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Sacrospinous hysteropexy versus vaginal hysterectomy with uterosacral ligament suspension in women with uterine prolapse stage 2 or higher: observational follow-up of a multicentre randomised trial

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ABSTRACT OBJECTIVE

To evaluate the effectiveness and success of uterus preserving sacrospinous hysteropexy as an alternative to vaginal hysterectomy with uterosacral ligament suspension in the surgical treatment of uterine prolapse five years after surgery.

DESIGN

Observational follow-up of SAVE U (sacrospinous fixation versus vaginal hysterectomy in treatment of uterine prolapse ≥ 2) randomised controlled trial.

SETTING

Four non-university teaching hospitals, the Netherlands.

PARTICIPANTS

204 of 208 healthy women in the initial trial (2009-12) with uterine prolapse stage 2 or higher requiring surgery and no history of pelvic floor surgery who had been randomised to sacrospinous hysteropexy or vaginal hysterectomy with uterosacral ligament suspension. The women were followed annually for five years after surgery. This extended trial reports the results at five years.

MAIN OUTCOME MEASURES

Prespecified primary outcome evaluated at five year follow-up was recurrent prolapse of the uterus or vaginal vault (apical compartment) stage 2 or higher evaluated by pelvic organ prolapse quantification system in combination with bothersome bulge symptoms or repeat surgery for recurrent apical prolapse. Secondary outcomes were overall

anatomical failure (recurrent prolapse stage 2 or higher in apical, anterior, or posterior compartment), composite outcome of success (defined as no prolapse beyond the hymen, no bothersome bulge symptoms, and no repeat surgery or pessary use for recurrent prolapse), functional outcome, quality of life, repeat surgery, and sexual functioning.

RESULTS

At five years, surgical failure of the apical compartment with bothersome bulge symptoms or repeat surgery occurred in one woman (1%) after sacrospinous hysteropexy compared with eight women (7.8%) after vaginal hysterectomy with uterosacral ligament suspension (difference -6.7%, 95% confidence interval -12.8% to -0.7%). A statistically significant difference was found in composite outcome of success between sacrospinous hysteropexy and vaginal hysterectomy (89/102 (87%) v 77/102 (76%). The other secondary outcomes did not differ. Time-to-event analysis at five years showed no differences between the interventions.

CONCLUSIONS

At five year follow-up significantly less anatomical recurrences of the apical compartment with bothersome bulge symptoms or repeat surgery were found after sacrospinous hysteropexy compared with vaginal hysterectomy with uterosacral ligament suspension. After hysteropexy a higher proportion of women had a composite outcome of success. Time-to-event analysis showed no differences in outcomes between the procedures.

TRIAL REGISTRATION

trialregister.nl NTR1866.

Introduction

Uterine prolapse is a common health problem, with increasing incidence due to aging populations and rising obesity rates.^{1,2} Women's lifetime risk for prolapse surgery is 11-20%, and worldwide vaginal hysterectomy is the most common surgical procedure for uterine prolapse.^{3,4} Studies comparing vaginal hysterectomy with uterus preserving procedures are limited, and no data are available on long term follow-up. Guidelines for pelvic organ prolapse are therefore ambiguous, resulting in variation in treatment.⁵ The SAVE U (sacrospinous fixation versus vaginal hysterectomy in treatment of uterine prolapse ≥ 2) randomised trial compared uterus preservation with hysterectomy on a large scale with relevant

WHAT IS ALREADY KNOWN ON THIS TOPIC

Vaginal hysterectomy is the standard treatment for uterine prolapse, but uterus preservation is gaining popularity

Sacrospinous hysteropexy was non-inferior to vaginal hysterectomy with suspension of the uterosacral ligaments for recurrent prolapse of the apical compartment with bothersome bulge symptoms or repeat surgery after 12 months' follow-up

Overall anatomical outcome, quality of life, subjective outcome, hospital stay, recovery, complications, and sexual functioning did not differ

WHAT THIS STUDY ADDS

Follow-up at five years shows that uterine preservation is more effective than vaginal hysterectomy with uterosacral ligament suspension, and the risk for retreatment of recurrent prolapse or malignancy is low

Women who require surgical correction of uterine prolapse should be given the opportunity to choose uterus preservation and avoid hysterectomy

outcome measures.⁶ Treatment with sacrospinous hysteropexy was non-inferior to vaginal hysterectomy with suspension of the uterosacral ligaments for surgical failure of the apical compartment after 12 months' follow-up. No notable differences were found between the interventions for overall anatomical and surgical failure, functional outcome, quality of life, complications, postoperative recovery, length of hospital stay, and sexual functioning. One of the study's limitations was short duration of follow-up (12 months). Two recent systematic reviews with meta-analysis on apical pelvic organ prolapse surgery confirmed the short term results of the SAVE U trial.⁷ The studies also concluded that long term follow-up of the comparison between vaginal hysterectomy with apical suspension and vaginal hysteropexy is necessary because the impact of the uterus on prolapse outcomes many years after surgery is still unknown. We report the five year outcomes in women after sacrospinous hysteropexy or vaginal hysterectomy with suspension of the uterosacral ligaments enrolled in the SAVE U randomised trial.

Methods

Study design

Details of the trial protocol have been published previously.^{6,9} All women gave written informed consent before randomisation.

