OXFORD

QJM: An International Journal of Medicine, 2015, 891–897

doi: 10.1093/qjmed/hcv052
Advance Access Publication Date: 27 February 2015
Original paper

ORIGINAL PAPER

Non-small cell lung cancer in young adults: presentation and survival in the English National Lung Cancer Audit

A.L. Rich[1], A. Khakwani[2], C.M. Free[3], L.J. Tata[2], R.A. Stanley[4], M.D. Peake[4], R.B. Hubbard[2] and D.R. Baldwin[1]

From the [1]Nottingham University Hospitals and [2]Epidemiology and Public Health, Clinical Sciences Building, City Campus, Hucknall Road, Nottingham NG5 1PB, UK, [3]University Hospitals of Leicester, Glenfield Hospital, Groby Road, Leicester LE3 9QP, UK and [4]Health and Social Care Information Centre (HSCIC), 1, Trevelyan Square, Leeds LS1 6AE, UK

Address correspondence to Dr A.L. Rich, Nottingham University Hospitals, City Campus, Hucknall Road, Nottingham NG5 1PB, UK.
email: anna.rich@nottingham.ac.uk

Summary

Background: Non-small cell lung cancer (NSCLC) in young adults is a rare but devastating illness with significant socioeconomic implications, and studies of this patient subgroup are limited.
Aim: This study employed the National Lung Cancer Audit to compare the clinical features and survival of young adults with NSCLC with the older age groups.
Design: A retrospective cohort review using a validated national audit dataset.
Methods: Data were analysed for the period between 1 January 2004 and 31 December 2011. Young adults were defined as between 18 and 39 years, and all others were divided into decade age groups, up to the 80 years and above group. We performed logistic and Cox regression analyses to assess clinical outcomes.
Results: Of a total of 1 46 422 patients, 651 (0.5%) were young adults, of whom a higher proportion had adenocarcinoma (48%) than in any other age group. Stage distribution of NSCLC was similar across the age groups and 71% of young patients had stage IIIb/IV. Performance status (PS) was 0–1 for 85%. Young adults were more likely to have surgery and chemotherapy compared with the older age groups and had better overall and post-operative survival. The proportion with adenocarcinoma, better PS and that receiving surgery or chemotherapy diminished progressively with advancing decade age groups.
Conclusion: In our cohort of young adults with NSCLC, the majority had good PS despite the same late-stage disease as older patients. They were more likely to have treatment and survive longer than older patients.

Introduction

The median age of presentation of lung cancer in England is 72 years and only ∼1–2% of people are younger than 40 years of age at diagnosis.[1] There has been one large study of 2775 younger patients based on the surveillance epidemiology and end results (SEER) programme in USA, but the clinical data were relatively limited.[2] The majority of studies have been small

Received: 11 December 2014; **Revised (in revised form):** 2 February 2015

scale (range 22–115), single centre, retrospective case note reviews[1,3–8]; although one study from Shanghai did compare clinical features and outcomes for 652 adults drawn from 175 hospitals in the surrounding area.[9] Cancer Registries may be more representative of the whole population, but they often lack clinical details such as performance status (PS) and co-morbid illness.[5,10,11] Some studies have reported a poorer prognosis in young adults,[4,7,12] without a clear explanation, whilst others have reported an equivalent prognosis to older patients following surgery.[6,13,14]

This study aimed to employ the previously validated English National Lung Cancer Audit dataset (NLCA)[15] to describe the sociodemographic and clinical features, as well as treatment and survival data for patients aged 18–39 years, and to compare these features with those of older patients.

Methods

Data from NLCA for all adult patients with primary lung cancer first presenting to their National Health Service (NHS) hospital between 1 January 2004 and 31 December 2011 were used. No formal ethical approval was required as all data are anonymous. Patients aged 18 to 39 years (inclusive) at diagnosis were grouped together and the remainder of the cohort divided into 10-year age groups at diagnosis, up to those aged 80 years and older. We excluded those patients with carcinoid tumours, mesothelioma and small cell lung cancer from all analyses.

