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## Deep and superficial endometriotic disease: the response to radical laparoscopic excision in the treatment of chronic pelvic pain

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**Abstract** A cohort of 108 women with chronic pelvic pain underwent a laparoscopy, and a diagnosis of endometriosis was made in 88 (81%). Pre-operative and 2 years post-operative pain scores, using a ranked ordinal scale, were calculated for 44 women with complete pelvic organs (50%) and full data sets. Endometriosis was diagnosed on the basis of histological confirmation of the presence of glands and stroma in excised specimens and endometriosis classified by the American Society of Reproductive Medicine r-ASRM or by the presence of superficial or deep disease. The r-ASRM was a poor predictor of pain relief following surgery, and women with superficial disease did not respond well (in terms of appreciable, reduced pain) to surgical treatment, but good pain relief was seen with some women with nodular or infiltrating ('deep') disease. Women were also asked to complete a General Health Questionnaire. This showed an appreciable degree of depressive morbidity, which improved over the time of the study. Severity of initial global pain scores did not equate to the severity of endometriosis as categorised by either the r-ASRM score or the type of disease. This small study suggests that surgical therapy does not reduce pain scores in superficial endometriosis but is valuable in the treatment of deep or infiltrating disease. Longer-term follow-up of a larger cohort is necessary to evaluate further

the value of surgery in this disease and to be further able to develop more accurate predictions of the outcome of surgical intervention in terms of pain relief.

**Keywords** Superficial · Deep · r-ASRM · Laparoscopic · Pain scores

### Introduction

The gold standard investigation for the diagnosis of endometriosis is laparoscopy, which not only allows visualisation or histology of the disease, but also any identified endometriotic lesions to be removed or destroyed at the same operation. Surgery has been shown to be an effective treatment of endometriosis, with a recent double-blind trial showing that both ablation and excision of superficial lesions provide equal relief of pain symptoms at 6 months in 65% of women [1]. A cohort study of 135 women has also revealed positive effects of surgery, with the majority of women reporting improvements in pain symptoms irrespective of stage or site of disease when followed up 2–5 years later [2]. However, 25% of this cohort underwent hysterectomy and bilateral salpingo-oophorectomy to reduce their symptoms. Moreover, over a third (36%) of these women required further surgery within the follow-up period. The authors report that the only significant predictor of the requirement for further surgery was an American Society of Reproductive Medicine (r-AFS) score >70 (r-AFS ranges from 0–150). Surgery also offers patients the advantage of limiting drug side effects and the possibility of a long-term improvement [3], and it can be argued that surgery is the only option for women with ovarian endometriomas or those with associated adhesive disease [4].

The r-AFS score, now called the r-ASRM (American Society of Reproductive Medicine) score is the most widely used operative assessment of endometriosis [5]. In common with other disease staging measurements and to help guide clinical decision making, the score needs to be predictive of treatment outcome. However, having been

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developed as a fertility score, the r-ASRM score is weighted towards the presence of adhesions, and has, so far, been shown to be of limited value for the assessment of endometriosis.

Laparoscopy, with its enlarged views deep into the posterior cul-de-sac, offers greater access to the pelvis than laparotomy and thus a greater chance of complete excision with reduced morbidity. It is still, though, a procedure that is associated with operative risk. Thus, surgical treatment should ideally be limited to those individuals that are most likely to benefit.

Garry has recently popularised the division of endometriosis into superficial peritoneal disease (Sampson's disease) and deep nodular or infiltrating disease (Cullen's disease) [6]. The division initially appears easy to assess at laparoscopy, and, based on the evidence from Koninckx et al. [7], might be predictive of the initial level and subsequent improvement of pain. This hypothesis is yet to be tested.

The aim of this study was to assess the ability of measures of initial level of pain and surgical findings, in terms of the r-ASRM score or the presence of superficial or deep disease, to predict improvement in global pain scores in the treatment of women with chronic pelvic pain and endometriosis.

