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Ageism in the management of lung cancer

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Abstract

Background: age-related differences in the treatment of lung cancer patients have been reported in the past, but most previous studies have not recorded case-mix factors, nor have they studied the impact of such ageism on survival.
Methods: a questionnaire-based study of diagnostic and case-mix factors was carried out across 48 hospital Trusts in the UK between 1997 and 1998. We identified 1,652 patients and followed through with regard to their treatment and survival for 6 months after diagnosis.
Results: the median age of the population was 69 years, and for this analysis, was divided into three age groups: under 65 years, 65–74 and 75 years and over. There were significant inverse correlations between age and histological diagnosis, any active treatment and survival, even when corrected for case-mix factors and non-cancer causes of death. For example, the surgical resection rate in patients with confirmed non-small cell lung cancer with good performance status, no chronic obstructive pulmonary disease and limited disease was 37% in the younger patients compared with 15% in those 75 and over. The overall mortality rates at 6 months ranged from 42% in patients under 65 to 58% in the over 75s.
Conclusions: this national study of lung cancer care in the UK has shown large age-related differences in management and survival in patients with lung cancer, largely independent of case-mix factors. The reasons for this are complex but such under-treatment in the elderly may be one factor underlying the poor outcomes in lung cancer patients in the UK.

Keywords: *lung cancer, ageism, elderly patients, treatment, survival*

Background

As with many other cancers, the age at diagnosis of lung cancer is gradually increasing in the UK and other countries [1–3]. It is therefore a matter of concern that evidence of under-treatment of older lung cancer patients has emerged from several studies in different settings [4–14].

For example, analysis of data for 22,600 lung cancer patients diagnosed in Yorkshire between 1986 and 1994 [1], revealed significantly lower treatment rates for all therapies with increasing age. The Yorkshire study's Non-Small Cell Lung Cancer (NSCLC) patients had surgical rates of 27% in those under 65, 19% in the 65–74 age group and 6.5% in those 75 and over. These data and indeed most of the published work in this field were, however, uncorrected for stage, performance status and co-morbidity.

Against this background, in 1997, the Royal College of Physicians of London began a prospective audit of lung cancer care and outcome in UK hospitals. Data on both case mix and survival were collected to enable clinically meaningful comparisons to be made in assessing standards of care across cancer units. This report presents the project's findings as they relate to age-specific treatment and outcome.

Methods

The questionnaires that provided source data for this report were developed by a multi-disciplinary committee

and piloted by the Royal College of Physicians in collaboration with the audit sub-committee of the British Thoracic Society.

Questionnaires at bronchoscopy and one month later were completed by the supervising doctor, whereas treatment and survival data at 6 months were recorded variously by medical staff and audit clerks. Final patient outcome at 6 months was as either dead or alive. If alive, then patient tumour status was reported either as 'active' or as 'controlled/cured/in remission'. Dates of bronchoscopy and death allowed time to death to be computed. Any patient death recorded after 6 months (183 days) was taken in analysis as being 'alive with active tumour at 6 months'. When death was known to have occurred but no date was recorded, patients were assumed to have died within the 6-month period. Though most would have died from lung cancer, the precise details of cause of death were not routinely recorded.

Respiratory physicians were asked to submit data on 25–50 consecutive patients with a working diagnosis of lung cancer following bronchoscopy. Although not all of these patients went on to have histological confirmation of the diagnosis, they were all managed as lung cancer patients and were included in the analysis.

A summary of the variables collected is shown below.

Data collected from the questionnaires:
At bronchoscopy:

- Referral route
- Presenting symptoms and signs with their duration
- Radiological appearances
- Presence or absence of metastatic disease
- Significant co-morbidity
- Performance status (ECOG/WHO) – with spirometry if appropriate
- Alkaline phosphatase
- Bronchoscopic findings
- Provisional treatment plan

At one month post bronchoscopy:

- Histological diagnosis (with date)
- Details of management plan – including referral to other speciality

At six months post bronchoscopy:

- Details of treatment since diagnosis (with dates)
- Final diagnosis

Statistical analysis

Results are expressed for all hospitals combined. Percentages are stated, with the appropriate frequencies and denominators stated in parentheses as text or within tables. The chi-squared test for linear trend, with 1 degree of freedom, was used to investigate trends in histological confirmation, treatment and mortality rates over the <65, 65–74 and $75+$ year age groups. Mortality rates at 6 months for these age groups were adjusted after taking deaths expected from other causes into consideration: applying 10 year age-sex England and Wales other-causes mortality rates for 1998 [15] to the study cohort gave expected rates for other-causes mortality which were then subtracted from the overall rates. Kaplan-Meier survival curves were constructed by age group for all cases and the groups compared using the log rank test for linear trend for the age groups. It was assumed that there was no loss of information to 6 months regarding the notification of death.

