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Original Research

Factors influencing treatment selection and 30-day mortality after chemotherapy for people with small-cell lung cancer: An analysis of national audit data

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Abstract ***Background:*** Thirty-day mortality after treatment for lung cancer is a measure of unsuccessful outcome and where treatment should have been avoided. Guidelines recommend offering chemotherapy to individuals with small-cell lung cancer (SCLC) who have poorer performance status (PS) because of its high initial response rate. However, this comes with an increased risk of toxicity and early death. We quantified real-world 30-day mortality in SCLC after chemotherapy, established the factors associated with this and compared these with the factors that influence receipt of chemotherapy.

Methods: We used linked national English data sets to define the factors associated with both receiving chemotherapy and 30-day mortality after chemotherapy.

Results: We identified 3715 people diagnosed with SCLC, of which 2235 (60.2%) received chemotherapy. There were 174 (7.8%) deaths within 30 days of chemotherapy. The adjusted odds of receiving chemotherapy decreased with older age, worsening PS and increasing comorbidities. Thirty-day mortality was independently associated with poor PS [PS 2 vs PS 0, adjusted odds ratio (OR) 3.75, 95% confidence interval (CI) 1.71–8.25] and stage (extensive vs limited adjusted OR 1.68, 95% CI 1.03–2.74) but in contrast was not associated with increasing age. Both chemotherapy administration and 30-day mortality varied by hospital network.

Abbreviations: CAV, cyclophosphamide, doxorubicin and vincristine; CbE, carboplatin + etoposide; SCLC, small-cell lung cancer; CI, confidence interval; ED-SCLC, extensive-stage small-cell lung cancer; EP, cisplatin + etoposide; LD-SCLC, limited-stage small-cell lung cancer; NLCA, National Lung Cancer Audit; OR, odds ratio; PS, performance status; SACT, Systemic Anti-Cancer Therapies; TNM, tumour node metastasis; WHO, World Health Organisation; VALSG, Veterans Administration Lung Study Group.

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Conclusions: To reduce variation in chemotherapy administration, predictors of 30-day mortality could be used as an adjunct to improve suboptimal patient selection. We have quantified 30-day mortality risk by the two independently associated factors, PS and stage, so that patients and clinicians can make better informed decisions about the potential risk of early death after chemotherapy.

1. Introduction

The median survival for people with small-cell lung cancer (SCLC) who do not receive chemotherapy is short, and this, coupled with the fact that this aggressive tumour is responsive to chemotherapy reflects treatment guidelines that recommend chemotherapy for extensive-stage SCLC (ED-SCLC) even in elderly people with poor performance status (PS) and significant comorbidities [1–4]. Administration of chemotherapy in this frail population means some individuals die shortly after treatment. It is recognised that death within 30 days of anticancer treatment is an indicator of avoidable harm and suboptimal patient selection as it reflects that treatment was either directly toxic or, in the case of non-treatment–related early death, e.g. disease progression, futile and unnecessary [5]. To minimise 30-day mortality and improve patient selection for chemotherapy, we have determined what factors influence receipt of chemotherapy and investigated how these are associated with 30-day mortality from the first chemotherapy dose.

2. Materials and methods

2.1. Study population

Ethical approval for this study was obtained from the NHS Health Research Authority (16/LO/0503). Our primary data set, the National Lung Cancer Audit (NLCA), consisted of people diagnosed with lung cancer in English hospitals between 01 January 2015 and 31 December 2015. These data were linked with Systemic Anti-Cancer Therapies (SACT) and Hospital Episode Statistics data. All data were prospectively collected via clinical coding or electronic prescription. People with SCLC were identified from their systematised nomenclature of medicine histological code.

2.2. Chemotherapy

If an individual had a date for administration of chemotherapy recorded within 6 months from the date of diagnosis, he/she was defined as having received chemotherapy. Those who did not have a date for chemotherapy administration or received chemotherapy after 6 months from diagnosis were assumed not to have received chemotherapy. We defined the location where chemotherapy was received by the lung cancer network. In England, there are 13 cancer networks based on geographical location and each is composed of several hospitals. The chemotherapy received was grouped according to the combination administered. The remaining groups were the following: single platinum (cisplatin or carboplatin), other (single-agent etoposide, topotecan and clinical trials) and missing (date of administration present but no drug details given).

2.3. Death date

We used a death date derived from the Office of National Statistics records. For this study, the date of death had last been updated on the 19 October 2016. We used these dates along with the SACT record for the date of the first chemotherapy dose received to calculate 30-day mortality.

2.4. Covariates

Our variables were primarily derived from NLCA data. The socio-economic status was calculated from postcode of residence and formatted into Townsend index of deprivation (1, least to 5, most). PS is a marker of a person's well-being and fitness. It is based on the World Health Organisation criteria (0, asymptomatic to 4, bedbound, unable to carry out self-care) and taken at the time of diagnosis.

Stage was obtained from pretreatment tumour node metastases (TNM) records. We divided the stage into limited (LD-SCLC) and extensive (ED-SCLC) based on the similar criteria to the Veterans Administration Lung Study Group (VALSG) [6]. ED-SCLC consisted of any tumour with M1a/b or any T and M0 with N3 nodal involvement. If TNM was not recorded, the stage was classed as missing.

We used a previously derived method to calculate a Charlson Comorbidity index using a list of diagnoses (excluding lung cancer) from previous hospital admissions up to the date of chemotherapy [7,8]. People with no hospital admissions or comorbidities were assigned a score of 0. The Charlson index was grouped into four categories (0, 1, 2–3 and $\geq$4).