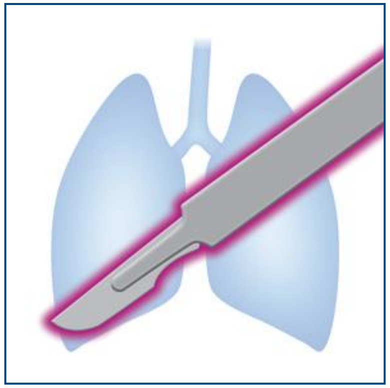
Pneumo Update Europe 2016

24-25 June, Prague

Thoracic Surgery & Lung Transplantation



Gilbert Massard, France

Methodology

- Review of the thoracic surgical literature
- Selection of papers which might be of interest for pulmonary physicians
- Preference to reviews, registry studies and meta-analyses

Thoracic Surgery

Clinical stage I NSCLC

State of the Art

Clinical stage I

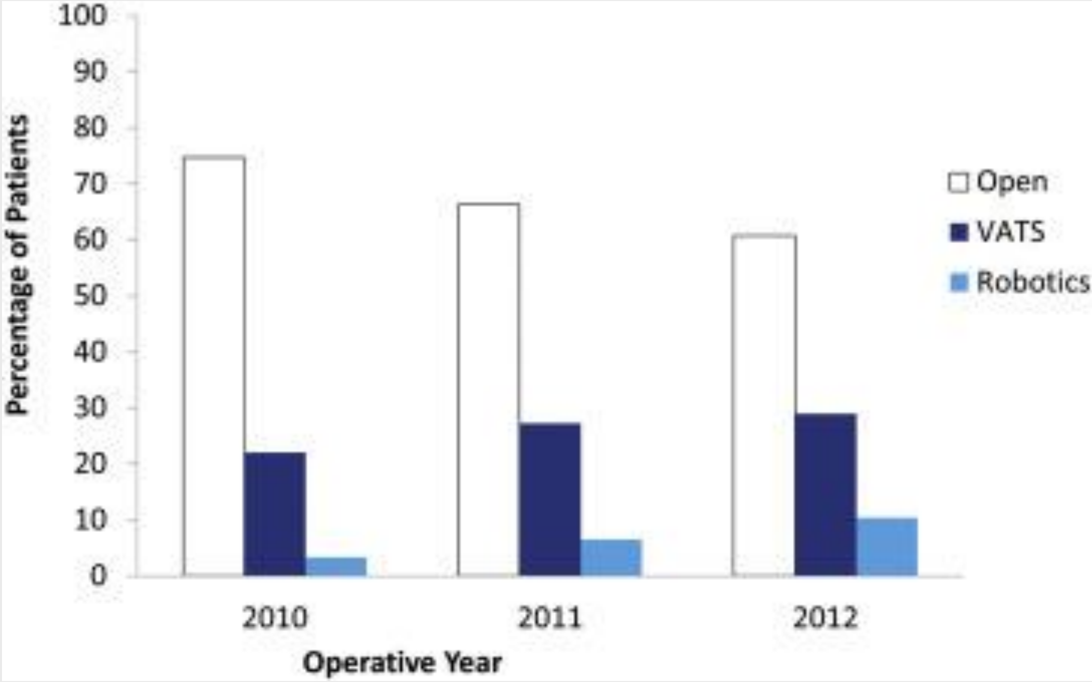
- (VATS) lobectomy
- Sublobar resection for cT1aN0
- Challenged by SBRT

Chang et al, Lancet Oncol 2015;16:630-7

Use and outcome of minimally invasive lobectomy for stage I NSCLC in the National Cancer Database

Registry study

- National cancer database
- 30040 lobectomies
  - 7824 VATS
  - 2025 RATS
- Propensity matching



Yang et al, Ann Thorac Surg 2016;101:1037-42

Use and outcome of minimally invasive lobectomy for stage I NSCLC in the National Cancer Database

- National cancer database
- 30040 lobectomies
  - 7824 VATS
  - 2025 RATS
- Propensity matching

Registry study

VATS = RATS

	MIS	Thoracotomy	p
Readmission 30 d	5%	4%	<0.02
Hospital stay	5 days	6 days	<0.01
2 year survival	87%	86%	=0.04

Yang et al, Ann Thorac Surg 2016;101:1037-42

Segmentectomy or lobectomy for early stage lung cancer: a meta-analysis

Bao F, et al. Eur J Cardio-Thorac Surg 2014;46:1-7.

Stade IA
T ≤ 2 cm

Meta-analysis

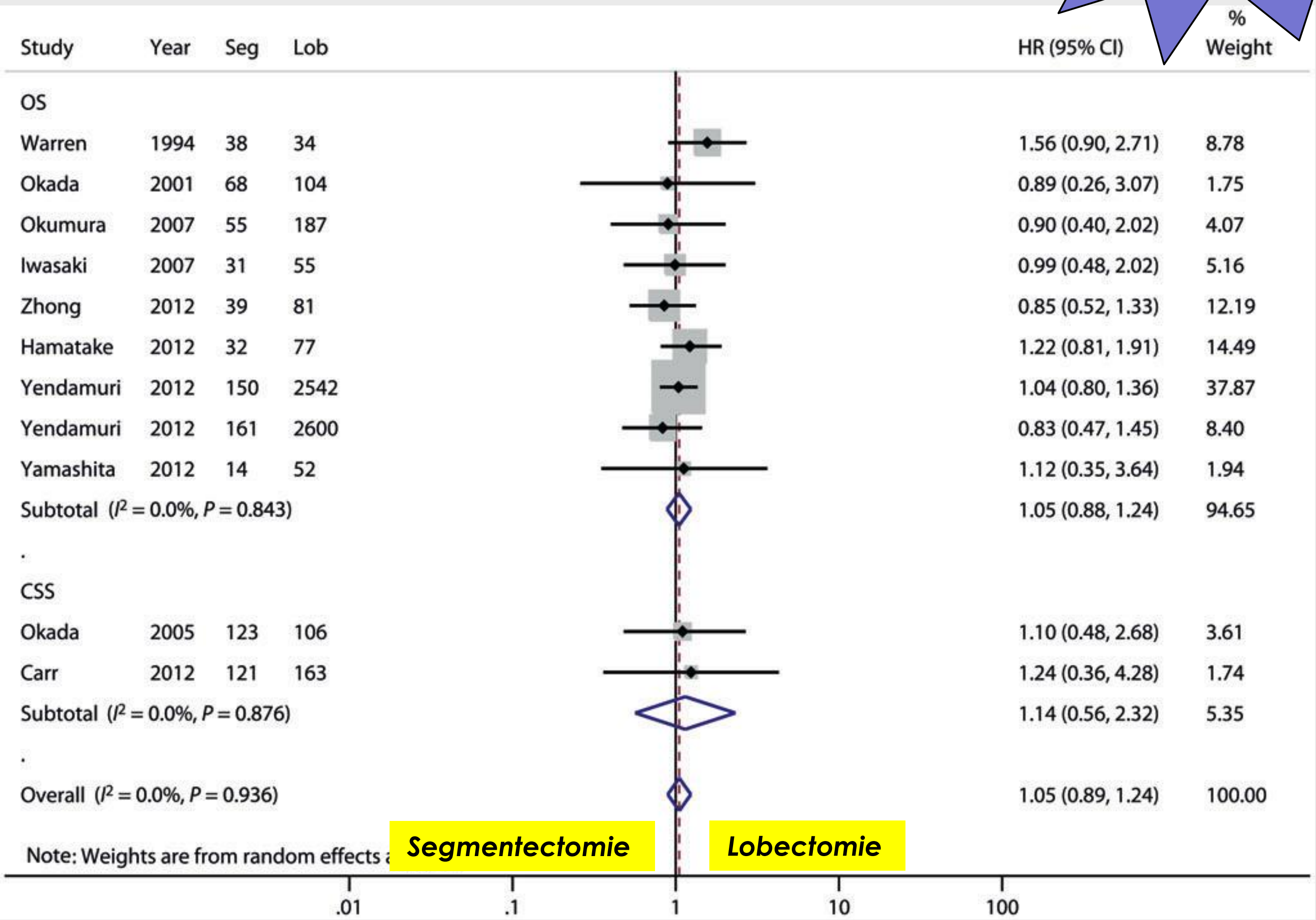
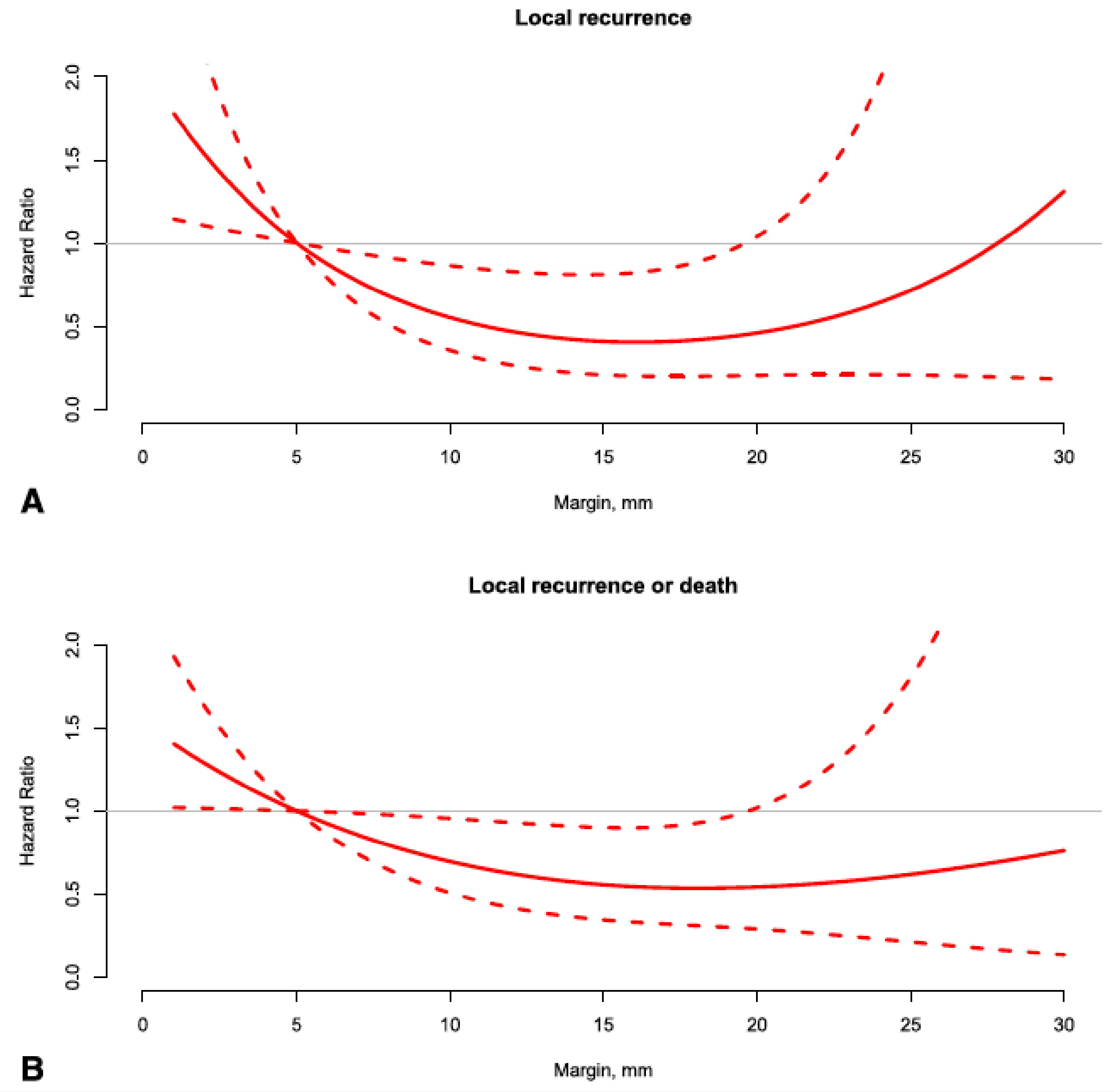


Figure 5: Overall survival/cancer-specific survival estimates for segmentectomy compared with lobectomy for Stage IA NSCLC patients with tumour 2 cm or smaller. Seg: segmentectomy; Lob: lobectomy.

Bao F, et al. Eur J Cardio-Thorac Surg 2014;46:1-7.

T≤2 cm
Wedges

Mohiuddin K et al.
J ThoracCardiovasc Surg
2014;147:1169-77



SBRT new standard for c-stage I ?

Stereotactic ablative radiotherapy versus lobectomy for operable stage I non-small-cell lung cancer: a pooled analysis of two randomised trials

Joe Y Chang*, Suresh Senan*, Marinus A Paul, Reza J Mehran, Alexander V Louie, Peter Balter, Harry J M Groen, Stephen E McRae, Joachim Widder, Lei Feng, Ben E E M van den Borne, Mark F Munsell, Coen Hurkmans, Donald A Berry, Erik van Werkhoven, John J Kresl, Anne-Marie Dingemans, Omar Dawood, Cornelis J A Haasbeek, Larry S Carpenter, Katrien De Jaeger, Ritsuko Komaki, Ben J Slotman, Egbert F Smit†, Jack A Roth†

Lancet Oncol 2015; 16: 630–37

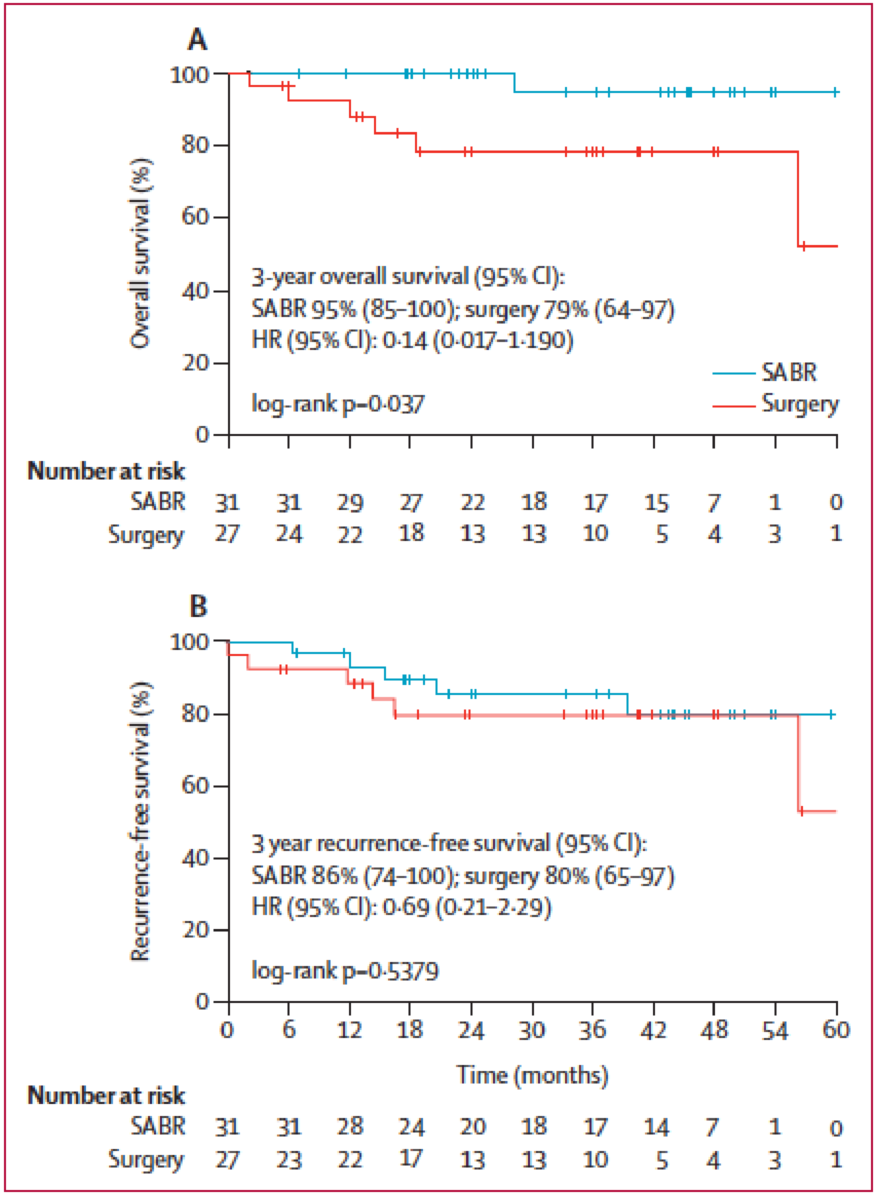


Figure 2: Overall survival (A) and recurrence-free survival (B)
One patient died and five had recurrence in the SABR group compared with six and six patients, respectively, in the surgery group. SABR=stereotactic ablative radiotherapy. HR=hazard ratio.

