IJMA

International Journal of Medical Arts

Volume 3, Issue 3 [Summer (July-September) 2021]

http://ijma.journals.ekb.eg/

Print ISSN: 2636-4174

Online ISSN: 2682-3780

About IJMA [last updated July, 1st, 2021]

- ✓ International Journal of Medical Arts is the Official Journal of the Damietta Faculty of Medicine, Al-Azhar University, Egypt
- ✓ It is an International, Open Access, Double-blind, Peer-reviewed Journal
- ✓ Published four times a year
- ✓ The First Issue was published in July 2019
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International Journal of Medical Arts 2021; 3 [3] July-September: 1530-1549

Available online at Journal Website
https://ijma.journals.ekb.eg/
Main subject [Obstetrics and Gynecology] *

Systematic review

Five-Years Outcomes of Different Procedures for the Treatment of Female Stress Urinary Incontinence: A Systematic Review and Network Meta-Analysis.

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Submission date: June 07, 2021; Revision date: June 26, 2021; Acceptance date: June 26, 2021.

DOI: 10.21608/IJMA.2021.79651.1323

ABSTRACT

Background: The current body of evidence is limited regarding the long-term outcomes of different modalities for stress urinary incontinence (SUI). We conducted this systematic review and network meta-analysis to compare the long-term follow-up outcomes of mid-urethral slings (MUS), Burch colpo-suspension, pubo-vaginal sling (PVS), anterior colporrhaphy with Kelly's plication, and laser therapy in the treatment of SUI.

Aim of the work: The current work aimed to compare the long-term follow-up outcomes of the following modalities in the management of SUI: MUS, Burch colpo-suspension, PVS, SIMS, anterior colporrhaphy with Kelly's plication, bulking agents, and laser therapy.

Methods: In this systematic review and network meta-analysis, we included prospective and retrospective studies that assessed the long-term outcomes of modalities for the management of SUI. We performed an online, bibliographic, search in four bibliographic databases: Cochrane Central Register of Controlled Trials (CENTRAL), Medline via PubMed, Web of Science, and Scopus.

Results: A total of 42 studies were included. For the subjective cure rate, five different interventions were compared; pooling direct and indirect comparisons revealed an advantage of tension-free vaginal tape (TVT) intervention over TVT-obturator (TVT-O), laparoscopic Burch colpo-suspension, trans-obturator tape (TOT), and TVT-sling (TVT-S). Concerning objective cure rate, the pooling direct and indirect comparisons showed an obvious advantage of TOT, followed by TVT, and then TVT-O, Burch lap, and TVT-S. For repeated surgery, four different interventions were compared, and the comparisons revealed an advantage of TVT intervention over TVT-O, PVS, and TOT. The comparisons revealed the advantage of TVT and TVT-O over other procedures for lower urinary symptoms and postoperative complications.

Conclusion: MUS appears to be the most effective and safe procedure for SUI at long-term follow-up. However, these findings should be interpreted with caution as there is scarcity in the published reports assessing long-term outcomes of other modalities, especially PVS and laser therapy.

Keywords: Stress Urinary incontinence; Mid-urethral slings; Burch Colpo-Suspension; Laser Therapy; Meta-analysis.

Citation: Effat DM, Alkafrawy MA, Soliman AA. Five-Year Outcomes of Different Procedures for The Treatment of Female Stress Urinary Incontinence: A Systematic Review and Network Meta-Analysis. IJMA 2021; 3 [3] July-September: 1530-1549 [DOI: 10.21608/IJMA.2021.79651.1323].

* Main subject and any subcategories have been classified according to the research topic.

INTRODUCTION

Stress urinary incontinence [SUI] is a troublesome disorder with the feature of impaired storage of urine and leakage after physical effort or exertion; the condition affects up to 40% of females in their lifetime [1]. Even though it is a non-life-threatening condition, SUI represents a substantial healthcare burden in the population, leading to negative repercussions on females' quality of life [2].