Results

Forty-eight hospital trusts took part. One site was excluded because they returned no outcome data. There were 1,652 patients, median 35 per hospital, inter-quartile range (IQR) 25–43. Only one hospital returned data on fewer than 20 patients. Cases were identified between June 1997 and September 1998. There were 37 District General Hospitals (1,278 patients) and 10 Teaching Hospitals (374 patients).

The distribution of patient age is shown in Figure 1. Nearly two-thirds (64%) were male. The distribution of ages of males and females was similar (males: mean age 69, SD 9; females: mean age 68, SD 10). The overall median age was also 69 years, with an IQR from 63–75 years.

A selection of the case-mix and prognostic factors that were recorded are shown in Table 1. The histological confirmation rate was inversely related to

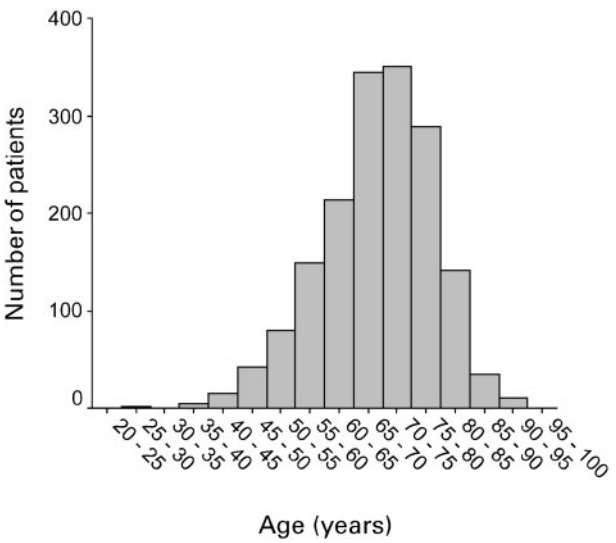

Figure 1. Age distribution for 1,647 patients.

Table 1. Patient characteristics

COPD noted	20% (324/652)
Any co-morbidity	51% (819/1620)
Performance status (known)	97% (1606/1652)
0. Normal activity without restriction or special care	31% (493)
1. Light work but physically strenuous activity limited	41% (651)
2. Self-care; unable to climb stairs; mobile > 50% of waking hours	19% (303)
3. Needs help with self care; bed/chair > 50% of waking hours	7% (116)
4. Completely disabled	3% (43)
Histology/cytology	
Unconfirmed tumours	15% (244)
Small cell lung cancer (SCLC)	18% (302)
Squamous cell	40% (664)
Adenocarcinoma	13% (222)
Large cell	2% (25)
Non-SCLC, type unknown	8% (136)
Carcinoma type unknown	2% (34)
Other (e.g. rare tumour, metastases from other primary site)	2% (25)

patient age (Table 2). No data on biopsies other than at bronchoscopy was obtained. Formal tumour, node and metastases (TNM) staging was not requested, but data included descriptions of radiological appearances, presence or absence of known metastases and the recording of other symptoms and signs that would have a bearing on operability (e.g. superior vena cava obstruction, recurrent laryngeal nerve palsy, phrenic nerve palsy and supraclavicular lymphadenopathy). Signs in addition to symptoms were reported in 521 cases. Of these, 100 (6% overall) were assessed by one of the authors (MDP) as evidence of definite metastases, 156 (9%) as indicating a high probability of metastases or inoperable disease and 265 (16%) as indeterminate. After integrating data on radiological appearances, evidence of metastases and presenting signs and symptoms, we constructed a proxy for stage and/or operability which was graded as (i) 'Potentially operable' (ii) 'Some concern' (iii) 'Unlikely to be operable' (iv) 'Clearly inoperable'. Almost half (49%) of patients were at least potentially operable (Table 3). Table 4 shows the frequency of recorded 'significant' co-morbidities by age group. Except for slightly lower rates in the youngest of the age bands (< 65), the incidence of co-morbidities did not appear to be related to age.

