AUDIT, RESEARCH AND GUIDELINE UPDATE

Clinical management of older people with non-small cell lung cancer in England

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ABSTRACT

Data for 25261 patients with non-small cell lung cancer whose details were submitted to the National Lung Cancer Audit in England were analysed to assess the effect of age at diagnosis on their clinical management, after accounting for sex, stage, performance status and comorbidity. Multivariate logistic regression showed the odds of having histocytological confirmation and anticancer treatment decreased progressively with age, and was also lower in women. It is likely that these results have a multifactorial explanation, and further research into the attitudes of patients, carers and healthcare professionals, and clinical trials of treatment in older populations, are necessary.

INTRODUCTION

Approximately 40 000 new cases of lung cancer are diagnosed in England and Wales each year, making it the second commonest cancer in men (after prostate) and women (after breast)[1] and the commonest cause of cancer-related death in both sexes. Treatment and survival rates vary across the UK and do not match those achieved in comparable healthcare systems. Despite recent scrutiny of primary care to try to explain these observations,[2] it is possible that lower levels of investigation and treatment in older patients in secondary care may explain some of the variation observed.

The National Lung Cancer Audit (NLCA) in the UK is commissioned by the Healthcare Quality Improvement Partnership with funds from the Department of Health and maintained jointly by the Health and Social Care Information Centre and the Royal College of Physicians. It has collected data of progressively improving completeness since 2005. These are now of sufficient quality to permit analysis of factors relating to treatment and outcome.[3] We have used NLCA data to quantify the association between age and the presence of histocytological confirmation of diagnosis and/or receipt of anticancer treatment (surgery, chemotherapy or radiotherapy) in people with non-small cell lung cancer (NSCLC).

METHODS

We obtained data for the 30 098 people with lung cancer first seen in England in 2009 submitted to the NLCA. A comparison of these cases with published lung cancer registrations from the Office of National Statistics for England[1] shows that the NLCA ascertained the vast majority of lung cancers and case distribution by age at diagnosis was representative of national registry data (see online supplementary figure 1). Of all cases, we excluded those with pathologically confirmed small cell lung cancer or confirmed/suspected mesothelioma, leaving 25 261 people with histocytologically confirmed or clinically diagnosed NSCLC.

The clinical management measures were patients' receipt of histocytological confirmation of NSCLC and receipt of any anticancer treatment (recorded treatment with surgery, radiotherapy or chemotherapy). We assessed these by age at diagnosis grouped into 10-year age bands (60–69 year olds were used as the reference group in analyses), sex, stage (as classified by the American Joint Committee on Cancer and Union Internationale Contre le Cancer V.6), performance status (as classified by the Eastern Cooperative Oncology Group) and recording of a significant diagnosed comorbidity.

We used multivariate logistic regression to quantify the association of age with our clinical management outcomes, adjusting for sex and the other important clinical features. Receipt of presence of histocytological confirmation was also included as a covariate in the multivariable model for anticancer treatment. Finally we looked for evidence of interaction between age and sex by fitting a multiplicative interaction term.

All statistical analyses were carried out using Stata V.SE11.

RESULTS

The 25 261 patients with NSCLC analysed had a median age of 72 years (interquartile range 64–80). Demographics and clinical features of the patients according to age and the clinical management outcomes are shown in online supplementary tables 1 and 2. Overall, 68% of patients had histocytological confirmation of the diagnosis and 57% received anticancer treatment.

Table 1 shows the ORs for histocytological confirmation by age and sex adjusted for clinical features. Other than for patients in the youngest age group (<40 years), the multivariable model showed the odds of histocytological confirmation decreased progressively with age. For example, compared with patients aged 60–69 years, the OR was 1.4 for patients aged 40–49 and 0.36 for those aged 80–89. Female sex (OR 0.81 compared with men) and having at least one recorded comorbidity (OR 0.75) were associated with reduced odds of

histocytological confirmation, which also decreased markedly with worsening performance status, whereas the relationship with stage was n-shaped with the largest odds being in those with stage IIIB cancer.

We found a statistically significant interaction between age and sex in our multivariate model (likelihood ratio test p=0.0009) which showed that, although similar between men and women under 60 years of age, women were less likely than men to receive histocytological confirmation as they became older. For example, the OR was 1.03 (95% CI 0.66 to 1.60) for women compared with men aged 40–49 and the OR was 0.72 (95% CI 0.65 to 0.81) for patients aged 80–89 (figure 1).