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## Method

This was a prospective, observational study of women with chronic pelvic pain and symptoms suggestive of endometriosis, presenting to the chronic pelvic pain clinics during 2002 and who underwent surgical treatment the same calendar year. The clinics are set in a UK district general hospital, providing both local and tertiary level referral services for the treatment of women with chronic pelvic pain and endometriosis. Surgery involved a diagnostic laparoscopy with the intention to proceed to excision of all observable abdominal and pelvic deposits of endometriosis. Local ethical and research governance approval was sought and granted prior to the study. All women were asked to complete a questionnaire in the clinic waiting room, before meeting the clinician. The questionnaire was a modification of that developed by Redwine [8] and Garry et al. [9]. It specifically looked at an analysis of symptoms with the degree of severity expressed on a 6-point scale (from 0 to 5). Women were asked to grade the level of the relevant seven symptoms: dysmenorrhoea, non-cyclical pelvic pain, dyschezia during and outside menses, back-ache during and outside menses and dyspareunia. A global pain score was also calculated by summation of the scores for these seven symptoms (range 0 to 35).

Level of depression was assessed with the General Health Questionnaire [10], which is a global measure of depression at the time of completing the questionnaire. It looks at depression by drawing on 12 dimensions: concentration, sleep, usefulness, decision making, psychological strain, coping, enjoyment, unhappiness, ability to face up to problems, self-confidence, worthlessness and

happiness. Each dimension is evaluated as either an improvement/unchanged (0) or worsening (1). The overall result is expressed as a numerical score from 0 to 12, with 12 indicating severe depression.

At laparoscopy, the intention was to identify a potential cause of the pain, and, if endometriosis was present, to excise completely all identifiable endometriotic lesions, with subsequent histological confirmation. All women were counselled as to the risks of the procedure and pre-operatively had a bowel cleansing preparation. This consisted of a 3-day, low-residue diet followed by an osmotic laxative (Citramag) 12 h prior to surgery. A further rectal washout was performed on the table if bowel involvement was suspected on pelvic examination under anaesthesia. All identified lesions were described in terms of their visual appearance, location and whether they presented as superficial peritoneal lesions, typically red, black or white, (class 1 or Sampson's disease), or deep lesions, typically infiltrating or nodular (class 2 or Cullen's disease). If a combination of lesions were present then these were grouped as 'deep' (class 2), since the assumption was made that this was more severe and thus the predominant feature. The r-ASRM score was also calculated during the surgical episode.

All lesions were then excised by monopolar diathermy. The technique employed has already been described in the literature [11]. A diagnosis of endometriosis was only made on histological confirmation, with the microscopic identification of the presence of endometrial-like glands and stroma [12]. If both uterosacral ligaments were involved or there was evidence of rectovaginal disease then the lesion was removed 'en bloc' [13]. Ovarian endometriomas were treated at the initial visit by drainage of the pseudo-cyst, flushing of the cavity, completely clean, and excision of the pseudo-capsule by blunt and sharp dissection.

These women were then followed-up on an outpatient basis. At 18 months they were then mailed a repeat identical questionnaire. If no reply was received a second, identical, reminder questionnaire was sent out, but, if still no reply was received, then no further effort was made to acquire the follow-up data.

All data were prospectively entered during each event using Endostat, a specifically designed database, and results tabulated on Excel.

Statistical analysis was carried out by two-sample pooled and paired *t*-tests and their non-parametric equivalents. Before and after test scores were examined by Altman-Bland plots and the correlated individual question scores by principal component analysis (PCA). All analyses were carried out using Minitab (Minitab Inc., State College, Pa., USA).

