NICE guidance

Microstructural scaffold (patch) insertion without autologous cell implantation for repairing symptomatic chondral knee defects

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. However, 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.

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.

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 microstructural scaffold insertion without autologous cell implantation for repairing symptomatic chondral knee defects raises no major safety concerns; however, current evidence on its efficacy is inadequate in both quality and quantity. Therefore, this procedure should only be used with special arrangements for clinical governance, consent, and audit or research. Find out what special arrangements mean on the NICE interventional procedures guidance page.

1.2 Clinicians wishing to do microstructural scaffold insertion without autologous cell implantation for repairing symptomatic chondral knee defects should:

- Inform the clinical governance leads in their NHS trusts.
- Ensure that patients understand the uncertainty about the procedure's safety and 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 microstructural scaffold insertion without autologous cell implantation for repairing symptomatic chondral knee defects (see section 7.1).

1.3 NICE encourages further data collection, including randomised controlled trials on microstructural scaffold insertion without autologous cell implantation for repairing symptomatic chondral knee defects. Studies should clearly describe patient selection, clinical indications and adjunctive treatments. Outcome measures should include symptom relief, functional ability, long-term outcomes measured by appropriate imaging techniques and patient-reported outcomes.

2 Indications and current treatments

2.1 Chondral damage (or localised damage to the articular cartilage) in the knee can be caused by injury or arthritis, or it can occur spontaneously (a condition called osteochondritis dissecans). It may also happen because of knee instability, muscle weakness, or abnormal unbalanced pressures, for example, after an injury to a ligament or meniscal cartilage. In young people, the most common cause of cartilage damage is sporting injuries. Symptoms associated with cartilage loss include pain, swelling, instability, joint catching and locking, and may lead to degenerative changes in the joint (osteoarthritis).

2.2 There is no uniform approach to managing cartilage defects in the knee. Treatment options depend on the size of the defect and its location. There are 2 main categories of procedure: those intended primarily for symptom relief and those that also try to re-establish the articular surface. Interventions that aim to re-establish the articular surface include marrow stimulation techniques (such as abrasion arthroplasty, Pridie drilling and microfracture), mosaicplasty (also known as osteochondral transplantation), and autologous chondrocyte implantation (in which chondrocytes harvested from the knee are cultured and implanted into the damaged cartilage). Interventions that aim to relieve symptoms include knee washout (lavage) with or without debridement, osteotomy, and knee replacement.

3 The procedure

3.1 Microstructural scaffold insertion without autologous cell implantation for repairing symptomatic chondral knee defects is done with the patient under general or local anaesthesia, using an open or arthroscopic approach. The damaged articular cartilage is removed and standard bone marrow stimulating procedures, such as microfracturing or Pridie drilling, are done. The microstructural scaffold is cut to fit the size of the defect and then fixed in place over the damaged area using, for example, fibrin glue, resorbable suture thread or absorbable tacks. The position of the implanted scaffold is checked by bending and extending the knee and the wound is sutured. The aim of this procedure is that the graft or

patch 'captures' the bone marrow cells and stem cells released by the microfracturing, and acts as a scaffold on which new articular cartilage can grow.

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 interventional procedure overview.

4.1 In a randomised controlled trial of 38 patients with cartilage knee defects, autologous matrix-induced chondrogenesis (AMIC) techniques (sutured [n=13] or glued [n=15]) were compared with microfracture (MFx; n=10). In the interim analyses, the mean modified Cincinnati scores (assessing knee function [6 to 30 points], clinical pathology [0 to 20 points], and highest activity level without pain [0 to 50 points]; a maximum possible score of 100 points) increased significantly from baseline values of 47±20 to 82±14 ($p<0.001$) for the sutured AMIC group, 47±15 to 67±27 ($p=0.02$) for the glued AMIC group and 37±14 to 68±17 ($p=0.002$) for MFx group respectively at 1-year follow-up. There were no statistically significant differences between the groups. At 2 years, mean scores increased significantly from baseline to 88±9 ($p<0.001$) for the sutured group, to 85±18 ($p<0.001$) for the glued AMIC group and to 83±8 ($p<0.001$) for the MFx group. There were no statistically significant differences between the groups. In a case series of 27 patients with 32 chondral lesions treated with AMIC, the mean Cincinnati scores improved significantly from baseline (46±18 to 66±23; $p<0.05$) at 1 year and further increased (to 74±23) at 2 years (level of significance not given). Non-significant declines in scores were reported at 36-month follow-up (62±26) and 48-month follow-up (37±9).