The problem arises from the weakened support of the pelvic diaphragm and vaginal connective tissue that surrounds the urinary bladder neck and urethra, as well as insufficiency of the urethral sphincter. Risk factors involve gravidity and parity, assisted vaginal delivery, older age, menopause, previous pelvic reconstructive surgeries, and persistent strain [3].

Conservative treatments for SUI usually involves pelvic floor muscle training and vaginal pessaries [4]. While the current international guidelines recommend pelvic floor muscle training as a first-line intervention, vaginal pessaries remain a powerful reversible option in symptoms management [5].

On the other hand, surgical procedures are often indicated when conservative interventions fail, or when operable patients prefer definitive treatment while accepting the hazards of surgery [6]. The three common operations include mid-urethral sling [MUS], Burch colpo-suspension, and pubo-vaginal sling [PVS] [7]. Surgery allows for a higher rate of cure in general, but the short and long-term success rates vary across different methods [8]. MUS continues to be the gold standard surgical treatment in SUI, although literature acknowledges the potentially serious complications of transvaginal mesh application [9, 10].

Generally, MUS is a minimally invasive surgical procedure with symptom-objective cure rates that reach up to 94% [9]. It involves the passing of a small band of an artificial mesh into either the retropubic space [known as tension-free vaginal tape, TVT] or through the obturator foramen [known as trans-obturator tape, TOT] [11].

The frequency of re-operation and mesh removal for MUS rises with time [10]. With the recent concerns about the transvaginal mesh, traditional PVS has re-emerged as an alternative to MUS [12]. The foremost advantage for PVS is the lack of erosion risk that follows inflammation and foreign body reaction associated with the mesh insertion [12]. However, this re-adoption is restrained by the technical challenges and surgeons' expertise [13].

While Burch colpo-suspension and PVS may be preferred to avoid mesh implant problems, their operative morbidities, and rigorous approach restrain their surgical value [13, 14]. Single-incision mini-sling [SIMS] is another modality that relies on anchors to support a pullout force; however, its mid and long-term efficacy is controversial [15].

Meanwhile, in the last decade: the adoption of different laser techniques has shown promising results in the treatment of SUI [16]. The concept of laser therapy is based on the thermal induction of neocollagenesis, elastogenesis, neoangiogenesis, and fibroblast recruitment in the nearby skin and pelvic floor tissue [17, 18]. However, laser treatment does not show efficacy in patients with weakened urethral sphincter, producing an additional intrinsic sphincter deficiency [19]. The injection of bulking agents around the urethra has been proposed as a promising modality that acts by enhancing the closure function of the urethral sphincter; thus, prevent urinary leakage [20].

Another option in the surgical management paradigm of SUI is anterior colporrhaphy with Kelly's plication; despite being considered as historical methods by many researchers; recent surveys indicated that the procedure is still popular among gynecologists [21]. In the short-term, it appears that anterior colporrhaphy with Kelly's plication had a similar cure rate to TOT [21]; however, the long-term results of anterior colporrhaphy with Kelly's plication showed controversies; previous reports demonstrated a high recurrence rate at five years of follow-up [22].

Given all these controversies, we conducted this systematic review and meta-analysis to compare the long-term follow-up outcomes of the following modalities in the management of SUI: MUS, Burch colpo-suspension, PVS, SIMS, anterior colporrhaphy with Kelly's plication, bulking agents, and laser therapy.

MATERIALS AND METHODS

All steps of the present network meta-analysis followed the instructions of the 2nd version of the Cochrane Handbook for Systematic Reviews of Intervention[23]. The writing of the present manuscript was done in strict adherent to the PRISMA for Network Meta-Analyses [PRISMA-NMA] statement [24].

Eligibility Criteria:

We included prospective and retrospective studies that assessed the long-term outcomes of one of the following modalities for the management of SUI: MUS, Burch colpo-suspension, PVS, SIMS, anterior colporrhaphy with Kelly's plication, bulking agents, and laser therapy in the treatment of SUI. Only RCTs that reported the five years' outcomes of

the above mentioned procedures were included. Studies that were written in other languages than English, thesis, conference abstracts, and studies with no reliable data for extraction were excluded.

