Review

Transvaginal mesh for POP: an endless story with a strong present and future in Italy and in all Europe

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Abstract: Vaginal vault prolapse is observed with increasing frequency in the era of increasingly aging populations. Various surgical techniques have been established, varying in performance, difficulty, outcomes and most importantly complications. A bilateral sacrospinous colposuspension technique (BSC) with a corresponding mesh prosthesis was developed using a direct I-Stitch fixation of the 38 microgram mesh from the vaginal apex or uterine cervix to the sacrospinous ligament or the parasacral tendinous region for the treatment of an anatomical central pelvic floor defect. As a minimally invasive approach with the potential for conservation of the uterus, this technique should be applicable to all age groups including the increasingly frequent elderly patient with significant co-morbidities.

Keywords: Pelvic organ prolapse; POP; Mesh; Fascial surgery; Women health; FDA; Urogynaecology

ONCE UPON A TIME...

Like all fairytales, this story will also have a happy ending. This article analyses the use and regulatory history of non-absorbable meshes implanted by vaginal way for the treatment of Pelvic Organ Prolapse (POP). The surgical mesh is a medical device used to provide additional support when repairing weakened or damaged tissue, most often made in polypropylene.

We will now outline a suite of guidelines and recommendations developed on the topic and we will assess its key strength and weakness points.

2016 COCHRANE REVIEW

In 2016, the Cochrane Library published a review of native tissue versus polypropylene absorbable meshes to determine the safety and effectiveness of surgery for anterior compartment prolapse[1]. The review found that 18% to 30% of women would be aware of prolapse after native tissue repair, versus only 13% of women after polypropylene mesh repair. Recurrent anterior compartment prolapse was more likely after native tissue repair compared with polypropylene mesh repair (RR 3.01, 95% CI 2.52 to 3.60; 16 RCT; 1976 women; I^2 = 39%; moderate-quality evidence), suggesting that if recurrent prolapse occurred in 13% of women after mesh repair, 32% to 45% would have recurrence after native tissue repair. Repeated surgery for prolapse, stress urinary incontinence or mesh exposure (composite outcome) was less likely after native tissue repair (RR 0.59, 95% CI 0.41 to 0.83; 12 RCT; 1,527 women; I^2 = 45%; moderate-quality evidence), suggesting that if 10% of women require repeated surgery after polypropylene mesh repair, 4% to 8% would do so after native tissue repair. For de novo stress urinary incontinence (SUI) and dyspareunia (de novo) there was few or no differences between groups (RR 0.54, 95% CI 0.27 to 1.06; 8 RCT; n = 583; I^2 = 0%; low-quality evidence).

FDA WARNINGS AND BOSTON SCIENTIFIC STUDIES

On January 5 2016, the FDA, after previous warnings since 2011[2], reclassified surgical mesh for transvaginal repair of POP into class III, and required submission of premarket approval (PMA) applications. The FDA mandated that premarket approval applications be filed by July 5 2018 for any surgical mesh marketed for transvaginal POP repair. Additionally, for women who had received transvaginal mesh for surgical repair of POP, routine check-ups and follow-up care were recommended, with no need to take additional action if they did not experience complications or symptoms. For women planning to have a mesh placed transvaginally for the repair of POP, the FDA recommended discussion of other treatment options with their doctor.

On April 16 2019, the FDA determined that the manufacturers Boston Scientific and Coloplast had not demonstrated reasonable assurance of safety and effectiveness for these devices. Due to this decision, no FDA-approved surgical mesh products for transvaginal repair of prolapse are currently available in the United States. Following these FDA changes, a literature review by Rizvi and Chughtai[3] aimed to look at the role of graft and mesh in vaginal surgery. They conducted a search for English-language articles published during 1997 to 2016, using MEDLINE, PubMed and United States National Library of Medicine databases, reviewing approximately 50 papers. The literature review provided a new insight regarding safety of mesh, demonstrating how polypropylene mesh is safe for vaginal surgery if used by experienced surgeons. The safety of mesh becomes compromised in the hands of commercial surgical kit providers, and therefore it was recommended all the new mesh tailored kits should undergo evidence-based trials to then be safely used worldwide. The FDA decision therefore seemed to be ill informed by not distinguishing between high-volume centers from low-levels ones, therefore overlooking the surgeons' level of experience. Furthermore, the negative attitude of the FDA stemmed from old generation meshes that do not share much with the modern ones except for the material, polypropylene. Cochrane itself stated in 2016 no recommendation can be made on current macroporous and ultralight meshes based on the current available reviews. This lack of clear direction is in turn reflected on patients, lawyers, and forensic doctors who never distinguish, often for opportunistic reasons, between the different available materials. Furthermore, the market seems to have failed to notice that the FDA did not impose any ban on the prolapse marketing in the USA, but simply requested additional studies from the two main companies marketing mesh in the USA, Coloplast and Boston Scientific. When these companies failed to comply and decided to exit the market due to urogynaecology representing a residual part of their revenues, this created a *de facto* unavailability of the devices in the country.

