NICE guidance

Cryotherapy for the treatment of liver metastases

Interventional procedures guidance
Published: 15 December 2010

www.nice.org.uk/guidance/ipg369

1 Guidance

1.1 Current evidence on the safety of cryotherapy for the treatment of liver metastases appears adequate in the context of treating patients whose condition has such a poor prognosis, but the evidence on efficacy is inadequate in quality. Therefore cryotherapy for the treatment of liver metastases should only be used with special arrangements for clinical governance, consent and audit or research.

1.2 Clinicians wishing to undertake cryotherapy for the treatment of liver metastases should take the following actions.

- Inform the clinical governance leads in their Trusts.
- Ensure that patients and their carers understand that other ablative treatments are available and provide them with clear written information. In addition, the use of NICE's information for patients ('Understanding NICE guidance') is recommended.

- Audit and review clinical outcomes of all patients having cryotherapy for liver metastases (see section 3.1).

1.3 Patient selection and treatment should be carried out by a hepatobiliary multidisciplinary team with expertise in the use of ablative techniques.

2 The procedure

2.1 Indications and current treatments

2.1.1 Liver metastases are commonly caused by colorectal cancer or other primary malignancies, such as lung and gastric cancer.

2.1.2 For a minority of patients, surgical resection of liver metastases with curative intent may be possible. For most patients however, treatment is palliative and options include systemic chemotherapy, external beam radiotherapy, other thermal ablation techniques, and selective internal radiation therapy. Multiple treatment modalities may be used for individual patients.

2.2 Outline of the procedure

2.2.1 Thermal ablation procedures including cryotherapy may be used as the primary treatment for liver metastases in patients who are not considered suitable for surgery, or to treat post-resection recurrence. They may also be used as an adjunct to hepatic resection. Cryotherapy can be delivered as part of an open resection procedure (requiring general anaesthesia and intraoperative ultrasound), or percutaneously (under local or general anaesthesia, with ultrasound, computed tomography [CT] or magnetic resonance imaging guidance).

2.2.2 Cryotherapy probes (single or multiple, depending on the size of the tumour) deliver coolant at subzero temperatures directly to the tumour in freeze-thaw cycles with the aim of destroying tumour cells.

2.2.3 The maximum recommended hepatic tumour size for cryotherapy is 4 cm. Cryotherapy for larger tumours requires multiple probes and is

associated with increased morbidity.

2.2.4 Various devices can be used for this procedure.

> Sections 2.3 and 2.4 describe efficacy and safety outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the overview.

2.3 Efficacy

2.3.1 A randomised controlled trial (RCT) of 123 patients treated by cryotherapy and chemotherapy or by surgical resection and chemotherapy reported disease-free survival in 14% (9/63) and 5% (3/60) of patients respectively at 10-year follow-up (significance not stated).

2.3.2 A non-randomised controlled trial of 415 patients treated by surgical resection and cryotherapy (for remnant lesions) or resection alone reported median survival of 29 and 34 months respectively ($p = 0.206$).

2.3.3 A case series of 326 patients reported median overall survival of 29 months after cryotherapy of colorectal liver metastases, with tumour recurrence in 42% (136/326) of patients at a median of 32 months. In a subset of 280 patients who had CT imaging at baseline and during follow-up, complete response was reported in 15% (41/280), partial response in 41% (115/280), stable disease in 24% (68/280), and progressive disease in 20% (56/280) (follow-up not stated).

2.3.4 The Specialist Advisers listed key efficacy outcomes as tumour destruction with small margins of additional tissue destruction, and survival.

2.4 Safety

2.4.1 A non-randomised controlled study of 223 patients reported no significant difference in perioperative mortality between the cryotherapy

group (2% [1/55]) and the surgical resection group (5% [8/168]) (p = 0.30). However overall perioperative morbidity was significantly lower in the cryotherapy group (11% [6/55] than in the resection group (26% [44/168]) (p = 0.01).

2.4.2 A case series of 326 patients reported mortality in 2% (7/326) of patients (follow-up period and details of causes were not reported, but 1 patient died from 'cryoshock' syndrome and 1 from liver failure).

2.4.3 A case report described death of a patient from hepatic failure related to portal vein thrombosis and intra-hepatic MRSA sepsis, 2 months after a second cryotherapy course via an open approach.

2.4.4 Infections directly related to cryotherapy were reported after 8% (12/158) of procedures in the case series of 150 patients (most occurred within 3 weeks of treatment). Fever over 38°C was reported in 33% (108/326) of patients in the case series of 326 patients (timing of events not stated).

2.4.5 Haemorrhage was reported in 4% (2/55) and 1% (2/168) of patients treated with cryotherapy and surgical resection respectively in the non randomised controlled trial of 223 patients (timing of event not stated).

2.4.6 The Specialist Advisers listed anecdotal adverse events as damage to bile ducts and structures outside the liver. The Specialist Advisers also cited reports of major haemorrhage, the rare but fatal complication of cryoshock syndrome, and a high local recurrence rate; they stated that cryotherapy is therefore no longer widely used.

2.5 Other comments

2.5.1 The Committee noted possible differences in the safety of this procedure when used intraoperatively, compared with the percutaneous approach that uses narrower probes. Evidence on the percutaneous approach is limited in quantity.

3 Further information

3.1 This guidance requires that clinicians undertaking the procedure make special arrangements for audit. NICE has identified relevant audit criteria and has developed an audit tool (which is for use at local discretion).

3.2 For related NICE guidance see our website.

Information for patients

NICE has produced information on this procedure for patients and carers ('Understanding NICE guidance'). It explains the nature of the procedure and the guidance issued by NICE, and has been written with patient consent in mind.

4 About this guidance

NICE interventional procedure guidance makes recommendations on the safety and efficacy of the procedure. It does not cover whether or not the NHS should fund a procedure. Funding decisions are taken by local NHS bodies after considering the clinical effectiveness of the procedure and whether it represents value for money for the NHS. It is for healthcare professionals and people using the NHS in England, Wales, Scotland and Northern Ireland, and is endorsed by Healthcare Improvement Scotland for implementation by NHSScotland.

This guidance was developed using the NICE interventional procedure guidance process.

It has been incorporated into the NICE pathway on colorectal cancer, along with other related guidance and products.

We have produced a summary of this guidance for patients and carers. Tools to help you put the guidance into practice and information about the evidence it is based on are also available.

Changes since publication

2 January 2012: minor maintenance.

Your responsibility

This guidance represents the views of NICE and was arrived at after careful consideration of the available evidence. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. This guidance does not, however, override the individual responsibility of healthcare professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way which would be inconsistent with compliance with those duties.

Contact NICE

National Institute for Health and Clinical Excellence
Level 1A, City Tower, Piccadilly Plaza, Manchester M1 4BT

www.nice.org.uk
nice@nice.org.uk
0845 033 7780

Endorsing organisation

This guidance has been endorsed by Healthcare Improvement Scotland.

Accreditation