Lung and Bronchus Cancer in Puerto Rico: Changes in Incidence and Mortality Rates by Histology and Sex During 1987-2003

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Objective: Major changes in the incidence of the most common histological types of lung and bronchus cancer have been observed around the world. Herein we report the overall incidence, stage at diagnosis and overall mortality of lung and bronchus cancer in Puerto Rico, and the incidence of the different histologic types.

Methods: Aggregate lung and bronchus cancer data from 1987 to 2003 were obtained from the Puerto Rico Central Cancer Registry. Incidence and mortality rates were age-standardized by the direct method to the 2000 standard population of the United States. For the incidence (overall, by histologic type, and by sex), and mortality we calculated the annual percent change (APC) using the Joinpoint Regression Program.

Results: There were 9,886 cases of lung and bronchus cancer (6,772 men, 3,114 women), for an overall age-adjusted incidence of 18.8 per 100,000. The incidence decreased significantly for the whole group, falling from 18.9 per 100,000 in 1987 to 17.1 in 2003 (APC: -0.74, $p<0.05$); for men, incidence decreased from 28.1 per 100,000 to 24.4 (APC: -1.02, $p<0.05$) over the same period of time. The mortality rate has decreased overall (APC: -0.62, $p<0.05$) and in men (APC: -0.71, $p<0.05$). Squamous cell carcinoma was the most common histologic type in 1987, but it decreased from 6.2 per 100,000 in 1987 to 3.5 in 2003 (APC: -3.86, $p<0.05$), while adenocarcinoma increased from 3.7 per 100,000 to 4.6 (APC: +1.51, $p<0.05$).

Conclusion: In Puerto Rico, over the period of 1987 to 2003, squamous cell carcinoma of the lung and bronchus decreased, while adenocarcinoma increased. As of 1999, the most common type of lung and bronchus cancer is adenocarcinoma. Both the incidence and the mortality of lung and bronchus cancer decreased for men but not for women. [*P R Health Sci J 2011;30:176-181*]

Key words: Lung, Cancer, Puerto Rico

Lung cancer is the leading cause of cancer death in the world (1). The mortality rate and incidence of lung cancer are both higher in developed countries than they are in less developed ones (2). In the United States, the overall 5-year survival rate of lung cancer is 16%, meaning that it causes more deaths than do breast, prostate, and colorectal cancer combined (3). The 5-year relative survival rates (1996-2002) for lung cancer patients were 15.8% for whites and 12.8% for blacks, pointing to the importance of access to health care in cancer survival (4). Up to 90% of lung cancer is attributed to smoking and is thus preventable (5).

It has been shown that the incidence of lung cancer in the Hispanic population is lower than is the incidence in non-Hispanic whites and blacks in the United States (4). For both male and female Hispanics combined, the age-adjusted (2000 US standard population) 2000-2003 incidence rates per 100,000 population for lung and bronchus cancer (32.6) were lower than the incidence rates of lung and bronchus cancer for whites (67.3), blacks (76.9), and Asian/Pacific Islanders (39.6) (4). The annual average percent change (1997-2006) evidenced a decrease in incidence in all ethnic groups as represented by data from 17 cancer registries operating under the auspices of the Surveillance Epidemiology and End Results program (SEER) of the National Cancer Institute. Mortality rates also presented a decreasing trend in all ethnic groups included in the SEER

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report. With regard to the SEER data, it is important to note that members of Hispanic groups may also be included in any one or combination of the following groups: white, black, Asian/Pacific Islander, or Native American/Alaskan native (4). Cancer data from Puerto Rico are not included in any SEER reports.

Major changes in the most common types of lung and bronchus cancer have been reported around the world (6). Several countries have reported an increasing incidence of adenocarcinoma and a decreasing incidence of squamous cell carcinoma since at least the 1980s (6, 7). Whether this pattern has also occurred, or is occurring, in Puerto Rico has not been reported. Our hypothesis is that the Puerto Rican population has experienced changes, similar to those reported around the world, in the incidence of the most common lung cancer histologies. We present data from the Puerto Rico Central Cancer Registry documenting overall, age- and sex-specific incidence and mortality, and the incidence of the most frequent types of lung and bronchus cancer.

