

Research Article

Epidemiology of Pancreatic Cancer in Puerto Rico (1987-2010): Incidence, Mortality and Survival

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Abstract

Background & Objective: Pancreatic cancer is an uncommon type of cancer worldwide. Nonetheless, even with early diagnosis, mortality rates are high. This study aims to perform an epidemiologic profile of pancreatic cancer in Puerto Rico (PR) from 1987-2010.

Methods: Using data from the Puerto Rico Central Cancer Registry, age-standardized incidence and mortality rates of pancreatic cancer in PR were compared with Hispanics, non-Hispanic Whites, and non-Hispanic Blacks in the United States of America (USA). Incidence and mortality trends of pancreatic cancer were estimated, and survival analyses were also performed.

Results: In 2005-2010, 5.8 per 100,000 persons were diagnosed with pancreatic cancer in PR and mortality rates were similar. Pancreatic cancer was more frequent in men (6.5 per 100,000 men) than women (5.2 per 100,000 women), and in persons older than 65 years (32.0 per 100,000 persons). Moreover, the median survival for the people diagnosed with pancreatic cancer in PR during 2006-2007 was 4 months and at the end of the third year after diagnosis, only 13% of the patients survived. Incidence trends of pancreatic cancer showed an increase for men (APC=13.0%, $p<0.05$) from 2006 to 2010, but not for women (APC=-0.4, $p>0.05$). However, mortality trends showed a slight decrease for men (APC=-1.0%, $p<0.05$), but not for women (APC=1.4, $p>0.05$) in the period of 1987 to 2010. Meanwhile, Puerto Ricans in comparison to other racial/ethnic groups living in the USA showed a lower risk for being diagnosed and of dying from pancreatic cancer.

Conclusion: Our results highlight the need for additional research in pancreatic cancer, in order to have an impact in disease survival in PR.

Keywords: Incidence; Mortality; Pancreatic cancer; Epidemiology; Puerto Rico

Abbreviations

PR: Puerto Rico; PRCCR: PR Central Cancer Registry; USH: Hispanics; NHW: non-Hispanic Whites; NHB: non-Hispanic Blacks; USA: United States of America; APC: Annual Percent Change; SRR: Standardized Rate Ratios

Introduction

Pancreatic cancer has received limited attention, in comparison to other cancer types, due to its low incidence; however, it is a highly fatal malignancy. Globally, among any type of cancer, pancreatic cancer is placed in the twelfth position for incidence and the eighth for mortality [1]. Pancreatic cancer is more common in developed countries, where 55.0% of cases occur. In the United States of America (USA), it is the fourth most frequent cause of cancer death after lung, breast, prostate, and colorectal cancer [2]. The survival of patients with pancreatic cancer is low, with 6% patients dying within 5 years of diagnosis because of cancer-related complications. It is expected that pancreatic cancer will occupy the second most common cause of cancer-related death in the USA by 2030 [2]. Although the specific reasons for the observed increase in the incidence of this disease are unknown, changes in the prevalence of risk factors associated with the

development of pancreatic cancer could help explain its increment, especially given that effective screening strategies are still unavailable for pancreatic cancer [3].

In Puerto Rico (PR), pancreatic cancer is also a common cause of cancer-related death, being the sixth most common cause of death from cancer among men (3.9% of all deaths) and the fourth most common cause of death from cancer among women (5.3% of all deaths) during 2010 [4]. Pancreatic cancer is one of the leading cancer sites that generate labor productivity loss in Puerto Rico. The productivity loss in the labor market due to pancreatic cancer in Puerto Rico during 2004 was \$1,701,248, which represents 2.65% of total cancer costs [5]. However, despite its public health burden; there are no recent detailed reports of the epidemiology of pancreatic cancer in PR. The aim of this study is to describe the incidence, mortality and survival from pancreatic cancer in PR, and thus, describe the burden of the disease in this population. In addition, comparisons are made with data from other racial/ethnic groups living in the USA. Results from this study can be useful for health education and health promotion, necessary for the creation of prevention programs and public policy that increase the awareness of pancreatic cancer in the Puerto Rican population.

