NICE National Institute for Health and Care Excellence

Appendix A: Summary of evidence from surveillance (exceptional review)

2019 surveillance of Lung cancer: diagnosis and management (2019) NICE guideline NG122

Summary of evidence from surveillance

As part of this exceptional review, feedback from topic experts was considered alongside the evidence to reach a view on the need to update guideline recommendations in a specific area.

Only recommendations relevant to the exceptional review are listed below concerning other palliative treatments for malignant pleural effusion. The full list of recommendations can be found under recommendation 1.5 palliative interventions and supportive care of the guideline.

1.5 Palliative interventions and supportive and palliative care

Other palliative treatments

1.5.7 Pleural aspiration or drainage should be performed in an attempt to relieve the symptoms of a pleural effusion. **[2005]**

1.5.8 Patients who benefit symptomatically from aspiration or drainage of fluid should be offered talc pleurodesis for longer-term benefit. **[2005]**

Surveillance decision

These recommendations should not be updated.

2019 surveillance summary

Studies identified from a focused search are summarised in the tables below from the information presented in their abstracts. To identify all studies of relevance to this review, the evidence search was expanded to include patients with malignant pleural effusion irrespective of cancer site.

Table 1: Effectiveness of indwelling pleural catheter (IPC) in palliation of malignant pleural effusion

A small body of evidence (1 Cochrane review, 2 systematic reviews and 5 RCTs) was identified concerning the effectiveness of IPC in managing malignant pleural effusion. Several studies comparing IPC and chemical/talc pleurodesis found no significant differences for certain outcomes, however noted that IPC may be associated with a shorter length of hospital stay and fewer repeat pleural interventions. Additionally, 1 RCT indicated that talc administered through an IPC resulted in a significantly higher chance of successful pleurodesis than IPC alone.

Study	Patient Characteristics	Comparison	Key Findings/Effect Size	Secondary Outcomes/Comments
Cochrane review included: 1) Pair-wise meta-analyses and 2) network meta-analysis (NMA) (1) 62 RCTs n=3,428	Adults with symptomatic malignant pleural effusion.	1) Talc slurry pleurodesis 2) NMA included 16 agents (including IPC)	Meta-analysis with 2 RCTs [4] [5] showed IPC patients had a higher rate of pleurodesis failure than those receiving talc slurry (OR 3.35; 95% CI 1.64 to 6.83). NMA for pleurodesis efficacy found that talc poudrage resulted in lowest rate of pleurodesis failure compared with 8 other agents, including IPC.	Both RCTs comparing IPC and talc slurry noted improved breathlessness with IPC.
Systematic review and meta-analysis (2) 5 RCTs (n=545)	Adult patients with symptomatic malignant pleural effusion.	Chemical pleurodesis	Studies reported no differences in dyspnoea or survival between both interventions.	Length of hospitalisation and repeat pleural interventions were less frequent in IPC patients compared with pleurodesis (RR 0.32; 95% CI 0.18 to 0.55). No differences in adverse events between groups, except for risk of cellulitis which was

				higher in IPC group (RR 5.83; 95% CI 1.56 to 21.8).
Systematic review and meta-analysis (3) 3 studies (n=307)	Patients with malignant pleural effusion.	Chemical pleurodesis	No significant differences were noted in the success rates between both groups (RR 0.8; 95% CI 0.53 to 1.19; p=0.27). No significant differences were noted in the complication rates between both groups (RR 2; 95% CI 0.91 to 4.4; p=0.09).	
Unblinded RCT (4) n=106 randomised	Patients with malignant pleural effusion, with no previous pleurodesis.	Chest tube and talc slurry pleurodesis	In the IPC group the mean VAS score* was 24.7 mm (95% CI 19.3 to 30.1) and 24.4 mm (95% CI 19.4 to 29.4) in the talc slurry group, with a non-significant difference of 0.16 mm (95% CI; -6.82 to 7.15, p= 0.96). At 6 months, there was a significant difference in VAS score between groups of -14.0 mm (95% CI, -25.2 to -2.8, p=0.01) in favour of IPC.	Duration of initial hospitalisation and repeat pleural interventions were significantly less in the IPC group compared with talc group. No significant difference in quality of life between groups, whilst adverse events were significantly higher in the IPC group.
Multi-institutional, prospective RCT (5) n=57 randomised	Patients of similar age, active chemotherapy status and histologic diagnosis with unilateral malignant pleural effusions.	Bedside talc pleurodesis	Combined success outcome (consistent/reliable drainage/pleurodesis, lung expansion and 30-day survival) was non-significantly higher in the tunneled catheter drainage** (TCD) group than talc pleurodesis group (62% versus 46% respectively, OR 5.0, p= 0.064).	TCD patients had significantly improved survival with effusion control at 30 days compared with talc pleurodesis patients.
Open-label RCT (6) n=146	Patients with symptomatic malignant pleural effusion with no previous pleurodesis or use of IPC.	Talc pleurodesis	Duration of hospitalisation from intervention to death or to 12 months was significantly less in the IPC arm (median 10.0 versus 12.0 days for talc, p=0.03).	No significant differences in improvements in breathlessness or quality of life between groups. Number of adverse events were greater in the IPC group and fewer IPC patients required repeat pleural drainage.

