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TITLE

A randomised controlled trial evaluating the use of polyglactin mesh, polydioxanone and polyglactin sutures for pelvic organ prolapse surgery

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ABSTRACT

Objective

To compare the effectiveness of polyglactin mesh, and polydioxanone or polyglactin sutures in women having pelvic organ prolapse surgery.

Methods

Randomised controlled trial with a factorial 2x2 design of polyglactin mesh or not, and polydioxanone or polyglactin suture. Outcomes were assessed using questionnaires at baseline and on the third day and at 6 months after surgery. Women were also examined clinically at 3 months after surgery. The primary outcome was the subjective improvement in prolapse symptoms and quality of life scores from baseline to 6 months.

Results

There was a subjective improvement in the prolapse symptom score from baseline to 6 months after surgery (mean difference of 9.2 (95% CI for difference 7.2 to 11.2, $P < 0.001$) and an improvement in the mean quality of life score over the same period with a reduction of 3.4 (95% CI for difference 2.4 to 4.3, $P < 0.001$). However there were no significant differences in the mean difference in prolapse system and quality of life score according to the randomised groups. The majority (86%) of women were satisfied with their surgery.

Conclusions

Our study demonstrated at short term follow up there were no significant differences in the mean difference in prolapse system and quality of life scores after surgery using polyglactin mesh or not, polyglactin or polyglactin sutures but the numbers were too small for a definitive conclusion. Longer term follow up and a larger trial are required.

(Keywords Pelvic organ prolapse, randomised control trial surgical mesh, polydioxanone, polyglactin)

INTRODUCTION

Surgery for pelvic organ prolapse (POP) is notoriously prone to failure: up to 30% of women require a second or subsequent repair (1). Surgical failure may be attributed to a number of factors. Both patient factors (poor tissues, impaired healing processes and high intra-abdominal pressure due to obesity, constipation or chest conditions) and surgical factors (inappropriate choice of suture material or operation, or poor surgical technique) may contribute to poor outcomes (2, 3).

In an attempt to improve surgical factors, reinforcement of the fascial defect and its repair has been advocated using mesh or graft placement. After surgical correction of the hernial defect the mesh reinforces the repair by acting as scaffolding for new tissue regeneration, and support to attenuated areas, thus augmenting the natural function of the damaged tissue. (1, 3). Mesh placement is easy to perform and has been successful elsewhere, notably in hernia surgery. However, controversy exists regarding the choice of mesh to use, especially in women having primary surgery.

Recent literature has highlighted the danger of erosion with non-absorbable grafts, but there is little evidence to guide the choice between biological or synthetic absorbable material, nor indeed whether any use of mesh is effective in prolapse surgery.

A recent update of the Cochrane Review of surgery for prolapse has identified six small RCTs which evaluated the use of mesh or not for women having anterior and/or posterior prolapse surgery. Differences in inclusion criteria or interventions (eg types of women, operations or mesh/graft inlay) generally precluded useful meta-analysis or reliable conclusions. However, there was some evidence from two of these (5, 6) that absorbable polyglactin mesh (Vicryl) might reduce objective (anatomical) prolapse recurrence compared with anterior repair alone, although the numbers were too few to evaluate morbidity or clinical outcomes. Polyglactin is a synthetic absorbable mesh which is inert, porous, and flexible. It loses 50% of its original strength at 14 days and so acts as initial scaffolding for new tissue regeneration after which it is completely absorbed. (5, 6)

The choice of suture material is also controversial, in that no RCTs exist to guide the choice of the most effective one. (4) Traditionally a polyglactin suture has been used for prolapse surgery. It is a synthetic polyfilament suture, which loses 50% of its original strength at 14 days. More recently polydioxanone, a single-stranded, absorbable suture has been adopted by some surgeons. This suture has similar tensile strength and knot security to polyglactin but has the advantage that it maintains 50% of its original strength for 21 days. (7) This may be particularly advantageous in POP reconstructive surgery where abdominal pressure may affect the healing tissue postoperatively by acting as a stress factor. Additionally, because it is a monofilament suture it may be associated with a lower risk of perioperative infection.