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## Results

One hundred and eight women with chronic pelvic pain completed the initial questionnaire; of these, 88 (81%) women had a positive diagnosis of endometriosis, of which

**Table 1** Change in pain scores with treatment with respect to initial surgical findings

Surgical findings	Global pain scores (SD)		Statistical significance ( <i>P</i> ) (paired <i>t</i> -test)
	Pre-operative	Post-operative	
No endometriosis ( <i>n</i> =2)	21.0 (2.8)	7.0 (7.1)	0.30
Superficial endometriosis only ( <i>n</i> =17)	17.5 (7.8)	16.1 (6.7)	0.43
Deep ± superficial endometriosis ( <i>n</i> =27)	19.2 (7.2)	14.5 (8.9)	0.004

eight (7%) women had had a previous pelvic clearance (removal of uterus and/or ovaries prior to recruitment) and six (6%) underwent simultaneous pelvic clearance (hysterectomy and bilateral salpingo-oophorectomy) during laparoscopy. These 14 women did not have complete data sets in view of the absence of menstrual symptoms and were excluded from the analysis. Of the remaining 74 women with complete pelvic organs and a positive diagnosis of endometriosis, 44 (59% of the target group of 74 cases) had complete data sets, both pre-operatively, intra-operatively and post-operatively. Two other women had complete data sets but no identifiable pelvic pathology. The data from these women were analysed.

### Surgical findings

The r-ASRM score was calculated for the 44 women with a histological diagnosis of endometriosis. Seventeen (39%) were stage 1, seven (16%) were stage 2, four (9%) were stage 3 and 16 (36%) were stage 4. The utero-sacral ligaments were involved in 26 (59%) and recto-vaginal disease in 19 (43%) women. Six (14%) women had ovarian endometriomas which were resected. The pouch of Douglas was uninvolved in 25 (57%), partially obliterated in four (9%), and completely obliterated in 15 (34%). One woman had a full-thickness lesion of the vagina excised, and one had a full-thickness bladder lesion. The disease was excised from the rectal serosa in 19 (43%) women, and three disc resections (rectal mucosal involvement) performed and completed laparoscopically. None of the women in this study required conversion to laparotomy or presented with a secondary complication.

**Table 2** Relationship between endometriosis classification and r-ASRM score

r-ASRM score	Endometriosis	
	1 (Superficial)	2 (Deep)
1	14	3
2	1	6
3	2	2
4	0	16
	17	27

Chi-square test of association:  $\chi^2_{(3)} = 25.8 P < 0.001$

### Pain scores

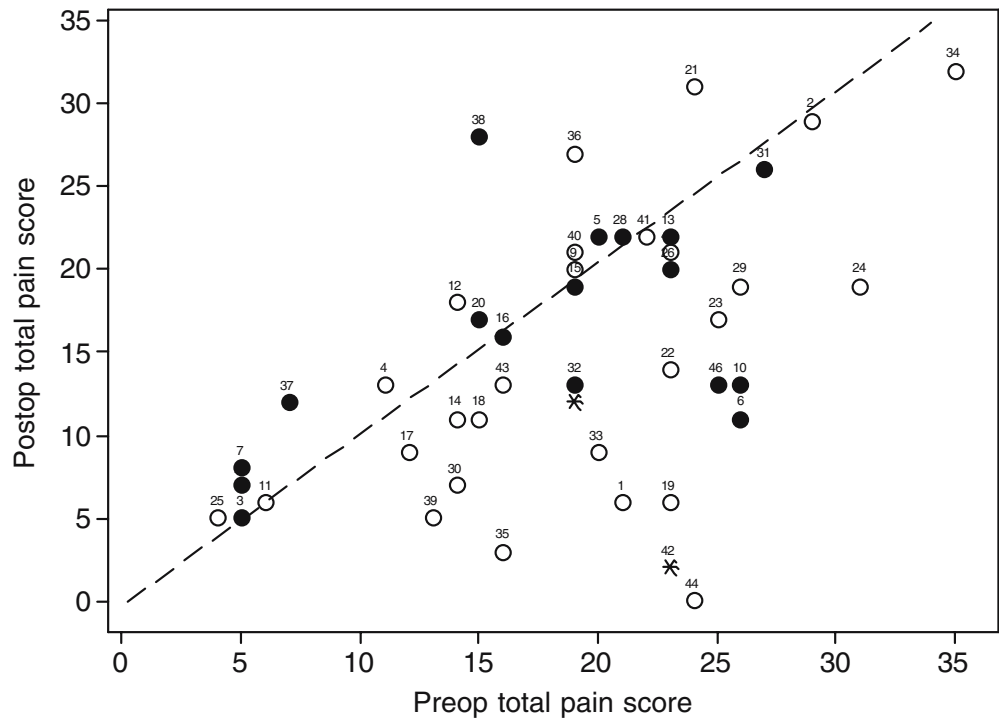
Table 1 summarises the results of the pain scores. Pre-operative questionnaires showed that the women in the study reported a significant degree of pain (mean score of 18.6 (SD 7.2) *n*=46), the severity of which was unrelated to their r-ASRM score (Kruskal–Wallis test, *P*=0.56) or to the presence or type of endometriotic disease (Sampson's or Cullen's disease) (Kruskal–Wallis test, *P*=0.90). Over the course of the study an appreciable but non-significant improvement in pain was observed in women with no disease (but there were only two cases), no improvement was seen with women classified as having superficial endometriosis (class 1), but significant improvements did occur in women who had undergone resection of their nodular endometriotic disease (class 2). Table 2 shows a highly statistically significant association between r-ASRM score and disease type, ( $\chi^2_{(3)} = 25.8 P < 0.001$ ). This shows that the majority of 'deep' (class 2) cases had an r-ASRM grade of 4, while the majority of 'superficial' cases (class 1) had an r-ASRM grade of 1.