In the original trial, women with uterine prolapse at stage 2 (uterine prolapse 1 cm above or beyond the hymen, according to the Pelvic Organ Prolapse Quantification (POP-Q) system) or higher were randomly assigned to sacrospinous hysteropexy or vaginal hysterectomy with suspension of the uterosacral ligaments in a non-blinded multicentre randomised controlled non-inferiority trial. Concomitant repair of anterior or posterior vaginal prolapse (colporrhaphy) was allowed, as was anti-incontinence surgery. We excluded women with previous pelvic floor or prolapse surgery, known malignancy, an abnormal cervical smear test result, a wish to preserve fertility, language barriers, immunological or haematological disorders interfering with recovery after surgery, abnormal ultrasound findings of the uterus or ovaries, and abnormal uterine bleeding. The women were randomly allocated in a 1:1 ratio using a web based application with computer generated randomisation tables in blocks of four, stratified by hospital and stage of uterine prolapse. The trial was non-blinded as it was impossible to blind surgeons and women to the allocated surgical procedure. An independent doctor or specialist nurse not involved in treatment carried out the follow-up visits.

Outcome measures

The primary outcome of the original SAVE U study was surgical failure of the apical compartment, defined as a recurrent prolapse stage 2 or higher of the uterus or vaginal vault (apical compartment) evaluated by the POP-Q system in combination with bothersome bulge symptoms or repeat surgery for recurrent apical

prolapse after 12 months follow-up. This outcome was also used as the primary outcome after five years. The predefined secondary outcomes at five year follow-up included overall anatomical failure (pelvic organ prolapse stage 2 or higher in any compartment), a composite outcome of success (defined as no prolapse beyond the hymen, no bothersome bulge symptoms, and no repeat surgery or pessary use for recurrent prolapse), functional outcome, quality of life, repeat surgery, and sexual functioning.

Interventions

The surgeons were provided with a detailed guideline of the study interventions to ensure a uniform technique.^{6,9}

Sacrospinous hysteropexy—Vaginal sacrospinous hysteropexy was performed unilaterally to the right sacrospinous ligament. The posterior vaginal wall was incised and the sacrospinous ligament accessed through the pararectal space. Two permanent sutures (Prolene 1.0; Ethicon, Somerville, NJ) were placed under direct vision through the sacrospinous ligament at least 2 cm from the ischial spine. Additional anterior or posterior vaginal wall repair or incontinence surgery was performed as required. Both ends of the permanent sutures were placed through the posterior side of the cervix and tightened and the uterus redressed. The posterior vaginal wall was closed with absorbable sutures (Vicryl 2; Ethicon, Somerville, NJ). (For further details see www.youtube.com/watch?v=ySSfy2A1_RM and www.youtube.com/watch?v=wjct1r37sTw).

Vaginal hysterectomy—The vaginal wall around the cervix was circumcised. After bladder and bowel dissection the anterior and posterior peritoneum were opened. The uterosacral ligaments—strong supportive ligaments that attach the cervix to the sacrum— were identified, ligated, and transected. The uterus was released in several steps using clamps and sutures. After removal of the uterus, the surgical pedicles were inspected for haemostasis and the adnexa were inspected for abnormalities. The peritoneum was closed using a delayed absorbable suture (Vicryl 1.0; Ethicon, Somerville, NJ). Additional vault suspension in this study was performed by suspension of the uterosacral ligaments. This technique has been described previously and involves the attachment of the uterosacral ligaments to the vaginal vault with two delayed absorbable sutures (Vicryl 1.0, Ethicon).⁹ The sutures were placed as high as possible on the visible part of the ligament, which in general was caudal to the level of the ischial spine thereby restoring normal support to the apical compartment.¹⁰ Again, concomitant anterior or posterior vaginal wall repair or anti-incontinence surgery was performed if indicated.

Measurements and procedures

After the initial 12 month follow-up, women attended annual appointments at hospital for five years after surgery. Pelvic organ prolapse was staged during follow-up using the POP-Q system, and women completed validated health related and disease specific

quality of life questionnaires: short form-36, Euroqol 5D, urogenital distress inventory, defecatory distress inventory, and incontinency impact questionnaire.¹¹⁻¹⁴ The presence of bothersome bulge symptoms after surgery was defined as a positive answer to any of the following questions from the urogenital distress inventory: “Do you experience a sensation of bulging or protrusion from the vagina?” and “Do you have a bulge or something fallen out that you can see in the vagina?” in combination with a response “somewhat bothered” to “very much bothered” to the question “how much does this bother you?” To assess sexual functioning, we used the 12 item pelvic organ prolapse/urinary incontinence sexual questionnaire, translated from the validated questionnaire but not validated for Dutch language at that time.¹⁵

Statistical analysis

The sample size for this trial was based on the primary outcome of the original trial at 12 months' follow-up and reported previously.⁹ We assessed study outcomes by intention-to-treat analysis and surgical failure and composite outcome of success also by per protocol analysis. This analysis included women who completed the entire treatment protocol as originally planned, with availability of the POP-Q scores at five year follow-up and absence of major deviations from the protocol. We evaluated the outcomes at five year follow-up by frequencies and proportions and used the Agresti-Coull method to calculate 95% confidence intervals for differences in proportions.¹⁶ To account for missing data on anatomical outcome at five year follow-up, we applied two strategies. For the first strategy, we used the last observation carried forward with data from the last available follow-up visit. If data were not available, we excluded the woman from the intention-to-treat last observation carried forward analysis. Furthermore, we applied conservative imputation by imputing a failure for all women with missing data at five year follow-up (worst case scenario). If questionnaires were missing, we obtained information on the presence or absence of bothersome bulge symptoms from the case record form of the follow-up visit. For the second strategy, we performed time-to-event (survival) analysis using a Kaplan-Meier approach to estimate the cumulative incidence at five years of follow-up, and calculated the difference in cumulative incidences with corresponding 95% confidence intervals.

Statistical significance was evaluated using Fisher's exact tests and Mann-Whitney U tests to compare proportions and continuous variables between the groups. We used paired sample *t* tests to compare mean continuous data within groups. All statistical analyses were performed with SPSS for windows (version 24.0.0.1).

