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MULTICENTRE RANDOMISED TRIAL OF VAGINAL PROLAPSE REPAIR VERSUS VAGINAL PROLAPSE REPAIR WITH A MIDURETHRAL SLING IN PATIENTS WITH PELVIC ORGAN PROLAPSE AND CO-EXISTING STRESS URINARY INCONTINENCE.

Hypothesis / aims of study
The hypothesis of this trial was that combining vaginal prolapse repair (VPR) with a midurethral sling (MUS) reduces postoperative stress urinary incontinence (SUI) in patients with pelvic organ prolapse (POP) and co-existing SUI.

Study design, materials and methods
A randomized trial was conducted at 14 hospitals. The trial protocol was previously published.[1] Patients with POP and co-existing SUI were randomized in a web-based system in a 1:1 ratio for combination surgery (VPR+MUS) or prolapse surgery (VPR) only. SUI was defined as a positive stress test with ≥ 300 mL bladder filling without redression of the POP and/or a positive response to the question regarding SUI in Urogenital Distress Inventory (UDI) ("Do you experience urine leakage related to physical activity, coughing, or sneezing?") in a frequency of more than once a week. POP had to be at least POPQ stage 2. The primary outcome was subjective SUI at 12 months defined as a positive response to the UDI question regarding SUI. Secondary outcomes were bothersome SUI at 12 months (defined as a response of at least "moderately" on the UDI question); objective SUI (defined as a positive cough stress-test at a bladder volume ≥ 300mL); any treatment for SUI; SUI as a composite endpoint (bothersome SUI, objective SUI and/or any treatment for SUI at 12 months) and adverse events. For a 80% power and a one-sided type I error of 5%, 126 patients were needed to detect a 20% difference in subjective SUI (accounting for 10% lost in follow-up). The analysis was performed according the intention to treat principle.

Results
Between October 2007 and October 2010 138 patients were randomized. Of those, 67 were allocated to VPR+MUS and 71 to VPR only. Data of 134 patients were available for evaluation. Baseline characteristics were similar between the VPR+MUS (n=63) and VPR (n=71) group. Twelve months after surgery, patients who were randomly assigned to receive VPR+MUS had a lower rate of subjective SUI (21 vs 59%) and SUI composite endpoint (16 vs 49%) than those in the VPR group (table 1). The differences for bothersome and objective SUI were statistically borderline significant (resp. 7 vs 19% and 6 vs 31%). During follow-up, 22 patients (31%) in the VPR group underwent subsequent treatment for SUI, including 8 patients (11%) who underwent a MUS. At 12 months the UDI subscale for urinary incontinence was better after VPR+MUS than after VPR only. We found no differences in bladder storage or voiding symptoms. Adverse events were more common in the VPR+MUS group vs the VPR group (table 1). In 7 patients the complication was related to the MUS procedure: 1 vaginal tape extrusion, 1 bladder perforation and later ureteral tape exposure, 1 urethrolysis because of persisting obstructive micturition and 4 MUS related pain (for which 2 partial tape removal). Including the MUS procedures for persisting SUI in the VPR group the reoperation rate was similar: 11 vs 15%. We found no differences in the PGI-severity and PGI-improvement.

Interpretation of results
The limitations of our study should be considered. First, patients with relatively mild SUI were included. It is to be expected that the effect of additional MUS in these patients is limited and therefore the difference between the groups is smaller than when only patients with bothersome or objective SUI were included. Second, the follow-up of 12 months is relatively short and some patients may have been unwilling to undergo subsequent MUS within the first year, even if they had symptoms. Finally, knowledge of the study intervention may have had an effect on the subjective outcomes, while blinding was not used.
The combination of VPR+MUS reduced significantly SUI and subsequent treatment for persisting SUI when compared with only VPR. But, we found no difference in PGI-improvement and PGI-severity at 12 months and in the combination group more complications (related to the MUS procedure) occurred. Therefore, it seems to be better not to combine VPR with MUS routinely, than to risk causing more harm than good. It is possible that the benefits of combination surgery will increase with more severe SUI and benefits must be balanced against the higher rates of adverse effects and the need for additional surgery in the individual patient.

Concluding message
The combination of VPR and a MUS in patients with POP and coexisting SUI resulted in a lower rate of SUI at 12 months but higher rates of adverse events.

Table 1

Outcome 12 months	**Combination Surgery (n=63)**	**POP surgery (n=71)**	
SUI			**RR (95% CI)**
Subjective SUI	13 (21%)	38 (59%)	2,8 (1,7-4,7)
Bothersome SUI	4 (7%)	12 (19%)	2,9 (1,0-8,5)
Objective SUI – ≥ 300 mL	1 (6%)	8 (31%)	5,5 (0,8-40,5)
Treatment for persisting SUI	7 (11%)	22 (31%)	2,8 (1,3-6,1)
Physiotherapy for SUI	7 (11%)	22 (31%)	2,8 (1,3-6,1)
MUS for SUI	0 (0%)	8 (11%)	n.a.

SUI composite endpoint	10 (16%)	35 (49%)	3,1 (1,7-5,8)
Patient Global Impression (PGI)			**p-value**
PGI-severity (no. "severe")	1 (2%)	2 (3%)	1,00
PGI-improvement (median, min-max)	2 (1-6)	2 (1-5)	0,47
Adverse events			**RR (95% CI)**
Total surgery related complications	11 (17%) ¥	3 (4%) §	11,8 (1,7-24,5)
Total reoperations related to index surgery (including MUS as second procedure)	7 (11%)	11 (15%)	1,3 (0,6-3,3)
Incomplete bladder emptying (CAD/CIS > 7 days)	11 (20%)	11 (18%)	0,9 (0,4-1,9)
UDI DOMAIN SCORES, mean (± SD)			**p-value**
Stress urinary incontinence	8 (± 21)	25 (± 27)	<0,01
Urgency urinary incontinence	10 (± 19)	23 (± 27)	<0,01
Bladder storage symptoms	11 (± 18)	12 (± 18)	0,83
Obstructive micturition	2 (± 0,4)	2 (± 0,4)	0,08

¥ 1 VVF related to hysterectomy (vaginally closed in second procedure); 1 rectal injury related to posterior repair (primary repair); 1 pyometra related to Manchester procedure (reoperation); 1 hematoma (conservative management); 1 lateral vaginal tape extrusion (uncomplicated excision); 1 bladder perforation during MUS procedure (TVT-O) for which primary closure, the patient developed later a ureteral tape exposure for which partial removal of the tape with a Martius flap; 1 urethrolysis for obstructive micturition; 2 MUS related transient pain (1 TVT, 1 TVT-O); 2 MUS related thigh pain for which (partial) tape removal (1 TVT-O, 1 TOT).

§ 1 pain (neuropathy) related to vaginal sacrospinous fixation of the uterus (sutures were removed in second procedure); 2 dyspareunia related to posterior repair for which small vaginoplasty.

References

1. Van der Steen A, van der Ploeg M, Dijkgraaf MG, van der Vaart H, Roovers JP. Protocol for the CUPIDO trials; multicenter randomized controlled trials to assess the value of combining prolapse surgery and incontinence surgery in patients with genital prolapse and evident stress incontinence (CUPIDO I) and in patients with genital prolapse and occult stress incontinence (CUPIDO II). BMC Womens Health. 2010 May 11;10:16.

Disclosures

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