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Safety and efficacy of non-absorbable mesh in contemporary gynaecological surgery

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Abstract

Mesh-augmented pelvic floor surgery evolved to address the limitations of native tissue repair in reconstructive surgery. The development of the synthetic mid-urethral tape signalled a revolution in the treatment of stress urinary incontinence, whilst the use of mesh in abdominal apical prolapse repair may confer benefits over native tissue alternatives. However, these procedures can be associated with mesh-specific complications, underlining the need for shared decision-making between physicians and patients prior to mesh surgery.

Transvaginal non-absorbable mesh implants for pelvic organ prolapse are associated with a high risk of serious adverse events, leading to withdrawal or restricted use in many countries. Increased scrutiny has led to growing concerns about complications associated with all types of mesh-augmented reconstructive surgery, attracting widespread media attention.

National and international reports have been commissioned examining the safety and efficacy of mesh surgery in gynaecology. They have all highlighted systemic failures in the development, regulation and clinical adoption of medical devices. The widespread application of novel devices prior to the availability of reliable safety and efficacy data, and delayed recognition of adverse events, is of serious concern. Notwithstanding, the available data continue to support a role for mesh augmentation. This review outlines the evolution of gynaecological mesh, the safety and efficacy of pelvic floor surgery using non-absorbable mesh materials, and an overview of specific complications.

Keywords: Surgical mesh, Pelvic organ prolapse, Urinary incontinence, Laparoscopy

Introduction

Gynaecological mesh refers to synthetic mesh materials used to augment the surgical repair of pelvic organ prolapse (POP) or stress urinary incontinence (SUI). These common conditions impair quality of life (QoL) and have associated healthcare costs. Whilst many women pursue conservative management initially, surgery is common. The lifetime incidence of surgery for SUI or POP by the age of 80 is 11.1% [1]. Traditional surgical techniques for the treatment of POP and SUI have well-recognised limitations. Transvaginal native tissue repair of POP is associated with a significant risk of recurrence, in the region of 30% [1]. Colposuspension, an abdominal procedure for SUI, has significant morbidity and is associated with the development of posterior compartment prolapse. These limitations fostered the development of surgical mesh applications to treat POP and SUI.

The principal applications of gynaecological mesh include transvaginal mesh (TVM) for SUI, TVM for POP, and transabdominal mesh for POP. The synthetic mid-urethral tape (MUT) has been the most common application of TVM for SUI. Approximately 3.7 million women underwent insertion of an MUT between 2005 and 2013 [2, 3]. Mesh used to surgically treat POP may be inserted either vaginally or abdominally, an important distinction due to significant differences in complication profiles and adverse events (AEs). Transabdominal mesh can be used to treat prolapse of the uterus or for post-hysterectomy vault prolapse (PHVP). Sacrohysteropexy suspends the uterus from a sacral anchor point, whilst sacrocolpopexy similarly suspends the vaginal vault. In contrast, TVM for POP uses a vaginal approach to implant a specific device or a mesh inlay at colporrhaphy.

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It is now clear that some women experience AEs associated with mesh procedures. In this review, the term mesh refers to synthetic, non-absorbable mesh used in gynaecological surgery and focuses on the evidence for these procedures, reflecting recent controversy. Absorbable mesh materials deserve further research however, they are beyond the scope of this review. Several national and international reports have examined the safety and efficacy of gynaecological mesh [4–7]. These reports have supported the safety and efficacy of the MUT for SUI, and transabdominal mesh for POP. However further research is required, and critics raise legitimate concerns about a lack of surveillance data and underreporting of serious adverse events (SAEs). In England, concerns have led to a pause in the use of mesh for SUI, pending further review [8]. None of the mesh reports have supported TVM for primary repair of POP outside of the research setting, and in some countries, TVM has been banned outright [9]. Given the potential for mesh-related morbidity and the complexity of managing mesh complications, a contemporary evidence-based approach is important for clinicians managing pelvic floor disorders. This article documents the development of mesh-augmented gynaecological surgery and reviews the evidence supporting safety and efficacy to guide clinicians.