Literature Search Strategy and Screening:

We used different combinations of the following queries and retrieved all online records, which were published until the end of August 2020: Urinary incontinence, stress urinary incontinence, urinary incontinence in women, mid-urethral sling, mid-urethral slings, tension-free vaginal tape, trans obturator tape, Burch colposuspension, Pubovaginal sling, anterior colporrhaphy, Kelly's plication, single-incision mini-sling, bulking agents, and laser therapy. The search was conducted in Cochrane Central Register of Controlled Trials [CENTRAL], Medline via PubMed, Web of Science, and Scopus. In order to remove duplicates from databases search, we downloaded the retrieved citations and imported them to EndNote X7 for duplicates removal. Then, the titles and abstracts of the remaining records were screened for eligibility. The second round of screening was conducted on full-texts of potentially eligible abstracts for final inclusion in the present systematic review.

Data Extraction and Quality Assessment:

The authors used a standardized Excel sheet to extract the following data independently: summary characteristics of study design and population, characteristics of studied procedures, cure rates [both objective and subjective], need for repeated surgery, lower urinary symptoms, and postoperative complications. The risk of bias of the randomized controlled trials [RCTs] was assessed using the Cochrane risk-of-bias tool [25]. The quality of observational studies was deemed low.

Data Analysis:

As all our outcomes were dichotomous, the odds ratio [OR] of adverse effects of interventions comparisons at the end of each study was calculated and pooled. Inconsistency between studies was assessed using Cochran's Q methods. For indirect comparisons, network meta-analyses were applied to assess all possible effects of treatment measured at different times if sufficient data were available for pooling [26]. A random-effect model was applied during pooling in all outcomes. The pooled OR and its 95% confidence intervals [CIs] were estimated by exponential coefficients of outcomes. All analyses were performed using MetaInsight version 12.0 [27]. A P value <0.05 was considered statistically significant.

RESULTS

Our literature search retrieved 8299 studies with only 4684 left after removing duplicates. Title and abstract screening yielded 572 articles that met the eligibility criteria for further full-text assessment. Only 42 studies were included in our study after full-text screening. Also, the manual approach of the reference lists of the included studies revealed no potential articles. [**Figure 1]** provides a summary of the search and inclusion process of the articles.

Characteristics and quality of included studies

A total of 44 studies, encompassing 6775 women at baseline, were included. Of them, 16 studies were RCTs, 14 were retrospective studies, and the rest were prospective cohort studies. All included studies assessed MUS, except one study that compared Burch colposuspension to fascial sling surgery and six studies that assessed the anterior colporrhaphy. Notably, there were no published studies with long-term outcomes [at least five years] assessing laser therapy, PVS, bulking agents, or SIMS for SUI. The average follow-up duration of the included studies was 74.3 months. **[Table 1]** presents the patient characteristics and the designs of the included studies. The results of the quality assessment of RCTs are present in **[appendix 1]**.

Subjective cure rate:

For the subjective cure rate, five different interventions were compared, and the network graph is showcased in **[Figure 2a]**. The total number of patients in the network meta-analysis was 2894 included from 14 studies. Pooling direct and indirect comparisons revealed an advantage of TVT intervention over TVT-O, Burch colposuspension, TOT, TVT-S, and anterior repair respectively [**Figure 3a**].

There was no significant inconsistency [P= 0.380]. Moreover, sensitivity analysis in our model did not materially affect the relative effect and the ranking of interventions. In the same context, pairwise comparisons of all interventions to TVT revealed that TVT was more effective than any other approach. However, this difference in cure rates was not statistically significant throughout all comparisons [**Figure 4A**].

