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Original Article

Primary lung cancer in women after previous breast cancer

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Abstract

Background: Breast cancer is the most common malignancy among women in the USA. Improved survival has resulted in increasing incidence of second primary malignancies, of which lung cancer is the most common. The United States Preventive Services Task Force (USPSTF) guidelines for lung-cancer screening do not include previous malignancy as a high-risk feature requiring evaluation. The aim of this study was to compare women undergoing resection for lung cancer with and without a history of breast cancer and to assess whether there were differences in stage at diagnosis, survival and eligibility for lung-cancer screening between the two groups.

Methods: Women who underwent lung-cancer resection between 2000 and 2017 were identified. Demographic, clinicopathological, treatment and outcomes data were compared between patients with a history of breast cancer (BC-Lung) and patients without a history of breast cancer (P-Lung) before lung cancer.

Results: Of 2192 patients included, 331 (15.1 per cent) were in the BC-Lung group. The most common method of lung-cancer diagnosis in the BC-Lung group was breast-cancer surveillance or work-up imaging. Patients in the BC-Lung group had an earlier stage of lung cancer at the time of diagnosis. Five-year overall survival was not statistically significantly different between groups (73.3 per cent for both). Overall, 58.4 per cent of patients (1281 patients) had a history of smoking, and 33.3 per cent (731 patients) met the current criteria for lung-cancer screening.

Conclusion: Differences in stage at diagnosis of lung cancer and treatment selection were observed between patients with and without a history of breast cancer. Overall, there were no statistically significant differences in genomic or oncogenic pathway alterations between the two groups, which suggests that lung cancer in patients who previously had breast cancer may not be affected at the genomic level by the previous breast cancer. The most important finding of the study was that a high percentage of women with lung cancer, regardless of breast-cancer history, did not meet the current USPSTF criteria for lung-cancer screening.

Introduction

There has been an increasing call in the surgical literature for better understanding of sex-specific differences in disease presentation and outcomes[1,2]. Breast cancer is the most commonly diagnosed malignancy among women in the USA, accounting for 30 per cent of new cancer diagnoses[3]. Improvements in screening and treatment have resulted in an increase in 5-year overall survival rate of more than 20 per cent in the last 40 years, with the current rate reaching 90 per cent[3]. With more early-stage diagnoses, long-term prognosis has improved, and the incidence of second primary malignancies, a leading cause of death among breast cancer survivors, has increased[4,5]. By 10 years after breast-cancer diagnosis, up to 10 per cent of women will have a second malignancy, of which lung cancer is the most common[6,7].

In the USA, 112 520 women were expected to be diagnosed with new lung cancer in 2020[3]. Given that lung cancer has a 5-year overall survival rate of less than 20 per cent (highlighting the benefits of early-stage diagnosis), a better understanding of lung cancer in women with a history of breast cancer could have important implications for screening and surveillance[3].

Because of the survival implications of diagnosis at an early stage, lung-cancer screening with low-dose computed tomography (LDCT) is recommended for selected high-risk adults by the United States Preventive Services Task Force (USPSTF) guidelines, which serve as the foundation for insurance reimbursement. The most recent guidelines from the USPSTF, published in 2014, recommend annual screening for lung cancer with LDCT in adults aged 55 to 80 years with a 30-pack-year smoking history[8]. However, in July 2020, it was announced that the USPSTF 2014 recommendation would be updated to expand screening for adults aged 50 to 80 years who have a 20-pack-year smoking history[9]. Changes to the previous guidelines reflect new evidence from a systematic review as well as from collaborative modelling studies commissioned by the USPSTF that suggested a benefit associated with screening patients at a younger age and with a shorter smoking history[10,11].