History of mesh

A range of materials and devices are covered by the term 'mesh', defined by the International Urogynecological Association (IUGA) and International Continence Society as 'a (prosthetic) network fabric or structure; open spaces or interstices between the strands of the net' [10]. Mesh is differentiated from a graft, which is typically a product derived from biological tissue. Surgical mesh was originally developed to augment abdominal hernia repair. A range of materials were used prior to the advent of plastics and ultimately polypropylene, which was first used to repair inguinal hernias in the 1960s [11]. Strengthening native tissue repair with mesh appeared to translate well to the surgical treatment of pelvic floor disorders. Contemporary mesh procedures are based on historical operations that utilised native tissue or suture material.

Some 150 surgical procedures for urinary incontinence have been described. Von Giordino is credited with undertaking the first pubovaginal incontinence sling, utilising gracilis muscle grafted around the urethra [12]. The use of synthetic material to do this was first described in 1965, and in 1996, the US Food and Drug Administration (FDA) approved the ProteGen™ sling to treat SUI [13, 14]. Work based on the integral theory undertaken by Petros and Ulmsten in the 1980s led to the development of the most popular MUT, the tension-free vaginal tape (TVT) [15]. The integral theory proposed that pelvic floor dysfunction resulted from laxity of the vagina or supporting ligaments as a result of connective tissue weakness [16]. Initial studies utilised mersilene which was associated a 14% risk of erosion. The technique was refined and polypropylene adopted, leading to FDA approval in 1998 [17]. Subsequent studies showed equivalent efficacy to colposuspension whilst avoiding laparotomy, and the MUT quickly became the 'gold standard' treatment for SUI [3, 18]. The original TVT was inserted via the retropubic route (RPR), although variations include the transobturator route (TOR) and the 'mini-sling'.

The surgical management of POP with mesh includes a variety of approaches and techniques. Surgeons may use a vaginal or abdominal approach, with the latter being developed in the mid-twentieth century. Uterine preserving abdominal hysteropexy utilises either sutures or mesh, with suspension to pelvic ligaments or the sacral promontory. The evolution of mesh hysteropexy is outlined in Table 1.

For women who have undergone hysterectomy, the reported incidence of PHVP is as high as 43%, with the rate

Table 1 Evolution of uterine sparing prolapse surgery

Year	Surgeon/technique	Description
1886	Howard Kelly 'Abdominal ventrosuspension'	Open abdominal approach. The uterus is sutured to the anterior abdominal wall at the level of the cervix using the peritoneum.
1891	Donald and Shaw 'Manchester Repair'	Vaginal approach. Anterior and posterior colporrhaphy with amputation of cervix [80].
1956	Arthure and Savage 'Suture sacral hysteropexy'	Open abdominal approach. The uterine fundus or posterior uterine corpus is sutured to the ligamentous tissue of the sacral promontory [81].
1979	SK Chaudhuri 'Abdominal autologous fascial uterine sling'	Fascial sling from external oblique is brought through the transversalis fascia and sutured to the anterior aspect of the cervix [82].
1993	Andrew Farkas 'Mesh hysterosacropexy'	Open abdominal approach. Goretex mesh is used to fix the uterus to the sacrum [83].
2010	Price and Jackson 'Laparoscopic hysteropexy'	Laparoscopic approach. Bifurcated polypropylene mesh is wrapped round the uterus through the broad ligament and suspended to the sacral promontory [84].

of surgical repair between 6 and 8% [19, 20]. Sacrocolpopexy permits abdominal suspension using mesh. Lane first described the use of autograft to suspend the vault in 1962 [21]. The first series of polypropylene abdominal vault suspension procedures was published in 1991 [22]. There are now over 25 years of data examining mesh-augmented sacrocolpopexy, with meta-analyses reporting advantages over vaginal alternatives [23]. Now considered a routine treatment for PHVP, it has been endorsed by the European Commission safety report and European consensus guidelines, which recommend the laparoscopic approach [6, 7]. A review of the CARE trial found concurrent sacrocolpopexy at the time of hysterectomy to be associated with a higher risk of mesh erosion than for those having the procedure for PHVP, and this technique is rarely advocated [24].

