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Marginal Pulmonary Function Should Not Preclude Lobectomy in Selected Patients with Non-Small Cell Lung Cancer

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Disclosures

None

Background

- Growing number of patients with NSCLC deemed high-risk for surgery based upon poor pulmonary function
- A number of alternative treatment strategies have been proposed including SBRT, RFA, brachytherapy, and sublobar resection
- Some patients have centrally located or larger tumors in which sublobar resection is not oncologically possible

Purpose

Compare post-operative morbidity and mortality in patients with NSCLC undergoing lobectomy based upon pulmonary function status

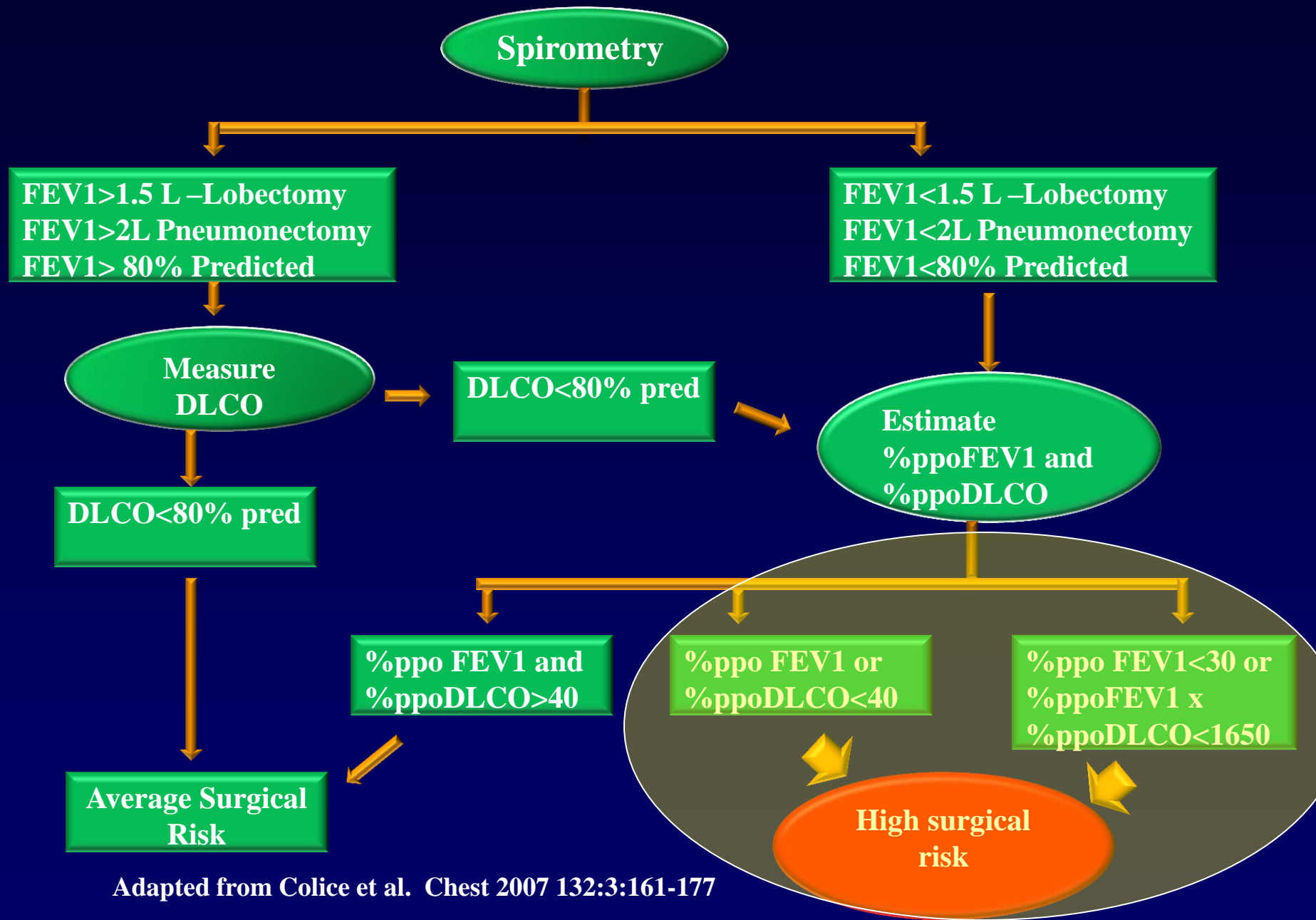
Hypothesis

Marginal PFT classification is not associated with increased post-operative morbidity or mortality following lobectomy in selected NSCLC patients