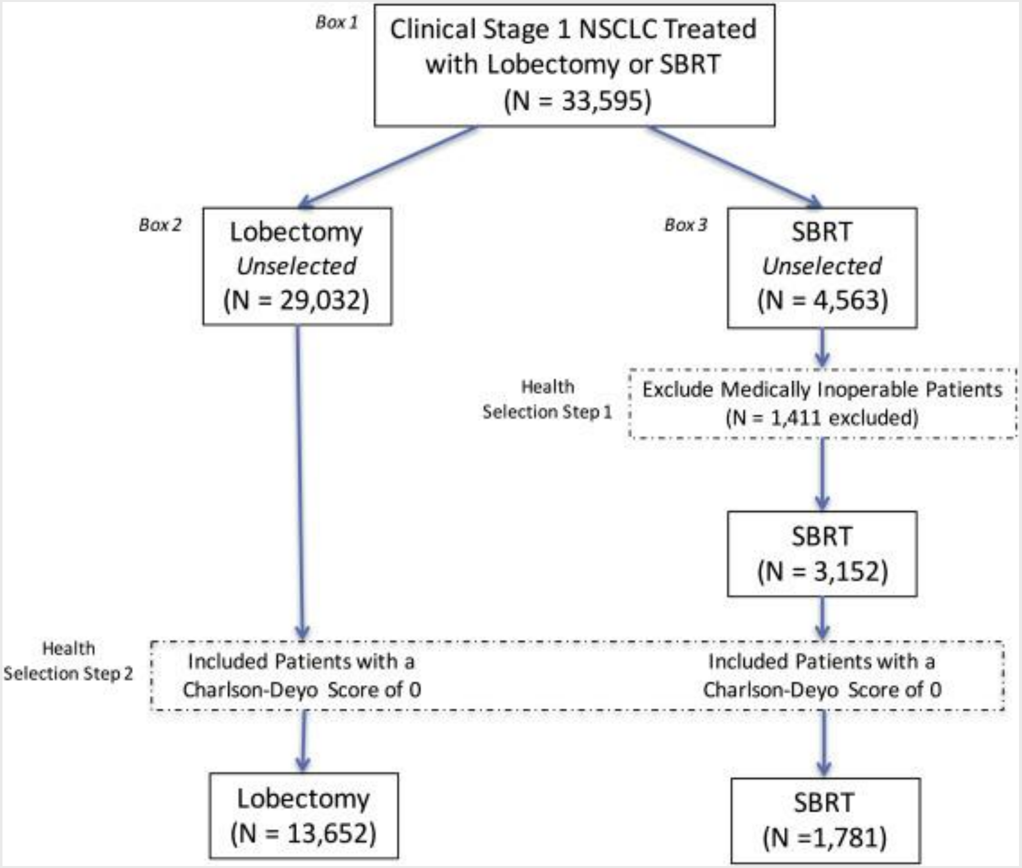
Chang et al. Lancet Oncol 2015;16: 630–37

Stereotactic ablative radiotherapy versus lobectomy for operable stage I non-small-cell lung cancer: a pooled analysis of two randomised trials.

- Both trials closed for lack of accrual
  - STARS trial : 28 sites - 36 patients
  - ROSEL study: 10 sites - 22 patients
- Overmortality of open lobectomy (3.7%)
- Undermortality of SBRT
- Lack of follow-up : median survival not joined
- Tissue diagnosis in SBRT 27% (ROSEL)
- Local recurrence
  - SBRT 16.1 %
  - Lobectomy: 4.1 %

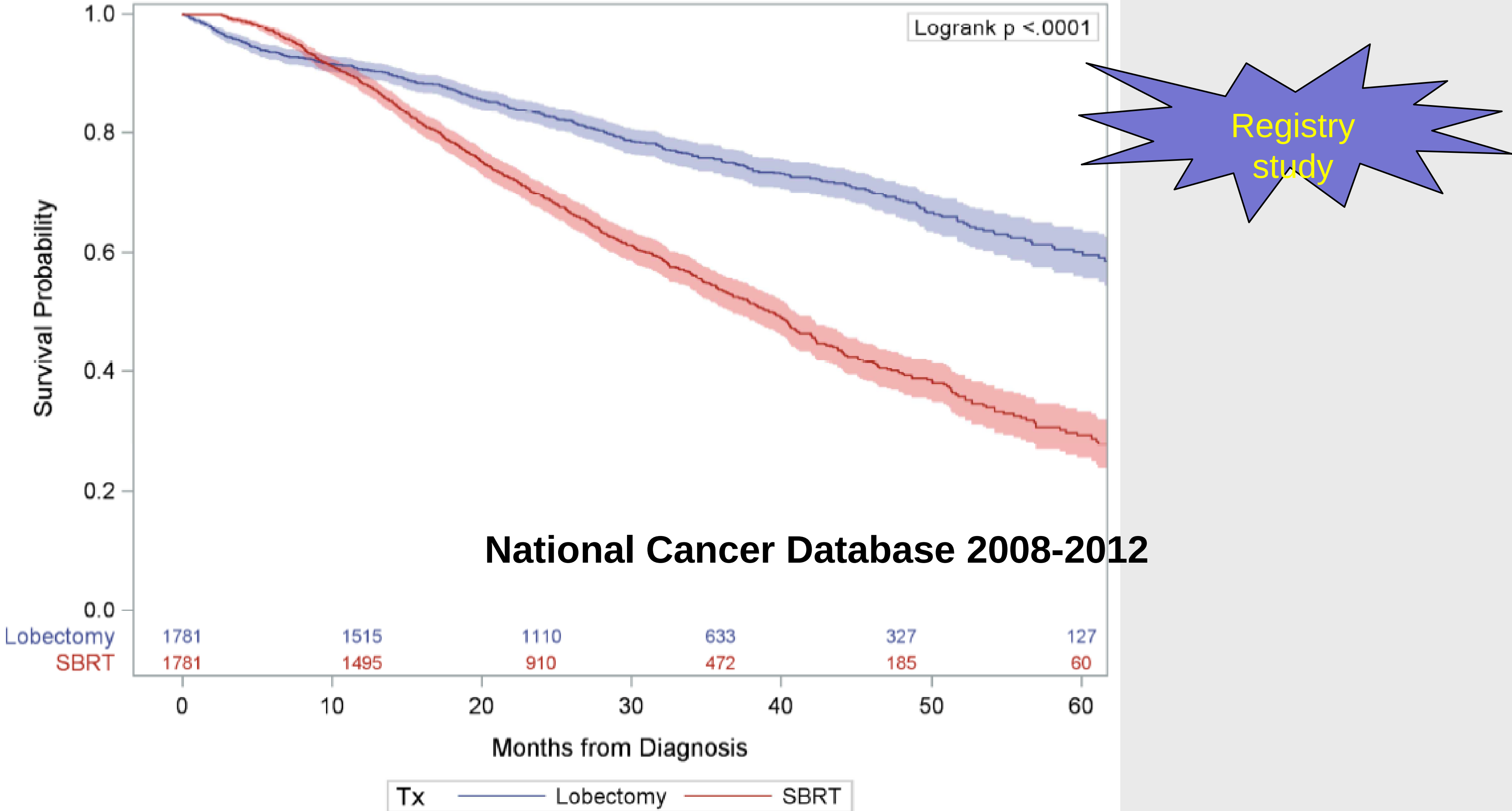
Chang et al. Lancet Oncol 2015;16: 630–37

Lobectomy versus stereotactic body radiotherapy in healthy patients with stage I lung cancer



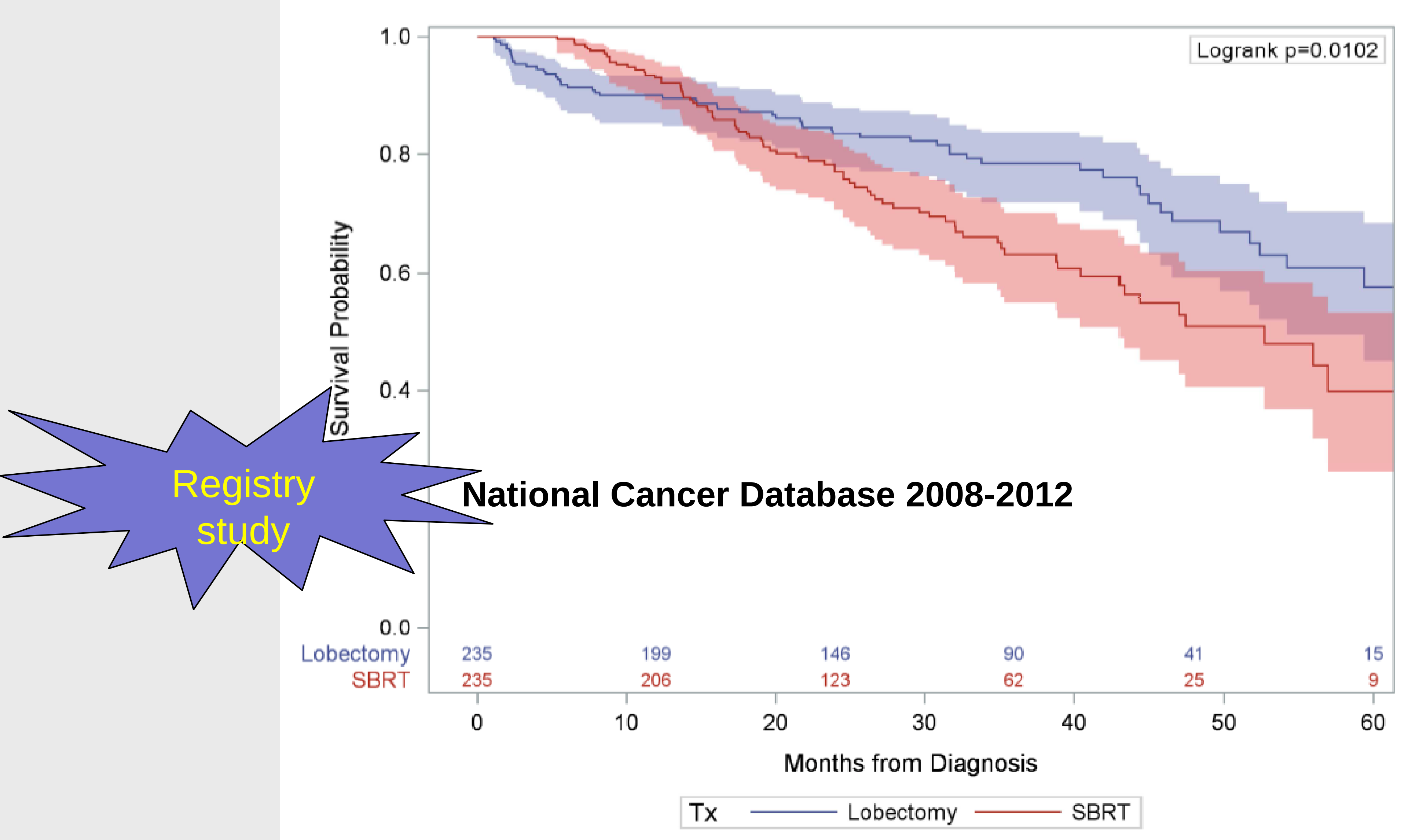
- National Cancer Data Base
- 13662 lobectomies
- 1781 SBRT

Rosen et al, J Thorac Cardiovasc Surg 2016 (in press)



1781 propensity-matched “healthy” lobectomy and SBRT patients pairs

Rosen JE et al. Lobectomy versus 1 Stereotactic Body Radiotherapy in Healthy Patients with Stage I Lung Cancer. J Thorac Cardiovasc Surg 2016; in press.



235 Propensity matched lobectomy patients and SBRT patients pairs who were recommended to have surgery, but refused.

Rosen JE et al. Lobectomy versus 1 Stereotactic Body Radiotherapy in Healthy Patients with Stage I Lung Cancer. J Thorac Cardiovasc Surg 2016; in press.

Tissue is the issue !