Table 1: Pancreatic cancer cases and deaths diagnosed in PR from 1987-2010.

	Incident Cases N (%)	Deaths N (%)
Sex		
Males	2,509 (52.4)	2,487 (52.3)
Females	2,281 (47.6)	2,270(47.7)
Age		
≤ 64 years	1,446(30.2)	1,284 (27.0)
≥ 65 years	3,342 (69.8)	3,471 (73.0)
Stage*		
Localized	536 (14.8)	--
Regional	608 (16.8)	--
Distant	1,093 (30.2)	--
Unknown	1,385 (38.2)	--
Total	4,790 (100)	4,757 (100)

Data for incidence cases and deaths include known and unknown age.
 *Incident cases obtained from death certificate only were excluded (n=3,622)

Methods

Study design and study subjects

A secondary data analysis was conducted using the database of the PR Central Cancer Registry (PRCCR). This database was used to estimate the incidence, mortality, and survival of diagnosed pancreatic cancer cases (ICD-O-3: C25.0-C25.4, C25.7-C25.9) in PR during the period of 1987-2010. The study population consisted of all individuals residing in PR who were diagnosed with pancreatic cancer throughout the period of 1987-2010.

Statistical analysis

Incidence and mortality rates of pancreatic cancer were analyzed by socio-demographic characteristics, specifically by age, sex and tumor stage. For most of the analysis, we included all diagnosed pancreas cases, including those found by death certificate only (DCO), except for the calculations of tumor stage since these cases

do not have additional information regarding to the type of tumor diagnosed. Data also includes information with known and unknown ages. Rates were calculated per 100,000 persons and age-adjusted to the 2000 USA Standard Population (19 age groups - Census P25-1130). Incidence rates were estimated using the PRCCR database, based on the pancreatic cancer cases that were diagnosed among residents from PR between January 1, 1987 and December 31, 2010. To calculate the variable of tumor stage we used the definitions different definitions depending on the year of diagnosis of the tumor. The SEER Summary Stage 1977 was used when for cases were diagnosed from 1987 to 2000, the SEER Summary Stage 2000, for the cases diagnosed from 2001 to 2003 and the Derived Summary Stage 2000 for cases diagnosed from 2004 to 2010. On the other hand, mortality rates were estimated using death certificates from the Demographic Registry of the Department of Health of PR, and the mortality case file from the Institute of Statistics of PR for the period of 1987-2010. Statistics were calculated using the SEER*Stat software version 8.1.5 [6,7]. In order to compare the incidence and mortality rates of pancreatic cancer of Puerto Ricans with other racial/ethnic groups (non-Hispanic Whites [NHW], non-Hispanic Blacks[NHB] and Hispanics [USH]) that live in the USA, rates were also calculated per 100,000 persons and age-adjusted to the 2000 USA Standard Population for the period 2006-2010. For this period, rates were stratified by sex. Finally, standardized rate ratios (SRR) using P R age-adjusted rates as the reference, were calculated, in order to determine statistical differences between Puerto Ricans and the other racial/ethnic groups. These results were also stratified by sex.

Age-adjusted temporal trends of the incidence and mortality of pancreatic cancer in PR were also evaluated for the period of 1987-2010. Estimation of time trends was performed overall and by sex. For this analysis, the annual percent change (APC) was calculated using the Join point Regression Program (Version 4.1.0), which identifies the number of change-points and calculates a *p*-value associated to that change [8]. This test allowed determining if an apparent change in trend was statistically significant [8]. Finally, the relative survival

Table 2: Age- adjusted incidence and mortality of pancreatic cancer by sex, age group, and period: Puerto Rico, 1987-2010.

