**TITLE PAGE**

**Manuscript title:** The use of synthetic mesh for vaginal prolapse in the UK: A review of cases submitted to the British Society of Urogynaecology database

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1. RD Trochez. Project development, data collection and manuscript writing
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**The use of synthetic mesh for vaginal prolapse in the UK: A review of cases submitted to the British Society of Urogynaecology database**

**Abstract**

***Introduction and hypothesis***. The use of mesh gained popularity during the 1990’s. More recently concerns have been raised regarding the safety of mesh procedures. Mesh can be inserted vaginally, laparoscopically or via an open abdominal route but there is little data comparing the outcomes. Most previous data relate to small numbers of procedures.

***Methods****.* This was a review of data submitted to the British Society of Urogynaecology (BSUG) database of all cases reporting the use of mesh placed vaginally or abdominally (open or laparoscopic) between January 2006 and December 2016. The primary outcome was based on the reported patient global impression of improvement (PGI-I).

***Results****.* 6709 cases of mesh prolapse repair were entered during the study period. Women in the laparoscopic group had a lower BMI and were younger. Significantly more patients in the open group (96.4%) described themselves as very much better or much better compared to the laparoscopic group (91%) and the vaginal mesh group (90.7%) (p<0.001). 0.5% of patients reported that they were worse or very much worse.

***Conclusions****.* This dataset suggests that the effectiveness of mesh repair is good regardless of the route of insertion. The improvement in PGI-I seems to be greatest with open sacrocolpopexy.

**Keywords:** vaginal mesh, vaginal prolapse

**Brief summary**: the insertion of vaginal mesh for prolapse seems effective whether the mesh is inserted vaginallly, laparoscopically or via open abdominal surgery.

**The use of synthetic mesh for vaginal prolapse in the UK: A review of cases submitted to the British Society of Urogynaecology database**

**Ruben Trochez, Steven Lane, Jonathan Duckett, on behalf of BSUG**

**Introduction**

The use of synthetic mesh for the management of vaginal prolapse gained popularity worldwide in the 1990’s. The rationale behind this related to a perceived high failure rate with conventional native tissue repairs [1]. However, more recently their use became controversial due to reports of serious complications, including pain, mesh erosion and revision surgery. This led to the Food and Drug Agency (FDA) in the USA [2] to issue warnings on their use and the Health Ministry in Scotland [3] banning their use altogether.

There is some evidence that synthetic mesh inserted by the vaginal route have a higher rate of complications compared to mesh inserted by the abdominal route, whether open or laparoscopically [4]. For vaginal vault prolapse, abdominal sacrocolpopexy is considered the gold standard treatment [5,6]. With advances in laparoscopic surgery, there has been a shift towards increased use of laparoscopic sacrocolpopexy over the open abdominal alternative.

Some studies have compared open vs laparoscopic sacrocolpopexy [7-9] and some have compared the vaginal versus the abdominal route (open or laparoscopic) [10,11]. However, few studies have investigated outcomes for the three surgical alternatives (vaginal, open abdominal and laparoscopic) [4].

Government reports and calls for more information on successes and complications prompted a review of the information available on the BSUG database (NHSE interim report). The aim of this study was to use a large national registry, the British Society of Urogynaecology (BSUG) database, to compare outcomes and complications for the three operative routes for the insertion of synthetic mesh for vaginal prolapse.

**Materials and Methods**

The authors obtained permission from the Research Committee of the British Society of Urogynaecology to access the database and review all cases of vaginal mesh for prolapse performed between January 2006 and December 2016. The database was anonymised for patient, operating surgeon and centre. Consent was obtained from individual patients for their data to be entered in the database and used for analyses, as agreed nationally with the Caldecott Guardians of the individual centres using the database. Ethics committee approval was therefore not required.

The primary outcome of the study was the Patient Global Impression of Improvement (PGII) for prolapse. This is a 7-point categorical scale including the answers “very much better”, “much better”, “a little better”, “no change”, “a little worse”, “much worse” and “very much worse”. They were divided into 3 categories for analyses: *Improved* (very much better, and much better); *Same* (a little better and no change); and *Worse* (a little worse, much worse and very much worse).

