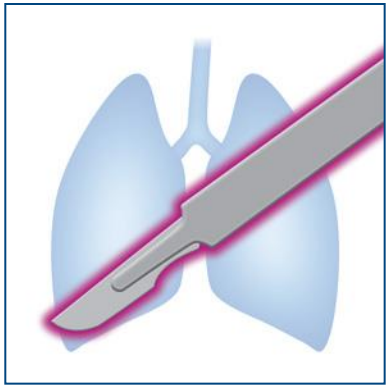
Pneumo Update Europe 2018

15 - 16 June, Budapest

Thoracic Surgery & Lung Transplantation



Gilbert Massard, France

Lung Transplantation

Ex-vivo Lung Perfusion

State of the Art

Ex-vivo lung perfusion (EVLP)

- Experimental work has demonstrated efficacy and safety for evaluation of lung function
- Observational studies have shown feasibility for assessment of marginal donor lungs

Cypel M et al; Am J Transplant 2009;9:2262-9
Cypel M et al, N Engl J Med 2011;364:1431-40
Reeb J et al, Clin Transplant 2016;30:183-94

State of the Art

Potential utilization of EVLP in clinical Lung TX

- Assessment of marginal donor lungs ✔
- Assessment of non-heart beating donor lungs ✔
- Improve quality of preservation for standard donor lungs
- Improve TX logistics owing to longer preservation time

Reeb J et al, Curr Opin Organ Transplant 2015;20:498-505

ISHLT-2016 consensus on PGD

Grade	Pulmonary edema On chest X-ray	PaO2/FIO2
PGD 0	No	Any
PGD 1	Yes	> 300
PGD 2	Yes	200 - 300
PGD 3	Yes	< 200

Expert consensus

Snell GI et al, J Heart Lung Transplant 2017;36:1097-103

To improve preservation: why?

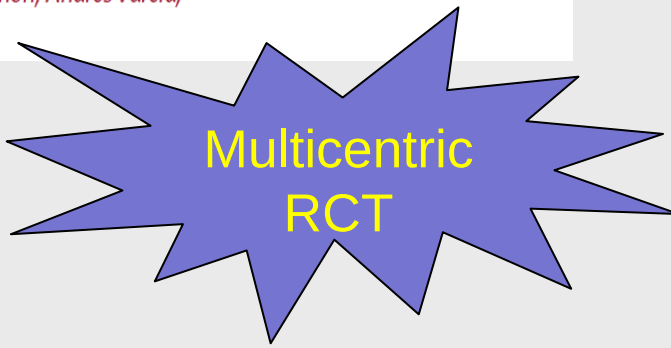
Improve quality of donor lungs

- To decrease primary graft dysfunction (PGD)
  - *30% of recipients during the first 72 hours !!*
- To decrease chronic lung allograft dysfunction (CLAD)
  - *Obvious link to PGD !!*
- To decrease bronchial complications
  - 20% of all recipients

Diamond JM et al., Am J Respir Crit Care Med 2013; 187: 527–534
Whitson BA et al., J Heart Lung Transplant 2007; 26:1004-1011
Olland A et al, J Heart Lung Transplant 2017;36:902-907

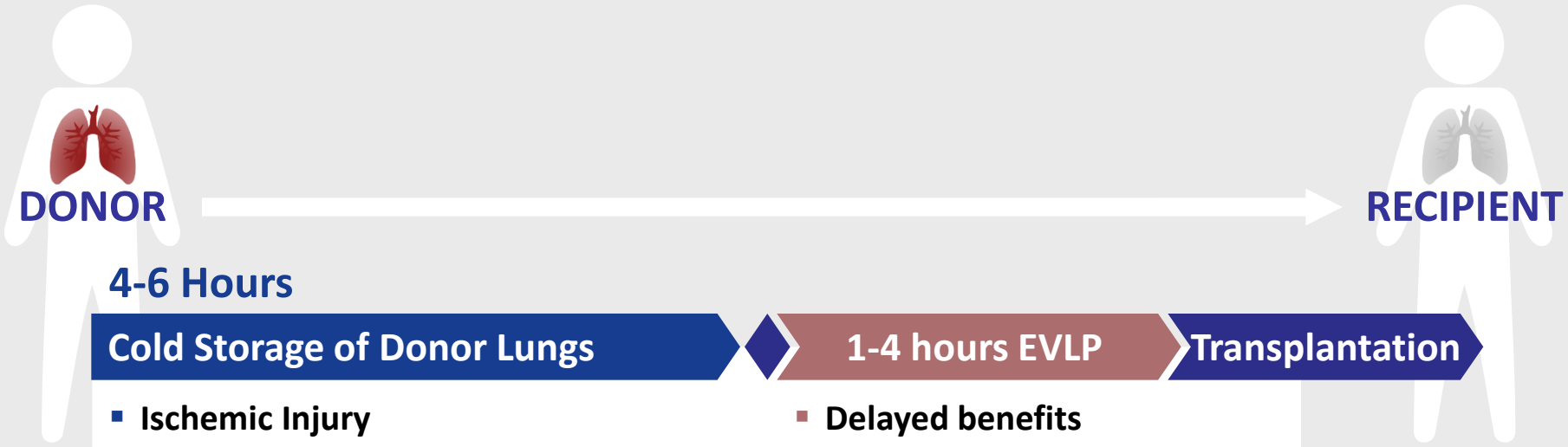
Normothermic ex-vivo preservation with the portable Organ Care System Lung device for bilateral lung transplantation (INSPIRE): a randomised, open-label, non-inferiority, phase 3 study

Gregor Warnecke, Dirk Van Raemdonck, Michael A Smith, Gilbert Massard, Jasleen Kukreja, Federico Rea, Gabriel Loor, Fabio De Robertis, Jayan Nagendran, Kumud K Dhital, Francisco Javier Moradiellos Díez, Christoph Knosalla, Christian A Bermudez, Steven Tsui, Kenneth McCurry, I-Wen Wang, Tobias Deuse, Guy Lesèche, Pascal Thomas, Igor Tudorache, Christian Kühn, Murat Avsar, Bettina Wiegmann, Wiebke Sommer, Arne Neyrinck, Marco Schiavon, Fiorella Calebrese, Nichola Santelmo, Anne Olland, Pierre-Emanuel Falcoz, Andre R Simon, Andres Varela, Joren C Madsen, Marshall Hertz, Axel Haverich, Abbas Ardehali



Warnecke G et al, Lancet Respir Med 2018;6:357-67

EVLP : static versus dynamic



4-6 Hours

Cold Storage of Donor Lungs → **1-4 hours EVLP** → **Transplantation**

- Ischemic Injury
- No recruitment or resuscitation
- No assessment

- Delayed benefits
- Limited capabilities
- Poor utilization of resources

10+ Hours

Portable OCS™ Physiologic Support → **Transplantation**

- Elimination of ischemia
- Immediate & sustained recruitment/resuscitation
- Continuous monitoring & assessment of function
- Efficient utilization of resources

Warnecke G et al
Lancet
2012;380:1851-8

The Organ Care System (OCS™)

Reduce Ischemic Injury
Warm Oxygenated
Blood Perfusion – Physiologic
Preservation

Optimize Organ Condition
Optimize O2 Delivery, Ventilation
& Replenish
Substrates/Hormones

Perform Ex-vivo Assessment
Functional, Metabolic &
Perfusion Parameters
Assessments

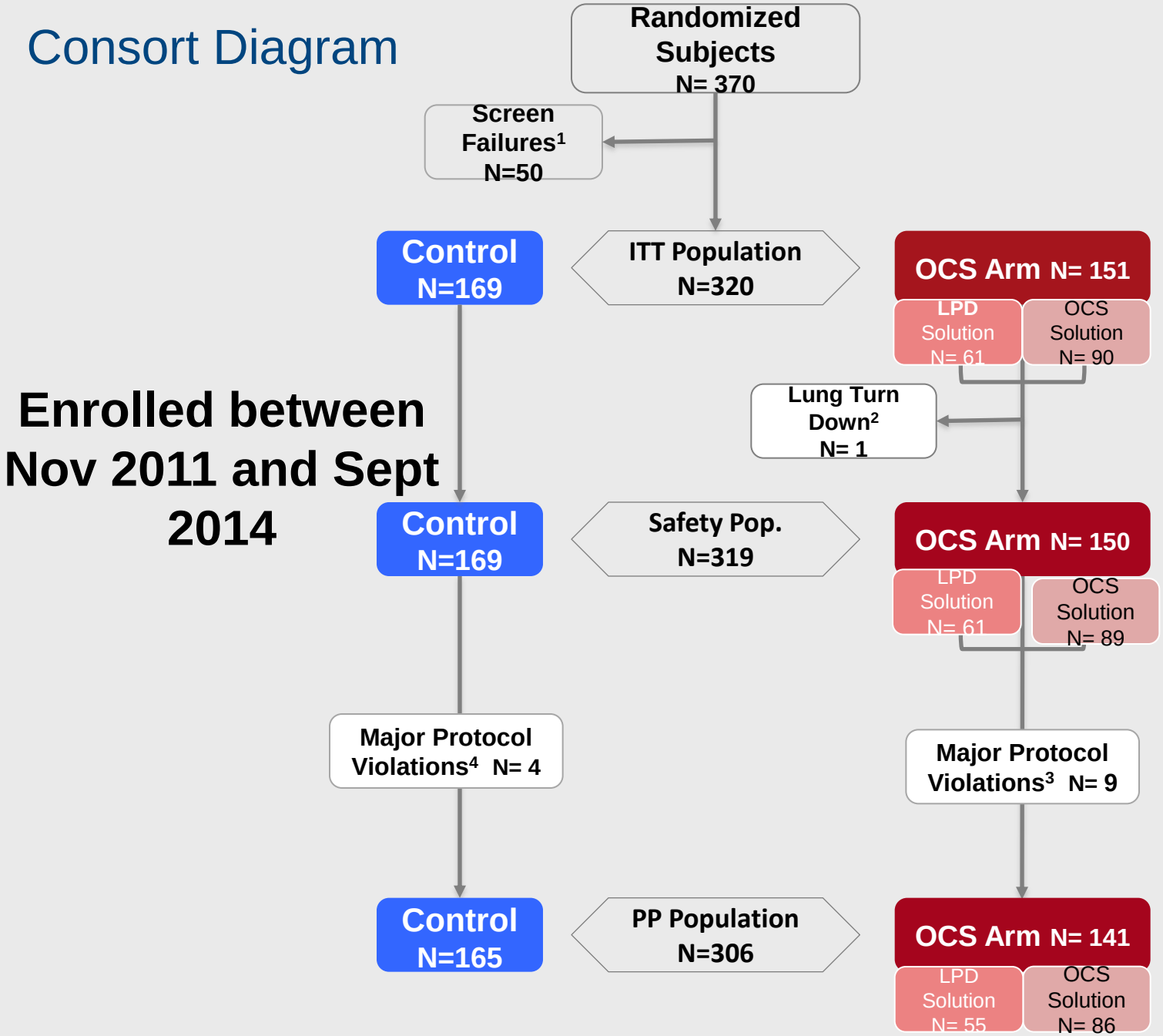
Organ Care System (OCS™) Platform Designed to Address Limitations of Cold Storage

REDUCE ISCHEMIC INJURY	OPTIMIZE ORGAN CONDITION	EX-VIVO FUNCTIONAL ASSESSMENT
Warm Oxygenated Blood Perfusion – Lung breathing, Heart beating etc.	Optimize O2 Delivery Replenish Substrates & Hormones	Metabolic Assessment & Perfusion Parameters

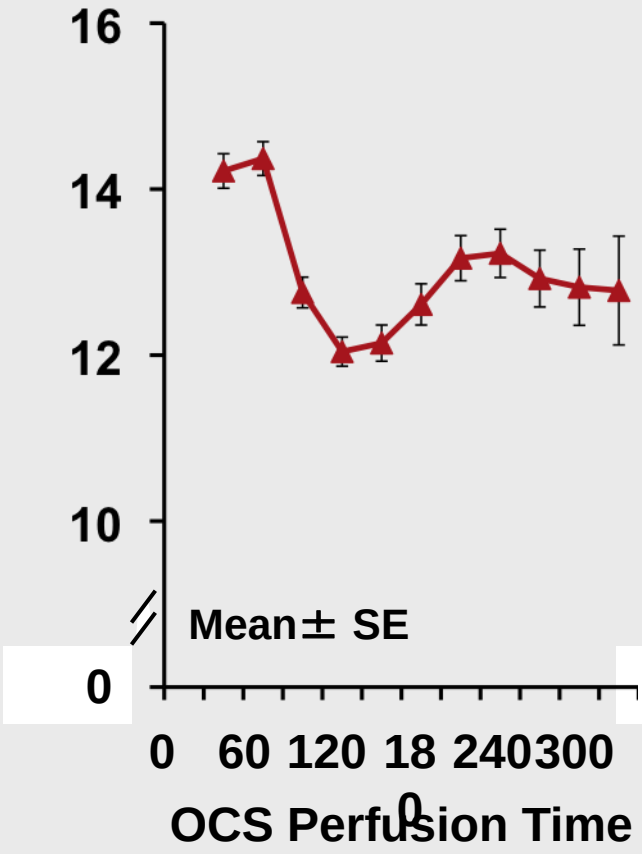
Donor Eligibility Criteria Reflect Standard Lung Transplantation

Inclusion	Exclusion
▪ Age <65 years old ▪ Normal gas exchange [PaO_2 / FiO_2 ≥ 300] at time of final acceptance of donor lung ▪ No active lung disease ▪ Lung suitable for both OCS or cold storage	▪ Presence of moderate to severe traumatic lung injury ▪ Presence of confirmed active pneumonia ▪ Positive serology (Hep. B/C, HIV etc.)