ACOSOG Z4099/RTOG1021 Definition of Marginal PFTs

- High-risk for surgery defined as one major criteria or two minor criteria
- Major criteria
 - $FEV1 \leq 50\%$ predicted
 - $DLCO \leq 50\%$ predicted
- Minor criteria
 - $Age \geq 75$
 - $FEV1$ 50-60% predicted
 - $DLCO$ 50-60% predicted

ACCP Definition of High –Risk Surgical Patient



**1259 patients
underwent lobectomy
for NSCLC**

Analysis #1

**ACOSOG
Z4099/RTOG1021
Marginal PFT definition**

**206
Marginal
PFT Patients**

**1053
Non-Marginal
PFT Patients**

Analysis #2

**ACCP Marginal PFT
definition**

**131
Marginal
PFT Patients**

**1128
Non-Marginal
PFT Patients**

Variables included in analysis

**Age
Gender
Pathologic stage
Zubrod function status
Hypertension
Coronary artery disease
Peripheral vascular disease
Diabetes
Pre-op oxygen therapy
Marginal PFT status**

Composite Major Morbidity

- Compare the likelihood of a major post-operative morbidity in patients undergoing lobectomy for NSCLC
- Complications included
 - Pneumonia
 - Myocardial infarction
 - Reintubation
 - Renal failure
 - Atrial arrhythmia
- Cox-regression model for both marginal PFT classifications was performed

Statistical Analysis

- Chi-square or Fisher's exact test for categorical variable comparisons
- Single factor analysis of variance (ANOVA) or the Mann Whitney U test to compare continuous data where appropriate
- Cox-proportional hazard regression analysis used to determine associations between variables

Results

Demographics

ACOSOG Z4099/RTOG1021 Marginal PFT definition

ACCP Marginal PFT definition

Variable	Marginal PFTs (N=206)	Non-Marginal PFTs (N=1053)	p-value	Marginal PFTs (N=131)	Non-Marginal PFTs (N=1128)	p-value
Age (Mean±SD)	69.4±9.6	66.8±10.5	0.34	66.4±9.7	66.0±10.1	0.48
Sex (M:F)	104:102	507:546	0.57	65:68	538:588	0.92
Tumor Location						
Upper lobe	138 (66.9%)	698 (66.2%)	0.95	93 (70.7%)	743 (65.9%)	0.20
Middle lobe	16 (7.9%)	41 (3.9%)	0.04	14 (10.5%)	43 (3.8%)	0.001
Lower lobe	52 (25.2%)	314 (29.9%)	0.23	26 (19.8%)	340 (30.3%)	0.17
Pathologic Stage						
Stage I	141 (66.5%)	702 (64.9%)	0.69	84 (64.4%)	759 (66.9%)	0.49
Stage II	46 (21.6%)	217 (20.0%)	0.58	50 (38.2%)	233 (20.6%)	0.57
Stage III	16 (10.5%)	118 (13.6%)	0.22	15 (11.5%)	119 (11.0%)	0.76
Stage IV	3 (1.4%)	16 (1.5%)	1.0	3 (2.3%)	16 (1.8%)	0.43
Co-morbidities						
Hypertension	56 (27.3%)	246 (23.4%)	0.25	34 (26.3%)	268 (23.7%)	0.59
Coronary artery disease	39 (19.3%)	210 (20.0%)	0.74	27 (20.3%)	222 (19.6%)	0.82
Peripheral vascular disease	62 (5.9%)	99 (9.4%)	0.65	10 (7.5%)	151 (13.4%)	0.07
Diabetes	21 (10.1%)	140 (13.3%)	0.20	12 (9.5%)	149 (13.2%)	0.21
Zubrod functional status>1	27 (13.1%)	69 (6.5%)	0.001	15 (11.3%)	81 (7.2%)	0.08
Home oxygen therapy	22 (10.7%)	37 (3.5%)	0.001	12 (9.5%)	47 (4.2%)	0.01

