Preoperative risk models:
The choice between surgery and stereotactic radiotherapy

Mr Eric Lim

MB ChB, MSc (Biostatistics), MD, FRCS (C-Th)

Consultant Thoracic Surgeon
Academic Division of Thoracic Surgery
Royal Brompton Hospital, London, United Kingdom

Clinical Senior Lecturer
National Heart and Lung Institute
Imperial College, London, United Kingdom

Imperial College London

Royal Brompton & Harefield NHS
NHS Foundation Trust

Disclosures

- Consultancy / Advisory Board
  - Strategen, Abbott Molecular, Glaxo Smith Klein, Pfizer, Norvatis, Covidien, Ethicon
- Educational presentations / speaker
  - Roche, Imedex, Glaxo Smith Klein, Lily, Pfizer, Medela, Boehringer Ingelheim
- Travel, accommodation and course fees
  - Covidien, Medela
- Research funding
  - ScreenCell®, Meleda
- Other
  - Founder of Informative Genomics (blood based molecular diagnostics laboratory)
  - Director of the BUPA Cromwell Lung Cancer Screening Programme

Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

J. Vansteenkiste[1], D. De Ruysscher[2], W. E. E. Eberhardt[3], E. Lim[4], S. Senan[5], E. Felip[6] & S. Peters[7], on behalf of the ESMO Guidelines Working Group*

primary radiotherapy

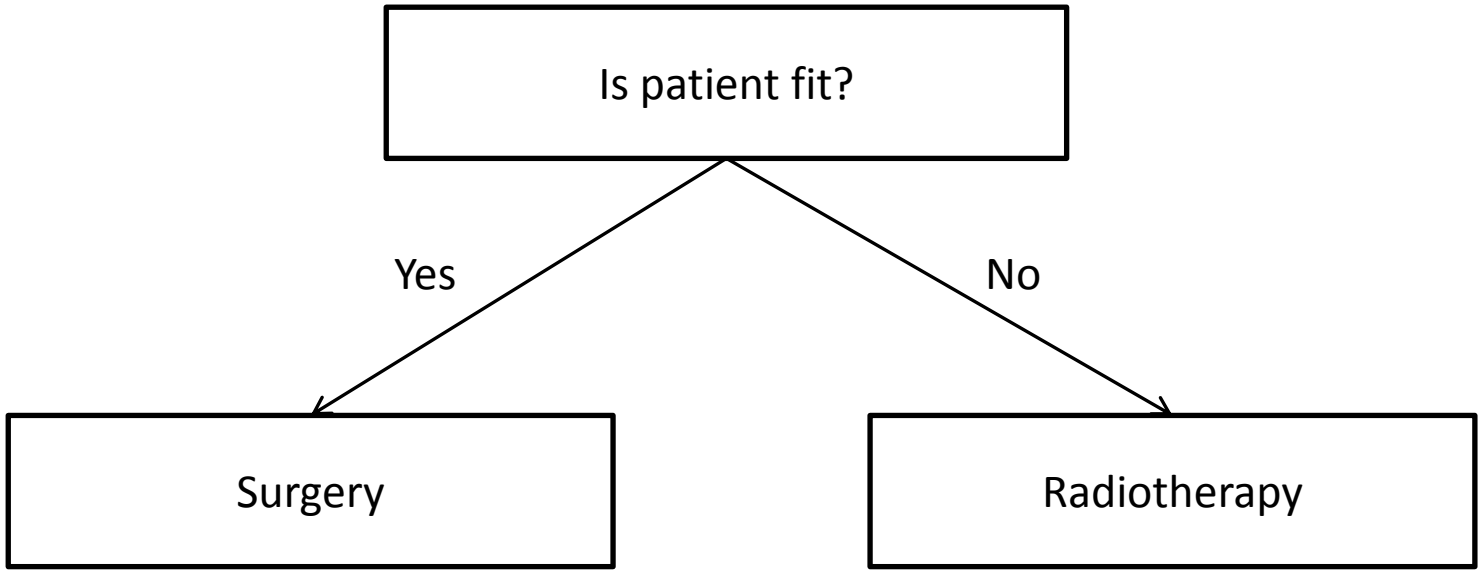
In patients unfit for surgery, SABR is the treatment of choice for peripherally located stage I NSCLC (if SABR is not available, a hypofractionated radiotherapy schedule with a high biologically equivalent dose is advised) [III, A].

