10th European Congress Perspectives in Lung Cancer
Brussels March 6-7, 2009

Management of pleural effusion

Prof. Dr. Kristiaan NACKAERTS

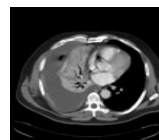
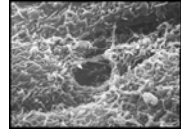
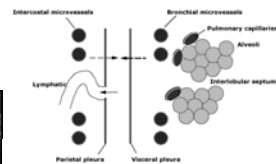
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• **Speaker Information and Disclosure**

- The commercial interests in which I have financial relationships do not produce health care-related products or services relevant to the content I am planning, developing, or presenting for this activity. I will identify these relationships:

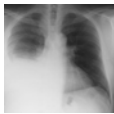
- *Novartis Oncology* - Honorarium/Advisory Board
- *Pfizer* - Educational Grant/Smoking cessation study



Broadus VC, Sahn SA, Hellingworth H.
Mechanisms of pleural fluid accumulation in disease
UpToDate® 2009 www.uptodate.com

Pleural effusion in malignancy

- Malignant effusion (pleuritis)
 - 22% of all pleural effusions
 - 50% of pleural effusions in malignancies are 'benign'
- "Paramalignant" effusions



- » Lymphatic obstruction
- » Airway obstruction
- » Pneumonia/atelectasis
- » Trapped lung
- » Chylothorax
- » Superior vena cava syndrome (SVCS)
- » Decreased oncotic pressure
- » Adverse effects of therapy

HE Davies et al. Thorax 2008;63:572-4
 Kulkarni G, Mariani AJ. Respiratory Med 2008;102:939-48
 Heflner JE, Klein JS. Mayo Clin Proc 2008;83:235-50

Pleural effusion in malignancy(2)

Tumour	n	%
Lung	641	36
Breast	449	25
Lymphoma	187	10
Ovary	88	5
Stomach	42	2
Unknown primary	129	7
Other causes	247	14

Sahn SA. Eur Respir J 1997;10:1907-13

Pleural effusion in lung cancer(1)

- Frequency of MPE in lung cancer
 - NSCLC/SCLC 25% of pts
 - Mesothelioma >90% of pts
- IASLC Staging: cT4 (wet T4) or M1a*
 - * Proposal for revision of the M descriptors in 7th Ed of TNM Classification
 - Lower median survival for wet cT4 vs other cT4
 - 8 m vs 13 m (p < 0.0001)
 - Lower 5 YSR
 - 2% vs 15%

HE Davies et al. Thorax 2008;63:572-4
 Postmus PE et al. J Thor Oncol 2007;2:686-93

Pleural effusion in lung cancer(2)

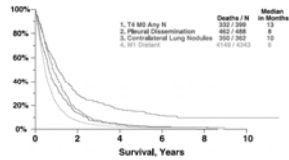


FIGURE 1. Overall survival comparisons for proposed clinical stage T4 (any N) N0 versus proposed categories M1a (pleural dissemination) and M1a (contralateral lung nodules) versus M1b (distant metastases). The T4 group includes cases with same-side nodules, in accordance with the proposal to move these cases to the T4. The T4 group excludes the cases with same-lobe nodules, in accordance with the proposal to move this group to the T3.

Postmus PE et al. J Thor Oncol 2007;2:686-93

Management of pleural effusion

- Palliative treatment
- Removal of pleural effusion
- Pleurodesis
- Drainage
- Stop pleural effusion formation(?)