We compared the young adult group with the older groups for the following key clinical features: sex, histological subtype, World Health Organisation PS (as a marker of physical fitness) and stage at presentation (Union for International Cancer Control versions 6 and 7). Patients with systematized nomenclature of medicine (SNOMED) codes representing unknown type of lung cancer and those missing codes were grouped with non-small cell lung cancer (NSCLC).[16] The histological subtype of NSCLC was based on SNOMED codes where recorded and followed the categories defined in the NLCA data manual.[17]

The NLCA was linked to hospital episode statistics (HES) allowing the calculation of the Charlson co-morbidity Index for every patient.[18] This creates a weighted score of co-morbid disease that has been validated in cohorts of men and women with both malignant and non-malignant diseases. We derived the Townsend quintile for socioeconomic deprivation for each patient, from the lower super output area based on the residential postcode of each patient. Quintile 1 is most affluent, and quintile 5 is the least affluent.

We performed multivariate logistic regression to assess the likelihood of receiving each treatment modality across the different age groups. Patients in their 70s were used as the reference group. The definitions of having had radiotherapy and chemotherapy were based on the recording of these treatments in the patients' NLCA record. To determine surgical treatment, we identified patients in HES with an Office of Population Censuses and Surveys classification of Interventions (OPCS-4) code consistent with potentially curative surgery, as described by Powell *et al.*[19]

We assessed survival from the date of diagnosis as recorded in the NLCA database. In the absence of a diagnosis date, we used the date of their first hospital appointment to derive a surrogate date. This was done by calculating the median number of days for the whole cohort between each patient's date of first appointment and their date of diagnosis and interpolating a surrogate date of diagnosis. Only 4981 patients (3%) did not have an existing diagnosis date. An end date was generated using either the date of death (obtained from the Personal Demographics Service), or the date the dataset was downloaded, which was 31 December 2011. Cox regression analysis was used to calculate unadjusted hazard ratios for mortality in each age group referenced to patients in the 70- to 79--year group, and a multivariate model constructed to adjust for the key clinical features.

Results

There were a total of 1 76 638 patients seen at English NHS Trusts between 1 January 2004 and 31 December 2011 (first appointment). We excluded 1500 patients (0.8%) for whom the end date was prior to the start date and 14 patients who were younger than 18 years of age, leaving a total of 1 75 124 patients. The 18- to 39-year group comprised 810 patients, 0.5% of the total. Within this group of young adults, 11 (1%) had proven mesothelioma, 47 (6%) had small cell lung cancer and 101 (12%) had carcinoid tumours. These tumour groups were then excluded, leaving 651 young adults and an overall cohort of 1 46 422 patients with NSCLC.

Key clinical features

Table 1 illustrates the key clinical features by age group. The sex ratio in the young adult group was 1.3 male to female, similar to that for the whole cohort (1.4–1). The proportion of individuals with adenocarcinoma reduced with increasing age: 30%, in the 18–39 group and 19% in the 70–79 group (χ^2 test $P < 0.001$). The proportion of individuals with squamous cell carcinoma increased with age: 8% in the 18- to 39-year-old group compared with 22% in the 70–79 group (χ^2 test $P < 0.001$).