Methods

The Puerto Rico Central Cancer Registry (PRCCR) provided lung and bronchus (ICD-O-3 site codes C340-C343, C348-349) cancer incidence and mortality rates for the years of 1987 to 2003. Only aggregate data were requested, resulting in the researchers being blinded to patient identifiers. Confidentiality agreements with the PRCCR required that study results be presented in summary form, precluding the identification of cases. The data were received on October 6, 2009.

From 1987 to 2000, the data were coded by PRCCR using the International Classification of Diseases for Oncology, Second Edition (ICD-O-2); starting in 2001, the Third Edition (ICD-O-3) was used. The National Cancer Institute guidelines were followed to assure consistent coding across the transition from ICD-O-2 to ICD-O-3 (8). Histologic confirmation was available for 75.2% of the cases; the rest were diagnosed by positive laboratory tests or markers, by direct visualization or imaging study (6.9%), or by death certificate (17.9%). Only histologically confirmed cases were used to define the major types of lung and bronchus cancer: small cell (ICD-O-3 codes 8041-8047), squamous cell (8050-8076), adenocarcinoma (8140, 8211, 8230-8231, 8250-8260, 8323, 8480-8490, 8550-8560, 8570-8572), and large cell (8012). Carcinoma in situ was excluded. The study protocol was approved by the Institutional Review Board at the University of Puerto Rico Medical Sciences Campus.

Age-adjusted and age-specific incidence rates were calculated by histological type. Incidence rates per 100,000 were calculated using SEER*Stat software, v.6.5.2 (9), and adjusted to the 2000 USA population data provided by Census 2000 (US Census Bureau) (10). Differences in age distribution were assessed using chi-square ($\chi 2$) statistics. The variables of interest for the analysis of lung and bronchus cancer incidence and mortality from 1987 to 2003 were as follows: 1) year of diagnosis, 2) sex, and 3) histologic type. Annual percent changes (APC) by histological type and age groups were calculated using the Joinpoint Regression Program, v.3.2 (11), to evaluate the incidence trends from 1987 to 2003. The parameters used in Joinpoint to estimate APCs were 1) log transformation of the rates, 2) zero-joinpoint model, 3) Poisson model using rate, 4) uncorrelated error model, 5) Hudson's method, and 6) permutation model selection methods. The level of significance was at an α level of 0.05; thus, significant results were reported at a P-value of <0.05. Microsoft Office Excel 2003 was used for graphs.

Results

A total of 9,886 new cases of lung and bronchus cancer (6,772 men, 3,114 women) were registered in Puerto Rico from 1987 to 2003, an average of 581 cases per year (Table 1). The overall average age-adjusted (US 2000 standard population) incidence of lung cancer was 18.8 per 100,000. The breakdown by stage at diagnosis (from 1987 to 2003) was as follows: 17% were diagnosed at a localized stage, 19% at a regional stage, and 27% at a distant stage. Unspecified stage was reported in a considerable proportion (37%) of cases. The distribution of lung and bronchus cancer cases by the major histological types (from 1987 to 2003) was squamous cell carcinoma, 26%; adenocarcinoma, 23%; small cell carcinoma, 11%; large cell carcinoma, 3%; and others, 37%.

Table 1. Age-adjusted lung and bronchus cancer incidence rates* by sex, 1987-2003.

Year of Diagnosis	Both Sexes		Male		Female	
	Rate	Count	Rate	Count	Rate	Count
1987-2003	18.8	9,886	28.5	6,772	10.8	3,114
1987	18.9	478	28.1	330	11.0	148
1988	18.9	492	29.0	352	10.2	140
1989	20.2	540	31.5	387	10.7	153
1990	20.1	557	31.0	396	10.9	161
1991	20.7	583	31.4	406	11.6	177
1992	19.4	559	29.2	387	11.1	172
1993	19.2	568	31.0	421	9.2	147
1994	18.6	560	28.7	391	10.2	169
1995	18.5	568	28.8	400	10.0	168
1996	18.7	584	27.4	385	11.6	199
1997	19.8	631	29.7	424	11.8	207
1998	18.7	621	29.0	430	10.4	191
1999	19.7	667	29.6	446	11.8	221
2000	18.0	615	26.2	393	11.7	222
2001	17.5	620	25.8	407	10.8	213
2002	16.8	604	26.2	416	9.4	188
2003	17.1	639	24.4	401	11.4	238

*Rates per 100,000 are age-adjusted to the 2000 US standard population.

