

## Lung Cancer Risk in Shoe Manufacturing

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**OBJECTIVE:** Workers in shoe manufacturing have been reported to be at a greater relative risk for bronchogenic carcinoma. Given the implications for our practice setting, we carried out a study to *a*) clarify whether working in shoe manufacturing is a risk factor for lung cancer and *b*) detect histological differences between lung cancers in shoe manufacturers and in other lung cancer patients.

**PATIENTS AND METHODS:** This case-control study compared all lung cancer patients diagnosed in Hospital Elda, Alicante, Spain, between January 1994 and December 1999, with a control group composed of patients admitted to the same hospital for accidental fractures. Information on occupational history and tobacco dependency was collected from all patients by telephone questionnaire.

**RESULTS:** One hundred and ninety-one case patients and 192 control patients were included in the study; 52 of the cases (27.2%) and 48 controls (25%) worked in shoe manufacturing. No statistically significant differences were found between the 2 groups, not even when we limited the cases and controls to only those who had worked more than 30 years in shoe manufacturing or when we analyzed only subjects who had had especially high risk occupations. No differences in tumor histology were found between cancer patients who worked in shoe manufacture and those who did not.

**CONCLUSIONS:** Working in shoe manufacturing has not proven to be a risk factor for bronchogenic carcinoma.

**Key words:** *Bronchogenic carcinoma. Occupational exposure. Risk factors. Shoe manufacture.*

Riesgo de presentar cáncer de pulmón en los trabajadores de la manufactura del calzado

**OBJETIVO:** Según algunos estudios, los trabajadores de la manufactura del calzado tienen mayor riesgo de presentar carcinoma broncogénico (CB). Dadas las implicaciones de esta afirmación para nuestra área, iniciamos un estudio cuyos objetivos fueron: *a*) aclarar si trabajar en este sector es un factor de riesgo para desarrollar CB, y *b*) detectar diferencias histológicas de los CB de trabajadores del calzado frente al resto.

**PACIENTES Y MÉTODOS:** Se ha realizado un estudio de casos y controles. Los casos fueron todos los pacientes diagnosticados de CB en el Hospital de Elda entre enero de 1994 y diciembre de 1999, y los controles fueron pacientes ingresados por fracturas accidentales. De todos se recogió una historia laboral y de tabaquismo mediante encuesta telefónica.

**RESULTADOS:** Incluimos en el estudio a 191 casos y 192 controles; 52 de los casos (27,2%) y 48 controles (25%) eran trabajadores del calzado. No hubo diferencias estadísticamente significativas entre ambos, ni siquiera cuando sólo incluimos a los que habían trabajado más de 30 años en el sector o a los que habían desempeñado ocupaciones de especial riesgo. Tampoco se encontraron diferencias histológicas en los CB de trabajadores del calzado frente al resto.

**CONCLUSIONES:** Trabajar en la manufactura del calzado no ha demostrado ser un factor de riesgo para presentar un CB.

**Palabras clave:** *Carcinoma broncogénico. Exposición ocupacional. Factor de riesgo. Manufactura del calzado.*

### Introduction

Shoe manufacturers are exposed to a group of substances that are known pulmonary carcinogens or suspected ones,<sup>1-6</sup> such as some disinfectants (arsenic and formaldehyde), pigments (chromium and nickel),

byproducts of polyvinyl chloride or other plastic breakdown processes, isocyanates, dust from polishing, and others. A higher incidence of certain tumors has been found in workers in shoe manufacturing.<sup>7</sup>

Few studies have considered the risk of bronchogenic carcinoma for these workers, the results have been contradictory, and most have been based on the analysis of causes of mortality.<sup>8-11</sup> The largest study designed to clarify the issue was carried out by a German group of public and occupational health epidemiologists.<sup>12</sup> The study was carried out as a result of a judicial order for an expert opinion in a lawsuit seeking compensation in

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a case of lung cancer in a shoe manufacturing worker. A total of 3180 patients with cancer and 3249 controls from the general population were studied. Seventy-six of the cancer patients and 42 of the controls had been shoe manufacturing workers. The authors concluded, after including smoking and asbestos contact in the model to calculate an adjusted odds ratio, that shoe manufacturing workers are subject to increased risk of lung cancer and that such risk doubles after 30 years working in the sector.

The present study was carried out in a geographic area where shoe manufacturing is one of the main sources of income and a large percentage of the population is involved. We were also aware that many workers engage in unregulated shoe manufacturing in their homes, without adequate ventilation or other safety measures. Our aim was to determine whether working in our area's shoe manufacturing industry is a risk factor for developing bronchogenic carcinoma and to detect possible differences in disease patterns of lung cancer patients who have worked in that industry in comparison with those who have not.