4.2 In the randomised controlled trial of 38 patients with cartilage knee defects comparing AMIC techniques (sutured [n=13] or glued [n=15]) against MFx (n=10), pain (measured on a visual analogue scale [VAS], 0 [no pain] to 100 [severe pain]) was rated less severe by patients at 1- and 2-year follow-up compared with baseline and was similar between the groups. At 1-year follow-up, pain decreased significantly from baseline for sutured AMIC (46±19 to 14±13; $p<0.001$), glued AMIC

(48±20 to 16±13; p< 0.001) and MFx (54±21 to 19±17; p=0.002), and was further reduced at 2-year follow-up without statistical significance (9±6 for sutured AMIC; 10±13 for glued AMIC; 5±3 for MFx). In a case series of 57 patients, knee pain (measured with a VAS) decreased significantly from baseline at 1-year follow-up (7.0±1.8 to 2.7± 2.4; p<0.001) and at 2-year follow-up (2.0±2.1; p<0.003). The mean VAS improvement from baseline to 1-year follow-up was 4.2±2.6 (p<0.001), from 1- to 2-year follow-up was 0.5±2.3 (p=0.003), and from baseline to 2-year follow-up was 4.7±2.7 (p<0.001).

4.3 In the randomised controlled trial of 38 patients with cartilage knee defects comparing AMIC techniques (sutured [n=13] or glued [n=15]) against MFx (n=10), at 1-year follow-up, patients in all groups (n=30) rated their functional status as improved (n=24) or stable (n=6; using the International Cartilage Repair Society [ICRS] Cartilage Injury Standard Evaluation Form 2000). At 2 years, patients in all groups rated their functional status as improved (n=12), stable (n=13) or deteriorated (from normal to nearly normal; n=2). Surgeon-rated assessments, based on the modified ICRS score (with respect to functional status, classification of the knee and crepitation using parts 3, 4 and 7 of the ICRS form), reported improvement in clinical symptoms and function and found no differences between the groups at 1- and 2-year follow-up. In the case series of 27 patients, mean ICRS scores improved significantly from baseline (31±15 to 59±24; p<0.05) at 1 year and further increased (to 68±22) at 2 years (level of significance not given). Scores declined non-significantly at 36-month follow-up (54±25) and 48-month follow-up (37±4).

4.4 In a randomised controlled trial of 80 patients with cartilage knee defects comparing a chitosan-based scaffold (n=40) with MFx alone (n=39), at 1-year follow-up, there were no significant differences in clinical benefit between the scaffold and MFx groups (measured on Western Ontario and McMaster Universities Osteoarthritis Index subscales for pain, stiffness and function), but significant improvement (p<0.0001) from baseline was seen for both groups. There were no significant differences in quality-of-life scores (measured with SF-36 health survey, higher positive scores indicating better results) between the scaffold and MFx treatment groups at 1-year follow-up; both the physical component

scores (13.02 in the scaffold group versus 14.76 in the MFx group; p=0.41) and the mental component scores (3.54 in the scaffold group versus 0.84 in the MFx group; p=0.22) were similar.

4.5 In a retrospective case series of 38 patients (40 knees) treated with AMIC for full-thickness chondral and osteochondral defects of the femoral condyles and patella, International Knee Documentation Committee (IKDC) scores (using the IKDC Subjective Knee Evaluation form 2000, score range 0 to 100, higher scores representing higher levels of function and lower levels of symptoms) improved significantly from baseline to a mean follow-up of 28.8 months in the osteochondral femoral condyle group (from 44±25 to 88±9; p=0.005) and the chondral patella group (from 51±25 to 74±17; p=0.0025). However, improvements in the chondral femoral condyle group were not significant (from 45±26 to 68±14). Significant differences were seen between the 3 groups (p=0.0016). There were no significant differences in outcomes in patients treated with AMIC alone compared with those who also had an osteotomy or realignment procedure. In a case series of 30 patients treated for chondral or osteochondral lesions with a cell-free collagen hydroxyapatite osteochondral scaffold, mean IKDC subjective scores improved significantly from 40.0±15.0 at baseline to 76.5±14.4 (p<0.0005) at 2-year follow-up and 77.1±18.0 (p<0.0005) at 5-year follow-up.

4.6 In the case series of 27 patients, mean Lysholm scores (a patient knee functional scoring scale with 8 items and a maximum possible score of 100) improved significantly from baseline (36±21 to 67±28; p<0.05) at 1-year follow-up and further increased (to 76±24) at 2-year follow-up (level of significance not given). Non-significant declines in scores were seen at 36-month follow-up (62±25) and 48-month follow-up (47±22).

4.7 In the case series of 27 patients, mean Tegner score (a patient activity level scale; score range 0 to 10, with higher scores representing participation in higher-level activities) improved significantly from baseline (not reported) to 3.4 (p<0.05) at 1-year follow-up and further increased to 4.1 at 2-year follow-up (level of significance not given). Non-significant decline in scores was seen at 36-month follow-up (4.0). In the case series of 30 patients with chondral or osteochondral lesions treated

with a cell-free collagen hydroxyapatite osteochondral scaffold, mean Tegner score improved significantly from 1.6±1.1 at baseline to 4.0±1.8 ($p<0.0005$) at 2-year follow-up and to 4.1±1.9 ($p<0.0005$) at 5-year follow-up.

