Lung Cancer xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

Lung Cancer

journal homepage: www.elsevier.com/locate/lungcan

The impact of comorbidity upon determinants of outcome in patients with lung cancer

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ARTICLE INFO

Article history:
Received 18 August 2014
Received in revised form 27 October 2014
Accepted 23 November 2014

Keywords:
Lung cancer
Epidemiology
Comorbidity
NSCLC
Outcomes
Treatment

ABSTRACT

Background: Survival from lung cancer remains poor in Scotland, UK. It is believed that comorbidity may play an important role in this. The goal of this study was to determine the value of a novel comorbidity scoring system (SCSS) and to compare it with the already established Charlson Comorbidity Index and the modified Glasgow Prognostic Score (mGPS). We also wished to explore the relationship between comorbidity, mGPS and Performance Status (PS). In addition we investigated a number of standard prognostic markers and demographics. This study aimed to determine which of these factors most accurately predicted survival.

Methods: Between 2005 and 2008 all newly diagnosed lung cancer patients coming through the Multi-Disciplinary Teams (MDTs) in four Scottish Centres were included in the study. Patient demographics, World Health Organization/Eastern Cooperative Oncology Group performance status, clinico-pathological features, mGPS, comorbidity and proposed primary treatment modality were recorded. Univariate survival analysis was carried out using Kaplan–Meier method and the log rank test.

Results: This large unselected population based cohort study of lung cancer patients has demonstrated that a number of important factors have significant impact in terms of survival. It has gone further by showing that the factors which influence survival are different, depending upon the stage of cancer at diagnosis and the potential treatment strategy. The novel comorbidity scoring system, the SCSS, has compared very favourably with the more established CCI.

Conclusion: This study has identified that a variety of factors are independent prognostic determinants of outcome in lung cancer. There appear to be clear differences between the early and late stage groups.

1. Introduction

Within Scotland lung cancer remains the commonest cause of cancer related death [1]. Survival lags significantly behind much of Western Europe and the United States [1,2]. The cause(s) are not fully understood but are likely to include late presentation and lower treatment rates [3–9]. Our own, previously published, work has identified very high levels of comorbidity within an unselected lung cancer population within Scotland [10]. It has also indicated that comorbidity may play an important part in the decision to offer active treatment both in the radical and palliative setting [11]. These findings have been supported by a number of studies, which have demonstrated the prognostic significance of comorbidities

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http://dx.doi.org/10.1016/j.lungcan.2014.11.012
0169-5002/

in many different types of cancer [12–23]. However the way that co-morbidity influences outcomes in lung cancer patients is not clear. In addition there are often significant differences between the methods used to document and grade the severity of comorbidity [23].

The most widely quoted tool to assess comorbidity is the Charlson Co-morbidity Index [15] (CCI). This was designed in 1987 and assigned 19 conditions with a weighting index of 1–6 in an attempt to quantify the likelihood of impact upon survival. Data were acquired via patients being admitted with medical conditions to a Washington Hospital, USA. This tool was initially validated in breast cancer patients with 10-year mortality as an endpoint. It has also been validated in predicting progression-free survival [15] in a variety of diseases such as breast and prostate cancer. However, limitations of applicability of this tool in lung cancer include the absence of some potentially relevant diseases such as pulmonary fibrosis, the inclusion of HIV when current treatments are so much more effective and a lack of severity grading of the specific diseases included in the index [15,23].

In addition to stage of disease [24] it is clear that the prognosis in lung cancer is determined by more than just comorbidity. Performance status is widely recognised as a very strong prognostic factor for patients with lung cancer [25–27]. Recent work shows that the effect of systemic inflammation is detrimental in terms of outcome in cancer in general [28,29] and in lung cancer specifically [30–37]. The combination of C reactive protein and albumin when combined to calculate the modified Glasgow Prognostic Score has previously been validated as an independent predictor of survival [38]. Two recent publications by Laird et al. [39] and Bozzetti et al. [40] have demonstrated that a combination of mGPS and PS is predictive in determining survival in advanced cancer patients and it is likely that a common pathophysiological association between all these factors determines outcome.

