

## Supplementary Online Content

Wei S, Guo C, He J, et al. Effect of vein-first vs artery-first surgical technique on circulating tumor cells and survival in patients with non-small cell lung cancer: a randomized clinical trial and registry-based propensity score matching analysis. *JAMA Surg*. Published online May 1, 2019. doi:10.1001/jamasurg.2019.0972

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**eFigure 4.** Kaplan-Meier survival estimates for 5-year overall survival (OS), disease-free survival (DFS) and lung cancer-specific survival (LCSS) in patients with different stage diseases undergoing vein-first lobectomy or artery-first lobectomy.

This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable 1 Perioperative outcomes of the enrolled patients in the randomized clinical trial**

Characteristics	V-first group (n=38)	A-first group (n=40)	<i>P</i> value
Operative time (min, median, IQR)	119 (100-150)	123 (110-155)	0.18
Blood loss (ml, median, IQR)	50 (20-55)	50 (20-95)	0.95
Post-operative length of stay (day, median, IQR)	6 (5-8)	6 (5-7)	0.99
Drainage time (day, median, IQR)	3 (3-4)	3 (2-5)	0.70
Post-operative complications (n, %)	5 (13.2)	5 (12.5)	0.93
Difference in FR <sup>+</sup> CTC levels after surgery (FU/3mL, median, IQR)	-0.50 (-2.53+0.79)	+0.73 (-0.86+1.58)	0.006
%Change of FR <sup>+</sup> CTC levels (% median, IQR)	-4.18 (-16.12- +6.26)	+6.23 (-4.73- +11.88)	0.002
Number of patients with FR <sup>+</sup> CTC levels increasing after surgery (n, %)	12 (31.6)	26 (65.0)	0.003

Abbreviations: IQR, interquartile range; FR<sup>+</sup>CTC, Folate Receptor-positive Circulating Tumor Cell.

**eTable 2 Univariate and multivariate analyzes of factors that may increase the levels of FR+CTC**

Covariates	Univariate analysis			Multivariate analysis		
	HR	95%CI	<i>P</i> value	HR	95%CI	<i>P</i> value
<b>Age</b>						
< 60 years old	Reference			Reference		
≥ 60 years old	3.18	1.01 to 10.04	0.05	3.19	0.95 to 10.72	0.06
<b>Sex</b>						
Female	Reference					
Male	1.02	0.41 to 2.53	0.96			
<b>Comorbidity</b>						
No	Reference					
Yes	1.01	0.41 to 2.47	0.98			
<b>Current or former smokers</b>						
No	Reference					
Yes	1.67	0.68 to 4.09	0.27			
<b>Tumor location</b>						
Left lobe	Reference					
Right lobe	2.53	0.98 to 6.56	0.06			
<b>Sequence of</b>						

<b>vessel ligation</b>						
V-first	Reference			Referenc e		
A-first	4.02	1.57 to 10.34	0.004	4.03	1.53 to 10.63	0.005
<b>Tumor size</b>						
< 3cm	Reference					
≥ 3cm	1.23	0.51 to 2.99	0.65			
<b>Histological type</b>						
Adenocarcino ma	Reference					
Non- adenocarcinom a	1.79	0.66 to 4.87	0.25			
<b>Pathological TNM stage</b>						
Stage I	Ref					
Stage II	2.57	0.83 to 7.93	0.10			
Stage III	2.14	0.68 to 6.80	0.20			
Stage IV	-	-	-			

Abbreviations: FR<sup>+</sup>CTC, Folate Receptor-positive Circulating Tumor Cell; HR, hazard ratio; CI, confidence interval.

