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ORIGINAL ARTICLE

A randomized controlled trial comparing three single-incision minislings for stress urinary incontinence

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Abstract
Introduction and hypothesis Studies have observed a significant heterogeneity in efficacy data for single-incision minislings (SIMS) as surgical treatment for female urinary incontinence (UI). Our study aim was to test the hypothesis that different vaginal kits for SIMS have different long-term outcomes.

Methods One hundred and twenty women with stress (SUI) or mixed (MUI) UI were enrolled in a multicenter randomized clinical trial (registration number NCT00751088) and treated with three different SIMS (Ajust®, MiniArc®, or TVT Secur System®). Duration of follow-up was at least 24 months from surgery. The primary outcome was the subjective cure rate at 24 months from surgery; secondary outcomes were rates of total failure and reoperations for UI.
Results At study end, no difference was detected between groups in terms of total subjective cure rate [21 (52.5 %) vs. 26 (65.0 %) vs. 21 (52.5 %), in Ajust®, MiniArc®, and TVT Secur System® group, respectively; P=0.412] or in terms of total failure rate [24 (60.0 %) vs. 22 (55.0 %) vs. 27 (67.5 %), in Ajust®, MiniArc®, and TVT Secur System® group, respectively; P=0.432]. The proportion of patients who received a second surgery for UI was also not significantly different between groups [13 (32.5 %) vs. 10 (25.0 %) vs. 13 (32.5 %), in Ajust®, MiniArc®, and TVT Secur System®, respectively; P=0.831].
Conclusion The long-term efficacy of SIMS does not differ between the vaginal kits examined.

Keywords Incontinence · Sling · Single-incision minislings · Surgery · Randomized controlled trial · Treatment

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Introduction

Single-incision minislings (SIMS) are third-generation midurethral slings (MUS) and have been proposed by many researchers as the new and minimally invasive surgery for female stress urinary incontinence (SUI) [1]. Several new types of SIMS vaginal kits are available for clinical practice. SIMS insertion has generally been considered an office procedure due to shorter operative time, increased feasibility of

performing the procedure under local anesthesia, less postoperative pain, and reduced morbidity [2–5]. In a randomized controlled trial (RCT) [6], we confirmed the feasibility inserting them in an office procedure, although we did register differences between vaginal kits used in terms of simplicity of insertion under local anesthesia in the ambulatory setting, complication rate, and patient satisfaction. Some doubt remains concerning the efficacy of SIMS, as some clinical data show conflicting results [7–12]. In 2011, a meta-analysis [7] of RCTs that aimed to compare SIMS with standard midurethral slings in terms of efficacy and safety in managing female SUI showed cumulative subjective and objective cure rates significantly lower for SIMS after just 6–12 months from surgery. However, a significant level of statistic heterogeneity in that data synthesis was detected [7]. In fact, a total cure rate of 73 % (207/281 patients) for patients treated with SIMS was detected [7], with a variation among studies in subjective cure rate from 97 % (29/30 patients) [4] to 62 % (26/42 patients) [5]. That difference of 35 % after short-term follow-up could be even higher after long-term follow-up.

One factor determining differences in efficacy rates among studies could be the different vaginal kits employed for SIMS. Moreover, to our knowledge, there is no study in literature that has as its primary endpoint differences in long-term efficacy between SIMS. Based on these considerations, the aim of this multicenter RCT was to test the hypothesis that different vaginal kits for SIMS have different long-term outcomes.

Materials and methods

This study involves the randomized arm of a wider clinical trial [6] comparing SIMS to retropubic tension-free vaginal tape (TVT). At study entry, eligible patients were extensively counseled about the risk-to-benefit ratio of the SIMS or retropubic TVT, and treatment allocation was initially based on patient choice.

Ethics

The procedures used in this study protocol are in accordance with the Declaration of Helsinki regarding human experimentation guidelines. The study was approved by the Ethical Committee of the Department of Obstetrics and Gynecology of the University "Magna Graecia" of Catanzaro, Italy. The purpose of the protocol was carefully explained to all women in each center, and their written consent was obtained before entering the study. The trial was registered on the website www.clinicaltrial.gov with the registration number NCT00751088.