The incidence rate of lung and bronchus cancer for males was 2.6 times greater than it was for females. The incidence rate difference by sex has been progressively narrowing. However the age-adjusted lung and bronchus cancer incidence rate per 100,000 in the male population (24.4) was still more than double that of females (11.4) during the last year of the study period. The age-adjusted lung and bronchus cancer incidence in Puerto Rico decreased from 18.9 per 100,000 in 1987 to 17.1 per 100,000 in 2003 (APC: - 0.74, $p<0.05$), with a parallel decreasing trend being seen for males, for whom the incidence rate fell from 28.1 per 100,000 in 1987 to 24.4 per 100,000 in 2003 (APC: -1.02, $p<0.05$). A small increase in the lung and bronchus cancer incidence rate for females was observed, but it was not statistically significant (APC: +0.19, $p>0.05$) (Figure 1). The peak age group for lung cancer diagnosis is 75 to 84 years (Figure 2). No significant shift in the age distribution of lung cancer was observed when the average age-specific rates of three time periods (1987-1991, 1992-1996, and 1997-2003) were compared. The overall mortality rate has decreased (APC: -0.62, $p<0.05$), mostly because the rate for males has significantly decreased (APC: -0.71, $p<0.05$). No significant change (APC: -0.05, $p>0.05$) was observed in the mortality rate for females (Figure 3).

In 1987, squamous cell carcinoma was the most frequent histological type of lung and bronchus cancer, with a rate of 6.2 per 100,000, significantly decreasing to 3.5 per 100,000 by 2003 (APC: -3.86, $p<0.05$) (Figure 4). The incidence of squamous cell carcinoma in men decreased from 10.2 per 100,000 in 1987 to 6.0 per 100,000 in 2003 (APC: -3.56, $p<0.05$); in females, incidence decreased from 2.7 per 100,000 to 1.6 per 100,000 (APC: - 3.99, $p<0.05$). Adenocarcinoma became the most common histological type by 1999 (specifically, by 1995 for women and by 2002 for men), increasing from 3.7 per 100,000 in 1987 to 4.6 per 100,000 in 2003 (APC: +1.51, $p<0.05$). For men adenocarcinoma incidence underwent no significant change from 1987 to 2003, while for women it increased from 1.8 per 100,000 to 3.8 per 100,000 (APC: + 3.59, $p<0.05$). The incidence of large cell carcinoma (APC: -2.57, $p>0.05$) and that of small cell carcinoma (APC: -0.25, $p>0.05$) experienced no significant changes from 1987 to 2003 (Figure 4). The incidence of lung and bronchus cancer cases of the other histologic groups was 6.3 per 100,000 in 1987, which increased over time to 6.6 per 100,000 by 2003.

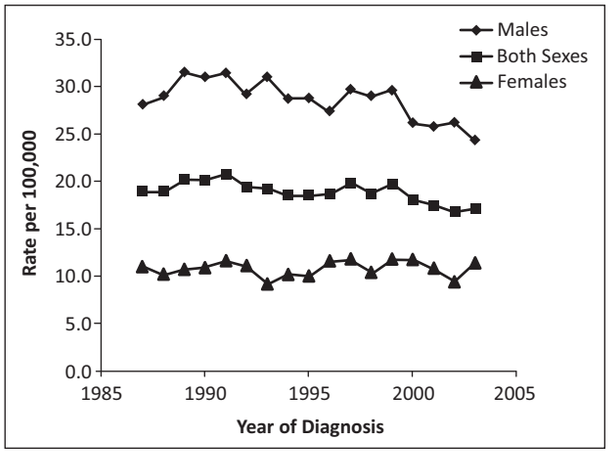

Figure 1. Age-adjusted lung and bronchus cancer incidence rates, 1987-2003. Annual Percent Change: both sexes = -0.74 ($p<0.05$); males = -1.02 ($p<0.05$); females = +0.19 ($p>0.05$).