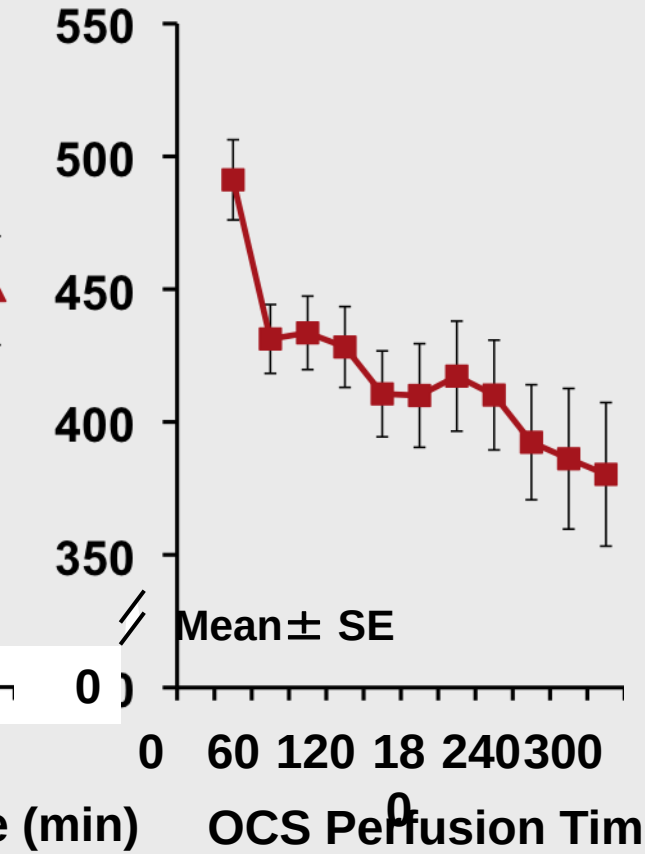
Consort Diagram



Peak Airway Pressure



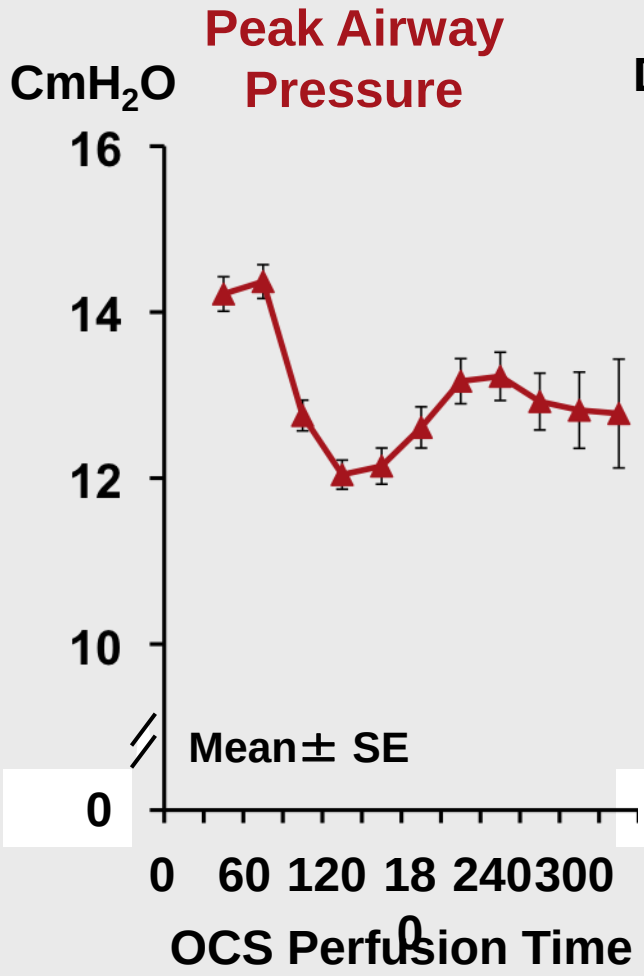
Vascular Resistance

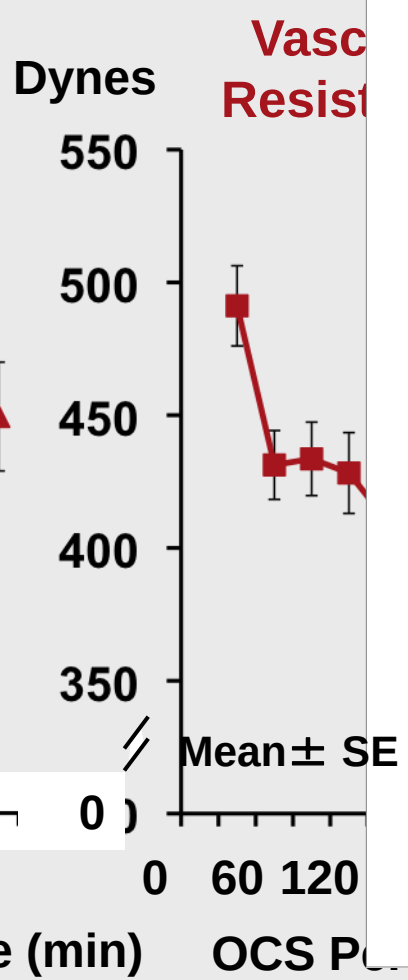


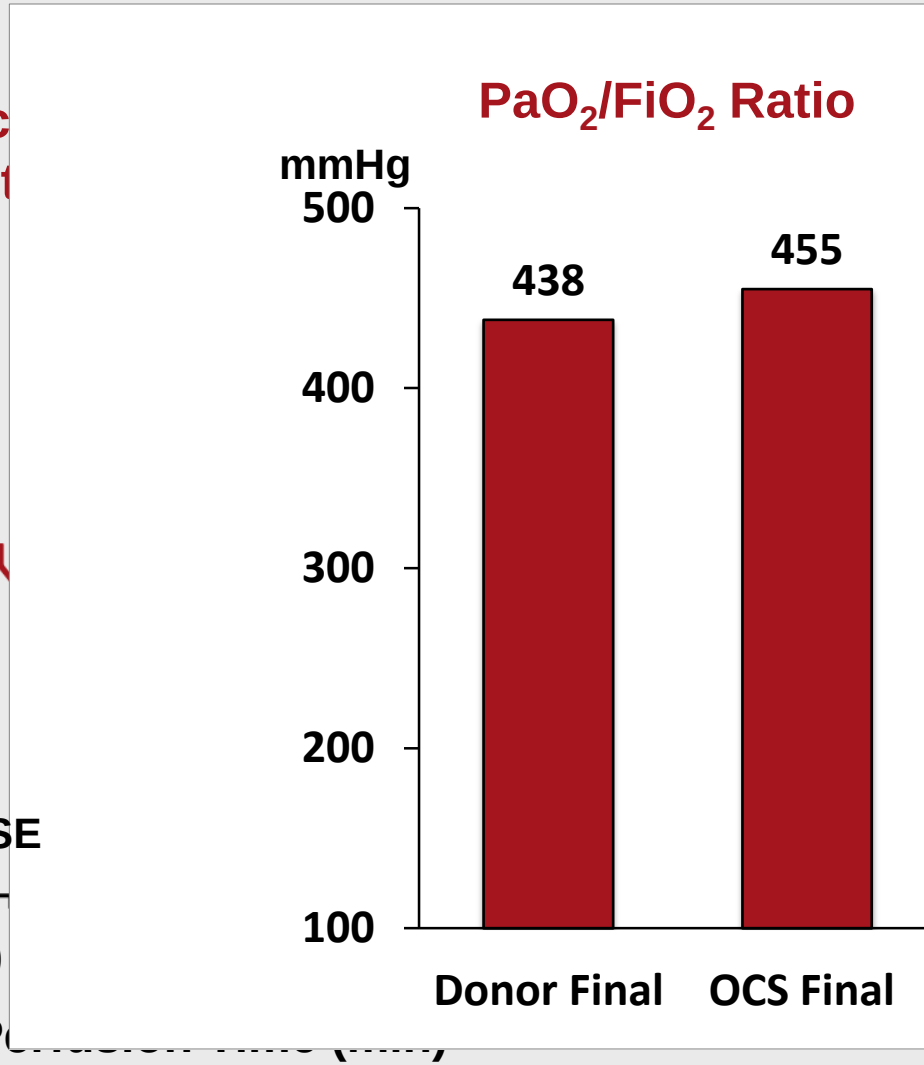
PaO_2/FiO_2 Ratio

mmHg

Improve lung condition/quality and clinical decision making



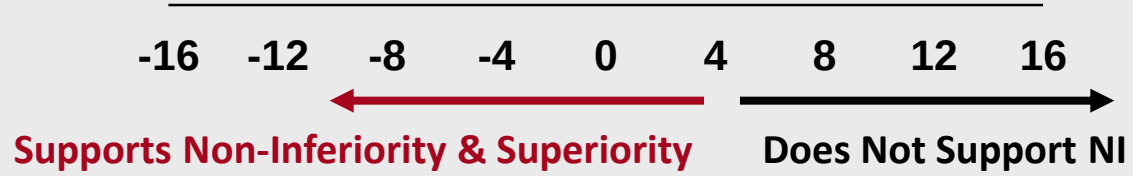




Improve lung condition/quality and clinical decision making

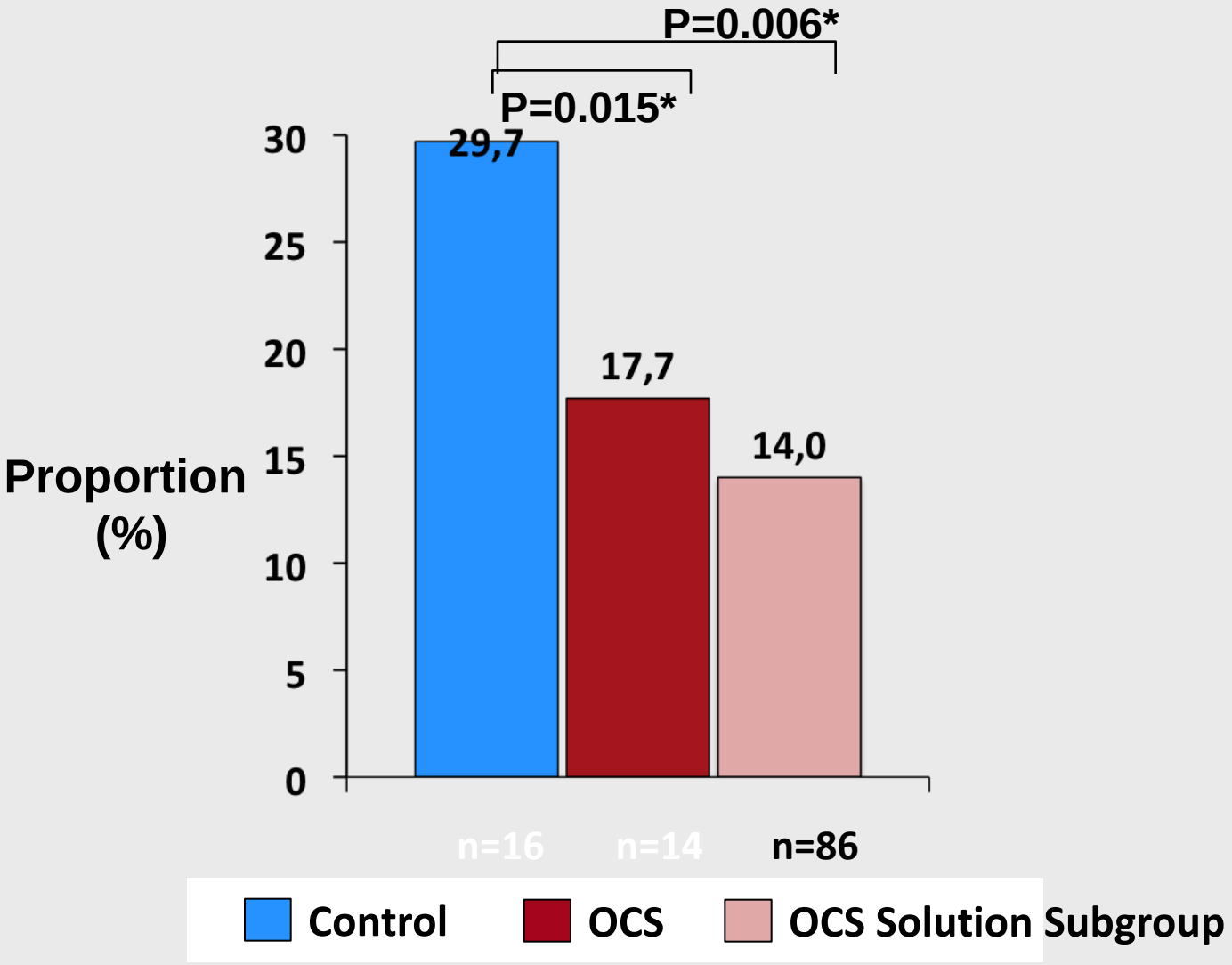
Met Primary Effectiveness Endpoint – 30-day Survival and Freedom from PGD3 within 72 Hours

	Point Estimates		Treatment Difference [Upper 95% CI]	P-Value
	Control	OCS	OCS Arm vs. Control	
PP Population	70.3%	79.4%	-9.1%	0.004
ITT Population	70.4%	74.2%	-3.8%	0.060
OCS Solution Subgroup vs. Control				
PP Population	70.3%	82.6%	-12.3%	0.001*
ITT Population	70.4%	78.9%	-8.5%	0.012

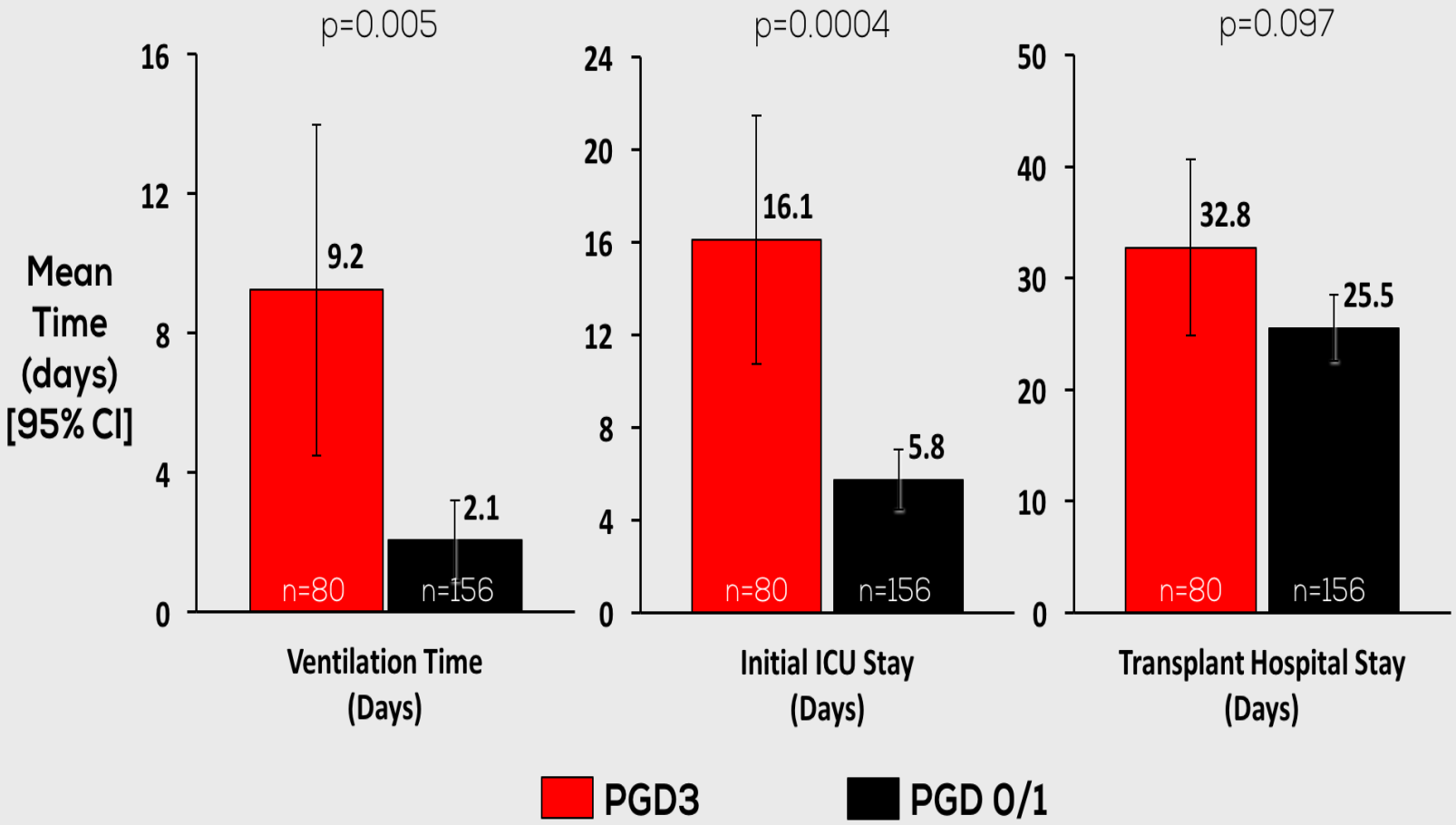


* met non-inferiority and superiority test

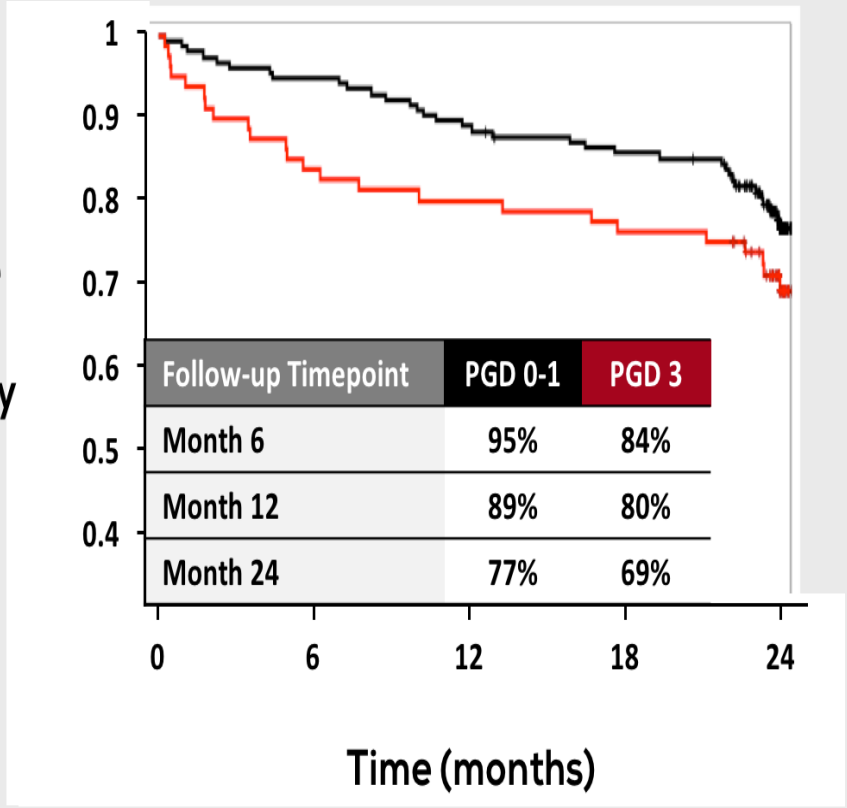
The OCS Resulted in Significant Reduction of PGD3 within the Initial 72 Hours Post-Tx.



Reduction in PGD3 Impacts Short Term Outcomes



Reduction in PGD3 Impacts Long-Term Outcomes

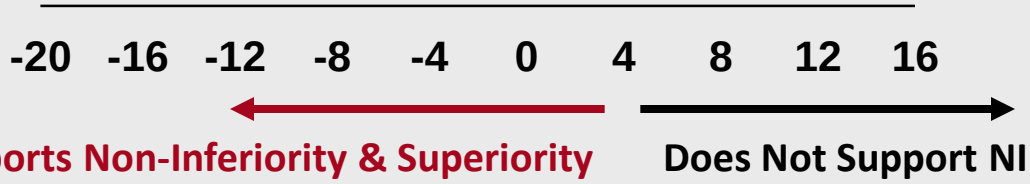


at risk

PGD 0-1	157	149	140	133	66
PGD 3	81	68	65	62	33

Adjunct Effectiveness Analysis – Survival Through Transplant Admission and Freedom from PGD3 within 72 hours

	Point Estimates		Treatment Difference [Upper 95% CI]	P-Value
	Control	OCS	OCS Arm vs. Control	
PP Population	66.7%	79.4%	-12.8%	0.0004*
ITT Population	66.9%	74.2%	-7.3%	0.013
			OCS Solution Subgroup vs. Control	
PP Population	66.7%	82.6%	-15.9%	0.0001*
ITT Population	66.9%	78.9%	-12%	0.002*



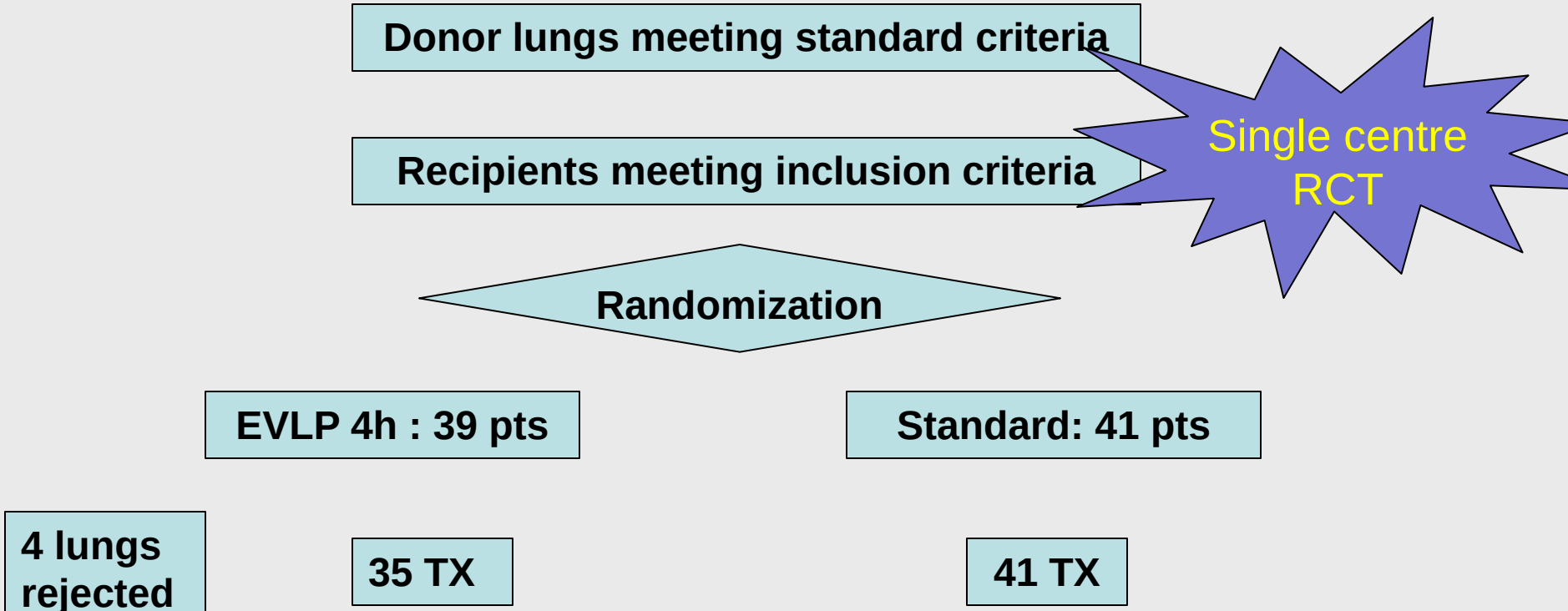
* met non-inferiority and superiority test

Conclusion

- Safe use of OCS is feasible and reproducible in a multi-center setting
- PGD 3 and 30-day mortality have been significantly reduced in the treatment arm
- Prevalence of BOS is reduced in recipients without PGD3

Warnecke G et al, Lancet Respir Med 2018;6:357-67

Standard donor lung procurement with normothermic ex-vivo lung perfusion



Slama A et al, J Heart Lung Transplant 2017;36:744-53

Standard donor lung procurement with normothermic ex-vivo lung perfusion

	EVLP N=35	Control N=41	p
Post-op intubation (days)	1.6	1.6	NS
Time in ICU (days)	6	6	NS
Hospital stay (days)	23	19	NS
Post-op ECMO, N pts	2 (6%)	5 (12%)	NS
30-day survival, N pts	34 (97%)	41 (100%)	NS
Hospital discharge, N pts	32 (91%)	41 (100%)	NS

No difference in terms of PGD at any time-point !!

Slama A et al, J Heart Lung Transplant 2017;36:744-53

Standard donor lung procurement with normothermic ex-vivo lung perfusion

Conclusion

- Use of EVLP with standard donor lungs is safe
- EVLP may increase duration of preservation
  - Allow for ex-vivo treatment
  - Improve logistics and planning

Slama A et al, J Heart Lung Transplant 2017;36:744-53

Extend preservation time:

- Prolonged cold ischemia might favour PGD
  - Yes: Consensus Statement ISHLT
  - No: ISHLT registry report 2017
- Prolonged EVLP technically possible

Gelman AE et al, J Heart Lung Transplant 2017;36:1114-9
Chambers DC et al, J Heart Lung Transplant 2017;36:1048-59
Cypel M et al, NJ Heart Lung Transplant 2008;27:1319-25

Outcomes after transplantation of lungs preserved for more than 12 hours: a retrospective study

- 906 transplants with full data, 2006-2015
- 2 modes of preservation
  - Cold ischemia alone
  - Cold ischemia – EVLP – cold ischemia
- Primary outcomes
  - 30-day survival
  - PGD at 72 hours

Yeung JC et al, Lancet Respir Med 2017;5:119-24

Outcomes after transplantation of lungs preserved for more than 12 hours: a retrospective study

	Pres. < 24h N = 809	Pres. > 24 h N = 97	p
Hospital stay (med, days)	23	25	NS
ICU stay (med, days)	4	4	NS

PGD score similar !!!