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It remains unknown whether the clinical presentation, tumour behaviour and prognosis of lung cancer in women with a history of breast cancer differ from those in other women presenting with lung cancer. Two available studies that compared cohorts drawn from the Surveillance, Epidemiology, and End Results (SEER) database were limited by their inability to evaluate smoking behaviour, a previously demonstrated risk factor for second primary lung cancer[12–14]. The objective of this study was to compare women undergoing resection for lung cancer with and without a history of breast cancer. More specifically, the aim was to assess whether there were differences in stage at diagnosis, survival and eligibility for lung-cancer screening between the two groups.

Methods

Patient cohort and data collection

Women who presented to Memorial Sloan Kettering Cancer Center for lung cancer resection between January 2000 and December 2017 were identified from a prospectively maintained institutional database. Only patients who underwent surgical resection for a first-time lung cancer during this period were included. This study was conducted in accordance with the amended Declaration of Helsinki. Demographic and clinicopathological characteristics and treatment and survival data were reviewed following approval from the institutional review board, which waived the need for patient consent. Characteristics and outcomes were compared between patients with a history of breast cancer before lung cancer (BC-Lung) and patients with primary lung cancer without a history of breast cancer (P-Lung). The BC-Lung group included patients with a diagnosis of breast cancer, ductal carcinoma *in situ* and lobular carcinoma *in situ* at any time before lung-cancer diagnosis.

Staging was performed in accordance with the American Joint Committee on Cancer, 8th edition guidelines[15]. Clinical stage was determined, in accordance with the standard institutional approach, using computed tomography (CT), positron emission tomography–CT and bronchoscopy. Induction therapy, including chemotherapy with or without radiation therapy, was administered for patients with locoregionally advanced disease unless contraindicated. The extent of surgical resection was determined by the location and stage of the tumour.

Among patients with a history of breast cancer, variables of interest included prior staging, receptor status and treatment. For patients with a history of multiple primary breast cancers, the date of breast-cancer diagnosis was selected as the first incidence of breast neoplasm. Treatments of interest included anti-oestrogen therapy and/or radiation therapy. Previous data suggested that a latency period of at least 10 years may be associated with lung cancer associated with mediastinal radiation therapy[14]. A subanalysis was performed among patients in the BC-Lung group who had undergone radiation therapy for breast cancer less than 10 and over 10 years before lung cancer diagnosis to assess for differences among those with presumed radiation-therapy-associated disease.

Genomic and oncogenic pathway alterations

Sequencing for the Memorial Sloan Kettering–Integrated Mutation Profiling of Actionable Cancer Targets (MSK-IMPACT) platform was performed as previously described[16]. Patient clinicopathological data were matched with genomic data and visualized using the cBioPortal for Cancer Genomics[17,18]. Tumour DNA and corresponding patient-matched blood DNA were extracted. All exons and selected introns were sequenced using the MSK-IMPACT panel to identify somatic alterations, copy number alterations and mutations. Median sequencing coverage was 764X (range, 164X to 1424X). Tumour mutational burden (TMB) was defined as the total number of non-synonymous single-nucleotide or insertion or deletion mutations divided by the number of Mbs in the coding region captured by each panel (0.98, 1.06 and 1.22 Mb in the 341-, 410- and 468-gene panels, respectively)[19]. The authors have previously shown that TMB calculations using this next-generation sequencing panel are strongly associated with the TMB assessed by whole-exome sequencing[19]. The fraction of genome altered, or the fraction of the genome that has been affected by copy number gains or losses, was defined as the fraction of log2 copy number variation (gain or loss) greater than 0.2 divided by the size of the genome whose copy number was profiled. This study evaluated 10 canonical signalling pathways using the templates provided in the signalling pathways manuscript from The Cancer Genome Atlas Pan Cancer Atlas project[20]. The pathways analysed were cell cycle, Hippo, Myc, Notch, oxidative stress response/Nrf2, PI3K, receptor-tyrosine kinase (RTK)/RAS/MAPK, TGFβ, p53 and β-catenin/Wnt. In total, 109 genes were identified at the intersection of the *a priori* pathway templates and the MSK-IMPACT panel[20]. A tumour was considered to be altered in the specific pathway when one or more gene relative to control in the corresponding pathway template was altered. The status of specific pathways was determined to be either altered or wild-type for each patient. Number of pathways altered was calculated as the total number of altered pathways out of the 10 identified pathways for each patient.

Statistical analysis

Outcomes of interest included lung cancer stage at diagnosis, smoking history, eligibility for lung cancer screening and overall survival after lung cancer resection. Patients who met the criteria for lung cancer screening as defined by the 2014 USPSTF guidelines were adults aged 55–80 years with a 30-pack-year smoking history; those who met the criteria by the 2020 USPSTF guidelines were adults aged 50–80 years with a 20-pack-year smoking history.

Categorical variables were compared using the χ^2 or Fisher's exact test, as appropriate, and are presented as percentages. Continuous data were compared using the Wilcoxon rank-sum test and are presented as median (i.q.r.). Overall survival, defined from the time of surgery to the time of death or last follow-up, was evaluated using Kaplan–Meier analysis and compared between groups using the log rank test. $P < 0.050$ was considered to indicate statistical significance. Analysis was performed using SAS, version 9.4 (SAS Institute, Cary, North Carolina, USA).

Results

In total, 2192 patients met the inclusion criteria and were included in the study (*Fig. 1*). Of these, 331 patients (15.1 per cent) were in the BC-Lung group and 1861 (84.9 per cent) were in the P-Lung group.

Characteristics of the BC-Lung group

The most common method of lung cancer diagnosis among patients in the BC-Lung group was breast cancer surveillance or work-up imaging (154 of 331 patients, 46.5 per cent) (*Fig. 2*). The median interval between breast cancer diagnosis and lung cancer diagnosis was 110 (range 1–644) months. Most patients had early-stage breast cancer; 61.0 per cent received breast radiation

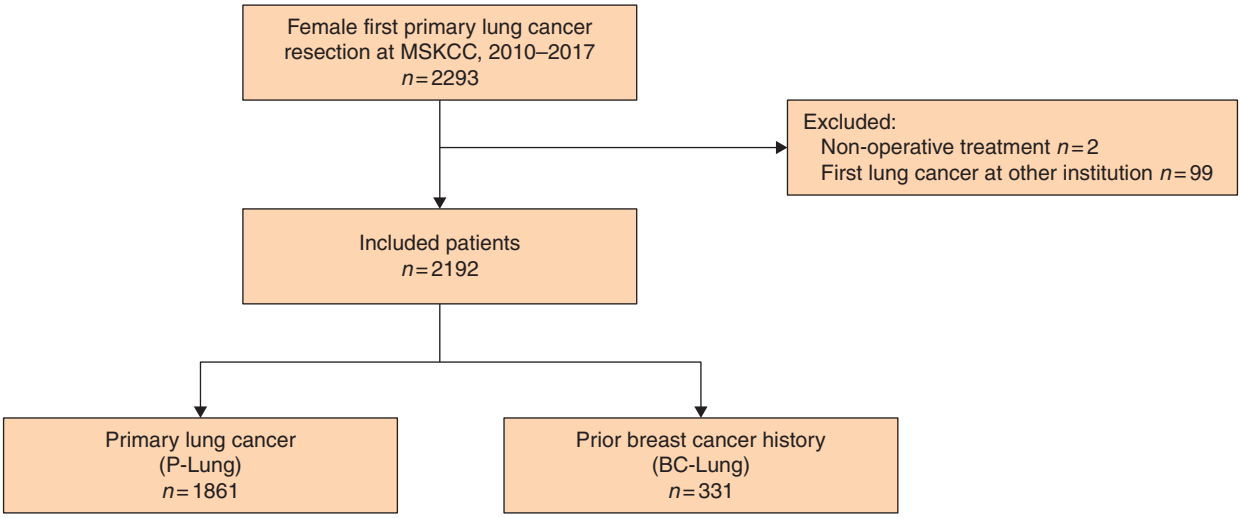

Fig. 1 Study flow chart MSKCC, Memorial Sloan Kettering Cancer Center

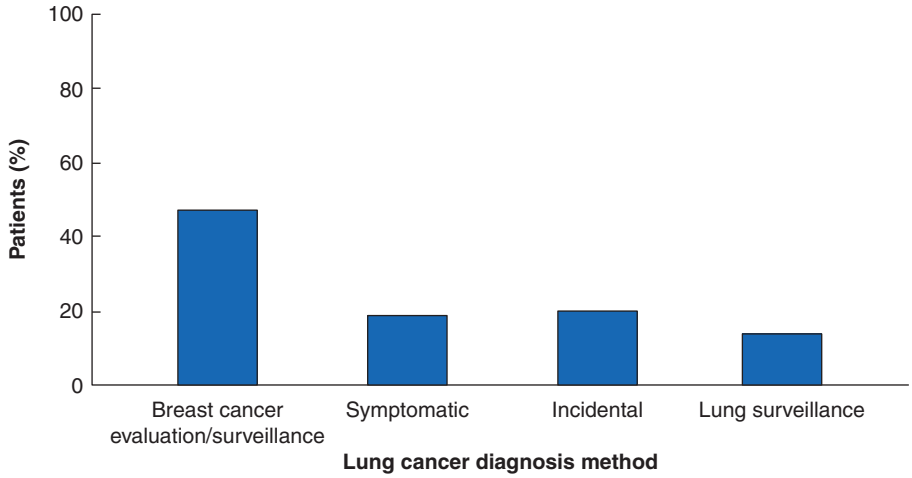

Fig. 2 Lung cancer diagnosis method among patients with breast cancer before lung cancer

therapy. Among patients with available data, most patients had oestrogen-receptor-positive and human epidermal receptor 2 (HER2)-negative breast cancer (*Table 1*).

Comparison between P-Lung and BC-Lung groups

Table 2 shows characteristics of the P-Lung and BC-Lung groups. Patients in the BC-Lung group were older at the time of lung cancer diagnosis (median, 70 *versus* 67 years; $P < 0.001$) and had a higher Zubrod score[21]. Tumour size on diagnostic CT scan was greater in the P-Lung group, and patients in the P-Lung group had more advanced clinical T stage tumours and were more likely to have node-positive disease. Patients in the P-Lung group received induction therapy more frequently and underwent more extensive resection. There were no statistically significant differences in histological subtype between the groups; however, patients in the BC-Lung group had earlier-stage disease. Survival was not statistically significantly different between the two groups: 5-year overall survival was 73 (95 per cent c.i. 71 to 76) per cent for the P-Lung group and 73 (95 per cent c.i. 68 to 79) per cent for the BC-Lung group (*Fig. 3*).

Smoking and lung-cancer screening

Overall, 58.4 per cent of patients (1281 patients) had a history of smoking. Using the 2014 USPSTF guidelines, 33.3 per cent of patients (731 patients) met the criteria for lung-cancer screening; using the 2020 guidelines, 44.9 per cent (985 patients) met the criteria. Although patients in the BC-Lung group had a significantly higher median pack-year history, there was no statistically significant difference between groups in terms of meeting the screening criteria. *Fig. 4* demonstrates that the majority of women overall, and especially those with a history of breast cancer, were below the thresholds for the 2014 USPSTF recommendations for lung-cancer screening; that is, younger and with a shorter pack-year history.

Radiation among the BC-Lung group

Among patients in the BC-Lung group, there were no statistically significant differences in clinicopathological characteristics or survival outcomes between those with and without a history of radiation therapy, with the exception of age: patients with a history of radiation therapy were older at the time of lung-cancer diagnosis (median (i.q.r.) age, 72 (54–89) *versus* 69 (27–91) years;

Table 1 Characteristics of patients with lung cancer after breast cancer

Characteristic	Patients ($n = 331$)
Age at breast cancer diagnosis (years)	
<50	95 (28.7)
50–59	84 (25.4)
60–69	97 (29.3)
70–79	45 (13.6)
≥80	10 (3.0)
Breast cancer stage ($n = 329$)	
Early	210 (63.8)
Advanced	92 (28.0)
NA	27 (8.2)
Oestrogen-receptor status ($n = 330$)	
Positive	152 (46.0)
Negative	38 (11.5)
NA	140 (42.4)
Progesterone-receptor status	
Positive	124 (37.6)
Negative	60 (18.2)
NA	147 (44.5)
HER2 status	
Positive	19 (5.8)
Negative	147 (44.5)
NA	165 (50.0)
Anti-oestrogen therapy	
Yes	166 (50.3)
No	148 (44.9)
NA	17 (5.2)
Radiation therapy	
Yes	202 (61.2)
No	119 (36.1)
NA	10 (3.0)
Interval to lung cancer (years) ($n = 319$)	
0–5	105 (33.0)
>5	214 (67.1)

Values in parentheses are percentages. HER2, human epidermal receptor 2; NA, not available.

$P = 0.002$). Of note, 79 of 100 patients (79.0 per cent) with a history of radiation therapy had a smoking history.

Genomic alterations and oncogenic pathways

An analysis of genomic alterations using 590 primary non-small-cell lung-cancer tumours for which MSK-IMPACT data were available was performed (P-Lung, 517 patients; BC-Lung, 73 patients). Common non-small-cell lung cancer driver genes were evenly distributed between the P-Lung and BC-Lung groups: *KRAS* (36 *versus* 27 per cent; $P = 0.159$), *EGFR* (26 *versus* 30 per cent; $P = 0.489$), *BRAF* (4 *versus* 6 per cent; $P = 0.523$), *ALK* (2 *versus* 3 per cent; $P = 0.669$), *ROS1* (1 *versus* 0 per cent; $P = >0.999$) and *MET* (4 *versus* 6 per cent; $P = 0.336$). Next, genes that were altered in 5 per cent of more of the cohort were compared. No statistically significant differences between the P-Lung and BC-Lung groups were identified: *PIK3CA* (5 *versus* 7 per cent; $P = 0.571$), *NF1* (6 *versus* 3 per cent; $P = 0.409$), *RBM10* (11 *versus* 10 per cent; $P = 0.784$), *STK11* (13 *versus* 15 per cent; $P = 0.653$) and *TP53* (38 *versus* 40 per cent; $P = 0.741$). In addition, there were no statistically significant differences in TMB (5.3 *versus* 4.4; $P = 0.084$) or fraction of genome altered (3.9 *versus* 4.7 per cent; $P = 0.813$) between the two groups.

Finally, the alteration frequencies of ten canonical oncogenic pathways between the two groups were assessed. Two pathways were commonly altered in both groups: p53 and RTK/RAS. The TGFβ pathway was least altered in the P-Lung group (11 of 517 patients, 2.1 per cent), whereas the Notch pathway was least altered in the BC-Lung group (0 of 73 patients, 0 per cent). There was a statistically significant difference in the alteration frequency of the Notch pathway between the P-Lung and BC-Lung groups (6.2 per cent (32 of 517 patients) *versus* 0 per cent (0 of 73 patients); $P = 0.024$). Mean number of pathways altered was not statistically significantly different between the two groups (1.99 *versus* 1.93; $P = 0.685$).

Discussion

The most common cancers among women in the USA are lung cancer and breast cancer. Given that the incidence of lung cancer is higher in breast cancer survivors than in the general population, a better understanding of the relationship between these two cancers is important to improve, potentially, long-term survival in this population[13]. There were differences in stage at diagnosis and treatment selection observed between patients in the BC-Lung and P-Lung groups. Additionally, overall, there were no statistically significant differences in genomic or oncogenic pathway alterations between the two groups, which suggests that lung cancer in patients who previously had breast cancer may not be affected at the genomic level by the previous breast cancer. The most important finding of the study was that a high percentage of women with lung cancer, regardless of breast cancer history, did not meet the current USPSTF criteria for lung cancer screening.

Like the SEER analysis of incidence by Milano and colleagues[22], the present study demonstrated that patients with a history of breast cancer had earlier-stage disease than patients without a history of breast cancer. Nearly half of patients in the BC-Lung group had their lung cancer diagnosed as a result of breast cancer surveillance imaging, which may play an important role in the observed disparities in stage. However, analyses of more than 6000 women with secondary primary lung cancer after breast cancer found that up to 42 per cent had distant-stage disease at the time of diagnosis, highlighting an ongoing need to improve the current screening recommendations for all populations[13,22].

Under the Affordable Care Act, insurers are required to cover all USPSTF Grade A and B screening recommendations, with no out-of-pocket costs[23]. The 2014 USPSTF guidelines for lung cancer screening recommend annual screening with LDCT for all adults aged 55–80 years with at least a 30-pack-year smoking history who are either current smokers or former smokers who have quit within the last 15 years (Grade B recommendation)[8]. This guideline was based on the 2011 National Lung Screening Trial, which demonstrated that LDCT screening was associated with an increased rate of early-stage lung cancer diagnosis and a 20 per cent reduction in mortality rate, compared with annual chest radiography[24].

There are important disparities in lung cancer screening that result from the USPSTF guidelines, as they do not account for variations in the risk of lung cancer among smokers. Women and racial and ethnic minorities have been repeatedly shown to have a higher risk of developing lung cancer with a shorter or lighter smoking history, and these individuals are often not considered eligible for screening as a result of the 30-pack-year limit[25–30]. As a result, most clinical trials do not adequately represent female patients, and often conclusions taken from studies that include mostly men are applied to women.

In 2019, the Nederlands–Leuvens Longkanker Screenings Onderzoek (NELSON) trial, which included more than 15 000 patients, revealed a statistically significant reduction in mortality rate with lung cancer screening performed among younger high-risk individuals with a lighter smoking history[31]. The Cancer Intervention and Surveillance Modeling Network (CISNET) studies provided further strong support for lung cancer screening

Table 2 Characteristics of patients with and without breast cancer before lung cancer

Characteristic	P-Lung ($n = 1861$)	BC-Lung ($n = 331$)	P
Age at lung cancer diagnosis (years)			
<50	117 (6.3)	12 (3.6)	<0.001
50–59	340 (18.3)	41 (12.4)	
60–69	661 (35.5)	99 (29.9)	
70–79	580 (31.2)	143 (43.2)	
80+	163 (8.8)	36 (10.9)	
Smoking			0.918
Current	202 (10.9)	34 (10.3)	
Former	1169 (62.8)	207 (62.5)	
Never	490 (26.3)	90 (27.2)	
Pack-years*	20 (0–272)	16 (0–118)	0.167
Zubrod score†			0.011
0	1364 (73.3)	229 (69.2)	
1–2	281 (15.1)	70 (21.1)	
Cardiac co-morbidity	984 (52.9)	185 (55.9)	0.345
Pulmonary co-morbidity	549 (29.5)	88 (26.6)	0.307
Eligible for screening‡	629 (33.8)	103 (31.1)	0.296
Clinical T stage			0.005
1	1267 (68.1)	259 (78.2)	
2	339 (18.2)	42 (12.7)	
3	164 (8.8)	20 (6.0)	
4	81 (4.4)	10 (3.0)	
Clinical node positive	362 (19.5)	48 (14.5)	0.036
Clinical stage			<0.001
1	1279 (68.1)	260 (78.5)	
2	258 (13.9)	37 (11.2)	
3	290 (15.6)	33 (10.0)	
4	34 (1.8)	0 (0)	
Induction therapy			
Any	302 (16.2)	28 (8.5)	<0.001
Chemotherapy	302 (16.2)	28 (8.5)	0.029
Radiation	37 (2.0)	3 (0.9)	0.605
Procedure			0.012
Bilobectomy/pneumonectomy	91 (4.9)	10 (3.0)	
Lobectomy	1202 (64.6)	191 (57.7)	
Segmentectomy	157 (8.4)	36 (10.9)	
Wedge	411 (22.1)	94 (28.4)	
Pathological size (cm)*	2 (0–19.5)	1.7 (0.1–10.5)	<0.001
Histological subtype			0.286
Adenocarcinoma	1386 (74.5)	255 (77.0)	
Neuroendocrine	216 (11.6)	27 (8.2)	
Squamous cell carcinoma	163 (8.8)	31 (9.4)	
Mixed/other non-small cell lung cancer	80 (4.3)	13 (3.9)	
Small cell carcinoma	16 (0.9)	5 (1.5)	
Pathological stage			0.006
0	34 (1.8)	6 (1.8)	
1	1201 (64.5)	245 (74.0)	
2	274 (14.7)	34 (10.3)	
3	301 (16.2)	44 (13.3)	
4	51 (2.7)	2 (0.6)	

