



Physiological Limits of Surgery for Early-Stage Lung Cancer: Interstitial Pneumonia Nullifies Survival Benefit in Critically Low Diffusing Capacity

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RESULTS SUMMARY

0.5%
30-day mortality
vs 0% in ppo%DLCO 30–40%

35%
Pulmonary complications
vs 24%; P=.004

20%
Home oxygen at discharge
vs 9%; P<.001

44.6%
5-year overall survival
vs 71.3%; P<.001

Selected ppo%DLCO <30% patients: low early mortality, substantial respiratory burden, and poor long-term survival

BACKGROUND

DLCO is central to lung-resection risk assessment, but thresholds describe a risk continuum rather than an absolute contraindication. Postoperative respiratory burden and competing causes of long-term death at ppo%DLCO <30% remain incompletely characterized.

OBJECTIVE

To evaluate perioperative and long-term outcomes after resection in clinical stage I lung cancer with ppo%DLCO <30%, including competing causes of death and the prognostic context of interstitial pneumonia (IP).

METHODS

Retrospective single-center cohort; resections from 2011–2022. Clinical stage I lung cancer with ppo%DLCO ≤40%; N=587. Groups: <30% (n=192) vs 30–40% (n=395). Outcomes: pulmonary complications, home oxygen therapy (HOT), 30-day mortality, OS, RFS, LCD, and NLCD. Statistics: Kaplan–Meier, Gray tests, and multivariable Fine–Gray regression.

STUDY DESIGN / FLOW PLACEHOLDER

Insert a simplified cohort flow diagram:
4,275 assessed → 1,040 with ppo%DLCO ≤40% → 587 stage I cases → 192 vs 395

Recommended visual: CONSORT-style flow, editable SVG/PNG at ≥300 dpi

Clinical characteristics of the patients

Variable	ppo%DLCO <30%	ppo%DLCO 30–40%	P
	(n=192)	(n=395)	value
Age, y, median	74 ± 5	74 ± 5	.335
Male sex	143 (74)	238 (60)	<.001
BMI, median	21.5 ± 2.1	22.0 ± 2.2	.050
Pack-years, median	50.0 ± 19.0	37.5 ± 27.0	<.001
CEA, ng/mL, median	4.5 ± 1.7	3.8 ± 1.7	.005
KL-6, U/mL, median	399 ± 165	327 ± 126	<.001
%FEV1, %, median	79.8 ± 12.1	85.9 ± 12.6	<.001
%DLCO, %, median	30.9 ± 4.8	44.5 ± 4.2	<.001
ppo%FEV1, median	63.4 ± 10.0	69.1 ± 10.8	<.001
ppo%DLCO, median	25.3 ± 3.2	36.0 ± 2.4	<.001
Major medical comorbidities			
COPD	43 (22)	65 (16)	.089
Interstitial pneumonia	60 (31)	73 (18)	<.001
Cardiovascular disease	57 (30)	124 (31)	.704
Cerebrovascular disease	12 (6)	23 (6)	.854
Diabetes mellitus	37 (19)	57 (14)	.150
Collagen disease	7 (4)	9 (2)	.418
Renal dysfunction	10 (5)	22 (6)	1.000
HRCT, solid with GGO	33 (17)	128 (32)	<.001

ETHICS, SUPPORT & REFERENCES

IRB: Juntendo University (E24-294); consent waived with opt-out. Funding: Uehara Memorial Foundation; no role in study conduct or reporting. Conflicts: None reported. Key references: Brunelli et al. Chest 2013; Pennathur et al. JTCVS 2021; Sato et al. JTCVS 2014; Vanstraelen et al. Ann Surg 2024 ; Fukui M et al. BMJopen 2022 ; Ueda T et al. EJCTS 2024