Annals of Oncology 24 (Supplement 6): vi89–vi98, 2013

Imperial College London

Royal Brompton & Harefield NHS
NHS Foundation Trust

The high risk patient with early lung cancer



What is fitness?

- "Fitness" is a loose term for risk assessment of an adverse outcome
- We need to clarify each outcome
  - Death
  - Post-operative shortness of breath
- Address risk for the individual outcome
- Conventionally undertaken though risk modeling

Logistic regression modelling

- 2-sided $1-\alpha$ CI for β: $b \pm t_{n-2,1-\alpha/2}\widehat{se}(b)$
- CI for *predictions* depend on what you want to predict even though $\hat{y}$ estimates both y [a] and $E(y|x)$
- Notation for these two goals: $\hat{y}$ and $\hat{E}(y|x)$
  - Predicting y with $\hat{y}$:
    $\widehat{s.e.}(\hat{y}) = s_{y\cdot x}\sqrt{1+\frac{1}{n}+\frac{(x-\bar{x})^2}{L_{xx}}}$
    Note: This s.e. $\rightarrow s_{y\cdot x}$ as $n \rightarrow \infty$.
  - Predicting $\hat{E}(y|x)$ with $\hat{y}$:
    $\widehat{s.e.}(\hat{E}(y|x)) = s_{y\cdot x}\sqrt{\frac{1}{n}+\frac{(x-\bar{x})^2}{L_{xx}}}$ See footnote[b]
    Note: This s.e. shrinks to 0 as $n \rightarrow \infty$

Imperial College London

Royal Brompton & Harefield NHS
NHS Foundation Trust

Application of risk models in clinical care

Personalisation of care

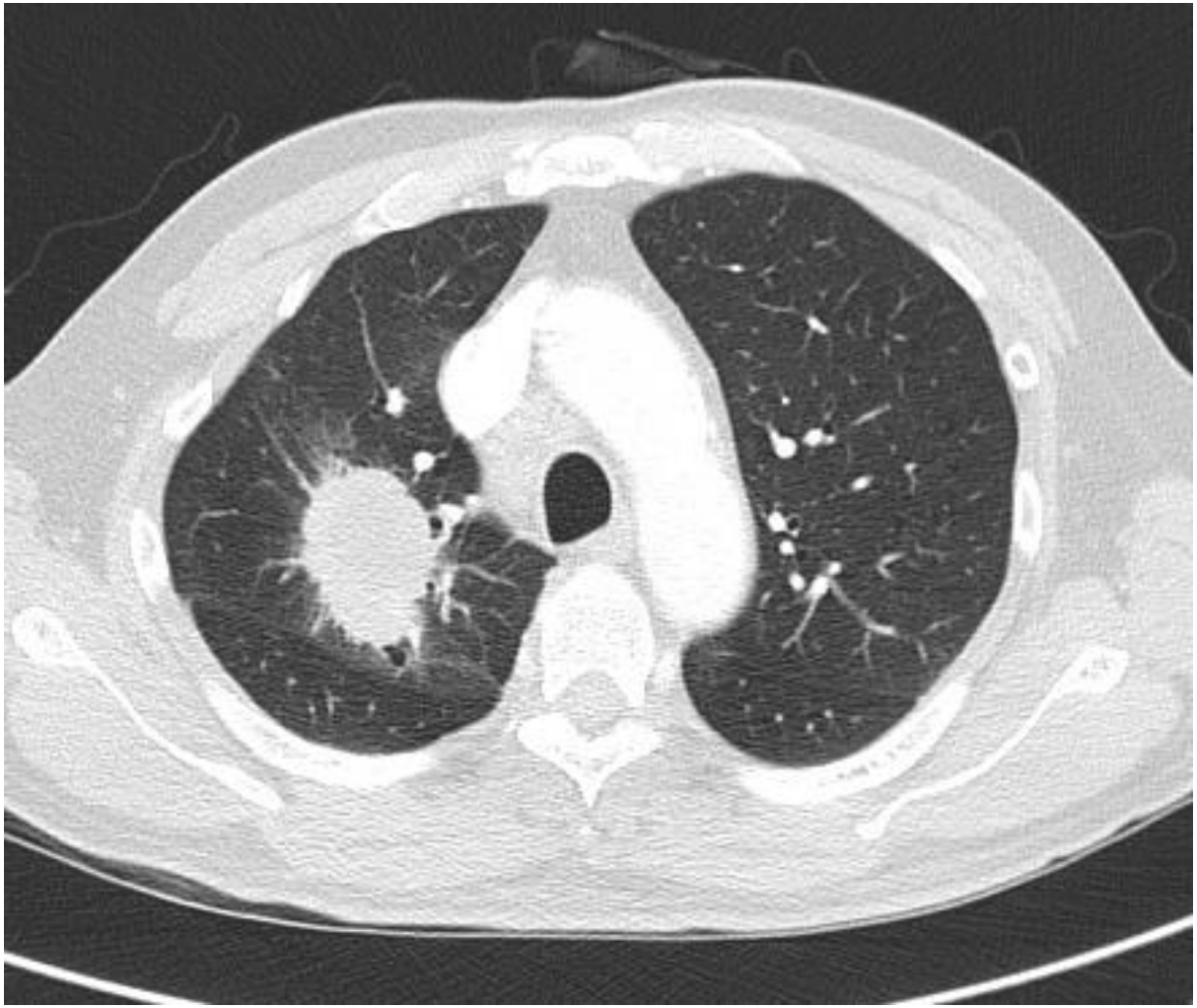
- Individualised treatment has been a theme throughout lung oncology
- Choice between surgery and radiotherapy should not be any different
- How can we make “correct” decisions for high risk patients?