4.8 In a case series of 23 patients with symptomatic knee osteochondritis dissecans, EQ-VAS score (a measure of patients' own global rating of their overall health, on a scale 0 [worst imaginable health state] to100 [best imaginable health state]) had improved significantly from baseline at 2-year follow-up (3.15±1.09 to 8.15±1.04; $p<0.0005$).

4.9 In the case series of 38 patients (40 knees), patient satisfaction (rated on a scale of 0% to 100%, 0 indicating completely dissatisfied and 100 indicating completely satisfied) was high in all subgroups and there was no significant difference between groups (osteochondral femoral group 94±8; chondral patella group 84±24; chondral femoral condyle group 74±43). In the case series of 23 patients with symptomatic knee osteochondritis dissecans, satisfaction was recorded in 85% (absolute numbers not given) of patients.

4.10 In the case series of 30 patients with chondral or osteochondral lesions treated with a cell-free collagen hydroxyapatite osteochondral scaffold, MRI evaluation showed an improvement in both the magnetic resonance observation of cartilage repair tissue (MOCART) score and subchondral bone status (part of MOCART, 5 variables rated on a scale of 1 to 3) at 2- and 5-year follow-up. At 5-year follow-up, complete filling of the cartilage was shown in 78% of lesions (absolute numbers not given), complete integration of the graft was detected in 70% of cases, the repair tissue surface was intact in 61% of cases and the structure of the repair tissue was homogenous in 61% of the cases. No correlation was found between MRI findings and clinical outcome. In the randomised controlled trial of 80 patients with cartilage knee defects comparing a chitosan-based scaffold (n=40) with MFx alone (n=39), at 1-year follow-up, the scaffold group achieved statistical superiority for greater lesion filling (92.8±2.0% versus 85.2±2.1% with MFx; $p=0.011$) and more hyaline cartilage-like T2 relaxation times (70.5±4.5 milliseconds versus 85.0±4.9 milliseconds with MFx; $p=0.033$) on MRI analysis.

4.11 The specialist advisers listed key efficacy outcomes as improved clinical benefit, MRI evidence of chondro-regeneration (for example, T2 mapping and d-GERMIC) and delayed replacement arthroplasty.

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 interventional procedure overview.

5.1 Haematoma, after the autologous matrix-induced chondrogenesis (AMIC) procedure, developed in 1 patient in a case series of 38 patients (40 knees) with full-thickness chondral and osteochondral defects of the femoral condyles and patella. The haematoma was excavated. Bleeding and swelling of the knee after surgery was reported in 12% (6/49) of patients in a case series of 49 patients, all of which resolved spontaneously within 1 week. Swelling, which resolved in a few days, was reported in 22% (17/79) of patients in a case series of 82 patients with chondral or osteochondral knee lesions.

5.2 Muscle vein thrombosis was reported in 1 patient in a case series of 27 patients with 32 chondral lesions treated with AMIC. This complication resolved after treatment.

5.3 Effusion 'after tumbling' was reported in 1 patient in the case series of 27 patients. This complication resolved after treatment.

5.4 Knee stiffness was reported in 23% (9/40) patients in the case series of 38 patients (40 knees) after the procedure. This was reported in patients in the chondral patella group. Patients regained full range of motion after mobilisation under anaesthesia.

5.5 Revision surgery, because of pain and limited function of the knee, was done in 10% (5/49) of patients in a case series of 49 patients with large osteochondral knee lesions treated with a biomimetic osteochondral scaffold. In 2 patients with osteonecrosis of the medial femoral condyle, unicompartmental knee replacement was done in 1 patient and a valgus high tibial osteotomy was done in the other patient. In 2 patients with

osteochondritis dissecans, autologous osteochondral transplantation revision surgery was done in 1 patient and osteochondral allograft transplantation and varus femoral osteotomy was done in the other patient. The fifth patient, who was lost to follow-up, had treatment at another centre. Revision surgery was done in 8% (2/27) of patients due to symptoms of grinding, catching, pain or swelling after the procedure in the case series of 27 patients. Clinical improvement was not seen in these patients.

5.6 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 the following anecdotal adverse events: delamination of repair tissue and the need for surgical removal of this tissue, and hypertrophy. They considered that allergic reaction to materials used in preparation or preservation of scaffold was a theoretical adverse event.

6 Committee comments

6.1 The committee was informed that there are several devices available for this procedure, with substantial differences in the materials used.

6.2 Clinicians are encouraged to enter details about all patients having microstructural scaffold insertion without autologous cell implantation for repairing symptomatic chondral knee defects onto the International Cartilage Repair Society Registry.

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 NICE's interventional procedure outcomes audit tool (which is for use at local discretion).

7.2 For related NICE guidance, see the NICE website.

Information for patients

NICE has produced information on this procedure for patients and carers (information for the public). 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.

Accreditation