Study population

Between September 2008 and November 2010, 141 women with SUI or mixed urinary incontinence (MUI) were checked for inclusion/exclusion criteria in five departments of obstetrics and gynecology [6]. The study population was initially screened using patient history and stress test. Specifically, SUI was defined as involuntary leakage with effort or physical exertion or upon sneezing or coughing, whereas MUI was defined as SUI associated with urgency. In all screened patients, the clinical diagnosis needed to be confirmed by urodynamic testing, including uroflowmetry, cystometry, abdominal leak-point pressure assessment, and a pressure-flow voiding study. All patients selected according to inclusion (clinical and instrumental diagnosis of SUI or MUI) and exclusion criteria were treated with a 3-month course of conservative management. Specifically, patients with SUI received pelvic floor muscle training (PFMT) alone, whereas patients with MUI were treated with PFMT in association with orally administered antimuscarinic drugs. Only patients who remained incontinent after conservative management and who reported persistent and clinically remarkable SUI were actually included in the study protocol [3, 6].

Randomization

A total of 120 patients were randomized into three different treatment arms [6]. Randomization was centrally performed with the use of a computer-generated randomization list and stratified by the study center. The random allocation sequence was made in single blocks using a single sequence of random assignment. The sequence was concealed from all investigators until the interventions were assigned. For this purpose, sequentially numbered opaque sealed envelopes were prepared in a site distant from investigational centers. The interventions (type of vaginal kit) were assigned by a nurse not directly involved in the study protocol just before the patient entered the operating room. The protocol had a double -blind design, i.e., patients and data assessors were blinded to treatment assigned up to the 24-month follow-up visit.

Surgical procedures

The study design aimed to minimize potential confounders by using a careful definition of all surgical procedures (including potential cointerventions), operators, surgical teams, and surgical instrumentations. In each investigational center, one experienced operator skilled in SIMS procedures performed the surgeries and was assisted by the same nurse each time. The operator was considered "skilled" if having performed each type of SIMS procedure >20 times in the year previous to study initiation [6]. All surgical procedures were performed after intravenous injection of prophylactic antibiotic therapy and under local anesthesia with conscious sedation. The same drug protocols were used in all centers [6]. Prophylactic antibiotic therapy was administrated at the beginning of surgery and consisted of a single dose of cefuroxime 1.5 mg or, in

case of documented allergy to cephalosporins, metronidazole 500 mg. Local anesthesia was performed by injection of an anesthetic solution composed of 50 ml of bupivacaine cloridrate 0.25 % plus 0.5 ml of epinephrine. Injections of local anesthetic solution were given into the vaginal wall sub- and paraurethrally, extending the injection up to the bone surface of the inferior pubic arm (a total of 10 ml) and into the internal obturator muscle (5 ml for each side); repeated aspirations were performed to prevent intravascular injection. Finally, conscious sedation consisted of intravenous administration of 0.5 mg of atropine and 0.25 mg of fentanyl, followed by a slow, intravenous injection of 2.0 mg of midazolam. Each patient was informed that she could change from local to general anesthesia, as required by perceived pain.

Patients were placed in the lithotomy position, thighs at right angle with the floor, knees at 90°. A 15-mm incision was made starting 10 mm down to the urethral meatus. Tunneling 12- to 15-mm wide up to the bone surface of the inferior pubic arm was made by spreading the scissor blades while withdrawing parallel to the vaginal wall. Epithelial undermining was performed at the level of the upper and lower frenulum, attaching the suburethral tissue to the vaginal wall, releasing it cephalically and caudally for 3 mm. Insertion of the device was performed through the tunnel created horizontally to the inferior pubic arm up to the internal obturator muscle.

Vaginal kits used were Ajust® (Bard SpA, Rome, Italy), MiniArc® (Tegea for AMS, Bologna, Italy), or TVT Secur System® (Johnson & Johnson, Rome, Italy). In the Ajust® group, the SIMS was placed using a safe-hook geometry introducer. In the MiniArc® group, it was placed using a curved, single-use needle; in the TVT Secur System® group, it was placed ihammock fashion using two curved stainless-steel, single-use introducers. In Ajust® and MiniArc® groups, the tape was readjusted, when necessary, using a flexible stylet and a polypropylene suture, respectively, whereas in the TVT Secur System® group, tape tension readjustment was not possible. Although no specific method was suggested to operators for adjusting sling tension, the recommendation at the start of the study was to place the tape in the proximity of the urethra, with mild tension that would not cause it to bend. Vaginal incision was closed with absorbable 2/0 polyglecaprone suture with continuous closure.