A recently published study by Boston Scientific[4] confirmed that in centres with high surgery volumes the results of the treatment with mesh are highly satisfactory. For Uphold Lite Vaginal Support System the percentage of anatomical success at three years was 83.3% compared with 73.8%

with native tissue repairs, particularly for the anterior compartment (97.6% vs 87.1%) and re-operations for prolapse (0.9% vs 3.7%). For apical compartment, the success rates are slightly lower than those of fascial surgery (95.2% vs 97.6%), as well as the subjective success rate (87.5% vs 92.6%) and a re-operation rate for mesh exposure of 1.3% by Altaman[5]. Nonetheless, even if safety and effectiveness remain higher with mesh compared to native tissue, Boston Scientific has renounced the American market due to the FDA lack of clear indications.

SCENHIR, 2017

In 2017 the Scientific Committee on Emerging and Newly Identified Health Risk (SCENHIR)[5] published an opinion on safety of surgical meshes used in urogynaecological surgery. This did not limit itself to the assessment of the current use of mesh, but also made recommendations. These included the idea that material properties, product design, overall mesh size, implantation route, patients' characteristics, associated procedures (e.g. hysterectomy) and surgeon's experience are aspects to consider when choosing appropriate therapy. The implantation of any mesh for the treatment of POP via the vaginal route was recommended to be considered only in complex cases in particular after failed primary repair surgery, and that for all procedures the amount of mesh should be limited where possible. A certification system for surgeons was promoted based on existing international guidelines and established in cooperation with the relevant European Surgical Associations. Therefore, SCENHIR 2017 stated no prohibition for use, but limited it to complex cases, including relapses, advanced cases, and patients at high risk of recurrence.

ICI, 2016

The International Consultation on Incontinence (ICI) in 2017[6] condensed the 2,000 pages of analysis of POP in a 20 pages summary, focusing on the meshes for the anterior compartment in the first surgery. The ICI considered the results from the Cochrane review, but also included additional studies which found much lower erosion rates, highlighting the contradictions in the FDA recommendations.

Newer lightweight transvaginal polypropylene mesh products have been introduced to decrease the complication rate, specifically mesh erosion. Among the ICI quoted studies, Altman et al[7] and similarly, De Tayrac et al[8] found in 79 women with grade 3-4 cystocoele an anatomic success rate of 95%, a satisfaction rate of 98% and a mesh exposure rate of 1.3% using a lightweight (28 g/m^2) polypropylene mesh (Surgimesh® Prolapse Xlight, Aspide Medical, France) at three years. Despite the current negative sentiment surrounding transvaginal meshes these newer lightweight meshes with very low rates of erosions require further evaluation.

GUIDELINE OF THE DGGG, SGGG E OEGG, 2016

In 2016 the German, Austrian and Swiss gynaecological societies developed guidelines for the treatment of POP[9]. These were based on the new generation of meshes with macropores >75µm and ultra-light, ≤32g/m^2, which also integrate the necessary apical fixation to the sacrospinous ligaments and are single-incision, avoiding the need for a transobturator insertion of the anchoring arms. From international studies on the treatment of anterior compartment defects, including studies not included in the Cochrane review in 2016, cumulative success rates of 93%, erosions of 8%, chronic pain and dyspareunia de novo of 7% were detected. The use of synthetic nets in the anterior compartment was therefore shown to reduce relapses of anatomical and subjective prolapse, even though no positive influence on quality of life was found.

Mesh use for the repair of posterior defect was considered appropriate as part of the guidelines, but not as a routine practice, as no supporting clinical studies are available. The extensive systematic review recommendations of these guidelines are based on an literature and practical experiences and evaluation of current literature and practical experiences in Germany, Austria and Switzerland. Interestingly, in the development of these guidelines the expert opinion of surgeons who perform mesh implantation was considered, representing an exception in the space.