Patient and public involvement

No patients were involved in the design and implementation of the study, the dissemination of results, setting the research question or the outcome measures, or recruitment.

Results

In the original trial, 208 women were randomly assigned to sacrospinous hysteropexy (n=103) or vaginal hysterectomy with uterosacral ligament suspension (n=105) between 27 November 2009 and 12 March 2012. Figure 1 shows the flow of women through the study. A total of 204 women were eligible for the last observation carried forward analysis at five year follow-up. One woman developed severe complications during hospital stay after vaginal hysterectomy and died eight days after surgery. Three women withdrew consent before the first follow-up visit at six months. All four women were excluded from the last observation carried forward analysis.

Two women were lost to follow-up because they died. These deaths were from causes unrelated to the study and we applied last observation carried forward on their outcomes.

Two women received sacrospinous hysteropexy instead of vaginal hysterectomy owing to technical difficulties during surgery.⁶ According to the intention-to-treat principle, we included these women in the intention-to-treat analysis, with all women analysed as randomised. For the per protocol analysis, we excluded women with major protocol deviations (n=9), women who were lost to follow-up (n=22,) and women with missing or incomplete POP-Q scores (n=18).

Baseline characteristics of women did not differ noticeably (table 1). Table 2 and figure 2 show the results for surgical and anatomical failure, success, and repeat surgery. Surgical failure of the apical compartment with bothersome bulge symptoms or repeat surgery occurred in only one of 102 women (1%) after sacrospinous hysteropexy compared with eight of 102 women (8%) after vaginal hysterectomy with uterosacral ligament suspension (difference -6.7%, 95% confidence interval -12.8% to -0.7%) for the last observation carried forward approach. In the intention-to-treat analysis with conservative imputation, surgical failure of the apical compartment with bothersome bulge symptoms or repeat surgery occurred in 16 of 103 women (16%) after sacrospinous hysteropexy and 27 of 105 women (26%) after vaginal hysterectomy (difference -9.8%, 95% confidence interval -20.9 to 1.2). The per protocol analysis showed surgical failure of the apical compartment in none of 88 women after sacrospinous hysteropexy and four of 78 women (5%) after vaginal hysterectomy (difference -5.1%, 95% confidence interval -10.9% to 0.7%). In the time-to-event analysis surgical failure was found in four of 102 women (4%) after sacrospinous hysteropexy and nine of 102 women (9%) after vaginal hysterectomy (difference -4.7%, 95% confidence interval -11.4% to 2.0%). Table 3 shows the characteristics of women with surgical failure of the apical compartment.

Overall anatomical failure occurred in 46 of 102 women (45%) after sacrospinous hysteropexy and 51 of 102 women (50%) after vaginal hysterectomy (difference -4.8%, 95% confidence interval -18.5% to 8.9%). No differences were found for anatomical failure in the different compartments except for the posterior compartment: five of 102 women (5%) had