Not Significant

Post-operative Complications

ACOSOG Z4099/RTOG1021 Marginal PFT definition

ACCP Marginal PFT definition

Variable	ACOSOG Z4099/RTOG1021 Marginal PFT definition			ACCP Marginal PFT definition		
	Marginal PFTs (N=206)	Non-Marginal PFTs (N=1053)	p-value	Marginal PFTs (N=131)	Non-Marginal PFTs (N=1128)	p-value
30-Day Mortality	0.5%	1.4%	0.10	0.8%	1.3%	0.48
Pneumonia	10.4%	5.6%	0.002	10.6%	5.8%	0.09
Re-intubation	1.1%	5.3%	0.62	4.6%	3.7%	0.44
Myocardial infarction	2.7%	0.7%	0.008	2.3%	0.8%	0.01
Acute renal failure	2.8%	0.7%	0.01	2.3%	0.8%	0.01
Supraventricular arrhythmia	12.4%	9.3%	0.16	13.7%	9.4%	0.06

Multivariable Analysis for Composite Major Morbidity

ACOSOG Z4099/RTOG1021 Marginal PFT definition

ACCP Marginal PFT definition

Variable	P-value	Hazard Ratio (95% CI)		P-value	Hazard Ratio (95% CI)	
Pathological stage	0.73			0.58		
Age	0.02	1.02	1.01-1.04	0.11	1.01	0.99-1.03
Zubrod status	0.16			0.17		
Hypertension	0.48	1.14	0.80-1.61	0.68	1.08	0.76-1.54
Coronary artery disease	0.66	1.09	0.75-1.58	0.66	1.09	0.75-1.59
Peripheral vascular disease	0.14	0.66	0.38-1.14	0.40	0.79	0.46-1.36
Gender (female)	0.91	0.98	0.73-1.33	0.76	0.95	0.70-1.29
Diabetes	0.29	0.78	0.50-1.23	0.23	0.75	0.47-1.20
Marginal PFT status	0.68	0.93	0.64-1.33	0.14	0.65	0.37-1.15
Home oxygen therapy	0.32	1.31	0.77-2.33	0.06	1.65	0.97-2.82

No variables were associated with the occurrence of any major complication

Multivariable Analysis for Overall Survival

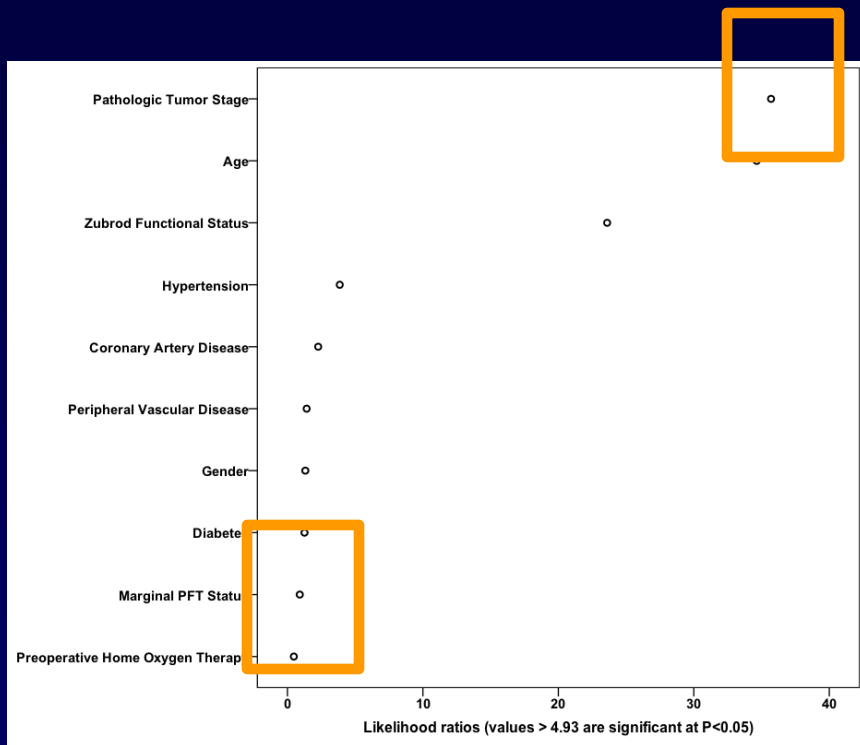
ACOSOG Z4099/RTOG1021
Marginal PFT definition

