Radiologically guided percutaneous cryotherapy for soft tissue tumours: A promising treatment

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Abstract
Studies of percutaneous cryotherapy in the treatment of benign or malignant soft tissue tumours are rare and mainly involve small populations. Nevertheless, results show cryotherapy’s potential in terms of local control of tumours, analgesic efficacy, reduced intra- and postoperative complications, and reduction in the length of convalescence after the procedure. The objective of this update is to set out the short-term prospects for this technique in the treatment of soft tissue tumours, so that it may be more widely offered in these indications.

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Radiologically controlled percutaneous thermal ablation procedures such as radiofrequency, microwaves and cryotherapy are increasingly used in a variety of indications as alternatives to surgery, particularly in patients where surgery is contraindicated or difficult.

Studies of percutaneous cryotherapy in the treatment of benign or malignant soft tissue tumours, with the exception of organs such as the kidneys \cite{1}, liver and lungs \cite{2}, appear to date to be rare, and mainly involve small populations \cite{3,4}. Their analysis, however,

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has meant that new prospects can be proposed, particularly for tumours of soft tissues, bone [5] or the prostate.

Because the technique is minimally invasive [6], the fact that it does not damage collagenous structures and the ablation zone can be monitored in real time by visualising the ice, cryoablation appears to cause less damage to surrounding tissues than surgery, particularly as regards the skin and nerve structures. In general, postoperative pain is slight and recovery after the procedure is rapid. The risk of complications is reduced, partly owing to easy planning and monitoring using ultrasound (US), computed tomography (CT) or magnetic resonance imaging (MRI). In addition, percutaneous cryoablation can be performed under local or general anaesthesia [7].

The aim of this update is less to provide a reminder of cryotherapy techniques than to present the short-term prospects of this technique in the treatment of soft tissue tumours, so that it may be more widely offered in these indications.

Cryotherapy of secondary locations

Soft tissue cryotherapy was initially proposed by Tuncali et al. [4] for the management of bone and/or soft tissue metastases resistant to the usual analgesic treatment. This study showed antitumoral and analgesic efficacy in a population of 22 patients (27 lesions with a mean long axis of 5.2 cm). In this study, the treatment was performed under general anaesthesia with MRi guidance, with the number of cryoprobes suited to the volume of the lesion (a mean of 1.6). Analysis showed that 89% of the lesions treated were the site of tumour necrosis greater than 75% and that tumour size regressed in 19% of cases, was stable in 43% of cases and increased in 38% of cases. The mean time to local progression was 5.3 months. Tolerance of the treatment was excellent with the complications observed after the procedure all being transient. In all, two cases were reported where the L4 and L5 sensory/motor roots were affected but resolved within a week, there were two cases of damage to the perineal nerve which resolved itself in a few months, and one case of serous vaginal discharge complicated by a gluteal abscess. In terms of analgesia, six patients spoke of complete improvement in pain, 11 of partial improvement and three said there was no improvement. The others were not symptomatic as regards pre- or postoperative pain.

In another study by Beland et al. [8], four patients were treated by percutaneous cryotherapy under general anaesthesia for secondary soft tissue lesions. These had occurred in the pelvic, presacral, and axillary areas and within paravertebral soft tissue. In all cases, the patients reported an improvement in pain after cryoablation. Local tumour control could only be assessed in two patients and showed stability in one and an increase in tumour size after 2.5 months in the other. No complication was found apart from brachial plexopathy considered as admissible at the time of treatment, since the initial lesion was invading the brachial plexus. In our experience (with 10 patients treated under general anaesthesia), similar results were obtained, particularly for painful intercostal locations (Fig. 1).

Desmoid tumours

Desmoid tumours, also known as aggressive fibromatosis, are rare [9]. Although they never present metastases, the treatment of extra-abdominal desmoid tumours is a challenge due to locally invasive extension. The main treatment for desmoid tumours is surgical ablation with wide margins, but local recurrence is common, even after apparently complete surgical ablation, and occurs in a mean of 40% of cases (19–77%). Cryotherapy has consequently been offered as an alternative to surgery (Fig. 2).

The initial study by Kujak et al. [3] reported local control of extra-abdominal desmoid tumours after cryotherapy in five patients who failed to respond to standard treatments (surgery, radiotherapy and chemotherapy). Of the five cases, three were referred for local tumour control and two for palliative care of inoperable tumours. The tumours were located in the neck, shoulders and trunk and their maximum dimension was between 3 and 10 cm. In each case, there was short and long-term follow-up of the size of the tumour and evolution of the pain, the data being compared with the data before cryotherapy. In all three patients referred for local tumour control, the ablatherapy zone completely and optimally covered the tumours, and for two of them, their tumours with long axes of 3 and 4.9 cm and the related pain had completely regressed in the short- (mean of 16 months) and long-term (mean of 46 months). The third patient, whose lesion had a long axis of 6.1 cm, showed a moderate decrease in both tumour size and pain after 6 months. The two patients referred for palliative care obtained partial relief of pain 2 weeks after the procedure; in the long-term (58 months follow-up), although there was a significant reduction in tumour size of the first patient’s initial lesion of 9.1 cm, pain returned at its original level, which was described as moderate; in the second patient, who had received partial treatment of a 10-cm mass, there was an increase in tumour size in the long-term (36-month follow-up) and pain returned at the same moderate level as before cryotherapy. Kujak et al. concluded that cryoablation may be an effective alternative to surgery for the treatment of extra-abdominal desmoid tumours if the ablation zone completely covers the tumour.