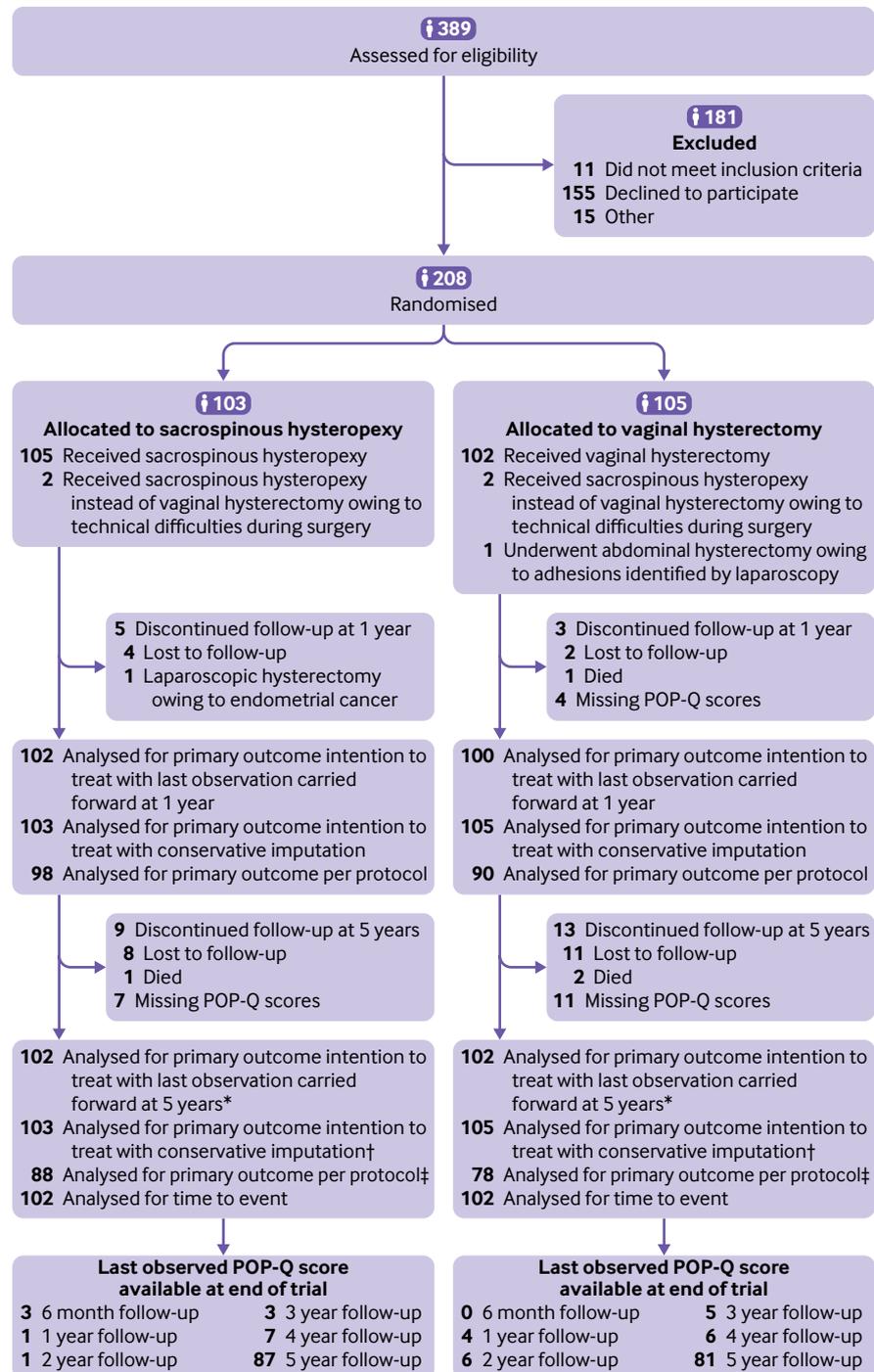


Fig 1 | Flow of women through study. *Intention to treat: two women allocated to vaginal hysterectomy received sacrospinous hysteropexy and were analysed in the vaginal hysterectomy group. One woman after vaginal hysterectomy had recurrent apical prolapse, but pelvic organ prolapse quantification (POP-Q) score was missing; this woman was included in the intention-to-treat last observation carried forward analysis. †Missing data imputed as failure. ‡Per protocol analysis: two women did not receive intended treatment. Excluded from per protocol analysis: discontinued follow-up at five year (n=22), missing or incomplete POP-Q score (n=18), and major protocol deviations (n=9); seven patients met two criteria for exclusion from per protocol analysis

prolapse stage 2 or higher of the posterior vaginal wall after sacrospinous hysteropexy and 18 of 101 women (18%) after vaginal hysterectomy (difference -12.7%, 95% confidence interval -21.5% to -3.9%). Time-to-event analysis showed overall anatomical failure in 73 of 102 women (72%) after sacrospinous hysteropexy

and 78 of 102 women (77%) after vaginal hysterectomy (difference -5.0%, -17.1% to 7.1%).

In the last observation carried forward approach, treatment success was significant in 89 of 102 women (87%) in the sacrospinous hysteropexy group compared with 77 of 102 women (76%) in the vaginal

Table 1 | Baseline characteristics of women in the extended trial. Value are numbers (percentages) unless stated otherwise

Characteristics	Sacrospinous hysteropexy (n=102)	Vaginal hysterectomy (n=102)
Median (range) age (years)	63 (45-85)	61 (33-82)
Highest educational level:		
Primary or secondary school	14 (14)	6 (6)
High school	77 (77)	80 (81)
Bachelor, master or academic degree	9 (9)	13 (13)
Comorbidity:		
Cardiovascular disease	39 (38)	31 (30)
Diabetes mellitus	5 (5)	5 (5)
Respiratory disease	3 (3)	7 (7)
Smoker	13 (15)	9 (10)
Median (range) No of vaginal deliveries	2 (0-7)	3 (0-7)
Median (range) No of caesarean deliveries	0 (0-1)	0 (0-2)
Mean (SD) body mass index	25.9 (3.3)	25.9 (3.5)
POP-Q stage uterine prolapse (point C)*:		
2	66 (65)	65 (64)
3	28 (28)	28 (28)
4	8 (8)	9 (9)
POP-Q stage 2-4:		
Anterior prolapse (Ba \geq 1)	93 (94)	92 (92)
Posterior prolapse (Bp \geq 1)	29 (29)	32 (32)
Prolapse beyond hymen:		
Apical (POP-Q C >0)	47 (48)	40 (40)
Anterior (POP-Q Aa or Ba >0)	70 (71)	70 (70)
Posterior (POP-Q Ap or Bp >0)	11 (11)	11 (11)
Overall POP-Q stage*:		
2	25 (25)	35 (35)
3	69 (70)	61 (61)
4	5 (5)	4 (4)

POP-Q= pelvic organ prolapse quantification.

Percentages were calculated using non-missing data. Women were analysed as allocated.

*System involves quantitative measurements of various points of vaginal wall, with hymen as reference point. Degree of prolapse of anterior vaginal wall (Aa and Ba), posterior vaginal wall (Ap and Bp), and uterus or vaginal vault (C) measured in centimetres both above or proximal to hymen (negative number) or beyond or distal to hymen (positive number), with plane of hymen defined as zero. A represents the descent of a measurement point 3 cm proximal to the hymen on the anterior (Aa) and posterior (Ap) vaginal wall. B is the most descended edge on the anterior (Ba) and posterior (Bp) vaginal wall. POP-Q stage 2: most distal prolapse is between 1 cm above and 1 cm beyond hymen; stage 3: most distal prolapse is prolapsed >1 cm beyond hymen but no further than 2 cm less than total vaginal length; stage 4: total prolapse.

hysterectomy group (difference 11.5%, 0.8% to 22.2%). Time-to-event analysis showed success in 70% of the women in the sacrospinous hysteropexy group and 65% of the women in the vaginal hysterectomy group (difference 5.3, -7.9 to 18.5).