**eTable 3 Baseline demographic and clinical characteristics of patients before propensity score matching in the retrospective analysis of the lung cancer registry**

Characteristics	V-first group (n=1,481)	A-first group (n=210)	<i>P</i> value
Age (n, %)			0.09
< 60 years old	739 (49.9)	118 (56.2)	
≥ 60 years old	742 (50.1)	92 (43.8)	
Sex (n, %)			0.39
Male	799 (54.0)	120 (57.1)	
Female	682 (46.0)	90 (42.9)	
Comorbidity (n, %)			0.009
No	747 (50.4)	126 (60.0)	
Yes	734 (49.6)	84 (40.0)	
Current or former smokers (n, %)			0.15
No	860 (58.1)	111 (52.9)	
Yes	621 (41.9)	99 (47.1)	
Family cancer history (n, %)			0.78
No	1,230 (83.1)	176 (83.8)	
Yes	251 (16.9)	34 (16.2)	
Tumor location (n, %)			0.55
Right lobe	856 (57.8)	126 (60.0)	
Left lobe	625 (42.2)	84 (40.0)	
Tumor size (n, %)			0.67
< 3cm	799 (54.0)	110 (52.4)	
≥ 3cm	682 (46.0)	100 (47.6)	
Histological type (n, %)			0.15
Adenocarcinoma	1,126 (76.0)	150 (71.4)	
Non-adenocarcinoma	355 (24.0)	60 (28.6)	

Pathological T stage (n, %)			0.69
T1	240 (16.2)	36 (17.1)	
T2	1,184 (80.0)	169 (80.5)	
T3	51 (3.4)	4 (1.9)	
T4	6 (0.4)	1 (0.5)	
Lymph node metastasis (n, %)			0.14
N0	1,033 (69.7)	138 (65.7)	
N1	179 (12.1)	22 (10.5)	
N2	269 (18.2)	50 (23.8)	
Pathological stage (n, %)			0.15
Stage I	957 (64.6)	128 (61.0)	
Stage II	241 (16.3)	30 (14.2)	
Stage III	283 (19.1)	52 (24.8)	
Post-operative adjuvant therapy (n, %)			0.33
No	737 (49.8)	112 (53.3)	
Yes	744 (50.2)	98 (46.7)	

**eTable 4 Comparison on perioperative outcomes of patients before propensity score matching in the retrospective analysis of the lung cancer registry**

Characteristics	V-first group (n=1,481)	A-first group (n=210)	<i>P</i> value
Operative time (min, median, IQR)	130 (105-165)	165 (130-205)	<0.001
Blood loss (ml, median, IQR)	50 (30-100)	60 (50-100)	0.007
Post-operative length of stay (day, median, IQR)	6 (5-8)	6 (5-8)	0.56
Drainage time (day, median, IQR)	3 (2-4)	4 (3-6)	<0.001
Post-operative complications (n, %)	241 (16.3)	34 (16.2)	0.98

Abbreviations: IQR, interquartile range.

**eTable 5 Baseline demographic and clinical characteristics of patients after propensity score matching in the retrospective analysis of the lung cancer registry**

Characteristics	V-first group (n=210)	A-first group (n=210)	<i>P</i> value
Age (n, %)			0.28
< 60 years old	129 (61.4)	118 (56.2)	
≥ 60 years old	81 (38.6)	92 (43.8)	
Sex (n, %)			0.49
Male	113 (53.8)	120 (57.1)	
Female	97 (46.2)	90 (42.9)	
Comorbidity (n, %)			0.77
No	123 (58.6)	126 (60.0)	
Yes	87 (41.4)	84 (40.0)	
Current or former smokers (n, %)			0.49
No	118 (56.2)	111 (52.9)	
Yes	92 (43.8)	99 (47.1)	
Family cancer history (n, %)			0.70
No	173 (82.4)	176 (83.8)	
Yes	37 (17.6)	34 (16.2)	
Tumor location (n, %)			0.19
Right lobe	139 (66.2)	126 (60.0)	
Left lobe	71 (33.8)	84 (40.0)	
Tumor size (n, %)			0.56
< 3cm	116 (55.2)	110 (52.4)	
≥ 3cm	94 (44.8)	100 (47.6)	
Histological type (n, %)			0.44
Adenocarcinoma	157 (74.8)	150 (71.4)	
Non-adenocarcinoma	53 (25.2)	60 (28.6)	
Pathological T stage (n, %)			0.64
T1	36 (17.1)	36 (17.1)	
T2	172 (81.9)	169 (80.5)	

