.

ference between white patients and black patients reflected that of the low- and medium-poverty groups.

Similarly, Kaplan-Meier survival analysis showed that although white and black patients did not significantly differ in survival times in 1981–1990 ($p = 0.8545$), white patients started to show longer survival than black patients in the second decade ($p = 0.0519$), and this gap kept widening in 2001–2010 ($p < 0.0001$; Fig. 4[c]). A similar trend was observed in Kaplan-Meier survival analysis for the three SES groups over the course of the three decades. Higher poverty was always associated with shorter survival, and the survival gaps between the low-, medium-, and high-poverty groups have kept widening, as reflected by an ever-decreasing p value (0.0078 in the first decade, 0.0036 in the second decade, and <0.0001 in the third decade; Fig. 4[d]).

Discussion

To our knowledge, this is the largest SEER-based analysis of the incidence and survival of PaCa in the United States so far. We found that overall PaCa incidence remained relatively stable from the second decade to the third decade and that the median overall survival of patients with PaCa improved each decade, from 4 months to 5 months to 7 months. However, the long-term survival rates have remained very low.

Table 4 | Six-month relative survival rates of PaCa patients according to SES, age group, and calendar period from 1981 to 2010 at nine SEER sites. Data are means ± standard error of the mean, with number of patients in parentheses

		SES		
Decade	Age Group	Low Poverty	Medium Poverty	High Poverty
81–90	6-mo RSR			
	All	36.2 ± 0.5 (10321)	32.9 ± 0.5 (8297)***	29.8 ± 2.3 (404)
	0–49	49.7 ± 2.0 (627)	49.2 ± 2.2 (529)	36.9 ± 11.1 (19)
	50–64	45.0 ± 1.0 (2723)	38.9 ± 1.0 (2307)***	33.2 ± 4.8 (97)
	65–79	35.2 ± 0.7 (4844)	30.9 ± 0.8 (3875)***	29.3 ± 3.2 (212)
	80+	23.2 ± 0.9 (2127)	23.6 ± 1.1 (1586)	25.1 ± 5.2 (76)
91–00	6-mo RSR			
	All	40.0 ± 0.5 (11219)	37.0 ± 0.5 (8452)***	36.0 ± 2.3 (430)
	0–49	58.6 ± 1.7 (818)	54.2 ± 2.0 (635)	48.4 ± 9.0 (31)
	50–64	47.8 ± 1.0 (2787)	43.5 ± 1.1 (2114)*	42.1 ± 4.8 (105)
	65–79	39.3 ± 0.7 (5235)	36.0 ± 0.8 (4055)*	33.2 ± 3.3 (208)
	80+	25.9 ± 0.9 (2379)	24.2 ± 1.1 (1648)	30.6 ± 5.1 (86)
01–10	6-mo RSR			
	All	49.8 ± 0.4 (14695)	44.8 ± 0.5 (9029)***	40.0 ± 2.2 (497)***
	0–49	68.9 ± 1.4 (1171)	62.6 ± 1.9 (682)*	58.1 ± 8.9 (31)
	50–64	58.9 ± 0.7 (4480)	52.3 ± 0.9 (2911)***	43.1 ± 3.9 (163)***
	65–79	48.7 ± 0.7 (5922)	43.9 ± 0.8 (3795)***	39.9 ± 3.3 (227)
	80+	31.3 ± 0.9 (3122)	27.7 ± 1.1 (1821)*	26.1 ± 5.2 (76)

Abbreviations: mo, month; RSR, relative survival rate; SEM, standard error of the mean.
*$p < 0.01$, **$p < 0.001$, and ***$p < 0.0001$ for comparisons with the White group.

We demonstrated that overall PaCa incidence declined by 11.34% from first decade to the second decade (from 9.7 to 8.6 per 100,000) but remained relatively stable through the third decade, at 8.8 per 100,000. Males had a higher incidence of PaCa than females over the 30 years analyzed, whereas the gap in incidence between sexes was declined from 2.9 to 2.1 to 1.9 per 100,000. In addition, Blacks showed a higher PaCa incidence than Whites and other races, and this incidence gap between Blacks and the other groups started to shrink between the second and third decade. Also there are differences in incidence between different SES groups, with highest incidence in medium-poverty group and lowest incidence in high-poverty group, on which racial composition is taken into account to have effect.