F Barlesi et al.
Lancet 2016;387:1415-26

Registry study

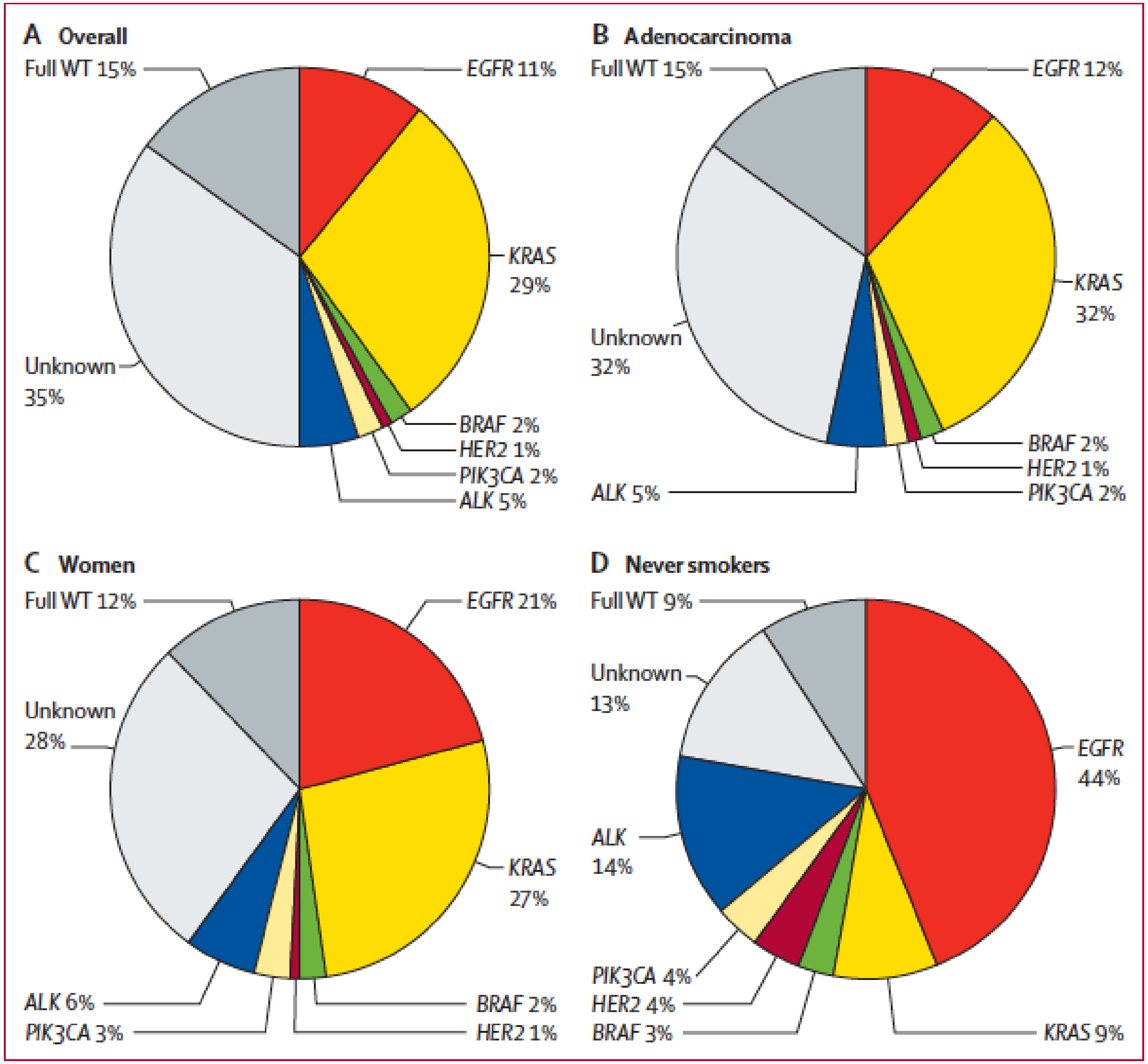


***Figure 2:* Frequency of genetic alterations**
Frequency of molecular alterations in six genes from 18 679 analysed samples (expressed as the percentage of positive samples for each molecular alteration relative to the number of available analyses, with unknown representing the cases with at least one unknown result after assessment of the six genes). Full WT=patients with an established molecular profile without an *EGFR*, *KRAS*, *BRAF*, *HER2* (*ERBB2*), or *PIK3CA* mutation or *ALK* rearrangement. (A) Overall population, (B) adenocarcinoma only, (C) women only, and (D) never smokers only.

SBRT suboptimal treatment !!

- Histology not always proven !!!
- Ignores lymph nodes !!!
- Ignores satellite nodes !!!

- Increased local recurrence
- Decreased survival

2 provocative open questions!

- **How dangerous is conversion from VATS to thoracotomy ?**
- How valuable is surgery compared to other treatment modalities ?

VATS : the fate of conversion to thoracotomy

- 1110 patients
- 69 conversions

Cause	N	%
Fibrocalcified nodes	28	40.6
Uncontrolled bleeding	20	29.0
Tumour extension	11	15.9
Incomplete fissure	3	4.3
Failing single lung ventilation	2	2.9

Byun et al, Ann Thorac Surg 2015;100:968-72

VATS : the fate of conversion to thoracotomy

Potential patient-related factors (univariate analysis)

Cause	conversion	VATS	p
Age	67.6	62.5	0.009
History of TB	29.0	8.7	0.029
COPD (%)	10.1	2.9	0.049
Smoking (P/Y)	22.6	14.7	0.042
FEV-1 (L)	2.18	2.47	0.023
Fibrocalcified nodes (%)	34.8	9.2	<0.001

Byun et al, Ann Thorac Surg 2015;100:968-72

VATS : the fate of conversion to thoracotomy

Potential patient-related factors (logistic regression analysis)

Cause	O.R.	p
Age > 65	1.81	0.031
FEV-1 (L)	2.01	0.005
Fibrocalcified nodes (%)	2.67	0.020

Byun et al, Ann Thorac Surg 2015;100:968-72

VATS : the fate of conversion to thoracotomy

Impact of conversion onto outcomes

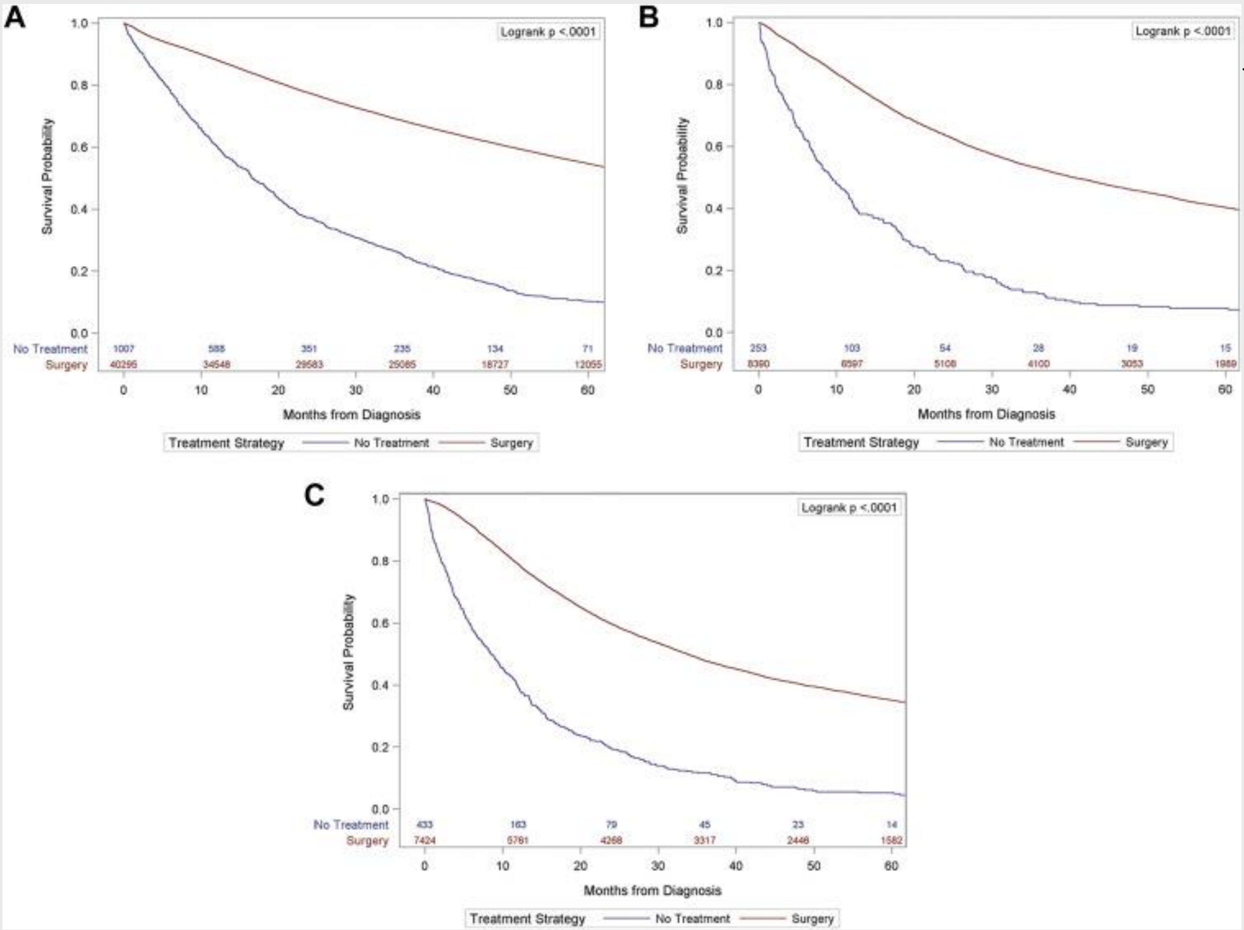
	conversion	VATS	p
Opereating time (min)	222	150	<0.001
Bleeding (mL)	693	227	<0.001
ICU stay (days)	3.3	1.4	0.047
Hospital stay (days)	9.4	8.4	NS
Pneumonia (%)	7.4	1.4	0.012

Byun et al, Ann Thorac Surg 2015;100:968-72

2 provocative open questions!

- How dangerous is conversion from VATS to thoracotomy ?
- **How valuable is surgery compared to other treatment modalities ?**

The Natural History of Operable Non-Small Cell Lung Cancer in the National Cancer Database



Registry study

NCDB = 70% of cancers in USA

2003-2009

1693 not operated operable patients

Rosen et al, Ann Thorac Surg 2016;101:1850-5

List of References

1. Chang et al. Lancet Oncol 2015;16: 630–37.
2. Yang et al, Ann Thorac Surg 2016;101:1037-42
3. Bao F, et al. Eur J Cardio-Thorac Surg 2014;46:1-7.
4. Mohiuddin K et al. J ThoracCardiovasc Surg 2014;147:1169-77
5. Rosen et al, J Thorac Cardiovasc Surg 2016 (in press)
6. F Barlesi et al. Lancet 2016;387:1415-26
7. Byun et al, Ann Thorac Surg 2015;100:968-72
8. Rosen et al, Ann Thorac Surg 2016;101:1850-5

Take-Home Message

- VATS is the preferable option for stage I
- Robotics has no added value
- Surgery is superior to SBRT

Thoracic Surgery

Locally Advanced NSCLC

State of the Art

Locally advanced NSCLC

- Surgery for N2 remains debated
  - Downstaging used to select operable patients
  - Surgery is not credited any survival advantage
- Surgery is an option for cT4N0

Betticher et al, J Clin Oncol 2003;21:1752-59
Van Meerbeck et al, J Natl Cancer Instit 2007 ; 99: 442-50

Postinduction positron emission tomography assessment of N2 nodes is not associated with ypN2 disease or overall survival in stage IIIA non–small cell lung cancer

2007-2012

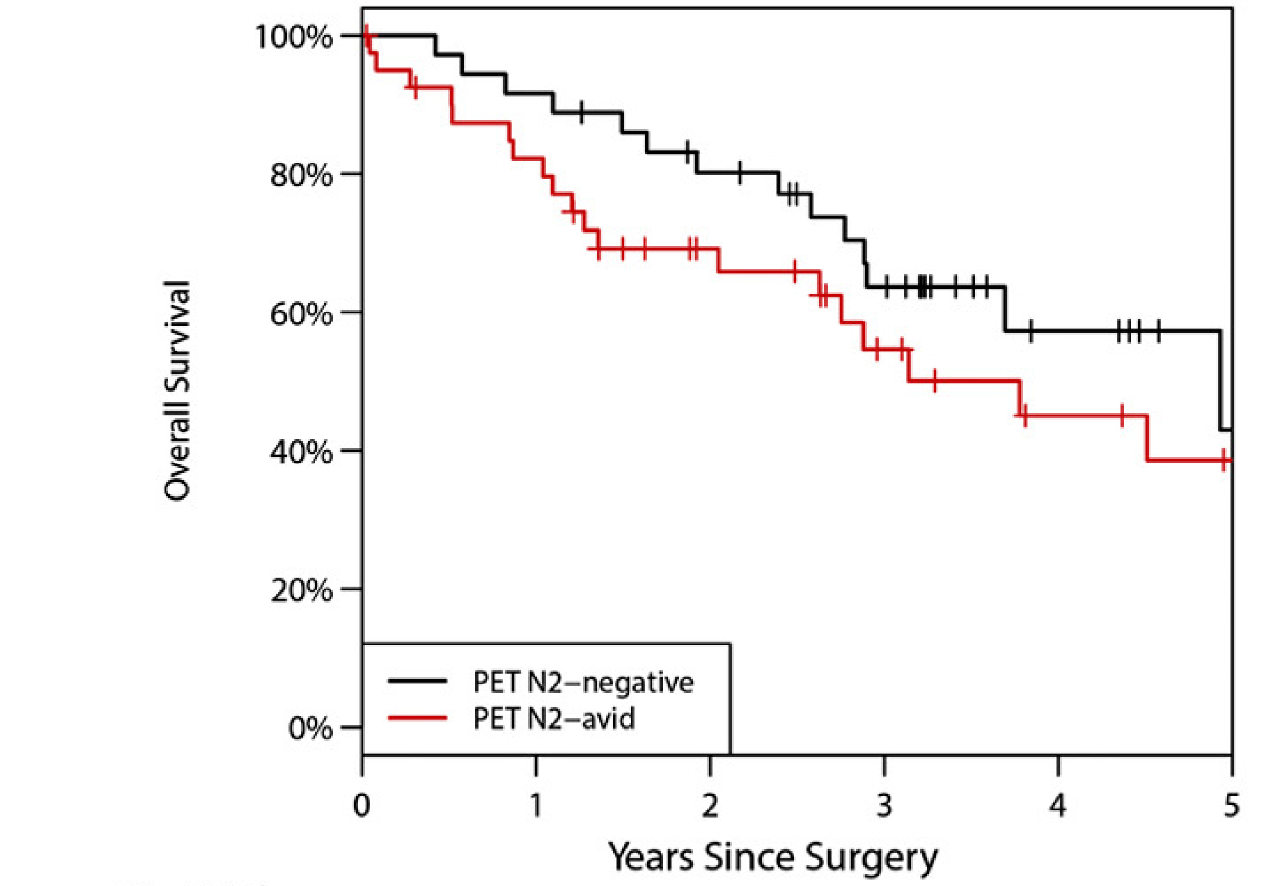
100 consecutive patients

Histologically proven N2

Induction chemotherapy

Restaging with PET

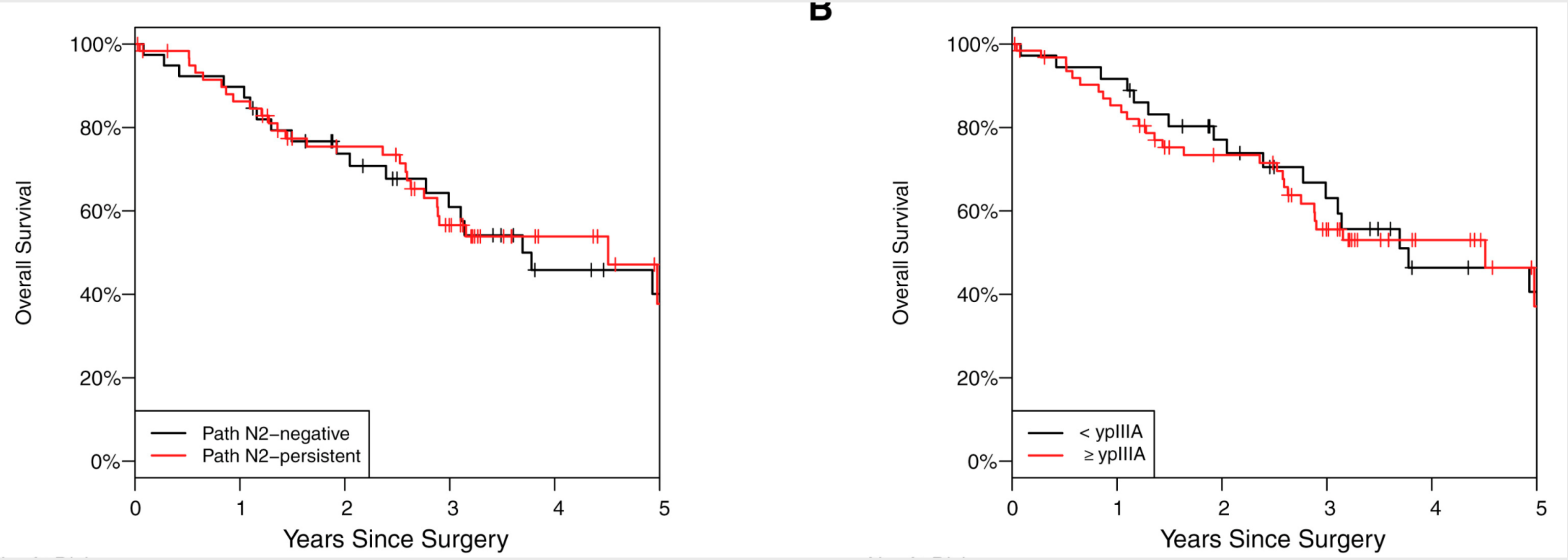
Overall survival



Ripley et al, J Thorac Cardiovasc Surg 2016;151:969-79

Postinduction positron emission tomography assessment of N2 nodes is not associated with ypN2 disease or overall survival in stage IIIA non–small cell lung cancer