Sex	Age Group	INCIDENCE						MORTALITY					
		1987-1995		1996-2004		2005-2010		1987-1995		1996-2004		2005-2010	
		Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count	Rate	Count
Male	≤64 years	2.9	322	2.1	283	2.3	247	2.6	288	2.0	272	2.0	214
	≥65 years	43.8	598	37.4	606	34.9	452	43.2	588	41.7	667	36.1	457
	Overall*	8.1	920	6.5	890	6.5	699	7.7	876	7.0	940	6.3	671
Female	≤64 years	1.4	184	1.3	214	1.6	196	1.3	170	1.2	193	1.2	147
	≥65 years	34.3	555	29.9	628	29.6	503	35.5	575	30.9	649	31.4	535
	Overall*	5.6	740	4.9	842	5.2	699	5.7	745	5.0	842	5.0	683
Overall	≤64 years	2.1	506	1.7	497	2.0	443	1.9	458	1.6	465	1.6	361
	≥65 years	38.7	1,153	33.3	1,234	32.0	955	39.1	1,163	35.6	1,316	33.5	992
	Overall*	6.7	1,660	5.7	1,732	5.8	1,398	6.6	1,621	5.9	1,782	5.6	1,354

Rates are per 100,000 and age-adjusted to the 2000 USA Standard Population (19 age groups - Census P25-1130).
 Incidence Data Source: Incidence Case File of Puerto Rico from the Puerto Rico Central Cancer Registry (March 16, 2014).
 Mortality Data Source: Mortality Case File provided by the Demographic Registry of Puerto Rico (February, 2013) & the Institute of Statistics of Puerto Rico (December, 2010).
 Population Source: Vintage 2012 estimates series from the Population Division of the United States Census Bureau.
 *Data include known and unknown age.

Table 3: Age-adjusted incidence and mortality (per 100,000) pancreatic carcinoma by sex and racial/ethnic groups during 2006-2010.

	Age-Adjusted Incidence				SRR (95% CI)		
	PR	NHW	USH	NHB	NHW vs. PR ^a	USH vs PR ^a	NHB vs PR ^a
Males	6.76	14.95	9.95	17.04	2.21 (2.04, 2.41)*	1.47 (1.33, 1.63)*	2.52 (2.29, 2.78)*
Females	5.51	8.36	12.03	14.92	2.19 (2.01, 2.38)*	1.52 (1.37, 1.68)*	2.71 (2.46, 2.98)*
	Age-Adjusted Mortality				SRR (95% CI)		
Males	6.21	13.68	8.12	14.57	2.20 (2.03, 2.40)*	1.30 (1.20, 1.43)*	2.35 (2.16, 2.56)*
Females	5.21	10.83	6.99	12.69	2.08 (1.92, 2.26)*	1.34 (1.23, 1.47)*	2.44 (2.25, 2.66)*

SRR= Standardized Rate Ratio

^a=Reference Group

*Statistically significant (p<0.05)

was defined as the ratio of the proportion of observed survivors (all causes of death) in a cohort of pancreatic cancer patients to the proportion of expected survivors in a comparable cohort of cancer-free individuals [9]. The cohort of pancreatic cancer patients for this analysis was cases diagnosed during 2006-2007. These cases were followed during 3 years in order to determine the proportion of cases that survived at the end of the period. STATA software (Version 11.2) was used to calculate the relative and median survival [9].

