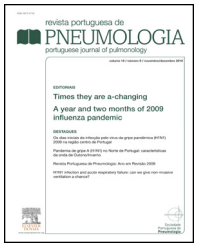
Rev Port Pneumol. 2013;19(6):241–242

revista portuguesa de PNEUMOLOGIA
portuguese journal of pulmonology
www.revportpneumol.org



EDITORIAL

Studies on lung cancer management in routine practice

Estudos sobre a abordagem clínica no cancro do pulmão

In the present issue of the Portuguese Journal of Pulmonology appears a hospital-based study about lung cancer in Northern Portugal[1] The authors have registered during an eleven years period (2000 – 2010) the cases of lung cancer managed in a network of hospitals in Northern Portugal. They collected information about 9767 patients with a significant increase in the number of cases from 2000 (634 cases) to 2010 (1284 cases). Collected data include demographic characteristics, smoking habits, performance status, histology, stage, treatment strategy. Survival, specific mortality and causes of death were not reported. There was an increase of adenocarcinoma histological type as well as more lung cancers in women. The authors observed also over time a significant increase of combined therapeutic modalities.

This type of study is important because it allows determining how thoracic oncology is practiced in specific settings or countries without selection of the patients according to trials criteria. It may somehow give a picture how guidelines or recent studies results are implemented in the daily practice. In the present report, the authors consider to have included about one third of the total number of lung cancer diagnosed in their catchment area. In comparison, registries have the advantage to include all the cases of the area without any selection but information about individual patients is often limited.

Other studies performed with unselected patients population are **implementation studies** where a specific treatment or approach is assessed in routine practice. This very important information is often lacking in the literature, particularly concerning guidelines. We have conducted a few implementation studies to determine if the results that are obtained with a given treatment in routine practice are consistent with those reported by the clinical trials. We assessed in advanced non-small cell lung cancer by such an approach the MIP (mitomycin + ifosfamide + cisplatin) regimen as first-line chemotherapy[2] and docetaxel[3] and pemetrexed[4] as salvage chemotherapy. The results that we obtained in all those retrospective studies showed similar activities than those reported in clinical prospective trials, suggesting their generalizability for routine practice if medical contra-indications are respected.

French authors have used a similar approach based on **unselected cohorts** as in the Northern Portugal study. This study, called KPB-CPHG, has been prospectively performed in general hospitals. Two cohorts have been follow up, one in 2000 and the other one in 2010 with the respective participation of 137 and 104 centres that have included 5667 and 7051 patients[5–8]. They observed that over ten years, lung cancer characteristics have changed with more women, more never-smokers, and more adenocarcinomas. That observation is similar to the presently reported. In the French study, survival was also registered and results with the first cohort were published, showing an overall 10.4% 5-year survival. The impact of treatment strategy has also been assessed with better survival when patients were treated.

Registries can also provide interesting information. They have the advantage to deal with large number of patients but the number of collected data is usually limited, precluding in-depth analysis. The SEER (for Surveillance, Epidemiology and End Results) registry is widely used for purposes as the study of lung cancer in women[9], the influence of hospital volume on survival after resection for lung cancer[10], the effect of race on invasive staging and surgery in non-small-cell lung cancer[11], the role of postoperative radiotherapy[12], or the management of stage III and IV NSCLC[13]. Other good registries are also available in the United Kingdom, Scandinavia and the Netherlands, allowing performing similar studies.

An important question is **the level of evidence** of the study reported in the present issue of the Portuguese Journal of Pulmonology. Whatever implementation, cohort or registries studies, all deal with unselected patients' population, contrary to clinical trials. In term of evidence-based medicine, randomised clinical trials are considered as the best level of evidence[14,15], followed by prospective studies with a control group, comparative studies with historical controls, prospective cohorts without control group, retrospective studies and case reports. If this is true from a

DOI of original article:
http://dx.doi.org/10.1016/j.rppneu.2013.05.005

http://dx.doi.org/10.1016/j.rppneu.2013.10.001

scientific point of view (internal validity) because randomisation minimises the risk of bias, it is less true for external validity. Indeed, the patients selected for trials are often a small part of the whole group of patients which we have to treat. Patients which are compromised by conditions such as poor performance status, organ failures, other severe diseases, or old age, are often excluded for trials but not for routine treatment. In fact, results of clinical trials should be confirmed by studies conducted in the context of the daily practice where patients do not receive the recommended therapy only in case of medical contra-indication to its administration. Those studies of which methodology should be better defined are the best level evidence for generalizability (**external validation**). A similar approach should be recommended for practice guidelines. Indeed, a lot of guidelines are today published but none have been so far validated by implementation studies.

Today, the performance of a prospective clinical trial has become very complicated and expansive. A lot of bureaucratic rules and a high cost have led to a considerable reduction of the number of academic trials. Most of the randomised clinical trials testing drugs are conducted by the pharmaceutical industry for registration purposes. A new role for academic research is to develop external validation in unselected patients' population, allowing generalisation of the registered treatment. Otherwise, the drug prescription should be restricted to the criteria and conditions with which the registration studies were performed.

Today, the external validation studies are mainly published in the national medical press and often in the native language. Indeed, an important parameter that has to be considered in such studies is the influence of the social security system (including rules for reimbursement) and of the local health care organisation. This is a barrier for publication in the journal with good impact factors, which are highly biased in favour of the native English-speaking world. Taking all those elements in consideration, studies like that presently reported can have major care impact, particularly if survival is taken into account and correlated with treatment administered over time. They also should allow validation of guidelines in the daily practice.

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