Transvaginal mesh for prolapse is either placed as a customisable inlay secured during colporrhaphy, or introduced using a kit or device. Despite a lack of quality evidence supporting superior outcome, TVM for POP was rapidly adopted. Mesh kits were constantly reinvented, endorsed, and implanted in large volumes prior to safety concerns being raised. Emerging evidence has subsequently demonstrated an unacceptable rate of SAEs associated with TVM. Heneghan et al. have described the history of the FDA regulatory process with respect to TVM devices for POP [13]. As Class II devices approved through the Food and Drug Administratio (FDA's) 510(k) process, products were marketed on the basis of 'equivalence' to existing devices, despite minimal clinical data. Limited prospective studies emerged in the early 2000s, and a host of TVM products for POP followed with FDA approval [13, 25]. In 2016, with increasing evidence demonstrating a high risk of AEs, TVM kits were upgraded to Class III devices. Post-marketing surveillance was requested and many TVM kits were withdrawn from the market, leading to a relatively short-lived period of widespread use [26]. European guidance suggests that TVM should be reserved for complex recurrent cases [7]. The UK National Institute and Health and Care Excellence (NICE) states that TVM for POP should not be used outside the research setting, and some countries such as Australia have banned TVM completely [9, 27].

Biocompatibility and biophysical profile of mesh

The pathophysiology of mesh erosion or extrusion remains unclear but is likely to be multifactorial. Polypropylene is the most commonly used material as it is relatively inert, cheap, and easily tailored [28, 29]. The biocompatibility and biophysical profile of an implant determines clinical outcomes and complications. Biocompatibility, defined as 'the ability of a material to perform with an appropriate host response in a specific application', is mediated by tissue integration and host immunological response [28, 30]. The interplay between these processes is known as the foreign body response (FBR) and varies according to the composition of the implant and individual immunogenic response [31].

Animal studies suggest there is a local implant-mediated immune response leading to overt or subclinical infection which may be implicated in mesh erosion or extrusion [32]. Mesh pore size influences the interaction between host immunological cells and smaller pathogens. Leucocytes average between 9 and 15 μm whilst a typical bacterium is 2 μm [33]. Small pore size may therefore inhibit clearance of pathogens within the mesh [34]. Mesh can be categorised according pore size using the Amid classification [33]. Additionally, heavyweight mesh materials have been found to be less biocompatible; lightweight, macroporous mesh is therefore favoured for implants [6].

Fibroblast deposition and granuloma formation associated with the FBR reduces tissue elasticity and alters tissue adaptation to physical forces. Animal studies have shown that the presence of mesh reduces biomechanical tissue compliance leading to stiffness, which may translate clinically into dyspareunia [35]. Transvaginal mesh has also been shown to alter the structure and function of vaginal smooth muscle which may be implicated in the development of AEs attributed to mesh [36]. The process of excess fibroblast deposition and adaptation to the extracellular matrix may lead to 'stress shielding', altering forces exerted on tissues. Tissues shielded from dynamic forces may then become thin and atrophy, perhaps causing mesh erosion or extrusion [37].

Intraoperative variables also alter the biological response to mesh. Both animal models and human studies have shown that reducing the volume of mesh implanted reduces the risk of erosion [38, 39]. The technique of mesh placement and its location also influences the likelihood of erosion. Ovine models demonstrate a greater risk of mesh erosion associated with TVM when compared to mesh placed abdominally [40]. Histological examination of mesh explants in these studies demonstrated a more pronounced FBR after vaginal placement perhaps reflecting clinical findings in human studies.

Concerns have also been raised over the malignant potential of mesh. However, a comprehensive review of five decades of data, during which time millions of implanted polypropylene mesh devices have been used, did not demonstrate a link to carcinogenesis [41].

Adverse events attributed to mesh

Mesh-specific AEs should be considered in the context of complications associated with native tissue surgery, or indeed no treatment at all. Complications following mesh-augmented surgery include vaginal mesh erosion (or exposure), extrusion, pain (affecting the abdomen,

pelvis, groins, vulva or vagina, and lower limbs), dyspareunia, hispareunia (pain for the partner during sexual intercourse), infection, urinary voiding dysfunction, functional bladder and bowel symptoms, and treatment failure or recurrence [42–44]. There are also reports of neuromuscular problems, vaginal scarring and implant shrinkage. Psychological sequelae as a result of physical problems are common. Whilst the presence of mesh outside its intended anatomical location is a clearly defined complication, the evidence linking mesh implants to other AEs is less clear.

To standardise the reporting of AEs associated with mesh surgery, IUGA has developed a coding system for the classification of mesh complications, as well as terminology guidance, outlined in Fig. 1 and Table 2 [10].