The PS at diagnosis was missing in 37% of the young group, but was recorded as 0 or 1 in 85% of the remainder. Only 9 patients were recorded with a PS of 4 (2%), compared with 2381 (6%) of the patients aged 70–79 years with PS recorded. The proportion of patients with a Charlson Index of zero (no recorded co-morbid illness in HES), declined from 55% in the young adult group to 31% in patients aged 70–79 years. Table 2 illustrates the co-morbid diseases recorded in HES at the point of diagnosis in our young adults; and although more than half had no co-morbid disease recorded, and 200 (31%) had metastatic disease from their lung cancer; a further 47 (7%) patients had another solid organ tumour prior to their lung cancer diagnosis. There were a handful of adults with conditions ranging from peptic ulcer disease, to stroke and diabetes. Data on socioeconomic status were missing in 11–13% of patients across all age groups (Table 1). In those with data, a third of young adult patients were from the least affluent socioeconomic quintile, whilst only 11% were from the most affluent. In contrast, 24% of patients aged 70–79 years at diagnosis were from the least affluent, and 16% were from the most affluent quintile (χ^2 test $P < 0.001$).

Our results showed 260 (40%) young adult patients did not have stage at diagnosis recorded in the NLCA dataset. Of the remaining 391 patients, 279 (71%) had stage 3b or stage 4 disease, and only 57 (15%) had stage I or II disease (Table 1).

Treatment

Surgical resection was performed in 134 (21%) of the young adult patients, of whom 63 also received chemotherapy, 11 radiotherapy and 10 trimodality treatment. Chemotherapy alone was given to 232 (36%) young patients with NSCLC, radiotherapy alone to 36 (6%) and combination chemo-radiotherapy

Table 1 Distribution of key clinical features across the age groups (N = 1 46 422)

Age (years)	18–39		40–49		50–59		60–69		70–79		>80 years	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
Sex												
Male	364	56	1919	52	8630	56	22749	58	30470	59	19669	55
Female	287	44	1795	48	6914	44	16272	42	21079	41	16274	45
Histological subtype												
AdenoCa	194	48	1114	43	4251	38	9116	34	9864	31	4524	31
Squamous cell	51	13	495	19	2848	26	8593	32	11124	35	5158	35
NSCLC NOS	138	34	937	36	3777	34	8684	32	10043	32	4701	32
Ca in situ	0		14	0.5	38	0.3	80	0.3	105	0.3	105	0.7
Mixed	1	0.2	13	0.5	56	0.5	128	0.5	140	0.4	59	0.4
Others	17	4	23	1	78	0.7	122	0.5	141	0.4	141	1
Missing	250		1118		4496		12298		20132		21255	
Stage												
I	37	9	280	10	1329	11	4218	14	5939	15	3756	14
II	20	5	148	5	709	6	2123	7	2774	7	1829	7
IIIA	35	9	276	10	1191	10	3290	11	4541	11	2859	11
IIIB&IV	279	71	1874	68	8011	66	18956	62	23571	59	16161	60
Uncertain	20	5	179	6	861	7	2221	7	3147	8	2369	9
Missing	260		957		3443		8213		11577		8969	
PS												
0	216	52	1062	42	3927	35	7806	27	6460	17	2168	8
1	136	33	911	36	4183	38	10676	37	12714	34	6045	23
2	25	6	317	12	1685	15	5261	19	8543	23	6676	26
3	27	7	185	7	1000	9	3606	13	7507	20	8202	32
4	9	2	64	3	346	3	1135	4	2381	6	2887	11
Missing	238		1175		4403		10637		13944		9965	
Charlson Index												
0	360	55	1882	51	6944	45	14553	37	15827	31	10697	30
1	51	8	451	12	2432	16	7750	20	10858	21	7418	21
2–3	52	8	253	7	1470	9	5660	15	10148	20	7681	21
4+	188	29	1128	30	4698	30	11058	28	14716	29	10147	28
Socioeconomic status												
1 (affluent)	64	11	408	13	1829	14	5325	15	7072	16	5410	17
2	85	15	506	16	2273	17	6187	18	8669	19	6443	20
3	107	19	598	18	2450	18	6781	20	8977	20	6778	21
4	125	22	708	22	3053	23	7658	22	9484	21	6869	21
5	185	33	1023	32	3882	29	8427	25	10826	24	6499	20
Missing	85		471		2057		4643		6521		3944	
Total	651		3714		15544		39021		51549		35943	

N, number; %, percentage excluding missing. Histology; Ca in situ, carcinoma in situ; Mixed=mixed tumour (malignant); Others, large cell carcinoma and carcinosarcoma.

to 122 (17%). A total of 147 patients (23%) in the young adult cohort had no treatment information recorded, compared with 22 600 (44%) of the 70- to 79-year-old group.