CANADIAN GUIDELINE, 2017

The Canadian guidelines published in 2017[10] highlighted how better recurrence rates were achieved with the use of mesh compared to fascial surgery without improving the quality of life. It was not clearly outlined though whether the re-intervention for recurrence did in fact worsen the quality of life. However, 12% erosion rate was reported with meshes, very differently from what was obtained in other comparable recent studies. Finally, the use of local oestrogen were found not to protect from erosions, whereas smoking and hysterectomy were identified as risk factor for small versus extensive erosions, a discriminating element of gravity and therefore crucial in prolapses.

EUGA, 2017

The European Urogynaecology Association (EUGA)[4] in 2017 highlighted how current data suggest the use of non-autologous durable materials in surgery has well-established benefits, but also significant risks, which are specific to the condition and location they are used for. Exposure in the vagina, shrinkage, erosion into other organs and other various mesh-related complications have been described, including infection, chronic pain and dyspareunia. According to the EUGA, patients need to be aware of the alternative therapy and potential risks and complications of this therapy. Synthetic mesh for treating prolapse should be used only in complex cases with recurrent prolapse in specialist referral centres. These conclusions were largely developed based on the PROSPECT and PROSPERE trials, which, as outlined further in the article, contained significant bias.

NICE, 2019

The National Institute for Health and Care Excellence (NICE)[11] reiterated the public concern about the use of mesh procedures, though contradicting the position of the government and the NHS on the period of "high vigilance restriction". The NHS stated that some evidence of benefit was present with the use of mesh, but limitations were present in terms of long-term effectiveness and adverse effects. In particular, the true prevalence of long-term complications was considered to be unknown. The NHS recommends to promote informed preference and shared decision-making when a woman is considering a surgical procedure for pelvic organ prolapse. This position, very different from that expressed by NICE in 2017, has raised a degree of dismay in Great Britain[12], but it supports the use of vaginal meshes as a safe and effective device and procedure for the treatment of POP.

REACTION FROM UROGYNAECOLOGICAL WORLD: CHANGE.ORG PETITION, IUGA TOOL AND NICE BBC INTERVIEW

The role of mesh in pelvic prolapse surgery has been under critical debate. A petition named "Women's Health Physicians: Ensure Ethical and Fair FDA Mesh Research" promoted through change.org and sent to Ben Fisher, the Director of the FDA Division Urologic Devices, represented an interest-

ing way to support the mesh use and a movement supporting the fact that provide an efficient and effective treatment for complex or recurrent prolapse, able to preserve the uterus compared to procedures such as hysterectomy (change.org).
In response to the issues raised around mesh use, the FDA mandated 522 post-market studies. These studies were conducted with great effort, expense, and with an ethical understanding that the 3-year assessment described in the study protocols would provide the key outcomes required to answer clinical questions and determine the best regulatory decisions. The physicians involved in these studies believe that FDA action occurred primarily due to outside pressures, and that these factors will ethically compromise interpretation of the 522 trials. More than 6,500 physicians and advocates have made their voices heard by supporting this petition, but the voices of countless patients remain the most important untold part of the story, and these voices have remained largely silent. This can change, starting today.
Indeed, in May 18, 2019 the International Urogynaecological Association (IUGA) has launched "Have Your Say: Your Pelvic Floor Story" (https://www.yourpelvicfloor.org/your-pelvic-floor-story), a new online tool within the IUGA website inviting women to share their stories, maintaining the privacy but allowing for submission of video stories and public sharing, depending on a patient's personal comfort level. This can finally allow millions of successful outcomes to be accurately represented and reported.
Another interesting intervention in April 2019 in support of mesh was done by Anna Collinson and Jessica Furst in the BBC Victoria Derbyshire programme, reporting that "vaginal mesh ban can be lifted with changes". Controversial vaginal mesh implants can be offered again on the NHS in England, as long as certain conditions are met, according to the health watchdog NICE. Nonetheless, the NHS is not compelled to act on the guidelines - which are for England only - and the "pause" on vaginal mesh surgery remains in place.