Active treatment

Active treatment was reported in 66% (1,082) of cases within 6 months of bronchoscopy. For a few patients, treatment started beyond 6 months (surgery 5, radiotherapy 27, chemotherapy 10 patients); these cases were taken as having had no active treatment within 6 months. Others had had treatment but no date was available; these were considered to have had treatment within 6 months (surgery 10, radiotherapy 188, chemotherapy 50 patients). Surgery was performed in 10% (170) of cases. If the proven small cell cancers are excluded, the surgical rate was 12% (167/1350). Three patients with a histological SCLC diagnosis (from bronchoscopy) underwent surgery. One was found to be an adenocarcinoma after resection. Radiotherapy was given in 44% (729) of cases and chemotherapy in 20% (335). Unfortunately, the questionnaire did not differentiate between radical or palliative thoracic or extrathoracic radiotherapy. For patients with SCLC, the chemotherapy rate was 67%

Table 4. Frequency of recorded co-morbidity by age group

Age	Patients	Any co-morbidity	COPD noted	IHD noted
< 65	484	40% (67)	14% (67)	9% (37)
65–74	670	50% (332)	22% (145)	12% (79)
75–79	281	64% (179)	27% (76)	17% (47)
80+	180	62% (112)	19% (35)	17% (31)
Unknown	5	60% (3)	20% (1)	– (–)
Total	1620	51% (819)	20% (324)	12% (194)

Table 2. Age and histological confirmation

% Histological confirmation								
	< 65 years % (*n*/*N*)	95%CI	65–74 years % (*n*/*N*)	95%CI	75+ years % (*n*/*N*)	95%CI	Chi-squared statistic*	*P* value
All patients	89% (442/496)	86–92	86% (587/683)	83–89	80% (374/468)	76–84	16.0	< 0.001
Ps = 0,1, no COPD	93% (317/342)	89–95	87% (357/412)	83–90	81% (179/220)	76–87	16.3	< 0.001

Table 3. Age and operability

	Age < 65	Age 65–74	Age 75+	Age unknown	All
Potentially operable	214 (43%)	324 (47%)	254 (54%)	2	794 (48%)
Some concern	99 (20%)	128 (19%)	87 (19%)	1	315 (19%)
Unlikely to be operable	94 (19%)	120 (18%)	81 (17%)	2	297 (18%)
Clearly inoperable	86 (17%)	98 (14%)	42 (9%)	–	226 (14%)
Indeterminate	3	13	4	–	20
All	496 (100%)	683 (100%)	468 (100%)	5	1652 (100%)

(201/302), and for the other cell types their combined rate was 10% (134/1350).

Older patients were less likely to receive active treatment of any sort (Table 5). As would be expected, patients with good performance scores were much more likely to receive active therapy. However, a much lower level of chemotherapy use in older patients with confirmed SCLC was observed in the subgroup with good performance scores and no chronic obstructive pulmonary disease (COPD). Similarly, the age related reduction in the surgical resection rate was observed even in those patients with good performance status, no significant COPD and graded as 'potentially operable'. The questionnaire did not make a distinction between radical and palliative radiotherapy and there was only a weak age-related drop in the use of recorded radiotherapy in the fittest group of patients.

Mortality

Almost half [46% (768)] of the patients died within 6 months of bronchoscopy, 16% (261) were classed as alive and either cured or in remission at 6 months, 33% (547) as alive with active tumour, whilst for 5% (76) the outcome at 6 months was unknown.

Overall mortality rates within 6 months of bronchoscopy are shown in Table 6, with survival curves set out in Figure 2. It is possible that some patients died of causes unrelated to their lung cancer. The overall mortality rates at 6 months ranged from 42% in patients aged under 65 years to 58% of those aged 75 and over.