Table 3 shows the relationship between the age of a patient and the treatment they received. Young adults with NSCLC were more likely to have both surgery and chemotherapy than those aged 70–79 years (adjusted OR 1.66, 95% CI 1.32, 2.09; and 3.96, 95% CI 3.33, 4.70, respectively). There was no clear variation in the use of radiotherapy across the age groups.

Survival

Cox regression analyses revealed young adults with NSCLC had a lower overall mortality than patients from all other age groups (Table 4). Young adults who had surgery were half as likely to die compared with those aged 70–79 years treated surgically (adjusted HR 0.49, CI 0.36, 0.67). When patients with presumed NSCLC were excluded, the survival benefit for those with proven NSCLC who had surgery was reduced, but no worse than those aged 70–79 years.

Discussion

Principal findings

We have found differences in clinical features between young adults with NSCLC and older patients with some progressive trends with increasing age. We found a higher proportion of young adults had adenocarcinoma, and significantly fewer had squamous cell carcinoma. A higher proportion of patients had late stage disease at diagnosis but the PS and level of co-morbidity was more favourable. Young adults with NSCLC were 66% more likely to have surgery compared with older patients and almost four times as likely to have chemotherapy. The likelihood of receiving radiotherapy was approximately equal amongst all patients, which may reflect the use of radiotherapy in palliative as well as potentially curative treatment regimens

Table 2 Co-morbid disease recorded in HES for young adults with NSCLC ($N = 651$)

CI score	Conditions included in Charlson Index	N	%
1	Myocardial infarction/heart failure	2	0.3
1	Cerebrovascular disease	5	0.8
1	Chronic pulmonary disease	47	7
1	Dementia	0	
1	Peptic ulcer disease	2	0.3
1	Diabetes mellitus	9	1.4
1	Peripheral vascular disease	2	0.3
1	Connective tissue disease	2	0.3
1	Mild liver disease	3	0.5
2	Any tumour (not including lung)	47	7
2	Haematological malignancy	13	2
2	Diabetes mellitus with complications	2	0.3
2	Hemiplegia	2	0.3
2	Moderate/severe renal failure	1	0.2
3	Moderate/severe liver disease	0	
6	AIDS	1	0.2
6	Metastatic solid tumour	200	31
	No disease recorded in HES	355	55
	Total patients	651	

CI score, score assigned to individual disease; N, number of patients with each condition; %, percentage.

as data recorded in the NLCA cannot reliably differentiate treatment intent.

Mortality was less in the young adult group overall, and this survival advantage was maintained in those who had surgery, even if no histology was recorded pre-surgical resection.

Our data confirm previously published evidence that adenocarcinoma is more common in this young adult group and squamous cell carcinoma less common.[1,2,5,8,11,12,20,21] This may reflect both a lower smoking prevalence[22] and duration of exposure to tobacco smoke in this age group, thereby reducing the proportion of tumour types most closely linked with smoking.[23] There is evidence that the incidence of adenocarcinoma is rising overall,[24,25] with an increase in younger women (15–49 years).[10]

Strengths and limitations

The strength of our study lies in the large cohort of patients aged between 18 and 39 years, drawn from a validated, contemporary national cohort of unselected patients with lung cancer.[15] The NLCA includes robust clinical and demographic data (enhanced by linkage with HES), which can be used to assess potential inequalities in patient care and survival based on age.