We prospectively investigated the survival of a large unselected lung cancer population assessing the impact of comorbidity along with more standard prognostic determinants. The goal of this study was to determine the role of a novel comorbidity scoring system (SCSS) and to compare it with the already established Charlson Comorbidity Index and the modified Glasgow Prognostic Score (mGPS). We also wished to explore the relationship between comorbidity, mGPS and PS. In addition we investigated a number of standard prognostic markers and demographics. This study aimed to determine which of these factors provided the most accurate information on survival.

2. Methods

2.1. Data source and patients

Four Scottish Centres were included in the study – Aberdeen, Glasgow (Stobhill Hospital), Inverclyde and Dunfermline. All four of these centres routinely investigate, diagnose and treat patients with lung cancer across demographically very different regions of Scotland [10]. National guidelines indicate that all newly diagnosed lung cancer patients must be discussed at a MDT. All four centres adhere to this with a greater than 90% success (Managed Clinical Network audit report [41]).

Between 2005 and 2008 all newly diagnosed lung cancer patients coming through the Multi-Disciplinary Team (MDT) meeting were included in the study. The actual timescale during which patients were included varied between centres. The study recruitment periods for each centre were Aberdeen, October 2005 to February 2007; Glasgow, December 2005 to April 2008; Inverclyde, October 2005 to December 2007 and Dunfermline, June 2007 to April 2008.

2.2. Data collection

At the time of the patient's case being discussed at the MDT, anonymised details were entered into a specifically designed Microsoft Access database. Patient demographics and baseline characteristics (age, sex, postcode and smoking history), PS, weight loss, laboratory parameters (C-reactive protein, albumin, creatinine and ventilatory function, wherever possible this was based on full lung function testing, if unavailable spirometry was used), co-morbidites (including severity), tumour stage [24], histology and primary treatment proposed by the MDT were all recorded. If the treatment proposed varied from the 2005 Scottish Intercollegiate Guidelines Network (SIGN) guidelines [42] on lung cancer management the reasons why were also recorded (i.e. age, poor Performance Status, comorbidity, size of tumour, etc.). Treatment recorded was on an intention to treat basis rather than that actually delivered.

All four MDTs had input from both a clinical oncologist and a thoracic surgeon. All data was recorded in real time at the MDT by one of the clinical staff, taking on average 2–3 min to enter the data. Details of the study design have previously been published [10]. For the purposes of data analysis it was decided to separate the population into 2 separate groups. The first included NSCLC st I to IIIa where the intent of treatment is curative. The second, much larger, group included patients with NSCLC st IIIb/IV and SCLC where treatment intent is almost always palliative.

Information on date of death was obtained via survival analysis undertaken by the Information Service Division (ISD) of NHS Scotland. Death records were complete until 1 June 2011, which served as the censor date for those alive.

2.3. Socioeconomic status

Information on patients' individual educational or occupational social class was not available, and we therefore used their postcode of residence as a proxy indicator of their socioeconomic status. Using the 2006 Scottish Index of Multiple Deprivation (SIMD) ranking [43] (see Box 1) the postcode enabled us to group patients into one of 5 quintiles.

2.4. Comorbidities and severity scores

For each patient the co-morbidities present at the time of the MDT discussion were recorded by one of the clinicians using a novel severity index [44–48]. This included use of the British Thoracic Society guidelines for Chronic Obstructive Pulmonary Disease, the Canadian Cardiovascular Society Classification for Ischaemic Heart Disease, the New York Heart Association classification for Heart Failure, the National Institutes of Health Stroke Scale for Cerebrovascular disease and the Clinical Dementia Rating. For co-morbidities without a validated severity scale we devised a scale based on discussion with local experts. The constituent components of the scale are shown in Table 1. A description of the scoring system and its components, including its impact upon treatment,

Box 1: Scottish Index of Multiple Deprivation (SIMD).
The 2006 SIMD is a validated area-based index that uses 37 indicators in seven domains to rank 6505 small geographic areas in Scotland (data zones) from 1 (most deprived) to 6505 (least deprived). These can be subsequently grouped into quintiles. These split up the data zones into 5 groups, each containing 20% of Scotland's data zones. The first quintile contains the 20% most deprived data zones with the fifth representing the 20% least deprived.

Please cite this article in press as: Grose D, et al. The impact of comorbidity upon determinants of outcome in patients with lung cancer. Lung Cancer (2014), http://dx.doi.org/10.1016/j.lungcan.2014.11.012