The most common symptom experienced by those reporting a mesh complication is pain. Unfortunately, few studies of gynaecological mesh have used a validated pain measure pre- and postoperatively. Thus, it is difficult to accurately determine the incidence of new-onset pain and more difficult still to confidently attribute pain to the mesh itself. Of those reporting AEs to the FDA, 38% of complaints reported pain or dyspareunia, and 89% of women reporting complications to the Scottish review reported pain [44, 45]. The incidence of new postoperative pain in patients who have undergone a procedure using gynaecological mesh is reportedly between 0 and 15% [46, 47]. It has been hypothesised that pain may be generated as a result of mesh contracture over time, causing tethering of fascia and muscles [48]. Pelvic floor hypertonia has also been reported in association with TVM

Table 2 IUGA terminology [10]

Contraction:	Shrinkage or reduction in size
Prominence:	Parts that protrude beyond the surface (e.g. due to wrinkling or folding with no epithelial separation)
Separation:	Physically disconnected, for example, vaginal epithelium.
Exposure:	A condition of displaying, revealing, exhibiting or making accessible (e.g. vaginal mesh visualised through separated vaginal epithelium)
Extrusion:	Passage gradually out of a body structure or tissue (e.g. a loop of tape protruding into the vaginal cavity)
Compromise:	Bring into danger
Perforation:	Abnormal opening into a hollow organ or viscus
Dehiscence:	A bursting open, splitting, or gaping along natural or sutured lines
Sinus tract formation:	(Localised) formation of a fistulous tract towards vagina or skin, where there is no visible implant material in the vaginal lumen or overlying skin

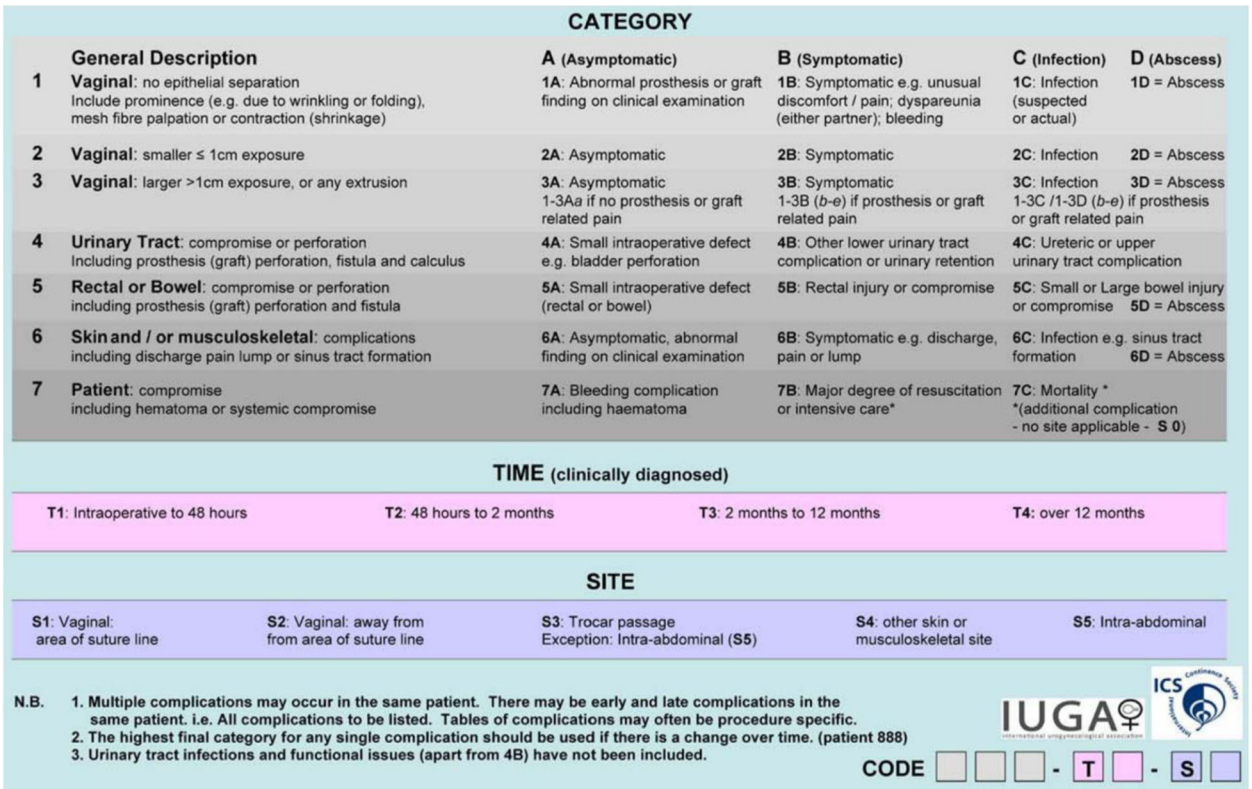

Fig. 1 IUGA classification of complications related directly to the insertion of prostheses (meshes, implants, tapes) or grafts in urogynecological surgery [10]

