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Tommaselli G A[1], Di Carlo C[1], Formisano C[1], Fabozzi A[1], Nappi C[1]
1. *University of Naples "Federico II"*

EFFECTIVENESS AND SAFETY OF RE-ADJUSTABLE MID-URETHRAL SLINGS FOR THE SURGICAL TREATMENT OF FEMALE STRESS URINARY INCONTINENCE: A SYSTEMATIC REVIEW AND META-ANALYSIS

Hypothesis / aims of study
Mid-urethral slings (MUS) are widespread procedures for the surgical treatment of female stress urinary incontinence (SUI), yielding high cure rates. Nevertheless, failures with recurrent SUI and post-operative voiding dysfunctions are still an issue. To reduce these risks, re-adjustable slings have been marketed [1-3]. The aim of this systematic review and meta-analysis of the literature was to evaluate the effectiveness and safety of re-adjustable slings for the surgical treatment of female stress urinary incontinence reported in randomized (RCT) and non randomized studies.

Study design, materials and methods
An updated meta-analysis was performed per the PRISMA guidance including all studies describing the effectiveness and safety of re-adjustable slings (meaning that re-adjustment could be performed after the procedure) in women affected by SUI. They were identified by searching the MEDLINE, EMBASE, National Library for Health, ClinicalTrials.gov, and Google Scholar databases (up to February, 2015). The abstracts from International Conferences were not included in this systematic review. The search terms included: “re-adjustable , re-adjustable sling, remeex, safyre, toa, tva” AND “stress urinary incontinence”. Hand search was performed on the bibliographies and citation lists of all relevant reviews and primary studies to identify articles not captured by electronic searches. All studies of women who underwent a re-adjustable sling for SUI with a mean follow-up of at least 3 months were included. Three reviewers (GAT, CF, and AF) selected the studies independently on the basis of the inclusion criteria. Clarifications were sought from the individual trial lists if required. In cases of duplication, the study reporting most recent data was included. In case of cohort studies with multiple publications, the last data-set on efficacy was used, while safety data were extracted by all published articles. Data included characteristics of patients (number, lost to follow-up and age), intervention, comparison for RCTs, follow-up length, exclusion criteria, preoperative and outcome assessment methodology, and results of the studies. The Jadad score was used to assess quality of RCTs and the Newcastle-Ottawa scale was used for the non-randomized studies. Risk of bias across studies was assessed according to the Cochrane Handbook for Systematic Reviews. For dichotomous data, results of each study were expressed as an odds ratio (OR) with 95% confidence interval (CI) and combined for meta-analysis using the Mantel-Haenszel method (fixed effects model). For non RCT studies, regression rates from individual studies were meta-analyzed using a fixed effect model. Heterogeneity among studies was assessed analyzing I^2. Differences in proportions were performed using the χ^2 test and were expressed as OR with 95% CI.

Results
A total of 37 potentially relevant studies were indentified and six were excluded (duplication: 5, follow-up not meeting the inclusion criteria, 1). Thus, a total of 31 studies was included regarding three devices (Remeex, TOA/TVA, and Safyre). There were 2 RCTs or quasi-RCT and 29 non randomized studies (prospective: 15, retrospective: 14) with a total of 2561 operated patients (120 in RCTs and 2441 in non-RCTs) aged 21-87 years. The number of patient evaluated patients evaluated at last follow-up was 2004 (83 in RCTs and 1921 in non-RCTs). One RCT showed a Jadad score of 5, while the other had a Jadad score of 1. In non-RCT studies, SUI was clinically diagnosed in 5 (no urodynamic studies performed) and only one reported a blinded assessment. The efficacy outcomes were assessed as subjective, objective cure rates or both. The follow-up was described in each study with a minimum of 3 and a maximum of 72 months. On meta-analysis of RCTs, the odds ratio of subjective cure was similar comparing the re-adjustable tape (Safyre-T) with the reference procedure (PVS and colposuspension) (OR 0.40; 95% CI 0.13-1.22; p = 0.11). Considering the non RCTs, cumulative subjective and objective cure rates of re-adjustable slings were 80% [95%CI 77.2-82.4%] and 82.8% [95%CI 80.1-86.3%], respectively. Cumulative subjective cure rates for the specific devices were 87% [95%CI 82.5-90.4], 81.4% [95%CI 76.8-85.2], and 78.9% [95%CI 73.9-83.2] for Remeex, TOA, and Safyre, respectively. Cumulative objective cure rates for the specific devices were 79.8% [95%CI 76.2-83.1], 88.6% [95%CI 83.8-92.2], and 90.1% [95%CI 81.4-95] for Remeex, TOA, and TVA, respectively. Only one study reported subjective cure for TVA (56.2%) and no study reported objective outcomes for Safyre. Cumulative re-adjustment rate was 43% [95%CI 40.5-45.6]. Re-adjustment rate was significantly higher for Remeex (55.3%; 95CI 52-58.6%) in comparison with TOA (30.8%; 95%CI 27.1-34.8; OR 1.87; 95%CI 1.54-2-27; p < .0001) and Safyre (7%; 95%CI 4.6-10.6; OR 7.31; 95%CI 4.51-12.0; p < .0001). Re-adjustment rate was also significantly higher for TOA/TVA in comparison with Safyre (OR 3.91; 95%CI 2.37-6.52; p < .0001). Cumulative re-adjustment rates for persistent SUI and voiding dysfunction were 17.1% [95%CI 14.8-19.8%] and 10.8% [95%CI 8.9-12.9%], respectively. Overall, there were 413 complications reported (16.6%) (246, 44, and 142 for Remeex, TOA/TVA, and Safyre, respectively). De novo overactive bladder (OAB) symptoms (9.1%) and bladder injuries (6.4%) were the most common complications. While de novo OAB symptoms were the most frequent complication for also in the Remeex and the Safyre group, in the TOA/TVA group the most reported complication was voiding dysfunction. Overall, vaginal erosions rate was 1.6% and was significantly higher in the Safyre group compared to both Remeex (OR 0.076; 95%CI 0.017-0.286; p < .0001) and TOA/TVA groups (OR 0.242; 95%CI 0.054-0.924; p = .02) Persistent or severe voiding problems (defined either by difficulties persisting beyond the peri-operative period) were observed in 32 cases (Remeex, 13, TOA/TVA 16, Safyre 4). No studies were excluded on the basis of methodological heterogeneity. In RCTs, there was a considerable estimate of statistical heterogeneity (I^2 = 77%). In non-RCT studies, there was moderate to high degree of statistical heterogeneity (I^2 from 48.8 to 95.7%).

Interpretation of results
Re-adjustable slings carry the advantage of potentially allowing a regulation of tension after the procedure to improve continence or to relieve voiding dysfunction/obstruction symptoms. This analysis of the literature showed high cure rates, both subjectively

and objectively, similar to traditional MUS. Complications were limited, mostly related to the onset of de novo OAB symptoms. Vaginal erosion were more common with Safyre than with the other devices. Heterogeneity of the studies included was mostly high and there were only 2 RCTs.

Concluding message

Considering the potential advantages they carry, re-adjustable slings should be tested in more RCTs and for longer follow-up periods in order to be able to suggest their used on an evidence-based basis.

References

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