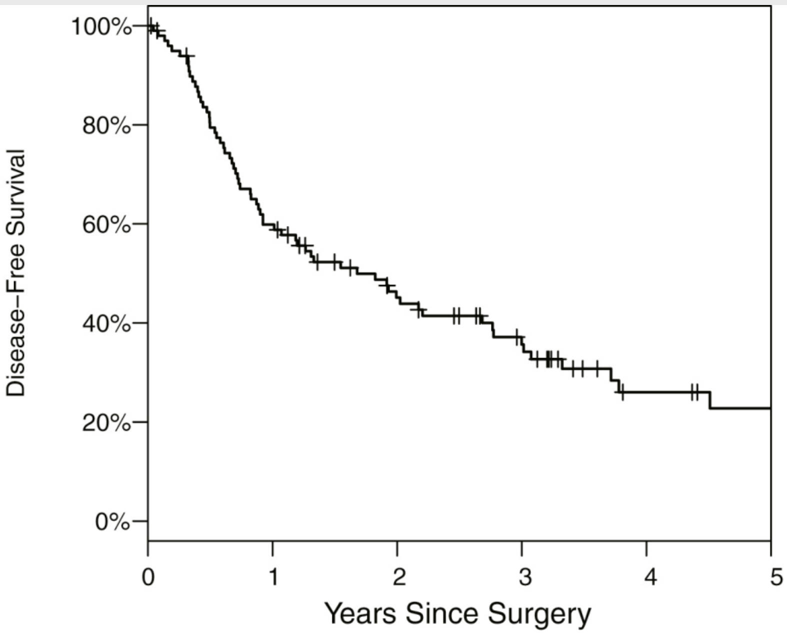
Overall survival

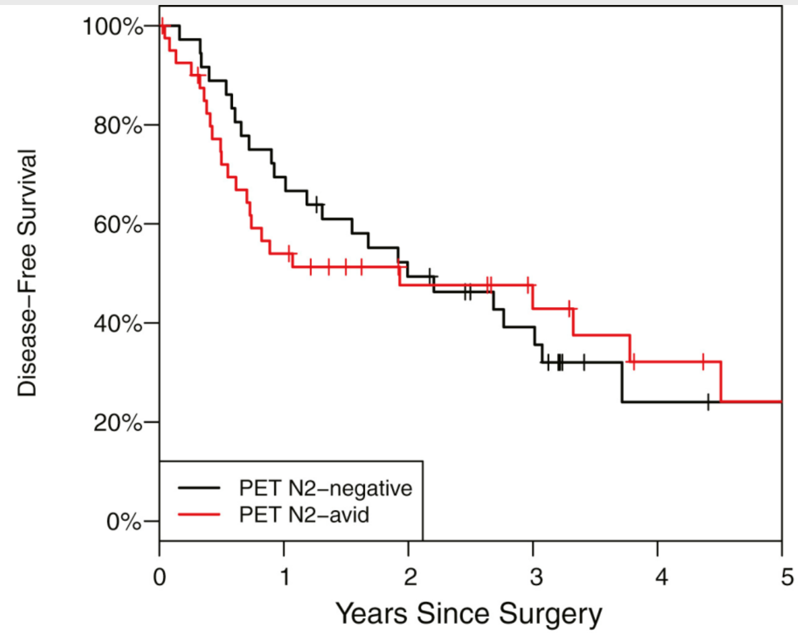


Ripley et al, J Thorac Cardiovasc Surg 2016;151:969-79

Postinduction positron emission tomography assessment of N2 nodes is not associated with ypN2 disease or overall survival in stage IIIA non–small cell lung cancer

Disease-free survival

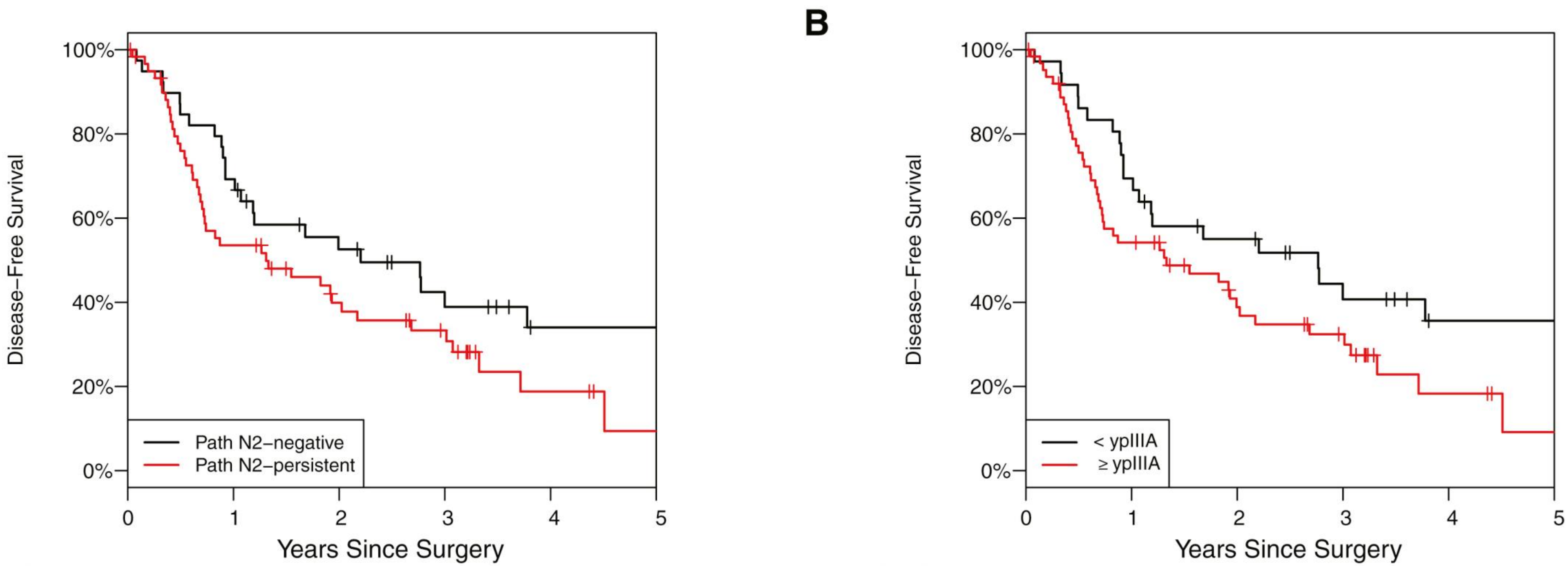




Ripley et al, J Thorac Cardiovasc Surg 2016;151:969-79

Postinduction positron emission tomography assessment of N2 nodes is not associated with ypN2 disease or overall survival in stage IIIA non–small cell lung cancer

Disease-free survival



Ripley et al, J Thorac Cardiovasc Surg 2016;151:969-79

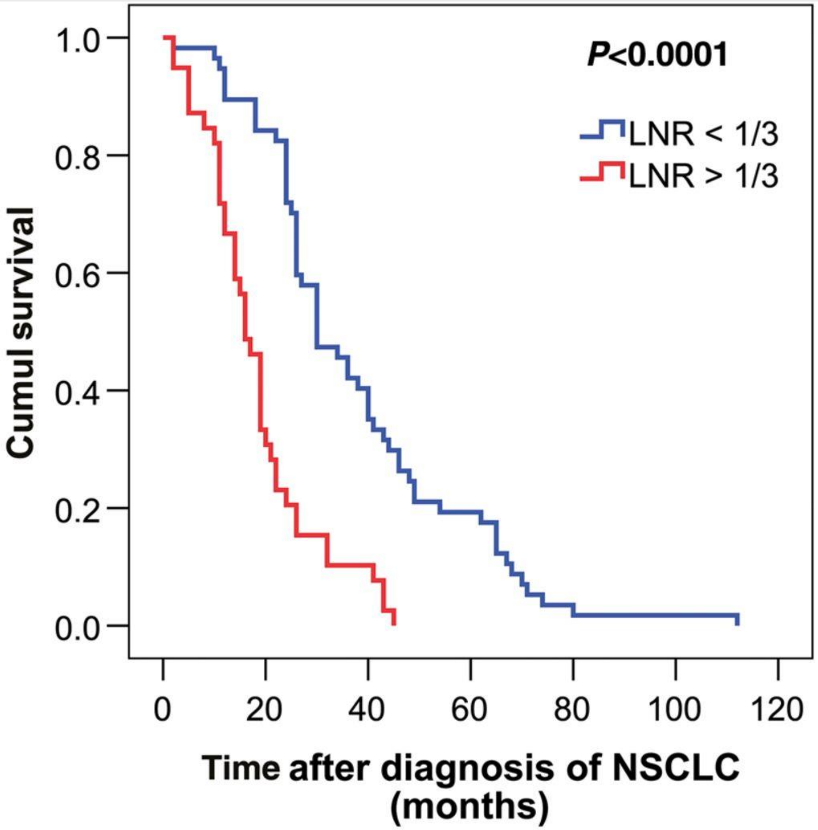
Postinduction positron emission tomography assessment of N2 nodes is not associated with ypN2 disease or overall survival in stage IIIA non–small cell lung cancer