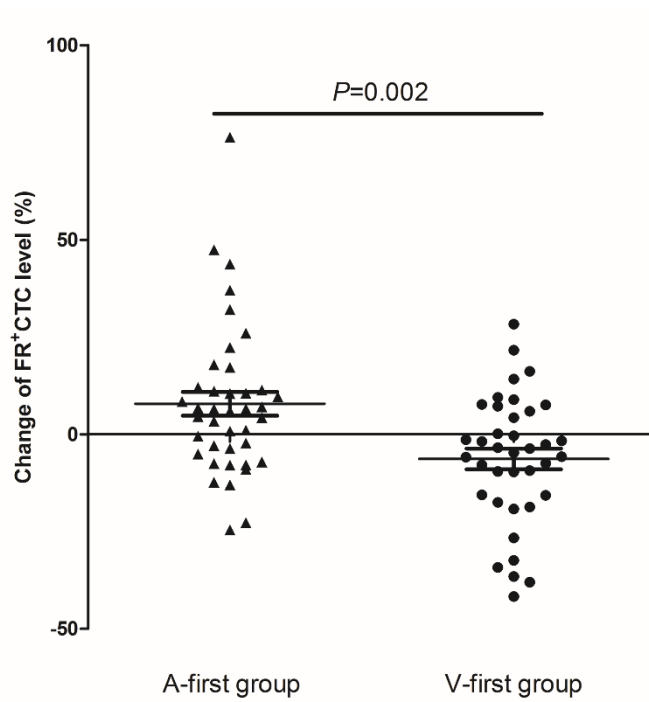


T3	2 (1.0)	4 (1.9)	
T4	0 (0.0)	1 (0.5)	
Lymph node metastasis (n, %)			0.35
N0	141 (67.2)	138 (65.7)	
N1	29 (13.8)	22 (10.5)	
N2	40 (19.0)	50 (23.8)	
Pathological stage (n, %)			0.37
Stage I	137 (65.2)	128 (61.0)	
Stage II	33 (15.7)	30 (14.2)	
Stage III	40 (19.1)	52 (24.8)	
Post-operative adjuvant therapy (n, %)			0.70
No	116 (55.2)	112 (53.3)	
Yes	94 (44.8)	98 (46.7)	

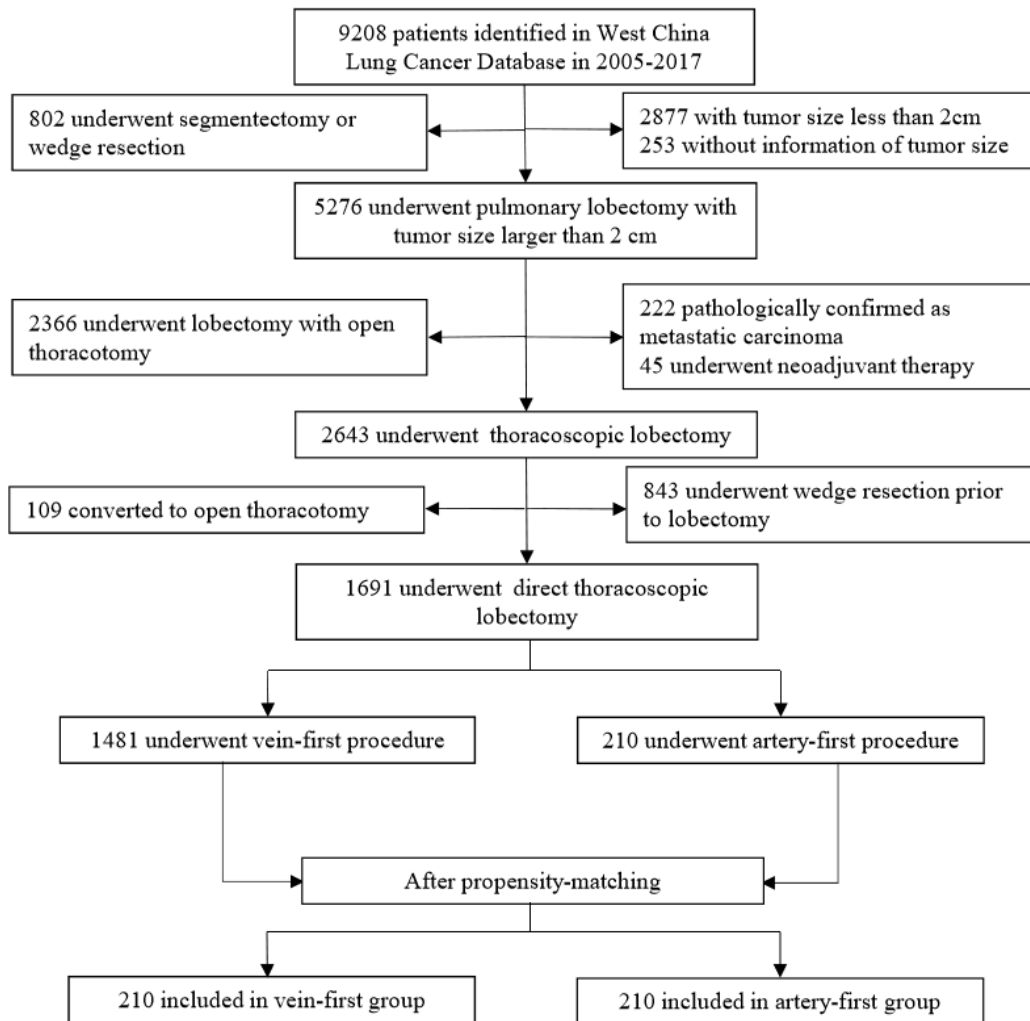
**eTable 6 Comparison on perioperative outcomes of patients after propensity score matching in the retrospective analysis of the lung cancer registry**