Kvale PA et al. Palliative Care in lung cancer. ACCP evidence-based clinical practice guidelines Chest 2007;132:368S-403S

Thoracentesis

- Symptomatic relief
- Alternative causes for dyspnea?
- Repeated thoracentesis
 - Pts who reaccumulate pleural fluid slowly
 - Pts who have cancers responding to Rx
 - Pts with limited survival (<1-3 m)
 - Pts who can't tolerate pleurodesis

Kvale PA et al. Chest 2007;132:368S-403S
Hoffner JE, Klein JS. Mayo Clin Proc 2008;83:235-50

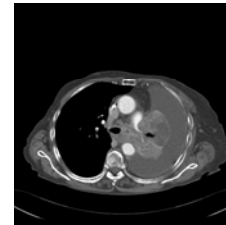
Pleurodesis

TABLE 3. Questions to Guide Selection of Patients for Pleurodesis

- Is the underlying tumor and resulting malignant pleural effusion responsive to chemotherapy or radiotherapy?
- Are the patient's respiratory symptoms caused by the effusion?
 - Does the patient's dyspnea improve after therapeutic thoracentesis?
 - Do alternative causes of dyspnea exist that will not respond to pleurodesis?
- Does the patient's life expectancy warrant pleurodesis (eg, is it longer than 2-3 months)?
- Will pleurodesis resolve the effusion and sufficiently improve the patient's symptoms?
 - Does the lung expand to the chest wall after therapeutic thoracentesis?
 - Do imaging studies suggest multiloculated effusions and thick visceral pleural membranes suggestive of a trapped lung?
- Will the amount of intrapleural tumor prevent an effective pleurodesis?
 - Do imaging studies detect large tumor masses along pleural surfaces?

Heffner JE, Klein JS. Mayo Clin Proc 2008;83:235-50

Pleurodesis



"Trapped" lung

Pleurodesis

- Selection of pts
- pH of pleural fluid > 7.30 ?
 - Poor predictive performance of pH<7.30
- Pleural manometry?
 - No predictive performance proven

Antony VB et al. Eur Respir J 2001;18:402-19
Heffner JE et al. Chest 2000;117:79-86

Pleurodesis

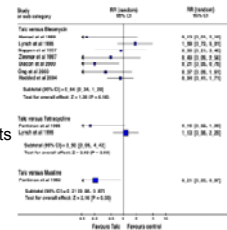
- Sclerosants
 - Talc [$Mg_3(Si_2O_5)(OH)_2$] most effective
 - Agent of choice
 - Safety?
 - Different talc preparations
 - Lung infiltrates/hypoxemia(30%)/resp. failure(4-8%)/ARDS
 - Best = with smallest (<10 μ) talc particles removed (graded talc)

Maskell NA et al. AJRCCM 2004;170:377-82
 Anthony VB et al. Eur Respir J 2001;16:402-19
 Dressler CM et al. Chest 2005;127:909-15

Janssen JP et al. Lancet 2007;369:1535-39
 Davies HE et al. Thorax 2008;63:572-4

Pleurodesis

- Sclerosants
- Other?
 - Tetracyclins
 - Bleomycin
 - Other antineoplastic agents
 - Corynebacterium parvum
- "...Trends favor talc..."



Tan C et al. Eur J Cardiothor Surg 2006;29:829-38

Pleurodesis

- Sclerosants
- Other?
 - TGF β (animals)
(Leo YC et al. Respirology 2002; Light RW et al. AJRCCM 2000)
 - OK-432 (Str.pyogenes)
(Kashi K et al. Eur Respir J 2004; Ishida A et al. Respirology 2006; Kasahara K et al. Anticancer Res 2006)
 - S. Aureus superantigen
(Ren S et al. Chest 2004)

Pleurodesis

- Chest tube/catheter + talc slurry
- Thoracoscopy + talc insufflation

– Shaw P et al, Cochrane Database Syst Rev 2004 TI
– Dressler CM et al, Chest 2005 =
– Crnjac A et al, Eur J CT Surg 2004 TI=cath



?