Results

Incidence and mortality rates

A total of 4,790 new cases were reported to during the study period (1987-2010), 52.4% were males and 69.8% were aged 65 years or older (Table 1). From 2006-2010, after excluding the cases reported by death certificates, 14.8% of the pancreatic cancer cases presented a localized tumor stage, 16.8% presented a regional tumor stage, 30.2% presented a distal tumor stage, and 38.2% of patients had an unknown tumor stage (Table 1). Results for the incidence and mortality rates are presented in three periods: 1987-1995, 1996-2004 and 2005-2010 (Table 2). During the last period (2005-2010), 5.8 per 100,000 persons were diagnosed with pancreatic cancer (n=1,398 new cases). For the same period, the incidence of pancreatic cancer by sex was very similar (6.5 per 100,000 males vs. 5.2 per 100,000 females). Also, significant differences were observed by age group, with an elevated incidence among persons 65 years or older (32.0 per 100,000 persons 65 years or older, n=955 new cases) compared to those under 65 years (2.0 per 100,000 persons under 65 years, n=443 new cases). For mortality, a total of 4,757 deaths were reported to during the complete study period (1987-2010), 52.3% were males and 73.0% were for persons aged 65 years or older (Table 1). From 2005-2010, 5.6 per 100,000 persons of all ages died from pancreatic cancer (n=1,354 deaths). Mortality rates were similar in males and females (6.3 per 100,000 males vs. 5.0 per 100,000 females). In addition, mortality rates were also higher among people aged 65 years or more, (33.5 per 100,000 persons of 65 years or older, n=992 deaths) compared to those less than 65 years (1.6 per 100,000 persons, n=361) (Table 2).

Incidence and mortality rates and SRR by racial/ethnic group

Age-adjusted incidence of pancreatic cancer was presented according to the race or ethnicity of the person, during the period of 2006-2010 (Table 3). Puerto Ricans had lower incidence rates of pancreatic cancer compared to other ethnic groups residing in the USA. During this period, 6.8 per 100,000 males in PR were diagnosed

with pancreatic cancer; this incidence rate is lower when compared to USH (9.9 per 100,000 males), NHW (14.9 per 100,000 males), and NHB (17.0 per 100,000 men) in the USA. The incidence of pancreatic cancer for NHW and NHB in PR was higher among men, compared to women. However, the incidence of pancreatic cancer in USH was higher among females, compared to males. For the same period, 5.5 per 100,000 Puerto Rican females were diagnosed with pancreatic cancer, this incidence rate is lower than NHW (8.36 per 100,000), USH (12.03 per 100,000) and NHB (14.9 per 100,000) females living in the USA. NHB had the highest incidence rate compared with the other racial/ethnic groups. Moreover, results from the standardized rate ratios show that NHW males (SRR=2.2, 95% CI: 2.0, 2.4) and females (SRR=2.2, 95% CI: 2.0, 2.4) had a two-fold excess risk of pancreatic cancer in comparison to their counterparts in PR. USH males (SRR=1.5, 95% CI: 1.3, 1.6) and females (SRR=1.5, 95% CI: 1.4, 1.7) also had a higher risk of pancreatic cancer in comparison to those living in PR. Furthermore, NHB males (SRR=2.5, 95% CI: 2.3, 2.8) and females (SRR=2.7, 95% CI: 2.5, 3.0) also had an excess risk of the disease in comparison to their counterparts in PR.

Age-adjusted mortality of pancreatic cancer was presented according to race or ethnicity during the period of 2006-2010 (Table 3). Results show that Puerto Ricans had lower mortality rates of pancreatic cancer compared to other racial/ethnic groups residing in the USA. During this period, 6.21 per 100,000 males in PR were diagnosed with pancreatic cancer, compared to higher estimates for USH (8.1 per 100,000 men), NHW (13.7 per 100,000 males), and NHB (14.6 per 100,000 males). The mortality of pancreatic cancer for all races was higher among males, compared to females. For the same period, 5.2 per 100,000 Puerto Rican females were diagnosed with pancreatic cancer, compared to higher estimates for NHW (10.8 per 100,000), USH (8.1 per 100,000) and NHB (14.6 per 100,000) females. NHB had the highest mortality rate compared with the other racial/ethnic groups. Moreover, results from the standardized rate ratios show that NHW males (SRR=2.2, 95% CI: 2.0, 2.4) and females (SRR=2.1, 95% CI: 1.9, 2.3) had two-fold excess risk of pancreatic cancer death in comparison to their counterparts in PR. USH males (SRR=1.3, 95% CI: 1.2, 1.4) and females (SRR=1.3, 95% CI: 1.2, 1.5) also had higher risk of pancreatic cancer death in comparison to those living in PR. Furthermore, NHB males (SRR=2.3, 95% CI: 2.2, 2.6) and females (SRR=2.5, 95% CI: 2.2, 2.7) also had excess risk of death from the disease in comparison to their counterparts in PR.