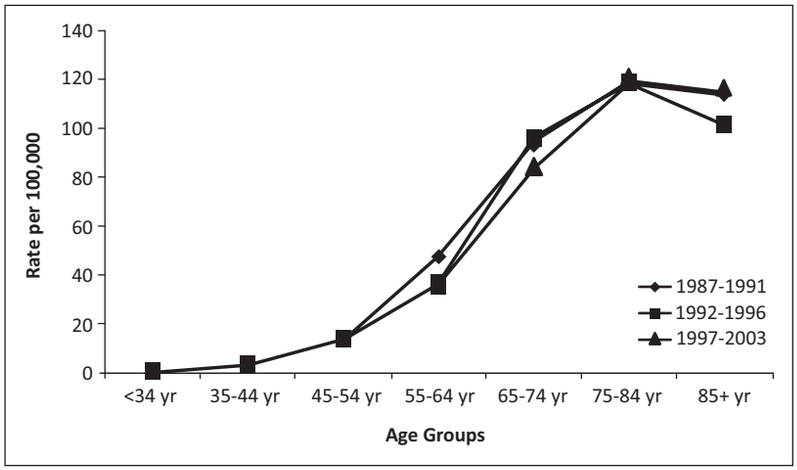

Figure 2. Age-specific lung and bronchus cancer incidence rates for three time periods (1987-1991, 1992-1996, and 1997-2003), both sexes.

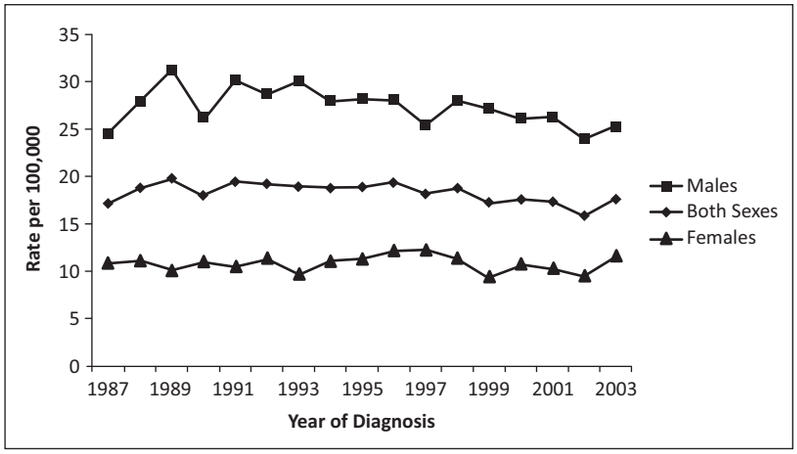

Figure 3. Age-adjusted lung and bronchus cancer mortality rates by sex, 1987-2003. Annual Percent Change: both sexes = -0.62 ($p<0.05$); males = -0.71 ($p<0.05$); females = -0.05 ($p>0.05$).

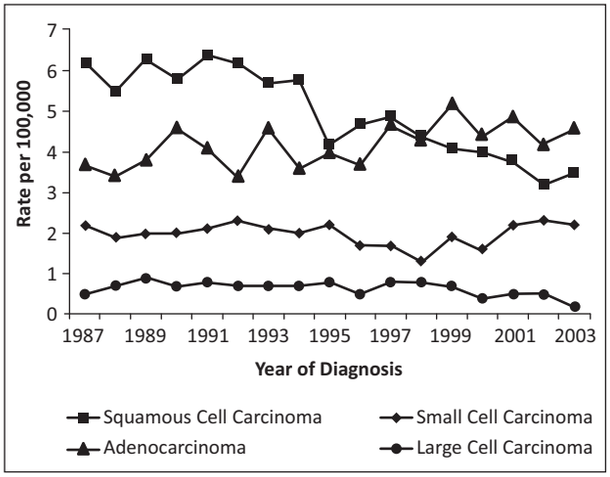

Figure 4. Age-adjusted lung and bronchus cancer incidence rates by histology for both sexes, 1987-2003. Annual Percent Change: squamous cell carcinoma = -3.86 ($p<0.05$); adenocarcinoma = +1.51 ($p<0.05$); small cell carcinoma = -0.25 ($p>0.05$); large cell carcinoma = -2.57 ($p>0.05$).