In view of these uncertainties, we carried out a randomised controlled trial to evaluate the use of absorbable polyglactin mesh and to compare the two sutures in women having POP surgery. The aim of our study was to assess the difference in the mean prolapse symptom and quality of life scores in the study groups at 6 months after surgery.

PATIENTS AND METHODS

Ethical approval was obtained from the Grampian Research Ethics Committee. Women scheduled for POP surgery were identified from the waiting lists or admission diaries of the consultants participating in the trial. Women were provided with trial information on admission and invited to participate.

Eligible women provided informed signed consent to the trial and long term follow up. All women admitted with grade 2 or more POP who were willing to participate in the trial were eligible. Women undergoing concurrent vaginal hysterectomy or continence procedures were also eligible. They were counselled and consented for the trial by a research assistant or their consultant gynaecologist and then completed a baseline questionnaire.

Women were randomised into receiving polyglactin mesh or not, and either a polydioxanone or a polyglactin suture for the repair of the pubocervical and/or the rectovaginal fascia using a 2x2 factorial design. XX

{Insert ref: FA McAlister, SE Straus, DL Sackett and DG Altman, Analysis and reporting of factorial trials: a systematic review, JAMA 289 (2003), pp. 2545–2553.}

Thus there were four groups, enabling separate analysis of mesh versus no mesh, and polydioxanone versus polyglactin sutures, as well as interactions between the two interventions. Allocation to groups was carried out using a secure method of concealment of randomisation (remote computer allocation) on the afternoon before surgery.

The group allocation was concealed from the women and the ward staff, although blinding in theatre was not possible, as theatre staff needed to prepare appropriate sutures and mesh for the surgeons before surgery. The surgeon performing the operation completed a questionnaire in theatre giving details of the operation performed, complications and deviation from the allocated treatment.

Women completed a postoperative questionnaire on the third day after their surgery. They were clinically reviewed at 3 months after surgery for a subjective and objective assessment of their symptoms by one of the authors (who was blind to group allocation until after examination), and were given advice or further treatment if required. Finally they completed a postal questionnaire six months after operation.

Primary outcome assessment was by participant self-complete questionnaire, thus avoiding interviewer bias. A researcher who was blind to the unit of randomisation conducted the data collection and analysis, using study numbers only to identify women and questionnaires. All women were actively followed up with analysis based on the intention to treat principle. All analyses were predefined to avoid bias. A data base was designed for data entry.

The primary outcome was based on change in a pelvic symptom score derived from the seven most common prolapse symptoms. (XX ref)
{insert ref to study: C. Bugge, S. Hagen, and C. M. A. Glazener. *The POPPY study: a qualitative evaluation of a pelvic organ prolapse outcome questionnaire (Abstract)*. ICS UK, Annual General Meeting, Glasgow, UK, March, 2005.}

The minimum score was 0 (all symptoms rated as 'never') and the maximum was 21 (all symptoms rated as 'all of the time'). The score was calculated at baseline (before surgery) and again at 6 months after surgery. A symptom score change was calculated for each woman for the difference between these two scores. Quality of life attributed to prolapse symptoms was calculated by asking, "Overall, how much do your prolapse symptoms interfere with your everyday life?" The minimum score was 0 ('not at all') and the maximum was 10 ('a great deal').

Data verification was carried out by having data entry limits in place, by querying outlying or suspect variables, and by spot checking data from 17 participants. A 2.9% data error rate was found and variables corrected if necessary. Data analysis was carried out using independent t-tests and Chi-squared tests as appropriate.

RESULTS

In total, 83 women were considered for randomisation (Figure 1). Of these, 5 refused and 5 were not eligible. Of the five women who refused to participate in the trial, four refused because they did not wish to or could not attend for follow up and one woman was worried about the use of a foreign material such as mesh. Of the 73 randomised women, a further 7 were found to be ineligible after randomisation (Figure 1), resulting in 66 properly randomised of 71 potentially eligible women (93%).