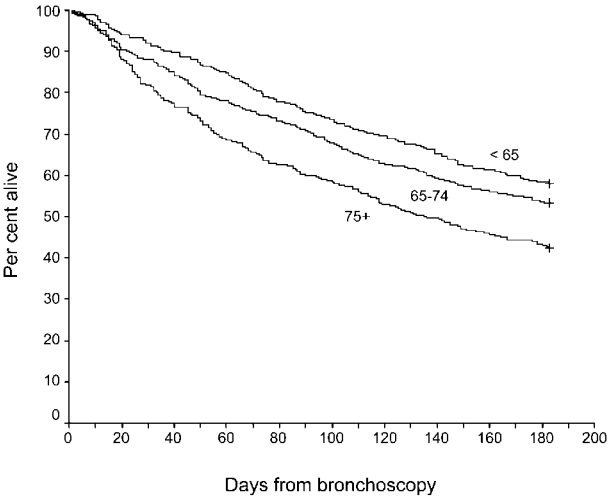

Figure 2. Survival experience by age group. Log rank statistic for linear trend = 27.3, df = 1, $P < 0.0001$.

Table 5. Age and treatment within 6 months of bronchoscopy

	< 65 years % (*n*/*N*)	95%CI	65–74 years % (*n*/*N*)	95%CI	75+ years % (*n*/*N*)	95%CI	Chi-squared statistic*	*P* value
% active treatment (surgery, chemotherapy, radiotherapy)								
All patients	78% (389/496)	75–82	67% (458/683)	64–71	49% (231/468)	45–54	89.5	< 0.001
Ps = 0, 1, no COPD, potentially operable	85% (128/151)	79–91	80% (168/209)	75–86	67% (87/129)	59–76	11.9	< 0.001
NSCLC – %Surgery								
All patients	19% (60/309)	15–24	12% (53/429)	9–16	6% (18/307)	4–9	25.8	< 0.001
Ps = 0, 1, no COPD, potentially operable	37% (40/107)	28–47	24% (34/140)	17–31	15% (13/89)	8–24	13.3	< 0.001
SCLC – %Chemotherapy								
All patients	77% (83/108)	69–85	66% (92/139)	58–74	48% (25/52)	34–62	12.7	< 0.001
Ps = 0, 1	82% (69/84)	72–90	75% (70/94)	64–83	59% (20/34)	41–75	6.6	0.01
% Radiotherapy								
All patients	45% (224/496)	41–50	47% (318/683)	43–50	39% (184/468)	35–44	3.2	0.07
Ps = 0, 1	47% (179/384)	42–52	49% (241/489)	45–54	45% (121/270)	39–51	0.1	0.75

*Test for linear trend over the age categories.

Table 6. Age and mortality within 6 months of bronchoscopy

% Mortality								
	< 65 years % (*n*/*N*)	95%CI	65–74 years % (*n*/*N*)	95%CI	75+ years % (*n*/*N*)	95%CI	Chi-squared statistic*	*P* value
All patients	42% (200/474)	38–47	47% (309/654)	43–51	58% (257/444)	53–63	22.4	< 0.001
Ps = 0, 1, no COPD, potentially operable	23% (34/145)	17–30	31% (62/200)	25–37	41% (50/123)	32–49	9.1	0.003

*Test for linear trend over the age categories.

Applying 10 year age-sex mortality rates for 1998 (England and Wales) [15] for all causes other than lung cancer to this study cohort, the expected death rates would have been 0.4%, 1.2% and 3.8% of such deaths for the three age groups. Subtraction gives adjusted rates of 42%, 46% and 54%. For the 'fittest group' of patients with good PS, no COPD and who were potentially operable, 23% of patients aged under 65 years died within 6 months of bronchoscopy, as compared to 31% aged 65–74 and 41% aged 75 and over. Adjusted rates were 23%, 30% and 36% for the three ascending age groups.

Discussion

There is good evidence that age alone is not a significant prognostic factor in lung cancer, [16, 17] with performance status, stage and certain biochemical markers being of much greater importance [17]. It therefore follows that patients should not be denied optimal treatment on the basis of chronological age alone.

Potentially operable NSCLC has been reported as being more common in the elderly [18], a finding supported by our own study (Table 3). In contrast to this we found, in common with others, that older patients are less likely to receive surgery or other therapies [13, 14, 18, 19] despite the fact that survival after surgery has been repeatedly reported to be independent of age [2, 12, 20, 21]. Zachariah *et al.* [22] found radiotherapy to be highly effective and well tolerated by patients aged 80 and older, recommending that age should not be considered a contraindication. Looking at radical radiotherapy specifically, Pignon *et al.* [23] found that the incidence of toxicity was independent of age.

