SYSTEMATIC REVIEW OF MULTIPLE STUDIES OF PROGNOSIS, ILLUSTRATED BY THE CASE OF ANGIogenesis AS A MARKER IN NON-SMALL CELL LUNG CANCER

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Abstract

The vast number of existing publications of prognostic factors has raised more controversy than certainty. Researchers use a variety of laboratory and statistical methods and reporting of methods and results is often incomplete. As a result, the overall quality of published work suffers [1] and the findings are frequently contradictory.

As with other types of research, all the relevant evidence is best assessed in a systematic review [2,3]. Compared with randomised trials and epidemiological studies of risk factors, studies of prognosis have received little attention by those carrying out systematic reviews. These studies typically combine all the difficulties of systematic reviews of survival data using information given in published reports [4], problems associated with non-randomised studies, and some problems specific to prognostic studies.

We will review methodological issues in the systematic reviews of a set of studies examining the association between a prognostic factor and survival. Among the difficulties are poor reporting of survival, a variety of ways for grouping values of continuous variables (some of which lead to bias), use of different assays, varying and often inadequately described patient
cohort, and adjustment for different other variables (often using data-dependent selection methods). In addition, publication bias is very likely for this type of study. Those reviews that have been done have illustrated many of the difficulties; as a consequence many have offered little more than a listing of P values. Meta-analysis has been performed in some reviews, but its reliability using just published results has been seriously questioned.[5]

In view of these difficulties, there is a strong argument in favour of attempting to obtain individual patient data. A multi-centre collaborative framework using raw data from as many relevant studies as possible is a highly desirable approach for investigating prognostic factors [6]. How feasible is it though?

The Prognosis in Lung Cancer project (PILC) was set-up as an international co-operative group aiming to examine microvessel density counts (MVD) (a measure of angiogenesis) as a potential prognostic factor in non-small cell lung cancer (NSCLC). The project’s other key objective was to explore the feasibility and practical difficulties of doing individual patient data (IPD) systematic reviews in studies of prognosis. The few previous such studies seem to have begun with a collaborative network already in place. For PILC, however, there was no existing group and procedures had to be set up from scratch.

We obtained MVD data from 17 centres around the world for over 3000 NSCLC cases. Methodological and logistic challenges will be discussed. These include identifying and recruiting research groups with appropriate data who were willing to participate in the project; collecting, understanding, and cleaning the data to an appropriate standard; and inconsistencies in the methods and results from different centres. We found that while such an exercise is feasible and worthwhile it is also very time-consuming.

We will present the results of the analyses of markers of angiogenesis in NSCLC. In the end it was impossible to combine all the available data due to incompatible laboratory methods. While this might not apply to other markers, collecting IPD is probably the safest way of finding out.

Finally, we will make some recommendations for future systematic reviews of studies of prognostic factors.
References:


