

The extent of lymph node dissection is not associated with disease-free survival following lobar or sublobar resection: results from CALGB 140503 (Alliance)

Objective

The extent of lymphadenectomy in patients (pts) with c-stage I non-small cell lung cancer (NSCLC) is controversial. CALGB 140503 (Alliance; NCT00499330) randomized pts with peripheral c-stage 1A NSCLC \geq 2 cm to lobar (LR) or sublobar resection (SLR). Pts were eligible for randomization after frozen section examination of \geq 2 mediastinal and 1 major hilar node (simple sampling) confirmed the absence of nodal metastases. After randomization, additional node dissection was performed at the investigator's discretion and included simple sampling (S), systematic sampling (SS), or complete lymph node dissection (CLND). We report the impact of the extent of LND on recurrence- and disease-free survival (RFS and DFS) in this trial.

Methods

Between 6/2007 and 3/2017, 697 pts were randomized to LR (357) or SLR (340). 182 had CLND, 349 had SS and 158 had S. DFS was defined as time to lung cancer (LC) recurrence and/or all-cause mortality. RFS was defined as the time to LC recurrence or death from LC. Survival endpoints were estimated by the Kaplan–Meier method. Hazard ratios and their confidence intervals were estimated using stratified Cox proportional-hazards models.

Results

Baseline characteristics were similar between groups (Table) except that pts who had S were more likely to have SLR, pts who had SS had more squamous cell cancers and pts who had CLND had more nodal stations sampled. 5-year (yr) DFS was 62.3% (95%CI: 55.2 \pm 70.4%) after CLND, 65.7% (95%CI: 60.7 \pm 71.2%) after SS, and 61.2% (95%CI: 53.7 \pm 69.7%) after S ($p=0.306$). DFS was not statistically significantly different between LR and SLR based on the extent of node dissection. 5-yr DFS among pts who had CLND was 65% (95%CI: 56.4 \pm 76.6%) after LR and 58.5% (95%CI: 48.2 \pm 71.1%) after SLR ($p=0.530$). 5-yr DFS in pts who had S/SS was 63.4% (95%CI: 57.5 \pm 69.8%) after LR and 65.0% (95%CI: 59.1 \pm 71.5%) after SLR ($p=0.702$). 5-yr RFS for pts who had CLND was 72.5% (95%CI: 63.5 \pm 82.9%) after LR and 68.9% (95%CI: 59.0 \pm 80.5%) after SLR ($p=0.526$). 5-yr RFS in pts who had S/SS was 70.6% (95%CI: 64.9 \pm 76.9%) after LR and 70.4% (95%CI: 64.6 \pm 76.7%) after SLR ($p=0.764$).

Conclusions

In pts with peripheral c-stage IA NSCLC \geq 2 cm in size who had no nodal metastases to at least 2 mediastinal and 1 major hilar lymph nodes, there was no difference in DFS or RFS based on the extent of lymph node dissection irrespective of the magnitude of parenchymal resection.

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Table: Demographic and clinical characteristics

	Node dissection (CLND) (N=182)	Systematic sampling (SS) (N=182)	Simple sampling (S) (N=158)	Total (N=689)	P-value
Split Window					
Age (Years)					0.2057
Median (Range)	69.1 (43.2, 89.7)	67.8 (43.1, 88.9)	66.7 (46.8, 85.2)	67.8 (43.1, 89.7)	
Treatment Randomized to	, n (%)				0.8238
Lobectomy	96 (52.7%)	179 (51.3%)	78 (49.4%)	353 (51.2%)	
Limited Resection	86 (47.3%)	170 (48.7%)	80 (50.6%)	336 (48.8%)	
Surgery Received, n (%)					0.0123
Lobectomy	96 (52.7%)	185 (53.0%)	77 (48.7%)	358 (52.0%)	
Wedge Resection	58 (31.9%)	84 (24.1%)	58 (36.7%)	200 (29.0%)	
Segmentectomy	28 (15.4%)	80 (22.9%)	23 (14.6%)	131 (19.0%)	
Gender, n (%)					0.7946
Male	81 (44.5%)	145 (41.5%)	66 (41.8%)	292 (42.4%)	
Female	101 (55.5%)	204 (58.5%)	92 (58.2%)	397 (57.6%)	
ECOG Performance Status	, n (%)				0.4494
0	138 (75.8%)	249 (71.3%)	119 (75.3%)	506 (73.4%)	
1/2	44 (24.2%)	100 (28.7%)	39 (24.7%)	183 (26.6%)	
Tumor Size (cm), n (%)					0.6427
<1.0	14 (7.7%)	27 (7.7%)	17 (10.8%)	58 (8.4%)	
1.0-1.5	90 (49.5%)	185 (53.0%)	75 (47.5%)	350 (50.8%)	
>1.5-2.0	78 (42.9%)	137 (39.3%)	66 (41.8%)	281 (40.8%)	
Smoking Status, n (%)					0.5505
Never	15 (8.2%)	32 (9.2%)	15 (9.5%)	62 (9.0%)	
Former	100 (54.9%)	174 (49.9%)	72 (45.6%)	346 (50.2%)	
Current	67 (36.8%)	143 (41.0%)	71 (44.9%)	281 (40.8%)	
Histology, n (%)					<.0001
Squamous Cell Carcinoma	44 (24.2%)	30 (8.6%)	24 (15.2%)	98 (14.2%)	
Adenocarcinoma	101 (55.5%)	256 (73.4%)	80 (50.6%)	437 (63.4%)	
Other	37 (20.3%)	63 (18.1%)	54 (34.2%)	154 (22.4%)	
Forced Expiratory Volume 1 (Percent Predicted FEV₁)					0.5836
Median (Range)	84.0 (37.0, 146.0)	83.0 (2.0, 141.0)	84.0 (2.0, 140.0)	83.0 (2.0, 146.0)	
Number of lymph node stations sampled					<.0001
Median (Range)	5.0 (2.0, 10.0)	4.0 (2.0, 10.0)	4.0 (1.0, 8.0)	4.0 (1.0, 10.0)	
Pathological T stage [T], n (%)					0.8884
[Tis] Carcinoma in situ	0 (0.0%)	2 (0.6%)	0 (0.0%)	2 (0.3%)	
[T1]	153 (84.1%)	281 (80.7%)	128 (81.5%)	562 (81.8%)	
[T2]	26 (14.3%)	57 (16.4%)	26 (16.6%)	109 (15.9%)	
[T3]	2 (1.1%)	7 (2.0%)	2 (1.3%)	11 (1.6%)	
[T4]	1 (0.5%)	1 (0.3%)	1 (0.6%)	3 (0.4%)	
Pathological N Stage [N], n (%)					0.3521
[N0] No regional lymph node metastasis	172 (94.5%)	330 (94.8%)	153 (97.5%)	655 (95.3%)	
[N1] Metastasis to peribronchovascular or the ipsilateral hilar region, or both, including direct extension	9 (4.9%)	11 (3.2%)	3 (1.9%)	23 (3.3%)	
[N2] Metastasis to ipsilateral mediastinal lymph nodes and subcarinal lymph nodes	1 (0.5%)	7 (2.0%)	1 (0.6%)	9 (1.3%)	