Three of 102 women (3%) underwent surgery for recurrent prolapse in the sacrospinous hysteropexy group compared with seven of 102 women (7%) in the vaginal hysterectomy group (difference -3.8%, -10.2% to 2.5%). No women (0%) had recurrent surgery for pelvic organ prolapse in a non-operated compartment in the sacrospinous hysteropexy group compared with four of 102 women (4%) in the vaginal hysterectomy group (difference -3.8%, 95% confidence interval -8.4% to 0.7%). In the time-to-event analysis three of 102 women (3%) had repeat surgery in any compartment in the sacrospinous hysteropexy group compared with nine of 102 women (9%) in the vaginal hysterectomy group (difference -5.9%, 95% confidence interval -12.3% to 0.5%).

During follow-up two women (2%) underwent hysterectomy after sacrospinous hysteropexy. Stage 1 endometrial carcinoma was diagnosed in one woman (1%) and laparoscopic hysterectomy was performed. The other woman had persistent buttock pain immediately after surgery, and the sutures and uterus were removed four months after surgery and

the symptoms resolved. Subsequent surgical treatment for stress urinary incontinence was necessary in two of 102 women (2%) in the sacrospinous hysteropexy group compared with six of 102 women (6%) in the vaginal hysterectomy group (difference -3.8%, 95% confidence interval -9.7% to 2.0%). Tables 4 and 5 provide information on functional outcome, quality of life, and sexual functioning. Functional outcome and quality of life did not differ statistically significantly between the groups (table 4). Among the women who completed the pelvic organ prolapse/urinary incontinence sexual questionnaire before and five years after surgery, scores showed statistically significant improvement in both groups but no significant difference in total scores between both interventions (table 5). All serious adverse events potentially related to surgical treatment occurred in the first 12 months after surgery and have been described previously.⁶

Discussion

This study provides evidence that treatment of uterine prolapse with sacrospinous hysteropexy is effective and has lower risk of recurrent bothersome uterine prolapse or retreatment of the apical compartment compared with vaginal hysterectomy with uterosacral ligament suspension. We found no differences in overall anatomical failure, functional outcome, quality

Table 2 | Outcomes for pelvic organ prolapse at five year follow-up. Values are numbers (percentages) of women unless stated otherwise

Outcomes	Sacrospinous hysteropexy	Vaginal hysterectomy	% difference (95% CI)
Surgical failure of apical compartment*:			
ITT analysis with LOCF	1/102 (1)	8/102 (8)	-6.7 (-12.8 to -0.7)
ITT analysis with conservative imputation	16/103 (16)	27/105 (26)	-9.8 (-20.9 to 1.2)
Per protocol analysis	0/88 (0)	4/78 (5)	-5.1 (-10.9 to 0.7)
Time-to-event analysis†	4/102 (4)	9/102 (9)	-4.7 (-11.4 to 2.0)
Anatomical failure‡:			
Overall anatomical failure	46/102 (45)	51/102 (50)	-4.8 (-18.5 to 8.9)
Apical compartment	3/102 (3)	7/102 (7)	-3.8 (-10.2 to 2.5)
Anterior compartment	41/102 (40)	36/101 (36)	4.5 (-8.9 to 17.8)
Posterior compartment	5/102 (5)	18/101 (18)	-12.7 (-21.5 to -3.9)
Time-to-event analysis	73/102 (72)	78/102 (77)	-5.0 (-17.1 to 7.1)
Composite outcome success§:			
ITT analysis with LOCF	89/102 (87)	77/102 (76)	11.5 (0.8 to 22.2)
ITT analysis with conservative imputation	77/103 (75)	65/105 (62)	12.6 (0.0 to 25.2)
Per protocol analysis	77/88 (88)	62/78 (80)	7.9 (-3.6 to 19.4)
Time-to-event analysis	71/102 (70)	65/102 (64)	5.3 (-7.9 to 18.5)
Prolapse beyond the hymen¶:			
Apical (POP-Q C >0)	0/102 (0)	4/101 (4)	-3.9 (-8.5 to 0.7)
Anterior (POP-Q Ba >0)	6/102 (6)	8/101 (8)	-2.0 (-9.4 to 5.3)
Posterior (POP-Q Bp >0)	0/102 (0)	3/101 (3)	-2.9 (-7.1 to 1.3)
Repeat surgery¶:			
Recurrent prolapse	3/102 (3)	7/102 (7)	-3.8 (-10.2 to 2.5)
Apical compartment	1/102 (1)	4/102 (4)	-2.9 (-7.8 to 2.0)
Anterior compartment	3/102 (3)	4/102 (4)	-1.0 (-6.5 to 4.6)
Posterior compartment	0/102 (0)	2/102 (2)	-1.9 (-5.7 to 1.8)
Different site from primary surgery**	0/102 (0)	4/102 (4)	-3.8 (-8.4 to 0.7)
Time-to-event analysis	3/102 (3)	9/102 (9)	-5.9 (-12.3 to 0.5)
Surgery for non-prolapse conditions:			
Surgery for stress urinary incontinence	2/102 (2)	6/102 (6)	-3.8 (-9.7 to 2.0)
Hysterectomy	2/102 (2)	-	-
Other	1/102 (1)	1/102 (1)	0 (-3.8 to 3.8)

ITT=intention to treat; LOCF=last observation carried forward; POP-Q=pelvic organ prolapse quantification. Percentages were calculated using non-missing data. Agresti-Coull method used to calculate 95% confidence intervals.
*Recurrent apical prolapse stage ≥2 with bothersome symptoms or repeat surgery for apical prolapse.
†Time-to-event analysis using Kaplan-Meier to calculate cumulative incidence until five year follow-up.
‡Prolapse POP-Q stage ≥2.
§No prolapse beyond hymen, absence of bothersome bulge symptoms, and no repeat surgery or pessary use.
¶ITT with LOCF.
**Reoperation for pelvic organ prolapse in non-operated compartment.

of life, repeat surgery, and sexual functioning between sacrospinous hysteropexy and vaginal hysterectomy with uterosacral ligament suspension at five year follow-up. However, the proportion of women with successful treatment was statistically significantly higher after sacrospinous hysteropexy.