Discussion

The major findings of our study are that the incidence of lung and bronchus cancer decreased for men from 1987 to 2003, narrowing the gap that exists between men and women with regard to said incidence, and that adenocarcinoma became the most frequent histologic type in 1999. In western countries, lung cancer incidence for both sexes combined has stabilized over the past decades (4,12). From 1987 to 2003 the age-adjusted lung and bronchus cancer incidence decreased significantly in Puerto Rican men and increased nonsignificantly in women. A similar pattern has been observed in Europe and in North America (6).

Lung and bronchus cancer risk in Puerto Rico is much lower than it is in the United States. In 2003, the age-adjusted lung and bronchus cancer incidence rate per 100,000 was 60.7 for U.S. whites compared to the 16.3 per 100,000 rate for Puerto Ricans (13). The lower lung and bronchus cancer incidence in Puerto Rico is compatible with other reports that also show a lower incidence of lung and bronchus cancer among Hispanics living in the United States (4, 14). This lower incidence makes lung and bronchus cancer the second highest cause of cancer death in men and the third highest among women in Puerto Rico, while in the United States , lung and bronchus cancer is the primary cause of cancer death, both for men and for women (13). The difference in incidence is explained, in part, by the lower prevalence of cigarette smoking in Puerto Rico (15). According to the Behavioral Risk Factor Surveillance System, the prevalence of adults who were current smokers in 1996 in Puerto Rico was 14.5%, decreasing to 11.6% by the time of the 2008 survey (16). Even with the recent decreases in smoking rates in the US, the prevalence of current smokers in the US in 2008 was still higher (median value 18.3%) than it was in Puerto Rico (16).

People 75 to 84 years of age had the highest incidence of lung and bronchus cancer. In the United States, this same fact applies to those individuals who are so aged regardless of their race (4). Puerto Ricans who migrate to the United States acquire a higher risk for lung (both men and women), prostate (men only), and female reproductive tract cancers (women only) (17,18), suggesting that environmental or cultural factors, such as increased smoking, contribute to the increased risk for immigrants. The mortality rate is decreasing for men and is stable in women. In the United States, the mortality rate is higher related to the higher incidence of lung and bronchus cancer. However, the same decreasing trend for men and lack of change for women is also being seen (3).

The change in trend of the two major histologic types, adenocarcinoma and squamous cell carcinoma, that was observed in this study in Puerto Rico has also been described in the United States (7) and in other countries (6). The causes for the decrease in the incidence of squamous cell carcinoma and the increase in that of adenocarcinoma evidenced in Puerto Rico and elsewhere are not completely understood (12).

Worldwide geographic and temporal patterns of lung cancer reflect cigarette consumption on a similar scale. The carcinogenic effects of tobacco were noted as early as the 1760s (19) and have been demonstrated in epidemiologic studies since the 1950s (20). This evidence has guided regulatory authorities to establish public health initiatives to reduce and control tobacco exposure as well as to deter smoking initiation in the community. In 1984, Lubin and others reported that smokers who inhaled deeply had a 1.5- to 3.0-times greater risk of lung cancer (21). Further, hemoglobin and DNA adducts associated with carcinogens found in tobacco products have been detected in the blood of cigarette smokers (22), and metabolites of known lung carcinogens have been found in the urine of cigarette smokers (23).

Changes in cigarette composition and in smokers' inhalation patterns have been proposed as a possible explanation regarding the shift in the anatomic tissue target of carcinogen exposure from the central to the peripheral airways (12). Media coverage, research reports, and increases in cigarette taxes also have modified cigarette smoking patterns in the United States (24). Following the first scientific reports linking smoking to various cancers and other chronic diseases, bans of TV and radio cigarette advertising, public awareness channeled by an increasing number of antismoking groups, and increases in state and federal cigarette taxes impacted per capita consumption of tobacco products (24). The difference in risk between men and women has narrowed in recent years. Decreases in smoking rates by men are mostly responsible for the decline in lung cancer in men (25). Finally, there is a possible hormonal influence on the pathogenesis of lung cancer (26, 27, 28).