The improvement in pain was independent (note: high pre-pain scores are 'predictive' of improvement' but probably a 'basement' effect) of the r-ASRM class but appears to be greater in women with nodular disease (class 2 deep) than in those with only superficial disease (class 1 superficial) or even absence (class 0) of disease. A scatter plot of global post-operation pain score vs pre-operation pain score demonstrates this (Fig. 1). When the disease is classified as none, mild (class 1) or severe (class 2), those below the line indicate improvement, but this is not seen when an Altman–Bland plot, widely used for method comparison, is used for the comparison of the pre- and post-operative scores and the r-ASRM classification is used (Fig. 2). (This plot shows the average improvement in global pain score of 3.8 points with the 95% limits of agreement).

Table 3 shows the effect of treatment on individual symptoms, with improvements in dysmenorrhoea and pelvic pain showing the most statistically significant improvements (*P*=0.006 and *P*=0.005, respectively). A statistically significant improvement was also seen with back pain during menses (*P*=0.025), while improvements for dyschezia during menses and dyspareunia were of borderline significance (*P*=0.047 and *P*=0.049). The global pain score over all 46 women was reduced, on average, by 3.8 points (95% CI 1.5 to 6.1).

A multivariate PCA was carried out on the correlation matrix of the seven individual symptom scores for each

**Fig. 1** Scatter plot of post-operative global pain score vs pre-operative global pain score. Symbols: \* no endometriosis, ● superficial endometriosis only, ○ deep ± superficial endometriosis. The numbers identify each subject's reference number