FROM THE NEW YORK TIMES, JULY 14, 2019
"WOMEN WHO SUED MAKERS OF PELVIC MESH ARE SUING THEIR OWN LAWYERS, TOO"
A nearly decade-long legal battle over the harm inflicted on tens of thousands of women by surgically implanted pelvic mesh, totaling about $8 billion in settlements, is moving away from manufacturers and towards the lawyers who helped women bring their cases to court. Indeed, these women have started suing their lawyers, accusing them of improperly enriching themselves with excessive fees or stretching themselves too thin to properly handle the pelvic mesh cases.
A potential class action lawsuit filed in July 2019 in a state court in New Jersey contends that the 40% fee a group of law firms charged about 1,400 of their clients violated state law. The law caps fees in personal injury lawsuits at about 33%. A separate suit filed in federal court in Houston alleges that another group of firms took too many cases, missing filing deadlines for hundreds of women, potentially reducing the value of their claims against the mesh manufacturers to negligible amounts.
A half-dozen medical device manufacturers, including Boston Scientific and Johnson & Johnson, have agreed to pay billions of dollars to tens of thousands of injured women. But one of the most troubling aspects of the mesh cases involves pushing women to have the implants removed, a procedure that is sometimes necessary but can be rather complex, as the mesh is made of a fibre designed to bond with human tissues. In addition, the removal of the mesh in itself can become an exploitable profitable business. In June 2019, federal prosecutors in Brooklyn indicted a doctor and a consultant in a scheme to profit from removing mesh implants. A lawsuit filed in a federal court in Houston raised a similar issue, with three women contending that lawyers from Clark, Love & Hutson and several other Texas firms helped arrange for them to have costly removal procedures that would increase the value of the women's claims and lift the lawyers' fees.

PROSPECT AND PROSPERE STUDIES
When discussing the safety of mesh in pelvic prolapse, two studies are most often cited, namely PROSPECT[13] and PROSPERE[14].
PROSPECT (PROlapse Surgery: Pragmatic Evaluation and randomised Controlled Trials) was the evaluation of two pragmatic, parallel-group, multicentre, randomized controlled trials conducted in a mix of secondary and tertiary centres in the UK. This study, representing the largest RCT to date on mesh, shows no advantages of vaginal repair reinforcement with mesh material in terms of anatomical cure and improvement of quality of life with higher rate of post-operative complications in comparison to standard surgery. Due to these findings the Authors concluded mesh use should be avoided in the surgical treatment of primary anterior or posterior compartment prolapse, except for specific categories of women with high risk of prolapse-recurrence. However, the detailed characteristics of such patients are not clearly defined, generating various misleading interpretations of this key message.
Most importantly, despite the large number of patients included in the study and its rigorous randomization protocol, PROSPECT results are potentially influenced by different sources of bias deserving a thorough analysis in order to avoid misinterpretation of evidence. Among others, no distinction between anterior e posterior defects is used, nor a subgroup analysis conducted, too many patients with functional and less inclined to improvement defects are included, such as faecal incontinence and severe dyspareunia, type of apical prolapse repair is varied, possible concomitant hysterectomy is included, and no distinction nor subgroup analysis is conducted on the heterogeneity of meshes in term of weight, size and surgical placement.
In response to these significant sources of bias that were overlooked in the study, we drafted a letter to the editor of the Lancet journal, which was unpublished due to a delay in submission – and not due to its content – titled *"Mesh use for transvaginal prolapse surgery: real 'evils' or viable alternatives to standard repair?"*.
In this letter, we outlined how the interpretation of results could potentially be misleading due to the lack of adequate definition of the patient population. In addition, we outlined the significant sources of bias which were not addressed in the study, detailing how each of them could substantially impact the results of the study.
A single large study such as PROSPECT can hardly lead to conclusive recommendations regarding the superiority of standard vaginal repair in comparison to mesh repair, whose application is supported by more than 20 years of scientific research, particularly with its level of heterogeneity and bias.
The second study often cited when discussing mesh effectiveness is PROSPERE (PROSthetic PElvic organ prolapse REpair). This was a randomized controlled trial conducted in 12 French hospitals; the main objective of the study was to compare the morbidity of laparoscopic sacropexy with vaginal mesh for cystocele repair. Also this study has significant issues undermining the validity of its results.
As a response, Dr M. Bologna, Dr A. Vitagliano and Dr M. Cervigni of the Associazione Italiana di Urologia Ginecologica e del Pavimento Pelvico (AIUG) wrote a letter on behalf of the organization, published on European Urology and titled

"Is There Enough Evidence To Prove Higher Safety of Laparoscopic Sacropexy in Comparison to Vaginal Surgery for Cystocele Mesh Repair?"[15]. Quoting from the letter:

We read with interest the article by Lucot et al. The authors conducted a multicentre trial (PROSPERE) to compare 1-yr morbidity between laparoscopic sacropexy (LS) and vaginal mesh repair (VMR). In view of their results, the authors concluded that "LS is safer, sexual function is better preserved and it can be performed, whenever possible, as first-line surgical treatment for cystocele mesh repair".