Incidence and mortality trends

Annual percent change (APC) for the total incidence demonstrates

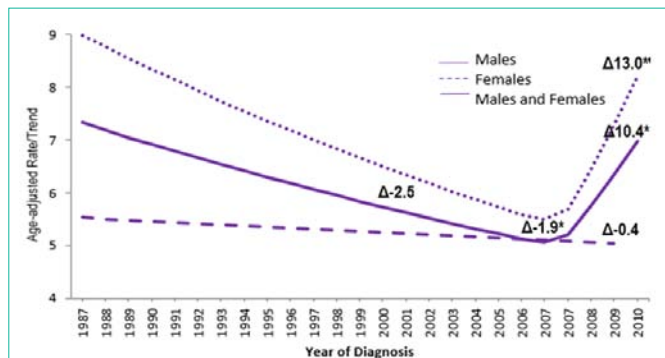


Figure 1: Age-adjusted incidence rates and annual percentage change (APC) for pancreatic cancer by sex: Puerto Rico, 1987-2010.

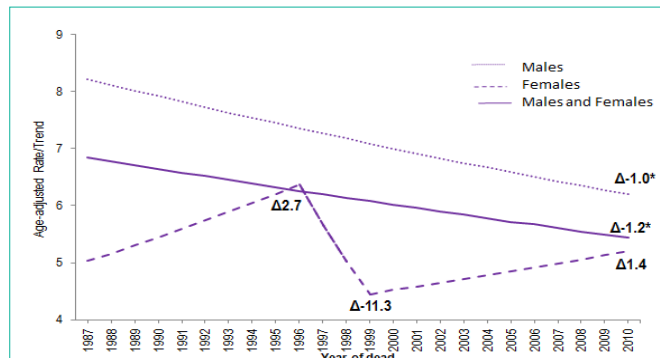


Figure 2: Age-adjusted mortality rates and annual percentage changes (APC) for pancreatic cancer by sex: Puerto Rico, 1987-2010.

an annual decrease of 1.9% in PR for the period of 1987- 2006 and an annual increase of 10.4% for the period of 2006-2010, these changes were statistically significant. For men, the APC indicates an annual decrease of 2.5% during 1987 to 2005, then between 2006 and 2010 the APC shows an annual increase of 13.0%, both changes were statistically significant. Finally, a decrease in females (APC = - 0.4%) is shown for the incidence of pancreatic cancer in the period 2003-2010, although, this change did not reach statistical significance (Figure 1). Mortality in the group of males and overall had an annual decrease of -1.0% and -1.2%, respectively. Both annual percentage changes were statistically significant ($p < 0.05$). However, females showed an increase in the APC of 1.4%, although it did not reach significance ($p > 0.05$) (Figure 2).

Survival

The relative survival for pancreatic cancer cases diagnosed during the period of 2006-2007 was computed by age and sex at 1, 2 and 3 years after diagnosis. The median survival for people diagnosed with pancreatic cancer during this time period in PR was 4 months. Approximately 24.0% of the people diagnosed with pancreatic cancer during 2006-2007 survived to the end of the first year. At the end of the second and third year, 16.0% and 13.0%, respectively, of those diagnosed with pancreatic cancer in the same period survived. When relative survival is assessed by gender, after a year of diagnosis, survival was the same for both genders (24.0%). However, relative survival was higher for males (18.0%) compared to females (14.0%) after two years of diagnosis and after the third year of diagnosis (15.0% vs. 11.0%), as well (Figure 3). With respect to relative survival assessed by age, those who were less than 65 years of age had a higher relative survival (32.0%) after one year of diagnosis, compared to those over 65 years (20.0%). The same results were observed after 2 years of diagnosis (20.0% vs. 13.0%) and after 3 years of diagnosis (13.0% vs. 11.0%).