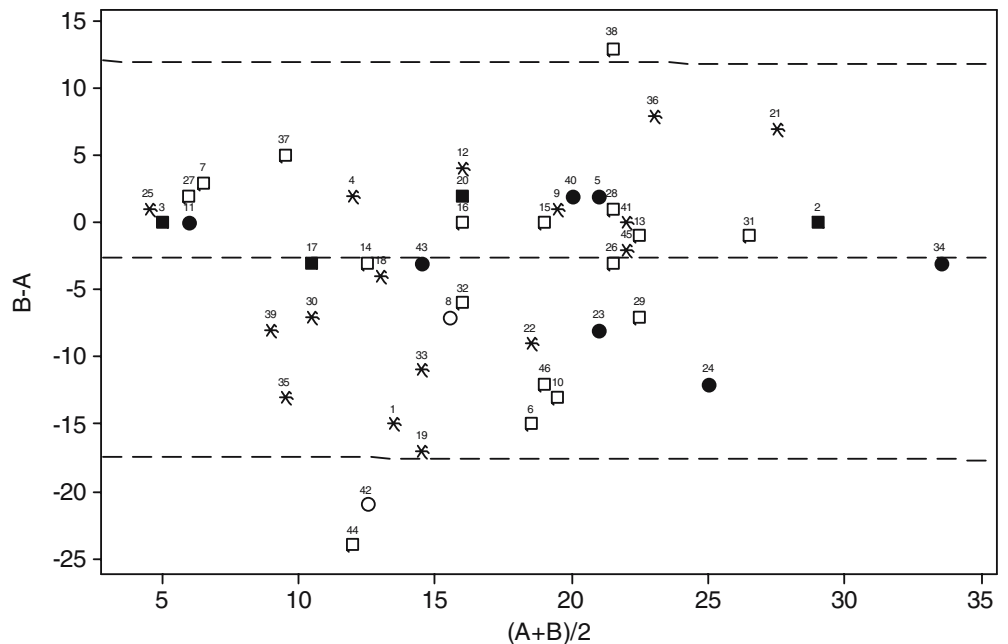


woman to identify the degree of inter-individual differences in the questionnaire responses. PCA is a multivariate statistical analysis that transforms the original set of correlated variables (here, the seven symptom scores from each completed questionnaire) into a new set of orthogonal or uncorrelated linear combinations called principal components [14]. These new variables are linear combinations of the original variables. The first component ‘accounts’ for as much of the variation in the original data as possible. Subsequent components are derived in decreasing order of importance: the second ‘accounts’ for

as much of the remaining variation as possible, and so on for the other components. This reduction of the ‘dimensionality’ of the original data sets provides a powerful statistical approach for the exploration of complex data sets. A plot, for instance, of the first and second principal component scores for the individuals can provide a concise description of the data, identifying patterns in the data and bringing out aberrant data or unusual results.

The plot of the first two principal component scores for the before and after scores for the 46 women is shown in Fig. 3. Principal component 1 (PCI) (which ‘explained’

**Fig. 2** Altman–Bland plot of difference (B–A) vs average of pre-operative and post-operative global pain scores (B+A)/2. Average change and ±95% limits of agreement are shown by dashed lines. The numbers identify each subject's reference number. Symbols indicate r-ASMR classification: ○ class 0, □ class 1, ● class 2, ■ class 3, \* class 4



**Table 3** Effect of treatment on individual symptoms ( $n=46$ . Includes two women without identifiable pelvic pathology)

Symptom	Pain scores (SD)		Statistical significance of difference (paired <i>t</i> -test)
	Initial visit	Follow-up visit	<i>P</i>
Dysmenorrhoea	3.85 (1.27)	3.04 (1.70)	0.006
Pelvic pain	2.85 (1.55)	2.22 (1.44)	0.005
Dyschezia throughout month	2.02 (1.78)	1.78 (1.57)	0.38
Dyschezia during menses	2.59 (1.87)	1.91 (1.93)	0.047
Back pain throughout month	2.17 (1.61)	1.85 (1.76)	0.17
Back pain during menses	2.61 (1.58)	1.96 (1.84)	0.025
Dyspareunia	2.54 (1.80)	2.09 (1.87)	0.049
<b>Global scores</b>	<b>18.6 (7.25)</b>	<b>14.8 (8.13)</b>	<b>0.002</b>

45% of the total variation in the scores) is derived by giving high negative weights to all the symptom scores, which results in high negative values for individuals with high scores on all symptom scores (i.e. high global pain scores). It can be seen from Fig. 3 that a large proportion of women show an overall improvement in pain scores, as shown by the shift rightwards of their PCI scores. There is, though, appreciable inter-individual differences with individuals such as no. 42 and no. 44 showing very big differences (improvements) in their scores before and after treatment, while individual no. 34 shows little difference. Principal component 2 (PCII) (which ‘explained’ 17% of the variability) provides a contrast between high scores for pelvic pain, back ache and back ache during menstruation (positive PCII values) with high scores for dyschezia, dyschezia during menstruation and dyspareunia (negative PCII values). Compare, for instance, the pre-operative scores for individual no. 40 (22 points) with individual no. 1 (21 points), where the profile of scores is very different. Note that Individual no. 17 shows a switch in the pattern of symptom scores before and after treatment,