Female steroid hormones are hypothesized to play a protective role against PaCa risk, and many epidemiologic studies have already investigated the association of PaCa risk with reproductive and hormone-related factors[14,15]. Poor vitamin D status in Blacks has been reported to contribute to their higher cancer incidence[16–18]. Racial variations in the prevalence of many established risk factors (e.g., cigarette smoking, diabetes, and the familial tendency to develop PaCa) and "speculative" risk factors (e.g., heavy alcohol intake, elevated BMI (body mass index), and low SES) are thought to account for the racial difference in the incidence of PaCa[19]. However, it has also been reported that Whites and Blacks share similar distributions of lifestyle factors such as heavy drinking and smoking[20]. Therefore, further research is needed to determine the extent of contribution of genetics and other factors to the observed differences in PaCa incidence between sexes and races.

Although the median survival of patients with PaCa improved each decade, the long-term survival rates are still very low. We found that the 1-year RSR for patients with PaCa improved each decade from 1981 to 2010, from 17.0% to 19.9% to 28.2%, with an increase of 42% from the second decade to the third decade, which may be due to accelerated improvements in the treatment of PaCa in the past decade. However, the 5-year RSRs increased from 3.1% to 4.4% to only 6.9% over these three decades, i.e., still only few patients with PaCa survive more than 5 years after resection. The prognosis of PaCa is still very poor, although the survival rates have been incrementally improving over time.

We observed an improving survival rate over time in both sexes. Although females seemed to have a slightly higher 6-month survival rate than males in 1981–1990 (35.4% vs. 33.9%), the difference was not statistically significant. However, interestingly, when patients were classified by age, females had significantly higher survival rates than males in each decade in younger age groups, especially for the groups of patients aged 0–49 and 50–54 years, and the difference was most pronounced in the youngest group. A similar trend in survival rates between the sexes was observed for 12-month and 18-month RSR and was further confirmed by Kaplan-Meier survival analysis. This age-related survival advantage in females together with the lower incidence of PaCa in females than in males supports the hypothesis that female hormones have a protective role in PaCa[14,15]. Indeed, in the late 1980s, some investigators reported an inhibitory effect of estrogen on preneoplastic pancreatic lesions or transplanted pancreatic carcinoma in rat models[21,22].

Our data also showed higher 6-month, 12-month, and 18-month survival rates in Whites than in Blacks. More importantly, this gap kept widening over time, suggesting that this survival difference between races resulted, at least partly, from factors other than genetic differences. Similarly, the low-poverty group showed higher survival, and the survival gaps between the SES groups also widened over time, especially between the second and third decade. When classified by SES, a higher percentage of Whites were categorized as having low poverty, whereas more Blacks were categorized as having medium poverty. This SES distribution disparity between Blacks and Whites may help explain the similar survival differences between races and between SES groups, since higher poverty is believed to prevent patients from accessing medical consultation and treatment and ultimately to lead to worse outcomes[23].

To obtain the most representative information of PaCa in the United States, we included all patients for the first time and without prior malignancy, from infants to the elderly, not only patients with 20 or 50 years of age or older, and excluded those whose PaCa was diagnosed by autopsy or reported only on a death certificate. Thus, the incidence rate we calculated was close to the real fact, and the survival rate was not affected by diseases other than PaCa itself. We did not consider the effects of pathologic type and stage on survival because they were not the main aims of the present study and because the standards for the pathologic types and stages of PaCa have changed over time.

It is important to note that although we used a large sample size from the SEER registries representing diverse populations over three decades to analyze PaCa incidence, survival rates, and trends in these measures, the study was limited by the fact that the data reflected only selected SEER areas and were not applicable to other geographic locations. In addition, if there is any under-registration or misclassification of cases and variation of socioeconomic status within and among counties[24,25], the study might have been affected by such sources of error and bias.