[49]. Chronic pain symptoms are likely to be multifactorial, perhaps initially driven by peripheral nervous system stimulation from the implant. The evolution of chronic pelvic pain after surgery may involve peripheral and central nervous system 'centralisation', with central changes implicated in the development of regional somatic and visceral pain symptoms. Referred pain is also commonly reported, believed to be a result of afferent neurons from different anatomic sites converging, with higher centres being unable to distinguish between these distinct inputs [50].

Mesh erosion may be asymptomatic or cause local discomfort, discharge and/or pain. In the absence of erosion, the aetiology of pain remains poorly understood. Some patients with chronic pain will be affected by mesh erosion or extrusion. For these patients, reasonable quality evidence supports excisional surgery [51]. In the absence of erosion or extrusion, there is very limited evidence to direct the management of pain attributed to mesh. Multi-disciplinary decision-making involving pain specialists, and careful counselling, are required until clear evidence-based pathways are developed [4, 45]. A recent systematic review has attempted to provide a management framework for mesh complications affecting patients and is discussed later [51].

Systemic Autoimmune Inflammatory Disorders (SAID) include fibromyalgia, rheumatoid arthritis and lupus, amongst many other conditions. Although anecdotally attributed to mesh, the background incidence of SAID in the female population undergoing mesh procedures is high. In a large study utilising a state-wide registry in the USA, Chughtai et al. estimated that 41% of women undergoing mesh-augmented surgery had an existing SAID diagnosis at the time of their operation [52]. In the same paper, at 6 years follow-up, there was no difference in rates of SAID amongst 2000 patients undergoing gynaecological mesh procedures when compared to matched cohorts undergoing screening colposcopy or vaginal hysterectomy without mesh. A recent study comparing 30,000 patients with hernia mesh to 70,000 control subjects also failed to illustrate an increased incidence of SAID in the mesh group [53]. Whilst these data provide some reassurance that mesh is not associated with SAID in the medium term, long-term studies are required.

TVM for SUI: safety and efficacy

Over the last decade, transvaginal mesh surgery for SUI in the form of the MUT has been widely regarded as the 'gold standard' surgical intervention for women [3]. It is the most common procedure performed for SUI and supported by numerous meta-analyses, and European and NICE guidelines [7, 54]. Table 3 outlines the subjective cure rates reported in two recent Cochrane reviews of the surgical management of SUI [55, 56].

A subgroup analysis of randomised controlled trials (RCT) comparing open colposuspension and MUT demonstrates superior subjective cure rates for the MUT. Colposuspension is less effective in the medium term (1 to 5 years; relative risk (RR) 1.35; 95% confidence interval (CI) = 1.11–1.64) and long term (more than 5 years; RR 1.19; 95% CI = 1.03–1.37) [56]. The reviews report inadequate evidence to make meaningful comparisons on QoL measures but report that the MUT is more cost effective than open colposuspension.

Concerning safety, the Cochrane reviews found favourable short- and mid-term data supporting the MUT. There was no evidence of a difference in complication rate as compared to open colposuspension at medium-term follow-up. The risk of mesh erosion after both RPR and TOR MUT is around 2% over this period. The RPR is associated with a higher incidence of visceral injury and voiding dysfunction. However, the TOR has significantly higher rates of groin pain (RR 4.12; 95% CI = 2.71–6.27), and in light of this, the Scottish mesh report recommended RPR MUT in preference to TOR [45].