Thus, 66 women were randomised (Figure 1): 32 were allocated to mesh and 34 to no mesh; 33 were allocated to polydioxanone and 33 to polyglactin. The groups were comparable on baseline characteristics (Table 1). Six women in the mesh/no mesh comparison did not receive the allocated treatment (see Figure 1). For the five women who did not receive mesh as allocated, the reasons included: lack of theatre time for the insertion of mesh; poor access to tissue; a concern that using mesh in addition to TVT would increase the infection risk. Only one woman in the no mesh arm actually received mesh as the gynaecologist deemed that the use of mesh was clinically indicated because the tissues were deficient and friable.

Two (3%) women experienced short term adverse effects: one returned to theatre for postoperative bleeding and one woman required suprapubic catheterisation for urinary retention.

In total, 58/66 (88%) women were reviewed by a gynaecologist 3 months after operation and 62/66 (94%) women completed the 6 month follow up questionnaire (Figure 1). At the 3 months examination, 10/58 (17%) of women reported a residual subjective feeling of something coming down, although this was unrelated to their randomised groups. Ten women said that their symptoms were unchanged (8) or worse (2) but only six women (10%) had a residual stage 2 anterior wall prolapse on objective examination. One woman had had a pessary fitted by her GP, and a further 7 were referred for formal physiotherapy or other conservative management.

At baseline, the mean prolapse symptom score was 13.5 (range 3 to 28), indicating that all of the women had at least one symptom. At 6 months after surgery, the mean prolapse symptom score was 4.3 (range 0 to 22). There was a significant improvement overall at 6 months, mean difference 9.2 (95% CI for difference 7.2 to 11.2, $P < 0.001$, paired t-test). However, there were no significant differences by randomised groups in the change in symptom score over 6 months (Table 2).

Similarly, the quality of life score at baseline was 4.8 (range 0 to 10), with no differences between the trial groups. The mean quality of life score at 6 months after surgery was 1.6 (range 0 to 10) this improved significantly after prolapse surgery, with a mean difference of 3.4 (95% CI for difference 2.4 to 4.3, $P < 0.001$, paired t-test). However, there were no differences between the groups in change in quality of life at 6 months (Table 2).

Regarding satisfaction, 49/59 (83%) women were very or fairly satisfied with their surgery 6 months later. However, there were no significant differences according to trial groups.

DISCUSSION

The results of this prospective randomised control trial showed that recruitment for POP surgery trials was very successful with 66 women (93%) out of the 71 eligible women agreeing to participate in the trial.

Our trial showed that there was a subjective improvement in mean prolapse symptom score from baseline to 6 months after surgery, with a mean decrease in score of 9.2 and an improvement in the mean quality of life score from the baseline to 6 month follow up with a mean decrease of 3.4 units. The majority (83%) of women were satisfied with their surgery and said that their prolapse did not bother them any more, and only a minority had residual prolapse of Stage 2 (10%).

However there were no significant differences in the mean difference in prolapse system score and quality of life score between the trial groups after surgery at short term follow up (Table 2). This differs from the results of a trial evaluating the use of polyglactin mesh evaluating the use absorbable mesh for anterior vaginal wall repair performed by Sand *et al.* (5) who analysed 143 women comparing anterior endopelvic fascial plication with and without the utilisation of Polyglactin mesh at 24 month follow up. The authors reported significantly higher objective success rates with the use of the mesh (75% versus 57%; $P = 0.02$) but did not report subjective prolapse symptoms or effect on quality of life. (5) Weber *et al.* (9) also compared classical anterior repair with and without the use of polyglactin mesh. Although at a mean follow-up of 24 months they found that the addition of polyglactin mesh did not improve the objective cure rate compared with standard anterior colporrhaphy, the groups were small. No data on subjective outcomes were provided.

The explanation for the difference in the findings of these three studies (Sand, Weber and the current study) may be explained in part by differences in sample sizes, in methods of assessing outcomes and types of outcomes, and length of follow-up. In addition, we analysed the data from women having anterior and posterior repairs together.

Complications related to mesh prosthesis include, infection, sinus tract formation, seroma, erosion and fistula formation. (10-12) Our study showed that surgery with the use of Polyglactin mesh was associated with very few perioperative and early post operative complications with no mesh erosions noted to date. This was comparable to the findings in the trials performed by Sand *et al.* (5) and Weber (9), who reported no mesh-related complications in their study.