For anticancer treatment, the results were very similar to those for histocytological confirmation (table 1) with the odds of anticancer treatment decreasing progressively with age. For example, compared with patients aged 60–69 years, the OR was 1.97 for patients aged 40–49 and 0.24 for those aged 80–89. Female sex (OR 0.91 compared with men) and having at least one recorded comorbidity (OR 0.75) were associated with reduced odds of anticancer treatment, which also decreased markedly with worsening performance status and disease stage. Again there was evidence of an interaction between age and sex (likelihood ratio test p=0.007), for example, the OR was 0.97 (95% CI 0.62 to 1.51) for women compared with men aged 40–49 and the OR was 0.78 (95% CI 0.69 to 0.89) for patients aged 80–89 (figure 1).

CONCLUSIONS

Our results suggest that age has an important impact on the investigation and treatment of people with lung cancer in England. After adjusting for the effects of sex, stage, performance status and comorbidity there was a progressive decline in patients' receipt of histocytological confirmation and anticancer treatment from age 50 years onwards. We also found that women with lung cancer were 19% less likely to have histocytological confirmation of their cancer than men and 9% less likely to have anticancer treatment after adjusting for important clinical features. These sex differences were mostly in patients aged 60–89 years, despite very similar proportions of lung cancers in men and women across these age groups.

The main strengths of our study are the large size of the NLCA datasets, which has been shown to be representative of people with lung cancer in the UK.[3] NLCA data completeness has progressively improved since its inception in 2005, with the result that the 30 098 patients analysed for this study represent almost 100% of the cases managed in secondary care that would be expected from population incidence figures. Furthermore comparison between our dataset and the most recently published data on cancer registrations for England does not suggest that older patients are under-represented in the audit dataset, a finding that supports more detailed previously published research.[3] The main weakness of our study is the lack of robust data on comorbidity routinely available in the NLCA, although information on stage and performance status are robust and more complete than other routine sources.

Our results are in line with earlier pilot research on a smaller cohort of 1652 patients from 48 English hospitals with all types of lung cancer which found significant inverse correlations between age and histocytological diagnosis, anticancer treatment and survival.[4] Histocytological confirmation was obtained in 89% of their patients under age 65 years and 80% in those over 75 years and anticancer treatment was given in 78%

Table 1 ORs for histocytological confirmation and anticancer treatment

	Histocytological confirmation			Anticancer treatment		
	OR*	95% CI	p Value	OR*	95% CI	p Value
Male	1	–	–	1	–	–
Female	0.81	0.77 to 0.86	<0.001	0.91	0.86 to 0.96	0.002
Age (years)						
<40	0.85	0.55 to 1.31	0.451	1.10	0.70 to 1.72	0.671
40–49	1.40	1.12 to 1.76	0.004	1.97	1.57 to 2.47	<0.001
50–59	1.34	1.19 to 1.52	<0.001	1.40	1.25 to 1.58	<0.001
60–69	1	–	–	1	–	–
70–79	0.71	0.65 to 0.76	<0.001	0.59	0.55 to 0.63	<0.001
80–89	0.36	0.33 to 0.39	<0.001	0.24	0.22 to 0.26	<0.001
>90	0.12	0.10 to 0.15	<0.001	0.07	0.05 to 0.10	<0.001
Cancer stage						
IA	1	–	–	1	–	–
IB	1.47	1.23 to 1.75	<0.001	1.29	1.07 to 1.56	0.007
IIA	1.07	0.72 to 1.58	0.735	0.99	0.65 to 1.49	0.946
IIB	1.65	1.34 to 2.02	<0.001	1.06	0.86 to 1.30	0.585
IIIA	1.66	1.40 to 1.98	<0.001	1.01	0.85 to 1.22	0.876
IIIB	1.92	1.65 to 2.25	<0.001	0.85	0.72 to 1.00	0.049
IV	1.38	1.20 to 1.59	<0.001	0.59	0.51 to 0.68	<0.001
Unknown	0.87	0.75 to 1.00	0.055	0.52	0.44 to 0.60	<0.001
Performance status						
0	1	–	–	1	–	–
1	0.93	0.83 to 1.04	0.205	0.84	0.76 to 0.94	0.002
2	0.47	0.42 to 0.53	<0.001	0.34	0.30 to 0.38	<0.001
3	0.20	0.18 to 0.23	<0.001	0.10	0.09 to 0.11	<0.001
4	0.10	0.09 to 0.12	<0.001	0.03	0.02 to 0.04	<0.001
Unknown	0.43	0.38 to 0.48	<0.001	0.31	0.28 to 0.34	<0.001
Diagnosed comorbidity	0.75	0.69 to 0.82	<0.001	0.75	0.69 to 0.82	<0.001
Histocytologically confirmed	–	–	–	4.02	3.75 to 4.30	<0.001

