NICE guidance

High-intensity focused ultrasound for symptomatic breast fibroadenoma

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 Recommendations

1.1 The evidence on high-intensity focused ultrasound for symptomatic breast fibroadenoma raises no major safety concerns. Evidence on its efficacy is inadequate in quantity and quality. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research.

1.2 Clinicians wishing to do high-intensity focused ultrasound for symptomatic breast fibroadenoma should:

- Inform the clinical governance leads in their NHS trusts.
- Ensure that patients understand the uncertainty about the procedure's efficacy and provide them with clear written information. In addition, the use of NICE's information for the public is recommended.
- Audit and review clinical outcomes of all patients having high-intensity focused ultrasound for symptomatic breast fibroadenoma (see section 7.1).

1.3 Patients should be informed about all the alternative treatment options, which could include conservative treatment.

1.4 Further research should include publication of patient-reported outcome measures and studies with long-term follow-up.

2 Indications and current treatments

2.1 Breast fibroadenomas are common benign masses that often develop during puberty, although they can occur in women of any age. The condition is rare in men. Simple fibroadenomas are usually 1 cm to 3 cm in size but giant fibroadenomas can be over 5 cm. They do not usually increase in size and some may disappear overtime. The condition is diagnosed by breast examination, and ultrasound or mammography. A needle core biopsy can be used for histological confirmation. Fibroadenomas are usually painless but can become painful and cause deformity.

2.2 If a fibroadenoma is asymptomatic, it does not need to be treated and no follow-up is necessary. However, any growth or other changes to the fibroadenoma should be reported. When symptomatic, fibroadenomas can be removed surgically or by vacuum-assisted mammotomy, which can be done under general or local anaesthesia.

3 The procedure

3.1 High-intensity focused ultrasound for breast fibroadenomas is a minimally invasive thermoablative technique that can be done at an outpatient clinic under local anaesthesia and sedation. A focusing ultrasound device delivers the treatment and allows for simultaneous imaging of the treatment area. The technology uses sound waves that propagate through the tissues, generating local heat and inducing coagulative necrosis, protein denaturation and cellular destruction. A strong acute inflammatory response follows. Remodelling of the chronic inflammatory response lasts for up to 3 months and involves cellular regeneration, proliferation, migration and removal of debris.

3.2 Tumour size reduction should happen gradually with no need for further intervention.

4 Efficacy

This section describes efficacy 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.

4.1 In a case series of 42 women (51 fibroadenomas) treated by high-intensity focused ultrasound (HIFU), 63% (29 out of 46) of the fibroadenomas had reduced in size by 30% at 2 months, 67% (32 out of 48) had reduced by 50% at 6 months and 87% (40 out of 46) had reduced by 60% at 12 months. In a non-randomised controlled study of 40 women, in which 20 were treated by HIFU and 20 were in a control group, fibroadenoma size was statistically significantly reduced by 17% at 2 weeks (standard deviation [SD] 19%, p=0.021) and by 31% at 3 months (SD 53%, p=0.022) in the HIFU group. In the same study, fibroadenoma size reduction was statistically significantly different in women treated by HIFU (44%, SD 39%, p=0.016) compared with women in the control group (5%, SD 46%, p=0.53) at 6-month follow-up; complete fibroadenoma reduction was reported in 33% (4 out of 20) of women in the HIFU group at 12-month follow-up. In a case series of 10 patients treated by HIFU, fibroadenoma diameter was reduced by 50% in 100% (10 out of 10) of patients at 3-month follow-up. In a case series of 9 patients treated by magnetic resonance-guided HIFU, fibroadenomas size was reduced to 1.3 cm^3 (mean, SD 1.1 cm^3) from a baseline of 1.9 cm^3 (mean, SD 1.5 cm^3) in 50% (6 out of 12) of treatments at 6-month follow-up. In a case series of 20 patients, fibroadenoma size was statistically significantly reduced in patients treated only once by HIFU from 0.78 ml (0.35 ml to 2.24 ml) at baseline to 0.35 ml (0.06 ml to 1.21 ml, p<0.001) at 2-year follow-up, and in patients treated twice from 2.66 ml (0.52 ml to 3.01 ml) to 0.21 ml (0.09 ml to 1.66 ml, p=0.003) at 2-year follow-up.

4.2 In the non-randomised controlled study of 40 women, 10% (2 out of 20) of fibroadenomas treated by HIFU did not change in size at 6-month follow-up.

4.3 In the case series of 9 patients treated by magnetic resonance-guided HIFU, technical failure was reported in 42% (5 out of 12) of fibroadenoma treatments.