A population study using UK Hospital Episode Statistics by Keltie et al. reported the 5-year complication rate following a mesh procedure for SUI to be 9.8% [57]. However, this included a wide range of complications, such as urinary tract infection, that are usually easily treated and equally common after non-mesh surgeries. Less than 2.3% of patients required readmission for complications from mesh surgery and 3.4% of women underwent readmission for removal or repair. A recent Scottish national database study supports the favourable safety profile of the MUT for SUI [58]. Compared with colposuspension, TVM procedures for SUI have a lower risk of immediate complications (adjusted relative risk [aRR] 0·44; 95% CI = 0·36–0·55). The two procedures carry a similar risk of further incontinence surgery (aRR 0·90; 95% CI = 0·73–1·11) and later complications (aRR 1·12; 95% CI = 0·98–1·27). Some commentators believe these data convincingly challenge the concerns raised regarding TVM for SUI [59]. Although a large body of high-quality evidence supports safety and efficacy of the MUT, the volume of surgeries undertaken has generated significant numbers of women with complications. This has led to media and political interest, some countries have banned mesh devices, and others such as England

Table 3 Subjective cure rate of procedures for SUI

Procedure	Subjective 1-year cure	Subjective 5-year cure
Retropubic route—MUT [55]	71–97%	51–88%
Transobturator route—MUT [55]	62–98%	43–92%
Colposuspension [56]	69–88%	70%

have implemented temporary restrictions. The future of the MUT remains uncertain whilst regulators and government agencies in these countries consider the plight of those affected by complications in the context of the available clinical data.

Transabdominal mesh for POP: safety and efficacy

Women without a uterus

Both European and UK guidelines support the use of sacrocolpopexy to treat PHVP [7, 60]. Vaginal alternatives include vault suspension to the sacrospinous or uterosacral ligaments, or introduction of a mesh device. Whilst widely adopted in clinical practice, the evidence base supporting sacrocolpopexy in preference to vaginal alternatives deserves proper scrutiny. It has been noted that there are twice as many published systematic reviews of apical prolapse repair than there are RCTs used within the reviews themselves [61].

A Cochrane review has strongly supported sacrocolpopexy as superior to vaginal alternatives [23]. Data from three RCTs suggested that women are more likely to be aware of prolapse after a vaginal procedure (14% vs 7%; RR 2.11; 95% CI = 1.06–4.21). From an anatomical perspective, authors found that 41% of women had recurrent prolapse after vaginal surgery as compared to 23% after sacrocolpopexy. However, the studies used within the Cochrane review are small and heterogenous and utilised vaginal procedures that are not in widespread routine use. The largest of the three studies included 53 patients and compared sacrocolpopexy to a total vaginal mesh device not widely employed (Prolift®) [62]. Half of the patients in one of the other studies by Benson et al. ($n = 42$) underwent concurrent hysterectomy, raising questions as to the applicability of these data in a review of PHVP [63].

Data from four RCTs showed an increased likelihood of repeat prolapse surgery for those who had a vaginal procedure (5–18% vs. 4%; RR 2.28; 95% CI = 1.20–4.32). This analysis used the data outlined above and outcomes from a study limited to 12 months follow-up, comparing sacrocolpopexy to uterosacral ligament suspension [64]. A retrospective comparative study has pooled data from three large RCTs ($n = 1022$), authors concluded that sacrocolpopexy offered an increased likelihood of successful prolapse treatment as compared native tissue vaginal alternatives at 24 months (odds ratio (OR) = 6.00, 95% CI = 3.45–10.44) [65]. Success was strictly defined as the absence of bothersome bulge symptoms, no prolapse beyond the hymen, and no subsequent retreatment of prolapse. However, a recent systematic review drew more cautious conclusions and did not find a statistically significant difference between the approaches [66]. Authors noted that evidence tended to favour laparoscopic sacrocolpopexy for some outcomes, such as satisfaction and length of stay.

Systematic reviews suggest that the risk of mesh erosion after sacrocolpopexy to be 2–3% [23, 66]. A large multi-centre study of sacrocolpopexy with median follow-up of 7 years modelled the risk of mesh erosion from available data, estimating the rate erosion to be 10.5% [67]. However, this study used a range of mesh materials according to the surgeons' discretion, including older heavier meshes that have been subsequently abandoned.

Meta-analysis suggests that dyspareunia is significantly more common after vaginal correction of apical prolapse as compared to sacrocolpopexy (RR 2.53; 95% CI = 1.17–5.50) [23]. This may be due to changes in vaginal axis or TVM used in some studies. Moderate quality evidence from the Cochrane review suggested a higher likelihood of reported urinary incontinence after vaginal procedures (RR 1.86, 95% CI 1.17 to 2.94). It is likely that this finding is also related to differences in postoperative pelvic floor dynamics related to the surgical approach, irrespective of whether a mesh-augmented or native tissue vaginal procedure is employed as a comparator.