Characteristics	V-first group (n=210)	A-first group (n=210)	<i>P</i> value
Operative time (min, median, IQR)	130 (100-165)	165 (130-205)	<0.001
Blood loss (ml, median, IQR)	50 (30-100)	60 (50-100)	0.04
Post-operative length of stay (day, median, IQR)	6 (4-8)	6 (5-8)	0.18
Drainage time (day, median, IQR)	3 (2-5)	4 (3-6)	0.001
Post-operative complications (n, %)	43 (20.5)	34 (16.2)	0.26

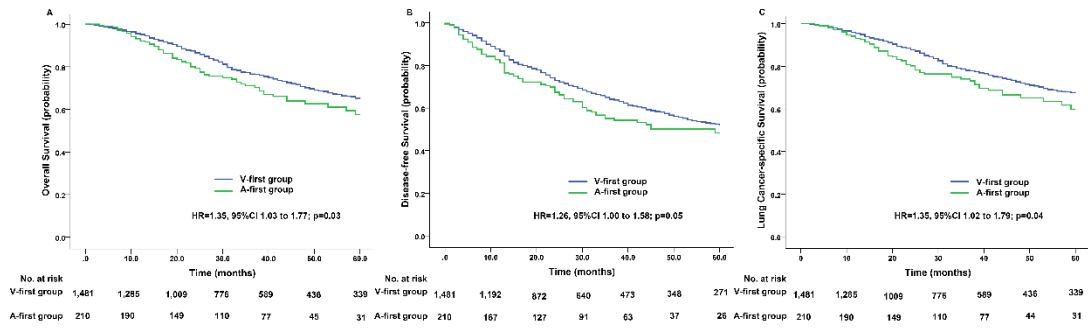
Abbreviations: IQR, interquartile range.