Post-induction PET identification pyN2

Sensitivity:	**59 %**
Specificity:	**57 %**
Accuracy:	**57 %**

Ripley et al, J Thorac Cardiovasc Surg 2016;151:969-79

Lymph node ratio is a significant prognostic indicator

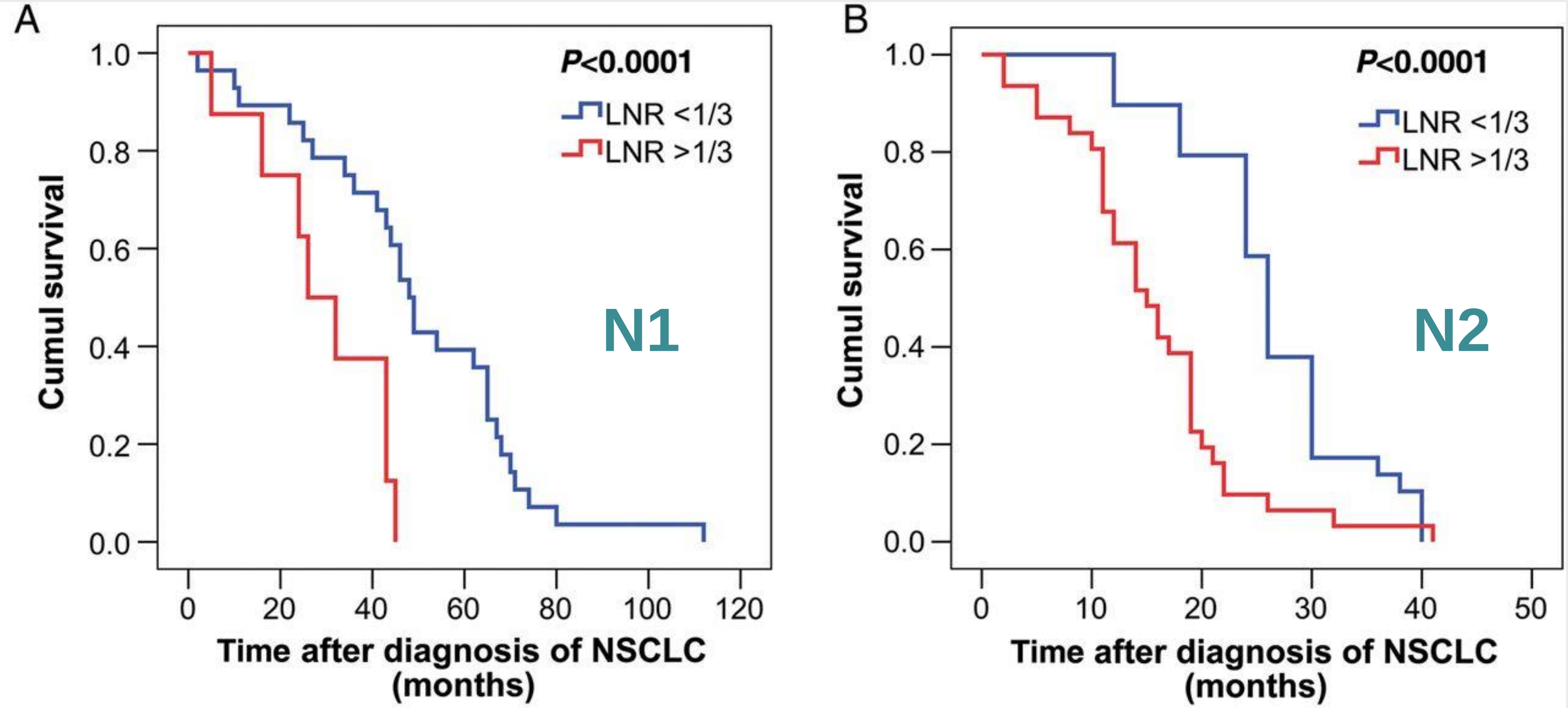


LNR <1/3	57	48	20	10	1	1	0
LNR ≥1/3	39	12	4	0	0	0	0

>1/3 is an adverse prognostic factor

Stéphane Renaud et al. Interact CardioVasc Thorac Surg 2015;20:222-227

Lymph node ratio applies to N1 and N2

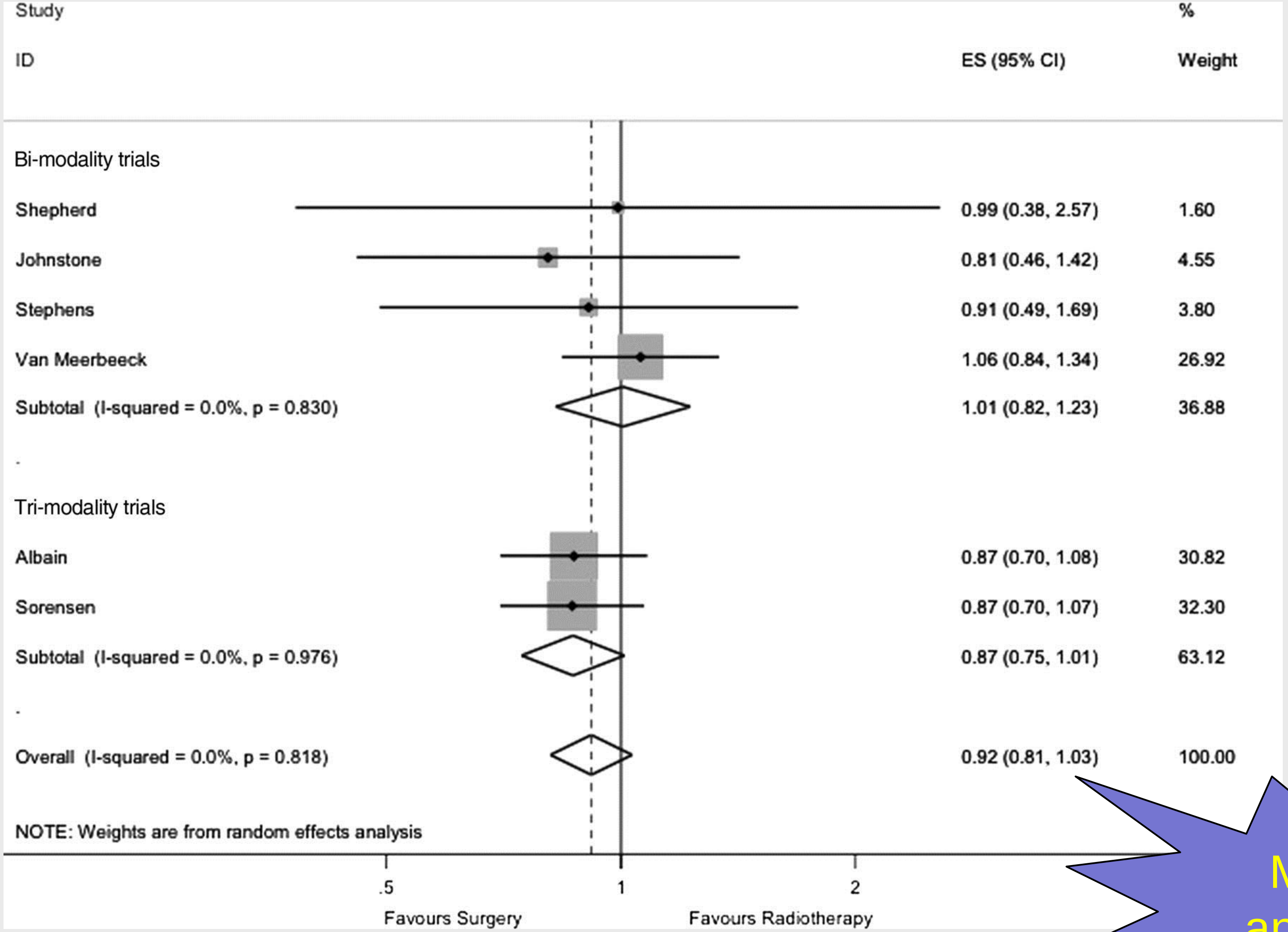


LNR <1/3	28	25	20	11	1	1	0
LNR ≥1/3	8	6	3	0	0	0	0

LNR <1/3	29	28	23	5	0	0
LNR ≥1/3	31	25	6	2	1	0

Stéphane Renaud et al. Interact CardioVasc Thorac Surg 2015;20:222-227

Surgery after induction therapy offers a survival advantage in a trimodality setting



Meta-analysis

P J McElnay et al. Thorax 2015;70:764-768

Lung cancer involving the spine :

a plea for combined resection

- cT4N0M0
- Combined en-bloc resection
- Anticipated R0 resection
- Fitness for operation confirmed

Combined resection of T4 (spine) NSCLC

- 20 patients
- No mortality
- Morbidity 40 %

- Adverse prognostic factors
  - R+ resection
  - Sublobar lung resection
- Trend towards improved survival
  - Age < 70 years
  - Adjuvant radiochemotherapy

Schirren et al, Eur J Cardiothorac Surg 2011;40:647-55

Combined resection of T4 (spine) NSCLC

- 48 patients
- Induction with chemoradiation (CDDP-45 Gy)

- Mortality 6 %
- Morbidity 38 %

- Complete resection 88 %
- Complete response 50 % ← MVA, p=0.048
- 5-year survival 61 %

Collaud et al, J Thorac Oncol 2013;8:1538-44

Combined resection of T4 (spine) NSCLC

pooled data analysis

- 135 patients from 4 centers
- Induction 63 %
- Adjuvant 52 %

- R0 89 %
- 3-year survival 57 %
- 5-year survival 43 %

- R0 improves survival

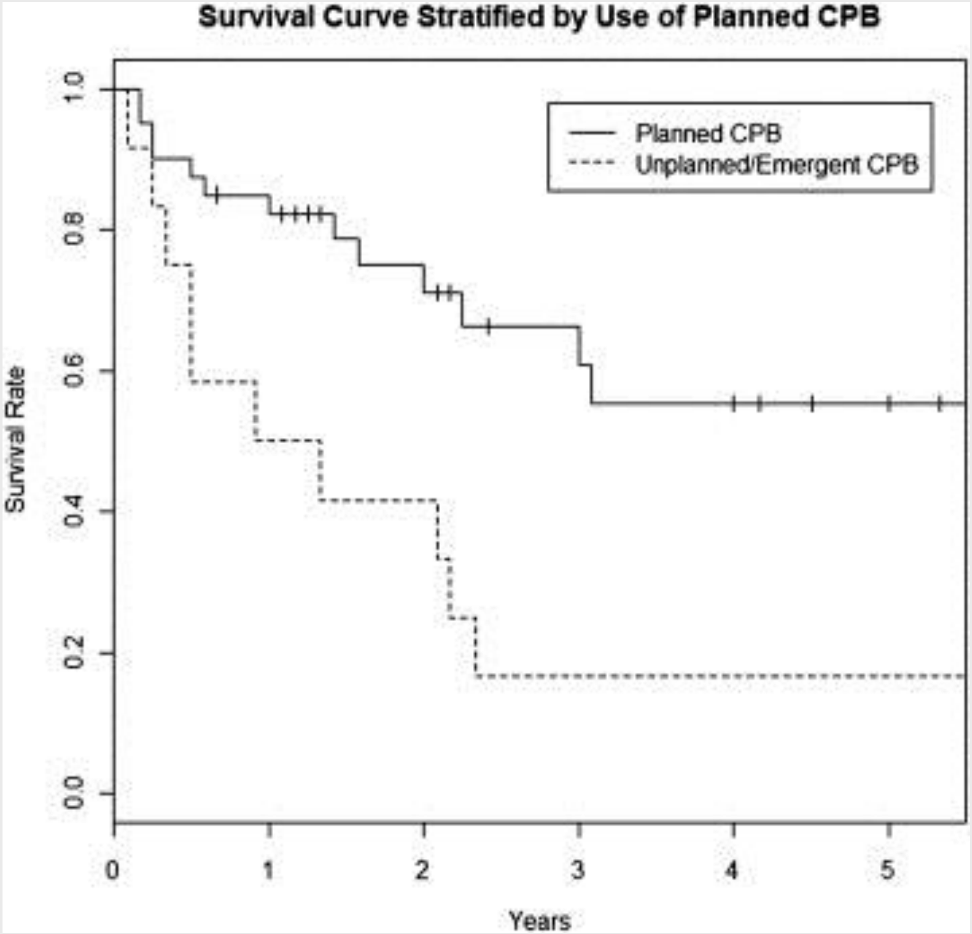
Collaud et al, Ann Surg 2015;262:184-8

Lung resection on cardio-pulmonary bypass

Clinical settings

- Lung cancer involving heart or great vessels
- Combined open heart surgery and lung resection
  - Ischemic heart disease
  - Valvular heart disease
- Intraoperative catastrophy

Long-term survival after lung resection for non–small cell lung cancer with circulatory bypass: A systematic review



Surgery on planned CBP :

- safe
- satisfactory survival

Muralidaran et al, J Thorac Cardiovasc Surg 2011;142:1137-42

National analysis of short-term outcomes after pulmonary resection on cardio-pulmonary bypass

NIS database 2001-2011 (20% of hospital stays US)

	Planned CPB	+ open heart surgery	Intraoperative catastrophy
N patients	265	376	202
Mortality %	22	16	57
Complications %	68	78	100
Discharge home %	48	34	18

Registry study

De Biasi et al, Ann Thorac Surg 2015;100:2064-71

National analysis of short-term outcomes after pulmonary resection on cardio-pulmonary bypass

- Risk factors for post-op. mortality (multivariate analysis)

	Odds ratio
Pneumonectomy	2.74
Combined heart & lung surgery	1.48
Intraoperative catastrophy	6.52

- Contrast with systematic review by Muralidaran et al (JTCS 2011;142:1137-42)

De Biasi et al, Ann Thorac Surg 2015;100:2064-71

List of References

1. Betticher et al, J Clin Oncol 2003;21:1752-59
2. Van Meerbeck et al, J Natl Cancer Instit 2007 ; 99: 442-50
3. Renaud et al, Interact CardioVasc Thorac Surg 2015;20:222-227
4. McElnay et al. Thorax 2015;70:764-768
5. Collaud et al, J Thorac Oncol 2013;8:1538-44
6. Collaud et al, Ann Surg 2015;262:184-8
7. Muralidaran et al, J Thorac Cardiovasc Surg 2011;142:1137-42
8. De Biasi et al, Ann Thorac Surg 2015;100:2064-71

Take-Home Message

- Meta-analysis credits a survival advantage to surgery in a trimodality strategy
- Surgery is effective in selmected patients with completely resectable T4 NSCLC
- Resection on CPB is subjected to a prohobotive mortality outside of highly specialized units

Lung Transplantation

Non heart beating donation

State of the Art

Brain dead donor so far gold standard

- **Ongoing shortage of donor lungs**
- **Increasing waiting lists**
- **Low rate of lung harvest in brain-dead donors : 15-20%**
- **Mortality on waiting list : 15-20 %**

J Reeb et al. Curr Opin Organ Transplant 2015;20:498-505
JJ Mooney et al. Am J Transplant 2016;16:1207-15.

State of the Art

Expanding the lung donor pool: advancements and emerging pathways

- **Optimisation of potential donor lungs**
- ***Ex vivo* Lung Perfusion (EVLP) of marginal lungs**
- **(Living related donor)**
- ***Lung donation after cardiac arrest***

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

State of the Art

Non-heart beating donor: Maastricht classification

	Category	Definition
« uncontrolled »	I	Dead on arrival
	II	Unsuccessful ressucitation
« controlled »	III	Awaiting cardiac arrest
	IV	Cardiac arrest while brain dead

Koostra et al, Transplant Proc 1995

Prevalence of DCD lung donation

Table 1 Characteristics of DCD Practices in Participating Centers

Center	Transplants 2012 to 2014 (n)	Percentage of Transplants from DCD (%)	Use of heparin pre-mortem	Use of Bronchoscopy Pre-mortem	Selective use of EVLP	Stand-off period	Maximum time allowed for WLST to arrest
Toronto	352	15	Yes	Yes	Yes	5 min	180 min
Sydney	139	23	No	No	Yes	2 min	90 min
Melbourne	214	23	Yes[a]	Yes	No	2 to 5 min	90 min
Brisbane	93	15	No	No	Yes	5 min	90 min
Leuven	199	14	Yes	No	Yes	5 min	120 min
Groningen	112	32	No	Yes	Yes	5 min	90 min
Minnesota	126	7	Yes	Yes	Yes	5 min	90 min
St. Louis	191	<1	Yes	Yes	No	5 min	30 min
Cleveland	302	8	Yes	Yes	No	5 min	60 min

DCD, donation after circulatory death donor; EVLP, ex vivo lung perfusion; WLST, withdrawal of life support therapy.
[a]When allowed by donor hospital.

DCD donors = marginal donors :

- ✓ **hypoxemia**
- ✓ **hypotension**
- ✓ **inhalation**

M Cypel et al.
J Heart Lung Transplant 2015;34:1278-82.

Organisation of DCD lung harvest
Maastricht III

- Acceptance on same criteria as brain dead donor
- OR is prepared in advance, all teams ready
- Vital support is discontinued

  close to the OR

  relatives present

  extubation, WSLT drugs discontinued
- Waiting for cardiac arrest < 3 hours
- At cardiac arrest

  no touch 5 minutes

  transfer to the OR

  harvest according to usual techniques

DCD / Results (1)

ORIGINAL CLINICAL SCIENCE

Lung transplantation from donation after cardiocirculatory death: a systematic review and meta-analysis

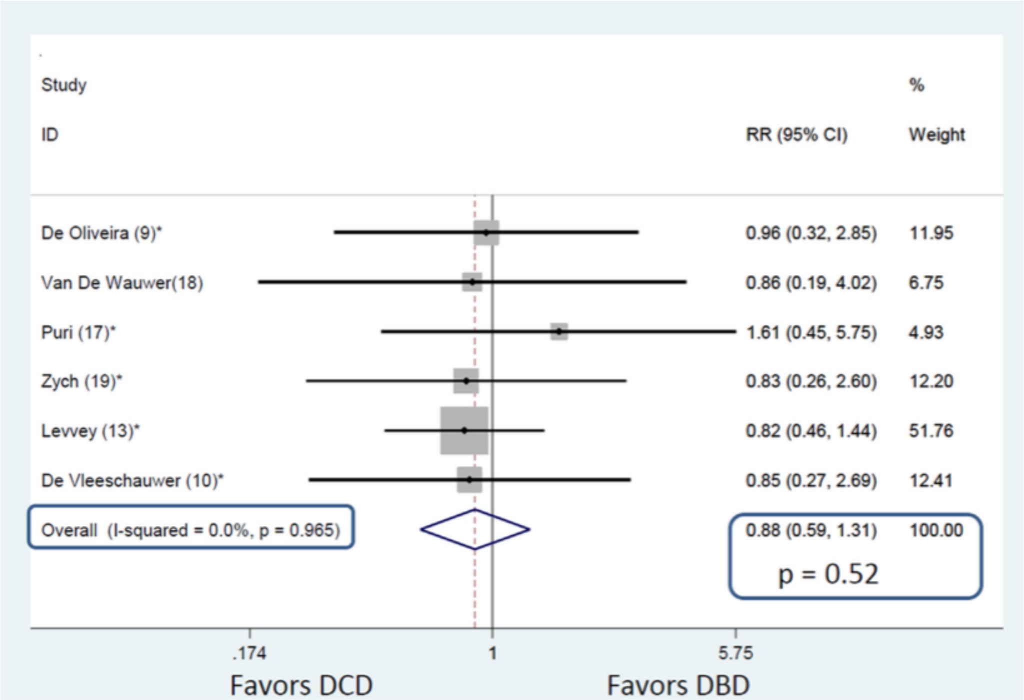
Dustin Krutsinger, MD,[a] Robert M. Reed, MD,[b] Amy Blevins, MALS,[c] Varun Puri, MD,[d] Nilto C. De Oliveira, MD,[e] Bartlomiej Zych, MD,[f] Servet Bolukbas, MD,[g] Dirk Van Raemdonck, MD, PhD,[h] Gregory I. Snell, MBBS, FRACP, MD,[i] and Michael Eberlein, MD, PhD[a,j]

- **meta-analysis from 6 studies**
- **203 DCD vs 1967 NDD**

D Krutsinger et al.
J Heart Lung Transplant
2015;34:675-84.

