Evidence Review for the Use of Biological Mesh in hernia repair in comparison to synthetic surgical mesh.

Questions to be addressed

1. In adults with a non-healed wound following hernia repair surgery using synthetic surgical mesh, is there evidence to support the use of biological mesh?
2. In adults are there clinical circumstances where the use of biological mesh in hernia repair would be clinically more effective than the use of synthetic surgical mesh?

Reason for review

NHS Birmingham and Solihull CCG, Sandwell and West Birmingham CCG, requested a rapid evidence review of the clinical and cost effectiveness of biological surgical mesh for hernia repair compared to alternative treatment options, in particular synthetic surgical mesh to inform their decisions on commissioning policy development.

Options for commissioners:

1. The Committee considers that due to the limited quality of evidence of clinical and cost effectiveness for the use of biological mesh compared to alternative treatment options, its use should be considered a low priority.
2. The Committee recommends that, due to the limited quality of evidence of its clinical and cost effectiveness, the use of biological mesh should be offered ONLY to patients who have failed wound healing following hernia repair using standard surgical mesh.
3. The Committee considers that there is sufficient evidence to suggest that the use of biological mesh in surgical hernia repair is at least as effective as alternative treatment options and the costs are comparable, therefore the decision about which approach to proceed with should be made after an informed discussion between the clinician and the individual person about the risks and benefits of each procedure.

Summary

Background

- Hernia most frequently occurs when an organ or internal tissue pokes through a hole or weakness in the abdominal muscle wall.
- Hernia repair surgery is one of the most common surgeries to be performed.
- Different types of mesh can be used in hernia repair: standard surgical mesh and biological mesh.

Clinical effectiveness

- Clinical effectiveness of biological mesh above synthetic mesh was not identified within the literature.
- 2 systematic reviews demonstrated a lack of clinically robust evidence to support the use of biological mesh above the use of synthetic mesh.
- The currently available clinical evidence demonstrated a lack of blinding within the studies and often retrospective studies of low to moderate quality.

Safety

NICE & MHRA support the use of surgical synthetic mesh in hernia repair surgery.

Cost effectiveness

Synthetic mesh is not excluded from National Tariff and the cost of synthetic mesh is within tariff and not funded separately.

Biological Mesh is currently excluded from PbR tariff. This is because of the variable and often high cost associated with its use; the product can range in cost from £750 to in excess of £8,500 per patient, depending on intended use, size of wound and product choice. All items listed as PbR exclusions are subject to locally agree payments taking into consideration existing tariff charges.

Equity issues

None were identified within the course of this review.

Context

1.1 Introduction

- A hernia occurs when an internal part of a body pushes through a weakness in the muscle or surrounding tissue wall. It usually takes the form of a lump, or swelling with or without some discomfort that may limit daily activities, including the ability to work.

- There are different types of hernia, inguinal hernias are the most common and the majority of these (approximately 98%) are found in men due to their particular anatomical structure.

- Other types include femoral (also in the groin), umbilical and incisional (this type occurs following surgery in the upper abdomen where an incision has caused weakness in tissue)

- Hernias cannot be treated medically and often require surgical repair if the patient is fit enough. Without surgery, there are risks of strangulation, bowel obstruction and incarceration, which could require emergency surgical intervention.

Management

- Hernia repair is a very common surgical intervention and significantly more patients have undergone hernia mesh procedures than have undergone vaginal mesh

procedures [with approximately 70,000 inguinal hernia repairs performed every year in England and 6,000 each year in Wales].

- Until the 1950's, the repair took the form of a suture technique at the site of weakness or defect. The stitching of such weak areas did not result in long lasting repair which led to the recurrence of the hernia.

- The use of prosthetic mesh has become increasingly common since then as a 'tension-free' or patching method for strengthening and reinforcing weak tissue, resulting in longer lasting repair.

- There has been significant change in the design and manufacture of synthetic mesh over the years, with a move to larger pore, lighter weight mesh, with early data suggesting better tolerance of such implants by the patient.

- There are broadly two techniques for mesh hernia repair - open or laparoscopic.