Survival (Kaplan-Meier) similar !!!

Yeung JC et al, Lancet Respir Med 2017;5:119-24

Take Home Message

EVLP has become part of clinical lung TX

- Improves preservation of standard donor lungs
- Allows to extent duration of preservation
- May increase the donor pool by evaluation of marginal donor lungs

Lung Transplantation

TX for pulmonary fibrosis

State of the Art

- *Median survival after TX for IPF is 1 year shorter*
- *Subcategories of IPF are credited worse prognosis*

- Scleroderma
  - Pulmonary death prevails over renal failure
  - TX validated by ISHLT consensus
- Short telomere syndrome
  - Isolated reports suggest dismal survival after TX
  - TERT/TERC mutations –hematologic & renal complications

Yusen et al, J Heart Lung Transplant 2014;33:1009-24
Steen VD et al, Ann Rheum Dis 2007;66:940-4
Weil D et al, J Heart Lung Transplant 2015;34:1-15
Silhan et al, Eur Respir J 2014;44:178-87
Borie R et al, j Heart Lung Transplant 2015;34:538-46

Long-term survival in bilateral lung transplantation for scleroderma-related lung disease

Jan 2006-Dec 2014

684 Lung TX

394 bilateral

181 IPF

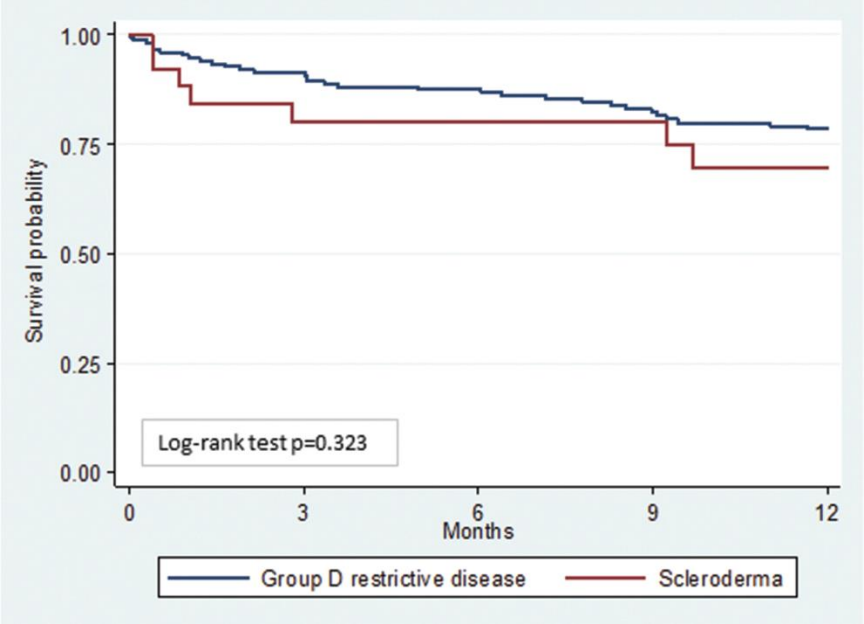
26 scleroderma

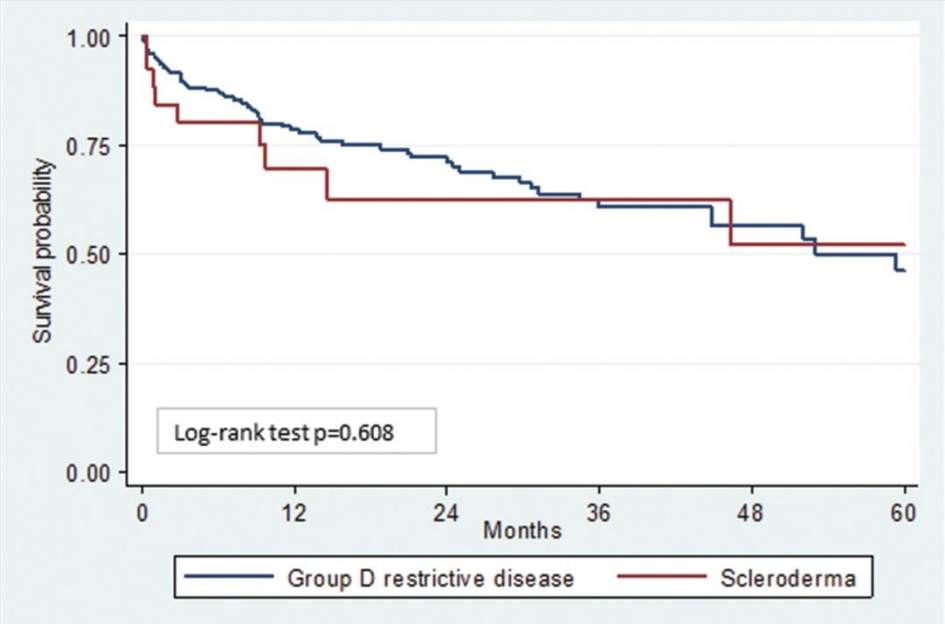
155 other

Single centre observational

Chan EY et al, Ann Thorac Surg 2018;105:893-900

Long-term survival in bilateral lung transplantation for scleroderma-related lung disease





Similar survival at 1 and 5 years

Chan EY et al, Ann Thorac Surg 2018;105:893-900

Long-term survival in bilateral lung transplantation for scleroderma-related lung disease

Risk factors at 1 year (Cox)

Variable	HR	95% CI	p
ECMO at listing	14.2	2-127	0.018
Diabetes	2.16	1-5	0.044
eGFR<60 mL/min/m2	5.95	2-15	<0.001
Donor smoker	2.25	1-5	0.047
Donor age > 50	2.57	1-6	0.018

Scleroderma isn't a significant risk factor !!!

Chan EY et al, Ann Thorac Surg 2018;105:893-900

Long-term survival in bilateral lung transplantation for scleroderma-related lung disease

Risk factors at 5 year (Cox)

Variable	HR	95% CI	p
ECMO at listing	13.84	2-118	0.016
eGFR<60 mL/min/m2	5.16	2-12	<0.001
Recipient age > 65	2.26	1-5	0.040
Recipient age > 70	2.74	1-6	0.005
Donor age > 50	2.67	1-5	0.002

Scleroderma isn't a significant risk factor !!!

Chan EY et al, Ann Thorac Surg 2018;105:893-900

Telomere length in patients with pulmonary fibrosis associated with CLAD and post-lung transplant survival

- Short telomeres (< 10th percentile) exist

  - in 40% of familial IPF

  - in 25% of sporadic IPF

- Prospective cohort study to investigate prognostic significance
- Methods
  - Measurement with PCR
  - Length adjusted to age
  - Comparison of < 10th percentile to > 10th percentile
- Outcome measurements
  - PGD garde 3
  - Acute Cellular Rejection
  - CLAD
  - Survival

Newton CA et al,
J Heart Lung Transplant
2017;36:845-53

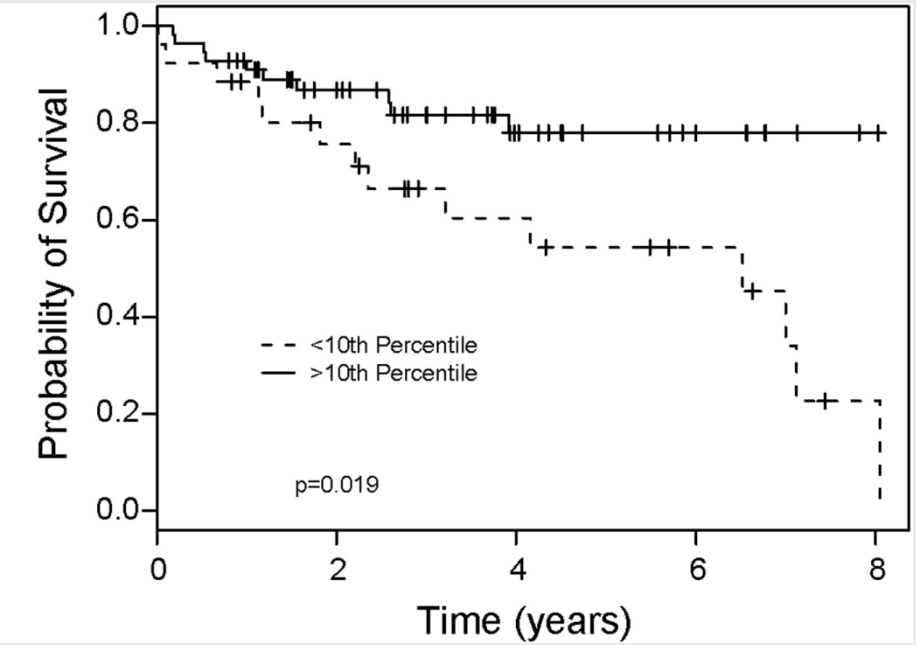
Telomere length in patients with pulmonary fibrosis associated with CLAD and post-lung transplant survival

	Total N=82	< 10th percentile	> 10th percentile	p
Death / FU	**29%**	**54%**	**18%**	0.0015
Median survival	7.1	6.2	NR	0.019
PGD 3	**12%**	**28%**	**6%**	0.034
Time to CLAD (Median)	5.3	2.7	NR	0.0054
CLAD present	**32%**	**50%**	**23%**	0.022

Newton CA et al, J Heart Lung Transplant 2017;36:845-53

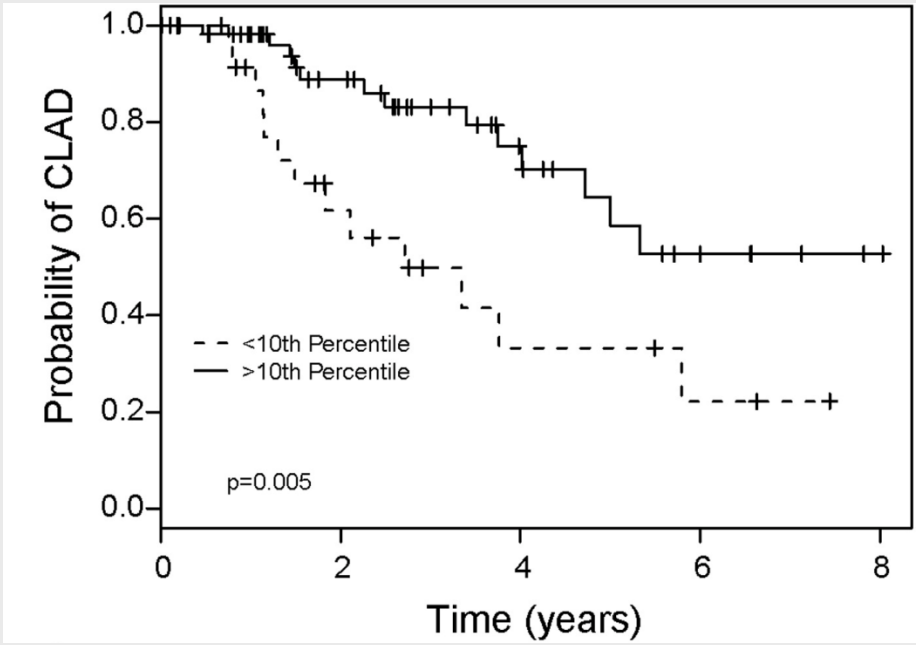
Telomere length in patients with pulmonary fibrosis associated with CLAD and post-lung transplant survival

Survival



H.R. 10.9 (p=0.001)

Time to CLAD



H.R. 6.3 (p=0.002

Newton CA et al, J Heart Lung Transplant 2017;36:845-53

Lung Transplantation

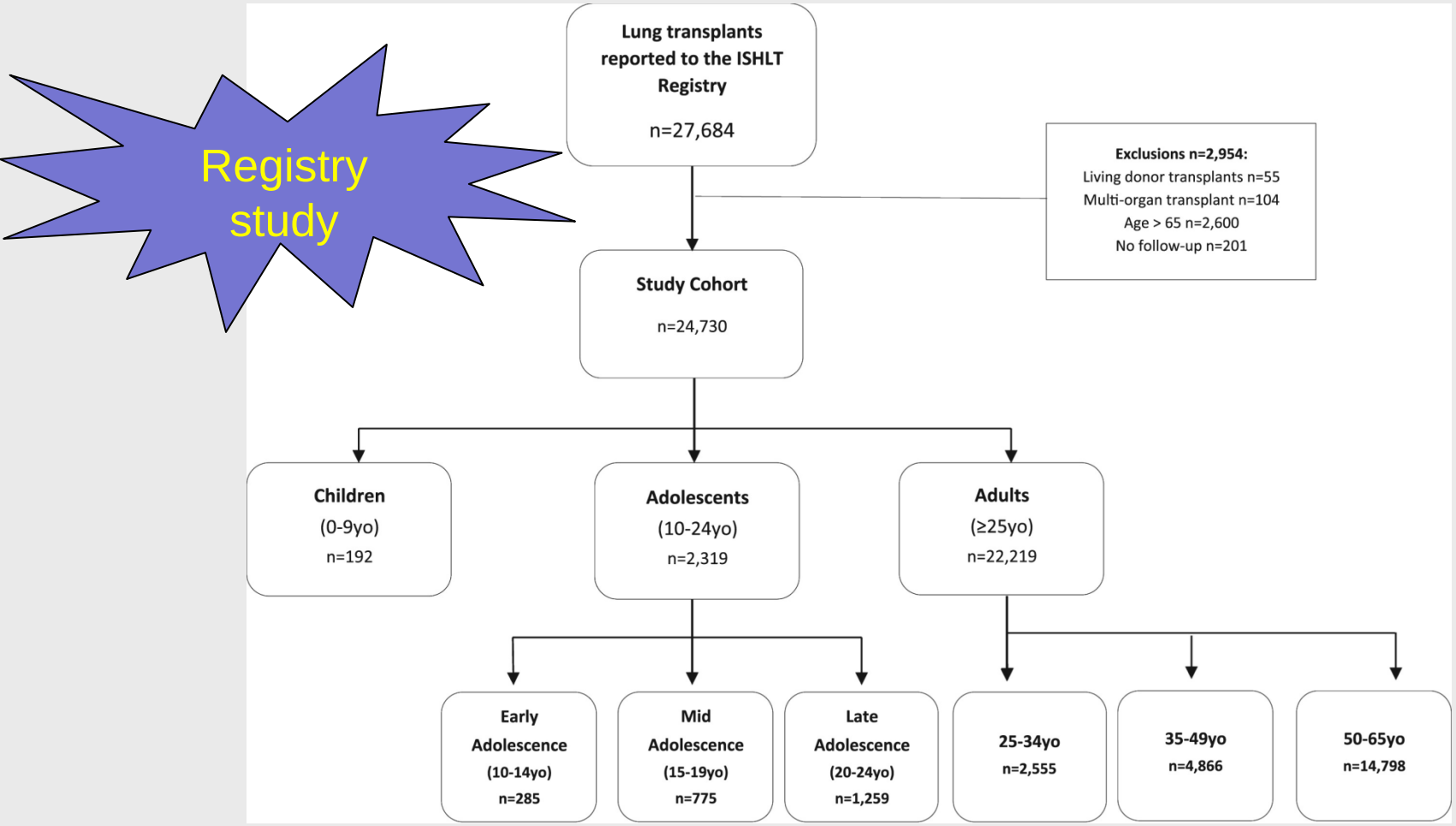
Younger patients' outcome

State of the Art

- Adolescents‘ outcomes after transplantation
  - Higher rate of acute and chronic rejection and mortality have been reported after renal, liver and heart transplantation
  - Transition to adulthood is period of risk
- Paediatric lung transplantation
  - Increased mortality and morbidity of lung TX
  - Case volume – outcome relationship accepted
  - Waiting list mortality under-explored

Bell LE et al, Am J Transplant 2008;8:2230-42
Dharnidharka VR et al, Pediatr Transplant 2015;19:471-6
Hsu DT. Pediatr Transplant 2005;9:416-21
Hayes D et al, Lung 2015;193:629-37
Kilic A et al, J Thorac Cardiovasc Surg 2012;144:1502-8

Outcomes of adolescent recipients after lung transplantation: an analysis of the ISHLT registry



Paraskeva MA et al, J Heart Lung Transplant 2018;37:323-331

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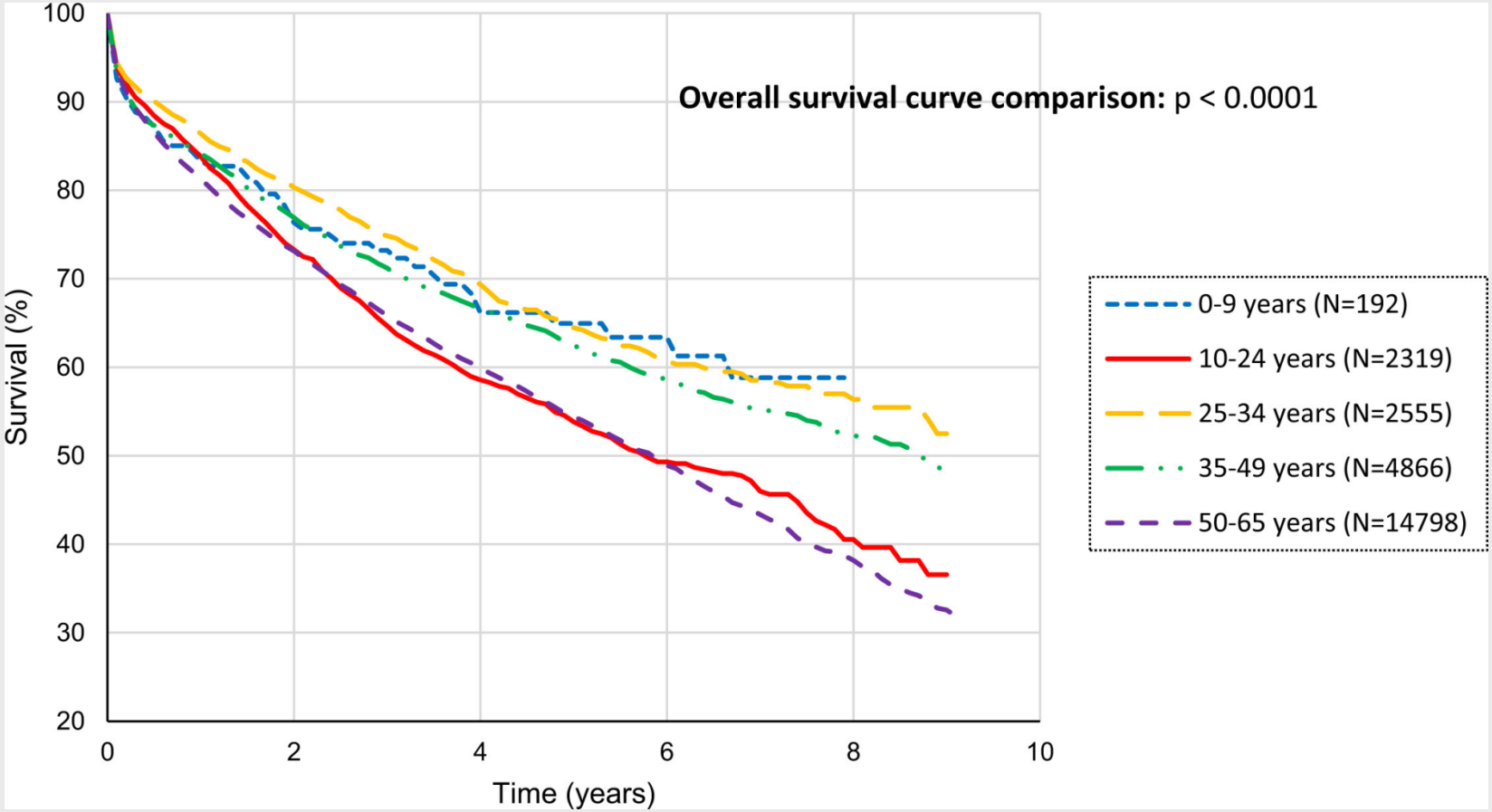