A limitation of the NLCA is that a number of data fields have missing data, although the proportion of missing data fields was similar across the age groups studied. The proportion of missing data has decreased progressively over time and the quality of the dataset is improving each year.[26,27] Despite this limitation, our cohort of 651 young adult patients with NSCLC is

Table 3 Results of logistic regression analyses examining the influence of age on treatment modality received for patients with NSCLC ($N = 1\,46\,422$)

				Unadjusted			Adjusted		
	Total N	N*	%	OR	95% CI	P-value	OR	95% CI	P-value
Surgery						<0.001			<0.001
18–39	651	134	21	1.43	(1.18–1.74)		1.66	(1.32–2.09)	
40–49	37 14	764	21	1.43	(1.32–1.56)		1.59	(1.44–1.77)	
50–59	15 544	3 064	20	1.36	(1.30–1.42)		1.43	(1.35–1.52)	
60–69	39 021	7 659	20	1.35	(1.31–1.40)		1.33	(1.27–1.39)	
70–79	51 549	7 864	15	1			1		
>80	35 943	1 922	5	0.31	(0.29–0.33)		0.34	(0.32–0.36)	
Chemotherapy						<0.001			<0.001
18–39	651	397	61	4.99	(4.26–5.85)		3.96	(3.33–4.70)	
40–49	3 714	2 165	58	4.46	(4.17–4.78)		3.63	(3.37–3.91)	
50–59	15 544	8 279	53	3.64	(3.50–3.78)		3.09	(2.96–3.22)	
60–69	39 021	16 586	43	2.36	(2.29–2.43)		2.16	(2.09–2.22)	
70–79	51 549	12 287	24	1			1		
>80	35 943	1 884	5	0.17	(0.30–0.31)		0.19	(0.18–0.20)	
Radiotherapy						<0.001			<0.001
18–39	651	149	23	0.81	(0.67–0.97)		0.87	(0.72–1.05)	
40–49	3714	1 094	29	1.13	(1.05–1.22)		1.11	(1.03–1.20)	
50–59	15 544	4 637	30	1.15	(1.11–1.20)		1.11	(1.06–1.15)	
60–69	39021	11 123	29	1.08	(1.05–1.11)		1.04	(1.01–1.07)	
70–79	51 549	13 842	27	1			1		
>80	35 943	7 628	21	0.73	(0.71–0.75)		0.79	(1.08–1.13)	

N, number; N*, number of patients who had treatment within each group; OR, odds ratio; %, percentage who had treatment within each age group; Adjusted OR, adjusted for sex, stage, PS, Townsend quintile and Charlson Index.

Table 4 Results of Cox regression analyses assessing overall survival by age group ($n = 1\,46\,422$); and also the subgroup who had surgery ($n = 21\,407$), and then those with proven NSCLC who had surgery ($n = 17\,544$).

				Unadjusted			Adjusted		
	Total *N*	*N**	%	HR	95% CI	*P*-value	HR	95% CI	*P*-value
All cases ($n = 1\,46\,422$)						<0.001			<0.001
18–39	651	406	62	0.44	(0.40–0.49)		0.43	(0.39–0.47)	
40–49	3 714	2 833	76	0.67	(0.64–0.69)		0.68	(0.65–0.71)	
50–59	15 544	12 645	81	0.77	(0.76–0.79)		0.80	(0.78–0.82)	
60–69	39 021	32 195	83	0.83	(0.82–0.84)		0.88	(0.87–0.89)	
70–79	51 549	45 025	87	1			1		
>80	35 943	33 350	93	1.3	(1.28–1.32)		1.14	(1.12–1.16)	
All cases who had surgery ($n = 21\,407$)						<0.001			<0.001
18–39	134	41	31	0.46	(0.34–0.63)		0.49	(0.36–0.67)	
40–49	764	298	39	0.61	(0.54–0.69)		0.62	(0.55–0.69)	
50–59	3 064	1 347	44	0.73	(0.69–0.78)		0.72	(0.68–0.77)	
60–69	7 659	3 367	44	0.77	(0.73–0.80)		0.78	(0.74–0.81)	
70–79	7 864	4 100	52	1			1		
>80	1 922	1 164	61	1.4	(1.31–1.49)		1.38	(1.29–1.47)	
Proven NSCLC who had surgery ($n = 17544$)						<0.001			<0.001
18–39	78	27	35	0.61	(0.41–0.88)		0.61	(0.41–0.89)	
40–49	580	241	42	0.71	(0.62–0.81)		0.69	(0.61–0.79)	
50–59	2 501	1 064	43	0.74	(0.69–0.80)		0.72	(0.67–0.78)	
60–69	6 369	2 703	42	0.77	(0.73–0.81)		0.77	(0.73–0.82)	
70–79	6 489	3 251	50	1			1		
>80	1 527	856	56	1.29	(1.20–1.39)		1.31	(1.21–1.40)	