    - In an open repair, the defect through which the hernia is protruding is identified and mesh placed over the defect and stitched in place, in effect creating a scaffold for the tissue to grow through to strengthen the weak area.

    - In a laparoscopic repair, a small incision is made near the umbilicus as well as two small incisions in the lower abdomen. Carbon dioxide is used to inflate the abdomen and a camera is inserted via one of the incisions so that the defect is viewed from the interior abdominal wall and mesh introduced.

- As with all types of surgery, there are associated risks. These include inter-operative complications such as bleeding or damage to surrounding structures as well as post-operative complications such as infection, pain (which can become chronic), thromboembolic complications as well as hernia recurrence.

There are 2 types of surgical mesh:

1. Standard Surgical Synthetic Mesh
2. Biological Mesh

Standard Surgical Synthetic mesh is made of either non-absorbable synthetic polymers (polypropylene) or absorbable synthetic polymers (polyglycolic acid or polycaprolactone).

A number of Biological Meshes are currently available on the market. Biological Meshes are derived from human (allograft) or animal (xenograft) dermis, pericardium or intestinal submucosa. These tissues are processed to remove any immunogenic material and, as a result, are rendered acellular. After processing, the extracellular matrix remains and is used as a scaffold by host tissues.

1.2 Existing national policies and guidance

National Institute for Health and Care Excellence (NICE) Guidance

- Guidance was published in 2004 on laparoscopic hernia repair which states that a laparoscopic repair should only be carried out by trained surgeons who perform the procedure regularly.

- The use of mesh in hernia repair is considered by NICE to be an 'Interventional Procedure', and therefore is not 'approved' as may be the case for a drug or procedure subject to technology appraisal. NICE do not examine interventional procedures which are considered established practice unless there are data demonstrating uncertainty about their efficacy or safety.

- The guidance with regard to laparoscopic repair was reviewed in 2016 but there was no new evidence to suggest a change in the guidelines was required.

Medicines and Healthcare Products Regulatory Authority (MHRA)

- It is understood that the MHRA broadly agrees with NICE's position outlined above and considers that the main determinant of success of an operation seems to be patient selection and surgical technique rather than choice of device. MHRA continues to encourage the reporting of adverse events following the use of surgical mesh.

2 Epidemiology

Groin hernia repairs are amongst the most commonly performed general surgical operations with over 71,000 inguinal and femoral hernias repairs carried out in England in 2014/15.

There is more than a 2-fold variation in the rate of inguinal hernia repair across the NHS. Patients and surgeons have the choice between various techniques and materials.
There is no national system of audit or follow-up, and the overall low reported recurrence rate following inguinal hernia repair makes it difficult to determine which procedure is best. However, outcomes should not be judged in only terms of hernia recurrence, but also wound complications, length of hospital stay, chronic pain, patient experience, quality of life and cost2.

The British Association of Day Surgery has suggested that 80% of inguinal hernia repairs should be carried out as day case procedures. In 2014/15 77.8% of primary inguinal hernia repairs (unilateral) were carried out as a day case, and rates varied from 67% to 88% across providers. (RCS, 2016).

Further data and analysis for England is yet to be undertaken, but Wales has undertaken a review of the use of surgical mesh and has found the following:

- In Wales between 2011/12 and 2017/18, 43,646 patients had a hernia repair
- Of those, 78.8% underwent a mesh-based technique
- A small number of patients will require removal of mesh due to complications, for example, chronic infection.
- The data showed that a very small minority of patients suffer complications that necessitates removal and those figures do not change dramatically on an annual basis
- Obviously some patients will have complications that do not warrant mesh removal but the interpretation is that those who undergo mesh removal suffer the most severe complications. The likelihood of the mesh being removed appears to be around 0.007%, consistent with international data and extremely low for any surgical complication. This is a rate which appears to have been largely consistent over the 5 year period of this review.

3 The interventions

Most hernias are found in the abdomen. Areas of weakness in the abdominal wall where hernias are commonly found include the groin, upper stomach, belly button and, where you have a surgical scar.