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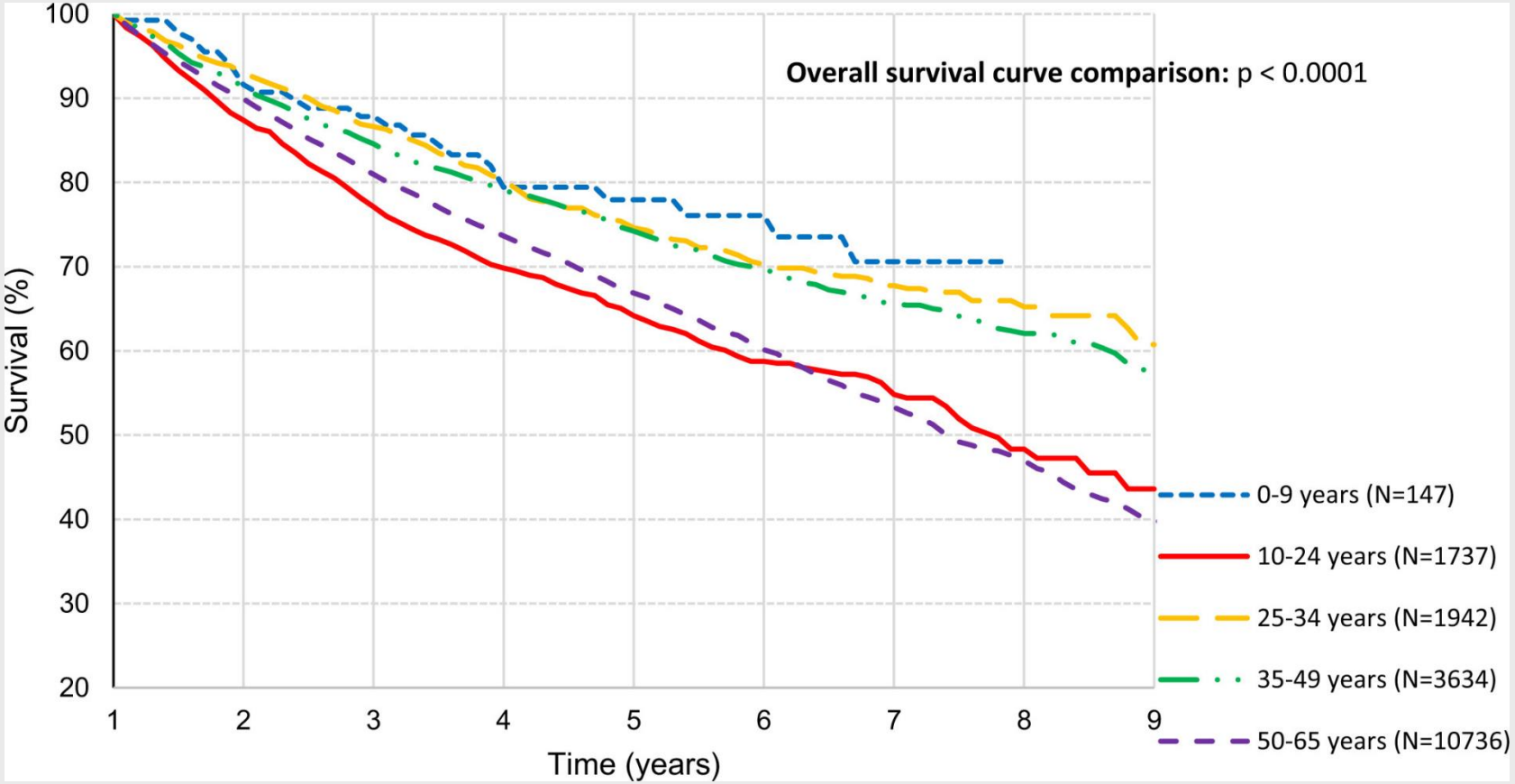

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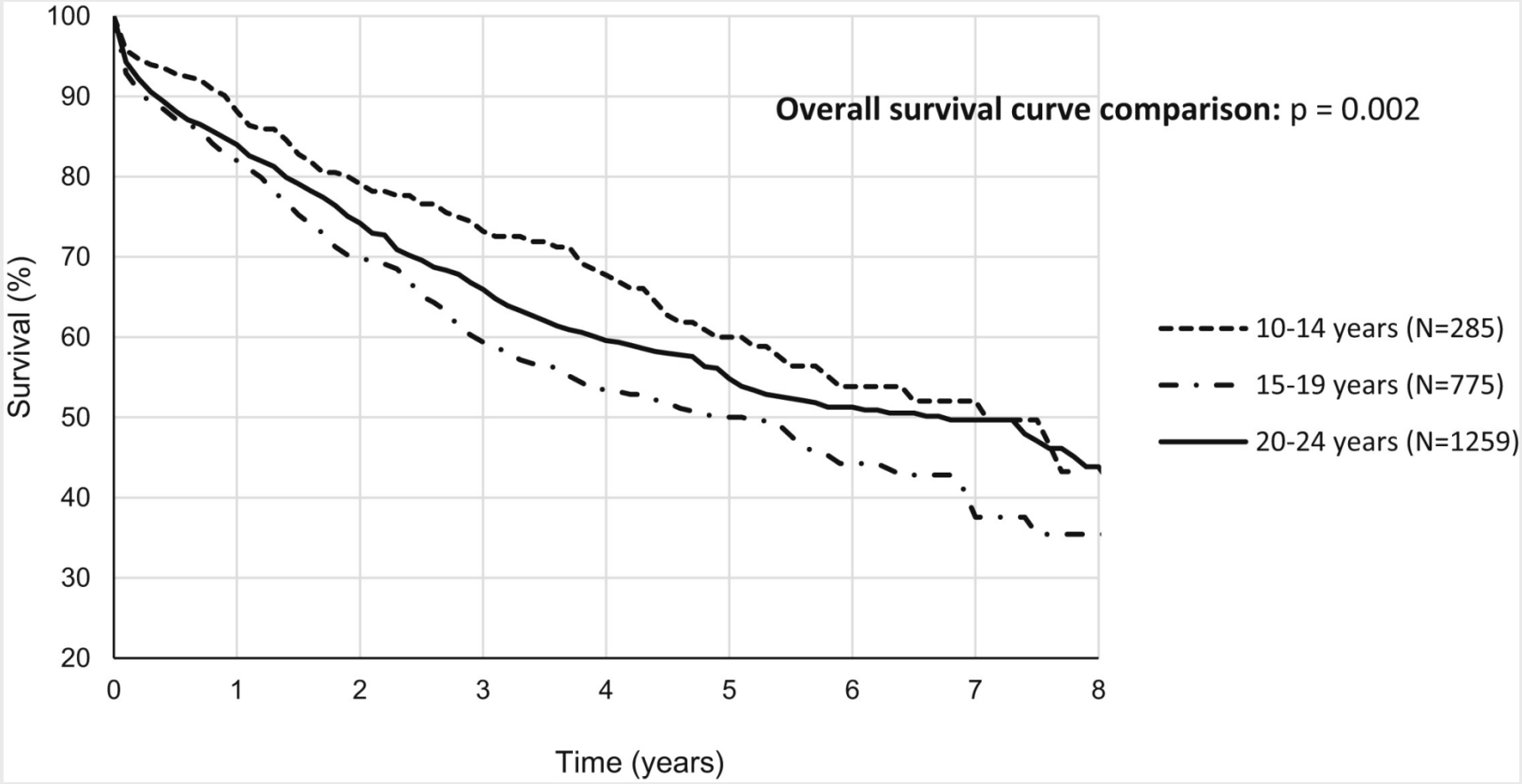

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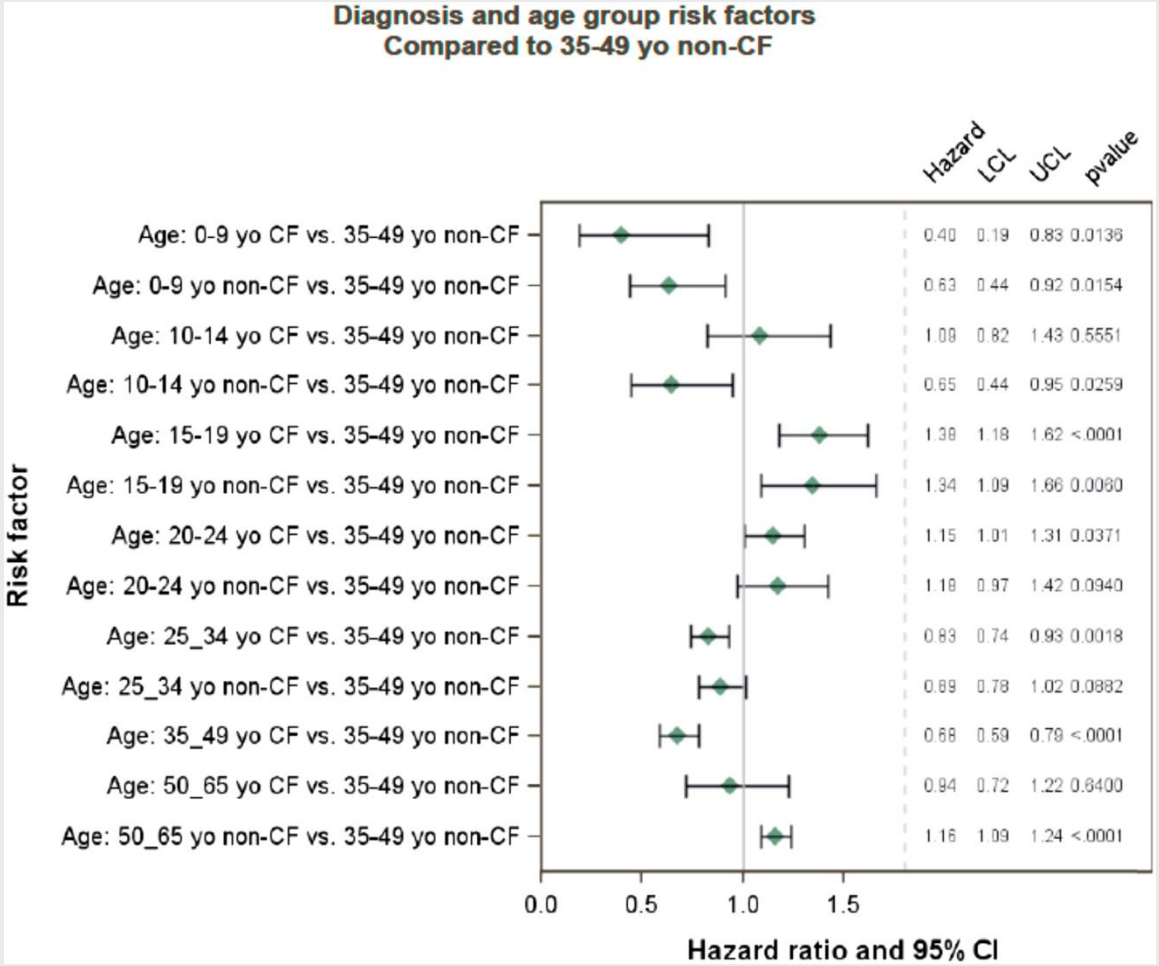


Paraskeva MA et al, J Heart Lung Transplant 2018;37:323-331

Outcomes of adolescent recipients after lung transplantation: an analysis of the ISHLT registry

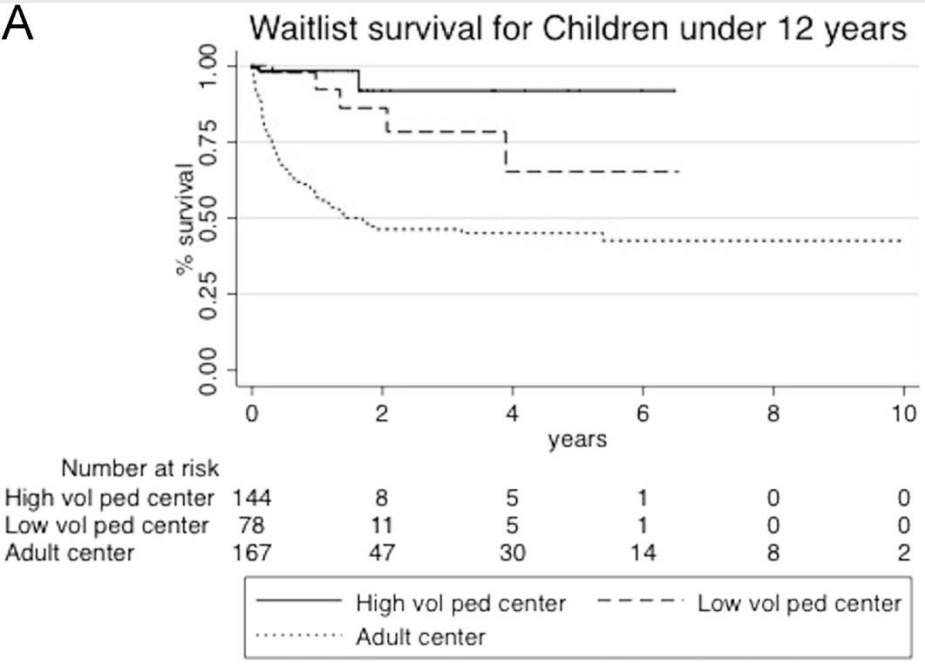
Age category 15-19 shows poorest prognosis

- Psychological profile ?
- Transition from paediatric to adult care teams ?
- Should be condidered apart in survival studies
- Requires particular care during follow-up

Paraskeva MA et al, J Heart Lung Transplant 2018;37:323-331

Waiting list outcomes in pediatric lung transplantation: poor results for children listed in adult TX programs

A



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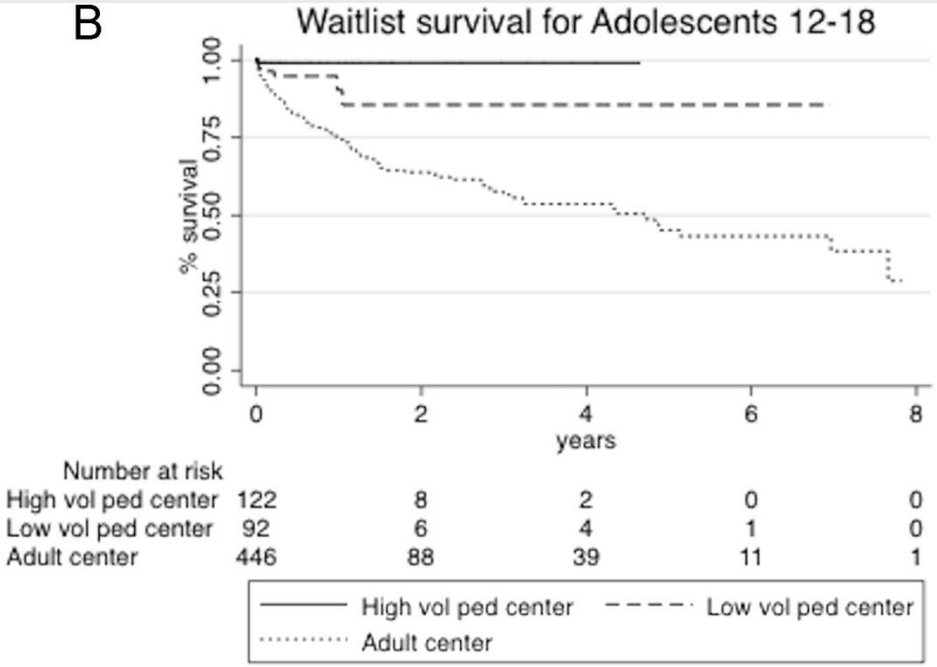
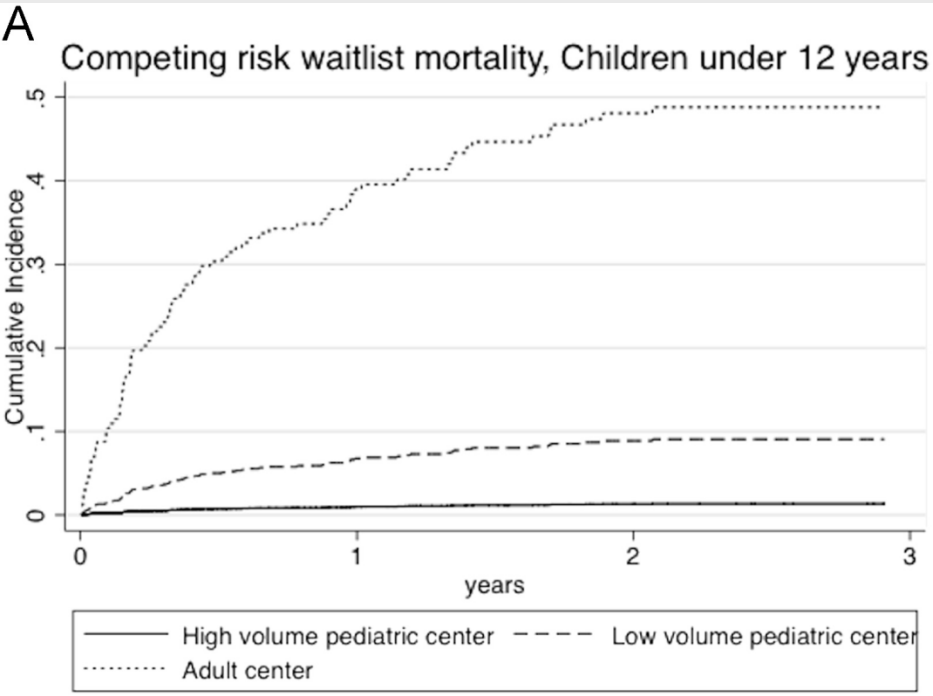


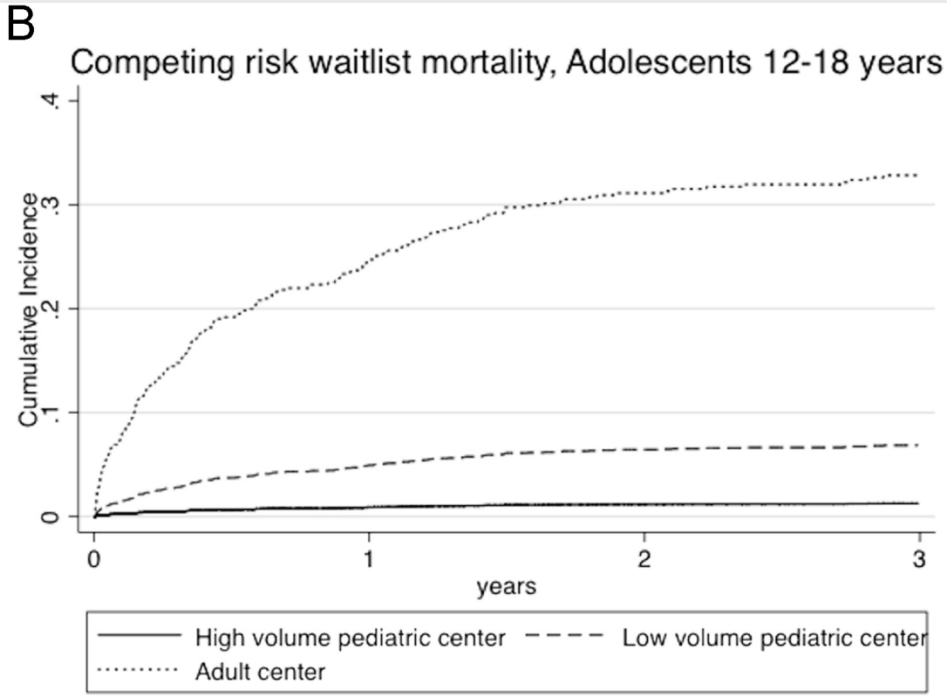
Registry study

	Hazard Ratio
Paediatric centre > 4/year	0.09
Paediatric centre < 4/year	0.56
Adult centre	6.56