At the end of each surgical procedure, a urethrocystoscopy was performed in order to formally exclude potentially unrecognized bladder and urethral lesions. Patients were allowed to eat and drink 2 h after surgery and ambulate as soon as they felt comfortable. A blood sample was taken 8 h after surgery. The urinary catheter was removed just before discharge from hospital (~12 h after surgery) and, in cases of postvoid residual urine (PVR)>100 ml, intermittent self-catheterization was suggested. Patients were not discharged in cases of perioperative complications and/or postoperative pain score (using the Wong-Baker FACES Pain Scale) >7 under analgesic treatment (one intravenous bolus of tramadol 100 mg, followed by 100 mg intramuscular injection) and/or hemoglobin drop >1 g/dl.

Clinical and instrumental assessments

At baseline, all eligible patients underwent a standardized evaluation, including urogynecological history, and anthropometric, gynecologic, and neurologic evaluation [3, 6]. Pelvic prolapse was graded using the Baden scale [14] during maximal straining in the standing position. The stress test was performed at room temperature by filling the patient's bladder to at least 300 ml or to symptomatic fullness and then asking her to relax and cough vigorously [15]. The test was considered positive when there was objective urine loss from the urethra [15]. The Q-tip test was also performed and considered positive if the excursion of a cotton swab placed in the proximal urethra, measured during straining, exceeded 30° [16]. Neurologic integrity of S2–S4 was evaluated by testing sensation of the inner thighs, vulvar and perirectal areas, and bulbocavernous reflex. All women underwent standard ultrasonographic gynecologic evaluation, bacterial culture of a midstream urine specimen, and urodynamic assessment [3, 6]. Urodynamic assessment consisted of uroflowmetry and PVR urine, multichannel cystometry, pressure flow study, urethral pressure profilometry, and leak pressures.

To evaluate UI severity, all patients were instructed to perform a 24-h pad test and to compile a frequency-volume-chart voiding diary of 3 days' duration [15]. A detrusor instability score (DIS) [13] was calculated for each patient in order to detect and measure the urge component, if any. King's Health Questionnaire (KHQ) [17] and Patient Global Impression of Severity (PGI-S) [18] were used to study the disease-specific impact of UI on quality of life (QoL), whereas the Short-Form Healthy Survey of 36 questions (SF-36) [19] was used to analyze global QoL. Finally, the Female Sexual Function Index (FSFI) [20] was administered to assess sexual function. The Italian version of each questionnaire was used. For each surgical procedure, operative time, blood loss, number of analgesic vials, intraoperative and postoperative complications, feasibility, degree of surgical difficulty, postoperative pain, and patient satisfaction were recorded [3, 6].

The first follow-up visit was performed 30 days after surgery to assess any postoperative complication, i.e., de novo or worsened urge incontinence. Further follow-up visits were scheduled at 6, 12, 18, and 24 months from surgery to assess the effectiveness of the procedure. Unscheduled evaluations were performed as required. Follow-up visits included clinical assessment to evaluate subjective and objective cure rates and to administer questionnaires, i.e., DIS [13], KHQ [17], PGI-S [18], SF-36 [19], FSFI [20], and Patient Global Impression of Improvement (PGI-I) [18]. Stress [15] and Q-tip [16] tests were repeated. Urodynamic evaluations were performed only

in cases of UI recurrence or micturition dysfunctions. In cases of UI, severity was assessed as described previously [15]. Subjective failure was defined as any UI after surgery or retreatment for UI. Specifically, the subjective cure rate was calculated as the proportion of women who reported being either dry or improved, whereas the subjective failure rate was calculated as the proportion of women who reported being unchanged or worse. Objective failure was defined as leakage of urine during the stress test. Total failure rate was calculated combining patients with subjective failure and those with objective failure. Long-term complications (observed after 30 days from surgery) and reoperations for UI were noted and analyzed for each patient.