Surgery versus radiotherapy

- What is the benefit?
  - No RCT evidence for either compared to medical therapy alone
- Will I be cured?
  - Recurrence is common after surgery (19% in stage IA, 30% in stage IB)
  - Is the disease still there after radiotherapy?
  - Survival is ultimately predicted by stage
- If I choose surgery:
  - What is the risk of death from the procedure?
  - What is the risk of shortness of breath?

Who should decide the upper limits of risk / safety?

a) Experts (guidelines committees), informed doctors?
b) Patients themselves?



Would you consider surgery?

What is the risk of death from the procedure?

The Thoracic Surgery Scoring System (Thoracoscore): Risk model for in-hospital death in 15,183 patients requiring thoracic surgery

Pierre Emmanuel Falcoz, MD, PhD,[a] Massimo Conti, MD,[b] Laurent Brouchet, MD,[c] Sidney Chocron, MD, PhD,[a] Marc Puyraveau, BSc,[d] Mariette Mercier, MD, PhD,[e] Joseph Philippe Etievent, MD,[a] and Marcel Dahan, MD[c]

TABLE 3. Prediction of risk of in-hospital mortality

Variable	Value	Code	β coefficient
Age (y)	<55	0	
	55-65	1	0.7679
	≥65	2	1.0073
Sex	Female	0	
	Male	1	0.4505
American Society of Anesthesiologists score	≤2	0	
	≥3	1	0.6057
Performance status classification	≤2	0	
	≥3	1	0.689
Dyspnea score	≤2	0	
	≥3	1	0.9075
Priority of surgery	Elective	0	
	Urgent or emergency	1	0.8443
Procedure class	Other	0	
	Pneumonectomy	1	1.2176
Diagnosis group	Benign	0	
	Malignant	1	1.2423
Comorbidity score	0	0	
	≤2	1	0.7447
	≥3	2	0.9065
Constant	—		−7.3737