The most frequently seen types of hernia include:

• Inguinal hernias – the most common hernia, seen more in men, causes a bulge in your groin. The inguinal hernia appears through your inguinal canal, a narrow passage that blood vessels pass through in your abdominal wall and, may reach your scrotum.
• Femoral hernias – also a bulge in your groin, relatively uncommon and seen more in women. The femoral hernia happens at the hole in your abdominal wall where the femoral artery and vein pass from the abdomen into your leg.
• Hiatus hernias - occur in your upper chest area when part of your stomach pushes up into your chest by squeezing through a gap in your diaphragm called the hiatus.
• Umbilical/periumbilical hernias – occur at the umbilicus, a natural weakness in your abdominal wall, when fatty tissue or a part of your bowel pokes through your abdomen near your naval.
• Incisional hernia – occurs through a scar from past abdominal surgery as tissue pokes through the weak healed site in your abdominal wall.

Hernia surgery is a routine procedure, but as with all surgeries there are risks of complications. These may vary depending upon the exact hernia operation required and the individual patient' health.

Often the greatest complication risk is a reoccurrence of the hernia. Other hernia surgery side effects include: build-up of seroma or a fluid-filled sac under the surface of the skin, inability or difficulty urinating, organ or tissue damage, wound infection and, rejection of the mesh.

4 Findings

4.1 Evidence of effectiveness

- A Cochrane systematic review was published in 2018 comparing mesh procedures and non-mesh procedures for the repair of inguinal and femoral hernias (which included 6,293 participants)

- It found that mesh repairs are associated with a reduced rate of hernia recurrence (hence reduced amount of patients needing more surgery) as well as reduced risk of visceral and neurovascular damage but non-mesh procedures carried a lower risk of seroma (pocket of serous fluid) formation.

- In terms of chronic pain a large systematic review published in 2018 found no statistical difference in the rates of chronic pain between mesh and non-mesh procedures in the first post-operative year. There is no evidence that the use of mesh increases the risk of pain

    - There are reports that moderate-severe chronic pain can affect 10-12% post-operatively, but that the risk is less with mesh than non-mesh repair. Reports from England also noted that up to 5 % of those undergoing inguinal hernia repairs can experience long-term discomfort or pain, lasting for more than three months after their operations.

    - An original piece of research looked at the rate of chronic infection following mesh insertion with only 0.005% requiring mesh removal due to chronic infection.

There is good evidence to support the use of synthetic mesh in hernia repair operations. Further evidence was reviewed to ascertain the clinical and cost effectiveness of synthetic vs biological mesh.

4.1.1 Clinical effectiveness

Con et al undertook a systematic review in 2019, , which aimed to review potential bias in the literature which reviewed the use of biological mesh in hernia repair:

A literature search in PubMed, Embase and Cochrane databases of systematic reviews on biologic mesh for ventral hernia repair. The literature review was conducted using the Population, Intervention, Comparisons, Outcomes and Design approach. 40 studies were identified which matched the stringent criteria set. A 13-point instrument was set to assess for bias and applied on the primary studies that were analyzed.

Most primary studies are case series or case reports of patients undergoing abdominal hernia repair with biologic mesh, without any comparison group, and the inclusion of cases was only specified to be consecutive in 6 out of 40 cases. In terms of assessing outcomes, in none of the 40 articles were the outcome assessors blinded to the intervention or exposure status of participants.

The instrument that created could allow assessment of the risk of bias in different kind of studies. The assessment of the studies based on the criteria set up in the instrument clearly identified that further research needs to be done due to the lack of unbiased studies regarding the use of biologic meshes for abdominal hernia repair.

Other earlier systematic reviews also support the need for further research in this area.

2017 Systematic Review of synthetic vs biological mesh (Knappen et al 2017) found the following: Forty-four studies were included: 5 reporting biologic mesh repairs; 21, synthetic mesh repairs; and 18, prophylactic mesh repairs. Most of the studies were retrospective cohorts of low to moderate quality. The hernia recurrence rate was higher after undergoing biologic compared to synthetic mesh repair (24.0% vs 15.1%, P = 0.01). No significant difference was found concerning wound and mesh infection (5.6% vs 2.8%; 0% vs 3.1%). Open and laparoscopic techniques were comparable regarding recurrences and infections. Prophylactic mesh placement reduced the occurrence of a parastomal hernia (OR = 0.20,

P < 0.0006) without increasing wound infection [7.8% vs 8.2% (OR = 1.04, P = 0.91)] and without differences between the mesh types.