Statistical analysis

The primary endpoint was subjective cure rate at the 24-month follow-up. Objective cure rates, reoperations for UI, total failure, and long-term complications were considered secondary endpoints. The superiority study design aimed to reject the null hypothesis that the difference between the most and least effective vaginal kit for SIMS according to subjective cure rate is higher than 20 %. In fact, the sample size was calculated on the arbitrary assumption of considering as clinically remarkable a difference in subjective cure rate of 0.20 and a mean subjective cure rate of 73 %, as reported in the literature [7]. Thus, we needed to enroll at least 38 patients for each group to yield a statistically significant result with a study power of 80 %. Thus, we included 40 patients per arm with the expectation that at least 38 patients would remain in each group. Power analysis and sample size calculation were performed using SamplePower (release 2.0) software. Data were analyzed using the intention-to-treat (ITT) principle, i.e., data of all randomized patients were included in the final analysis regardless of treatment received. Specifically, all randomized patients who had at least one follow-up visit were included in the final analysis. Patients subsequently lost to follow-up were included in the ITT analysis, and data from the last visit were used (Fig. 1).

The normal distribution of continuous variables was evaluated using the Kolmogrov–Smirnov test. As continuous data were normally distributed, they were expressed as mean± standard deviation (SD). Continuous variables were analyzed with one-way analysis of variance (ANOVA) and ANOVA for repeated measures, and the Bonferroni test was used for post hoc analysis. Categorical variables were compared using the Pearson chi-square test or Fisher's exact test, as required. Differences in questionnaire scores between and among groups were determined using repeated ANOVA that used a post hoc *t* test to compare individual domains of interest. Data were also analyzed using general linear model (GLM) univariate procedure, which provides regression analysis, and ANOVA for one dependent variable by one factor. ANOVA is robust to departures from normality, although data should be symmetric. The model included, as the dependent variable, the subjective/objective cure rate and the overall complication rate, and, as the independent variable, investigational centers involved. The level of statistical significance was set at $P<0.05$ for all statistical analyses. The Statistics Package for Social Sciences (SPSS 15.0.1; SPSS Inc., Chicago, IL, US) was used for all calculations.

Results

Baseline data

Figure 1 illustrates the study flowchart according to the last Consolidated Standards of Reporting Trials (CONSORT) guidelines and extension of the CONSORT statement to RCTs of nonpharmacologic treatment [21, 22]. All five investigational centers were high-volume referral hospitals. Internal meetings were held every 6 months throughout the study period to implement adherence to the single steps of surgical procedures and to the use of surgical instrumentation on the part of the predefined surgical team. After randomization, no difference in age, parity, body mass index (BMI), proportions of postmenopausal patients and patients with SUI or MUI, UI severity and duration, and/or main urodynamic parameters was detected among the three arms (Table 1). All patients were Caucasian, and none had cointerventions.

Efficacy data

Subjective and objective cure rates are detailed in Table 2.

Both subjective and objective cure rates at 6-, 12-, 18-, and 24-month follow-ups were not significantly different among arms. Subjective cure rates were significantly ($P<0.05$) lower after 12, 18, and 24 months from surgery in comparison with 6-month follow-up in each group. In Ajust® and TVT Secur System® arms, objective cure rate was not different between 6- and 12-month follow-ups, but it was significantly ($P<0.05$) lower after 18 and 24 months from surgery in comparison with 6-month follow-ups. In the MiniArc® arm, the objective cure rate was not different between the 6-, 12-, and 18-month follow-ups but was significantly lower at the 24-month follow-up in comparison with the 6-month follow-up. At the 24-month follow-up, no difference was detected between groups in terms of the total failure rate [24 (60.0 %) vs. 22 (55.0 %) vs. 27 (67.5 %), in Ajust®, MiniArc®, and TVT Secur System® groups, respectively; $P=0.432$]. In two (5.0 %) and three (7.5 %) patients in Ajust® and TVT Secur System® groups, respectively, incontinence was reported to be worse. In all other cases, incontinence was reported to be unchanged. After 24 months of follow-up, the proportion of patients who underwent a second surgery for SUI was not significantly