DCD / Results (1)

1-year survival



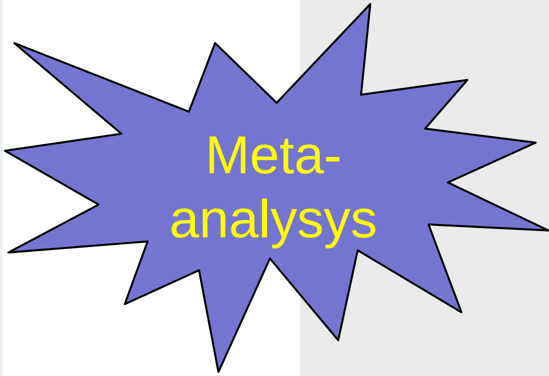


Figure 2 Forest plot of pooled analysis of 1-year survival. Vertical line is the "no difference" point in mortality between DCD and DBD cohorts. Horizontal lines are 95% confidence intervals. Squares indicate relative risk (RR), and the size of each square denotes the proportion of information provided by each trial. Diamond indicates pooled RR for all studies combined. *Updated 1-year survival data were provided (see Table 2 for further details). Numbers in parentheses are reference numbers.

D Krutsinger et al. J Heart Lung Transplant 2015;34:675-84.

DCD / Results (1)

PGD3 ≤ 3 days

s

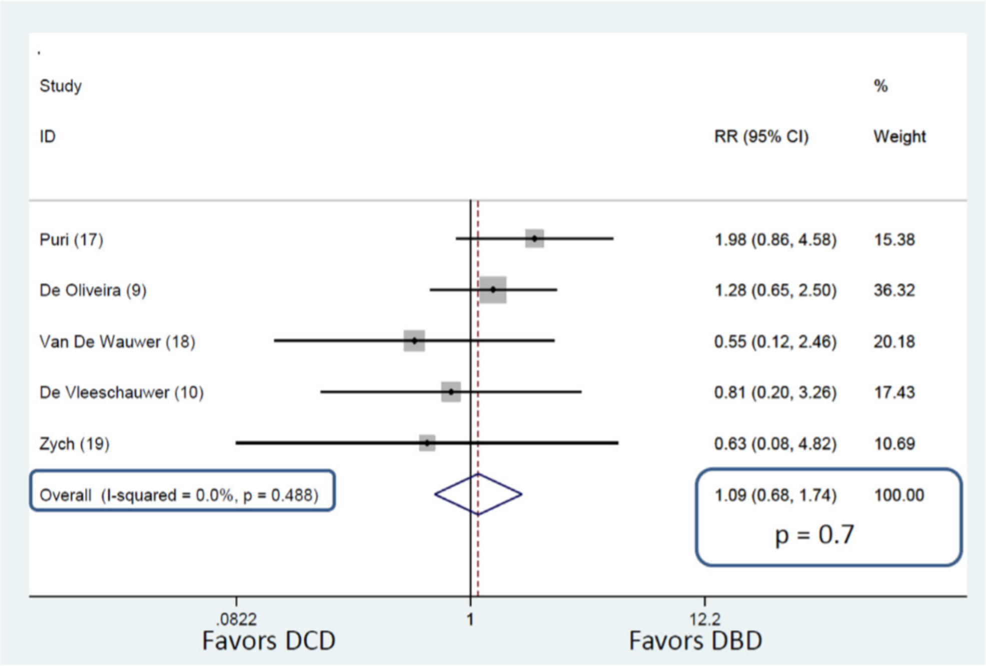


Figure 3 Forest plot of pooled analysis of primary graft dysfunction. Vertical line is the "no difference" point in primary graft dysfunction between DCD and DBD cohorts. Horizontal lines are 95% confidence intervals. Squares indicate relative risk (RR), and the size of each square denotes the proportion of information provided by each trial. Diamond indicates pooled RR for all studies combined. Numbers in parentheses are reference numbers.

Meta-analysys

D Krutsinger et al. J Heart Lung Transplant 2015;34:675-84.

DCD / Results (1)

Acute cellular rejection

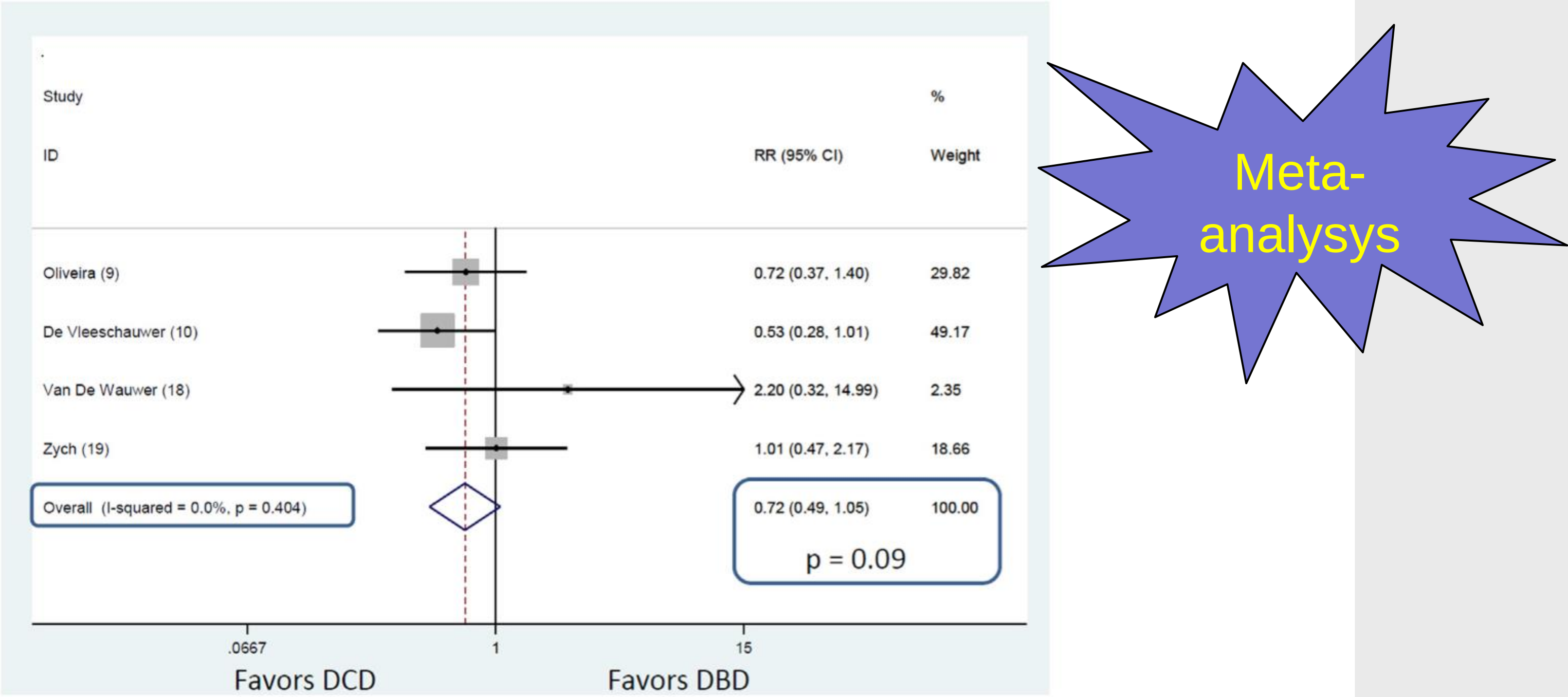


Figure 4 Forest plot of pooled analysis of acute rejection. Vertical line is the "no difference" point in acute rejection between DCD and DBD cohorts. Horizontal lines are 95% confidence intervals. Squares indicate relative risk (RR), and the size of each square denotes the proportion of information provided by each trial. Diamond indicates pooled RR for all studies combined. Numbers in parentheses are reference numbers.

D Krutsinger et al. J Heart Lung Transplant 2015;34:675-84.

DCD / Results (2)

European Journal of Cardio-Thoracic Surgery Advance Access published March 15, 2015

European Journal of Cardio-Thoracic Surgery (2015) 1–8
doi:10.1093/ejcts/ezv051

ORIGINAL ARTICLE

Cite this article as: Sabashnikov A, Patil NP, Popov A-F, Soresi S, Zych B, Weymann A *et al*. Long-term results after lung transplantation using organs from circulatory death donors: a propensity score-matched analysis. Eur J Cardiothorac Surg 2015; doi:10.1093/ejcts/ezv051.

Long-term results after lung transplantation using organs from circulatory death donors: a propensity score-matched analysis[†]

Anton Sabashnikov[a,*], Nikhil P. Patil[a], Aron-Frederik Popov[a], Simona Soresi[a], Bartlomiej Zych[a], Alexander Weymann[a], Prashant N. Mohite[a], Diana García Sáez[a], Mohamed Zeriouh[a], Thorsten Wahlers[b], Yeong-Hoon Choi[b], Jens Wippermann[b], Thorsten Wittwer[b], Fabio De Robertis[a], Toufan Bahrami[a], Mohamed Amrani[a] and André R. Simon[a]

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- **302 LTx**
- **60 DCD**

A Sabashnikov et al. Eur J Cardio Thorac Surg (2015) March: 1-8.

Table 1: Donor baseline and organ procurement data

	DBD	DCD	*P*-values
Age (years)	41 ± 14	42 ± 13	0.67
Female	75 (63%)	33 (55%)	0.33
Height (cm)	170 ± 10	171 ± 10	0.44
Weight (kg)	73 ± 14	73 ± 15	0.88
Blood group			0.55
O	53 (44%)	22 (37%)	
A	53 (44%)	33 (54%)	
B	10 (9%)	4 (7%)	
AB	4 (3%)	1 (2%)	
pO_2/FiO_2 ratio preretrieval	442 ± 100	449 ± 93	0.62
Ventilation duration (days)	3.2 ± 4.0	3.2 ± 2.0	0.92
Total ischaemic time (min)	363 (255;480)	346 (304;506)	0.24
History of cardiac arrest	32 (27%)	12 (20%)	0.29
Cardiac arrest duration (min)	22 ± 17	26 ± 13	0.57
Abnormal CXR	26 (22%)	17 (29%)	0.32
Abnormal bronchoscopy	35 (29%)	17 (28%)	0.88
Smoking history	55 (46%)	25 (41%)	0.53
Extent of smoking (pack-years)	11 (4;22)	10 (4;20)	0.72
Heavy smokers	5 (4.3%)	2 (3.4%)	1.00
Cannabis smokers	8 (6.7%)	4 (6.7%)	1.00
Extended donor criteria[a]	27 (28%)	10 (21%)	0.38
Other institute retrieval teams	41 (34%)	23 (38%)	0.10
Female-to-male transplantation	11 (11%)	8 (17%)	0.35
Male-to-female transplantation	5 (5%)	5 (10%)	0.29
Use of OCS	3 (2.5%)	1 (1.7%)	1.00
Use of EVLP	3 (3.1%)	3 (6.4%)	0.39
Cause of death/event			0.21
ICH	74 (62%)	35 (58%)	
HBI	17 (14%)	11 (18%)	
Trauma	11 (9%)	6 (10%)	
CVA	8 (6%)	7 (11%)	
Meningitis	10 (8%)	0	
Other	1 (0.8%)	1 (1.7%)	

EVLP: *ex vivo* lung perfusion; OCS: organ care system; DCD: donors after cardiac death; CXR: chest X-ray; ICH: intracranial haemorrhage; HBI: hypoxic brain injury; CVA: cerebrovascular accident.
[a]Donors outside standard criteria: PaO_2/FiO_2 ratio <300, age over 55 years and history of smoking >20 pack-years

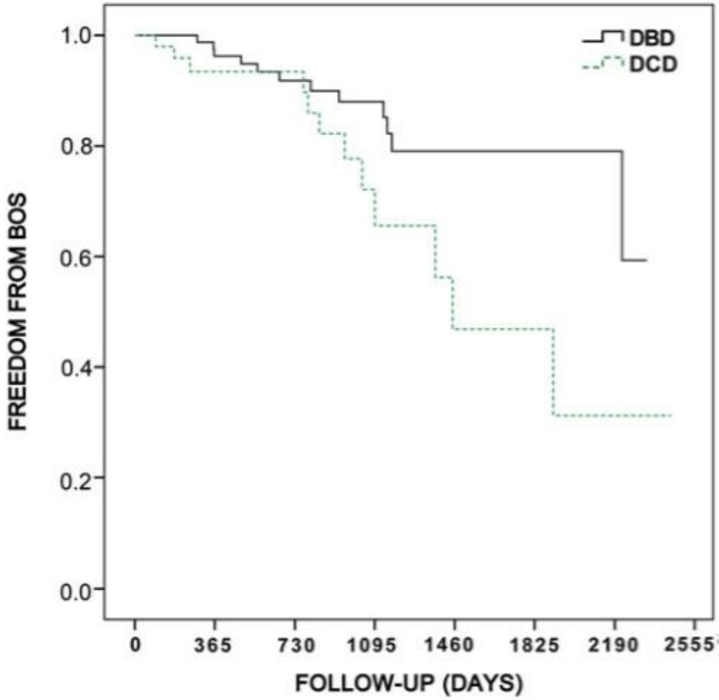
Table 3: Intraoperative data and postoperative outcome

	DBD	DCD	*P*-value
Use of CPB			0.81
Elective CPB	70 (58%)	38 (63%)	
Off-pump	26 (22%)	12 (20%)	
Converted	24 (20%)	10 (17%)	
CPB time	172 ± 90	160 ± 49	0.45
SLTx	1 (1.0%)	1 (2.1%)	0.55
pO_2/FiO_2 ratio on arrival	341 ± 125	284 ± 139	**0.018**
pO_2/FiO_2 ratio 24 h	358 ± 100	317 ± 106	**0.032**
pO_2/FiO_2 ratio 48 h	369 ± 123	349 ± 109	0.37
pO_2/FiO_2 ratio 72 h	355 ± 112	355 ± 130	0.99
Ventilation (hours)	32 (20;398)	32 (17;134)	0.66
ICU stay (days)	6 (3;21)	5 (3;25)	0.65
Hospital stay (days)	32 (22;48)	30 (10;60)	0.70
ECLS	6 (6%)	7 (15%)	0.08
BOS	12 (12%)	12 (24%)	**0.049**
PGD on arrival	10 (11%)	12 (27%)	**0.014**
PGD 24 h	5 (5%)	4 (9%)	0.46
PGD 48 h	6 (7%)	2 (5%)	1.00
PGD 72 h	7 (9%)	2 (5%)	0.71
Rejection			0.98
A0	93 (78%)	45 (75%)	
A1	11 (9%)	6 (10%)	
A2	13 (11%)	7 (12%)	
A3	3 (3%)	2 (3%)	

CPB: cardiopulmonary bypass; SLTx: single lung transplant; ICU: intensive care unit; ECLS: extracorporeal life support; PGD: primary graft dysfunction.