J Thorac Cardiovasc Surg 2007;133:325-32

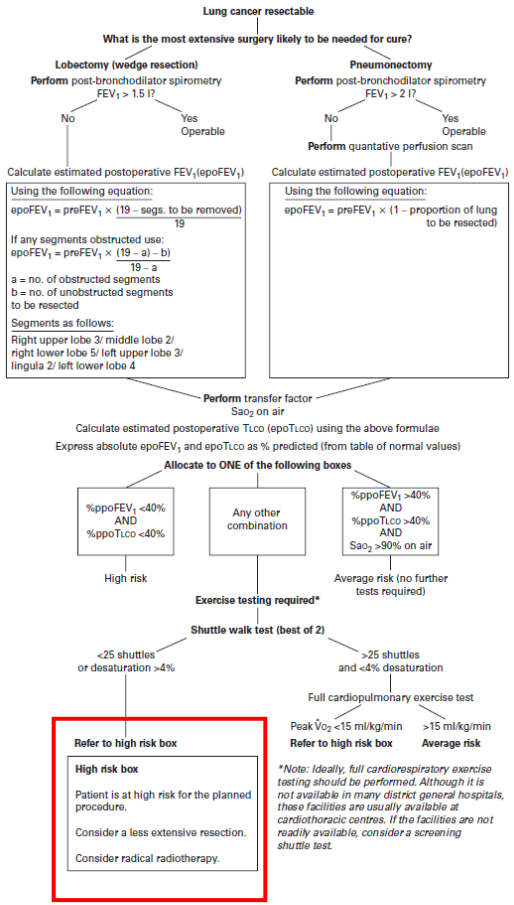
What is your risk threshold for in-hospital death?

< 1%
2%
5%
10%
20%
30%

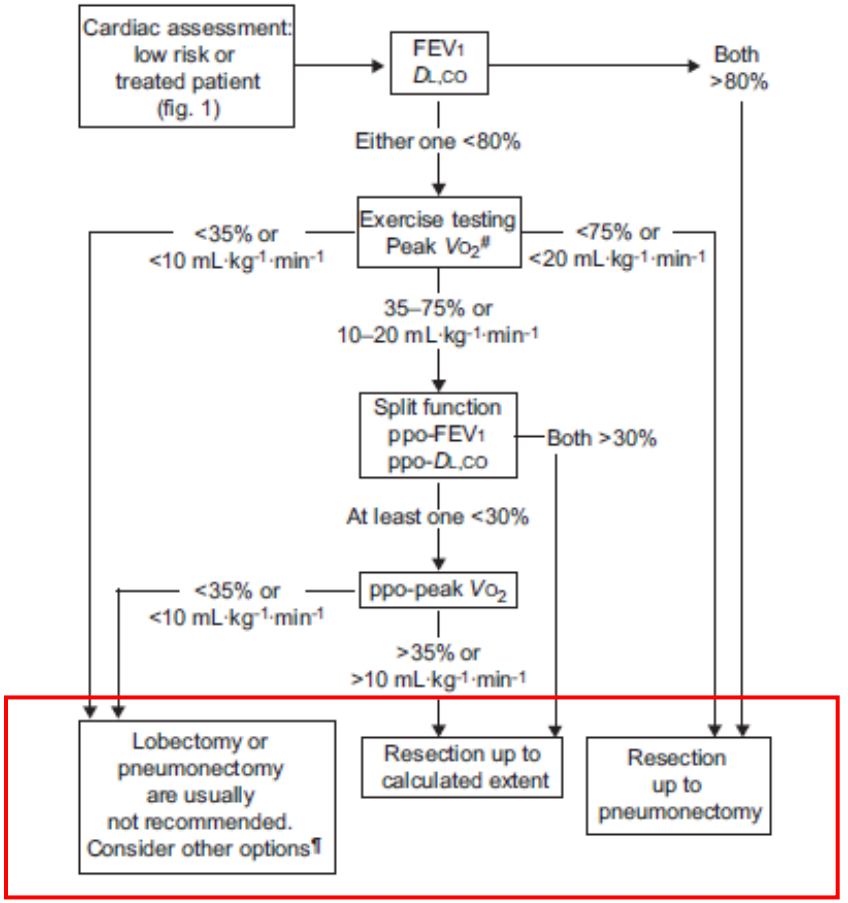
Learning points

- It is straightforward to obtain a estimate of risk of death from surgery
- Ultimately, the absolute number is unimportant
- Different people attach different interpretation to risk
  - What is high for some will be low for others
- It is impossible for “experts” to define that is a high or unacceptable risk
  - Interpretation of risk is personal

What is the risk of shortness of breath?