Objective cure rate

[Figure 2b] is a network plot of the comparisons of objective cure rates among five different interventions. Pooling direct and indirect comparisons showed an obvious advantage of TOT, followed by TVT and then TVT-O, Burch colposuspension, TVT-S, and anterior repair respectively. [Detailed ranks for all outcomes in **Figure 3b**]. but, there

was no significant difference [P= 0.175]. Moreover, sensitivity analysis revealed no alternations in ranks and the effects of the different interventions. Furthermore, pairwise comparisons of all approaches to TVT revealed TOT was the best. Interestingly, this difference in cure rate was not statistically significant across all interventions. [**Figure 4b**].

Repeated surgery

For repeated surgery, four different interventions were compared, and the network graph is showcased in **[Figure 2c]**. The total number of patients in the network meta-analysis was 584 included from 4 studies. Pooling direct and indirect comparisons revealed an advantage of TVT intervention over TVT-O, PVS, and TOT [**Figure 3c**].

There was no significant difference [P= 0.999]. Also, sensitivity analysis in our model revealed no effect on the overall ranking of interventions and the efficacy. In the same context, pairwise comparisons of all interventions to TVT revealed that TVT had the least repeated surgery rate than any other approach. However, this difference in outcome was not statistically significant throughout all comparisons [**Figure 4c**].

Improvements in the storage lower urinary symptoms at the end of follow-up

Regarding lower urinary symptoms [storage], three different interventions were compared, and the network graph is showcased in [**Appendix 2; Figure 1]**.

The total number of patients was 618 included from 4 studies. Pooling direct and indirect comparisons revealed an advantage of TVT-O intervention over TVT and PVS. There was insignificant difference [P= 0.245]. The sensitivity analysis in our model revealed no effect on the overall ranking of interventions and the efficacy. Furthermore, pairwise comparisons of all interventions to TVT revealed that TVT-O had the least repeated lower urinary symptoms [storage] than any other approach [**Appendix 2; Figure 2]**. However, this difference in outcome was not statistically significant throughout all comparisons [**Appendix 2; Figure 3**].

Improvements in the voiding lower urinary symptoms at the end of follow-up

Regarding voiding symptoms, there were four different interventions for comparison, and the network graph is showcased in [**Appendix 2; Figure 4**].

The total number of patients was 1117 included from 7 studies. Pooling direct and indirect comparisons revealed an advantage of TVT-S intervention over TVT-O, TVT, and TOT **[Appendix 2; Figure 5]**.

There was no significant inconsistency [P= 0.642]. Also, sensitivity analysis in our model revealed no effect on the overall ranking of interventions and the efficacy. Furthermore, pairwise comparisons of all interventions to TVT revealed that TVT-S had the least voiding symptoms rate than any other approach. However, the difference in voiding symptoms was not statistically significant throughout all comparisons [**Appendix 2; Figure 6**].

Pelvic hematoma

[Figure5a] is a network plot of the comparisons of pelvic hematoma rate among five two interventions included from four studies. The total number of patients encompassed in this model was 572. Pooling direct and indirect comparisons showed an obvious advantage of TVT-O, over TVT [**Figure 6a**].

TVT-O was associated with the lowest rate of pelvic hematoma. However, this difference was not statistically significant between both interventions [P= 0.234] [**Figure 7a**].

Vaginal erosion

[Figure 5b] is a network plot of the comparisons of vaginal erosion among seven different interventions. The total number of patients in this model was 2269, recruited from 11 studies. Pooling direct and indirect comparisons showed an obvious advantage of Burch colposuspension approach, followed by the facial sling and then PVS, TVT, TVT-S, TVT-O, and TOT, respectively. [Detailed ranks for all outcomes in **[Figure 6b**].

There was no significant inconsistency [P= 0.496]. Moreover, sensitivity analysis revealed no alternations in ranks and the effects of the different interventions. Furthermore, pairwise comparisons of all approaches to TVT revealed Burch was associated with the least vaginal erosion. Interestingly, this difference in vaginal erosion was statistically significant between interventions [**Figure 7b**].