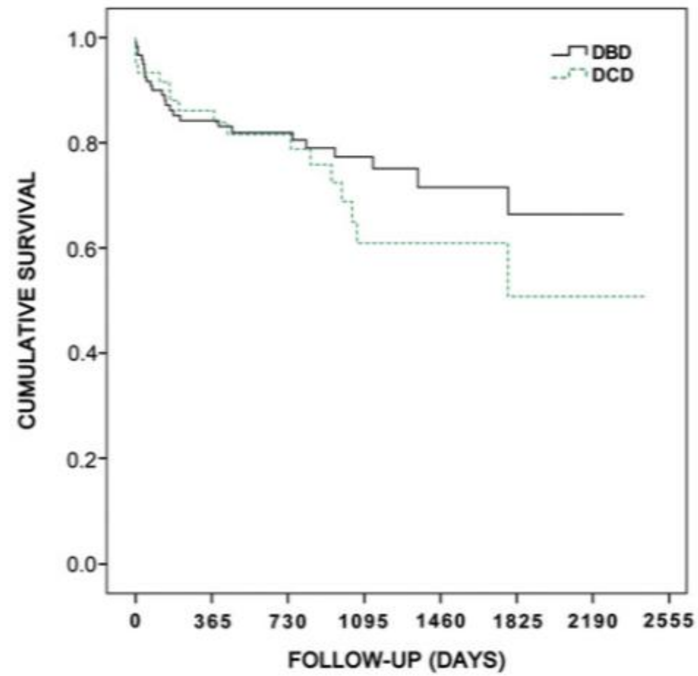
A Sabashnikov et al. Eur J Cardio Thorac Surg (2015) March: 1-8.

DCD / Results



Group	1 year	2 years	3 years	4 years	5 years	6 years	7 years
DBD							
Survival (%)	96.3	91.8	88.0	79.1	79.1	79.1	59.3
Standard deviation	2.1	3.2	4.1	6.1	6.1	6.1	17.7
Patients at risk	77	54	32	16	11	5	2
DCD							
Survival (%)	93.5	93.5	72.1	46.8	46.8	31.2	31.2
Standard deviation	3.7	3.7	9.1	13.4	13.4	15.6	15.6
Patients at risk	34	26	11	5	3	2	1

Figure 2: Propensity score-adjusted survival free of BOS (bronchiolitis obliterans syndrome) for patients after bilateral sequential lung transplantation with organs from DCD donors compared with DBD donors (log-rank *P* = 0.028).



Group	1 year	2 years	3 years	4 years	5 years	6 years	7 years
DBD							
Survival (%)	84.2	82.0	77.3	71.5	66.4	66.4	66.4
Standard deviation	3.4	3.7	4.4	5.7	7.2	7.2	7.2
Patients at risk	80	58	46	17	11	5	3
DCD							
Survival (%)	86.1	81.6	60.9	60.9	50.8	50.8	50.8
Standard deviation	4.6	5.3	8.4	8.4	11.6	11.6	11.6
Patients at risk	38	29	14	8	5	4	2

Figure 3: Propensity score-adjusted Kaplan–Meier survival estimate for patients after bilateral sequential lung transplantation with organs from DCD donors compared with DBD donors (log-rank *P* = 0.352).

A Sabashnikov et al. Eur J Cardio Thorac Surg 2016;49:46-53.

DCD / Results (3)

International Society for Heart and Lung Transplantation Donation After Circulatory Death Registry Report

Marcelo Cypel, MD, Bronwyn Levvey, RN, Dirk Van Raemdonck, MD, Michiel Erasmus, MD, John Dark, MB, FRCS, Robert Love, MD, David Mason, MD, Allan R. Glanville, MD, Daniel Chambers, MD, Leah B. Edwards, PhD, Josef Stehlik, MD, Marshall Hertz, MD, Brian A. Whitson, MD, Roger D. Yusen, MD, Varun Puri, MD, Peter Hopkins, MD, Greg Snell, MD, and Shaf Keshavjee, MD; for the International Society for Heart and Lung Transplantation

From the International Society for Heart and Lung Transplantation Donation after Circulatory Death Registry, Dallas, Texas.

Registry

M Cypel et al.
J Heart Lung Transplant
2015;34:1278-82.

- 306 DCD vs 3992 NDD

DCD / Results (3)

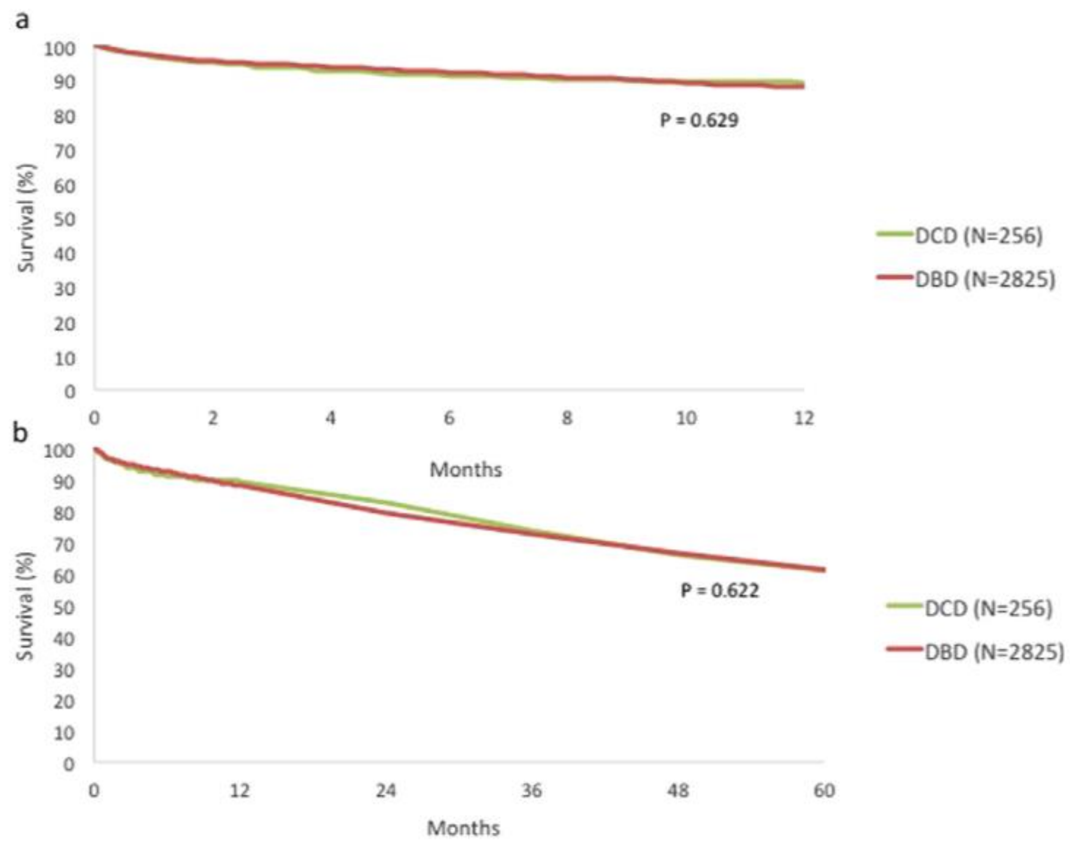


Figure 4 One-year (a) and 5-year (b) post-transplant survival in the DCD vs DBD groups. Asterisk indicates that only transplants performed between January 2006 and December 2012 used for survival calculations.

Registry

M Cypel et al.
J Heart Lung Transplant
2015;34:1278-82.

DCD / Results (4)

American Journal of Transplantation 2015; XX: 1–9
Wiley Periodicals Inc.

doi: 10.1111/ajt.13599

J. J. Mooney[1,*], H. Hedlin[1], P. K. Mohabir[1], R. Vazquez[2], J. Nguyen[3], R. Ha[4], P. Chiu[4], K. Patel[1], M. R. Zamora[5], D. Weill[1], M. R. Nicolls[1] and G. S. Dhillon[1]

Lung Quality and Utilization in Controlled Donation After Circulatory Determination of Death Within the United States

Registry

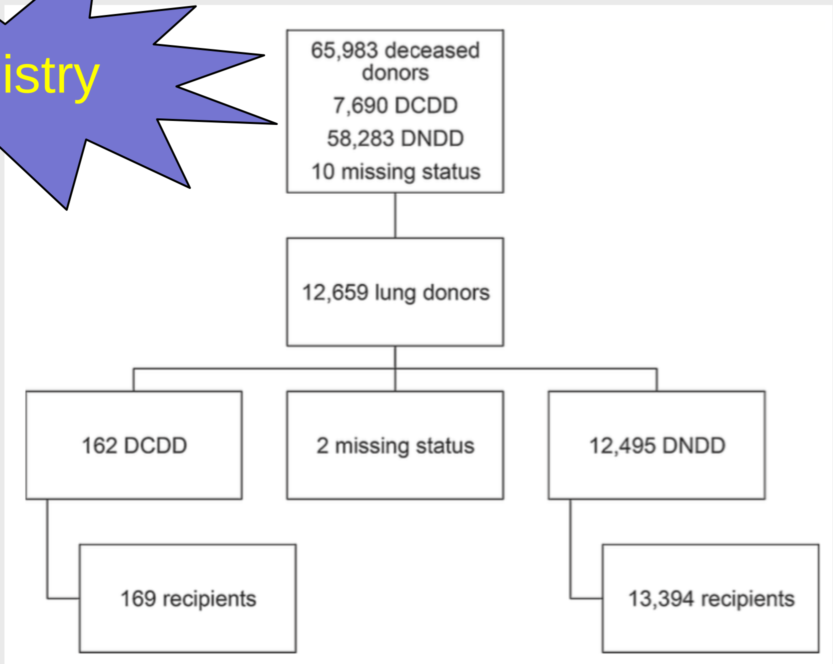


Figure 1: Flow diagram of donors and recipients. DCDD, donation after circulatory determination of death; DNDD, donation after neurologic determination of death.

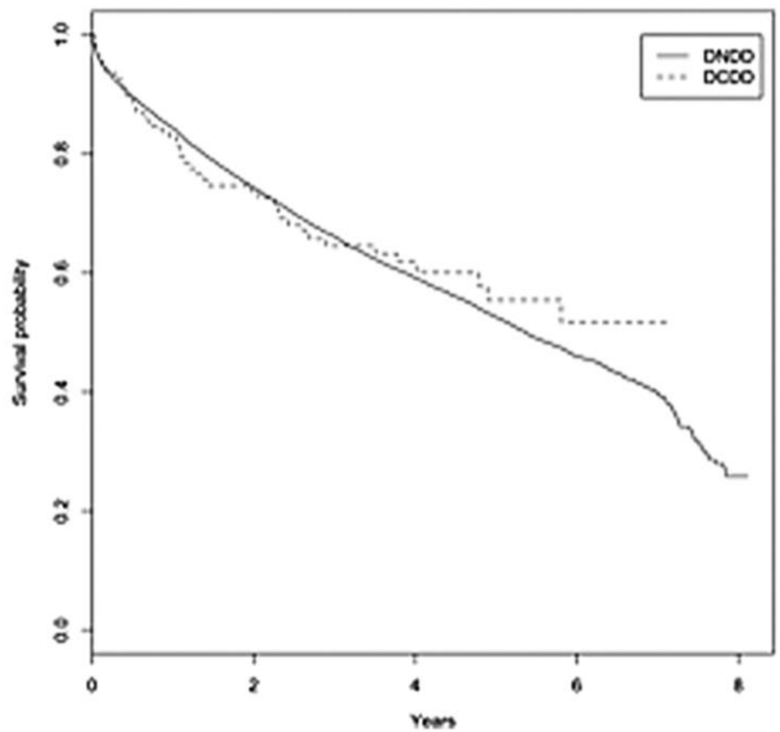


Figure 4: Recipient survival by controlled DCDD status. Kaplan-Meier survival curve for posttransplant recipient survival in controlled DCDD recipients (dashed line) and DNDD recipients (solid line). DCDD, donation after circulatory determination of death; DNDD, donation after neurologic determination of death.

DCD / Do we need EVLP ?

Lung Transplantation With Donation After Circulatory Determination of Death Donors and the Impact of *Ex Vivo* Lung Perfusion

T. N. Machuca, O. Mercier, S. Collaud, J. Tikkanen, T. Krueger, J. C. Yeung, M. Chen, S. Azad, L. Singer, K. Yasufuku, M. de Perrot, A. Pierre, T. K. Waddell, S. Keshavjee and M. Cypel*

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**TN Machuca et al.
Am J Transplant
2015;15:993-1002**

DCD / Do we need EVLP ?

