

On collagen, ageing and surgical treatment options following commercial kit withdrawals- a critical analysis

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Abstract: The banning of all mesh for prolapse by the FDA has failed to recognize that there is a major difference between mesh sheets applied behind the vagina for POP and repair of POP by shortening and reinforcing damaged suspensory ligaments, much as is used in the midurethral sling (MUS) which retains endorsement by the FDA. Mesh sheets interfere with the vaginal elasticity essential for function and may cause pain and massive urine loss post-operatively, in some cases; tapes far less so, as they have little contact with vagina and work by shortening and reinforcing damaged ligaments in the same way as the MUS operation. The main pathogenesis of POP is leaching out of collagen after the menopause. Weakened ligaments cannot support the organs so they prolapse. Only artificial collagenous neoligaments created by implanted tapes (as per the MUS) can create the new collagen required to repair these ligaments.

The major advances developed over the past 30 years for treatment of POP using these ligament repair techniques has in one stroke been abolished. The treatment of POP has been set back 100 years. In their twilight years, many women will suffer the consequences of loose posterior ligaments, major prolapse, urge, nocturia, chronic pelvic pain, obstructed micturition defecation and fecal incontinence. The FDA needs to reconsider its ban, at least for tapes, which are supported by individual, multicentre and long-term studies.

Keywords FDA; Mesh sheets; Mesh tapes; Neoligaments; Collagen; Menopause

COMMENTARY

The stimulus for this commentary was two news items, withdrawal of Bard's mini sling followed later by the announcement by the FDA of recall of all mesh kits, for pelvic organ prolapse (POP).

<https://news.sky.com/story/major-surgical-mesh-manufacturer-bard-to-pull-vaginal-implant-products-11657919>

<https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm636114.htm>

Both are grim reminders of Dr Nager's insightful 2016 predictions¹. The end point of his well-reasoned analysis was that despite overwhelming scientific evidence and recommendations from learned societies, even the midurethral sling (MUS), the most validated operation in history, was in danger of disappearing.

Our aim in this brief commentary is to elaborate on three main points from Nager's article and add a 4th, the rationale behind the MUS, collagen loss in the PUL suspensory ligament in an ageing female population.

1. Midurethral slings 'MUS', tape surgery, is very different from mesh sheets used for repair of pelvic organ prolapse.
2. MUS is minimal surgery. Complications are far less than those of major surgery; no surgery for MUS is disastrous as regards QOL.
3. Disappearance of midurethral slings from the market is a dire situation for women.

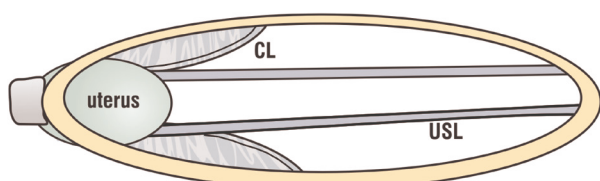


Fig 1. Uterine prolapse caused by weakened level 1 supports. If collagen leaches out of the cardinal (CL) and uterosacral (USL) ligaments, they will elongate. Shortening and reinforcing of ligaments is required. Critical for any long-lasting repair is the quality of ligament collagen.

Collagen 1 (breaking strain 18,000 lbs/sq inch) is the key structural component of the body. At menopause, there is a twofold increase in excretion of urinary collagen I breakdown products, which persists for the entire postmenopausal period². Collagen loss causes joint, osteoporosis and organ prolapse problems, the latter generally attributed to loss of level 1 supports, fig 1. Collagen I is the major structural component of ligaments, (breaking strain 300mg/mm²); collagen III, weaker, more elastic, allows vagina (breaking strain 60mg/mm²) to stretch extensively (VIDEO Xray <https://youtu.be/eiF4G1mk6EA>). We can deduce from collagen breakdown data², that if collagen deficiency in a structural ligament is the cause of a pelvic floor problem, whether it be prolapse or symptoms, no "native tissue repair" will fix it. New collagen needs to be created.