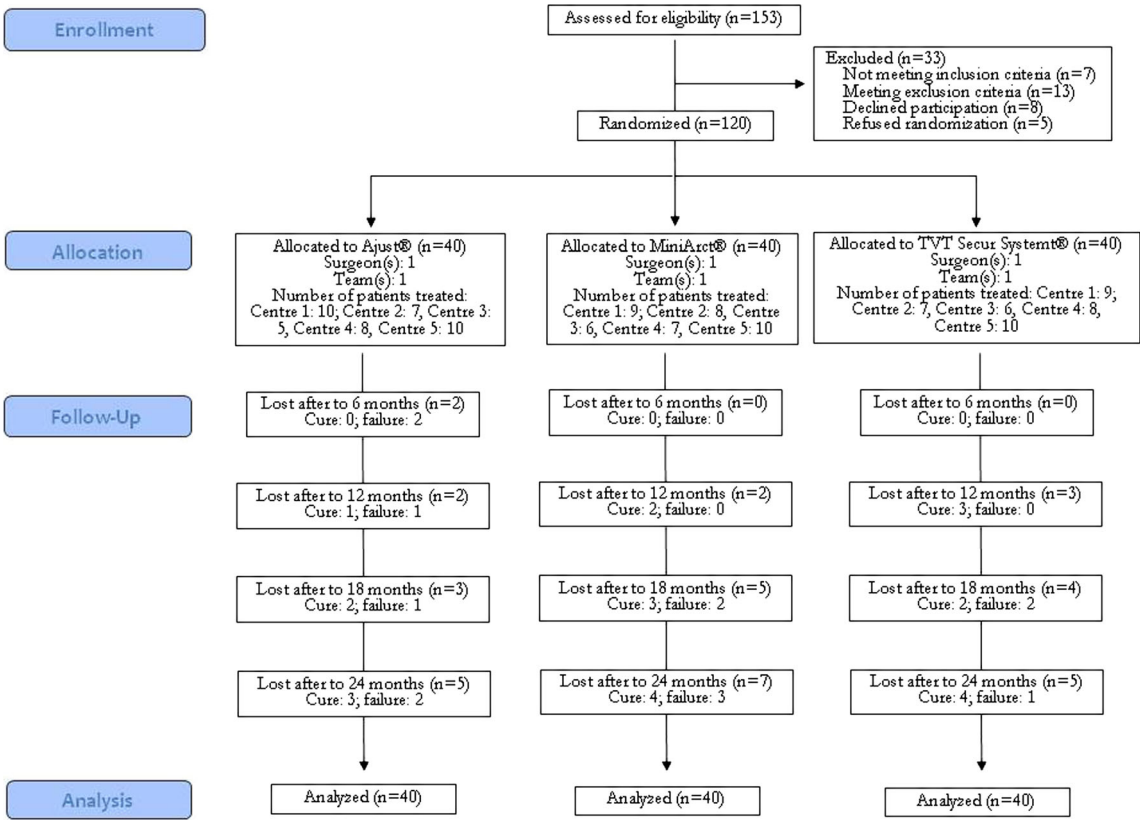

Fig. 1 Study according to the Consolidated Standards of Reporting Trials (CONSORT) guidelines and extension of the CONSORT statement to randomized controlled trials (RCTs) of nonpharmacologic treatment [21, 22]. *Cure* and *failure* refer to randomized patients subjectively cured or not at the previous follow-up visit

significantly different between groups [13 (32.5 %) vs. 10 (25.0 %) vs. 13 (32.5 %), in Ajust®, MiniArc®, and TVT Secur System®, respectively; P=0.831]. Using the GLM univariate procedure, investigational center did not significantly

Table 1 Demographic and clinical data of randomized patients [6]

Group	Ajust® (*n* 40)	MiniArc® (*n* 40)	TVT Secur System® (*n* 40)
Age (years)	62.5±12.3	64.2±13.8	63.6±10.9
Parity (*n*)	3.2±2.1	3.0±2.4	2.8±2.4
BMI (kg/m^2)	27.7±7.9	28.2±6.5	27.9±5.8
Patients who smoke [*n* (%)]	21 (52.5)	18 (45.0)	20 (50.0)
Postmenopausal [*n* (%)]	34 (85.0)	36 (90.0)	35 (87.5)
Patients with SUI [*n* (%)]	30 (75.0)	31 (77.5)	32 (80.0)
Patients with MUI [*n* (%)]	10 (25.0)	9 (22.5)	8 (20.0)
UI severity			
Mild [*n* (%)]	22 (55.0)	20 (50.0)	22 (55.0)
Moderate [*n* (%)]	18 (45.0)	20 (50.0)	18 (45.0)
UI duration (years)	5.2±3.9	4.9±3.7	5.0±3.5
Main urodynamic parameters			
FUL (mm)	25.4±6.8	24.9±6.3	25.2±6.1
PTR	80.3±5.2	83.1±6.4	82.5±5.7
MCC (ml)	411.5±49.4	415.8±51.3	413.2±50.2
MUCP (cm H_2O)	68.9±50.3	69.9±51.6	70.1±52.0
VLPP (cm H_2O)	113.2±53.8	115.0±58.9	114.2±55.7