Discussion

The current study provides the first comprehensive epidemiological profile of pancreatic cancer in PR, with comparisons with other racial/ethnic groups in the USA. Compared to NHW, NHB and USH, Puerto Ricans have lower risk of developing and dying from pancreatic cancer. Trends for pancreatic cancer during 1987-2010 suggest that the incidence of this disease has increased in PR since 2006, particularly for men. Also, significant differences were observed by age group, with an elevated incidence and mortality

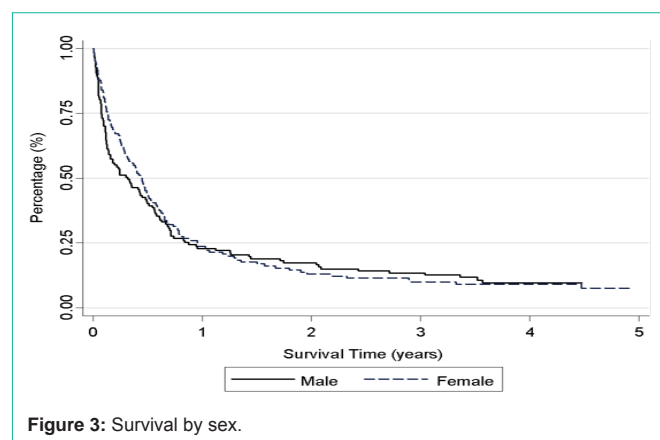


Figure 3: Survival by sex.

among persons 65 years or older. Consistent with previous studies, these results evidence that younger individuals are less likely to develop pancreatic cancer than older individuals, and that the incidence and mortality of pancreatic cancer increases with age [3]. At the same time, the results of the present study show that males were more likely to develop pancreatic cancer than females. In the USA, the American Cancer Society indicates that men are about 30% more likely to develop pancreatic cancer in comparison to females and they suggest that this could be explained, at least in part, to an elevated use of tobacco in men, one of the most influential risk factors for pancreatic cancer. They highlight that in fact, differences in the incidence of pancreatic cancer were more pronounced in the past, where tobacco use was more frequent among men than females [10]. Nonetheless, this gap has closed in recent years, as smoking use is rising among females, specifically women 45 years or older. [10-12]. In PR, although historical data is limited, data from the Behavioral Risk Factor Surveillance System (BRFSS-PR) show that the prevalence of tobacco use is lower in women in comparison to men (8.3% vs. 15.9% in 2010) [13].

In the present study, trends for pancreatic cancer during 1987-2010 suggest that the incidence of this disease is increasing in PR since 2006. This finding could be explained by some factors: (1) improvements in the collection of pancreatic cancer cases by the PRCCR, (2) elevated exposure of the population to risk factors associated with the disease (e.g. smoking, obesity, diabetes mellitus), (3) increased life expectancy in the population, (4) test improvement for the detection of pancreatic cancer, and (5) genetic predisposition

of the new generations [2,14,15]. Regarding pancreatic cancer risk factors [16,17], based on data from the BRFSS-PR [13], the prevalence of diabetes remained relatively constant on the island from 1996 (10.8%) to 2010 (12.8%), although the prevalence of overweight and obesity increased dramatically during this period (16.8% in 1996 to 34.4% in 2010). Meanwhile, slight decreases have been observed for tobacco consumption (14.5% in 1996 and 11.9% in 2010). Analytic studies should further evaluate the reasons for the observed disease trends, in order to be able to develop in the future appropriate prevention and control strategies.