RESULTS

SURGICAL OUTCOMES

Variables	ppo%DLCO <30%	IP(+)	IP(–)	ppo%DLCO 30–40%	IP(+)	IP(–)
	(n=192)	(n=60)	(n=132)	(n=395)	(n=73)	(n=322)
Reoperative procedure, n (%)	27 (14)	11 (18)	16 (12)	56 (14)	11 (15)	45 (14)
Surgical procedure						
Sublobar	66 (34)	19 (32)	47 (36)	116 (29)	23 (32)	93 (29)
Wedge	31 (47)	12 (63)	19 (40)	52 (45)	15 (65)	37 (40)
Segmentectomy	35 (53)	7 (37)	28 (60)	64 (55)	8 (35)	56 (60)
Sleeve/bronchoplasty ±	2/35 (6)	0/7 (0)	2/28 (7)	1/64 (2)	0/8 (0)	1/56 (2)
arterioplasty*						
Lobectomy or greater	126 (66)	41 (68)	85 (64)	279 (71)	50 (68)	229 (71)
Lobectomy	123 (98)	39 (95)	84 (99)	271 (97)	49 (98)	222 (97)
Sleeve/bronchoplasty ±	8/123 (7)	2/39 (5)	6/84 (7)	9/271 (3)	1/49 (2)	8/222 (4)
arterioplasty*						
Bilobectomy	3 (2)	2 (5)	1 (1)	8 (3)	1 (2)	7 (3)
Procedure approach						
Thoracotomy/hybrid VATS	182 (95)	59 (98)	123 (93)	371 (94)	70 (96)	301 (93)
RATS	10 (5)	1 (2)	9 (7)	24 (6)	3 (4)	21 (7)
Surgical side, right, n (%)	108 (56)	35 (58)	73 (55)	227 (57)	45 (62)	182 (57)
Lobe variation						
Upper lobe	81 (42)	21 (35)	60 (45)	197 (50)	33 (45)	164 (51)
Middle lobe	6 (3)	2 (3)	4 (3)	13 (3)	1 (2)	12 (4)
Lower lobe	105 (55)	37 (62)	68 (52)	185 (47)	39 (53)	146 (45)
Mediastinal lymph node dissection	96 (50)	31 (52)	65 (49)	212 (54)	39 (53)	173 (54)
Operative time, min	128 [100–161]	125 [88–161]	132 [101–161]	128 [101–161]	121 [96–147]	129 [102–165]
Blood loss, mL	15 [6–20]	13 [7–20]	15 [6–24]	10 [6–20]	10 [10–20]	10 [5–20]
Histologic type, adenocarcinoma, n (%)	80 (42)	17 (28)	63 (48)	260 (66)	35 (48)	225 (70)

EARLY POSTOPERATIVE OUTCOMES

Variables	ppo%DLCO <30%	IP(+)	IP(–)	ppo%DLCO 30–40%	IP(+)	IP(–)
	(n=192)	(n=60)	(n=132)	(n=395)	(n=73)	(n=322)
Pulmonary complications, n (%)	68 (35)	28 (47)	40 (30)	94 (24)	18 (25)	76 (24)
Atelectasis	5 (3)	1 (2)	4 (3)	16 (4)	3 (4)	13 (4)
Empyema	2 (1)	1 (2)	1 (1)	3 (1)	2 (3)	1 (0)
Pneumonia	9 (5)	1 (2)	8 (6)	10 (3)	2 (3)	8 (2)
Prolonged air leakage (>5 d)	24 (13)	7 (12)	17 (13)	39 (10)	4 (5)	35 (11)
IP-AE, n (%)	7 (4)	2 (3)	5 (4)	5 (1)	4 (5)	1 (0)
BPF, n (%)	2 (1)	2 (3)	0	2 (1)	0	2 (1)
HOT at discharge	38 (20)	20 (33)	18 (14)	35 (9)	10 (14)	25 (8)
Arrhythmia	16 (8)	5 (8)	11 (8)	38 (10)	7 (10)	31 (10)
Chylothorax	0	0	0	4 (1)	0	4 (1)
Delirium	3 (2)	2 (3)	1 (1)	13 (3)	2 (3)	11 (3)
Length of stay, d	7 [6–10]	7 [6–10]	7 [5–10]	6 [5–8]	6 [5–8]	6 [5–8]
Reoperation	3 (2)	1 (2)	2 (2)	3 (1)	2 (3)	1 (0)
Readmission	8 (4)	3 (5)	5 (4)	12 (3)	6 (8)	6 (2)
30-day mortality	1 (0.5)	1 (2)	0	0	0	0

