Effectiveness of blinding: sham suprapubic incisions in a randomized trial of retropubic midurethral sling in women undergoing vaginal prolapse surgery

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OBJECTIVE: This planned secondary analysis of the Outcomes Following Vaginal Prolapse Repairs and Midurethral Sling trial assessed whether treatment knowledge differed between randomized groups at 12 months and whether treatment success was affected by treatment perception.

STUDY DESIGN: Sham suprapubic tension-free vaginal tape (TVT) incisions were made in the Outcomes Following Vaginal Prolapse Repairs and Midurethral Sling trial participants randomized to no-TVT. Primary surgical outcomes and maintenance of blinding was assessed at 12 months. Knowledge of treatment assignment was compared between groups, and the relationship with treatment success rates was assessed.

RESULTS: Prior to the 12 month postoperative visit, only 4% of treated participants (13 of 336) formally reported unmasking. At 12 months, 94% of the randomized participants (315 of 336) provided treatment knowledge data. Sixteen TVT participants (10%) reported treatment knowledge; most (n = 15, 94%) were correct; 17 of the sham participants (11%) reported treatment knowledge; half (n = 8, 47%) were correct. Similar proportions of unmasked participants who reported no treatment knowledge correctly guessed/perceived treatment assignment (sham, 46 [33%] vs TVT, 44 [33%]). We did not detect significant differences in treatment success rates based on perception within and across received treatment groups (perceived sham vs TVT overall [$P = .76$]). Of those receiving TVT, more participants perceiving TVT had treatment success compared with those who perceived sham (84% vs 74%; $P = .29$). Among sham participants, more participants perceiving sham had success compared with those who perceived receiving TVT (65% vs 56%; $P = .42$).

CONCLUSION: Sham surgical incisions effectively mask TVT randomization. These findings may help to inform future surgical trial designs.

Key words: pelvic organ prolapse, sham incision, stress urinary incontinence, surgical trial

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Two critical principles for the proper conduct of a masked randomized trial include successful randomization and maintenance of the randomization assignment masking, also called blinding. Placebo controls have been introduced into clinical study design to enhance these basic tenets of scientifically sound human subject research and to minimize participant and evaluator knowledge of treatment.

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Placebo controls have traditionally been useful in situations in which there is a potential for a significant placebo effect, as in the case of studies utilizing outcomes based on subjective measures and those involving patient perception. Surgical sham incisions are designed to allow the conduct of a study so that treatment arms are indistinguishable to both participant and evaluator and should be low risk.

Although many placebo-controlled trials in the study of pelvic floor disorders have focused on pharmacological or behavioral therapy, there are fewer placebo-controlled trials in the surgical literature. For example, Jarrell et al[1] compared sham surgery (with sham skin incisions) with the excision of endometriosis in a randomized controlled trial assessing pain. They reported that active surgery (excision) was not associated with improvement in pain over sham incision, as measured by time to repeat surgery.

The Outcomes Following Vaginal Prolapse Repairs and Midurethral Sling (OPUS) trial provided an ideal environment to study the efficacy of sham incisions. The OPUS study evaluated the role of prophylactic tension-free vaginal tape (commonly known as TVT) to reduce the risk of de novo stress urinary incontinence. In the OPUS study, women undergoing vaginal prolapse repair were randomized to TVT vs no TVT with sham suprapubic incisions to mask the TVT assignment. We hypothesized that if sham incisions were effective and masking was maintained throughout the course of a trial, then the participants' perception of treatment would not differ between study groups.

The objective of this planned secondary analysis of the OPUS trial was to determine whether the participant's knowledge of treatment arm differed between randomized groups at 12 months and to assess whether treatment success was affected by the perception of receiving active treatment (TVT).

Materials and Methods

This is a planned secondary analysis of the OPUS trial. The design and primary outcome of this trial have been reported.[2,3] Briefly, treatment success was defined at 3 months by the absence of a positive cough stress test and/or bothersome urinary incontinence or a need for urinary incontinence treatment.

All participating sites of the Pelvic Floor Disorders Network had institutional review board approval, and written informed consent was obtained on all patients. Briefly, participants were women considering apical and/or anterior vaginal wall vaginal prolapse repair for stage 2 or greater prolapse without subjective complaints of stress urinary incontinence.

At the time of their vaginal prolapse repair, they were randomized to a concomitant TVT or sham incisions. At the time of the vaginal prolapse surgery in the randomized participants, participants randomized to the control group underwent partial thickness suprapubic skin incisions with the use of a scalpel, located and sized to be identical to the 2 cm suprapubic TVT trocar exit incisions performed in women randomized to and receiving the TVT. The study protocol required all incisions, sham and real, to be covered by skin tape for 1 week unless there was a clinical reason for removal (ie, suspicion of a postoperative incision-related bleeding or infection).

This research effort also included a patient preference cohort, which was a systematic sample of women declining participation in the randomized trial but otherwise eligible for the study who agreed to participate in the patient preference cohort. Patient preference cohort participants were not randomized; instead, they decided whether they wanted to receive a TVT at the time of their vaginal prolapse surgery, and those not receiving a TVT did not have sham incisions placed.

Treatment knowledge (whether a participant believed they knew their group assignment: TVT vs no TVT) was assessed. When unmasking occurred at any point after study surgery and prior to the 12 month primary outcome surgical assessment, participants or evaluators completed a report detailing any unmasking circumstances.

At the time of the surgical outcome assessment at 12 months, treatment knowledge in both randomized and patient preference cohorts was also assessed by the participant responding to the query: "Have you found out or been told (by clinical personnel) whether you had the additional study procedure (TVT) at the time of your prolapse surgery?" (yes or no). Participants who reported yes to this question were considered unmasked. Additionally, participants were asked: "Did you have (do you think you had) the additional procedure?" (yes, no, or do not know).

We compared treatment knowledge in the randomized cohort, at 12 months. We also assessed whether treatment success was affected by the perception of receiving active treatment (TVT). In the patient preference cohort, only the assessment of treatment knowledge and treatment received were assessed. Treatment perception was compared between treatment groups, and the relationship with treatment success rates was assessed.

All analyses are presented based on treatment received. Participants who did not complete the treatment knowledge form were excluded from further analyses. Because all analyses are considered secondary, they are exploratory in nature, and the resulting P values are considered descriptive measures of relationship as opposed to formal tests of hypotheses, and therefore, no adjustments for multiple comparisons were made.

The percentage of participants reporting knowledge of treatment received and those correctly identifying treatment assignment among those reporting knowledge as well as those reporting no knowledge was compared by treatment groups using a 2-sided χ^2 test statistic. These analyses were completed for participants with primary outcome data.

We separately analyzed the randomized and patient preference cohorts. The relationship of treatment received and perception with treatment success was assessed via a logistic model, which included only randomized participants with no treatment knowledge and no unmasking event reported; the model incorporated the outcome of treatment success and explanatory variables of treatment received, treatment perceived, and their interaction.