n, number; *N**, number in each age group who had died; %, percentage; HR, hazard ratios; Adjusted HR, adjusted for sex, PS, stage, Townsend quintile and Charlson Index.

the third largest described in the literature and has more comprehensive clinical data.

Comparison with other studies

There is very little published literature on lung cancer in a young adult population, and these studies are usually small, retrospective case series in one medical institution.[1,3–7] Unlike the paper from Liu *et al.*[28] our data are not restricted to one histological subtype, nor to one treatment modality, or one medical institution. Retrospective studies have confirmed the low rate of early stage disease in the young adult group demonstrated here.[4,7,8,28] Lara *et al.*[29] reported 80% of their cohort, adults <50 years of age with NSCLC from the California Registry, had stage 3 or 4 disease. Late stage at diagnosis could be attributed to young adults taking longer to present and being more likely to be symptomatic at diagnosis.[30,31] Unfortunately data regarding time from symptoms to presentation and diagnosis are not available in the NLCA. The proportion of patients without evidence of treatment appears high (23%), but it may reflect inconsistent data entry into the NLCA dataset, in addition to late stage at presentation. Green *et al.*[7] described a population with a similar high proportion of late stage disease, and the rate of 'no treatment' was 42%.

We found evidence that mortality was better in the young adult group overall, in contrast to some published data,[4,7,12,30] but in keeping with others.[1,2,28,29,31] Bourke *et al.*[8] published a multicentre retrospective study looking at variation in clinical features, treatment received and survival in young adult patients in Chicago, Israel and northern Italy. Young adult patients were compared in three distinct geographical areas, and variation found in survival which was likely to be a reflection of stage of disease at diagnosis. Within the Chicago cohort ($n = 83$), only 7% were stage I, compared with 16% of the cohort in Israel ($N = 43$). Five-year survival in Chicago was 8% compared with 25% in the Israeli young adult group. Only 5% of our patients had stage I disease. Five-year survival for our cohort is not yet available, but the results of Cox regression found no increased rate of mortality in the young compared with older patients. The largest cohort of young adult patients was described using data from the SEER programme[2] in 2010. This cohort of 2775 young adults demonstrated similar features to our English cohort, with an increased proportion of adenocarcinoma, and reduced squamous cell carcinomas. Stage 4 disease was present in 58%, compared with 36% in our cohort (with stage recorded). Five-year overall survival was better in the young adult cohort in SEER, which is in keeping with our results of overall mortality. In contrast to our linked dataset from the NLCA and HES, the SEER programme does not record information on PS, comorbidity and treatment.

Surgical case series with between 20 and 110 young adult patients[3,6,13,14] have shown no adverse survival in the young adults, which is in keeping with our findings ($n = 134$ with resected NSCLC). Duan *et al.*[32] performed a retrospective case note review of 68 patients with primary lung cancer aged <30 years, and reported a 5-year survival of 31%, and in those who had radical surgery it was 36%.