We want to commend authors for their efforts in undertaking such a unique and much needed trial. Nevertheless, we feel it is important to point out some aspects of the PROSPERE that may help readers in a more cautious interpretation of the results.

First, as honestly recognized by the authors, they found a statistically nonsignificant result for the primary outcome of grade II or higher postoperative complications (p=0.088). As their study was adequately powered to detect a statistical difference for the primary outcome (but not for secondary ones), a fully substantiated conclusion would be that LS and VMR were similar in terms of grade II and higher postoperative complications[16].

Besides type II error in the analysis of secondary outcomes and error for intention-to.treat approach we were surprised to note that some specific grade III complications (umbilical abscess, vaginal polyp, macroscopic haematuria after 6 wk) were judged as being definitely correlated to VMR[17,18]. *But what is of serious concern is that inclusion of an umbilical abscess in calculation of VMR-related complications (Table 3 in Lucot's article*[14]*)may suggest an inadvertent shift of a patient from the original allocation group (LS) to the other one (VMR).*

Finally, the heterogeneity in mesh composition (polypropylene alone or combined with absorbable components), kits, and techniques for VMR (variable mesh dimension, with or without sacrospinous fixation), as well as the considerable number of LS requiring a conversion to the vaginal route (n=7) may have affected comparison between the groups in terms of severe complications. Nevertheless, the total number of events (n=12) would in any case have been insufficient to draw any firm conclusion about the safety of each technique[14].

ITALIAN DEBATE INSIDE THE AIUG

These studies and international controversies have sparked a debate within the Italian UroGynecological Association (AIUG). It all begun with a request to the 2019 National Congress of the AIUG in Lecce for the association to take a position on the issues and to assume responsibility of the use of mesh in Italy, bearing in mind that there were no significant reports of mesh related complications in the country. Many Italian surgeons use mesh in the first surgery for POP and, so far, the Italian Ministry of Health has not received reports of the danger of using vaginal meshes and therefore there are no limitations in their use.

On behalf of the Scientific Secretary, I put forward the request for a "Position Paper" from the AIUG Board which, although not bearing a legal medical relevance, certainly would have reassured all the doctors who use this therapeutic strategy, and provided support in front of the Health Directorates of the Hospitals and patients suffering from POP. The agreement was that if the majority had approved the Position Paper, this would be published on the AIUG Association website.

The Position Paper prepared together with forensic doctors reads as follows:

Italian doctors can use, even if not routinely, synthetic material meshes for treatment of genital prolapse by vaginal way in first and second surgery in patients with correct indication, recorded in the Data Base (SRD) AIUG, with specific and detailed informed consent and with meshes certified for the purpose.

This would have been a significant opportunity for the AIUG to be the spokesperson for a scientific community wishing to pursue a research for the best cure for our patients.

However, after the approval by the majority of the Board, the scientific secretary objected to the publication of the statement on the AIUG website, proposing a modification, by adding the following statement at the beginning of the Position Paper:

Despite the current international concerns about the use of synthetic mesh.

It was the belief of the proponents that otherwise the Position Paper would have exposed doctors to legal medical disputes.

All this has generated a discussion that involved 90 Italian gynaecologists and urologists, activating an interesting online debate according to a modern style of discussion in which the Aristotelian principle "Ipse dixit" ceases to be valid. For all I quote a reply by Dr. Daniela Viviani (Gynecology Department, Montecchio Emilia, IT):

I would like to express only one thought. I believe that the indecision is the less protective attitude from a medical-legal point of view. I also believe that those who enthusiastically supported F. Deltetto's initiative are professionals who, in their treated cases, in small or large numbers, related to prosthetic surgery, have not recognized all the dangers feared by the FDA. Perhaps in Italy those who "adventure" in prosthetic surgery have always done so after having acquired a good expertise in fascial surgery, with good reasons and with religious respect for the rules of prosthetic surgery. I therefore believe that we are ready to face any struggle for approving our Position Paper.

Other colleagues have asked for guidelines to be developed, others for a short paper to be submitted to the AIUG board. My personal position on the matter was summarised in a question I posed: does the AIUG want to defend surgeons or not?