The original hypothesis which led to the MUS was that SUI (stress urinary incontinence) was mainly caused by collagen-deficient pubourethral ligaments. A new surgical principle, using an implanted tape to create artificial collagenous pubourethral ligaments, became the basis of the MUS, now implanted in >5,000,000 women¹.

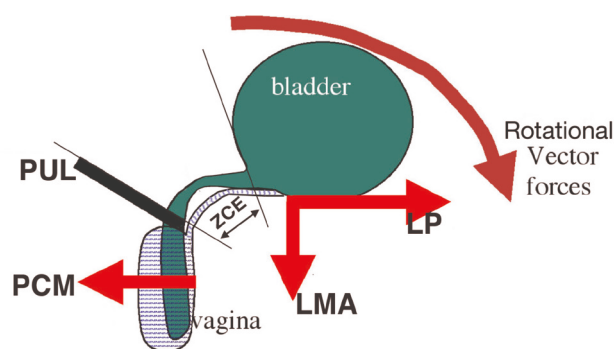


Fig 2. Normal urethral closure in the female during coughing or straining
PCM = m.pubococcygeus. LP= levator plate; LMA= conjoint longitudinal muscle of the anus; PUL=pubourethral ligament. ZCE (zone of critical elasticity), allows separate action of forward and backward vectors.

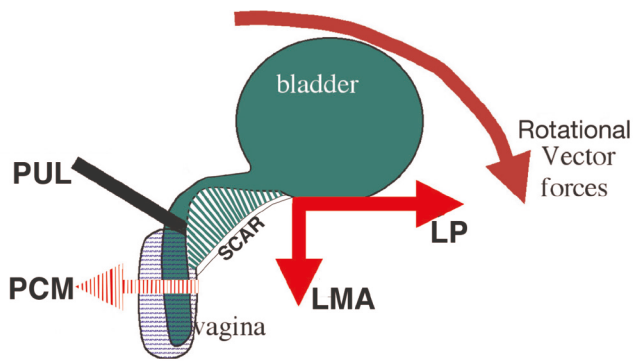


Fig 3. Xray Normal patient, sitting position, straining. Oppositely acting vector forces during straining (arrows) indicates the imperative of an elastic zone at ZCE so as to allow the vector closure forces to operate independently. Labelling as in 1A. CX=cervix; R=rectum; B=bladder; USL=uterosacral ligaments; S=sacrum.

Added to Nager's statement¹ that midurethral slings (MUS) are very different from mesh sheets as they implant much less mesh is the effect of mesh on vaginal elasticity. The VIDEO XRAY <https://youtu.be/eiF4G1mk6EA> shows that vagina requires very significant elasticity to implement its functional roles during straining, micturition, squeezing upwards; in contrast, the vaginal anchoring points, pubourethral ligament and uterosacral ligaments remain immobile. Placing a mesh sheet behind vagina, or removing a segment of vagina ("native tissue repair") will only fibrose vagina. One complication from fibrosis is sudden massive incontinence immediately after mesh sheet implant. Its cause, "Tethered Vagina Syndrome" (TVS), explains ongoing massive urine loss following Obstetric Fistula closure in 50% of patients³.

Pathogenesis

Excess scarring, whether from fistula or mesh fibrosis may "tether" (connect) the more powerful posterior muscle closure forces to the weaker anterior forces, so the urethra is forcibly pulled open on the signal to close, resulting in massive uncontrolled urine loss³, figs2&3. A skin graft to the anterior vagina restores elasticity and function³, fig4. Tapes rarely cause this problem as they attach directly to the skeleton with minimal contact with vagina.

Is there a difference between tapes and mesh sheets?

Mesh sheets work by blocking organ descent; post-op. 2D ultrasound reveals continued presence of the prolapse. The MUS tape principle, fig1, works by shortening and reinforced the elongated USLs, with a posterior sling, literally a "reverse TVT." A sling in front of cervix reduces post-surgical cystocele. A tensioned mini sling repairs all 5 suspensory ligaments, with 79% anatomical cure rate for major prolapse at 5 years, using 3rd generation lightweight tapes with no vaginal excision and low erosion/"surfacing" rates.