Values are reported as mean± standard deviation (SD) or as number (*n*) and percentage (%). No comparison was statistically significant

SUI stress urinary incontinence, *MUI* mixed urinary incontinence, *FUL* functional urethral length, *PTR* pressure transmission ratio, *MCC* maximal cystometric bladder capacity, *MUCP* maximal urethral closure pressure, *VLPP* Valsava leak-point pressure.

Table 2 Subjective and objective cure rates of randomized patients

Group	Ajust® (*n* 40)	MiniArc® (*n* 40)	TVT Secur System® (*n* 40)
Subjective cure rate [*n* (%)]			
6 months	36 (90.0)	37 (92.5)	34 (85.0)
12 months	26 (65.0)*	29 (72.5)*	23 (57.5)*
18 months	21 (52.5)*	27 (67.5)*	20 (50.0)*
24 months	21 (52.5)*	26 (65.0)*	21 (52.5)*
Objective cure rate [*n* (%)]			
6 months	32 (80)	33 (82.5)	31 (77.5)
12 months	25 (62.5)	26 (65.0)	22 (55.0)
18 months	20 (50.0)*	24 (60.0)	19 (47.5)*
24 months	19 (47.5)*	22 (55.0)*	17 (42.5)*

Data were analyzed according to intention-to-treat principle

*$P<0.05$ vs. 6-month follow-up

influence the objective ($P=0.310$) or subjective ($P=0.543$) cure rate.

Safety data

A complete description of surgical data, including operative and postoperative complications, was previously detailed [6]. Long-term complications were one case of pelvic pain [one (2.5 %) in TVT Secur System® arm], two cases of de novo or worsened urge UI [one (2.5 %) and one (2.5 %) in Ajust® and MiniArc® arms, respectively], and one case of mesh erosion [one (2.5 %) in Ajust® arm]. Mesh erosion did not require surgical revision.

Urinary symptoms, QoL, and sexual function

Table 3 provides questionnaire scores at baseline and at each follow-up visit.

Discussion

To our knowledge, at the moment this is the first multicenter RCT comparing the long-term efficacy of three different SIMS. In fact, only one study [2] assessed the efficacy and complications of two different SIMS in a randomized controlled fashion. Our clinical study demonstrated a similar and satisfying efficacy of all approaches in the short term, with an increase in differences after 12 months from surgery. In fact, the subjective cure rate of all SIMS was markedly reduced by the 12-month follow-up visit in comparison with previous assessments. Similarly, objective efficacy decreased from 18 months after surgery in the Ajust® and TVT Secur System® groups and from 24 months in the MiniArc® group. At the 24-

Table 3 Questionnaire scores assessed in patients randomized to receive Ajust®, MiniArc®, and TVT Secur System® at baseline and at 6-, 12-, 18-, and 24-month follow-ups