In addition, we reported to the group that the 2017 German, Austrian and Swiss guidelines state that the vaginal meshes for prolapse can be used in first and second surgery with the correct indications, and therefore we would not be "adventuring" nor failing to recognize international trends and recommendations.

Some have questioned the validity of the online voting mechanism that was used to communicate the approval of the Position Paper by the Board. Nonetheless, this is routinely used to gather consent and it gives clear evidence of unbiased and unpressured personal opinions. Finally, the publication on the AIUG website is only a formal and transitory formalization of the support, as the European MDR of 2020 will clarify the European positioning on mesh use.

At this point in the discussion, a clarification on the words used was requested – not routinely, correct indication, registration on the SRD Data Base, as informed consent, CE certification.

A finalized Position Paper was developed, which became the flag of a group of 60 experts (Mesh Italian Skilled Surgeons) (MISS). The new Position Paper reads as follows:

The meshes in synthetic material can be used by skilled surgeons in vaginal surgery for the treatment of some situations of genital prolapse (degree equal to or greater than 3, lateral detachment, relapse prolapse or with risk factors for recurrence - collagen diseases, chronic bronchopneumopathy, physically heavy work , etc). The cases treated must be recorded in a certified Data Base, as a guarantee of the access procedures, the preoperative checks and the correct

follow up. The treatments must be preceded by the signing of the specific informed consent and precise information to the patients, with the of meshes certified for the purpose and with the CE mark.

The debate continued with the statement of someone that no one can "ban" a method if not the professionals. The important thing is "not to wait for Godot" as a Becket comedy. Others talk about "open source" medical dynamics.

In July 2019 an Opinion Statement was published on the AIUG website by the Scientific Commitee. This statement outlined a position that not only appears unfavourable towards meshes implantations, but it will also give a potential tool to forensic doctors in lawsuits when arguing against surgeons. This Opinion Statement was actually defined as the AIUG Scientific Committee positioning, rather than guidelines.

Some AIUG members promptly expressed their disagreement, particularly Dr Antonello Azzena (Gynaecology department, Conegliano Veneto, TV). He expressed specific reservations about the nine points the Opinion Statement. Following, an analysis of the 9 points and the criticisms:

1. Better anatomical results are reported with prosthetics, but no evidence of improved quality of life for the patients is shown - if it is true in the treatment of the anterior prolapse the anatomical results are superior with the synthetic vaginal mesh and the percentage of relapse with facial surgery is higher, we should consider improving how we evaluate quality of life for prolapse surgery, as it is clear the current questionnaires are not able to capture the nuances of this patients' quality of life.
2. Mesh-related complications are 10-15% and often not definitively treatable - it would be useful to once and for all specify what are the key complications included in such assessments, and to subgroup them by gravity. To affirm mesh-related complications are 10-15% of all cases only raises concerns in doctors, patients and ultimately forensic doctors; truth is that new generation meshes have complication rates of 2-5%, as reported in the numerous sources quoted above.
3. Based on the evidence, the transvaginal implantation of synthetic prosthesis as first-line treatment of vaginal prolapse mono- or pluricompartimental should be discouraged, in the absence of specific risk factors - this represent a misleading medical lexicon, not really affirming whether they can or cannot be used (as it was originally requested in the MISS Position Paper), simply offering a legal tool for those suing surgeons for malpractice. In addition, to affirm that specific risk factors (identified in Friedman et al[19] as weight, stage 3-4, familiarity, avulsion to elevation and width of vaginal hiatus) would then allow the use of meshes do not clarify the Committee position, as most prolapses expert surgeons treat with meshes are indeed a grade 3 or superior. Nonetheless, this seems not to represent a good enough reason, according to point 8.
4. The use of meshes can be useful and appropriate in patients with specific risk factors, but in the apical defects then transabdominal route is better - again, this statement does not really represent a clear positioning, as according to the previous point the use of meshes for patients with specific risk factors seems actually recommended. In addition, the claim that the transabdominal route is free of significant complications related to the prosthetic material, and therefore preferable, overlooks crucial aspects such as mesh erosion, and issues related to the surgical practice, operating time and type of anaesthesia. Patients should be informed of all risks, whereas it appears from the statement that the vaginal route is more risky.
5. The treatment of prolapse relapse represents an indication for the use of vaginal meshes if it includes adequate informed consent and adequate surgical skills of the operator - it seems curious how the statement affirms the centrality of expert surgeons for the good success of the implant procedures, but also how no expert surgeon opinion was not considered by the Scientific Committee, and rather the evidence from bias studies such as PROSPECT and PROSPERE was considered more informative.
6. Most mesh kits have an apical attachments mechanism, but the in the apical prolapse no difference is present between native tissues and prosthesis vaginal surgeries - this statement does not find grounds in the other guidelines, as outlined in this article. It is also necessary to understand what is the vaginal referred to, whether with suspension of the sacrospinous ligament or uterosacral ligaments, with device or without. Every surgery has specific complications and to flatly criticize the use of vaginal meshes without any specification only increases the level of confusion in the already murky guidelines environment. This point of the statement also affirms that in the multicompartimental defect the abdominal route has a clear efficacy with no significant complication rate, even though no bibliographic evidence is provided to support such statement.
7. Synthetic meshes should not be used for the treatment of the posterior segment, except for exceptional cases - the highly problematic posterior vaginal segment has not yet found a certain surgical solution. Nonetheless, to affirm the use of meshes should be avoided completely without considering the specific case highlights the prejudicial and unscientific attitude, which only considers the anatomic results ignoring the functional one.
8. New devices and new meshes - this point of the statement is quite ambiguous, as it argues that modern meshes are likely to improve performances, but at the same time it affirms their use must only be in the context of controlled clinical studies, approved by ethics committees. The AIUG Scientific Committee seems unaware of the current Italian landscape, where it is extremely hard to obtain approval from ethical committees, in particular for vaginal meshes. In addition, all meshes used in Italy have been approved by the European Union. Therefore, not only the Committee is not using the available literature to back its members, but it further weakens them in the face of legal medical disputes. Moreover, limiting the use of meshes to controlled clinical studies would significant damage the companies currently on the market, a damage they could potentially seek compensation for.
9. The AIUG is committed to create centres of excellence for the use of vaginal meshes - no clear definition of who will determine the criteria for an excellence centre, nor who will assess such centres. In addition, no mention is made on how the AIUG will ensure a fair competition for all the meshes available on the market, nor indication that the skill of the surgeons will be considered as a criteria in making the excellence assessment, despite the literature clearly indicating this as a crucial factor in ensuring meshes effectiveness and safety.