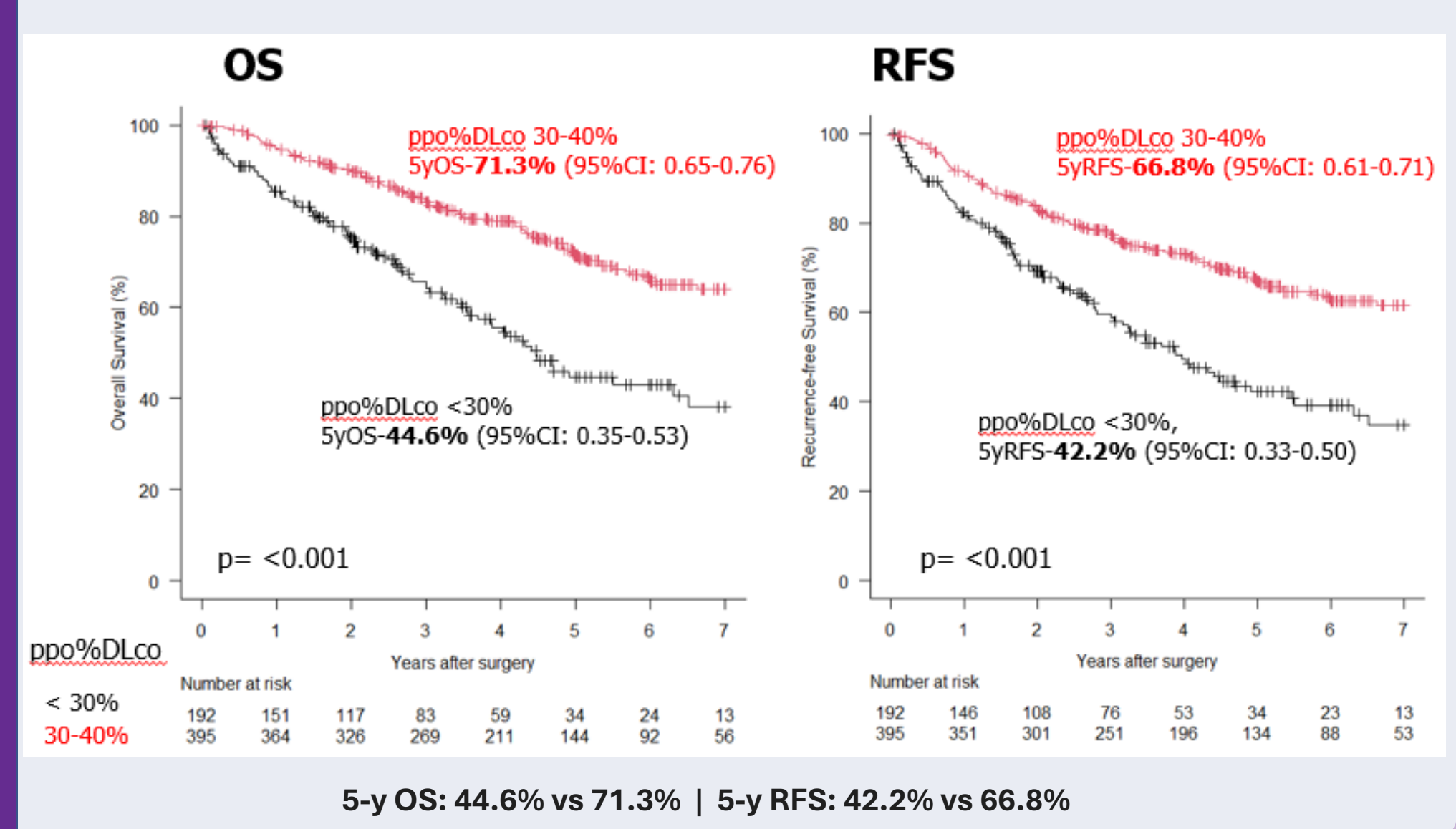
MULTIVARIABLE MODEL

Multivariable Fine–Gray competing-risk regression analyses for lung cancer-related and non–lung cancer-related death