It would appear that sacrocolpopexy is at least comparable to vaginal alternatives and potentially allows for better vault elevation optimising anatomical support and symptomatic success. Nonetheless, functional superiority across multiple domains, repeatedly cited in systematic reviews, may not be as definitive as previously thought.

Women with a uterus

Studies suggest that up to 60% would prefer to retain their uterus when undergoing surgery for uterine prolapse [68]. Mesh hysteropexy allows for uterine preservation by suspending the uterus to the sacral promontory. One RCT and one non-randomised prospective study have compared vaginal hysterectomy, the current 'gold standard' intervention, to 'wrap round' laparoscopic sacrohysteropexy, which is a specific surgical variant of the technique. These data demonstrated no difference in patient-reported prolapse symptoms at 1 and 2 years after surgery [69, 70]. Both the RCT and recent meta-analysis report superior anatomical outcome following laparoscopic sacrohysteropexy, although how this impacts on long-term objective and subjective outcome is unknown [71]. Larger cohort studies of this approach have shown 94% of patient report prolapse symptoms as 'much better' or 'very much better' in the medium term and a 5% risk of repeat POP surgery at 2.6 years follow-up [72, 73].

The UK's NICE guidance concluded that there were adequate safety and efficacy data supporting mesh hysteropexy, provided adequate clinical governance and

audit processes [74]. As a relatively emergent operation, much of these data are drawn from studies employing a laparoscopic approach. A recent meta-analysis and a systematic review reported difficulties in formal statistical analysis owing to the heterogeneity of outcome measures and surgical techniques [71, 75]. Nonetheless, the reviews demonstrated high rates of objective and subjective success, associated with excellent patient satisfaction rates, exceeding 90%.

As with some other applications of gynaecological mesh, there is a lack of high-quality, long-term safety data. The two largest cohort studies did not report any cases of mesh erosion at median follow-up of almost 3 years; however, other cohorts report an incidence of between 0 and 2.7% [72, 73, 76, 77]. One study reported three cases (0.6%) of symptomatic intra-abdominal adhesions attributed to non-peritonealised mesh [73]. Differences may well be driven by variations in surgical technique. Most studies have failed to identify dyspareunia or pelvic pain as an outcome measure. One study ($n = 110$) reported similar rates of dyspareunia and pelvic pain both preoperatively and postoperatively [72].

Subtotal hysterectomy with stump cervicopexy has been shown in some studies to offer superiority to hysteropexy, without the risk of mesh erosion associated with sacrocolpopexy. However, further research is required and meta-analyses have not supported such advantages. Rates of mesh erosion are higher with these procedures than uterine sparing or native tissue alternatives (OR 0.16; 95% CI, 0.03 to 0.97), without clear evidence of anatomical or symptomatic superiority [71]. This is reflected in the UK NICE guidelines that recommend the procedure is only undertaken in the context of research or with special clinical governance, consent and audit arrangements [78].

TVM for POP: efficacy and safety

A Cochrane meta-analysis in 2016 reviewed data from studies involving absorbable and permanent synthetic mesh, biological mesh and native tissue repair [25]. When compared to native tissue repair, data from 12 RCTs showed that mesh repair at 1 to 3 years is associated with a lower reported awareness of prolapse (RR 0.66; 95% CI 0.54 to 0.81). Additionally, women were less likely to undergo repeat surgery for prolapse if mesh was used (RR 0.53; CI 0.31 to 0.88). This is in contrast to the findings from the largest RCT to date, the PROSPECT trial [79]. This study did not report improved outcomes associated with the use of mesh, and no difference in validated patient-reported outcome measures or QoL measures at 1 to 3 years follow-up.

TVM for the primary repair of POP is not supported by the European guidelines, national mesh reviews or UK guidelines, due to high rates of mesh complications [4, 5, 7]. A Cochrane review has reported a composite risk of mesh exposure at 12%, with 8% of women undergoing surgical treatment [25]. Additionally, TVM was associated with higher rates of bladder injury and new-onset SUI. The PROSPECT trial also reported a mesh complication rate of 12%. A population-based cohort study that compared mesh and non-mesh procedures for POP in Scotland over a 20-year period found a substantially higher likelihood of late complications in the cohort having mesh repair of anterior wall POP (adjusted incidence rate ratio 3·15; 95% CI 2.46–4.04) [58].