Time-to-event analysis showed no differences in surgical failure of the apical compartment, overall anatomical failure, success, and repeat surgery between sacrospinous hysteropexy and vaginal hysterectomy with uterosacral ligament suspension.

Strengths and limitations of this study

This randomised trial evaluated efficacy and safety of uterus preserving sacrospinous hysteropexy and vaginal hysterectomy with uterosacral ligament suspension after five year follow-up. A major strength of this trial is the sample size and the large group of women who completed follow-up. POP-Q scores of 168 women (81%) were available for analysis. A recent systematic review on definitions of success in pelvic organ prolapse surgery concluded that most studies on such surgery use definitions solely based on anatomical criteria.¹⁷ We included definitions

for subjective outcomes and retreatment rates and analysed a composite outcome measure in which treatment was considered as success when women had no bothersome symptoms of prolapse, no surgical retreatment or pessary use, and no pelvic organ prolapse beyond the hymen as different studies have shown that the hymen is an important cut off point for symptom development.¹⁸⁻²⁰

The trial also has some limitations. We used the last observation carried forward method for missing data, with the advantage that it minimises the number of dropouts. In our trial, five out of nine (56%) women with recurrent pelvic organ prolapse of the apical compartment with bothersome symptoms or repeat surgery for recurrent apical prolapse withdrew from the study before the last study visit. As we evaluated outcomes solely at five year follow-up, these recurrences would not have been taken into account. However, there is a possibility that this method gives a biased estimate of the treatment effect and underestimates the variability of the estimated result. Prolapse recurrence could have occurred after withdrawal. By adding a time-to-event analysis using Kaplan-Meier this bias was minimised. Another limitation is the use of different types of sutures.

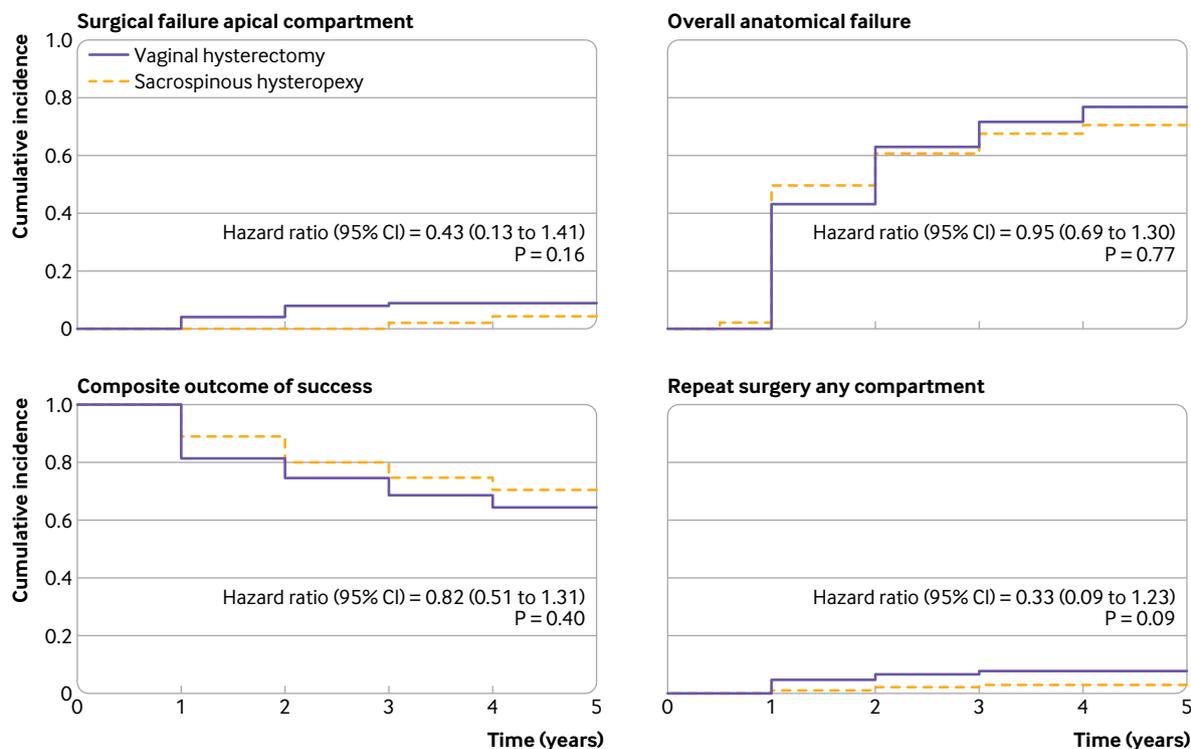


Fig 2 | Survival analysis to estimate the cumulative incidence of surgical failure of the apical compartment, overall anatomical failure, composite outcome of success and repeat surgery in any compartment at five year follow-up after sacrospinous hysteropexy and vaginal hysterectomy with uterosacral ligament suspension. *Cumulative incidence was number of events (%) that occurred during five year follow-up. Hazard ratios and 95% confidence intervals were calculated using Cox regression. (Top left) Recurrent apical prolapse stage ≥ 2 with bothersome symptoms or repeat surgery for apical prolapse. (Top right) Pelvic organ prolapse quantification (POP-Q) stage ≥ 2 in any compartment. (Bottom left) No prolapse beyond the hymen, no bothersome bulge symptoms and no repeat surgery or pessary use for recurrent prolapse. (Bottom right) Repeat surgery in any compartment

Permanent sutures were used in the sacrospinous hysteropexy procedure and delayed absorbable sutures in uterosacral ligament suspension after vaginal hysterectomy as this was the standard procedure in the participating hospitals at that time. This difference corresponds in general with the way both procedures are described in the literature. Currently, evidence is unclear about which type of suture material is preferable (delayed absorbable versus permanent or a combination of the two) and more research is needed on this topic.