Variable	LCD, sHR	95% CI	P value	NLCD, sHR	95% CI	P value
ppo%DLCO <30% vs 30–40%	1.53	0.90–2.58	.11	1.53	1.05–2.23	.027
CEA, per 1-ng/mL increase	1.04	1.02–1.05	<.001	—	—	—
BMI, per 1-kg/m ² increase	—	—	—	0.95	0.88–1.02	.18
Pack-years, per 1-pack-year increase	—	—	—	1.00	0.99–1.00	.23
ppo%FEV1, per 1% increase	1.01	0.99–1.03	.28	0.99	0.98–1.00	.020
GGO component, present vs absent	0.44	0.16–1.16	.095	—	—	—
Interstitial pneumonia, present vs absent	1.35	0.79–2.30	.27	1.62	1.08–2.45	.021
Male vs female sex	2.47	1.09–5.58	.030	2.03	1.24–3.32	.005
Age, per 1-year increase	1.01	0.98–1.05	.55	1.03	1.00–1.05	.022

NLCD: sHR 1.53 (95% CI 1.05–2.23); P=.027

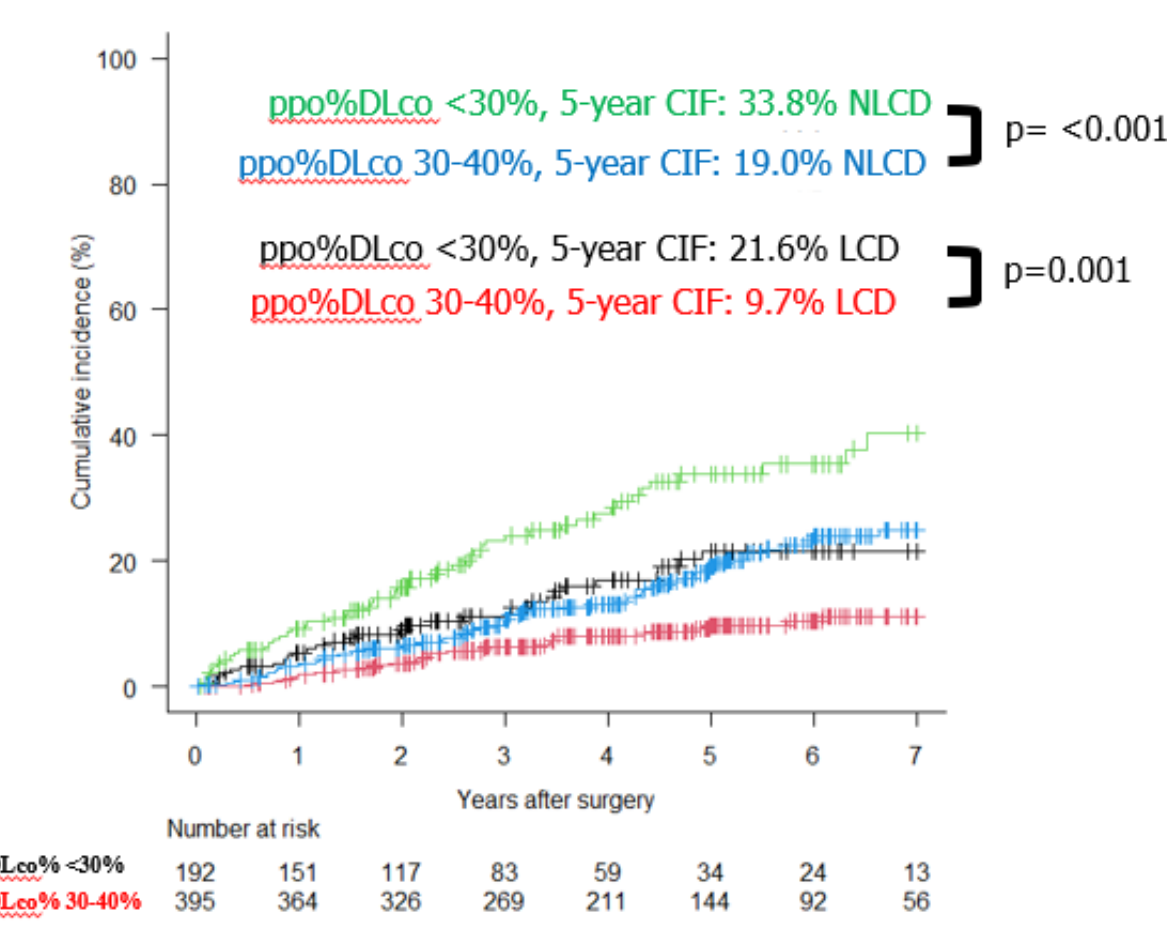
OVERALL & RECURRENCE-FREE SURVIVAL



COMPETING CAUSES OF DEATH