The overall 5-year survival rate for the years spanning from 1999 to 2005 for the 17 SEER geographic areas was 15.6%, but this varied by sex and ethnicity: 13.7% for white men, 18.3% for white women, 10.8% for black men, and 14.5% for black women (29). Given that in Puerto Rico 37% of the lung cancer cases in the PRCCR data bank were unstaged, conclusions regarding survival must be drawn with caution. In Puerto Rico, the 5-year relative survival rate for lung cancer was 5.6% for the years of 1987 to 1994, which percentage decreased to 3.9% in the 1995 to 2001 span of years. During the years ranging from 1995 to 2001, females over 50 years of age had a 5-year survival rate of 7.9% for lung and bronchus cancer, while among males over 50 years of age, the 5-year survival rate was only 2.0% (30).

There are some limitations to this study. The percentage of cases at an unspecified stage is high (37%) compared to the 8% reported in the United States (28). This high number will have reduced the validity of the survival analysis by tumor stage. The proportion of other histological types is also 37%, comparing more favorably to reports from Europe, where this number varies from less than 10% in France, Sweden, the Netherlands, and Switzerland to over 20% in Italy and Spain (8). The reason for these findings is not clear but may be related to limited access to radiology, nuclear medicine, cytology, pathology, and the procedural services needed for staging and histologic diagnosis. Further studies may explain why the unspecified stage and other histology groups are so large.

The Puerto Rico Central Cancer Registry has the most comprehensive population-based data bank for lung and bronchus cancer currently available. This is the first report that documents the changes that have been seen in the most common type of lung and bronchus cancer in Puerto Rico, from squamous cell carcinoma (before 1999) to adenocarcinoma (from 1999). In summary, squamous cell carcinoma of the lung and bronchus decreased and adenocarcinoma increased in Puerto Rico from 1987 to 2003. As of 1999, the most common type of lung and bronchus cancer is adenocarcinoma. Both the incidence and the mortality rate of lung and bronchus cancer decreased for men, but not for women, during the study period.

Resumen

Objetivo: Se han reportado cambios en el tipo más común de cáncer de pulmón y bronquios alrededor del mundo. Reportamos la incidencia, etapa al diagnóstico, mortalidad y tipo histológico de cáncer de pulmón y bronquio en Puerto Rico. Métodos: Obtuvimos del Registro Central de Cáncer de Puerto Rico información agregada de cáncer de pulmón y bronquios de 1987 a 2003. La incidencia y mortalidad se ajustaron por edad por el método directo a la población estándar USA 2000. Para la incidencia (total, por tipo histológico y por sexo) y mortalidad, calculamos el cambio porcentual anual (CPA) utilizando el programa Joinpoint Regression Program. Resultados: Se reportaron 9,886 casos de cáncer de pulmón y bronquio (6,772 hombres y 3,114 mujeres) entre 1987 y 2003 para una incidencia ajustada de 18.8 por 100,000. La incidencia disminuyó de 18.9 por 100,000 en 1987 a 17.1 en 2003 para el grupo completo (CPA: -0.74, $p<0.05$) y para hombres de 28.1 por 100,000 a 24.4 (CPA: -1.02, $p<0.05$). La tasa ajustada de mortalidad disminuyó para el grupo completo (CPA: -0.62, $p<0.05$) y en los hombres (CPA: -0.71, $p<0.05$). El tumor de célula escamosa era el tipo histológico más común en 1987 pero su incidencia disminuyó progresivamente de forma significativa (CPA: -3.86, $p<0.05$) mientras la de adenocarcinoma aumentó significativamente (CPA: +1.51, $p<0.05$). Conclusión: El cáncer de pulmón y bronquios de tipo de célula escamosa disminuyó y adenocarcinoma aumentó en Puerto Rico entre 1987 y 2003. Desde 1999 el tipo más común de cáncer de pulmón y bronquios es adenocarcinoma. La incidencia y mortalidad del cáncer de pulmón y bronquios disminuyó para los hombres, pero no para las mujeres.

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