NICE guidance

Irreversible electroporation for treating liver metastases

Interventional procedures guidance
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Your responsibility

This guidance represents the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take this guidance fully into account, and specifically any special arrangements relating to the introduction of new interventional procedures. The guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with

those duties. Providers should ensure that governance structures are in place to review, authorise and monitor the introduction of new devices and procedures.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

1 Guidance

1.1 Current evidence on the safety and efficacy of irreversible electroporation for treating liver metastases is inadequate in quantity and quality. Therefore, this procedure should only be used in the context of research. In particular, studies should report the effect of the procedure on local tumour control and patient survival.

2 The procedure

2.1 Indications and current treatments

2.1.1 Liver metastases are most commonly caused by colorectal cancer but may also result from other malignancies, such as lung and gastric cancer.

2.1.2 Treatment of liver metastases depends on their extent and location. Treatment options include surgical resection, thermal ablation, chemotherapy, different types of arterial embolisation, external beam radiotherapy and selective internal radiation therapy. Irreversible electroporation is a non-thermal cell-destruction technique, which is claimed to allow targeted destruction of cancerous cells with less damage to surrounding supporting connective tissue (such as nearby blood vessels and nerves) than other types of treatment.

2.2 Outline of the procedure

2.2.1 The aim of irreversible electroporation is to destroy cancerous cells by subjecting

them to a series of short electrical pulses using high-voltage direct current. This creates multiple holes in the cell membrane, irreversibly damaging the cell's homeostasis mechanisms and leading to cell death.

2.2.2 The procedure is performed with the patient under general anaesthesia. A neuromuscular blocking agent is essential to prevent uncontrolled severe muscle contractions caused by the electric current. Bipolar or unipolar electrode needles are introduced percutaneously (or by open surgical or laparoscopic approaches) and guided into place in and adjacent to the target tumour using imaging guidance. A series of very short electrical pulses is delivered over several minutes to ablate the tumour. The electrodes may then be repositioned to extend the zone of electroporation until the entire tumour and an appropriate margin have been ablated. Cardiac synchronisation is used to time delivery of the electrical pulse within the refractory period of the heart cycle, minimising the risk of arrhythmia.

2.3 Efficacy

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.

2.3.1 In a case series of 38 patients (including 69 procedures for tumours in the liver, lung and kidney), a response rate of 50% was reported in 45 procedures to treat liver metastases (number of patients not reported; response rate was not defined; exact timing of assessment unclear). Liver metastases larger than 5 cm in any dimension showed no response in terms of tumour control and all patients with liver metastases had other tumours that progressed.

2.3.2 A case series of 44 patients (including 30 with liver metastases) reported local recurrence-free survival of 95% at 6 months and 60% at 12 months. A case series of 28 patients with hepatic tumours (including 21 patients with colorectal liver metastases) reported local recurrence in 6% (3 out of 54) of tumours and 1 tumour with persistent disease at a median follow-up of 6 months.

2.3.3 The Specialist Advisers listed key efficacy outcomes as survival (including

progression-free survival and overall survival), local tumour control and/or tumour recurrence rate, and preservation of vascular and biliary structures.

2.4 Safety

2.4.1 The case series of 38 patients reported transient cardiac arrhythmia in 6 patients (4 patients had ventricular tachycardia, 1 patient had supraventricular tachycardia and 1 patient had atrial fibrillation). Two of these patients had cardiac synchronisation and 4 did not. All the arrhythmias resolved without treatment except for atrial fibrillation in 1 patient, which was treated by cardioversion.

2.4.2 A case series of 21 patients with primary or metastatic cancer (liver, kidney and lung) reported transient ventricular tachycardia in 25% (7 out of 28) of procedures. In 4 of the 7 procedures, arterial blood pressure was 'markedly decreased' (not defined). A case series of 18 procedures reported ventricular tachycardia associated with a fall in blood pressure in 1 patient (cardiac synchronisation was not used in this patient). A case series of 9 patients reported sustained intraoperative new-onset atrial fibrillation in 1 patient. This was treated medically and the atrial fibrillation resolved before the patient was discharged.

2.4.3 A case series of 45 patients (with different types of tumours) reported pneumothorax in 14% (7 out of 50) of procedures. It was treated with small-calibre thoracostomy tubes in 6 cases; it was not stated whether patients were treated for tumours in the liver. The case series of 38 and 21 patients reported treatment of 12 liver metastases and 17 liver tumours respectively; pneumothorax occurred after 1 of these cases in each series (an incidence of 8% and 6% respectively).

2.4.4 The case series of 28 patients reported 1 patient with postoperative portal vein thrombosis (there was no associated biliary dilatation).

2.4.5 The case series of 44 patients reported 1 patient with neurogenic bladder within 90 days of the procedure; this resolved within 30 days.

2.4.6 The case series of 38 patients reported increases in alanine aminotransferase (ALT) level of between 19 and 1,747 international units per litre 24 hours after 95%

(40 out of 42) of procedures (ALT levels available for 42 of 49 liver tumour ablation procedures). Levels returned to normal or baseline at 1-month follow-up after 98% (39 out of 40) of the procedures. The same case series reported transient increases in bilirubin level, which returned to normal or baseline levels at 1-month follow-up, in 18% (9 out of 49) of liver tumour ablation procedures.

2.4.7 The Specialist Advisers reported an anecdotal adverse event of post-ablation syndrome (flu-like symptoms, tiredness and lethargy lasting for 2 to 3 days). They listed theoretical adverse events as puncture or damage of non-target organs, sepsis, tumour seeding in needle tracks and bleeding.

3 Further information

Sources of evidence

The evidence considered by the Interventional Procedures Advisory Committee is described in the overview.

Information for patients

NICE has produced information for the public on this procedure. It explains the nature of the procedure and the guidance issued by NICE, and has been written with patient consent in mind.

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Endorsing organisation

This guidance has been endorsed by Healthcare Improvement Scotland.