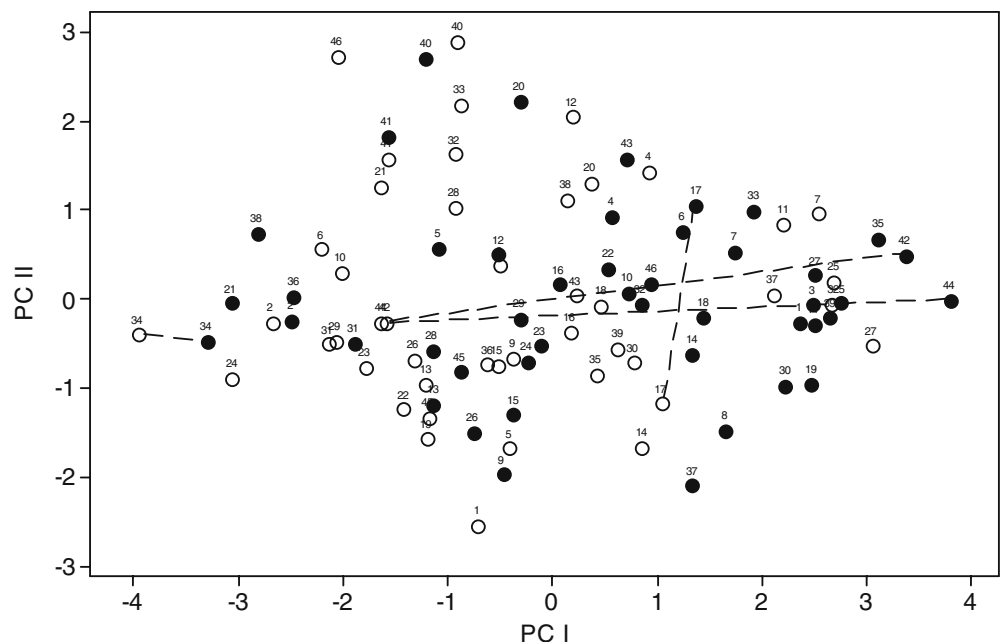
although her overall global scores were similar (12 before and 9 after).

The women in this cohort presented with a significant level of depressive morbidity, 66% of women at the initial visit demonstrating clinically significant depression, a score >9, with 19% at the extreme, severe end of the spectrum. With the use of a paired *t*-test, there was an improvement in this level of depression, which approached statistical significance ( $P=0.065$ ). This improvement was more prominent in those at the severe end of the spectrum, with those women with the high depression scores having the greatest chance of improvement.

**Discussion**

This study demonstrates that, like many chronic illnesses, endometriosis, with its concomitant pelvic pain, increases depression. The severity of the pain before treatment, however, does not correlate with the operative findings of endometriosis described either in terms of r-ASRM score or type of disease (class 1/superficial, Sampson’s or class

**Fig. 3** Scatter plot of second principal component scores (PCII) against first principal component scores (PCI) from principal component analysis of individual questionnaire scores for pre-operative questionnaires. ○ post-operative questionnaires ●. The numbers identify each subject’s reference number, and dotted lines link scores for pre- and post-operative scores for subjects who are discussed in the text