Values in parentheses are percentages unless indicated otherwise; *values are median (range). † $n3 = 1645$ and $n = 299$. ‡ Aged 55–80 years, smoking history of 30+ pack-years. Continuous variables were compared using the Wilcoxon rank sum test. Categorical variables were compared using the $\chi 2$ test or Fisher's exact test when the expected cell count was <5. P-lung, no breast cancer before lung-cancer diagnosis; BC-Lung, breast cancer before lung-cancer diagnosis.

among younger high-risk individuals[10]. Both of these studies ultimately prompted the recent expansion of these guidelines to include adults aged 50–80 years who have a 20-pack-year smoking history and currently smoke or have quit within the last 15 years[32]. Although the new guidelines reduce the pack-year history and age cutoffs for screening, non-smokers are not included. This is very important given the observation that nearly half of the women included in the study did not have a history of smoking. As such, the role of imaging for other causes, such as cancer surveillance, becomes especially important for early cancer diagnosis.

The recent expansion of the USPSTF guidelines was predicted to lead to a relative increase in the percentage of persons eligible for screening to 81 per cent in men and 96 per cent in women[10]. Additionally, although women represented only 14 per cent of the patients enrolled in the NELSON trial, data from long-term follow-up suggest greater survival benefits for screening in women than in men, highlighting the need for further studies specifically aimed at understanding the unique aspects of lung-cancer screening in women[31].

Despite differences in stage at diagnosis, patients in the BC-Lung group did not have better survival. Possible explanations for

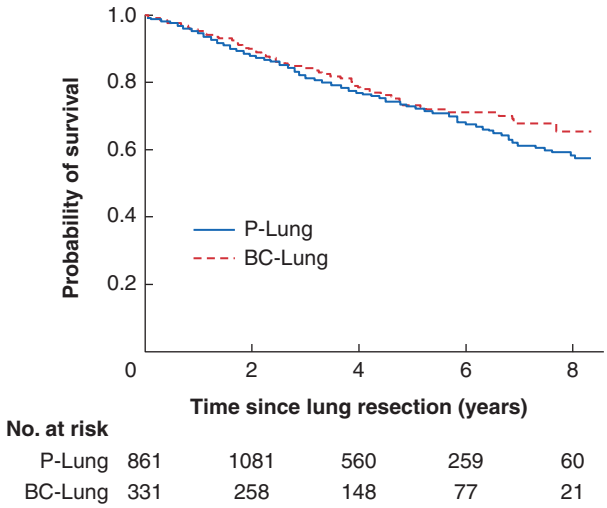

Fig. 3 Overall survival

Comparison of overall survival between patients with (BC-Lung) and without (P-Lung) breast cancer before lung cancer. Log-rank test $P = 0.241$.

