The Influence of Sex in Non-Small Cell Lung Cancer

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In this issue of ONKOLOGIE, Dr. Cerny and colleagues [1] report the results of a study of patients presenting to the cancer centre in St. Gallen with a diagnosis of lung cancer. The major emphasis of this paper is the reporting of different characteristics observed in women and men. In particular, women were generally younger than men, were more likely to have adenocarcinoma and smoked fewer cigarettes than men. The never-smokers in this series were more likely to be women. These observations are not new; all have been reported on previous occasions as acknowledged by the authors. It is this interplay between patient sex, histology and smoking history that has increasingly become an issue of interest. Many series have previously reported that female sex is a positive prognostic factor in both small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) [2–7]. In addition there are now series that have demonstrated prolonged survival for non-smokers with lung cancer compared to smokers [8, 9]. It is also well reported that never-smokers with NSCLC are more likely to be women and are more likely to have adenocarcinoma [9–11]. Furthermore, a few series have demonstrated that the longer survival observed in women with NSCLC may be entirely due to the effect seen in adenocarcinoma [12, 13]. Therefore whether the predominant prognostic factor is sex, histology or smoking currently remains unclear. It may be that female sex is purely a surrogate in this instance, backed up by Japanese data showing that, while mutations of the epidermal growth factor receptor (EGFR) gene are overall more common in women, when the rates are analysed among never-smokers then the EGFR mutation rates are actually similar between sexes [14].

It is certainly commendable that the smoking history was available in two-thirds of the patients, as in many clinical trials of this era smoking history was not necessarily recorded, as the concept of never-smoking lung cancer as a distinct clinical and biological entity was not yet established. As this becomes

established clearer definitions are available. Never-smokers are now defined as those who have smoked fewer than 100 cigarettes in their lifetime, ex-smokers must have quit for more than 1 year, and current-smokers include those who quit within the prior 12 months. The recent IPASS study also defined light former smokers as those with a fewer than 10 pack year smoking history who had not smoked for 2 years. This group seemed to behave in a similar fashion to the never-smokers. The authors wisely identify the current public health concerns regarding smoking rates, in particular with increasing rates of cigarette smoking being observed in teenagers, a trend that has been reported in other countries, in some cases where the only population with increasing smoking rates are young women.

Generally over recent decades smoking rates have been falling in western countries, but at a faster rate in men than women, such that in many places smoking rates are now approaching parity. This has been mirrored in mortality rates from lung cancer, which have been falling in men but staying level or even increasing in women [15, 16].

While the St. Gallen series does not show any significant survival difference (10 months in both sexes), it should be noted that this is a relatively small patient population and is quite heterogeneous, where patients are included at all stages of disease and all histological subgroups except carcinoid. However the hazard ratio (HR) for death of 0.92 (95% confidence interval 0.76–1.12) would be in line with other series, most of which report a HR of between 0.80–0.90, favouring women. There are no reports that demonstrate even a trend towards improved survival in men [5–7, 17–19]. The authors make an interesting observation that, while overall survival is similar, the survival curves did start to separate and that the 18-month survival rate was 30% higher in women. Actual numbers still at risk at each time point are not shown in the Kaplan-Meier curve and, given the relatively small size of the

overall population and the median overall survival of only 10 months, it is likely that there would be only small numbers alive at 18 months to make this observation. However it is an interesting theory, previously proposed in a sex analysis of SCLC chemotherapy trials from the UK [4], that the strength of female sex as a prognostic factor may be outweighed by stronger factors of poor prognosis, such as poor performance status or advanced disease stage.

In summary, Cerny et al. [1] demonstrate that the population of lung cancer patients seen in St. Gallen are representative of lung cancer seen in other western countries,

particularly in respect to age, histology and smoking history. Not too many prognostic factors can be confirmed because of the small numbers and heterogeneity of the cohort, but the emerging differences in lung cancer between women and men are increasingly of interest in the public health and lung cancer communities.

Conflict of Interest

The authors did not provide a conflict of interest statement.

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