2/deep, Cullen's disease). Sustained improvement in the level of global pain scores at 18 months was only statistically significantly improved in those with infiltrating or nodular disease (class 2 'deep') as opposed to those with only superficial disease (class 1). This study supports the classification by Garry et al. into superficial (Sampson's) and deep (Cullen's) disease [10] but does not add to the evidence about aetiology of the two situations: superficial disease co-existing with deep disease. The more visually obvious superficial lesions, although associated with adhesions and appearing more severe and sometimes with a higher r-ASRM score, are relatively resistant to surgical treatment [14]. Infiltrating lesions are visually easy to miss. They often require palpation using a secondary port at laparoscopy and appear visually less severe, scoring lower in the r-ASRM score. These lesions are, however, associated with an appreciable relief of pain after surgery in a proportion (22/27, 81%) of cases (as measured by the questionnaire). Superficial disease is equally distributed throughout all (r-ASRM) stages except stage IV in this cohort. The r-ASRM score [9] is heavily dependent on the presence of adhesions and obliteration of cul-de-sac, which accounts for 104 out of the 150 points available, with the remaining 46 points scored for the type and amount of endometriotic lesions present. This may be important in terms of fertility, but this study suggests that it is not so valuable in the surgical assessment of pelvic pain (and as a predictor of who will experience pain relief).

High initial global pain scores did not differentiate between severity of endometriosis as defined by either r-ASRM score or type of disease (superficial or deep) or identify those women whose pain scores were more likely to improve. Therefore, severity of symptoms does not appear to help predict improvement. It may be that details of the site and nature of the pain may be more useful in distinguishing between superficial and deep disease.

A limitation of this study was the number of incomplete data sets that were excluded from the analysis and the small size of the data set used. This limits the analysis, and we therefore did not use this data set to create our own model to predict the type of endometriosis by using pelvic pain scores. The results do indicate the possible benefit in repeating this study on a larger scale in order to develop a useful clinical diagnostic tool. The data collected can then be used to create a prognostic model, give guidance as to the value of any surgery and thus aid patient counselling.

The high dropout rate is related to the nature of the data collection, in that the follow-up data were acquired by postal questionnaire, with only one written reminder and no direct patient contact. This design was necessary to improve the integrity of the data, given the 2-year follow-up period and to ensure that any placebo effect following surgery would have passed. It is possible that the women who did not respond to the second questionnaire were more likely to have been discharged from the clinic than women who had not been discharged and where follow-up data could be collected in clinics. The former group of poor responders could, therefore, be women who had responded better to treatment. This is a limitation of the study, as it

may lead to underestimation of the size of the reduction in pain achieved. If this is so, then it may be proposed that surgical excision may be appropriate for deep disease but that women with chronic pelvic pain with no evidence of endometriosis, women with superficial disease only and not complaining of sub-fertility, irrespective of r-ASRM score, were less likely to show reduced pain and should be offered alternative treatments.

A major finding of this study is the apparent failure of surgical therapy to have a sustained reduction in global pain scores for women with superficial disease, in contrast to the report by Abbott and colleagues [2], which showed good relief at 5 years, and the randomised controlled trial by Wright et al. [1], which showed pain relief for 65% of women at 6 months. Abbott and colleagues' cohort did not distinguish between superficial and deep disease or the number requiring hysterectomy, although they did subgroup the data by r-ASRM stage. Also, 34% required further surgery, and these patients were still included in the analysis. In the study by Wright et al. [1], 6 months as the end point of the randomised trial is probably too early for a definitive assessment to be made of sustained benefit.

r-ASRM, unlike most other disease staging systems, is not dependant solely on the disease itself, as it is derived from an assessment of the presence of pelvic adhesions, as well as endometriotic deposits. The most useful intra-operative predictor of pain relief appears to be depth of invasion of the lesion [13]. The limitation of this assessment is in its clinical practicality. The division of endometriosis into superficial or deep disease may so far in clinical practice be the best prognostic indicator.

This surgery can be complex and is thus limited by the availability of the appropriate level of surgical experience and expertise [15].

Endometriosis may not be fully excised because of anxiety about damage to underlying structures, and this too may reduce the effectiveness of surgical management. Like all treatments, success in either terms of disease eradication or improvement in symptoms will not always be the case [10].

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## Conclusion

The r-ASRM classification does not assist in patient treatment either in terms of symptom severity or prognosis. Deep endometriotic disease, as compared with superficial disease, in the long term, is responsive to complete surgical excision in the treatment of chronic pelvic pain.

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