4.4 In the case series of 42 women, 61% (31 out of 51) of the fibroadenomas had caused discomfort before the procedure, which had resolved in 100% of the women at 12-month follow-up. In the same study, at baseline, 35% (18 out of 51) of fibroadenomas were associated with pain, which had resolved in 100% of patients at 12-month follow-up. In the non-randomised controlled study of

40 women, complete pain reduction was reported by 75% (6 out of 8) of women treated by HIFU at 6-month follow-up.

4.5 In the case series of 20 patients treated by HIFU, for symptom disappearance, 45% (9 out of 20) of patients were completely satisfied, and satisfaction was high in 50% (10 out of 20) and low in 5% (1 out of 20) of patients. In the same case series, for cosmetic results, 95% (19 out of 20) of patients were completely satisfied and satisfaction was high in 5% (1 out of 20) of patients.

4.6 The specialist advisers listed key efficacy outcomes as reduction in lesion size, relief or resolution of symptoms, cost effectiveness, recurrence of symptoms in the short and long term, and time taken to do the procedure.

5 Safety

This section describes 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.

5.1 Discomfort or burning sensation assessed with a visual analogue scale (VAS, 0=no pain, 10=very severe pain) was reported by 90% (18 out of 20) of women (mean score 6.4, standard deviation [SD] 3.2) treated by high-intensity focused ultrasound (HIFU) in a non-randomised controlled study of 40 women. In the same study, persistent pain assessed with a VAS was reported by 10% (2 out of 20) of women in the HIFU group (mean score 1.6, SD 1.9) within 3 months of treatment. Pain during treatment was reported as being slight in 36% (4 out of 11), moderate in 18% (2 out of 11) and severe in 9% (1 out of 11) of the procedures in a case series of 9 women (11 fibroadenomas) treated by magnetic resonance-guided HIFU. Pain after treatment measured by a VAS (0=no pain to 100=extreme pain) was 40.7 (±24.6) after the first ablation and 34.9 (±17.9) after the second ablation (p value not reported), in a case series of 20 patients treated by HIFU.

5.2 Numbness of the skin was reported by 1 woman of 20 treated by HIFU in the non-randomised controlled study of 40 women. Mild to moderate tenderness was reported by 45% (9 out of 20) of patients up to 1 week after the first HIFU session, and by 57% (4 out of 7) of patients after the second HIFU session in the

case series of 20 patients.

5.3 Superficial skin burn with blistering was reported in 6% (3 out of 51) of fibroadenomas after the procedure in a case series of 42 women (51 fibroadenomas) treated by HIFU. A first-degree skin burn was reported in 1 woman of 20 treated by HIFU in the non-randomised controlled study of 40 women. A first-degree skin burn with hyperpigmentation visible after 6 months was reported in 1 woman of 7, who had more than 1 fibroadenoma, in the case series of 20 women treated by HIFU.

5.4 Hyperpigmentation of the skin was reported in 1 woman within days after the procedure in the case series of 42 women treated by HIFU. Hyperpigmentation of the skin was reported by 30% (6 out of 20) of women treated by HIFU at 3 months and 20% (4 out of 20) at 6 months in the non-randomised controlled study of 40 women.

5.5 Subcutaneous induration was reported in 1 woman of 42 at 12-month follow-up in the case series of 42 women treated by HIFU. Subcutaneous oedema was reported in 25% (4 out of 20) of women in the case series of 20 women treated by HIFU.

5.6 Ecchymosis was reported by 45% (9 out of 20) of women treated by HIFU in the non-randomised controlled study of 40 women.

5.7 Erythema was reported by 30% (6 out of 20) of women treated by HIFU in the non-randomised controlled study of 40 women. Mild to moderate erythema that resolved within 1 week was reported by 29% (2 out of 7) of women, who had more than 1 fibroadenoma, treated by HIFU in the case series of 20 patients.

5.8 Dimpling of the skin was reported by 1 woman of 20 treated by HIFU in the non-randomised controlled study of 40 women.

5.9 In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never done so). For this procedure, specialist advisers listed no anecdotal adverse events. They considered that the following were theoretical

adverse events: poor cosmetic outcome, infection and severe fibrosis.

6 Committee comments

6.1 Patients should have appropriate assessment in a breast clinic to exclude malignancy.

6.2 In the published evidence, there was a variation in treatment time, and patients reported pain or discomfort during the procedure.

7 Further information

7.1 This guidance requires that clinicians doing 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).

7.2 Patient commentary was sought but none was received.

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.