The secondary outcomes included answers to the vaginal symptoms (VS) and sexual matters (SM) domains of the International Consultation on Incontinence Questionnaire (ICIQ); intra and postoperative complications.

Since revision surgery, particularly excision of mesh is considered one of the serious complications of this type of surgery, we looked separately at all cases of excision of mesh erosion registered on the database.

**Statistical analyses**

The data was first stratified into three categories depending on type of surgery: vaginal (V), open abdominal (A) and Laparoscopic (L). Summary statistics were calculated, again stratified by surgery type, for demographic, primary and secondary outcomes. Hypothesis tests to determine possible differences between categories were initially undertaken using Analysis of Variance (ANOVA) and Kruskal-Wallis test if data was not normally distributed. If a difference was observed, post-hoc pairwise testing was undertaken using either independent sample t-test or Mann-Whitney U test depending on the distribution of the data. Categorical data was assessed using the chi-squared statistic. All hypothesis tests were undertaken at the 5% significance level; however, Bonferroni correction was used to adjust the significance level of the pairwise test to allow for multiple testing. All analyses were carried-out using SPSS version 22, IBM Statistics for Windows.

**Results**

There were 6709 cases of mesh prolapse repair entered into the database during the study period. The number of centres entering their data onto the database increased from 20 in 2006 to 126 in 2016. The number of individual surgeons inputting their data from those centres also increased from 21 to 221 during the same period. More than 95% of all meshes used (by any method of insertion) were type 1 polypropylene. PGI outcome data was available for 61% (1034/1694) of patients undergoing vaginal surgery: 58% (1156/1999) of open abdominal cases and 59% (1771/3016) of laparoscopic procedures.

Table 1 shows the distribution of age and body mass index (BMI) according to operative route. Women in the laparoscopic group were younger and had a lower body mass index.

PGII was high for all three operative groups (table 2) suggesting that synthetic vaginal mesh for prolapse is effective in the short term regardless of the route of insertion. Post hoc tests suggest that PGII is statistically significantly better in the open abdominal group compared to the other two groups. There are no significant differences between the vaginal and laparoscopic groups. In the laparoscopic group 91% (1612/1771) described themselves as much better or very much better; in the open abdominal group this was 96.4% (1114/1156) and in the vaginal mesh group 90.7% (938/1034). Only 19 patients from 3961 giving PGI-I outcome reported that they were worse of very much worse. This was 0.6% in the laparoscopic group (11/1771); 0.3% in the open group (3/1156) and 0.5% (5/1034) in the vaginal group.

These results look different when the cases are split between mesh insertion done as a primary or a secondary procedure. In this case, as shown in table 3, the open abdominal route is less effective. There is no significant difference between the vaginal and the laparoscopic route. In 14% (551/3961) of cases data were missing on whether the mesh was inserted as a primary or a repeat procedure. Repeat surgical procedures for a failed primary procedure were more common in the vaginal mesh group (67.8%) than in the open abdominal (45.7%) and laparoscopic procedures (26.0%). Women in the laparoscopic group were more likely to have the mesh inserted as a primary procedure.

Table 4 summarises the results for the ICIQ VS and SM questionnaires. There is no difference between the three groups for pre-operative ICIQ VS. For post-operative ICIQ VS the analysis suggests that Laparoscopic is different from both vaginal and open abdominal. However, there is no difference between vaginal and open abdominal.

For the pre-operative ICIQ SM scores there is no difference between the groups and only borderline significance for the ICIQ SM post-operative scores, which disappears after post-hoc testing with adjustment for multiple testing.

Figure 1 shows the distribution of operative routes during the study period.

There were 174 cases of excision of mesh erosion entered into the database during the study period. However, none of the cases could be associated with the original operation. The very small proportion of erosions entered onto the database in relation to the number of meshes inserted (0.03%) is unlikely to represent the true rate of erosion.

Small numbers of intraoperative complications were reported as per table 5. The numbers were too small for formal statistical tests

**Discussion**

This large dataset suggests that the short-term effectiveness of mesh prolapse repair is good regardless of the route of insertion. Over 96% of women reported improvement on the PGII scale at 3-12 months follow up. This is in keeping with the existing literature.