### Patients and Methods

All cases of bronchogenic carcinoma diagnosed and confirmed by histology or cytology in Hospital de Elda (Area 17 of the Public Health Service of Valencia) from January 1994 through December 1999 were included for study.

Controls were patients, matched for age and sex, who were admitted to the same public health area with accidental bone fractures. Patients were excluded if fractures were pathological or due to occupational accidents or if they had a medical history of any type of cancer in any location. We thus tried to avoid selection bias. The aim was to create a control population that reflected the general population of those requiring hospitalization due to accidents.

Information for lung cancer patients was extracted from pathology reports and medical records. To select controls, we contacted the traumatology department and reviewed patients' charts. Data collection was complemented by a telephone interview with patients in both groups. If patients had died, a relative was interviewed. The same investigator conducted all interviews in both the lung cancer and control groups. A full occupational history (employment and time in each job), in order to detect other occupational risk factors. Subjects who reported working in shoe manufacturing were asked what specific jobs they had performed. Smoking history was also recorded.

Patients for whom no work history could be obtained were excluded. Persons who had worked in contact with other pulmonary carcinogens, such as asbestos, radon, and diesel fumes, were also excluded.

### Statistical Analysis

The information was organized in a Microsoft Access 2000 database and a Microsoft Excel 2000 spreadsheet. The statistical package SPSS, version 9.0 for Windows, was used to analyze the data. Causality was analyzed retrospectively as contingency (cases and controls) and the  $\chi^2$  test was used for bivariate comparisons.

### Results

A total of 211 patients were diagnosed with lung cancer in Hospital de Elda in the study period. Nineteen were excluded because it was impossible to contact them or their families to complete data collection. One more was excluded because he had worked in contact with diesel motor fuels. None of the patients with lung cancer had worked in contact with asbestos or radon. The characteristics of patients with lung cancer are shown in Table 1.

Histologic diagnoses obtained with samples from bronchoscopy or transthoracic needle biopsy guided by computed tomography were small-cell carcinoma in 40 cases (20.9%), squamous cell carcinoma in 87 (45.5%), adenocarcinoma in 32 (16.8%), undifferentiated large-cell carcinoma in 15 (7.9%), and undetermined in 17 (8.9%) cases. The clinical stage was IIIB or IV at the time of diagnosis for 67.9% of the cases according to the 1998 TNM classification system revised by the Working Group on Bronchogenic Carcinoma of the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR).<sup>13</sup>

Also selected were 192 age- and sex-matched controls for whom occupational histories were available. A total of 52 case (27.2%) and 48 control (25%) patients had worked in occupations related to shoe manufacturing. The 2 percentages were not significantly different.

Given the diversity of occupations within the shoe manufacturing industry, we decided to analyze only those considered to involve exposure to potential carcinogens: dyes, paints, solvents, glues, and leather dust. Unexposed patients who had worked as designers; clerical workers; proprietors and managers; stitchers; press workers, stampers and cutters, etc were excluded. The following shoe industry workers were considered to have possibly have been at risk: trimmers of soles, buffers, makers and handlers of outsoles and insoles, dyers, assemblers, basters, bespoke shoemakers, foremen and supervisors, sales clerks, and warehouse

TABLE 1  
Patient Characteristics

	Cases	Controls
Total number	191	192
Mean (SD) age, years	65.9 (10.2)	66.9 (11.1)
Number of males (%)	181 (94.8)	182 (94.8)

TABLE 2  
Summary of Results for Cases and Controls\*

	Shoe Manufacturing Workers		
	All Specialities	At-Risk Specialty	≥30 Years in the Industry
Cases (n=191)	52 (27.2%)	30 (16.7%)	29 (16.2%)
Controls (n=192)	48 (25%)	36 (18.8%)	30 (15.7%)

\* $P > .05$  in all comparisons.

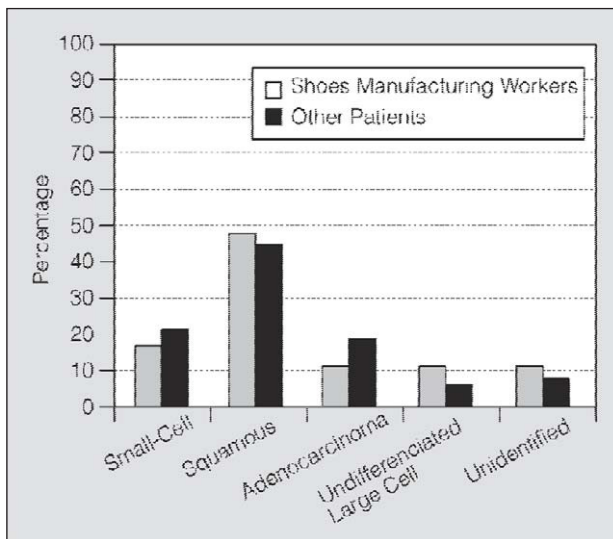


Figure. Distribution of histologic diagnoses in patients with bronchogenic carcinoma who worked in shoe manufacturing and in those who did not.

workers. Persons in risk-related occupations accounted for 16.7% of the cases and 18.8% of the controls; once again the percentages were not significantly different. Nor did we find differences when we analyzed the percentage of patients who had worked at least 30 years in the shoe manufacturing industry (Table 2).