ACCP
Marginal PFT definition

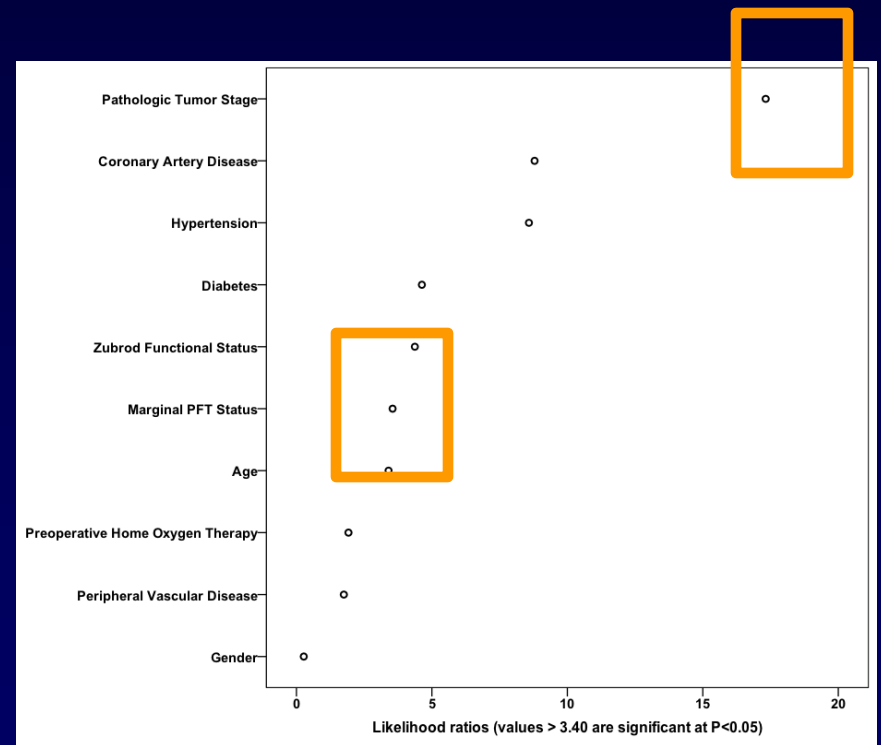
Variable	P-value	Hazard Ratio (95% CI)		P-value	Hazard Ratio (95% CI)	
Pathological stage	<0.001			<0.001		
Stage IB	0.11	1.20	0.96-1.50	0.11	1.20	0.96-1.50
Stage IIA	0.66	0.92	0.63-1.34	0.52	0.88	0.60-1.29
Stage IIB	0.15	1.25	0.92-1.70	0.15	1.25	0.92-1.69
Stage IIIA	<0.001	1.81	1.34-2.46	<0.001	1.79	1.32-2.44
Stage IIIB	<0.001	2.34	1.60-3.44	<0.001	2.38	1.62-3.48
Stage IV	0.009	2.38	1.25-4.55	0.008	2.42	1.26-4.64
Age	<0.001	1.03	1.02-1.04	<0.001	1.03	1.02-1.04
Zubrod status	<0.001			<0.001		
1	0.001	1.37	1.13-1.66	<0.001	1.41	1.16-1.71
2	<0.001	2.02	1.44-2.83	<0.001	2.01	1.43-2.83
3	0.03	2.38	1.11-5.10	0.03	2.38	1.11-5.11
Marginal PFT status	0.34	1.12	0.89-1.42	0.83	0.97	0.71-1.32