Table [1]: Summary Characteristics of the Included Studies [n =36]

Study ID	Year	Study Design	Population	No. at baseline	Technique	No. at baseline	Control	No. at baseline	FU Duration [mon]	Objective cure	Subjective cure	Urodynamic studies	QoI
Xian-Hue et al.,	2019	Retrospective cohort	Female patients with SUI	170	TVT	30 non-ISD; 16 ISD	TOT	87 non-ISD; 37 ISD	110		X		
Ward et al.,	2008	Multicentre randomized controlled trial	Women with urodynamically confirmed SUI	316	TVT [Retropubic]	170	Burch [Colposuspension]	146	60	X	X		X
Angioli et al.,	2010	Prospective randomized controlled trial	Patients affected by SUI	72	TVT [Retropubic]	35	TVT-O [transobturator tension-free vaginal tape]	37	60	X	x	X	X
Sivaslioglu et al.,	2012	Prospective single blind randomized controlled trial	Female patients with urodynamic SUI	80	TFS [Tissue Fixation System]	40	TOT I-Stop [Transobturator Tape]	40	60	X	X	X	
Laurikainen et al.,	2014	Multicentre randomized controlled trial	women with SUI	268	TVT [Retropubic]	136	TVT-O [transobturator tension-free vaginal tape]	132	60	X	X		X
Costantini et al.,	2015	Multicentre prospective randomized controlled trial	Patients with stress or mixed UI associated with urethral hypermobility, according to ICS classification	95	TVT [Retropubic]	44	TOT [Transobturator Tape]	51	100	X	X	X	X
Khan et al.,	2015	Multicentre prospective randomized controlled trial	Women with clinically and urodynamically confirmed SUI, requiring surgical intervention after failed trial of pelvic floor muscle training.	151	TVT	72	AFS [autologous fascial sling]	79	120	X	X		
Kenton et al.,	2014	Prospective randomized controlled trial	Women with SUI	597	TVT	298	TOT	299	60	X	X		X
Ross et al.,	2016	Prospective randomized controlled trial	Women with SUI	199	TVT	105	TVT-O [transobturator tension-free vaginal tape]	94	60	X	X		X
Tommaselli et al.,	2015	Prospective single blind randomized controlled trial	Patients affected by urodynamic SUI.	154	TVT-O	77	TVT-S	77	60	X	X		X
Valpas et al.,	2015	Multicentre randomized controlled trial	Women WHO had urodynamically proven SUI	121	TVT [Retropubic]	70	Burch lap [M laparoscopic mesh colposuspension]	51	60	X	X		X
Zhang et al.,	2016	Prospective randomized controlled trial	Patients affected by urodynamic SUI.	140	TVT	70	TVT-O	70	95	X	X		X
Ankardal et al.,	2006	Prospective observational study		707	TVT	704			60		X		
Athanasiou et al.,	2014	Retrospective cohort	Women who underwent a TVT-O procedure with or without a concomitant pelvic floor reconstructive surgery.	145	TVT-O	145			90.3	X	X	X	X
Bjelic-Radisic et al.,	2011	Retrospective cohort	women with a predominant symptom of SUI who underwent a TVT procedure with or without concomitant surgery	158	TVT	158			60	X	X	X	X
Li et al.,	2011	Retrospective cohort	Women with SUI	55	TVT	55			84	X	X	X	
Seratia et al	2017	Prospective observational study	Women with SUI	160	TVT-O	160			120	X	X	X	
Cañete	2013	Retrospective cohort	Women underwent a TOT operation due to SUI.	63	TOT Monarc	26	TOT Obtape	37	60	X	X	X	X
Celebi et al.,	2009	Retrospective cohort	Patients undergoing TVT for genuine SUI.	600	TVT	600			63.1	X	X	X	X
Chêne et al.,	2007	prospective series	Patients treated for stress urinary incontinence with a single TVT procedure	64	TVT	64			60			X	X
Cheng et al.,	2012	prospective study	Patients diagnosed with SUI, based on subjective complaints and objective clinical signs and confirmed with urodynamic diagnosis including a stress test and uroflowmetry.	10	TVT-O	103			65	X	X	x	X