Our trial was too small to demonstrate differences attributable to the two sutures and no other trials have been identified that address this issue (ref Cochrane review 4). Nevertheless, the theoretical differences between the sutures in terms of tensile strength, half life, potential for infection and handling ease would suggest that further evaluation by RCT would be warranted.

The satisfaction rate recorded at 6 month follow up showed that the majority of women were fairly or very satisfied with the results of their surgery (83%) but the numbers were too few to differentiate between the randomised groups. Four (13%) women were very dissatisfied with their surgery: two of them had recurrent prolapse.

The strengths of our study were that it was a prospective randomised control trial in which the principal outcome assessors were blinded to the randomisation and the patients were blinded to the treatment that they received thus reducing bias. The recruitment to the trial was excellent (93%) with 88% being reviewed at 3 months and 94% women responding to the 6 month questionnaire. The study groups were comparable at baseline on mean prolapse symptom score, quality of life score and other clinical and sociodemographic factors.

The weakness of our study was that participant numbers were too small to demonstrate statistical significance between the randomised groups. Furthermore, the follow up period of 6 months was too short to demonstrate clinical effectiveness, but long term follow up is planned.

We would also suggest that an objective assessment of the POP by a validated and standardised system such as the POPQ scoring system should be used before and after surgery to enhance generalisability. The randomisation of trial participants should be done on the day of surgery or as late as possible to reduce the numbers of women who are not fit or unsuitable for surgery being randomised. Larger numbers of participants and longer term follow up will help to more accurately assess the impact of the use of polyglactin mesh, polydioxanone and polyglactin sutures.

Future research is particularly warranted to compare the use of non absorbable or partially absorbable mesh with no mesh to assess the impact on POP surgery, as this is becoming increasingly common in clinical practice without an adequate evidence base.

CONCLUSIONS

Our trial established that running an RCT of different methods of prolapse surgery in a busy tertiary referral unit involving seven gynaecologists could be carried out with minimal disruption to routine services. The recruitment, randomisation and retention of the women was excellent. Although our trial did not demonstrate any significant difference in prolapse symptoms and quality of life after surgery at short term follow up, the numbers were too small to give reliable results. A larger trial is warranted.

Table 1 Baseline characteristics by randomised allocation

	Mesh (32)	No mesh (34)	Polydioxanone (33)	Polyglactin (33)
Age >= 60 years	18/32	20/34	19/33	19/33
Parity				
Para 1 or less	15/32	17/34	14/33	18/33
Para 2 or more	17/32	16/34	19/33	14/33
Menopause	28/32	28/34	28/33	28/33
Smoking	1/32	3/34	3/33	1/33
HRT	5/32	2/34	2/33	5/33
COPD	7/32	7/34	7/33	7/33
PFMT	9/32	9/34	8/33	10/33
Primary operation	27/32	30/34	28/33	29/33
Secondary operation	5/32	4/34	5/33	4/33
Preoperative ring use	8/32	4/33	4/33	8/32
Type of prolapse				
Cystocele	16/32	12/34	16/33	12/33
Rectocele	7/32	6/34	5/33	8/33
Both (19)	8/32	11/34	9/33	10/33
Paravaginal	2/32	0/34	1/33	1/33
Concomitant operations				
Hysterectomy	6/32	8/34	9/33	5/33
Cervical amputation	8/32	10/34	8/33	10/33
TVT	7/32	6/34	5/33	8/33
Other	0/32	2/34	0/33	2/33