In the sacrospinous hysteropexy group the proportion of women with anterior compartment anatomical failure, defined as a stage 2 pelvic organ prolapse or higher of the anterior vaginal wall, was greater after 12 months (47%) compared with the results at five year follow-up (40%). The most plausible explanation seems to be interobserver and intraobserver variability. The variability of the POP-Q score is, however, regarded as low and this scoring system is the only accepted

one used internationally in scientific research at this moment. Overall, a clinically relevant worsening of cystoceles over time seems unlikely.

Finally, it was not possible to blind the independent doctor or specialist nurse at follow-up to surgical intervention, because the cervix is present or absent in POP-Q. This is a limitation as it could lead to potential bias.

Comparison with other studies

Other randomised studies evaluating uterus preserving surgery versus vaginal hysterectomy with apical suspension after long term follow-up are not available. The risk of recurrent vaginal prolapse in a five year retrospective cohort study was 20% after vaginal hysterectomy with uterosacral ligament suspension based on a composite outcome definition of any anatomical prolapse beyond the hymen, or pessary, or repeat surgery.²⁰ The risk of recurrent surgery

Table 3 | Details for women with surgical failure of apical compartment at 60 months follow-up

Type of surgical failure by procedure	Time after primary surgery (follow-up)
Sacrospinous hysteropexy:	
Repeat surgery for apical prolapse	28 months (5 years)
Vaginal hysterectomy:	
Repeat surgery for apical prolapse	27 months (5 years); 11 months (5 years); 10 months (48 months); 23 months (48 months)
Recurrent apical prolapse with bothersome symptoms	48 months (5 years); 12 months (24 months); 24 months (24 months); 12 months (12 months)

Table 4 | Functional outcome and quality of life after sacrospinous hysteropexy and vaginal hysterectomy of women included in extended trial at baseline and five year follow-up. Values are medians (interquartile ranges) of domain scores unless stated otherwise

Domains	Before surgery		5 years after surgery		P value*
	Sacrospinous hysteropexy	Vaginal hysterectomy	Sacrospinous hysteropexy	Vaginal hysterectomy	
Urogenital distress inventory†:					
Overactive bladder	22 (0-44)	22 (0-33)	11 (0-22)	0 (0-19)	0.31
Urinary incontinence	17 (0-33)	17 (0-33)	0 (0-17)	0 (0-17)	0.33
Obstructive micturition	0 (0-33)	17 (0-33)	0 (0-17)	0 (0-17)	0.75
Genital prolapse	50 (33-67)	67 (33-67)	0 (0-0)	0 (0-0)	0.50
Pain	17 (0-33)	17 (0-33)	0 (0-8)	0 (0-17)	0.72
Defecatory distress inventory†:					
Obstipation	0 (0-17)	0 (0-17)	0 (0-0)	0 (0-0)	0.81
Obstructive defecation	0 (0-17)	0 (0-15)	0 (0-8)	0 (0-8)	0.93
Pain	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0.60
Incontinence	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0.93
Flatus	33 (0-33)	33 (0-33)	33 (0-33)	33 (0-33)	0.23
Incontinence impact questionnaire‡:					
Mobility	11 (0-33)	11 (0-22)	0 (0-11)	0 (0-11)	0.61
Physical	0 (0-33)	0 (0-33)	0 (0-0)	0 (0-0)	0.32
Social	11 (0-22)	0 (0-11)	0 (0-0)	0 (0-0)	0.49
Embarrassment	0 (0-17)	0 (0-17)	0 (0-0)	0 (0-0)	0.43
Emotion	0 (0-33)	0 (0-22)	0 (0-11)	0 (0-0)	0.18
Short form-36§:					
Physical functioning	80 (55-90)	80 (70-90)	90 (75-100)	90 (75-100)	0.71
Social functioning	100 (75-100)	88 (75-100)	88 (75-100)	100 (88-100)	0.18
Role limitations physical	75 (25-100)	100 (63-100)	100 (94-100)	100 (100-100)	0.99
Role limitations emotional	100 (100-100)	100 (100-100)	100 (100-100)	100 (100-100)	0.62
Mental health	84 (72-92)	84 (72-88)	80 (68-88)	84 (76-92)	0.18
Vitality	70 (50-80)	70 (55-80)	70 (55-80)	75 (61-85)	0.07
Bodily pain	78 (65-100)	80 (67-100)	90 (67-100)	100 (78-100)	0.39
General health perception	75 (58-85)	75 (65-85)	75 (60-90)	75 (60-90)	0.72
Health change	50 (25-50)	50 (50-50)	50 (50-50)	50 (50-50)	0.29

All women were analysed as allocated.

*P value for exploratory purposes: Mann-Whitney U test of sacrospinous hysteropexy versus vaginal hysterectomy at 5 years after surgery.

†0=no symptoms or not bothersome to 100=most bothersome symptoms.

‡0=best quality of life to 100=worst quality of life.