Multicentre RCT (7) n=94 randomised	Patients with recurrent malignant pleural effusion.	Talc pleurodesis	No significant between-group differences in improvement of dyspnoea*** (median 3 for talc pleurodesis and 1 for IPC at rest, p=0.16 and median 3 for talc pleurodesis and 1 for IPC during exercise, p=0.72).	Number of repeat interventions were significantly less in IPC group, whilst there was no difference in number of adverse events between groups.
Placebo-controlled RCT, single-blinded (8) n=154 randomised	Patients with malignant pleural effusion.	IPC and talc slurry	43% of patients in the IPC/talc group had successful pleurodesis at day 35 after randomisation, compared with 23% in the IPC/placebo group (HR 2.20; 95% CI 1.23 to 3.92; p=0.008).	No significant differences in effusion size and complexity, number of inpatient hospital days, mortality or adverse events between groups.

* Dyspnoea measured by 100 mm line visual analogue scale (VAS) over 42 days. (0mm = no dyspnoea, 100 mm = maximum dyspnoea; 10 mm = minimum clinically significant difference).

** Note that tunnelled catheter drainage refers to IPC.

*** Assessed by improvement in Modified Borg Scale score from baseline to 6 weeks after either treatment.

Table 2: Economic analyses of indwelling pleural catheter (IPC) versus chest tube and talc slurry pleurodesis in patients with symptomatic malignant pleural effusion using data from the Second Therapeutic Intervention in Malignant Effusion (TIME2) RCT[4]

Evidence was identified (1 cost-effectiveness analysis and 1 cost-analysis from a healthcare perspective) that suggested no significant differences in costs and/or quality-adjusted life years (QALYs) gained between IPCs and talc pleurodesis for malignant pleural effusion. There was some indication that IPC may be less costly and more cost-effective if patient survival is less than 14 weeks.

Study	Source of costs	Effectiveness measure	Key Findings	Comments
Cost-effectiveness analysis (9) n=106 randomised	Healthcare utilisation and costs were captured. Sources not reported in abstract.	QALY* - calculated using patient survival and utility weights obtained from EQ-5D*. Quality of life data used in the study was unpublished.	No significant differences in utility scores, cost and QALYs gained between both arms. Mean ICER (over 1-year study period) for IPC compared with talc was found to be $10,870 US dollars per QALY gained. IPC was found to be less costly compared with talc pleurodesis with a probability of >95% of being cost-effective if survival was less than 14 weeks.	IPC was found to be more expensive if catheter drainage required 2 hours weekly nursing time.
Cost-analysis (10) n=106 randomised	NHS reference costs and University of Kent's Unit Costs of Health and Social Care 2011. Intervention supply costs were obtained from the manufacturer. Costs were inflated to 2013 and converted from UK pounds to US dollars.	-	Mean cost for treating with IPC was $4,993 (SD $5,529) compared to $4,581 (SD $4,359) for talc. Incremental mean cost difference was $401 (95% CI -$1,387 to $2,261). IPC was significantly less costly compared with talc in individuals with survival less than 14 weeks.	No significant difference between groups in terms of cost of initial intervention or adverse events.

* QALY refers to Quality-adjusted life year

** EQ-5D refers to EuroQol Group five-dimensional questionnaire

Intelligence gathering

Initial intelligence noted that the updated NICE guideline on lung cancer would be published on 28 March 2019. During consultation on the draft guideline, a stakeholder commented that recommendation 1.5.8 should reflect the use of indwelling pleural catheters (IPCs). As this area was out of scope of the 2019 update, any impact was examined in this exceptional review.

Topic expert feedback indicated that IPC is widely used in the management of malignant pleural effusions. Experts commented that the clinical implications of recommending IPC in this small population would not be extensive, but the benefit for patients could be substantial. Several experts suggested that significant work in this area influencing practice has been published, however the cost-effectiveness of IPC is uncertain.

Impact statement

NICE guideline NG122 currently recommends pleural aspiration/drainage for relieving symptoms of malignant pleural effusion, however there are no specific recommendations concerning the use of indwelling pleural catheter (IPC). Chemical pleurodesis is currently recommended as a treatment option for pleural effusion using talc as the agent, for longer-term benefit.

Several studies comparing IPC and chemical/talc pleurodesis found no significant differences in outcomes including success rate and improvement of dyspnoea. One identified Cochrane review indicated that whilst IPC patients had improved breathlessness, pleurodesis failure rate was higher in IPC compared with talc slurry pleurodesis patients. There was mixed evidence concerning adverse event rate with IPC use, however several studies noted that IPC may be associated with a shorter length of hospital stay and fewer repeat pleural interventions. Two studies indicated that IPC may be less costly and more cost-effective in individuals with limited survival, however further evidence synthesis is needed to understand the cost implications associated with IPC use.

Whilst we acknowledge that IPC is being used in clinical practice, at present there is insufficient consistent evidence to impact the recommendations on pleural effusion. We will keep abreast of research in this area and assess any implications for NICE guideline NG122.

New evidence is unlikely to change guideline recommendations.

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