BTS 2001



ERS/ESTS 2009

Imperial College London

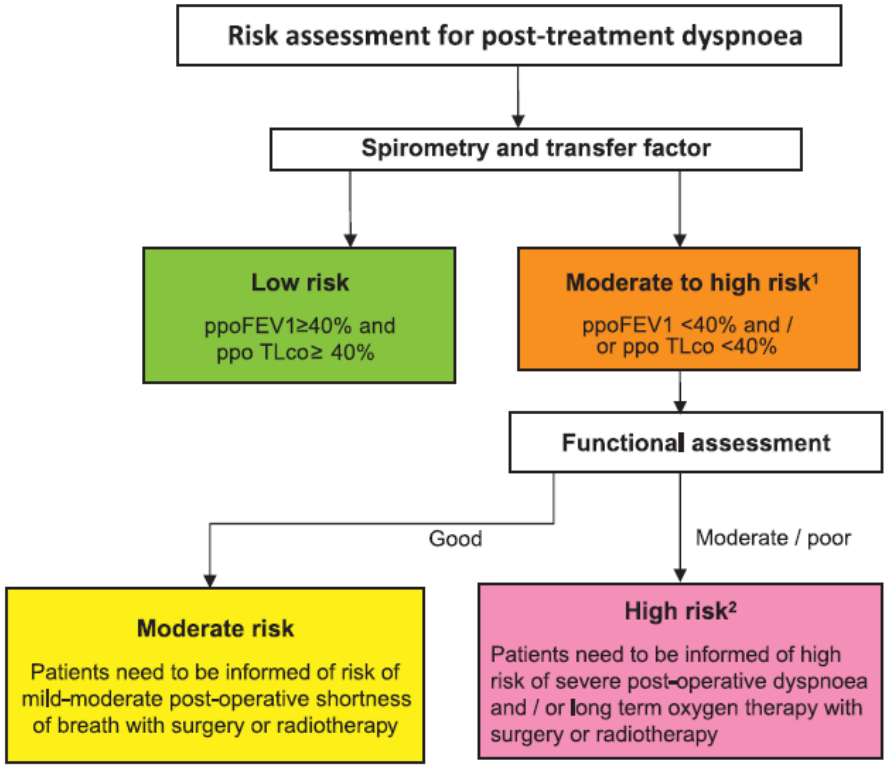
Royal Brompton & Harefield NHS
NHS Foundation Trust

What is your risk threshold for post-op shortness of breath?

a) No shortness of breath?
b) Shortness of breath on severe exertion?
c) Shortness of breath on moderate exertion?
d) Shortness of breath on activities of daily living?
e) Shortness of breath at rest / home oxygen?

Guidelines on the radical management of patients with lung cancer

Eric Lim,[1] David Baldwin,[2] Michael Beckles,[3] John Duffy,[2] James Entwisle,[4] Corinne Faivre-Finn,[5] Keith Kerr,[6] Alistair Macfie,[7] Jim McGuigan,[8] Simon Padley,[9] Sanjay Popat,[10] Nicholas Screaton,[11] Michael Snee,[12] David Waller,[13] Chris Warburton,[14] Thida Win,[15] British Thoracic Society and the Society for Cardiothoracic Surgery in Great Britain and Ireland



Thorax 2010;**65**(Suppl III):iii1—iii27.