Our data suggest that inserting a mesh via open abdominal surgery is more effective than either laparoscopically or vaginally, and that there is no difference between the laparoscopic and the vaginal groups. This contrasts with the study by Dandolu et al [4] in the USA in which laparoscopic sacrocolpopexy had the lowest failure rate (4.3%) and total vaginal mesh (TVM) had the highest (6.2%). However, this comparison should be taken cautiously since this study included meshes used for all vaginal compartments whilst the study by Dandolu was only investigating apical prolapse surgery. In addition, the outcomes of the studies are different (PGI-I in this study and reoperation rate/pessary use in theirs). On the other hand, the statistical differences found in this study could be due to the small number of events in the “no change” and “worse” categories in all three surgical groups.

However, the results are different when the cases are separated between mesh insertion done as a primary or a secondary procedure. In this case, an open abdominal insertion of mesh is less effective than a vaginal or a laparoscopic insertion; and there is no statistically significant difference between a vaginal and a laparoscopic insertion. It is difficult to fully explain these contrasting results, but it is possible that the difference may be explained, at least in part, by the 14% of cases with missing data with regards to classification (primary or repeat surgery)

Women having laparoscopic mesh insertion in this cohort were younger and had a lower BMI than those having either vaginal or open abdominal surgery. This may indicate patient selection which could have been expected to favor better outcomes in the laparoscopic group. Also they were more likely to be having primary surgery.

The controversy surrounding synthetic mesh for vaginal prolapse is not so much in its effectiveness but in the risks of complications. There are data [12,4] suggesting that the risk of mesh complications; particularly mesh erosion, reoperation and chronic pain; are higher when they are inserted by the vaginal route. Our data do not allow us to comment on this, as the reported complications on the database relate to intra and perioperative complications; and the data on mesh erosions do not discriminate by route of insertion. Furthermore, women having excision of mesh erosion may or may not had the index surgery (insertion of mesh) entered onto the database.

Overall, there was a gradual increase in the number of meshes entered into the database during the study period. This is likely due, at least in part, to the gradual increase in the number of centers and surgeons using the database. Figure 1 indicates that there was a change in surgical preferences for prolapse mesh over time. The most significant change is an increase in the use of laparoscopic insertion of mesh between 2012 and 2014. The decline for all types of surgery in 2015 and 2016 may relate to delayed data entry onto the database, but may also reflect a somewhat delayed reduction in the overall use of prolapse mesh following the FDA warnings and the Scottish Health Ministry directive.

The limitations of this study include the fact that the BSUG database is voluntary and is unlikely to capture all prolapse mesh surgery in the UK. The length of follow up is variable but generally short and there is a significant amount of missing data, especially post-operative outcomes. In addition, the number of women whose PGII fell in the no change and worse categories are small, which may have led to the observed statistical differences. The lack of objective data is also a drawback and the results very much rely on the outcome reported by a single measure. Long term complications such as mesh removal for pain or erosion were not captured as the results relate to the immediate surgery and post-operative follow up for only one year (maximum).

The main strengths of the study include the very large number of cases on the database and the use of a patient reported outcome measure. Unfortunately PGI-I data was only available for around 60% of patients and it was short term. The multicenter nature of the data makes it more robust. The differences in outcomes are small but the size of the dataset allows small statistical differences to become apparent. It is more difficult to interpret whether these differences are significant clinically. As with any database the data is only as good as the enthusiasm and rigor of the people entering the data. This can lead to bias but overall the numbers included make this less likely.

In conclusion, synthetic meshes for vaginal prolapse seem effective in the short term, whether inserted abdominally (open or laparoscopic) or vaginally, but the improvement is greatest with open sacrocolpopexy. However, it is unclear whether their effectiveness is sustained in the long term and doubts remain with regards to their safety.