The message emerging from the AIUG Opinion Statement is that not only are meshes not necessary to correct the pelvic floor defects, but they are dangerous. The most worrisome aspect is the final table reported in the statement, which states how in first-line surgery, even with relapse risk factors, it is optional to use vaginal meshes. This would expose patients to the 36% relapse risk[19] associated with traditional fascial surgery, rather than with meshes, which carry a significant lower risk. In this case, it would be much more

appropriately recommended to use meshes, as per point 4.
In addition, given all meshes have been approved for use, therefore previously assessed for safety and effectiveness, why should we limit their use in controlled clinical studies, rather than making them available to patients in need that would benefit from them?
Therefore, an open access debate including all key opinion leaders and expert professionals on the current guidelines would represent for us the best and most modern and scientific approach to debate the issue. The polypropylene meshes represent a great advancement in the care of our patients and we regret that some of us are now not using them only for fear of malpractices backlashes, even when used in the correct indications. It is for this reason that the AIUG must hear the voice of skilled experts on mesh implantation, by sharing the proposed Position Paper and modifying the Opinion Statement.
The question we should ask ourselves is what does the word *science* mean? During high school, I was passionate about physics and I remember a phrase by the great genius Richard Feyman, which has always been since then a guide in my life:
What is science? Science sometimes means a special method of discovering things; sometimes it means the set of knowledge that originates from the things discovered, but it can also mean all the new things that can be done using the acquired knowledge, or actually doing these things.
For us, a group of 60 colleagues who are passionate about surgery, who follow the debate and want to be at the forefront of the urogynaecology care, the only science is to look ahead using documentary evidence.
It is useful to clarify that when we talk about polypropylene, we mean all modern macroporous, light and ultra-light meshes[19-23]. Erosion is exceptionally rare and, when this happens, it is often due to implantation errors on the part of the surgeons. Today, no such thing as good polypropylene or bad polypropylene exists. There is a trend to believe that titanium coated propylene is the only safe option, even though this is happening in the absence of clinical studies that affirm its validity of safety and efficacy, evidence that does instead exist for the other polypropylene meshes.
Faced with the Anglo-Saxon world decisions it is necessary to react. This is a great scientific opportunity for the AIUG to be a driving voice in Europe, but the Opinion Statement, published on website, is not going in the right direction. The E.B.M. is obviously based on the evidence, but is there evidence that the current meshes are harmful? Certainly not as our Position Paper states.
But there is good news on the horizon. The European community regulation *"The medical device in Europe has less than one year until 26 May 2020, the Date of Application of the Medical Device Regulation (MDR - 745/2017)"* will come into practice in the next year. This regulation will allow the meshes currently used in Italy, as they all meet the biological criteria to be safely implanted.
As stated in the Position Paper by the Mesh Italian Skilled Surgeons (MISS), today it can therefore be affirmed that all polypropylene meshes with the CE mark have equal dignity of use, with equal and low risks of complications, when applied with expertise. Our wish is to be allowed to use the best available device to ensure the highest level of care for our patients. We are conscious that no surgery is free of complications, but also that most often these are caused by the surgical act in itself. The polypropylene meshes do not erode the tissues around them, except for when the vaginal wall is too thin for the procedure or the mesh is embedded above the pubocervical fascia.
A MISS study on prosthetic correction of anterior vaginal defects with different types of meshes, all in polypropylene, of low or ultra-low molecular weight currently available in Italy is underway, which is expected to shed some light on the issue and support our claims. This is an observational study involving more than 700 patients, with a mean follow-up of 18 months. The interim results already show that well applied meshes are a valid and safe surgical instrument and Italy is a vanguard country in their use, supporting the idea that POP surgery in 2019 must also be a vaginal mesh surgery. The data will be presented in October 2019 in Treviso, at the ISPP (International Society of PelviPerineology) world congress.
However in Europe the most important date will be 2020 MDR.