Group	Ajust® (*n* 40)	MiniArc® (*n* 40)	TVT Secur System® (*n* 40)
DIS			
Baseline	1.8±1.2	2.3±1.3	2.2±1.3
6 months	2.2±1.9	2.3±1.7	2.3±1.4
12 months	2.1±1.6	2.2±1.4	2.2±1.2
18 months	2.1±1.4	2.2±1.3	2.3±1.2
24 months	2.1±1.4	2.3±1.3	2.2±1.2
KHQ			
Baseline	284.9±96.2	273.8±98.7	293.3±95.0
6 months	153.8±83.4*	163.8±78.2*	162.8±86.9*
12 months	185.6±85.2*	178.9±86.3*	181.3±89.0*
18 months	197.7±84.7*	187.6±87.3*	220.7±105.1*
24 months	230.6±103.2*	209.5±107.8*	277.1±124.6*
PGI-S			
Baseline	2.7±1.1	2.7±1.1	2.9±1.1
6 months	1.6±1.0*	1.8±1.0*	1.7±1.0*
12 months	2.1±1.0*	1.8±1.0*	2.0±1.1*
18 months	2.0±1.0*	1.8±0.9*	2.1±1.1*
24 months	2.3±1.1	2.1±1.2*	2.5±1.2
PGI-I			
Baseline	—	—	—
6 months	2.3±1.6	2.2±1.5	2.3±1.5
12 months	2.7±1.5	2.5±1.7	2.7±1.5
18 months	2.9±1.6	2.4±1.6	2.9±1.9
24 months	3.2±1.9*	2.8±1.9	3.5±2.0*
FSFI			
Baseline	22.2±9.7	23.4±9.6	21.6±9.4
6 months	22.1±9.5	24.0±9.5*	21.9±9.4
12 months	22.3±9.3	24.2±9.6*	22.2±9.5
18 months	22.7±9.6	24.3±9.5*	22.3±9.7
24 months	22.4±9.4	24.6±9.1*	22.3±10.0
SF-36			
Baseline	70.1±8.9	67.6±9.0	69.8±9.2
6 months	76.4±7.9*	77.2±7.8*	76.4±7.7*
12 months	75.4±7.3*	77.0±7.9*	76.8±7.0*
18 months	75.8±8.2*	77.7±8.3*	76.9±7.5*
24 months	76.4±8.8*	77.0±8.5*	76.9±7.5*

Data were analyzed according to intention-to-treat principle. Values are reported as mean±standard deviation (SD). PGI-I scores were calculated considering as score the number used on a seven-point Likert scale to describe the change in symptoms (1: very much better, 2: much better, 3: a little bit better, 4: no change, 5: a little bit worse, 6: much worse, 7: very much worse) by each patient after surgery

DIS Detrusor Instability Score, *FSFI* Female Sexual Function Index, *PGI-I* Patient Global Impression of Improvement, *PGI-S* Patient Global Impression of Severity, *SF-36* Short-Form Health Survey of 36 questions, *KHQ* King's Health Questionnaire.
* $P<0.05$ vs. baseline

month follow-up, the subjective cure rate, i.e., our primary endpoint, was similar between SIMS. However, the total failure rate was very high for all SIMS studied, without any statistical and clinical difference between groups. Specifically, at 24 months from surgery, the failure rate was >50 % for all SIMS (60.0 %, 55.0 %, and 67.5 % for Ajust®, MiniArc®, and TVT Secur System®, respectively). The lack of efficacy of all three devices was also confirmed and strengthened by reintervention rate, ranging from 25.0 % to 32.5 %. This rate is to be considered clinically remarkable.

All procedures were performed using a transobturator-like hammock approach in order to create a suburethral hammock and to minimize the risk of intraoperative complications. This point is particularly important for TVT Secur System®, which was also placed in a U position using a retropubic approach. Due to the pillowing effect, this placement seemed to be more obstructive and efficacious, resulting in better postoperative QoL and treatment satisfaction [23–25]. However, in June 2012, Johnson & Johnson's Ethicon Division announced a voluntary withdrawal of the TVT Secur System® from the market after a safety communication of the US Food and Drug Administration (FDA) stated the risk of serious complications.

No substantial differences were detected between vaginal kits with regard to the score used to assess the disease-specific impact of UI on QoL or general QoL. The absence of variations in DIS scores in all groups reflects the absence of effects on detrusor activity of these devices. In addition, improvement in KHQ, SF-36, and PGS-I scores at each follow-up suggest that improvement in incontinence might be associated with a better QoL, albeit minimal and not prolonged over time. However, a placebo effect of the surgery cannot be ruled out.

In agreement with a recent prospective study [26] showing a significant benefit on sexual function after 6 months of follow-up, an improvement in FSFI score was observed after the MiniArc® surgery, which remained unchanged throughout the 24 months of follow-up. This finding may be related both to better, even if not significantly, cure rates and to the mini-invasiveness of this device, for which the smaller needle introducer probably reduces the risks of vascular and nerve damage. At the moment, only Olivera's RCT [2] compared the efficacy of two SIMS, i.e., TVT Secur System® and MiniArc®, with control surgery being a transobturator TVT. After 12 months from surgery, the cure rate for TVT Secur System®, MiniArc®, and transobturator TVT were 67 %, 87 %, and 83 %, respectively; on the other hand, failures were 20 %, 7 %, and 7 %, respectively [2].