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**Figure Legends.**

Figure 1. Distribution of operative route for insertion of vaginal meshes

**Tables**

Table 1: Demographics

|  |  |  |  |
| --- | --- | --- | --- |
|  | Vaginal | Open abdominal | Laparoscopic |
| n | 1694 | 1999 | 3016 |
| Age mean (st. dev.) | 63.79 (10.46) | 61.38 (11.34) | 59.45 (12.69) |
| BMI mean (st. dev.) | 25.75 (9.35) | 25.46 (8.04) | 24.19 (9.53) |

Table 2. Patient Global impression of Improvement – PGII (categorised)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Vaginal | Open abdominal | Laparoscopic | Significance |
| n | 1034 | 1156 | 1771 |  |
| Improved n (%)  Same  Worse | 938 (90.7)  91 (8.8)  5 (0.5) | 1114 (96.4)  39 (3.4)  3 (0.3) | 1612 (91.0)  148 (8.4)  11 (0.6) | P<0.0011 |
| Pairwise comparison | Vaginal v Open abdominal  Vaginal v Laparoscopic  Open abdominal v Laparoscopic | | | P<0.0011  P=0.831  P=0.0011 |

1 Chi-squared test

Table 3. Primary and secondary surgery

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| PRIMARY | | | | |
|  | Vaginal | Open abdominal | Laparoscopic | Significance |
| n | 290 | 518 | 1155 |  |
| Improved n (%)  Same  Worse | 181 (62.4%)  76 (26.6%)  33 (11.4%) | 259 (50.0%)  206 (39.8%)  53 (10.2%) | 735 (63.6%)  296 (15.6%)  124 (10.7%) | P<0.0011 |
| Pairwise comparison | Vaginal v Open abdominal  Vaginal v Laparoscopic  Open abdominal v Laparoscopic | | | P<0.0011  P=0.921  P<0.0011 |
| SECONDARY | | | | |
|  | Vaginal | Open abdominal | Laparoscopic | Significance |
| n | 611 | 437 | 399 |  |
| Improved n (%)  Same  Worse | 350 (57.3%)  160 (26.2%)  101 (16.5%) | 219 (50.1%)  181 (41.4%)  37 (8.5%) | 253 (63.4%)  106 (26.6%)  40 (10.0%) | P<0.0011 |
| Pairwise comparison | Vaginal v Open abdominal  Vaginal v Laparoscopic  Open abdominal v Laparoscopic | | | P<0.0011  P=0.011  P<0.0011 |

Table 4: Secondary Outcomes

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Vaginal | Open abdominal | Laparoscopic | Significance |
| n | 656 | 604 | 508 |  |
| ICIQ VS pre median (IQR)a | 26 (15) | 26 (13) | 26 (15) | P=0.592 |
| n | 511 | 446 | 360 |  |
| ICIQ VS post median(IQR) | 3(8) | 3(8) | 4(9) | P<0.0012 |
| Pairwise comparison | Vaginal v Open abdominal  Vaginal v Laparoscopic  Open abdominal v Laparoscopic | | | P=0.953  P<0.0013  P<0.0013 |
| n | 314 | 343 | 278 |  |
| ICIQ SM pre mean (st. dev.) | 21(38) | 21 (41) | 23 (41) | P=0.462 |
| N | 207 | 209 | 172 |  |
| ICIQ SM post median(IQR) | 0 (13) | 0 (17) | 1 (19) | P=0.052 |

2 Kruskal-Wallis test

3 Mann-Whitney U test

a N = 656, 604 and 508 respectively

Table 5: Complications by procedure type

|  |  |  |  |
| --- | --- | --- | --- |
| N (%) | Vaginal | Open abdominal | Laparoscopic |
| Ureteric | 1 (0.1) | 0 | 1 (0.1) |
| Bladder | 11 (0.7) | 32 (1.6) | 41 (1.4) |
| Vaginal | 6 (0.6) | 3 (0.2) | 30 (1.1) |
| Bowel | 6 (0.4) | 4 (0.4) | 8 (0.3) |
| Vascular | 1 (0.1) | 4 (0.2) | 4 (0.1) |
| Neurological |  | 1 (0.1) |  |
| Blood loss > 500ml | 26 (1.2) | 12 (0.6) | 10 (0.3) |
| Blood transfusion | 4 (0.2) | 2 (0.4) | 3 (0.1) |
| Thromboembolism | 1 (0.1) |  | 2 ().1) |

**Figures**

Figure 1. Distribution of operative route for insertion of vaginal meshes

|  |  |
| --- | --- |
|  | Vaginal |
|  | Open abdominal |
|  | Laparoscopic |