COPD chronic obstructive airway disease

HRT hormone replacement therapy

Polydioxanone

PFMT pelvic floor muscle training

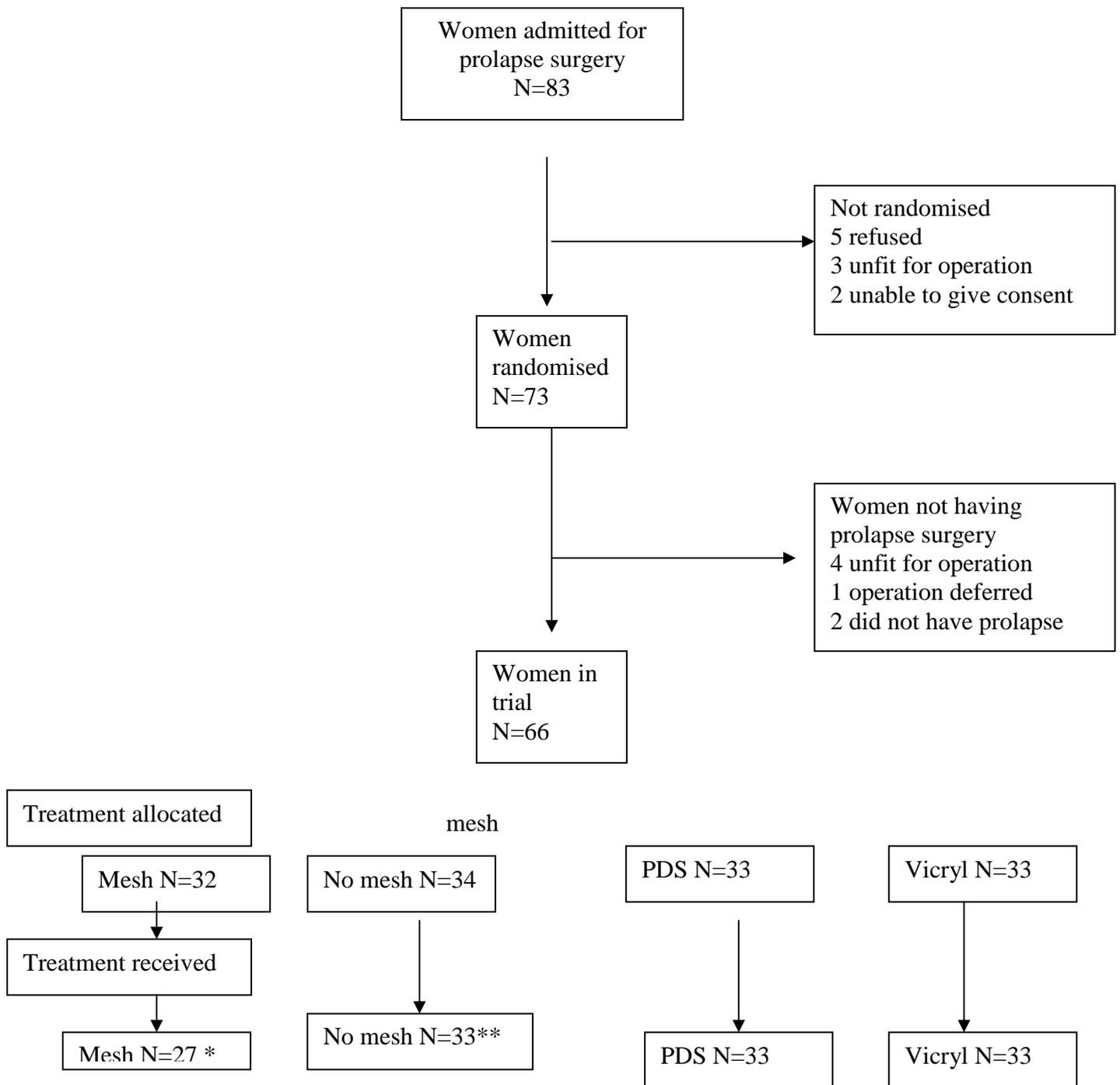
TVT tension free vaginal tape

Table 2 Change in prolapse symptom and quality of life score between baseline and at 6 months after prolapse surgery

	Mean change in Symptom Score at 6 months N, mean (SD)	Mean difference [95% CI for difference]	Mean change in QoL from baseline to 6 months N, mean (SD)	Mean difference [95% CI for difference]
Mesh	29, -9.6 (8.6)	-0.8 [-4.9 to +3.3]	26, -3.8 (3.5)	-0.8 [-2.8 to +1.1]
No mesh	32, -8.8 (7.3)		32, -3.0 (3.8)	
Polydioxanone	29, -9.1 (9.0)	0.2 [-3.8 to +4.3]	26, -3.1 (3.5)	0.5 [-1.5 to +2.4]
Polyglactin	32, -9.3 (6.9)		32, -3.6 (3.8)	