We also found that young adults with NSCLC were slightly more likely to come from less affluent areas, which may be important, given Lara *et al.*[29] described more affluent status was a marker of good prognosis. Individuals from deprived backgrounds are often hard to reach in terms of engaging with

health services and will be more likely to present with late-stage disease.

Conclusion

Our research has shown that young adult patients with NSCLC in England are more likely to have adenocarcinoma. They are less likely to have early-stage disease at presentation, but have less co-morbidities and a better PS at diagnosis than older patients. We have shown these young adults are more likely to have surgery and chemotherapy than older patients, and they are less likely to die. There was a progressive trend in the differences according to age rather than the young adult patients representing a unique or idiosyncratic group.

Funding

This work was supported by a Royal College of Physicians research fellowship. The second, fourth and seventh authors are funded by the British Lung Foundation. The authors acknowledge the support offered by the Biomedical Research Unit at Nottingham University; The NHS Information Centre for Health and Social Care; and the British Lung Foundation.

Conflict of interest: None declared.

References

1. Minami H, Yoshimura M, Matsuoka H, Toshihiko S, Tsubota N. Lung cancer treated surgically in patients <50 years of age. *Chest* 2001; **120**:32–6.
2. Subramanian J, Morgensztern D, Goodgame B, Baggstrom MQ, Gao F, Piccirillo J, *et al*. Distinctive characteristics of non-small cell lung cancer (NSCLC) in the young: a surveillance, epidemiology, and end results (SEER) analysis. *J Thorac Oncol* 2010; **5**:23–8.
3. Icard P, Regnard JF, de Napoli S, Rojas-Miranda A, Dartevelle P, Levasseur P. Primary lung cancer in young patients: a study of 82 surgically treated patients. *Ann Thorac Surg* 1992; **54**: 99–103.
4. Antkowiak JG, Regal AM, Takita H. Bronchogenic carcinoma in patients under age 40. *Ann Thorac Surg* 1989; **47**: 391–3.
5. Mauri D, Pentheroudakis G, Bafaloukos D, Pectasides D, Samantas E, Efstathiou E, *et al*. Non-small cell lung cancer in the young: a retrospective analysis of diagnosis, management and outcome data. *Anticancer Res* 2006; **26**: 3175–81.
6. Sugio K, Ishida T, Kaneko S, Yokoyama H, Sugimachi K. Surgically resected lung cancer in young adults. *Ann Thorac Surg* 1992; **53**:127–31.
7. Green LS, Fortoul TI, Ponciano G, Robles C, Rivero O. Bronchogenic cancer in patients under 40 years old. The experience of a Latin American country. *Chest* 1993; **104**: 1477–81.
8. Bourke W, Milstein D, Giura R, Donghi M, Luisetti M, Rubin AH, *et al*. Lung cancer in young adults. *Chest* 1992; **102**: 1723–9.
9. Zhang J, Chen SF, Zhen Y, Xiang J, Wu C, Bao P, *et al*. Multicenter analysis of lung cancer patients younger than 45 years in Shanghai. *Cancer* 2010; **116**:3656–62.
10. Ellis L, Fox J, Peake MD, Coleman MP. Lung cancer in young women remains rare. *Lung Cancer* 2010; **67**:124–5.
11. Lienert T, Serke M, Schonfeld N, Loddenkemper R. Lung cancer in young females. *Eur Respir J* 2000; **16**:986–90.
12. Jiang W, Kang Y, Shi GY, Zhang HY, Cai L, Sun XW, *et al*. Comparisons of multiple characteristics between young and old lung cancer patients. *Chin Med J* 2012; **125**:72–80.