Elderly patients' response rates to chemotherapy have been shown to be comparable to those of younger patient groups [24–26]. Others have concluded that for both limited and extensive Small Cell disease, chemotherapy should not be withheld from patients with SCLC on the basis of age [27].

The literature on age-related treatment rates for lung cancer generally relies on analyses that have not been controlled for key case-mix factors. In studies where some corrections were made, significantly lower treatment rates in the older age group have still been disclosed. Mor *et al.* [9] controlled for stage and co-morbidity, and found a significant inverse relationship between age and treatment with radiotherapy or chemotherapy. Guadagnoli *et al.* [13], after allowing for co-morbidity, sex, marital and socio-economic status, reported that US patients aged 74 or older with local disease had surgery less often than younger patients.

Our study was designed to control for case-mix factors like performance status, co-morbidity and a proxy for stage/operability, in order to ensure a clinically credible basis for comparison. Although formal staging was not recorded, the surrogate categorisation that we derived from the available data was equally applied to all groups. Even after adjusting for case mix, we still found a clear pattern of decreasing 'diagnostic zeal' and active treatment with increasing age. Older patients, including those with good performance status and no COPD were less likely to have a positive histological diagnosis. Since all patients in the study had had a bronchoscopy, this finding is most likely to be the result of a reluctance to carry out further invasive investigations (such as CT guided needle biopsy, mediastinoscopy etc.) in older patients. For the older patient group with a confirmed diagnosis, patients with 'potentially operable' Non-Small Cell Cancer of good performance status with no significant COPD remained significantly less likely to receive surgery. Similarly, older patients with confirmed Small Cell lung cancer were less likely to receive chemotherapy. The failure to differentiate between palliative and radical radiotherapy limits the value of our data for this treatment modality. The most concerning observation from this study, however, is the age-related mortality gradient. Patients over 75 were 50% more likely to die within 6 months of diagnosis than those aged under 65, even when adjusted for non-cancer causes of death. The mortality gradient is of similar magnitude in those with the best performance status and no obvious adverse prognostic features, so it cannot be explained by the systematic exclusion of those too ill to benefit from treatment. We did not correct for smoking status when analysing the mortality data because we did not record smoking status in our population; it is highly unlikely, however, that this would have significantly influenced the interpretation of the results.

It is possible that our findings could be explained by a number of factors other than deliberate or unconscious 'ageism' or therapeutic nihilism [28]. Various explanations have been proposed in earlier published reflections on these issues [29, 30]. For example, the elderly may be more likely to decline treatment, although there is evidence that some therapies may be equally acceptable to older and younger patients [31]. They may be perceived by clinicians (both specialist and non-specialist) or by relatives to be too 'frail' to withstand and/or benefit from aggressive interventions [29, 30].

Our data relate to those patients initially managed by respiratory physicians and who had a bronchoscopy. Since it is well recognised that many patients with lung cancer never get to see a specialist at all and that this shortcoming is more common in the elderly [1], it is highly likely that our results give an overoptimistic picture of age-related under-treatment. There will have been a number of patients in the participating centres in whom a histological diagnosis was obtained but did not undergo a bronchoscopy. They would not have been included, but the number of such patients is likely to have been small and is highly unlikely to have significantly altered the findings. This study was carried

out in the early days of the implementation of the cancer services reconfiguration process in the UK which followed the publication of the Calman and Hine report [32], the Clinical Outcomes Group Guidelines [33] and before the Urgent Referral Guidelines [34] were introduced. One would hope that these measures would lead to an increase in the proportion of elderly patients being referred to specialist multi-disciplinary teams and thus to an improvement in this particular form of discrimination in health care. Mortality rates for lung cancer are reported as being higher in the UK than in most of Europe and the USA [35, 36]. This study raises the possibility that ageism may be one of the underlying factors to explain this.

Key points

- Median age of lung cancer patients in the UK is around 69 years.
- Lower rates of histological diagnosis, active treatment, and survival were seen in older age groups, even when corrected for major case-mix factors.
- Under-treatment of lung cancer in older patients may be one factor underlying the poor survival statistics for this disease in the UK.

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