Scully BS et al, J Heart Lung Transplant 2017;36:1201-8

Waiting list outcomes in pediatric lung transplantation: poor results for children listed in adult TX programs





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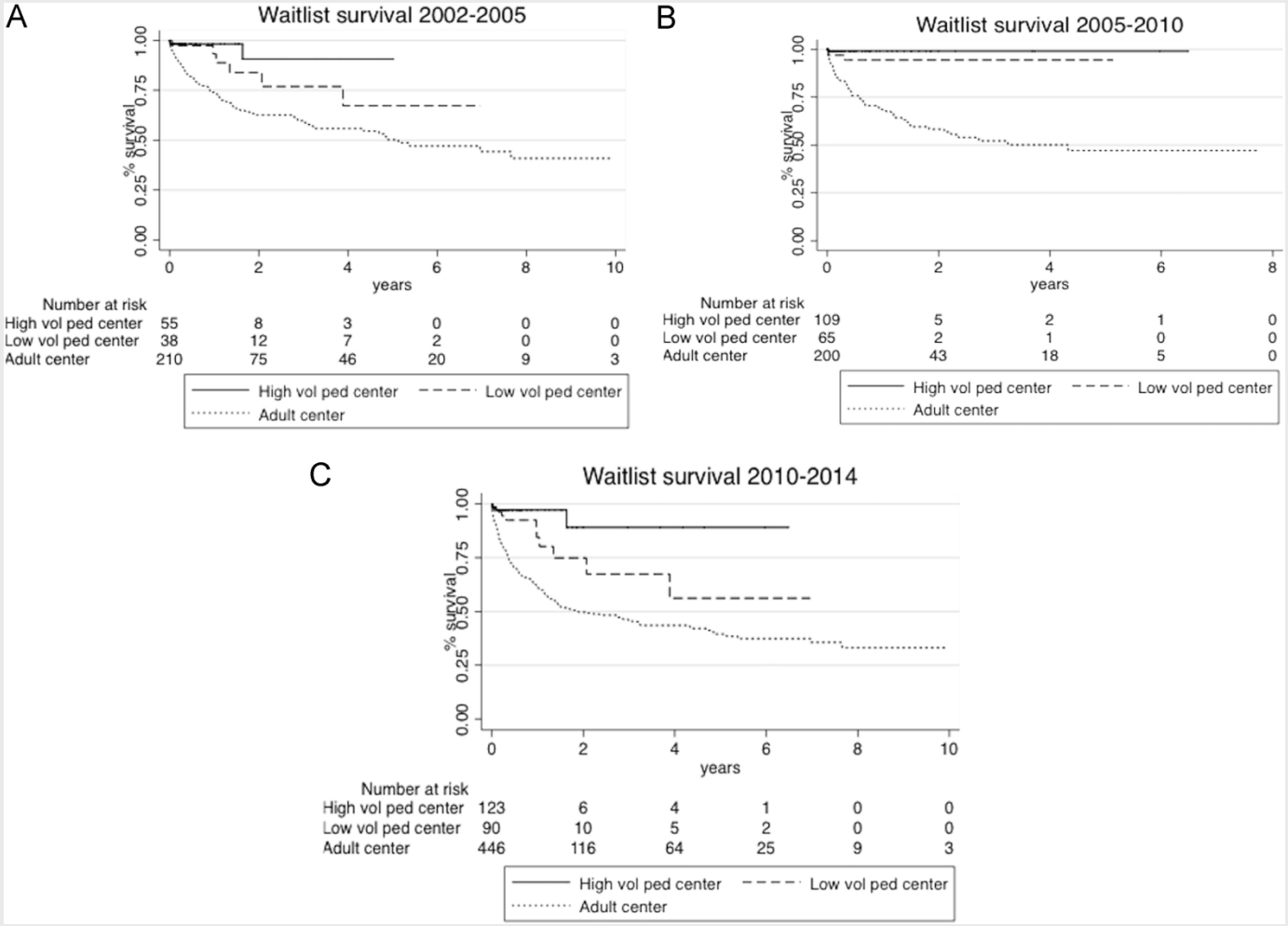


Scully BS et al, J Heart Lung Transplant 2017;36:1201-8

Waiting list outcomes in pediatric lung transplantation: poor results for children listed in adult TX programs

Mortality by type of centre

	Paediatric > 4 TX/year	Paediatric <4 TX/year	Adult
Alive after TX	59%	54.4%	20.2 %
Dead after TX	31.5 %	33.5 %	22.0 %
Alive without TX	2.1 %	6 %	27.1 %
Dead on waitlist	1.4 %	6.0 %	30.8 %

Scully BS et al, J Heart Lung Transplant 2017;36:1201-8

Waiting list outcomes in pediatric lung transplantation: poor results for children listed in adult TX programs

Paediatric lung TX waitlist survival (Cox)

Risk factor	H.R.	p
Adult centre	15.6	<0.001
Paediatric centre < 4 TX/year	4.06	0.02
Ventilator	2.78	0.02

Scully BS et al, J Heart Lung Transplant 2017;36:1201-8

Waiting list outcomes in pediatric lung transplantation: poor results for children listed in adult TX programs

Paediatric lung TX: competing on waitlist (Cox)

Risk factor	H.R.	p
Adult centre	32.97	0
Paediatric centre < 4 TX/year	5.43	0.004
Inotropes	2.87	0.026
Ventilator	2.26	0.09

Scully BS et al, J Heart Lung Transplant 2017;36:1201-8

Take Home Message

- Post-TX outcome of adolescents aged 15-19 is suboptimal
- Access to lung TX for children is best in high volume paediatric transplant centres

Thoracic Surgery

Thoracic Surgery

Patient Safety Issues
In the context of early discharge

State of the Art

Enhanced Recovery After Surgery (ERAS)

- Morbidity after lung cancer surgery close to 50%
- ERAS designed for colorectal surgery
  - multi-modal pathway from referral to discharge
  - Stress response decreased, outcome improved
- ERAS is new in thoracic surgery
  - How does it work ???

Phillips JD et al, J Am Coll Surg 2012;215:206-15
Kehlet H et al, Am J Surg202;183:630-11
Madani A et al, Surgery 2015;158:899-910
Gimenez-Mila M et al, J Thorac Dis 2016;8:31-45

The impact of ERAS protocol compliance on morbidity from resection for primary lung cancer

Thoracic surgery ERAS pathway: Patient Diary

Outlines protocol
Daily targets
Planned discharge

Preop.

1. Preop assessment
2. Patient education
3. Smoking cessation
4. Preop. Rehab.
5. Admission day 0
6. Preop carbohydrate
7. Avoid sedation

Periop.

1. Antibioprophylaxy
2. Regional anesthesia
3. Avoid fluid overload
4. Intraop warming
5. VTE prophylaxis
6. Avoid Foley
7. Favour VATS
8. Single chest tube

Postop

1. Avoid IV fluid
2. Avoid opiates
3. Early feeding
4. Treat nausea
5. Early mobilization
6. Remove drains early

Rogers LJ et al, J Thorac Cardiovasc Surg 2018;155:1843-52

The impact of ERAS protocol compliance on morbidity from resection for primary lung cancer

Results

- 422 resections
- Surgical approach
  - VATS 71.6%
  - Conversion 9.7%
  - Open 18.2%
- Lobectomy 70.4 %
- Risk category
  - ASA 3 : 28%
  - WHO PS 0/1: 84.4%
- Avoid sedation

- Hospital stay: 5 days
- ICU 0 days
- 30-day read. 5.5 %
- 30-day reop. 1.6 %
- 30-day morbidity
  - None : 61.4%
  - Minor: 24.6%
  - Major: 13%
- Mortality
  - 30-day: 1.4%
  - 90-day: 2.1%

Rogers LJ et al, J Thorac Cardiovasc Surg 2018;155:1843-52

The impact of ERAS protocol compliance on morbidity from resection for primary lung cancer

Multivariate analysis: predictors

Morbidity

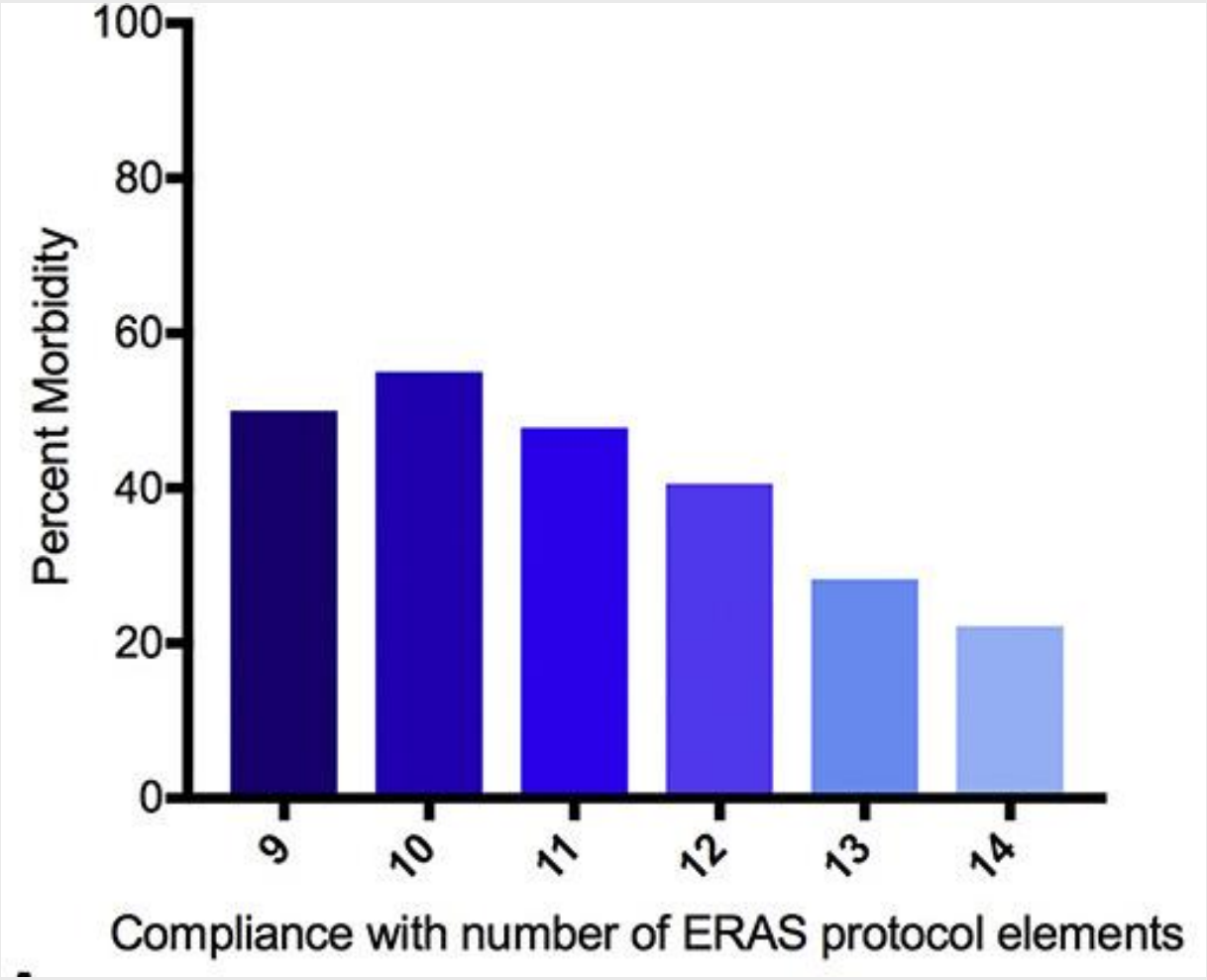
	O.R.	p
Age	1.20	0.01
Sublobar resection	0.45	<0.01
> 1 resection	2.21	0.02
Complicance score	0.72	<0.01
ICU stay	2.00	0.02

Prolonged hospital stay

	O.R.	p
Age	1.03	< 0.01
VATS	0.54	0.01
Carbohydrate drink	0.59	0.04
Early mobilization	0.43	<0.01
HDU	2.86	<0.01
ICU	3.81	<0.01

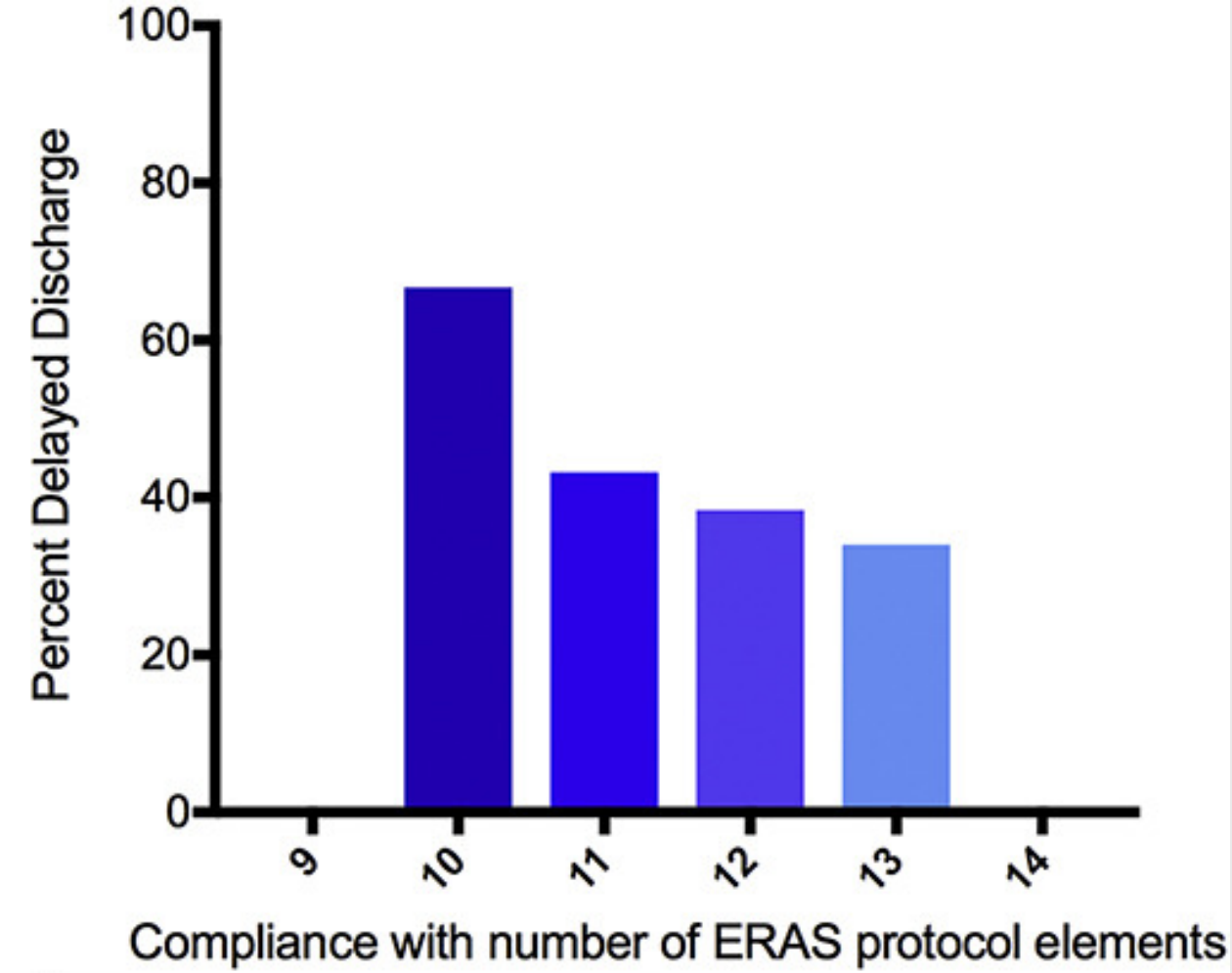
Rogers LJ et al, J Thorac Cardiovasc Surg 2018;155:1843-52

The impact of ERAS protocol compliance on morbidity from resection for primary lung cancer



Rogers LJ et al, J Thorac Cardiovasc Surg 2018;155:1843-52

The impact of ERAS protocol compliance on morbidity from resection for primary lung cancer

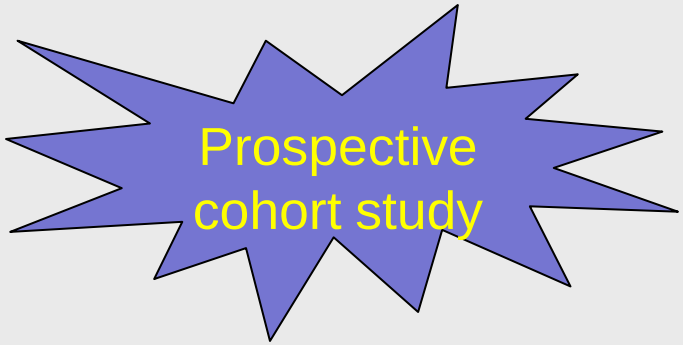


Rogers LJ et al, J Thorac Cardiovasc Surg 2018;155:1843-52

The impact of ERAS protocol compliance on morbidity from resection for primary lung cancer

Take home message

- Compliance to ERAS decreases morbidity
- Length of stay reduced with
  - Early mobilization
  - Use of VATS
- ERAS should become standard of care



Rogers LJ et al, J Thorac Cardiovasc Surg 2018;155:1843-52

State of the Art

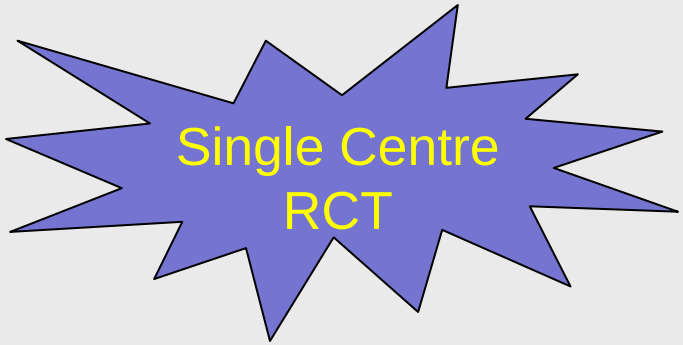
Post-op pain management

- Multimodal non-opioid protocols well accepted
  - Paracetamol
  - Non-steroid anti-inflammatory drugs
  - Locoregional anaesthesia
- Preop steroids seem effective

Wildgaard K et al, Eur J Cardiothorac Surg 2012;41:1072-7
De Oliveira GSJ et al, Anesthesiology 2011;115:575-88

High-dose methylprednisolone in VATS lobectomy: a randomized controlled trial

- Single centre randomized trial
- 125 mg methylprednisolone IV after induction
- Non-opioid analgesia per os + paravertebral block
- Outcome parameters:
  - **Pain**
  - Sedation
  - Glycemia
  - Nausea
  - Fatigue/sleep quality



Bjerregaard et al, Eur J Cardiothorac Surg 2018;53:209-15

High-dose methylprednisolone in VATS lobectomy: a randomized controlled trial

- 120 patients included
- 96 available for final analysis
  - 49 methylprednisolone group
  - 47 placebo
- Pain scores significantly reduced on day of surgery
  - At rest : 1.6 – 2.0 (p=0.019
  - At mobilisation 1.7 – 2.5 (p=0.004)
- Secondary outcomes
  - Less nausea (p=0.04)
  - Less fatigue (p=0.03)

