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Review

The role of image-guided therapy in the management of colorectal cancer metastatic disease

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Abstract The European Society for Medical Oncology (ESMO) have stressed that the option for treating oligometastatic disease is a strategy of local ablative therapy, the goal of which is to improve disease control. The spectrum of the local ablative therapy toolbox described by the ESMO includes surgical R0 resection, percutaneous ablation and intra-arterial therapies, the choice of treatment being left to the multidisciplinary team. Interventional therapy involving image-guided treatment offers the possibility of less invasive treatments for colorectal cancer metastases in the liver, lung and bone by preserving from toxicity distant healthy organs or even parts of the diseased organs. Oligometastases can be targeted by image-guided puncture for percutaneous ablation by delivering locally, through inserted probes, heat (radiofrequency, microwaves), extreme cold (cryoablation) or electric pulses (electroporation). Radiofrequency (RFA) is the mainstay of percutaneous ablation and provides local control rates of around 90% when metastases are small (<3 cm), located away from hilum and large vessels, and perfectly visible under imaging guidance. The lung provides a specific environment with excellent visibility of the target tumour, and insulation of the tumour by the healthy lung improves thermal delivery. RFA of colorectal lung metastases provides a 5-year overall survival of 56.0%, with a 91.6% control rate for metastases with a diameter <3 cm. These results are comparable to results of surgical series. Non-resectable, non-ablatable liver metastases can be targeted through their preferential arterial vascularisation with hepatic arterial infusion chemotherapy (HAIC) or selective internal radiation therapy (SIRT) with radioactive microspheres. HAIC with oxaliplatin has demonstrated an impressive response rate when patients

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who have previously failed intravenous oxaliplatin are rechallenged. The response rate in first-line therapy is around 90%, with conversion to surgery in roughly 40% of patients. SIRT has recently demonstrated a benefit for progression-free survival in the liver when used as first-line treatment in combination with systemic therapy.

1. Introduction

Interventional oncology involves the application of image-guided procedures to treat cancerous tumours and related complications. The treatments encompass the goals of cancer cure and palliation, by either interventional technique alone or in concert with medical oncology, surgical oncology and radiation therapy. All interventional oncological treatments aim to deliver a focussed treatment that provides maximal therapeutic effect while also lowering systemic side-effects and same-organ toxicity.

Interventional oncology treatments target tumours either by direct percutaneous tumour puncture or by selective intra-arterial methods that isolate tumour-feeding arteries. Treatments can consequently be categorised as percutaneous ablation therapy or intra-arterial therapy. Percutaneous ablation modalities currently include radiofrequency ablation (RFA), microwave ablation, cryoablation and irreversible electroporation. Intra-arterial therapies for liver metastases encompass hepatic artery infusion chemotherapy (HAIC), trans-arterial chemoembolisation (TACE; which involves the delivery of chemotherapy and embolic material) and selective internal radiation therapy (SIRT; also named radioembolisation) which involves delivery of ^{90}yttrium- or ^{166}holmium-loaded microspheres.

This paper aims to review current therapeutic approaches applied specifically to the treatment of metastatic colorectal cancer. It will not discuss interventional radiology procedures that provide cancer diagnosis (biopsy) and palliative treatment of pain or secondary obstructions in the urinary, biliary and digestive systems. Figs. 1 and 2.

2. Percutaneous thermal ablation

2.1. Principle

In the recent European Society for Medical Oncology (ESMO) clinical practice guidelines for metastatic colorectal cancer, both surgical resection and thermal ablation are classified as 'local ablative treatments' and are acknowledged as part of the treatment algorithm for oligometastatic disease [1]. Obviously systemic therapy remains the cornerstone of the treatment strategy, but patients with single or few liver or lung metastases should benefit from the best local treatment selected from a 'local ablative treatments toolbox' where ablation therapies include widely reported radiofrequency ablation, commonly used microwave or cryoablation, and very centre-specific image-guided brachytherapy or yet experimental irreversible electroporation. All percutaneous tumour ablation techniques hinge on insertion of a needle applicator directly into a target tumour under image guidance. Then complete destruction of tumour cells is achieved by focal administration of extreme heat (+60 °C) in radiofrequency ablation and microwave ablation [2], extreme cold in cryoablation [2,3], radiation in brachytherapy or opening cell pores with high voltage in electroporation.

The following will discuss only RFA, which is the more mature technique for the treatment of colorectal metastases; more recently, other ablation technologies have become available and show preliminary clinical promise in surpassing the limits of RFA by the enlargement and improved homogeneity of the ablation zone, with decreased sensitivity to convective cooling by adjacent blood vessels [4,5].

2.2. Metastatic liver disease

Factors that influence the success of ablation are size, location, and visibility of the target tumour. Evidence suggests that metastases >3 cm are more likely to undergo incomplete ablation, with an incomplete ablation rate of 2.6% for 190 metastases <3 cm versus 21.6% for 37 metastases ≥3 cm [6] and incomplete ablation rates of 9%, 26.5% and 45% for 290 metastases measuring 0–3 cm, 3–5 cm, and >5 cm, respectively [7]. The risk of incomplete ablation increases incrementally by approximately 22% for each additional 5 mm in tumour size greater than 3 cm, and conversely decreases incrementally by approximately 46% for each 5 mm in tumour size below 3 cm [8]. Although thermal ablation can effectively cauterise small blood vessels, blood vessels >3 mm in diameter may cause decay in tissue heating through convection [9–11]. This impact is commonly referred to as the 'heat-sink effect', and can result in 23% incomplete treatment for metastases immediately adjacent to vessels ≥3 mm in diameter versus 3% for metastases located a short distance from such vessels [6]. The effects of the heat-sink effect may be mitigated by