Variables	ppo%DLCO <30%	IP(+)	IP(–)	ppo%DLCO 30–40%	IP(+)	IP(–)
	(n=192)	(n=60)	(n=132)	(n=395)	(n=73)	(n=322)
Lung cancer-related death	31 (16)	12 (20)	19 (14)	37 (9)	13 (18)	24 (8)
Radiologically confirmed recurrence	31 (16)	12 (20)	19 (14)	55 (14)	15 (21)	40 (12)
Local	13 (42)	6 (50)	7 (37)	21 (38)	7 (47)	14 (35)
Distant	13 (42)	4 (33)	9 (47)	23 (42)	5 (33)	18 (45)
Both	5 (16)	2 (17)	3 (16)	11 (20)	3 (20)	8 (20)
Therapy for recurrence, yes	15/31 (48)	5/12 (42)	10/19 (53)	36/55 (66)	8/15 (53)	28/40 (70)
Non–lung cancer-related death	52 (27)	22 (37)	30 (23)	73 (18)	18 (25)	55 (17)
Respiratory disease	23 (44)	10 (45)	13 (43)	36 (49)	13 (72)	23 (42)
Cardiac disease	3 (6)	1 (5)	2 (7)	0	0	0
Other cancer	3 (6)	0	3 (10)	3 (4)	1 (6)	2 (4)
Other cause	23 (44)	11 (50)	12 (40)	34 (47)	4 (22)	30 (54)