Bjerregaard et al, Eur J Cardiothorac Surg 2018;53:209-15

Take Home Message

- Non opioid multimodal analgesia is the contemporary standard for fast track surgery
- High dose preoperative methylprednisolone improves pain control without adverse effects on the day of surgery

State of the Art

Venous thrombo-embolism

- Well documented in oncologic surgery
- Risk higher in patients with lung cancer
- Cumulated risk
  - Personal factors
  - Cancer
  - Post-op immobility
  - Extent of resection

Trinh VQ et al, JAMA Surg 2014;149:43-9
Dentali F et al, J Thorac Cardiovasc Surg 2008;135:705-6
Corrales-Rodriguez L et al, Lung Cancer 2012;75:1-8
Christensen TD et al, Ann Thorac Surg 2014;97:394-400

Timing and risk factors associated with venous thromboembolism after lung cancer resection

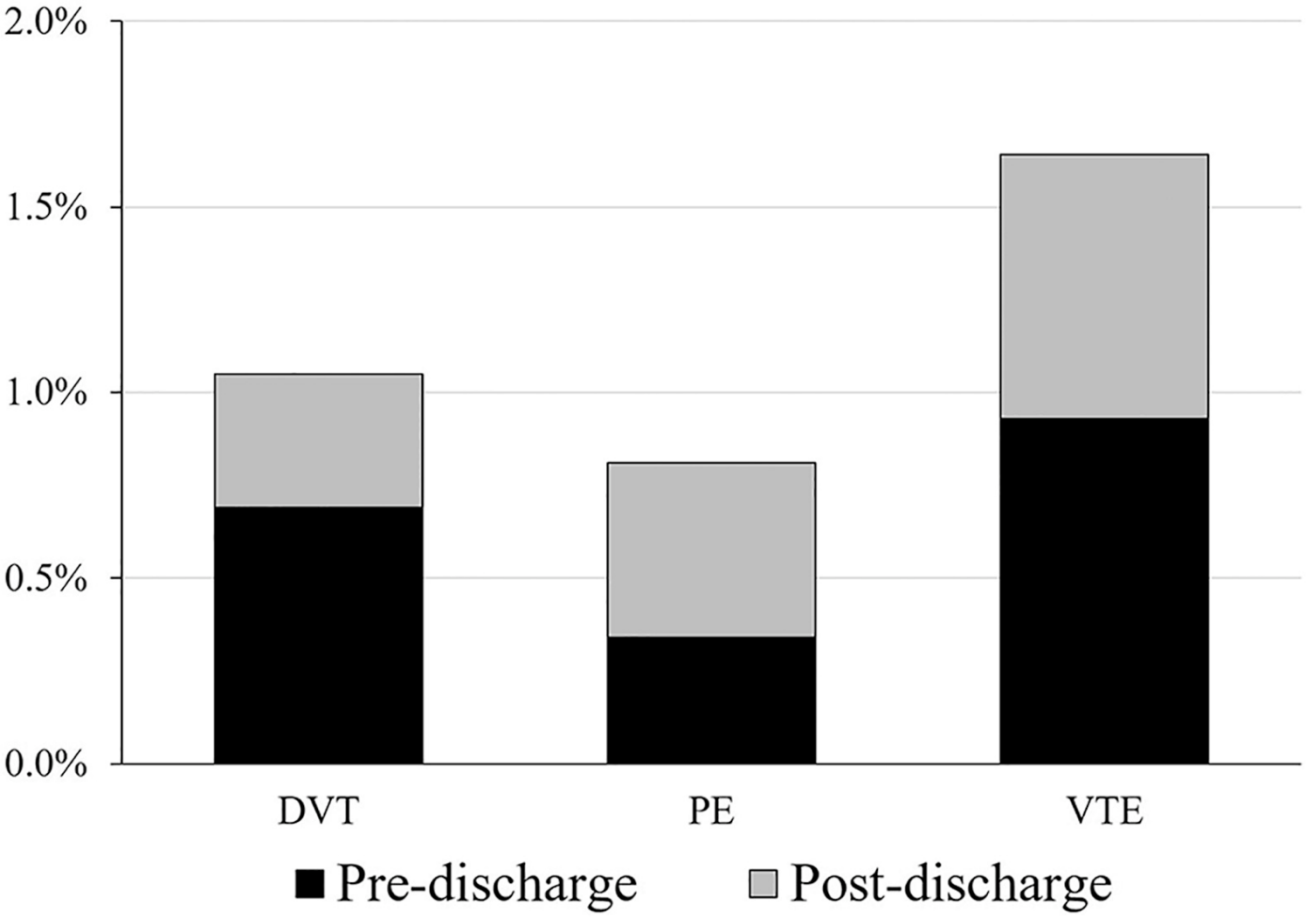
No data on timing & duration of prophylaxis

- Frequency overall / post-discharge ?
- Profile of high risk patients

- ACS NSQIP 2005-2015
- Patients > 18 years, anatomic lung resection

Thomas DC et al, Ann Thorac Surg 2018;105:1460-75

Timing and risk factors associated with venous thromboembolism after lung cancer resection



Thomas DC et al, Ann Thorac Surg 2018;105:1460-75

Timing and risk factors associated with venous thromboembolism after lung cancer resection

Timing of thromboembolic event

	N	%	Median delay
DVT	150	1.1	10 (5-16)
PE	116	0.8	11 (5-17)
VTE	234	1.6	10 (5-17)

Thomas DC et al, Ann Thorac Surg 2018;105:1460-75

Timing and risk factors associated with venous thromboembolism after lung cancer resection

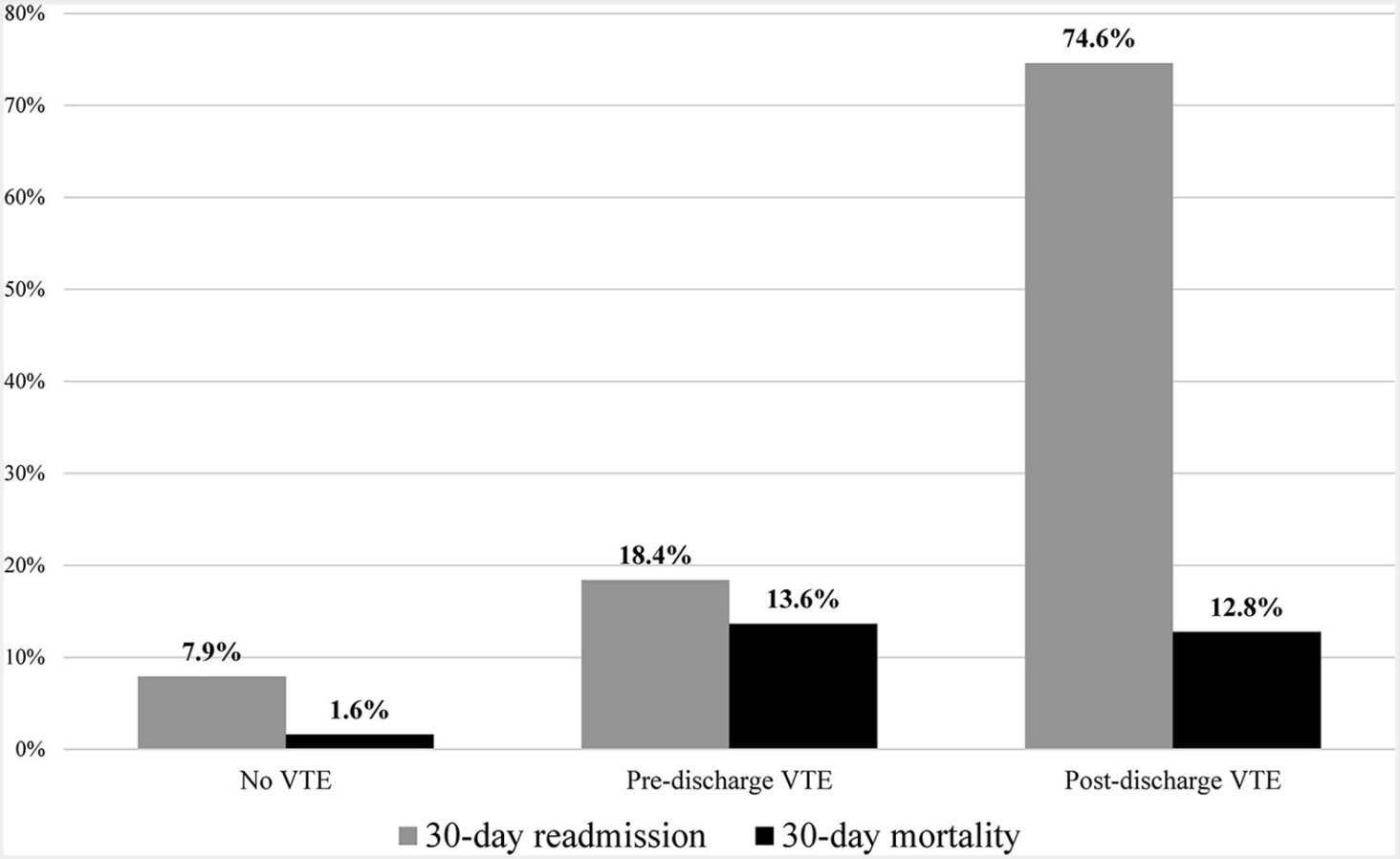
Risk factors (univariate)

- **Age > 65 years***
- Male gender
- **Underweight or obese***
- Weight loss > 10% / 6 months
- Severe COPD
- Hypertension
- Diabetes
- **Pneumonectomy = 3 x lobectomy***
- Thoracotomy > VATS

*Confirmed multivariate

Thomas DC et al, Ann Thorac Surg 2018;105:1460-75

Timing and risk factors associated with venous thromboembolism after lung cancer resection



Thomas DC et al, Ann Thorac Surg 2018;105:1460-75

Take Home Message

- VTE occurs at a median interval of 10 days after surgery
- Half of the events occur after discharge
- Risk factors are
  - age
  - high or low BMI
  - extent of parenchymal resection

State of the Art

Air leak after surgery

- A common problem !
  - COPD, steroids
  - Upper lobectomy
  - Adhesions
- Many adjuncts with variable success
- Pressure for early discharge
  - Cost control
  - VATS
  - Enhaced recovery after surgery

Brunelli A et al, Ann Thorac Surg 2010;90:204-9
Rice T et al, Thorac Surg Clin 2010;20:377-89
Varela G et al, Eur J Cardiothorac Surg 2005;27:329-33

Analysis of patients discharged from the hospital with a chest tube in place

Empyema in patients discharged with a chest tube

- 236 patients from 2004-2013
- 4% of all lung resections
  - Wedge resection 29%
  - Lobectomy 40%
  - Lung volume reduction 3%
  - Miscellaneous 28%
- 27 patients (11.4%) discharged on antibiotics

Reinerman JM et al, Ann Thorac Surg 2018;105:1038-43

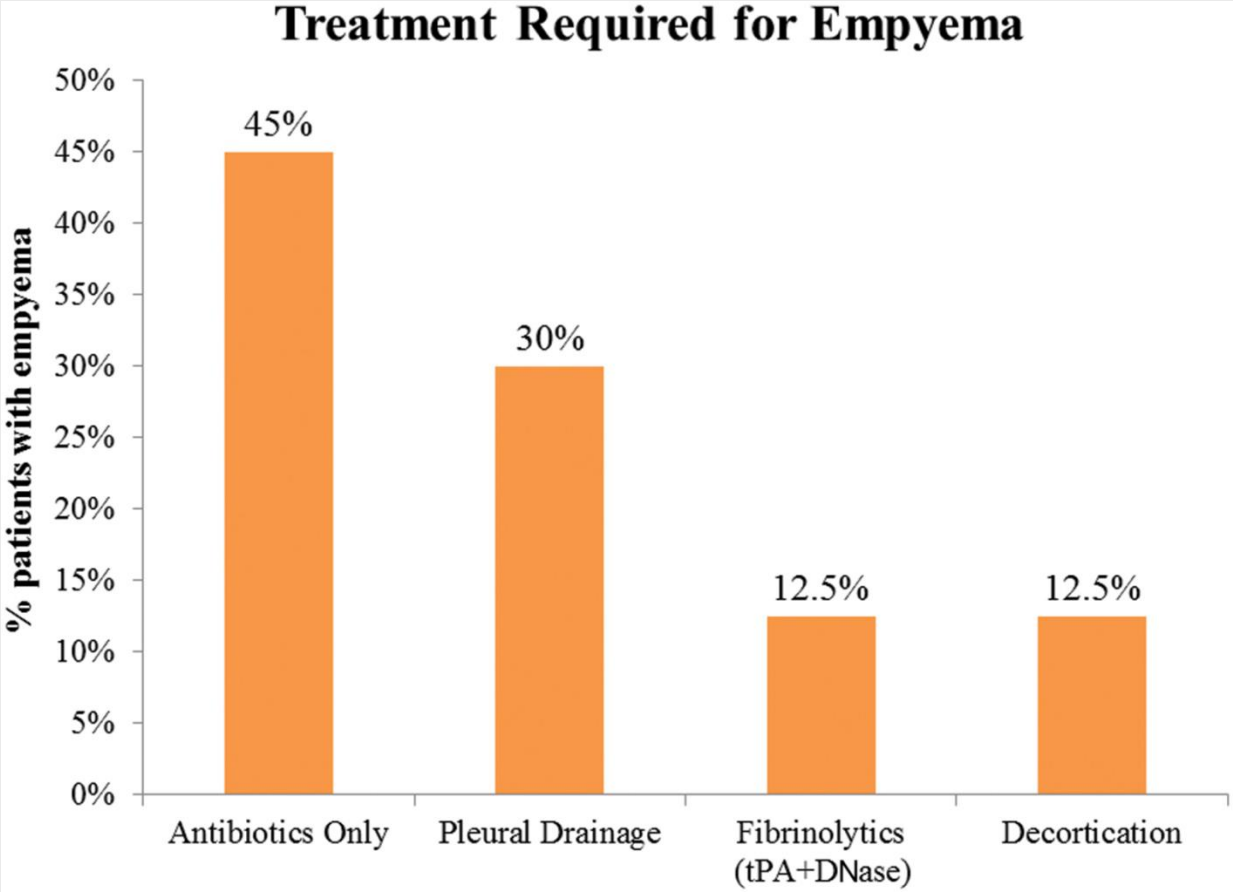
Analysis of patients discharged from the hospital with a chest tube in place

	Median (days)	Range
Initial hospital stay	7	2-373
Chest tube duration (total)	18	6-90
Chest tube after discharge	11	1-56

- Empyema : 40 patients (16.9 %)
- Readmission : 62 patients (26.3%)
  - Related to chest tube: 57 patients (92%)

Reinerman JM et al, Ann Thorac Surg 2018;105:1038-43

Analysis of patients discharged from the hospital with a chest tube in place



Reinerman JM et al, Ann Thorac Surg 2018;105:1038-43

Take Home Message

- Safety of discharge on Heimlich valve is questionnable
- Empyema has been observed in 16%
- 1 patient out of 4 requires readmission
- Careful outpatient fommow-up is mandatory

Thoracic Surgery

Miscellaneous
Matter for ongoing debate !

State of the Art

Tumour upstaging during surgery

- Unforeseen positive nodes are found at surgery in 10-20% of cN0 patients
- Nodal upstaging can be used to monitor quality of surgery
- Retrospective studies show lower upstaging with VATS, although survival rates are similar

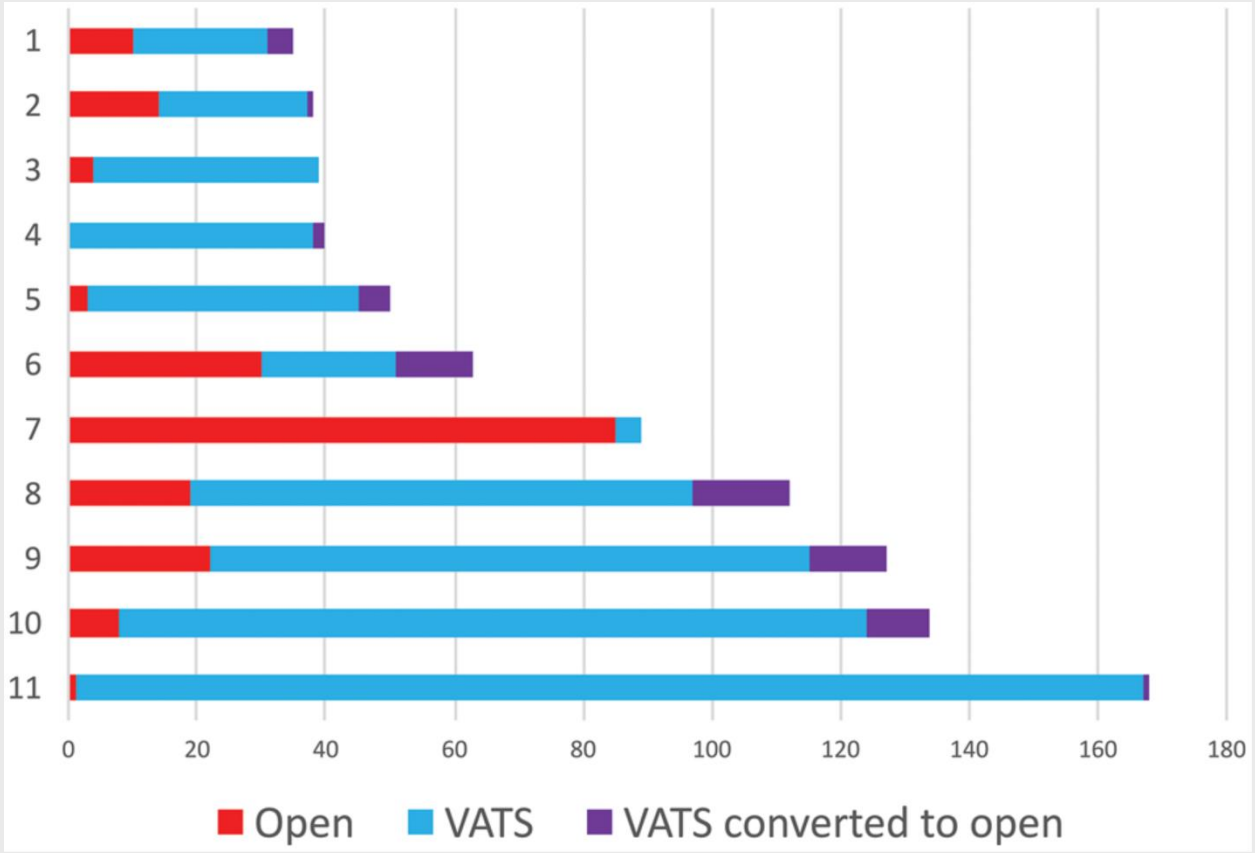
Boffa DJ et al, Ann Thorac Surg 2012;94:347-53
Licht PB et al, Ann Thorac Surg 2013;96:943-50
Martin JT el al, Ann Thorac Surg 2016;101:238-44

Multicentric evaluation of the impact of tumour location when comparing rates of N1 upstaging in patients undergoing VATS and open surgery for clinical stage I NCSLC

- Aim:
  - To check whether tumour location is associated to upstaging
  - More central tumours in the thoracotomy group?
  - More unforeseen N1+ with central tumours?
- Patients operated in 2014 in 11 leading centres
- Central tumours defined as
  - CT contact with lobar artery, vein, or bronchus
  - Tumour visible on standard bronchoscopy

Decaluwe H et al, Eur J Cardiothorac Surg 2018;53:359-65

Multicentric evaluation of the impact of tumour location when comparing rates of N1 upstaging in patients undergoing VATS and open surgery for clinical stage I NCSLC



Case load of centres paticipating in this study

Decaluwe H et al, Eur J Cardiothorac Surg 2018;53:359-65

Multicentric evaluation of the impact of tumour location when comparing rates of N1 upstaging in patients undergoing VATS and open surgery for clinical stage I NSCLC

		Open	VATS	p
N		196	699	
Histology %	Squamous	34	21	<0.0001
	Other	66	79	
cT	cT1a	31	46	<0.0001
	cT1b	30	22	
	cT2a	40	32	
Location CT	Central	28	12	<0.0001
	Peripheral	68	84	
Visible at bronch.	Yes	17	4	<0.0001
	No	66	78	

More central T in the thoracotomy group !