13. Hanagiri T, Sugio K, Uramoto H, Sugaya M, Ono K, So T, *et al*. Results of surgical treatment for lung cancer in young adults. *Int Surg* 2008; **93**:50–4.
14. Yazgan S, Gursoy S, Yaldiz S, Basok O. Outcome of surgery for lung cancer in young and elderly patients. *Surg Today* 2005; **35**:823–7.
15. Rich AL, Tata LJ, Stanley RA, Free CM, Peake MD, Baldwin DR, *et al*. Lung cancer in England: information from the National Lung Cancer Audit (LUCADA). *Lung Cancer* 2011; **72**: 16–22.
16. Khakwani A, Rich AL, Tata LJ, Powell HA, Stanley RA, Baldwin DR, *et al*. The pathological confirmation rate of lung cancer in England using the NLCA database. *Lung Cancer* 2013; **79**: 125–31.
17. NHS Health and Social Care Information Centre. National Lung Cancer Audit: Data manual. v3.1.5. 2013.
18. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; **40**: 373–83.
19. Powell HA, Tata LJ, Baldwin DR, Stanley RA, Khakwani A, Hubbard RB. Early mortality after surgical resection for lung cancer: an analysis of the English National Lung Cancer Audit. *Thorax* 2013; **68**:826–34.
20. Kreuzer M, Wichmann HE. Lung cancer in young females. *Eur Respir J* 2001; **17**:1333–4.
21. Kreuzer M, Kreienbrock L, Gerken M, Heinrich J, Bruske-Hohlfeld I, Muller KM, *et al*. Risk factors for lung cancer in young adults. *Am J Epidemiol* 1998; **147**:1028–37.
22. Peto R, Darby S, Deo H, Silcocks P, Whitley E, Doll R. Smoking, smoking cessation, and lung cancer in the UK since 1950: combination of national statistics with two case-control studies. *BMJ* 2000; **321**:323–9.
23. Alberg AJ, Ford JG, Samet JM. Epidemiology of lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition). *Chest* 2007; **132**(**3 Suppl**):29S–55S.
24. Charloux A, Quoix E, Wolkove N, Small D, Pauli G, Kreisman H. The increasing incidence of lung adenocarcinoma: reality or artefact? A review of the epidemiology of lung adenocarcinoma. *Int J Epidemiol* 1997; **26**:14–23.
25. Devesa SS, Bray F, Vizcaino AP, Parkin DM. International lung cancer trends by histologic type: male:female differences diminishing and adenocarcinoma rates rising. *Int J Cancer* 2005; **117**:294–9.
26. NHS Health and Social Care Information Centre. National Lung Cancer Audit Report. 2010. http://www.hscic.gov.uk/catalogue/PUB02684/clin-audi-supp-prog-lung-canc-nlca-2010-rep1.pdf
27. NHS Health and Social Care Information Centre. National Lung Cancer Audit report. 2011. http://www.hscic.gov.uk/catalogue/PUB02676/clin-audi-supp-prog-lung-canc-nlca-2011-rep.pdf
28. Liu NS, Spitz MR, Kemp BL, Cooksley C, Fossella FV, Lee JS, *et al*. Adenocarcinoma of the lung in young patients: the M. D. Anderson experience. *Cancer* 2000; **88**:1837–41.

29. Lara MS, Brunson A, Wun T, Tomlinson B, Qi L, Cress R, *et al*. Predictors of survival for younger patients less than 50 years of age with non-small cell lung cancer (NSCLC): a California Cancer Registry analysis. *Lung Cancer* 2014; **85**:264–9.
30. Bryant AS, Cerfolio RJ. Differences in outcomes between younger and older patients with non-small cell lung cancer. *Ann Thorac Surg* 2008; **85**:1735–9; discussion 9.
31. Dell'Amore A, Monteverde M, Martucci N, Davoli F, Caroli G, Pipitone E, *et al*. Surgery for non-small cell lung cancer in younger patients: what are the differences? *Heart Lung Circ* 2015; **24**:62–8.
32. Duan L, You Q, Chen X, Wang H, Zhang H, Xie D, *et al*. Outcome and prognosis for patients younger than thirty with primary lung cancer. *Minerva Chir* 2013; **68**:175–82.