Histologic diagnoses and frequencies among the shoe manufacturing workers with lung cancer were as follows: small-cell carcinoma in 9 cases (17.3%), squamous cell carcinoma in 25 (48.1%), adenocarcinoma in 5 (9.6%), adenosquamous carcinoma in 1 (1.9%), undifferentiated large-cell carcinoma in 6 (11.5%), and undetermined in 6 (11.5%). No statistically significant differences were found between the frequencies of the different histological types in shoe manufacturing workers and other patients (Figure).

We were able to rule out smoking as a confounding factor in our study because it was not a variable associated with the risk factor under study. Seventy-six percent of shoe manufacturing workers with lung cancer and 74.5% of those who had never worked in the sector had been smokers; the mean (SD) number of pack-years was 43.6 (39.65) for the former and 43.85 (38.95) for the latter. The differences, were not statistically significant.

## Discussion

The main finding of the present study was that working in the shoe manufacturing industry did not prove to be a risk factor for developing lung cancer, unlike the findings of Jökel et al<sup>12</sup> and Garabrant and Wegman.<sup>10</sup> Even when we selected and analyzed by occupations within the industry that might suggest greater contact with potential carcinogens or when we looked at workers who had been exposed for more than 30 years, we found no indication of significant risk.

Garabrant and Wegman<sup>10</sup> demonstrated a higher rate of lung cancer in men who worked with leather but did not control for other risk factors such as smoking, which we and Jökel et al<sup>12</sup> have taken into consideration. Although our population sample is smaller than those studied by Jökel and colleagues, the absolute number of exposed individuals was not very different because of the large percentage of the population in our health care area who work in shoe manufacturing. In comparison with the 76 lung cancer cases and 42 controls those authors found to have worked in the sector, our study identified 52 cases and 48 controls in the sector. We therefore believe it is unlikely that the differences between our results and theirs can be attributed to differences in sample size.

A possible limitation of our study is lack of assurance that the interviewees gave accurate information regarding employment, given that those who worked in the worst conditions with greater exposure to potential carcinogens (shoe manufacturers in unregulated operations) might have lied. However, we believe this is unlikely. During the interview, we identified ourselves as pneumologists from the hospital and, with reference to the patient's own hospital records, we explained that we were studying the association between the patient's disease (a serious one for those with cancer) and profession and we never asked whether work had been done legally or not. Moreover, in most cases the patient with cancer had died and information was obtained from a relative. No one refused to respond and most were grateful that we were carrying out the study. We do not believe anyone lied but if anyone did, it is unlikely that more cases than controls did so.

To support our study we decided to analyze whether death from lung cancer in our area had been greater than expected in the Community of Valencia as a whole during the study period. The mortality rate for lung cancer was calculated based on data from the registry of deaths by health care area for Valencia.<sup>14</sup> Our health care area had a rate of 0.67, lower than in the rest of the Valencian community. In this sense, our results are similar to other authors' whose studies were based on mortality reports, such as those of Decouflé and Walrath,<sup>9</sup> Garabrant and Wegman,<sup>10</sup> and Pippard and Acheson,<sup>11</sup> although our findings are inconsistent with those of Walker et al,<sup>8</sup> who demonstrated a significantly higher rate of mortality due to bronchogenic carcinoma in shoe manufacturing workers in a study based on historical cohorts. Although data from death records should be interpreted cautiously, in this case they support findings from our case-control study.

We also found no differences in the distribution of histological types of cancer in patients who had worked in the shoe manufacturing industry (Figure). A review of the literature reporting on other areas in Spain (Extremadura<sup>15</sup>; Tarragona, the Basque Country, and Murcia<sup>16</sup>) and evidence on the distribution of histologic diagnoses in our study suggest that the pattern for shoe manufacturing workers is similar to that reported for the general population.

The present study raises questions and adds controversy to the discussion of this topic and supports the opinion of those who believe that shoe manufacturing work is not a risk factor for lung cancer, at least not in our geographic area. In any case, given that all the studies on this question published to date are based on populations in different countries, it may be that safety measures and materials used—which probably vary from one location to another—are responsible for the observed differences.

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