Decaluwe H et al, Eur J Cardiothorac Surg 2018;53:359-65

Multicentric evaluation of the impact of tumour location when comparing rates of N1 upstaging in patients undergoing VATS and open surgery for clinical stage I NCSLC

Upstaging: rough data

Upstaging	Open (%)	VATS (%)
pT > T2aN0	6	5
pN1	15	8
pN2	6	7
Total	27	20

Decaluwe H et al, Eur J Cardiothorac Surg 2018;53:359-65

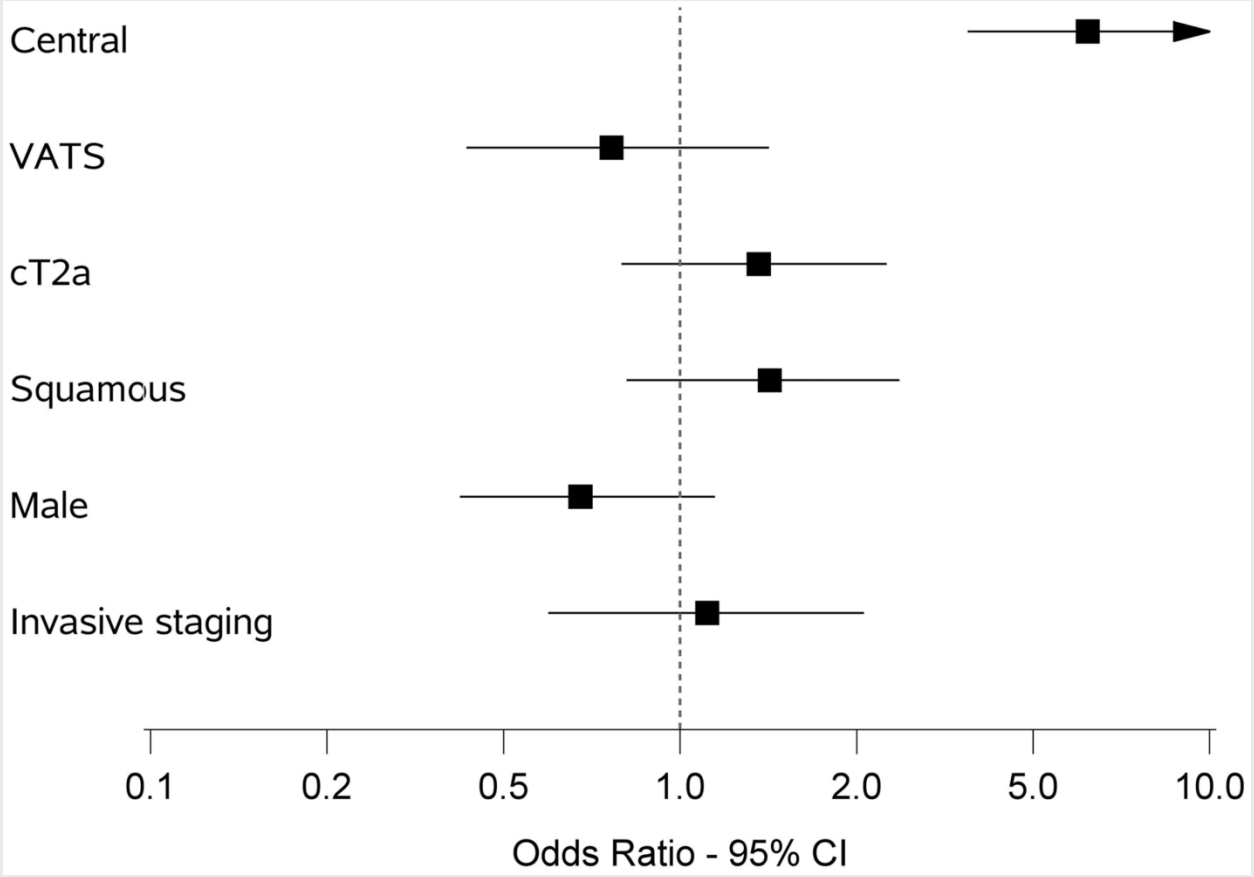
Multicentric evaluation of the impact of tumour location when comparing rates of N1 upstaging in patients undergoing VATS and open surgery for clinical stage I NCSLC

Univariate analysis: risfactors for upstaging cN0 to pN1

	0.R.	p
Central (CT)	7.43	<0.001
Visible at bronch	6.08	<0.001
VATS	0.48	0.003
Squamous	2.42	<0.001
cT2a	1.99	0.003

Decaluwe H et al, Eur J Cardiothorac Surg 2018;53:359-65

Multicentric evaluation of the impact of tumour location when comparing rates of N1 upstaging in patients undergoing VATS and open surgery for clinical stage I NCSLC



Multivariate analysis:

Upstaging cN0 to pN1

Decaluwe H et al, Eur J Cardiothorac Surg 2018;53:359-65

Take-Home Message

Nodal upstaging

- Is dependent on tumour location
- Surgical approach is not determining
- VATS is reliable !!

Decaluwe H et al, Eur J Cardiothorac Surg 2018;53:359-65

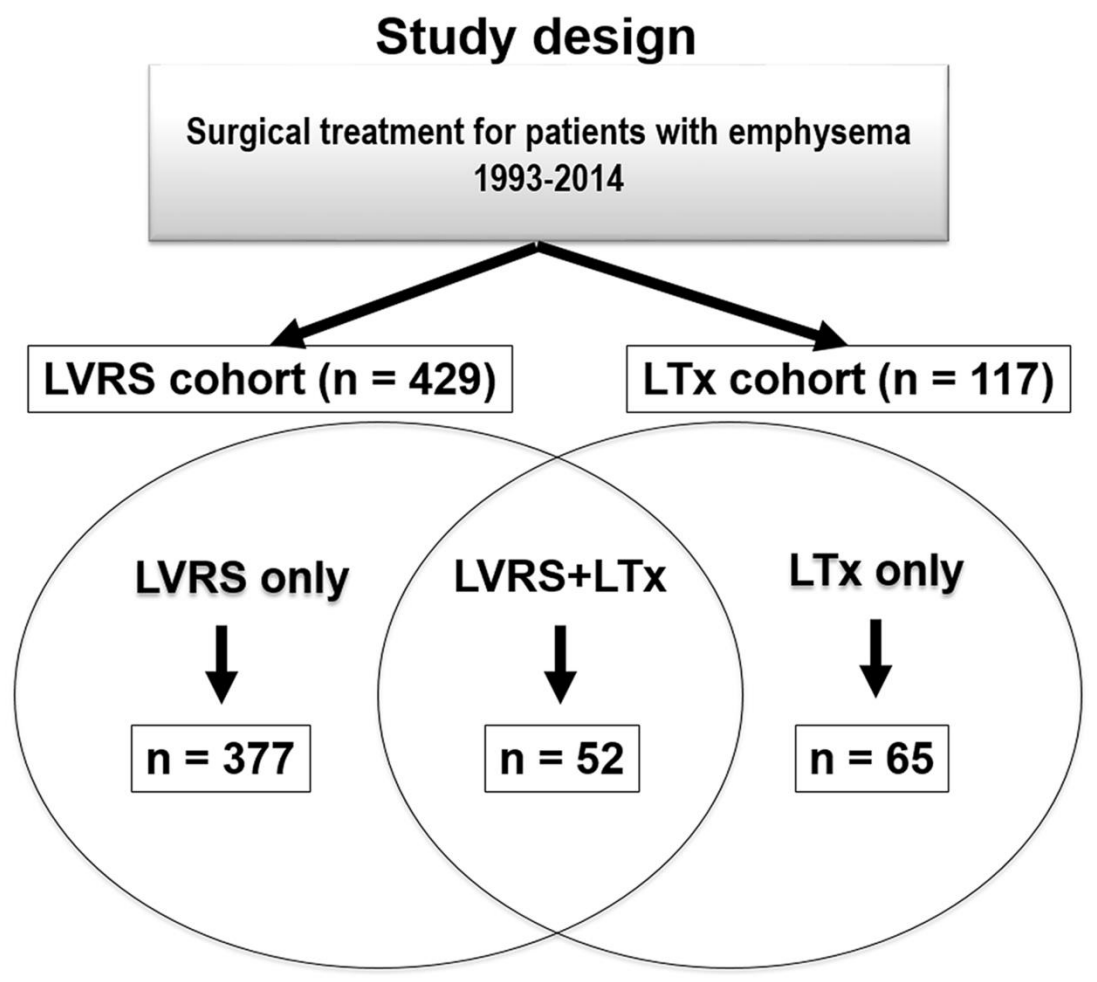
State of the Art

Lung TX after previous Lung Volume Reduction Surgery

- LVRS and TX provide superior survival rates
- LVRS is offered in less advanced disease
- LVRS may be used as bridge to TX
- Effect of LVRS on TX outcomes is matter of controverse

Marchetti N et al, Semin Respir Crit Care Med 2015;36:592-608
Tutic M et al, Ann Thorac Surg 2006;82:208-13
Backhus L et al, J Thorac Cardiovasc Surg 2014;147:1678-83

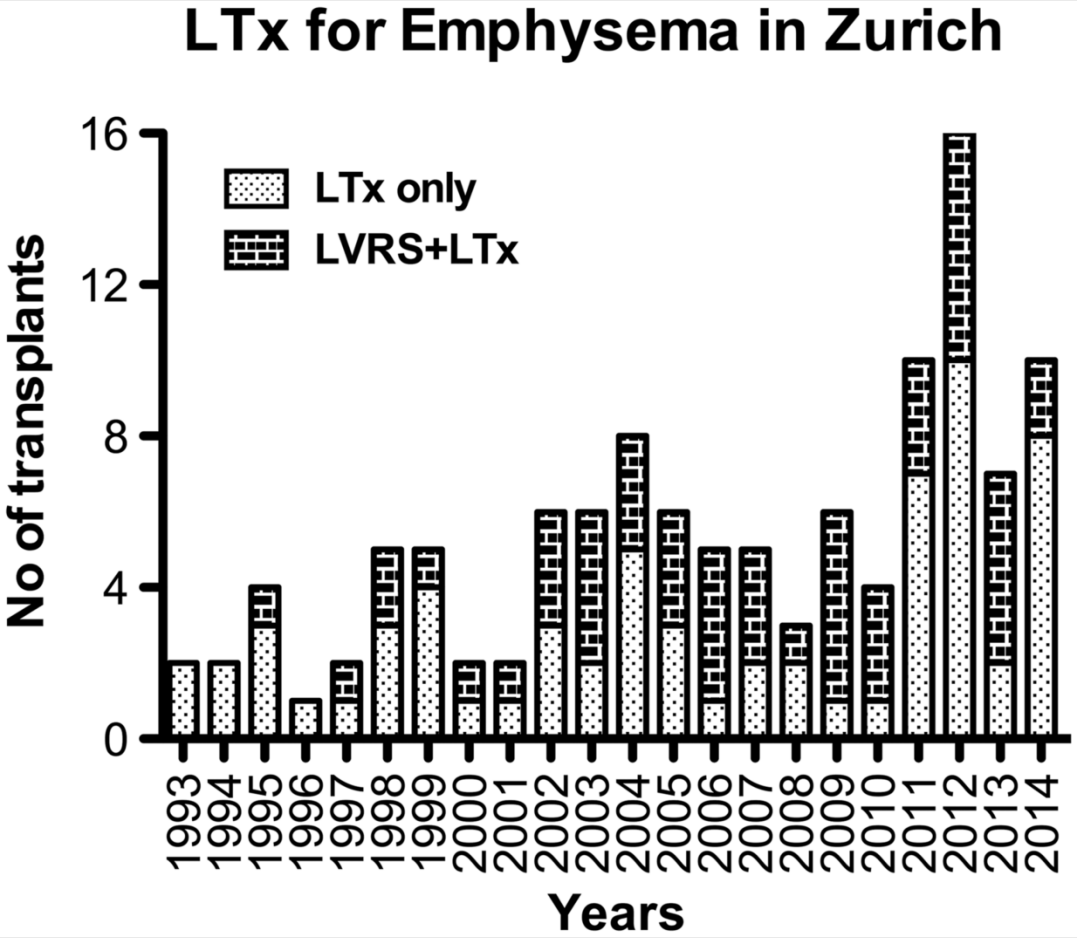
Previous LVRS does not negatively affect survival after lung TX



Single centre retrospective

Inci I et al, Eur J Cardiothorac Surg 2018;53:596-602

Previous LVRS does not negatively affect survival after lung TX



Inci I et al, Eur J Cardiothorac Surg 2018;53:596-602

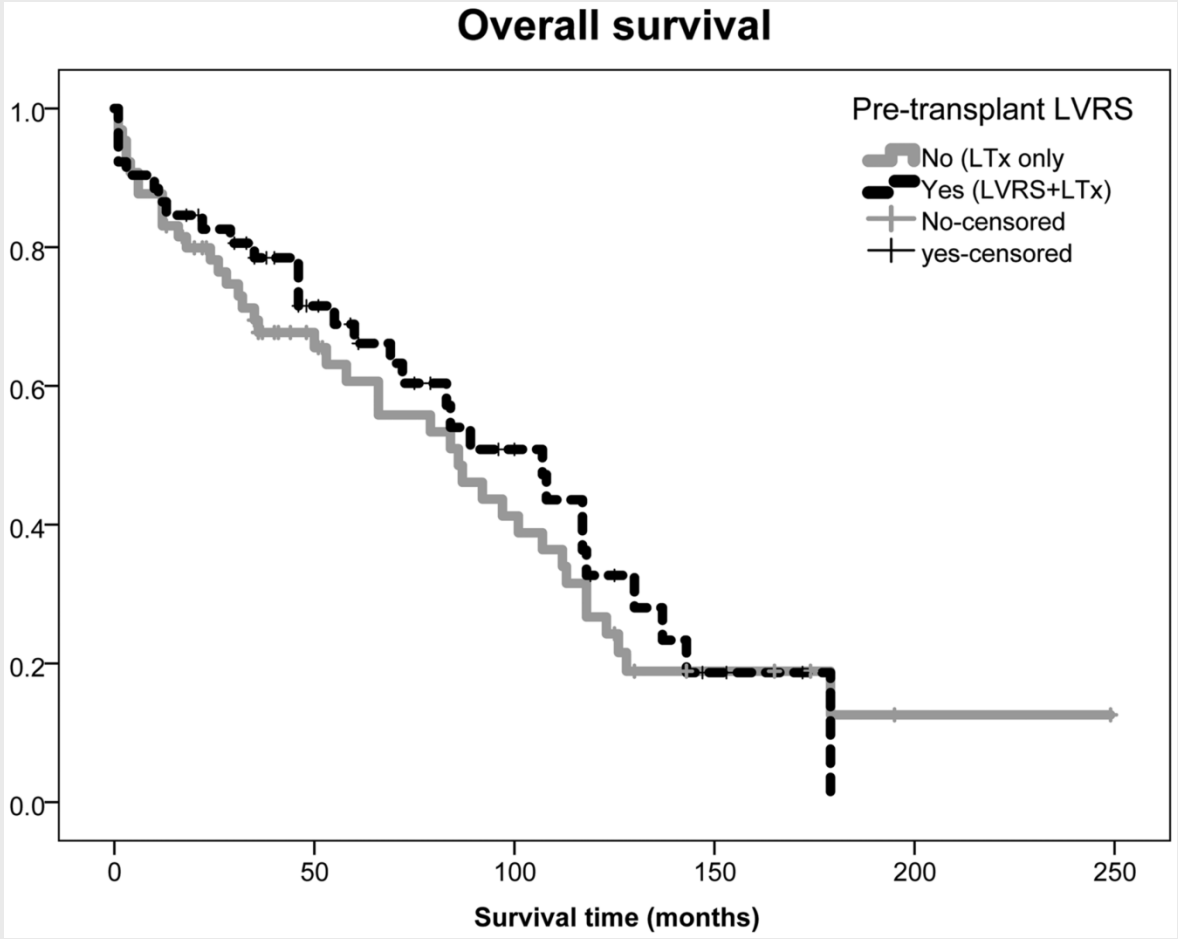
Previous LVRS does not negatively affect survival after lung TX

Perioperative outcomes

Parameters	LVRS + TX (N=52)	TX only (N=65)	p
TX procedure single-bilateral (%)	6 - 94	12 - 88	ns
Intraoperative ECLS (%)	19	23	ns
Theatre time (min, median))	380	351	ns
Blood loss (ml, median))	1000	1000	ns
ICU stay (days, median)	4	4	ns
Duration of ventilation (days, median)	1	1	ns
Hospital stay (days, median)	33	34	ns
30-day mortality (%)	7.7	3.1	ns
In-hospital mortality (%)	9.6	10.8	ns

Inci I et al, Eur J Cardiothorac Surg 2018;53:596-602

Previous LVRS does not negatively affect survival after lung TX



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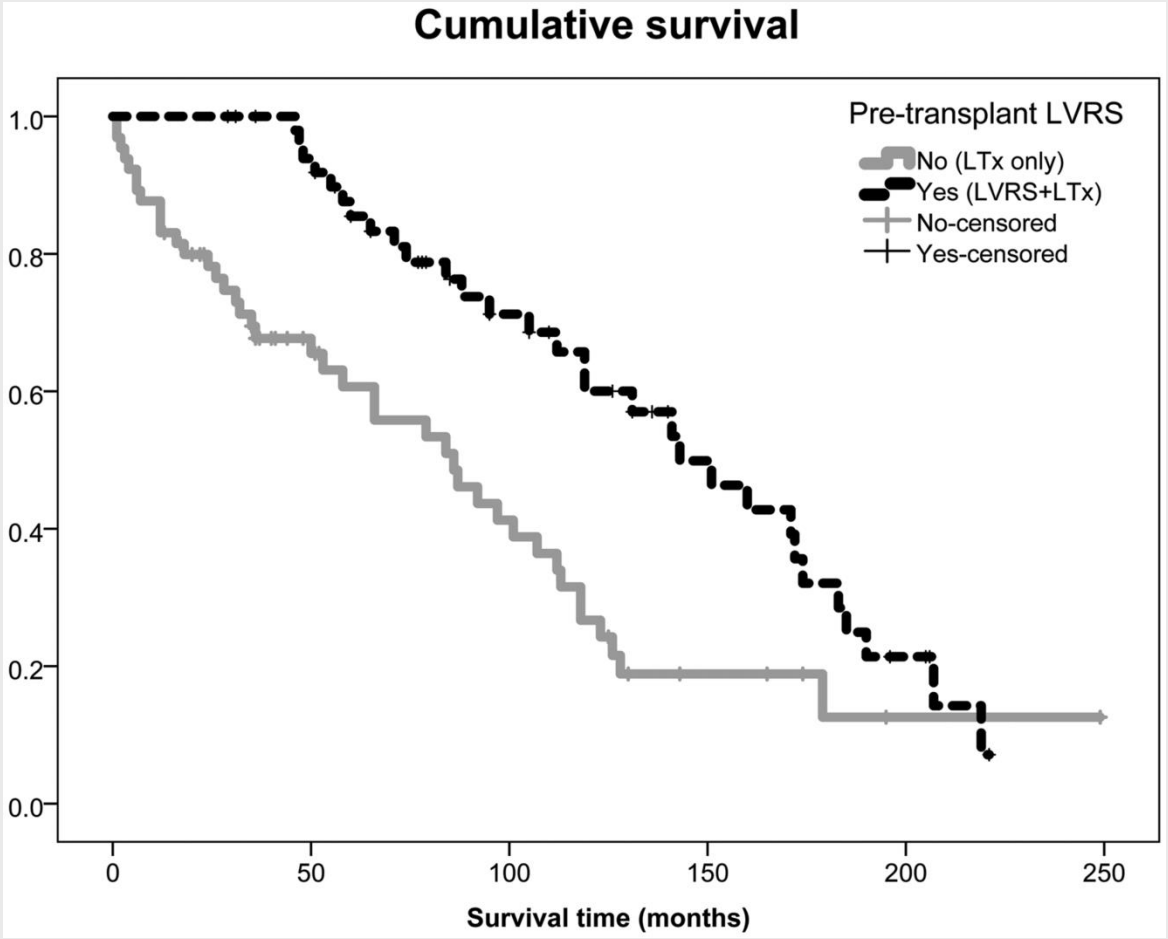