"Native tissue" repair

There is no greater condemnation of 'native' vaginal repair than the 2016 Lancet PROSPECT study. Failure rate at 6 months was >85%. CL/USL plication may be a better "native tissue" option. Evidence for this is from an RCT, CL/USL plication against Tropicium which was stopped by the St Petersburg University EC because of rapidly deteriorating cure rates in the post-menopausal

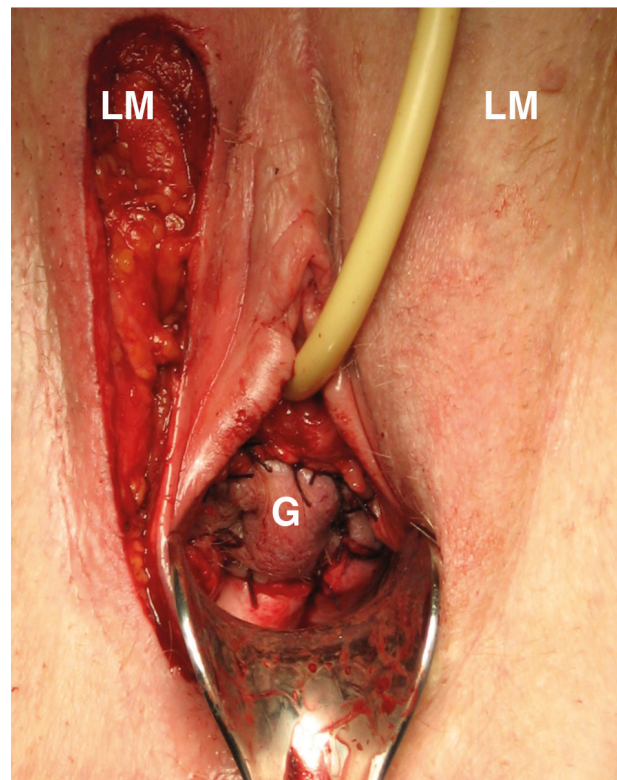


Fig 4. Augmentation of ZCE with a skin-on Martius Graft restores independent movement of the vector forces. LM=labium majus ; G=graft sutured to bladder neck area of vagina to cover the tissue deficit.

arm, 17% cure (n=48) at 18 months post-op, as against 80% cure for pre-menopausal women (n=40), (Shkapura, as yet unpublished data). The high failure rate was attributed to collagen leaching out postmenopausally from the ligaments, consistent raised collagen1 breakdown products².

CONCLUSIONS

It is unfortunate that whatever the expert opinion guiding the FDA's actions, it was ignorant of the fact that posterior slings for POP work in exactly the same way as the midurethral sling which it has endorsed. Posterior slings do not have the same severe pain or tethered vagina syndrome complications as mesh sheet kits. This FDA decision will have severe unintended consequences. After the menopause, women lose the collagen which supports their ligaments². Weak ligaments cannot be repaired by any type of "native tissue repair". They can only be repaired by the artificial neoligament technique developed on experimental animals in the years 1987-8 at Royal Perth Hospital⁴, the very method endorsed by the FDA for cure of SUI. The major advances developed over the past 30 years for treatment of POP using these ligament repair techniques has in one stroke been abolished. The treatment of POP has been set back 100 years. In their twilight years, many women will suffer the consequences of loose posterior ligaments, major prolapse, urge ,nocturia,chronic pelvic pain, obstructed micturition defecation and fecal incontinence. The FDA needs to reconsider its ban, at least for tapes, which are supported by individual, multicentre and long-term studies⁵⁻¹⁹.

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NOTES

VIDEO <https://youtu.be/eiF4G1mk6EA> Note the enormous elasticity of the vagina which is required to squeeze (lift up) the organs and also during micturition.