Overall, in this study, our SEER analysis demonstrated a moderate improvement in survival among PaCa patients over the past three decades. However, the relative survival rates of patients with PaCa remained low. Knowing the incidence and survival of PaCa over the past 30 years will not only help predict future trends but also contribute to better-designed clinical trials by eliminating disparities that may affect the results. Looking ahead, studies to gain a better understanding of the mechanisms and regulation of molecular interactions in PaCa should enable the design of novel and effective targeted therapies that together with improved health care accessibility will yield improved survival.

Methods

The SEER program. All data were obtained from the SEER program of the National Cancer Institute in the United States, which has grown through the addition of new sites since 1973. In this study, we obtained PaCa incidence and survival data across the three decades studied only for patients registered at the original nine SEER sites: the states of Connecticut, Iowa, New Mexico, Utah, and Hawaii and the metropolitan areas of Atlanta, Detroit, San Francisco-Oakland, and Seattle-Puget Sound, comprising approximately 10% of the U.S. population. The SEER program registries routinely collect data on patient demographics, primary tumor site, tumor morphology and stage at diagnosis, first course of treatment, and follow-up for vital status. SEER is the only comprehensive source of population-based information in the United States that includes stage of cancer at the time of diagnosis and patient survival data. The population covered by SEER is comparable to the general U.S. population with regard to measures of poverty and education but has a higher proportion of foreign-born persons than the general U.S. population[26].

Categorized PaCa cases over the course of three decades. Patients with PaCa were identified in the SEER registries using the criteria established by the World Health Organization International Classification of Diseases for Oncology. We analyzed PaCa patients diagnosed between 1981 and 2010. Data obtained included the incidence of PaCa and the relative survival rates for patients diagnosed with PaCa for the periods from 1981 to 1990, from 1991 to 2000, and from 2001 to 2010. Cases of PaCa that was diagnosed by autopsy or reported only on a death certificate were excluded. Cases were stratified by sex, SES, race (White, Black, and Other), and age at diagnosis (0–49 years, 50–64 years, 65–79 years, and 80+ years). Area SES was determined by the county poverty rate[24,25], which was defined as the percentage of people in the county living below the national poverty threshold in the 2000 U.S. Census. The county poverty rates were categorized into three levels using the same cut points used in the National Cancer Institute monograph[27]: $<$10% (low-poverty areas), 10%–19.99% (medium-poverty areas), and $\geq$20% (high-poverty areas). For incidence and survival rate calculations, the SEER program recoded detailed race information into four major categories: White, Black, Other (American Indian/Alaska Native, Asian/Pacific islander), and Unknown. Patients whose race or county-level poverty rate was defined as "unknown" or "blank" were excluded during the stratification analysis.

Incidence and survival data analysis. Incidence rates were expressed per 100,000 people, and age was adjusted to the 2000 U.S. standard population. Cancer patient

survival was typically measured from the date of diagnosis to the date of death. Period analysis methodology was applied to calculate the relative survival rate, which indicates deaths attributable to PaCa either directly or indirectly. The relative survival rate is calculated as the ratio of the absolute survival rate of PaCa patients divided by the expected survival rate for a group of age-, sex-, and race-matched individuals in the general population[28]. This analysis was designed to identify trends in patient outcomes over time. Relative survival point estimates (expressed as percentages), means, and standard errors were calculated in SEER*Stat software (available at seer.cancer.gov/seerstat) according to standard statistical methodology using the Ederer II method[29]. Kaplan-Meier curves were constructed to estimate overall survival, and differences between the curves were assessed using a two-tailed log-rank test. Stata 12.0 software (StataCorp) was used for analyses. A two-tailed p value < 0.01 was considered statistically significant.

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Author contributions

H.H.S., H.Q.M. and J.W. planned the study. H.H.S., H.Q.M., G.B.H. and H.L.S. calculated statistics and analyzed the data. H.H.S., H.Q.M., H.L.S. and J.W. wrote the manuscript. H.Q.M. and J.W. supervised the entire project. All authors reviewed the manuscript.

Additional information

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