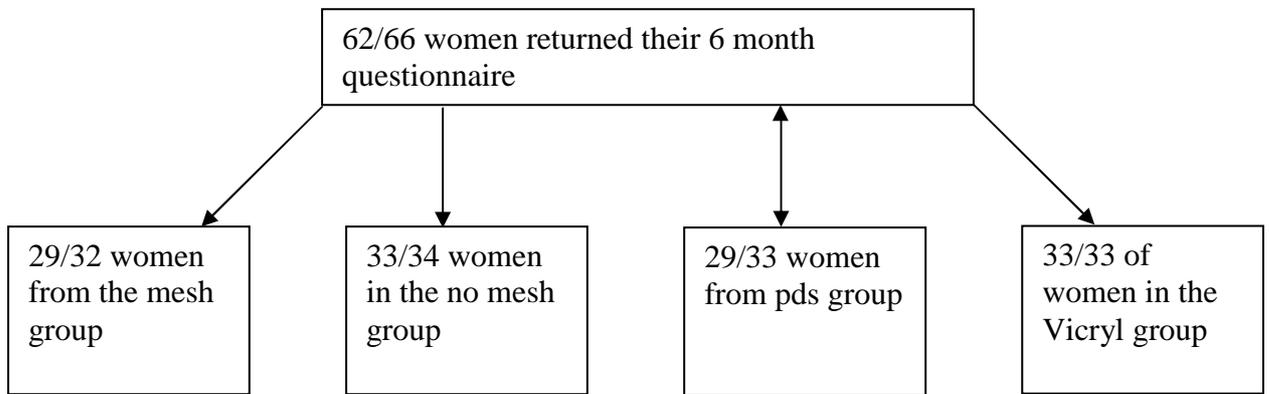
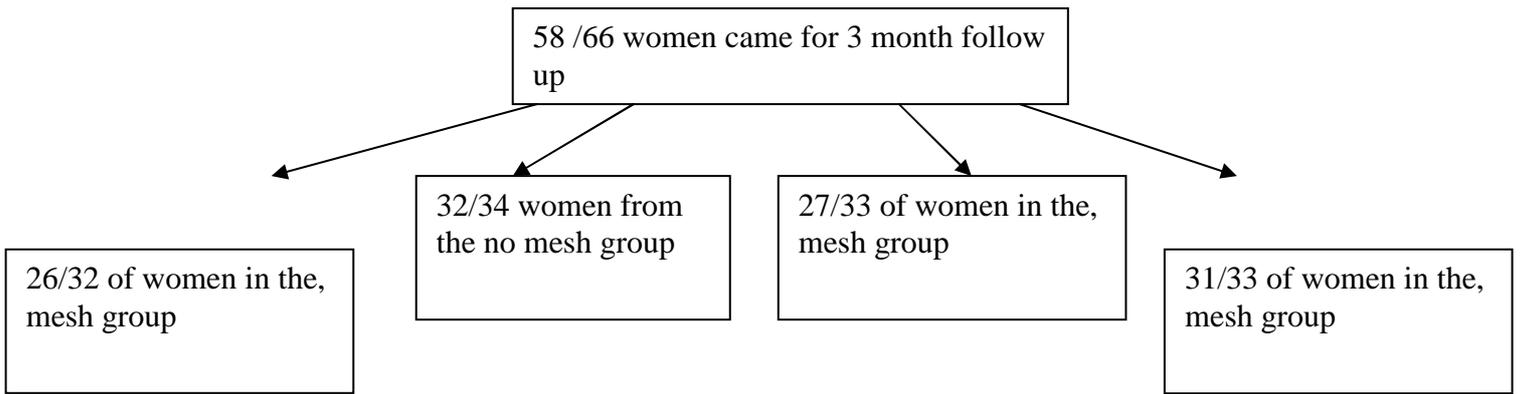
CI confidence interval
 N number
 Polydioxanone
 QoL quality of life
 SD standard deviation

Impress Flow diagram (figure 1)



* Mesh not used due to poor access (2); not enough theatre time (2); TVT caused worries re increased infection risk (1)

** Mesh used as tissue were deficient and friable



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