Pleurodesis

Talc poudrage

- N=242
- 78% 30d outcome
- 9 deaths
- 8% respir failure (6†)

Talc slurry (tube)

- N=240
- 71% 30d outcome
- 7 deaths
- 4% respir failure (5†)

“Both methods of talc delivery are similar in efficacy”

Dressler CM et al, Chest 2005;127:909-15

Pleurodesis

- chest tube/thoracoscopy

“In lung cancer pts with symptomatic pleural effusions that recur after thoracentesis, chest tube drainage and pleurodesis are recommended. Grade of recommendation: 1B”

Kivale PA et al.
Palliative Care in lung cancer. ACCP evidence-based clinical practice guidelines
Chest 2007;132:368S-403S

Pleural Catheters

- Long-term indwelling pleural catheters, or subcutaneously tunnelled indwelling PC
 - Pts who have failed pleurodesis
 - Lung incapable of re-expanding
 - 1st line use??
 - Outpatient care
 - Patient controlled fluid drainage
 - Spontaneous pleurodesis (40-58% of pts)

Davies HE, Gary Lee YC, Davies RJO. Thorax 2008;63:572-4
Heffner JE, Klein JS. Mayo Clin Proc 2008;83:235-50

Pleural Catheters

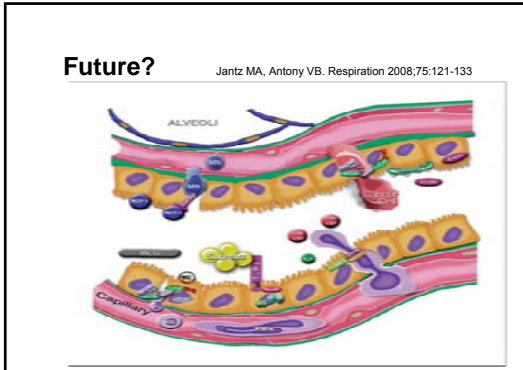
- Long-term indwelling pleural catheters (IPC)
 - Additional prospective data needed !
 - IPC vs doxycycline (tube) pleurodesis:
 - Equal symptomatic improvement
 - 13% vs 21% late recurrence of pleural effusion
 - British Lung Foundation trial
 - IPC vs standard care (talc pleurodesis)

Putnam JB et al. Cancer 1999;86:1992-9
Davies HE, Gary Lee YC, Davies RJO. Thorax 2008;63:572-4
Heffner JE, Klein JS. Mayo Clin Proc 2008;83:235-50
Tremblay A et al. Chest 2006; 129:362-8

Pleuroperitoneal shunt

- Pts who don't benefit from pleurodesis
- No randomised trials
- Effective palliation in 73-100% of pts
- Shunt complications

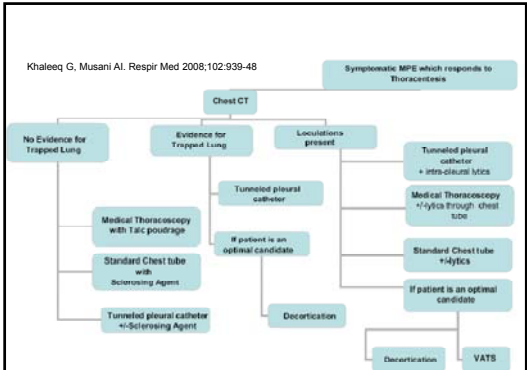
Tan C et al. Eur J CT Surg 2006;29:829-38
Heffner JE, Klein JS. Mayo Clin Proc 2008;83:235-50
Kvale PA et al. Chest 2007;132:368S-403S



Future?

- Multiple cytokines: VEGF, bFGF, TGFβ, PDGF...
- Effect of bisphosphonates?
 - Murine MPE model (Lewis LC cells)
 - Zoledronate sc
 - Reduction in pleural vascular permeability
 - Reduction in pleural fluid accumulation

Mutsaers SE et al. Cancer Treat Res 2007;134:1-19
 Gary Lee YC. AJRCCM 2008;178:3-5
 Stathopoulos GT et al. AJRCCM 2008;178:50-59



Management of pleural effusion (PE)

- Removal of pleural effusion
- Talc pleurodesis
- Future?
 - Pleural catheters
 - New sclerosing agents
 - New agents to stop PE formation