Cumulative benefit
LVRS + TX = 143 months

Median delay
LVRS to TX 21 months

Inci I et al, Eur J Cardiothorac Surg 2018;53:596-602

Take – Home Message

LTx	LVRS-LTx	LVRS
Age <65 years	Age ≤ 65 years	Age : any
FEV1 <15-20% DLCO <20% Moderate to severe PAH In combination with homogeneous distribution in CT	FEV1 20-45% DLCO>20% CT: Heterogeneous distribution	FEV1<45% TLC > 100% RV > 150% RV/TLC > 0.58 CT: - Preferentially heterogeneous distribution, upper lobe predominant - All morphologies in the absence of DLCO <20% and/or PAH
Significant bronchiectasis		No significant bronchiectasis
Steroid intake >20mg/d		

Inci I et al, Eur J Cardiothorac Surg 2018;53:596-602

State of the Art

Surgery for multidrug resistant tuberculosis (TB)

- High failure rate of medical treatment for MDR and XDR TB
- Cavitary TB and bilateral TB are adverse prognostic factors
- Operation most often denied for bilateral TB

Migliori GB et al, Eur Respir J 2007;30:623-6
Dravniece G et al, Eur Respir J 2009;34:180-3
Iddriss A et al, Ann Thorac Surg 2012;94:381-6

Bilateral cavitary MDR of XDR tuberculosis: role of surgery

Inclusion criteria

- Fibro-cavernous TB
- At least 1 segment on either side affectes with lesion > 1 cm
- MDR / XDR confirmed in atleast 1/3 cultures > 6 months

- 57 patients
  - 22 MDR
  - 35 XDR
- Operation scheduled > 6 months of best available treatment

Marfina GY et al. Eur J Cardiothorac Surg 2018;53:618-24

Bilateral cavitary MDR of XDR tuberculosis: role of surgery

Patient data

	MDR N=22	XDR N=35	p
Male gender (%)	72.3	80	
Age < 30 years (%)	45.5	25.7	
Treatment < 2 years (%)	40.9	11.0	0.005
History of imprisonment (%)	13.6	20	
Positive sputum (%)	72.3	94.3	0.027
Median number of drug resistance	5	8	
Destroyed lung (%)	36.4	57.1	
BMI < 18.5 (%)	13.6	22.9	
Hepatitis B, C (%)	9.1	28.6	0.059

Marfina GY et al. Eur J Cardiothorac Surg 2018;53:618-24

Bilateral cavitary MDR of XDR tuberculosis: role of surgery

- Group A: 8 patients
  - Well localized bilateral disease
  - < 10 segments in total
  - Eligible for staged bilateral resection
- Group B: 28 patients
  - Destroyed lung + contralateral cavitary disease limited to 3 segments
- Group C: 21 patients
  - Not eligible for bilateral resection
  - >14 segments affected
  - Or poor lung function
  - Palliative management (thoracoplasty, endobronchial valves)

Marfina GY et al. Eur J Cardiothorac Surg 2018;53:618-24

Bilateral cavitary MDR of XDR tuberculosis: role of surgery

Post-op sputum conversion

	MDR (%)	XDR (%)	All (%)
Group A	100	0	75
Group B	66.7	42.1	48
Group C	57.1	53.8	55
All patients	68.8	45.5	53

Post-op culture conversion

	MDR (%)	XDR (%)	All (%)
Group A	100	100	100
Group B	100	70	78.6
Group C	85.7	64.3	71.4
All patients	95.5	68.6	78.9

Marfina GY et al. Eur J Cardiothorac Surg 2018;53:618-24

Take-Home Message

Surgery for MDR-XDR TB

- May achieve conversion of sputum culture
- Should be considered
  - In patients fit to undergo surgery
  - If complete resection is feasible
  - After at least 6 months of best possible treatment

Marfina GY et al. Eur J Cardiothorac Surg 2018;53:618-24

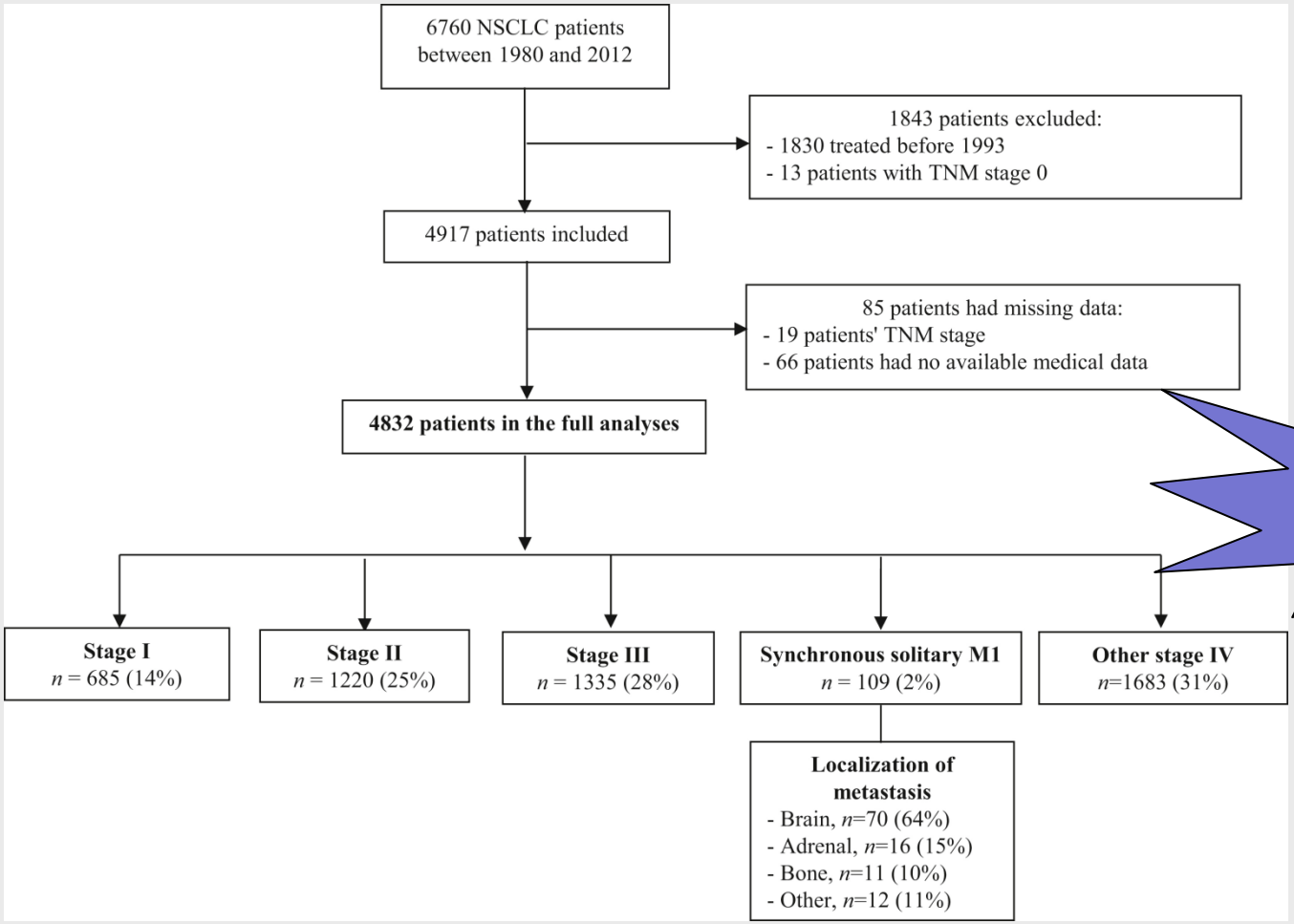
State of the Art

Oligometastatic lung cancer

- Stage IV NSCLC considered inoperable,
- Median survival 12 months
- Operated oligo-metastatic (< 5 metastases) cancer
  - Resection of liver metastases in colorectal cancer
  - Valuable for NSCLC : progression free survival 12 months

Hellman S et al. J Clin Oncol 1995;13:8-10
Tomlinson JS et al. J Clin Oncol 2007;25:4575-80
De Ruysscher D et al. J Thorac Oncol 2012;7:1547-55

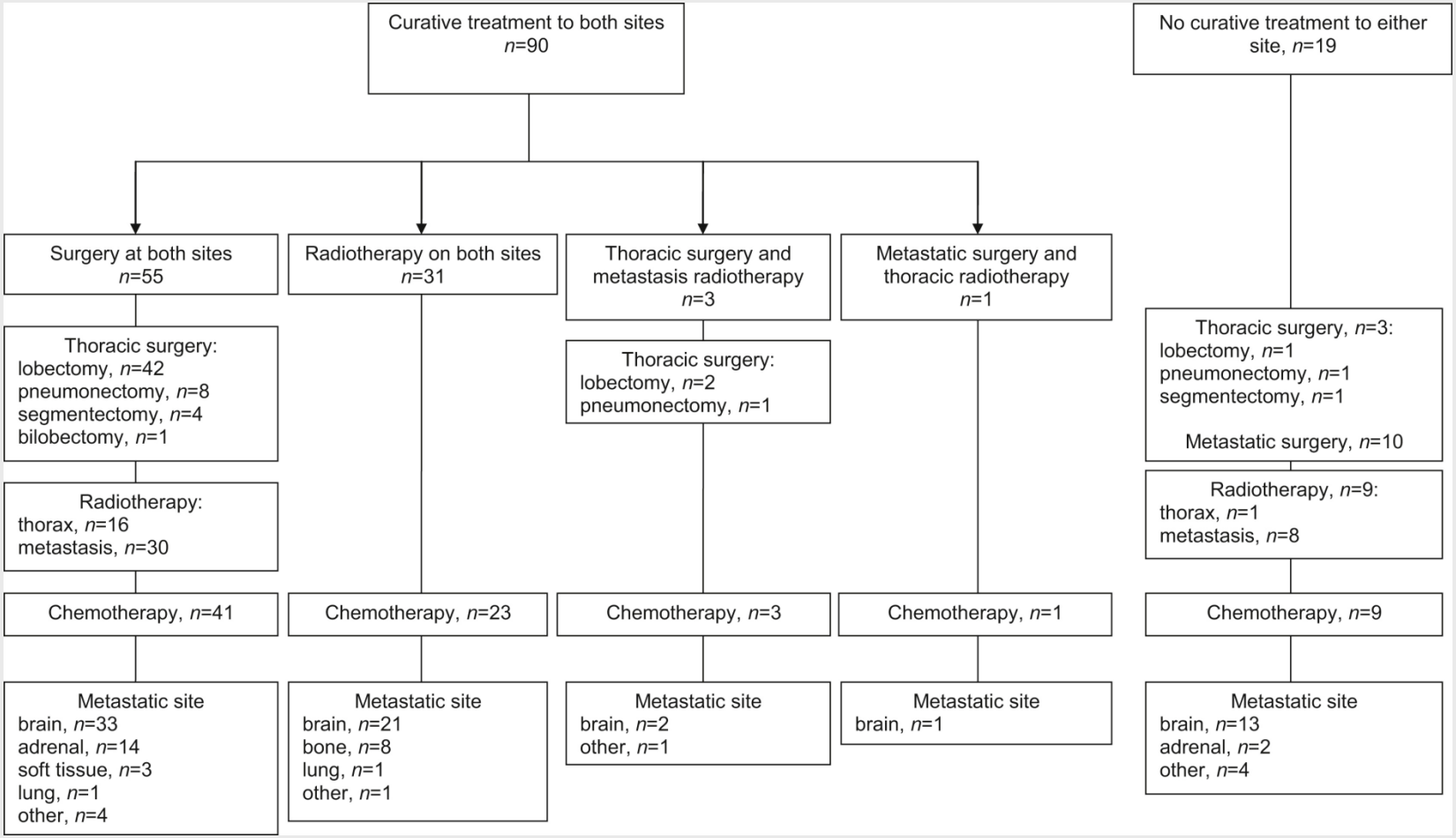
Operation and Chemotherapy: Prognostic Factors for Lung Cancer With One Synchronous Metastasis



Single centre retrospective

Toffart AC et al. Ann Thorac Surg 2018;105; 957-65

Operation and Chemotherapy: Prognostic Factors for Lung Cancer With One Synchronous Metastasis



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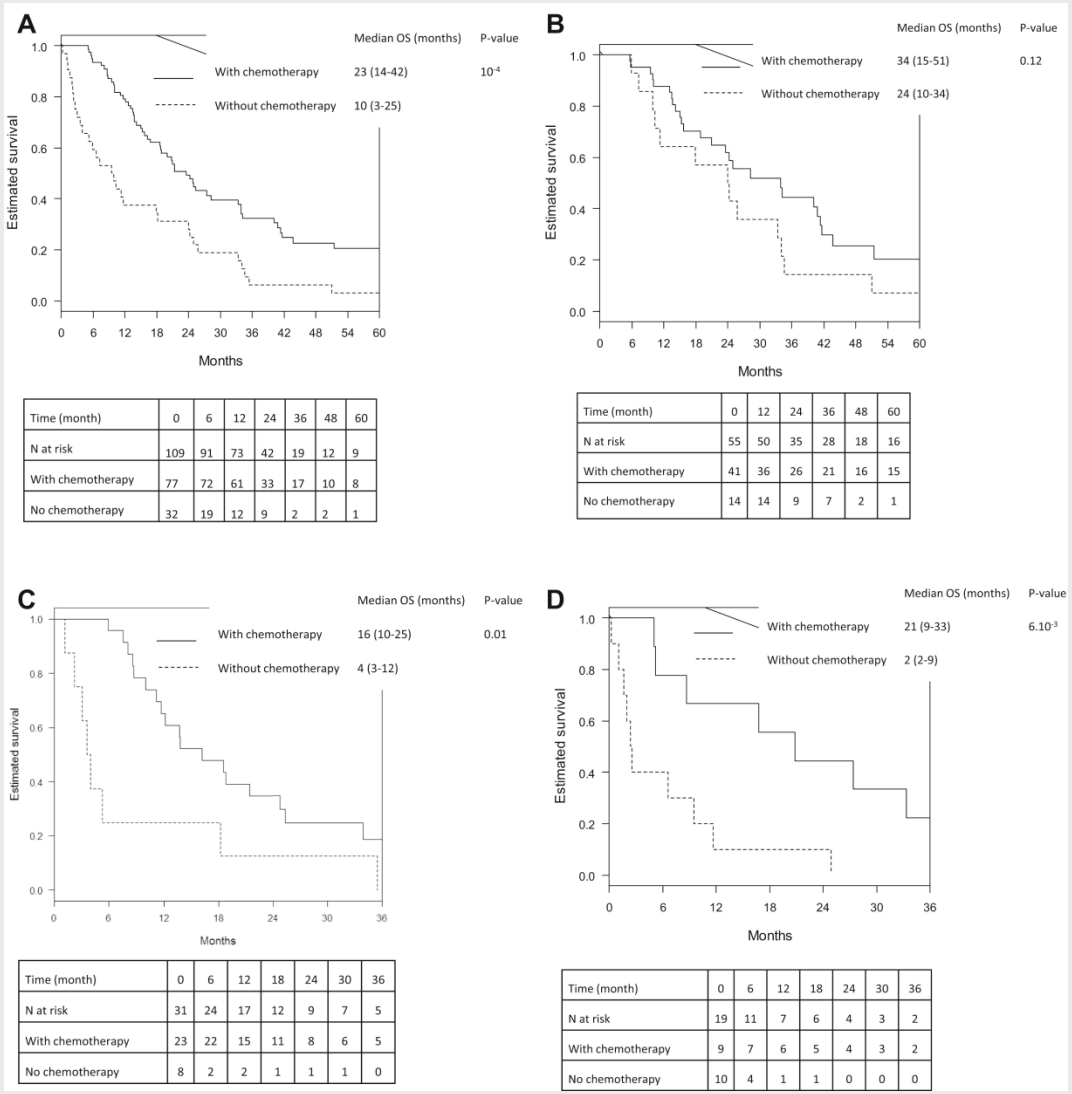

Time (month)	0	6	12	24	36	48	60
N at risk	109	91	73	42	19	12	9
With chemotherapy	77	72	61	33	17	10	8
No chemotherapy	32	19	12	9	2	2	1

Time (month)	0	12	24	36	48	60
N at risk	55	50	35	28	18	16
With chemotherapy	41	36	26	21	16	15
No chemotherapy	14	14	9	7	2	1

Time (month)	0	6	12	18	24	30	36
N at risk	31	24	17	12	9	7	5
With chemotherapy	23	22	15	11	8	6	5
No chemotherapy	8	2	2	1	1	1	0

Time (month)	0	6	12	18	24	30	36
N at risk	19	11	7	6	4	3	2
With chemotherapy	9	7	6	5	4	3	2
No chemotherapy	10	4	1	1	0	0	0

Toffart AC et al. Ann Thorac Surg 2018;105; 957-65

Operation and Chemotherapy: Prognostic Factors for Lung Cancer With One Synchronous Metastasis

Factors associated with death from cancer

	H.R.	p
Age > 63 years	1.63	0.04
ECOG 3,4	6.99	0.01
Chemotherapy	0.47	0.002
Operation on both sites	0.41	0.02

Compared survival after radical resection

	Median survival (months)
Stage III	30.3
Single site M1	25.8

Toffart AC et al. Ann Thorac Surg 2018;105; 957-65

Take-Home Message

Surgery for single site M1 NSCLC

- May achieve prolonged survival similar to stage III
- Should be integrated into a multimodal strategy
- Validation by multidisciplinary tumour board

Marfina GY et al. Eur J Cardiothorac Surg 2018;53:618-24

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List of Abbreviations

- BOS: Bronchiolitis Obliterans Syndrome
- BMI: Body Mass Index
- CLAD: Chronic Lung Allograft Dysfunction
- COPD: Chronic Obstructive Pulmonary Disease
- DVT: Deep Venous Thrombosis
- ECMO: Extra-Corporal Membrane Oxygenation
- ERAS: Enhanced Recovery After Surgery
- EVLP: Ex Vivo Lung Perfusion
- ICU: Intensive Care Unit
- IV: Intra-Venous
- IPF: Interstitial Pulmonary Fibrosis
- ISHLT: International Society for Heart and Lung Transplantation

List of Abbreviations

- LVRS: Lung Volume Reduction Surgery
- MDR: Multi-Drug Resistance
- NSCLC: Non Small Cell Lung Cancer
- PE: Pulmonary Embolism
- PGD: Primaty Graft Dysfunction
- RCT: Randomized Controlled Trial
- TB: Tuberculosis
- TX: Transplantation
- VATS: Video-Assisted Thoracoscopic Surgery
- VTE: Venous Thrombo-Embolism
- XDR: Extensive Drug Resistance