*Fully adjusted for all variables in the table.

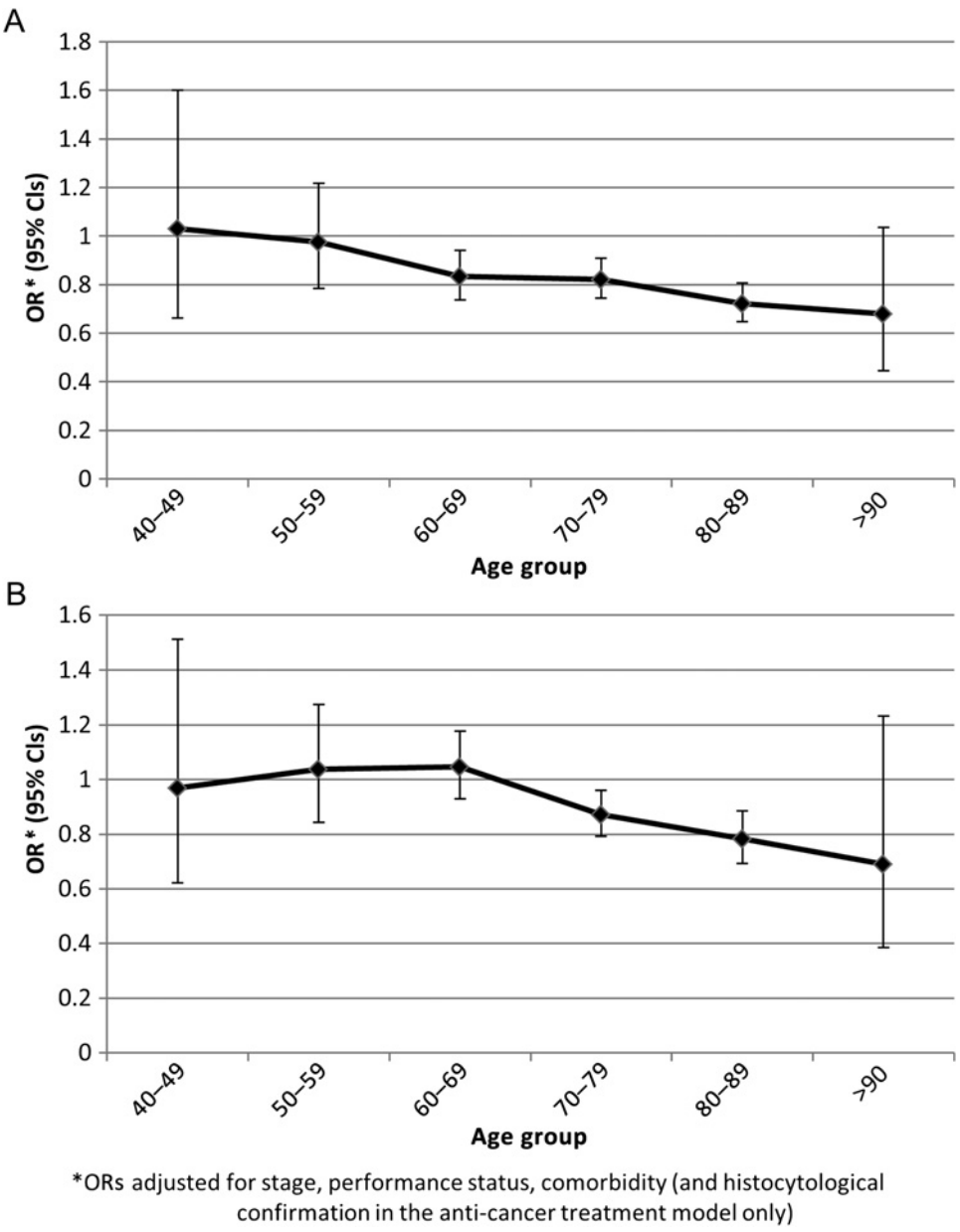

Figure 1 Odds ratios for histocytological confirmation (A) and anti-cancer treatment (B) in women compared with men (reference group), stratified by age group.

