

## THE PREVALENCE OF CLUBBING IN DIFFERENT TYPES OF LUNG CANCER

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**Background:** The aim of the study was to determine the relative frequency of digital clubbing in small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC), and to find out whether there is a gender predominance in the frequency of clubbing.

**Patients and Methods:** The study was a single center prospective study conducted at the Pulmonary Medicine Department in a university hospital. Between January 1988 and December 1998, 738 patients with histopathologic diagnoses of SCLC or NSCLC were enrolled. Twenty-six patients with a diagnosis of indifferntiated lung cancer were excluded.

**Results:** Clubbing was present in 128 (17.3%) of the 738 patients and was detected in 17.5% of patients with NSCLC vs. 16.7% of patients with SCLC ( $X^2$  test,  $P>0.05$ ), and it was more common in males (18.6%) than in females (4.4%, Fisher's exact test,  $\chi^2=8.74$ ,  $P<0.01$ ).

**Conclusion:** The incidence of clubbing was similar in both SCLC and NSCLC patients, which is inconsistent with classical knowledge in the literature, and digital clubbing was significantly more common in males than in females with lung cancer.

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**Key words:** Clubbing, small cell lung cancer, non-small cell lung cancer.

Digital clubbing, or "hippocratism digital," can be defined as the bulbous enlargement of the distal segment of a digit due to an increase in soft tissue. Although its pathogenesis remains unknown, it appears that vasodilatation of the vessels in the fingertips causes elevated hydrostatic pressure in the capillaries, and this promotes fluid movement into the interstitial tissue and results in soft tissue enlargement.<sup>1</sup> In adults, malignant neoplasms account for nearly 90% of clubbing associated with lung disease, the majority being the non-small cell type. The prevalence of clubbing in lung cancer reported in the literature ranges from 5% to 50%, and is noted most often in squamous cell carcinoma. Except for one study in the literature, it was generally accepted that small cell lung cancer rarely causes digital clubbing.<sup>2</sup> This prospective study was designed to determine the relative frequency of digital clubbing in small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC).

### Patients and Methods

The eligibility criteria of the study were histologically and/or cytologically documented SCLC and NSCLC cases encountered in our clinic between January 1998 and December 1998.

Clubbing can be graded as a five-step process:<sup>3</sup> grade 1 is the fluctuation and softening of the nail bed; grade 2 is the loss of the normal 15-degree angle between the nail and the cuticle; grade 3 is the accentuated convexity of the nail; grade 4 is a clubbed appearance of the fingertip; grade 5 is the development of a shiny or glossy change in nail and adjacent skin with longitudinal striations. In our clinic, the diagnosis of clubbing was made when a patient presented with symptoms or changes regarded as grade 2 or greater.

Demographic characteristics and clinical measures including sex, age, family history of lung cancer, family history of cancer, tobacco history, and clubbing were compared between NSCLC and SCLC groups. If a patient with a diagnosis of lung cancer had any associated disease which has a potential of causing clubbing, the patient was excluded from the study. Statistical analyses including summary statistics (mean, standard deviation and median),  $X^2$  test and Fisher's exact test. The levels of significance were set at  $P<0.05$ .

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## Results

Between January 1988 and December 1998, 738 patients with a histopathological diagnosis of lung cancer were enrolled. Among the 738 lung cancer patients, 559 (75.8%) were diagnosed as NSCLC and 179 (24.2%) were diagnosed as SCLC. Clubbing was present in 128 patients (17.3%). The incidence of clubbing was greater in males than in females—125 of 670 males (18.6%) and only 3 of 68 females (4.4 %) (Fisher's exact test,  $\chi^2=8.74$ ,  $P<0.01$ ). Clubbing was present in 98 of 559 patients with NSCLC (17.5%) and in 30 of 179 patients with SCLC (16.7%) ( $\chi^2$  test,  $P>0.05$ ). Demographic factors such as age, family history of lung or other cancers were not different between SCLC and NSCLC groups.

## Discussion

Clubbing is generally acquired, but may also be hereditary. Acquired clubbing is seen in a wide variety of clinical disorders including both extrathoracic and intrathoracic pathologies. In adults, it occurs most commonly in association with lung cancer, especially the NSCLC type, and is regarded as a paraneoplastic syndrome. Radiographic findings of clubbing include an initial sign of the loss of the curvilinear radiolucency normally present at the nail-skin junction, and later on in more advanced cases, a prominent bulbous deformity of the distal end of the digit.<sup>4</sup> It has been stated in many studies in the literature that patients with NSCLC were more likely to have clubbing than patients with SCLC, and that SCLC rarely causes clubbing.<sup>5-7</sup> But Baughman et al.<sup>2</sup> have reported that by using a new index, which is a comparison of distal interphalangeal length (DIL) and mid-distal phalangeal length (MPL) (presence of clubbing was accepted if MPL/DIL ratio was  $>1$ ), the incidence of clubbing was not different between NSCLC and SCLC groups, and concluded that if this index is used for clubbing, similar results would be reached in other series.

Our results were similar to the results of Baughman's study. The relative frequencies of clubbing in SCLC and in NSCLC in our study were similar at 16.7% and 17.5%, respectively, and statistical analysis showed that the difference between the groups was insignificant ( $P>0.05$ ). In a clinical aspect, our study showed that in contrast to the classical knowledge, the presence or absence of clubbing does not determine lung cancer subtype of SCLC or NSCLC. The other important finding of the study was that males had more prevalence of clubbing than females, and that the difference was statistically significant. This finding was similar to previous series in the literature, except one in which the incidence was greater in women than in men with values of 40% and 19%, respectively.<sup>8</sup> The underlying cause for gender difference of clubbing is unknown.

In conclusion, our study showed that the incidence of clubbing is nearly the same for both SCLC and NSCLC patients, and that the incidence of clubbing occurs in men much more than in women.

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