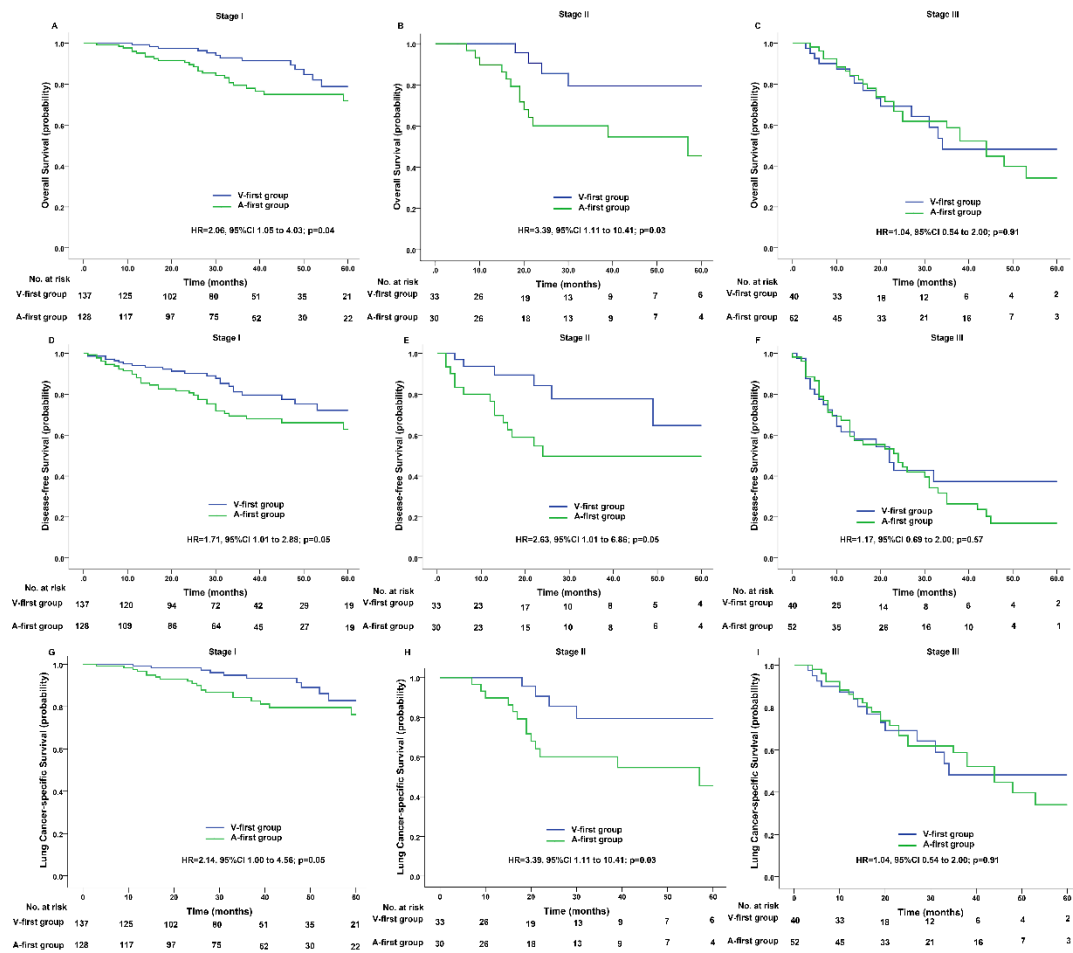
**eFigure 1.** The percentage of the changes of FR<sup>+</sup>CTC level during surgery in the A-first group and the V-first group.



**eFigure 2.** Study flow diagram of the enrolled patients and propensity matching in the lung cancer registry.



**eFigure 3.** Kaplan-Meier survival estimates for (A) 5-year overall survival (OS), (B) 5-year disease-free survival (DFS) and (C) 5-year lung cancer-specific survival (LCSS) in patients undergoing vein-first lobectomy or artery-first lobectomy. (HR, hazard ratio)



**eFigure 4.** Kaplan-Meier survival estimates for 5-year overall survival (OS), disease-free survival (DFS) and lung cancer-specific survival (LCSS) in patients with different stage diseases undergoing vein-first lobectomy or artery-first lobectomy. (A) OS of patients with stage I disease. (B) OS of patients with stage II disease. (C) OS of patients with stage III disease. (D) DFS of patients with stage I disease. (E) DFS of patients with stage II disease. (F) DFS of patients with stage III disease. (G) LCSS of patients with stage I disease. (H) LCSS of patients with stage II disease. (I) LCSS of patients with stage III disease. (HR, hazard ratio)