Results from the present study also suggest that Puerto Ricans have a lower incidence and mortality of pancreatic cancer in comparison to NHB, NHW and Hispanics that live in the USA. Lower incidence of pancreatic cancer was also reported by Ho and colleagues from 1998-2002, when comparing island Puerto Ricans with Puerto Ricans living in various USA states [18], although in that study, no differences were observed between mainland Puerto Ricans and NHW. This result from Ho and colleagues suggests that the protective effect of Puerto Ricans living in PR with respect to pancreatic cancer risk is lost once they move to the mainland USA, supporting the stronger importance of social and lifestyle risk factors, rather than genetic ones. Previous studies conducted in the USA indicate that the observed differences by race/ethnicity observed in this population may be explained by greater exposure to risk factors for pancreatic cancer by African Americans such as smoking, diabetes, alcohol consumption and, obesity. Nonetheless, the excess of pancreatic cancer incidence and mortality in this group cannot be attributed only to currently known risk factors, suggesting that the predisposition of genetic mutations for pancreatic cancer could be present. However, further research is needed in this area in order to elucidate the reasons behind these differences [19,20].

Regarding survival, results of this study showed that relative survival at the end of the third year after a diagnosis of pancreatic cancer was low in PR (13.0%), however, the population that lives in the US presents an even lower relative survival (8.0%) [21]. Furthermore, the median survival for persons diagnosed with pancreatic cancer in PR during the period of 2006-2007 was only 4 months. This low survival could be explained by the fact that 29% of the patient's tumors were in a distal area relative to the pancreas at the time of diagnosis during that period (data not shown); at this point, the malignancy has progressed to the point where surgical removal is difficult to perform. Nonetheless, the high proportion of pancreatic cancer cases with an unstated tumor in the PRCCR limits our ability to hypothesize on this factor. Despite this limitation, the reduced survival of pancreatic cancer is of concern and needs to be further addressed by research and intervention efforts, as although uncommon, pancreatic cancer is highly fatal. In fact, pancreatic cancer is one of the few cancers for which survival has not improved substantially over the last 40 years [22]. Furthermore, in 2012, the National Cancer Institute (NCI) merely spent an estimated \$105.3 million for performed pancreatic cancer research, repressing 1.8% of NCI's approximate \$5.8 billion cancer research budget for that year [23]. Therefore, research efforts have to focus on performing more research on pancreatic cancer, across the cancer control continuum, in order to improve prevention and treatment options for pancreatic cancer, as well as the prognosis of these patients.

This study was performed in the presence of some limitations. First, assessment of risk factors that could explain the incidence, mortality, time trends and survival of pancreatic cancer occurrence in PR was limited, as much of this information is not collected through the PRCCR. Second, given the observational nature of our study, an evaluation of the possible factors that could explain differences observed in the incidence and mortality rates among Puerto Ricans and other ethnic groups that live in the USA could not be performed. These limitations should be addressed by future, multi-centric analytic studies.

Conclusion

This study provides updated information on the burden of pancreatic cancer in PR; essential data for the assessment of research priorities and public health efforts in this population. We can conclude that in PR, the incidence and mortality of pancreatic cancer is lower than among other racial/ethnic groups in the USA. Nonetheless, incidence trends are increasing, particularly in men, and relative survival is poor in this population. These trends should continue to be monitored in the upcoming years, in order to conclude whether these trends persist. In addition, further studies are necessary in order to elucidate the reasons that could explain the observed differences in disease occurrence between Puerto Ricans and other racial/ethnic groups living in the USA. In addition, the assessment of pancreatic cancer risk factors and characteristics, access, and response to treatment are required to further understand these results. Thus, future analytic studies are strongly necessary and should focus on further understanding the social, lifestyle, genetic and environmental risk factors of pancreatic cancer, to achieve a decrease in its incidence and mortality. Moreover, efforts should be made to obtain early stage diagnoses in order to improve prognosis.

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