An important strength of our study is the randomized design, which allows correct treatment allocation in the setting of a clinical trial and improves scientific relevance of the study. To this end, in order to avoid bias, minimize random error, and preserve the power of the study, a true ITT principle was followed: all randomized patients were included in the final analysis and, for patients lost to follow-up, data recorded at the last visit was considered. A further strength is the multicentricity of the trial, which formally allows external reproducibility of surgical procedures and their efficacy, although no influence of investigational center on objective and subjective cure rates was detected.

The study also has some limits. First, there was no control arm, which in a nonpharmacological trial is usually standard care or placebo/waiting list [22]. However, at study design, the Ethical Committee refused randomization between SIMS and retropubic TVT due to the lack of adequate safety and efficacy data about SIMS. Thus, after providing patients with an impartial and careful explanation of the study protocol, only patients choosing to receive a SIMS were randomized. Second, in order to strictly follow the ITT principle (and to have comparable study arms), the last observation of each patient dropped from study was used for statistical analysis. This method could bias results according to the timing of patient dropout. However, analysis of the dropout rate was not statistically significant for the three arms throughout the study period, suggesting a limited bias. Only two patients in the Ajust® group dropped out only after surgery; this event (in comparison with no dropout from the other two arms) probably slightly biased negatively the final results for that arm. Third, at study design, we used a large difference in subjective cure rate among groups for the power calculation, and at study end, the RCT was strongly underpowered. In fact, a postpower study of 50 % was calculated to detect the maximal observed difference in subjective cure rate between the best and worst SIMS, i.e., 12.5 %. Thus, according to that difference in subjective cure rate between SIMS and requiring a power of 90 %, a well-designed and powered two-arm RCT must include at least 500 patients per arm. Thus, it is obvious that obtaining evidence-based data about the most effective SIMS to adopt in clinical practice is highly improbable. In addition, the multiarm approach, as used in this trial—although shown to require a lower total sample size compared with conducting separate RCTs for each intervention, and the fact that it is also very appealing to patients and physicians because it provides an increased probability of receiving an experimental intervention rather than a traditional (control) treatment—requires a multiplicity adjustment, such as the Bonferroni adjustment; its use, however, reduces dramatically the advantage of using the multiarm trial [27].

Recently, Mostafa et al. [28] reported an update of a previous meta-analysis of RCTs and quasi-RCTs aimed at comparing SIMS with traditional MUS [7]. After excluding from data synthesis papers reporting on the TVT Secur System®, no difference between SIMS and traditional MUS was detected in subjective and objective cure rates after a follow-up of 18.6 months, suggesting that TVT Secur System® potentially biased results [7]. A long-term prospective evaluation of the effectiveness of the TVT Secur System® showed a frustrating cure rate of 31 % after 4.5 years of follow-up [29]. Current

data are partially in agreement with that observation, as, at 12 months from surgery, a difference of ~20 % between TVT Secur System® and the other two SIMS was detected. However, as suggested by Serati [30], results [28] must be interpreted with caution. In the RCT reported here, although it was not designed for that purpose, a very low cure rate was observed for all three SIMS vaginal kits. Our previous paper [3], assessing the same population studied for this report, showed no difference in efficacy between SIMS and retropubic TVT only during the first 6 months from surgery. In fact, at the 12-month follow-up, SIMS efficacy was significantly reduced, and their subjective and objective cure rates were significantly worse in comparison with the retropubic TVT, which sustained its effectiveness up to 2 years after surgery. The lack of efficacy of SIMS was also confirmed and strengthened by our reported reintervention rate, which was more than three times higher in patients treated with SIMS (35 % vs. 11 % for SIMS and retropubic TVT, respectively) [3].

In conclusion, the multicenter RCT reported here demonstrates that the long-term efficacy of SIMS is similar between vaginal kits, with similar and very low cure rates and a high risk of secondary surgery for UI.

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