and 49% respectively. These are slightly higher confirmation and treatment proportions than in NLCA cases overall, however these 1652 patients were a more selected population by virtue of all undergoing bronchoscopy. Similar results have been obtained from studies carried out in the USA, Canada and Europe.

Although there is considerable evidence that tumours behave differently, and outcomes differ, in men and women, there is very little published research on the effect of gender on disease management in patients with lung cancer, since most research has adjusted for sex rather than examining its effect. It is difficult to find a satisfactory explanation for the results observed in our analyses. It is possible that men and women perceive the benefits of a histocytological diagnosis and anticancer treatment differently or that healthcare professionals have a different attitude to a more aggressive management approach in women.

There is good evidence that older patients with comparable clinical features to younger patients can tolerate and benefit equally from investigation and treatment. A recent European Organisation for Research and Treatment of Cancer statement on treatment in older people, based on a detailed literature review and expert consensus, acknowledges the lack of research evidence to guide clinical decisions about treatment but also clearly states that suitability for treatment should not be defined upon chronological age alone.[5]

How are patients and lung cancer multidisciplinary teams to interpret these results? It is likely that the less active approach to management of lung cancer observed in older people has a multifactorial explanation. Difficulty of access to services, therapeutic nihilism in primary and secondary care, overestimation of the risks of treatment-related toxicity, and ill-informed patient choice, based perhaps upon the experiences of friends or relatives undergoing different treatment for different cancers, may all play a part. However, it is the multidisciplinary teams who provide key decisions and it is incumbent upon them to examine more closely their own results through local audit and to consider whether their investigation and treatment protocols may inadvertently discriminate against older patients. Further research into attitudes of patients, carers and healthcare

professionals, and clinical trials of treatment in older populations are vital if we are to ensure that all patients receive the very best care, regardless of their age.

Contributors PB, RS, MDP and IW lead the team responsible for audit data. RH provided the initial idea for the analysis. PB analysed the data under the supervision of RBH and LJT. PB wrote the paper with substantial input from all authors on content, style and presentation.

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Competing interests None.

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Journal club

CPAP may reduce cardiovascular mortality in patients with OSA

This double-blind randomised crossover study of patients with moderate-to-severe obstructive sleep apnoea (OSA) compared 3 months of therapeutic continuous positive airway pressure (CPAP) with 3 months of sham CPAP with a 1 month wash-out period in between. Markers of the metabolic syndrome were measured before and after each CPAP treatment.

The study population comprised 86 CPAP naïve patients aged 30—65 who were recruited from a sleep laboratory in New Delhi, India. Exclusion criteria were previous or current treatment for hypertension, diabetes, dyslipidemia or any evidence of end-organ damage due to these conditions.

There were modest, statistically significant, reductions in systolic and diastolic blood pressure, glycated haemoglobin, triglycerides, low-density lipoprotein, non-high-density lipoprotein and total cholesterol after CPAP therapy as compared with sham therapy. Additionally, there were significant decreases in body mass index and visceral and subcutaneous fat. Carotid intimal thickness and insulin resistance did not differ significantly. Applying the authors' criteria for the metabolic syndrome, there was a net reduction in the number of patients affected.

Predefined subgroup analysis of patients whose mean adherence with CPAP was five or more hours per night (n=51) revealed, compared with the whole population, significantly greater reductions in systolic and diastolic blood pressure, glycated haemoglobin, triglyceride, LDH and total cholesterol.

The study uses surrogate end points for cardiovascular mortality. CPAP reduces cardiovascular mortality in patients with OSA and CPAP is the recommended treatment for patients with moderate-to-severe OSA.

Further research is needed before we can conclude that additional cardiovascular mortality reduction benefit accrues to this subset of patients with moderate OSA who have the metabolic syndrome.

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