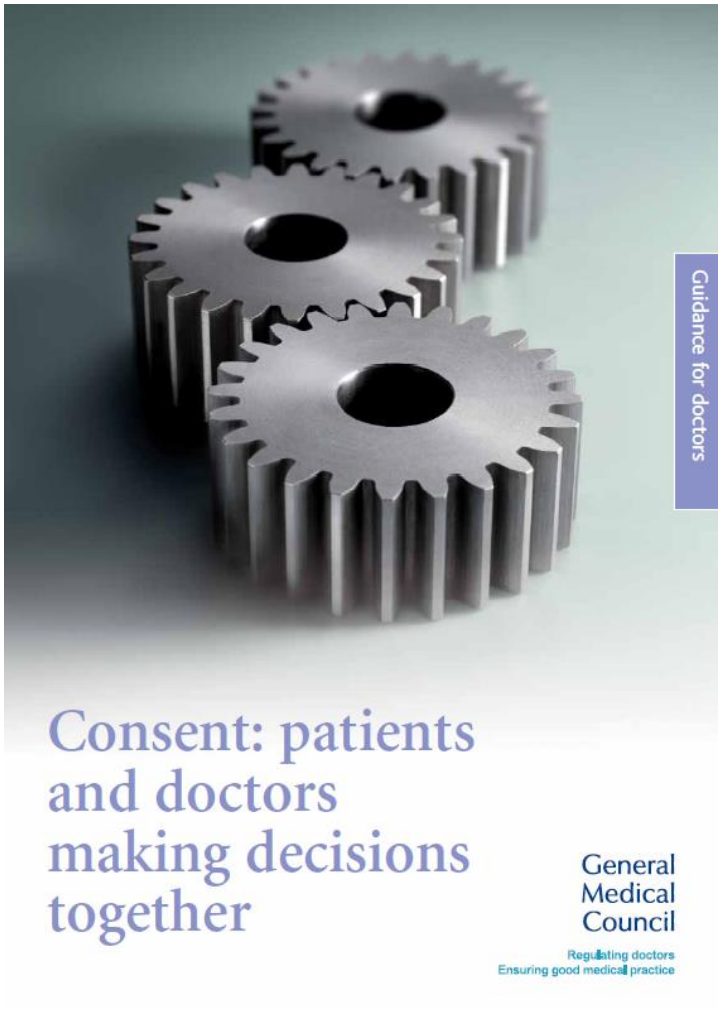
Imperial College London

Royal Brompton & Harefield NHS
NHS Foundation Trust

Learning points

- Post-operative shortness of breath can only be a rough estimate as there is no evidence to support what is an acceptable threshold in this setting
- No study will ever be conducted to determine the unacceptable threshold because it is unethical
- Ultimately it is not the risk of shortness of breath but the degree of adaptation considered acceptable by the patient that is pivotal in the decision to undergo surgery
- In other words it is a measure of “happiness”

Patient and clinician joint decision making



Clear, accurate information about the risks of any proposed investigation or treatment, presented in a way patients can understand, can help them make informed decisions. The amount of information about risk that you should share with patients will depend on the individual patient and what they want or need to know. Your discussions with patients should focus on their individual situation and the risk to them.

You should do your best to understand the patient's views and preferences about any proposed investigation or treatment, and the adverse outcomes they are most concerned about. You must not make assumptions about a patient's understanding of risk or the importance they attach to different outcomes. You should discuss these issues with your patient.[8]

The patient weighs up the potential benefits, risks and burdens of the various options as well as any non-clinical issues that are relevant to them. The patient decides whether to accept any of the options and, if so, which one. They also have the right to accept or refuse an option for a reason that may seem irrational to the doctor, or for no reason at all.[2]

What if patients cannot decide?

- Decide with them (95%)
  - Understand their individual fears and preferences
  - Weigh up and give a balanced opinion
- Decide for them (5%)
  - Insufficient mental capacity
  - Refuse to participate / make a decision

Summary and conclusions

Conclusions

- Preoperative risk models are an important starting point to initiate conversations with patients when deciding care
- Ultimately predicted risk or high risk definition is unimportant
  - Patients decide on individual perception of risk
- Clinicians need to give balanced opinion on treatment options
  - Need to be prepared to explore individual fears and lifestyle preferences to help make decisions with patients

Thank you!