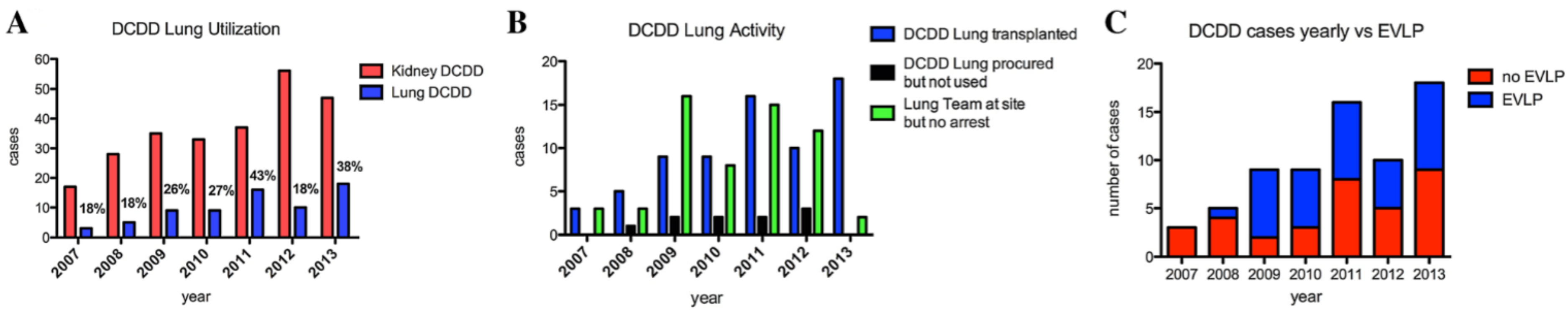

Figure 1: (A) DDCD lung utilization. Displays the annual number of DDCD kidney transplants as a denominator and the percentage of DDCD lung transplants performed. (B) DDCD Lung Activity. Displays the number of DDCD lungs transplanted. Along with the number of times the lungs were actually procured but not transplanted and finally the numbers to instances the procurement team was onsite but the potential donor did not arrest within 120 minutes. (C) Annual EVLP Activity in DDCD. Yearly lung transplants performed with DDCD donor lungs with and without EVLP. DDCD, donation after determination of circulatory death; EVLP, *ex vivo* lung perfusion.

TN Machuca et al.
Am J Transplant
2015;15:993-1002

DCD / Do we need EVLP ?

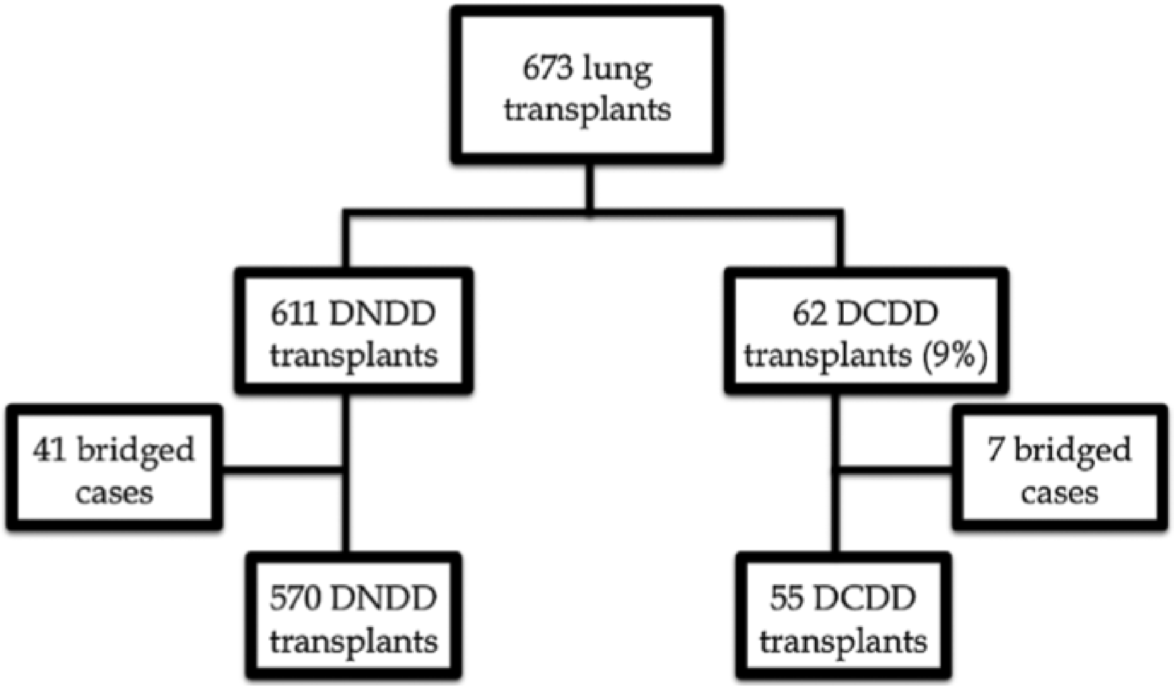

Figure 2: Study flow diagram including lung transplants performed from January 2007 to November 2013. Patients bridged to transplant with mechanical ventilation and/or extracorporeal life support were excluded. DDND, donation after determination of neurological death; DDCD, donation after determination of circulatory death.

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2015;15:993-1002

DCD / Do we need EVLP ?

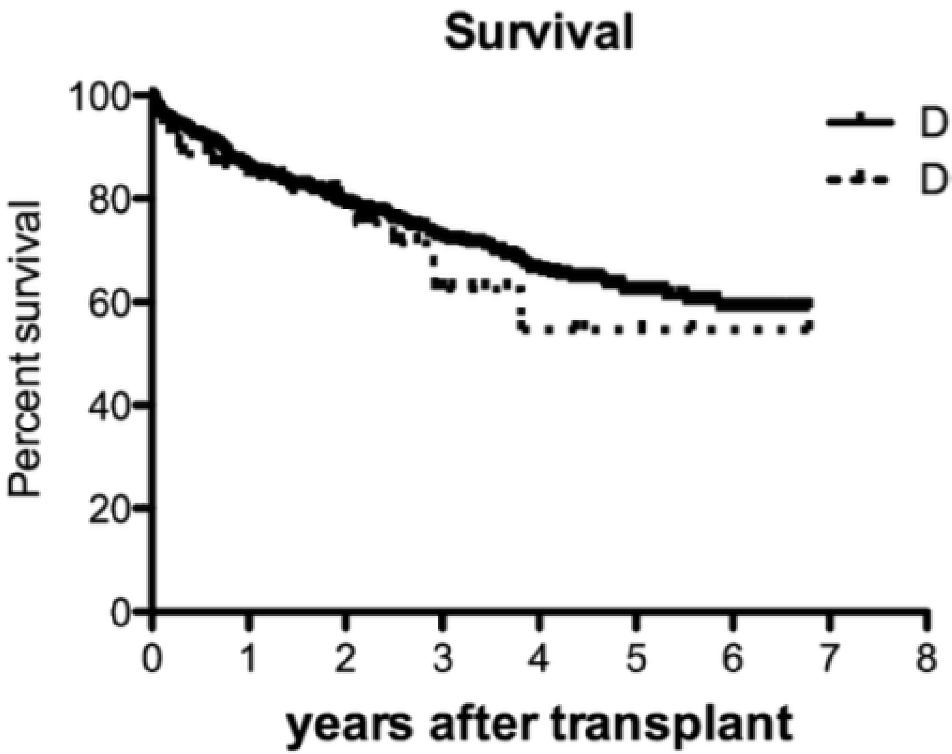

Figure 3: Kaplan–Meier survival curve for lung transplants with donation after neurological determination of death (DNDD) donors and donation after circulatory determination of death (DDCD) donors. ($p = 0.6$).

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2015;15:993-1002

DCD / Do we need EVLP ?

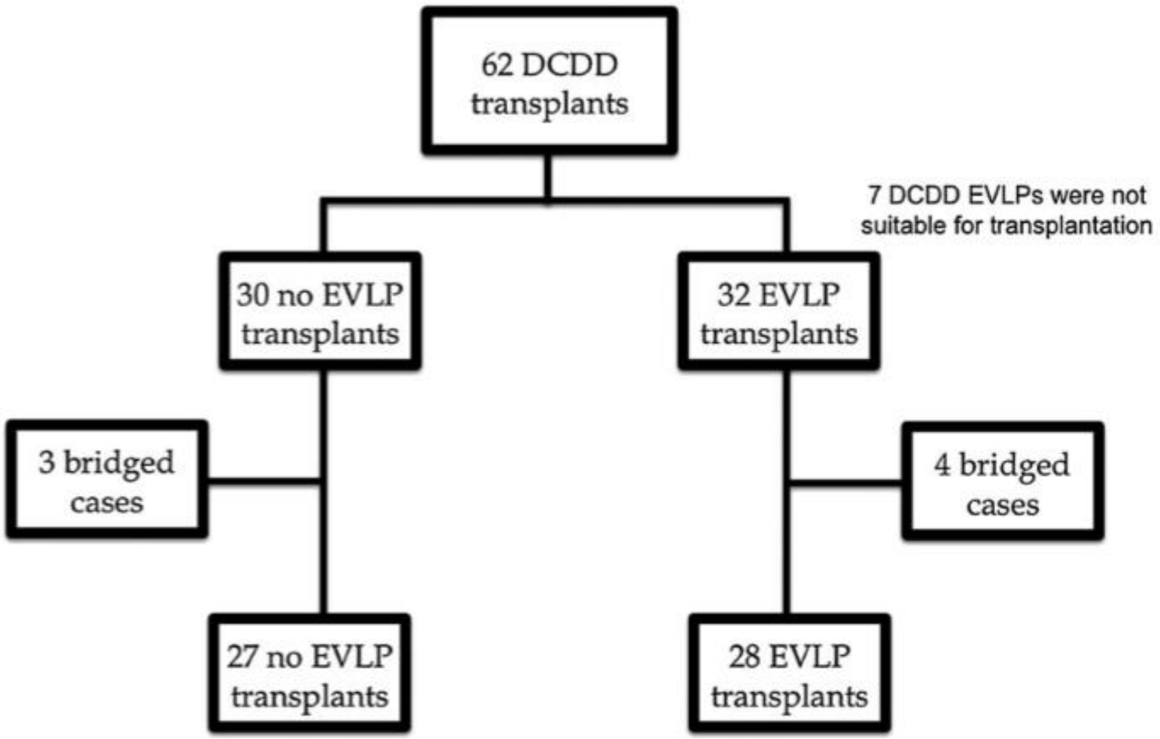

Figure 4: Study flow diagram focusing in the donation after circulatory determination of death (DCDD) cohort. Patients bridged to transplant with mechanical ventilation and/or extracorporeal life support were excluded. EVLP, *ex vivo* lung perfusion.

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2015;15:993-1002

DCD / Do we need EVLP ?

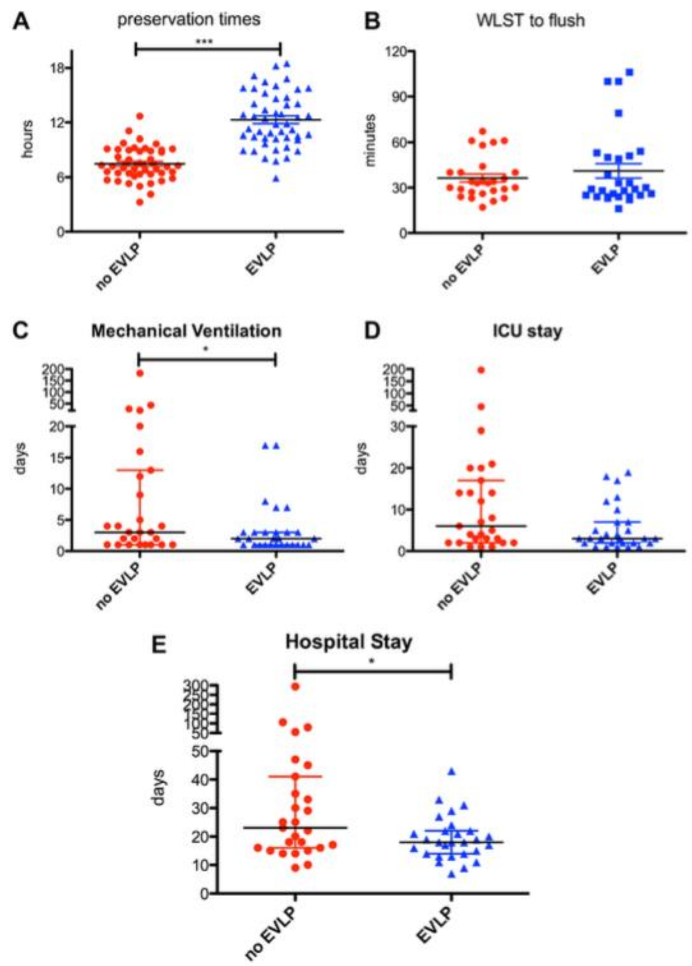

Figure 5: (A) Preservation times (including cold ischemic times before and after EVLP, EVLP time and warm ischemic time), *** $p < 0.0001$. (B) Length of time from withdrawal of life sustaining therapies to pulmonary artery flush. Although there is significant difference between groups ($p = 0.40$), the presence of outliers in the EVLP group is noted. (C) Comparison of length of mechanical ventilation requirement between DCDD-no EVLP and DCDD + EVLP, * $p = 0.059$. (D) Comparison between ICU length of stay between DCDD-no EVLP and DCDD + EVLP, $p = 0.072$. (E) Comparison between hospital length of stay between DCDD-no EVLP and DCDD + EVLP, * $p = 0.047$. EVLP, *ex vivo* lung perfusion. For A and B, the bars in the scatter plot represent mean with standard error of the mean. For C–E, the bars in the scatter plot represent median with interquartile ranges.

Survival	DCD-no EVLP	DCD-EVLP
6-month	92 %	86 %
1-year	92 %	77 %
3-year	51 %	71 %

***p* = 0.68**

TN Machuca et al.
Am J Transplant
2015;15:993-1002

DCD / Conclusions

REVIEW

DCD lung donation: donor criteria, procedural criteria, pulmonary graft function validation, and preservation

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Erasmus M. et al., Transpl Int. 2015 Dec 31. doi: 10.1111/tri.12738. [Epub ahead of print] Review

Recommendation table DCD lung

Recommendation	Grade
Use same donor selection criteria for DCD as already established for DBD.	B
DCD lungs should not be discarded as quality and outcome is at least similar to DBD lungs.	B
Perform antegrade and retrograde flush perfusion.	C
Use same terminology and definition for warm ischemia times as used for other organs	D
Protect the airway early after declaration of death to avoid aspiration during abdominal organ retrieval.	D
Pretransplant *ex vivo* lung perfusion (EVLP) is advised in case of uncertain graft performance to safely extend donor and procedural criteria (long WI, bad flush, clots), lungs with a $PO_2/FiO_2 < 40$ kPa and/or agonal phase >90 min and/or warm ischemia >60 min might be used after testing with EVLP.	C–D
Acceptance criteria on EVLP may include measures of pulmonary compliance, vascular resistance, and gas exchange.	C

Take home messages

- DCD lung grafts are a way to decrease donor organ shortage and death on waiting list
- DCD lungs do not adversely affect short and medium term outcomes

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7. TN Machuca et al. Am J Transplant 2015;15:993-1002
8. Erasmus M. et al., Transpl Int. 2015 Dec 31. doi: 10.1111/tri.12738. [Epub ahead of print] Review

List of Abbreviations

CPB:	cardio-pulmonary bypass
BOS:	bronchiolitis obliterans syndrome
DBD:	donation after brain death
DCD:	donation after cardiac death
EVLP:	ex-vivo lung perfusion
MIS:	minimally invasive surgery
NSCLC:	non-small cell lung cancer
PGD:	primary graft failure
RATS:	robot-assisted thoracic surgery
SBRT:	stereotaxic beam radiation therapy
VATS:	video-assisted thoracic surgery