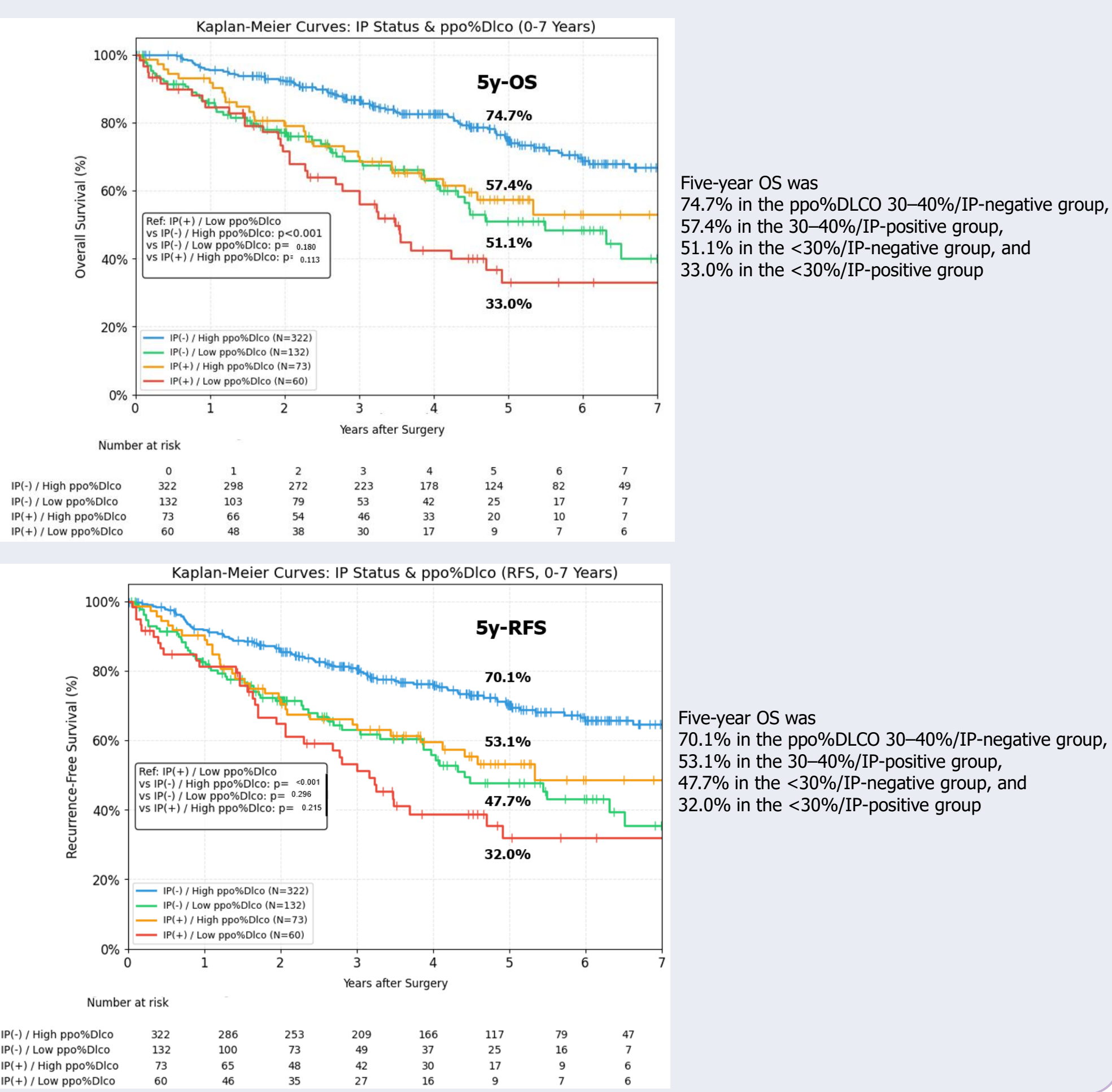
Cumulative incidence of Cause-Specific Death



KEY FINDINGS

Early feasibility: 0.5% 30-day mortality in carefully selected patients. Respiratory burden: 35% pulmonary complications and 20% HOT at discharge. Long-term risk: ppo%DLCO <30% independently associated with NLCD.

OVERALL & RECURRENCE-FREE SURVIVAL For ppo%DLCO-by-IP interaction



IP PROVIDES ADDITIONAL RISK CONTEXT

Within ppo%DLCO <30%, HOT at discharge was 33% with IP vs 14% without IP. Five-year OS was 33.0% with IP vs 51.1% without IP (P=.180). No significant ppo%DLCO-by-IP interaction was detected (categorical P=.544); the analysis was exploratory and not powered for modest interactions.

DISCUSSION

Perioperative feasibility and long-term benefit are distinct clinical questions. Very low ppo%DLCO should trigger intensified, multidimensional assessment—not an isolated binary prohibition. The evidence for an independent association was stronger for NLCD; the LCD estimate had the same point estimate but wider uncertainty.

CONCLUSIONS

- Patients with a ppo%DLCO of less than 30% exhibited low 30-day mortality; however, they experienced significant respiratory morbidity and poor long-term survival.
- These findings enhance risk assessment by not only considering perioperative mortality but also quantifying postoperative respiratory burden and other competing causes of long-term mortality.
- This supports a multidimensional approach to patient selection and counseling, rather than relying solely on a binary pulmonary function threshold.

LIMITATIONS

Retrospective, single-center, surgically selected cohort; no nonsurgical comparator; CPET not uniform; HOT duration and quality of life unavailable; limited power for IP interaction testing.

ARTIFICIAL INTELLIGENCE (AI) USE DISCLOSURE

In accordance with ACCME disclosure guidance, the authors disclose that Gemini and ChatGPT (OpenAI) were used to assist manuscript organization and English-language refinement. ChatGPT (OpenAI), including Codex, was additionally used to organize and format this poster. The authors reviewed and revised all AI-assisted output and take full responsibility for the content. AI did not replace clinical expertise or independent medical judgment.

Data availability
Available from the corresponding author on reasonable request.

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