Managing adverse events attributed to mesh

A recurrent theme in both the Scottish Report and UK Mesh Oversight Group Report was the failure of clinicians and regulators to recognise the existence of complications due to mesh. Many women report feeling as if their problems were dismissed or not taken seriously. The Scottish Report has outlined the need for multi-disciplinary working, patient-centred care, the collection of long-term safety and efficacy data, and the development of care pathways [5].

In an attempt to ensure high-quality care, 24 units in the UK have identified themselves as having the expertise to assess mesh complications. All centres have a multi-disciplinary team comprising of a gynaecologist, urologist, colorectal surgeon and pain management specialist, in addition to clinical nurse specialists and pelvic floor physiotherapists. There is no agreed guidance as to who should be referred to specialist centres. In the primary or secondary care setting, patients with signs or symptoms of erosion or extrusion should be referred to a specialist unit, as well as those not alleviated by conservative interventions. Further management is dictated by the route of mesh insertion, mesh type and the nature of the complication.

Cundiff et al. have systematically appraised the published evidence for the treatment of AEs attributed to gynaecological mesh, in an attempt to develop an evidence-based algorithm [51]. The management of complications lacks high-quality evidence to guide clinicians. Options include expectant and conservative management and partial and/or complete mesh excision. In the absence of convincing evidence of extrusion into or injury of adjacent organs, management requires careful consideration. Mesh excision is technically demanding and evidence to support surgery is lacking for many indications. Particularly in the context of pain, it is important that patients are aware of a paucity of supportive evidence before embarking on surgery. The management of complications attributed to mesh after sacrohysteropexy was not reviewed by Cundiff et al. For pain attributed to adhesions between bowel and exposed mesh, adhesiolysis and endoscopic re-peritonealisation has

been described with success [73]. For exposed vaginal mesh, authors have advocated expectant and office management with positive short-term results [76].

Conclusion

Gynaecological mesh has broadened the surgical options available for the treatment of pelvic floor disorders with numerous international and national reports appraising available data with respect to safety and efficacy [4, 6, 7, 45]. High-quality, long-term data support the use of TVM for SUI in the form of the RPR MUT. Sacrocolpopexy for PHVP is effective and safe, and may offer advantages over vaginal alternatives; however, meta-analyses deserve closer scrutiny. For uterine prolapse, good quality evidence from short-term randomised studies and cohort studies support the use of mesh hysteropexy. It is the most effective option for uterine-sparing apical prolapse surgery, with a low complication profile, although more high-quality, long-term data are needed. Evidence supports advantages of a laparoscopic approach for both procedures.

The use of TVM for primary repair of POP is not supported by the available evidence. Data from the most recent randomised trials have failed to show superiority over native tissue repair, and TVM for POP is associated with a high rate of mesh-specific SAEs. The treatment of these complications is complex, and insufficient evidence exists to confidently guide management. Reports have consistently highlighted the human cost of mesh-associated complications, and it is critically important that clinicians acknowledge this.

There has been a collective failure to regulate, appraise and audit many mesh devices used to treat POP and SUI. Going forward, further research is needed to clearly define treatment benefit and inform the management of complications attributed to mesh. In the interim, multi-disciplinary, specialist centres should provide individualised care that is evidence based where possible. Finally, clinicians in all care settings must recognise the myriad of symptoms and complications attributed to, and associated with, gynaecological mesh to ensure that women who require treatment receive the care they need.

Abbreviations

AEs: Adverse events; aRR: Adjusted relative risk; CI: Confidence interval; FBR: Foreign body response; FDA: Food and Drug Administration; IUGA: International Urogynecological Association; MUT: Mid-urethral tape; NICE: National Institute for Health and Care Excellence; OR: Odds ratio; PHVP: Post-hysterectomy vault prolapse; POP: Pelvic organ prolapse; QoL: Quality of life; RCT: Randomised controlled trials; RPR: Retropubic route; RR: Relative risk; SAE: Serious adverse event; SAID: Systemic Autoimmune and Inflammatory Disorder; SUI: Stress urinary incontinence; TOR: Transobturator route; TVM: Transvaginal mesh; TVT: Tension-free vaginal tape

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MI contributed to the project development and manuscript writing. AK contributed to the project development and manuscript editing. AV contributed to the project development and manuscript editing. All authors read and approved the final manuscript.

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