Variable Effect Size on Overall Survival

ACOSOG Z4099/RTOG1021 Marginal PFT definition

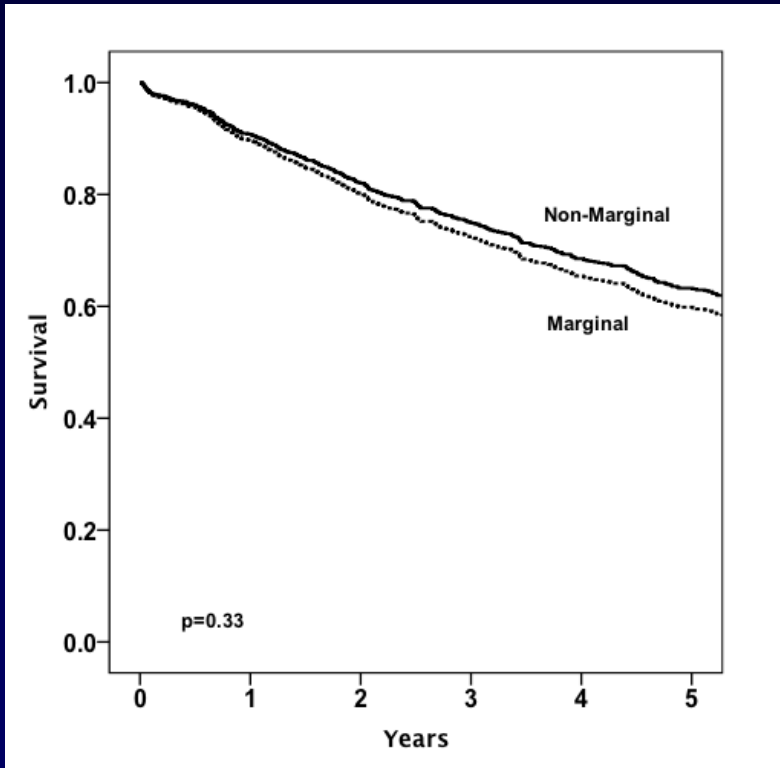


ACCP Marginal PFT definition

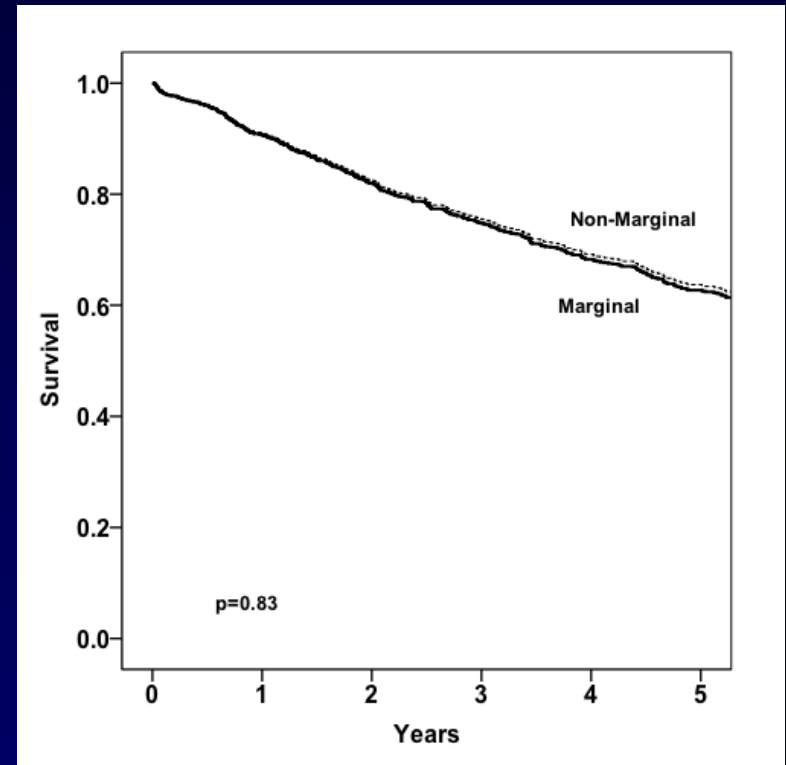


Risk-Adjusted Survival Curves for Overall Survival

ACOSOG Z4099/RTOG1021
Marginal PFT definition



ACCP
Marginal PFT definition



At Risk	0	1-year	2-year	3-year	4-year	5-year
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Non-Marginal	1053	971	809	667	506	368
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Marginal	206	173	134	110	80	55
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At Risk	0	1-year	2-year	3-year	4-year	5-year
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Non-Marginal	1128	1051	862	713	542	386
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Marginal	131	97	88	71	52	40
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Strengths/Limitations of Study

- Strengths
 - Prospective collected
 - Internal audit for accuracy
 - Risk-adjusted analysis
 - Compared two different marginal PFT definitions
- Limitations
 - Single institution
 - Retrospective review- Selection bias

Conclusions

- Marginal PFTs, as classified by two methodologies, are not associated with decreased overall survival in selected patients undergoing lobectomy for NSCLC
- Risk-adjusting for preoperative and pathological variables, the incidence of a significant morbidity was not greater in patients with marginal PFTs