§0=worst quality of life to 100=best quality of life.

was 10%. Additional analysis of our data using this definition confirmed this finding. The risk of recurrent prolapse after vaginal hysterectomy with uterosacral ligament suspension was 20% (20/102 women). In the sacrospinous hysteropexy group this risk was lower (9%, 9/102 women, $P=0.04$). The risk of recurrent surgery after vaginal hysterectomy was 9% (9/102 women) when we included women who had surgery for recurrent pelvic organ prolapse or primary surgery for a prolapse in a non-treated compartment, or both. After sacrospinous hysteropexy this was 3% (3/102 women). After five years we found more anatomical recurrences of the posterior compartment after vaginal hysterectomy with suspension of the uterosacral ligaments, although more posterior repairs were performed in the vaginal hysterectomy group (50%) compared with sacrospinous hysteropexy group (29%). This finding is in line with the results after 12 months' follow-up. Generally, it is believed that the more dorsal axis of the vagina after sacrospinous hysteropexy might prevent recurrent prolapse of the posterior vaginal wall. This is, however, speculative because the POP-Q system is not an appropriate instrument to show this change in axis, and studies with, for example, magnetic resonance imaging are lacking. Another possible explanation could be the difference in apical suspension between

the procedures. Because of the low percentage of surgical failure of the apical compartment we analysed the anatomical features of this compartment. We compared the level of the cervix or vaginal vault in relation to the hymen (POP-Q point C) at five year follow-up. Overall this was significantly lower after vaginal hysterectomy with uterosacral ligament suspension compared with sacrospinous hysteropexy (-5.9 cm v -7.2 cm, $P=0.01$). Women with posterior vaginal wall prolapse stage 2 or higher after both types of surgery had statistically significantly lower POP-Q point C scores compared with women without posterior vaginal wall prolapse. Other anatomical differences that could affect the posterior vaginal wall such as preoperative and postoperative genital hiatus (distance between the external urethral meatus and posterior midline hymen) were not found, and perineorrhaphy, which can influence the genital hiatus, was not routinely performed in both procedures. After vaginal hysterectomy, two thirds of the repeat surgeries were performed because of recurrent or de novo pelvic organ prolapse of the posterior compartment. The number of women who underwent repeat surgery was overall low, however, and most recurrences were proximal to the hymen. The clinical significance of these findings is therefore debatable.

A recent published cohort study from Denmark showed that the highest risk for undergoing reoperation is within the first year.²¹ We found that 50% of the reoperations were in the first year and 83% in the two years after primary surgery. Endometrial carcinoma was diagnosed in one woman during follow-up (1%) and she underwent laparoscopic hysterectomy. In most cases, endometrial carcinoma presents with symptoms at a low stage, as was the case here. We believe that future risk of malignancy should not be regarded as a valid reason for removal of the uterus before adequate preoperative investigations have been done.⁶

Clinical implications and future research

Vaginal hysterectomy is still widely regarded as the ideal treatment for uterine prolapse. A recent survey among UK practitioners showed that vaginal hysterectomy and repair is still the procedure of first choice (75%) for uterovaginal prolapse.²² Comparable findings were described in a study from Australia and New Zealand.²³ However, uterus preserving surgery is gaining popularity among doctors and women. A recent published study on trends in prolapse surgery in England found an increase in uterine sparing surgery.²⁴ This trend is in line with a change in women's attitudes and preference for uterus preservation.²⁵⁻²⁷ On the other hand, in response to our previous report on the SAVE U study, some argued that the uterus is an atrophic, non-functional organ and that uterus preservation on cultural or ideological grounds should be rejected.²⁸ In our opinion this reflects a serious disregard of women's attitudes and feelings. Although vaginal hysterectomy is still the preferred treatment we believe that the results of our study together with the increasing knowledge of women's preference will lead to better informed decision making by women and their gynaecologists, in which sacrospinous hysteropexy is a valid option.

A recent review discussed several variations in technique of the sacrospinous hysteropexy.²⁹ In our study the sutures were placed under direct vision through the sacrospinous ligament. Newer disposable ligature carriers are used to facilitate blind suture application using minimal dissection. A study comparing open sacrospinous colpopexy with colpopexy using the Capio suture capturing device (Boston Scientific, MA) in 86 women after hysterectomy reported no difference in objective and subjective success after three years.³⁰ However, no randomised trials are available that compare this device or other suture capturing devices with open sacrospinous hysteropexy, as performed in our study. Although suturing devices might be potentially beneficial for blood loss and duration of operation, they should only be implemented after adequate clinical research. The SAVE U study group consisted of women with POP-Q stage 2 and higher. The effect of sacrospinous hysteropexy in a lower stage pelvic organ prolapse still needs to be established, as well as the effect on a predominant cystocele or rectocele.

More randomised trials comparing other uterus preserving surgical techniques are needed to compare efficacy and safety of the different procedures. In the Netherlands two large randomised controlled studies comparing modified Manchester procedure with sacrospinous hysteropexy (trialregister.nl NTR 6978) and laparoscopic hysteropexy with sacrospinous hysteropexy (trialregister.nl NTR 4029) have started.³¹

Conclusions

We conclude that, based on results five years after surgery, sacrospinous hysteropexy is an effective and safe alternative to vaginal hysterectomy with suspension of the uterosacral ligaments for treatment of uterine prolapse. Surgical failure, defined as recurrent apical prolapse with bothersome symptoms or repeat surgery for recurrent apical prolapse, was less often found after uterus preservation, and the proportion of women with successful treatment was higher at five year follow-up. Overall anatomical failure, functional outcome, repeat surgery, and sexual functioning did not differ between the two procedures. Furthermore, time-to-event (survival) analysis at five years showed no differences in surgical failure of the apical compartment, overall anatomical failure, surgical retreatment, and composite outcome of success between sacrospinous hysteropexy and vaginal hysterectomy with suspension of the uterosacral ligaments.

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Data sharing: No additional data available.

The study guarantor (RJD) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; No important aspects of the study have been omitted and any discrepancies from the study as planned have been explained.

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