Further research in this area is required to identify the clinical circumstances in which the use of biological mesh would be clinically superior and cost effective.

4.1.2 Trials in progress

A search of clinicaltrials.gov found the following trials currently recruiting:

1. https://clinicaltrials.gov/ct2/show/NCT03034213?cond=biological+surgical+mesh&rank=2

The hypothesis for this study is complex incisional hernia repair using the separation of

components technique reinforced with retrorectus placement of Gentrix™ Surgical Matrix will lead to fewer incisional hernia recurrences and fewer wound complications compared to the same incisional hernia repair techniques reinforced with other prosthetic or biologically-derived mesh.

2. Performance of biological mesh materials in abdominal wall reconstruction: study rotocol for a randomised controlled trial

Carver DA, *et al*. *BMJ Open* 2019;9:e024091. doi:10.1136/bmjopen-2018-024091

3. Seedfelt et al (2019) BIOLAP: biological versus synthetic mesh in laparo-endoscopic inguinal hernia repair: study protocol for a randomized, multicenter, self-controlled clinical trial. Trials. 2019 Jan 16;20(1):55. doi: 10.1186/s13063-018-3122-5.

https://www.ncbi.nlm.nih.gov/pubmed/30651127

4.1.3 Cost-effectiveness

Biological meshes are excluded from National Tariff.

Biological Mesh is currently excluded from PbR tariff. This is because of the variable and often high cost associated with its use; the product can range in cost from £750 to in excess of £8,500 per patient, depending on intended use, size of wound and product choice. All items listed as PbR exclusions are subject to locally agree payments taking into consideration existing tariff charges.

For a device to be considered as an exclusion from PbR it must meet all 3 of the following criteria:
I. high cost and represent a disproportionate cost relative to the relevant HRG
II. used in a subset of cases within an HRG and/or used in a subset of providers delivering services under a specific HRG
III. relatively high cost in terms of volume and cost.

Synthetic mesh is not excluded from National Tariff and the cost of synthetic mesh is within tariff and not funded separately.

Synthetic Equivalents This wording was included within PbR exclusions and is intended to allow for the possibility that there are synthetic materials in use which may represent a similar disproportionate cost as biological mesh – synthetic equivalents to biologic mesh are therefore also excluded.

4.2 Safety

National Institute for Health and Care Excellence (NICE) Guidance

- Guidance was published in 2004 on laparoscopic hernia repair which states that a laparoscopic repair should only be carried out by trained surgeons who perform the procedure regularly.

- The use of mesh in hernia repair is considered by NICE to be an 'Interventional Procedure', and therefore is not 'approved' as may be the case for a drug or procedure subject to technology appraisal. NICE do not examine interventional procedures which are considered established practice unless there are data demonstrating uncertainty about their efficacy or safety.

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4.3 Summary of findings

There is a significant amount of evidence to currently support the use of surgical synthetic mesh in hernia repair surgery at the present time. However, there is a lack of evidence to support the use of biological mesh above standard synthetic mesh in hernia repair surgery. The evidence to support the use of biological mesh when standard surgical mesh has failed is also scant and the disproportionate higher cost of biological mesh is also a factor to be considered.

5 Equity issues

Whilst there is a greater occurrence rates of inguinal hernia in men, there is currently insufficient evidence to support a wider equity issue.

6 Discussion and conclusions

Systematic reviews of the use of biological mesh found that there were issues with many of the studies carried out in this area. Many studies had no comparison group, assessors were not blinded to either the intervention or exposure status of participants.

Further unbiased studies are required to identify the true clinical effectiveness of biological mesh and the most cost effective clinical circumstances for use should be identified.

7 Search Strategy

Medline:

Surgical mesh

Biological mesh

Hernia repair

Synthetic mesh

PubMed:

Surgical mesh

Biological mesh

Hernia repair

Synthetic mesh

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