this observation include a compromised immune response in patients with a history of cancer treatment and decreased use of multimodality treatment owing to concerns of toxicity secondary to prior treatment. However, because of the retrospective nature of the data, the analysis did not account for death specific to treatment-related toxicity in breast cancer treatment. This may account for the failure to observe a difference in overall survival between groups despite earlier stage of diagnosis.

The relationship between breast cancer and second primary cancers is likely to be multifactorial. Previous population-based studies have demonstrated that the relationship between radiation therapy and increased risk of lung cancer after breast cancer may begin at over 10 years[33,34]. Interestingly, the relationship between radiation therapy and lung cancer after breast cancer may be especially pertinent to women with a history of smoking. In a population-based case-control study of women with breast cancer, smokers who underwent radiation therapy had an 18.9-times greater chance of developing lung cancer, compared with non-smokers who did not undergo radiation therapy. In comparison, among women who did not receive radiation therapy, smoking imposed an increased risk of only 5.9 times[35]. In the present series, 80 per cent of women who had received radiation therapy had a history of smoking. Unfortunately, the study nature does not allow for calculation of the incidence of lung cancer among all patients with breast cancer who underwent radiation therapy; however, once lung cancer was diagnosed, there was no statistically significant difference in outcomes between patients who did and did not receive radiation therapy for previous breast cancer.

Oestrogen plays an important role in lung cancer carcinogenesis through *EGFR* activation[36]. Although data on hormone receptor and anti-oestrogen therapy use are missing for many patients, the available data demonstrated a low rate of HER2-positive breast cancers in the BC-Lung group. Previous data suggest an increased risk of lung cancer in patients with oestrogen receptor-negative, progesterone receptor-negative, HER2-negative, or triple-negative breast cancer[13]. Anti-oestrogen treatment has been demonstrated to decrease the incidence of lung cancer and has been associated with improved long-term survival in patients with lung cancer after breast cancer[12,37]. Future studies should seek to identify high-risk populations on the basis of hormone-receptor status and anti-oestrogen therapy use.

This study has several limitations. The patients only came under the care of the study institution at the time of lung cancer resection, and therefore the results cannot comment on the incidence of lung cancer after breast cancer or risk factors that predict it (that is, radiation, chemotherapy, anti-oestrogen therapy). Future genetic analysis may allow for better prediction of which patients are at the highest risk of developing secondary lung cancer. Furthermore, in determination of eligibility for lung cancer screening according to the USPSTF guidelines, all patients

Fig. 4 Scatterplot by age and pack-years

The yellow shaded area indicates eligibility for screening. P-lung, no breast cancer before lung-cancer diagnosis; BC-Lung, breast cancer before lung-cancer diagnosis.

with an over 30-pack-year smoking history were included, and the analysis did not account for time since quitting smoking. However, if the results had accounted for time since quitting smoking, even fewer patients would have been considered to be eligible by the USPSTF criteria, highlighting the important need for identification of better screening criteria for lung cancer in women. Finally, this study evaluated overall survival rather than cancer-specific survival. However, given that the risk of secondary cancer after primary lung cancer treatment is up to 12 per cent, a limitation of many studies of this nature is the inability to determine which cancer was truly responsible for cancer-specific death[38].

In this population of women undergoing lung cancer resection, the majority did not meet the current guidelines for lung cancer screening, despite a high rate of smoking. The earlier stage of disease at the time of diagnosis observed among women with a history of breast cancer may reflect better surveillance and underscores the need for adherence to cancer-screening guidelines as part of survivorship care. To reduce late-stage cancer diagnoses, further assessment of guidelines for lung cancer screening for all women may be needed.

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