MDR EUROPE 2020: HARMONISATION OF STANDARDS FOR MEDICAL DEVICES

"The Medical Device Regulation (745/2017, to become applicable in May 2020)[24] is the most impactful legislative change for the medical devices sector since 1993, when the medical devices directive (93/42/EC) was published. Both legislative schemes follow the "New Approach" (NA) that was updated and replaced by the New Legal Framework (NLF) in 2007. The essence of the NA/NLF is that product regulations provide for general safety and performance requirements called "essential requirements" or "general safety and performance requirements", and that testable technical requirements addressing them are laid down in standards, developed jointly by all interested stakeholders. Those standards, following regulatory assessment, then become harmonized standards, are referenced in the Official Journal of the EU (OJEU) and thus provide for legal certainty for all stakeholders. Harmonized standards support the competitiveness of European industry, including small and

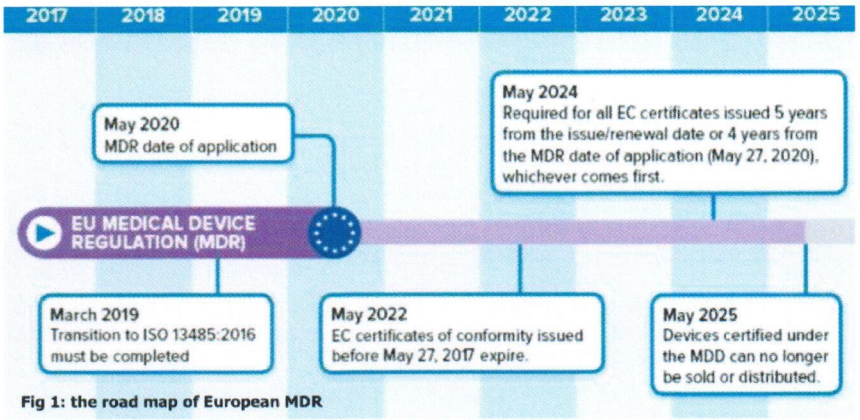

Fig 1: the road map of European MDR

medium enterprises as well as large global companies based in the EU and beyond" (Fig. 1).

CONCLUSIONS: "WHAT CAN WE LEARN FROM THE VAGINAL MESH STORY?"

What we can learn from the vaginal mesh story is effectively summarised in the abstract Karmaker and Hayward[25]:

The use of vaginal mesh in prolapse surgery has created enormous controversy and unprecedented media interest; it has become the most emotive topic in urogynaecology today. The US Food and Drug Administration 510(k) system allowed the proliferation of mesh products which were rapidly adopted by surgeons internationally. The importance of a firm understanding of the biomechanical properties of tissue and implants, surgical skill, patient selection, communication skills, informed consent, and high-quality research are all important lessons we can learn from the mesh story. These lessons need to be applied to all novel treatments in the field of urogynaecology and beyond.

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Disclosure Statements

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