In addition to our experience with 15 procedures under general (13 cases) and local (2 cases) anaesthesia that showed similar results to Kujak et al.’s study, we recently reported the possibility of repeated cryotherapy treatment of multiple extra-abdominal desmoid tumours in a single female patient with Gardner’s syndrome [10]. For this patient, efficacy and tolerance were excellent and therefore she had one of the procedures under sedation alone. This observation suggests that cryoablation can be repeated successfully with complete safety when clinically necessary. In addition, as indicated by the absence of progression of untreated abdominal lesions present in this patient, it seems that cryoablation does not promote the disease outside of the ablated tumour site. This point is particularly important because it has been shown that surgical trauma was associated with the growth of untreated tumours and local recurrence [11]. A multicentre trial should begin soon to evaluate these data on a larger population.
Vascular malformations

Despite the very preliminary nature of this type of procedure in this indication, cryoablation may also be effective for relieving symptoms, preventing the growth and/or local recurrence of venous vascular malformations (VM). In particular cryotherapy could be an alternative solution in the event of recurrence after sclerotherapy or in the case of vascular malformations with a mainly solid component [12].

In our experience with four patients, including one recently reported case [13], all the patients, including two recurrences, reported total absence of pain in the short-term without complications after cryotherapy performed under general anaesthesia (Fig. 3). Patients were referred after discussion in a multidisciplinary meeting for local control of symptomatic VM. For all these patients, VM decreased by more than 90% on follow-up images obtained 6 months after the procedure. A single centre prospective trial is currently in progress to validate these preliminary results on a larger scale.

Soft tissue sarcomas

In the absence of a prospective study, the initial management of soft tissue sarcomas (STS) is not at present a matter for cryotherapy. Nevertheless, in our centre, we have successfully performed several procedures in cases referred to us of recurrence inoperable under general anaesthesia (Fig. 4). A recent feasibility study [14] showed that in a population with STS relapse, only 28% of patients (13/48) could be treated in this way if the strict criteria are observed: maximum tumour diameter less or equal to 10 cm, distance of the tumour from the skin greater than 5 mm and from neurovascular structures greater than 3 mm, accessibility, absence of articular invasion and volume of the projected cryoablation
Radiologically guided percutaneous cryotherapy for soft tissue tumours

Figure 2. Ultrasound-guided cryotherapy of a desmoid tumour: a, b: T1-weighted sagittal and axial MRI images after contrast injection showing a 35-mm recurrence (arrows) of a desmoid tumour 2 years after initial treatment in a 46-year-old man. The patient was symptomatic; c: ultrasound-guided insertion of two cryotherapy needles. The bottom image shows the ice forming; d: T1-weighted MRI control after 6 months, with fat saturation and after contrast injection: no tumour remains can be seen. The patient was no longer in pain.
Figure 3. Ultrasound and CT-guided cryotherapy of vascular malformation: a: T2-weighted coronal MRI with fat saturation showing a 35-mm, clearly hyperintense, intramuscular mass. This mass was symptomatic and palpable in a 45-year-old female patient. Histological examination confirmed the diagnosis of venous vascular malformation; b: T1-weighted axial slices showing the hypointense mass (arrow); c: pretreatment axial CT scan with contrast injection showing discrete enhancement; d: axial CT slice after removing the two cryoablation needles; e: T1-weighted axial control MRI 3 months after treatment showing a hypointense ring reflecting post-treatment inflammatory changes; f: T1-weighted axial MRI slice after injection of contrast agent no longer showing enhancement in the treated mass. The patient no longer reported pain 1 year after the procedure.
Radiologically guided percutaneous cryotherapy for soft tissue tumours

Figure 4. CT-guided cryotherapy on a relapsed soft tissue sarcoma: a, b: axial MRI slices with T1 and T2 weighting after injection of contrast agent showing a 15-mm pelvic recurrence (arrows) of a high-grade myxoid sarcoma. The patient had a history of multiple surgery (3 resections) and had already been treated with radiotherapy; c: insertion of a cryotherapy needle with ultrasound guidance; d: appearance of the ablation zone after removing the needle. The axial section shows the ice covering the entire target lesion. The control at 6 months did not find any remains of the tumour.

zone covering the entire volume of the lesion. After univariate analysis and comparison with other patients, locations in the wall of the trunk, in the shoulders and pelvic girdle (P = 0.002), tumours with local aggressiveness (P = 0.016), deep tumours (P = 0.002) or less or equal to 5 cm (P = 0.044), and liposarcoma and myxofibrosarcoma (P = 0.007) subtypes appeared as eligibility criteria for such a treatment.

Conclusion

These results show the potential of radiologically guided cryotherapy as concerns local control of tumours, analgesic efficacy and reduced intra- and postoperative complications. Because it is tolerated extremely well, cryotherapy has the advantage of being able to be performed under local anaesthesia and in an outpatient clinic. In addition, this minimally invasive technique seems better tolerated by nearby structures than radiofrequency or microwave treatment. At the present time, the cost is still a limitation (approximately twice as expensive as radiofrequency) but can be put into perspective when compared with the costs of surgery or convalescence for patients for whom "conventional" treatment is no longer an option. This technique now needs to be validated prospectively and on a larger scale.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.
References