Study ID	Year	Study Design	Population	No. at baseline	Technique	No. at baseline	Control	No. at baseline	FU Duration [mon]	Objective cure	Subjective cure	Urodynamic studies	QoI
Cheung et al.,	2014	Prospective observational cohort	audit database involving all patients presenting to the outpatients department with urinary incontinence	213	TOT Monarc	124	TVT-O	89	60	X	X	X	
Deffieux et al.,	2007	Retrospective cohort	women who underwent TVT surgery	61	TVT	61			83		X		
Doo et al.,	2006	Prospective cohort	women with complaints of SUI underwent the TVT procedure	155	TVT	155			67			X	
Glavind et al.,	2012		Patients with genuine stress SUI.	173	TVT	173			60		X		X
Goktolga et al.,	2008	prospective study	patients undergoing TVT for Intrinsic Sphincter Deficiency	50	TVT	50			67	X	X		
Groutz et al.,	2011	Retrospective cohort	women with urodynamically confirmed SUI	60	TVT [Retropubic]	60			120		X	X	
Han et al.,	2014	Retrospective cohort	patients who underwent retropubic TVT sling for urodynamic SUI	113	TVT [Retropubic]	113			144		X	X	X
Heinonen et aal.,	2014	Retrospective cohort	Patients operated using the outside-in TOT procedure.	191	TOT Monarc	191			78	X	X		X
Holdø et al.,	2018	Retrospective cohort	patients having undergone a possible Unrelated surgical procedure	390	TVT [Retropubic]	390			120		X	X	
Brubaker et al.,	2012	Prospective randomized observational study		482	Burch	239	Fascial Sling Surgery	243	60				X
Diniz et al.,	2018	Retrospective cohort	Patients who had surgical correction using the transobturator sling technique	152	TOT [Transobturator Tape]	152			60		X	X	
Golbasi et al.,	2019	Prospective cohort	Patients with SUI.	62	single incision minisling	62			60		X		X
Karmakar et al.,	2017	randomized controlled trial	Patients with urodynamic SUI or stress-predominant mixed urinary incontinence [MUI],	208	TVT-O	104	TOT-ARIS	104	110.4		X		X
Natale et al.,	2019	single-center prospective study	Women who underwent “out-in” TOT with “complicated” and “uncomplicated” SUI.	136	TOT	136			120	X	X	X	X
Sun et al.,	2019	prospective cohort	Patients with stress urinary incontinence	64	TVT-O	31	TVT-S	33	120	X	X		X
Shirvan.,	2014	randomized prospective clinical trial,	Women with SUI.	100	TVT	50	TOT	50	60				
Zhua et al.,	2007	comparative randomized clinical trial study	Women with SUI.	55	TVT	28	TVT-O	27	67.6				
Thaweekul et al.,	2004	Retrospective cohort	Women with SUI.	52	Anterior colporrhaphy with Kelly plication	52			60	X	X	X	
Pelusi et al.	1990	Retrospective cohort	Women with SUI.	160	Anterior colporrhaphy	160			60-120	X	X	X	
Hajihashemy	2008	prospective cohort	Women with SUI.	20	Anterior colporrhaphy	20			64	X	X	XX	
Colombo et al.,	2005	randomized prospective clinical trial,	Women with SUI.	78	Anterior colporrhaphy	33	Burch colposuspension	35	8 to 17 years	X	X	X	
LIAPIS et al.,	1996	prospective cohort	Women with SUI.	170	Anterior colporrhaphy		Marshall-Marchetti-Krantz [MMK] - Burch colposuspension		60	X	X	XX	
Bergman and Elia	1995	randomized prospective clinical trial,	Women with SUI.	127	Anterior colporrhaphy				60	X	X	X	

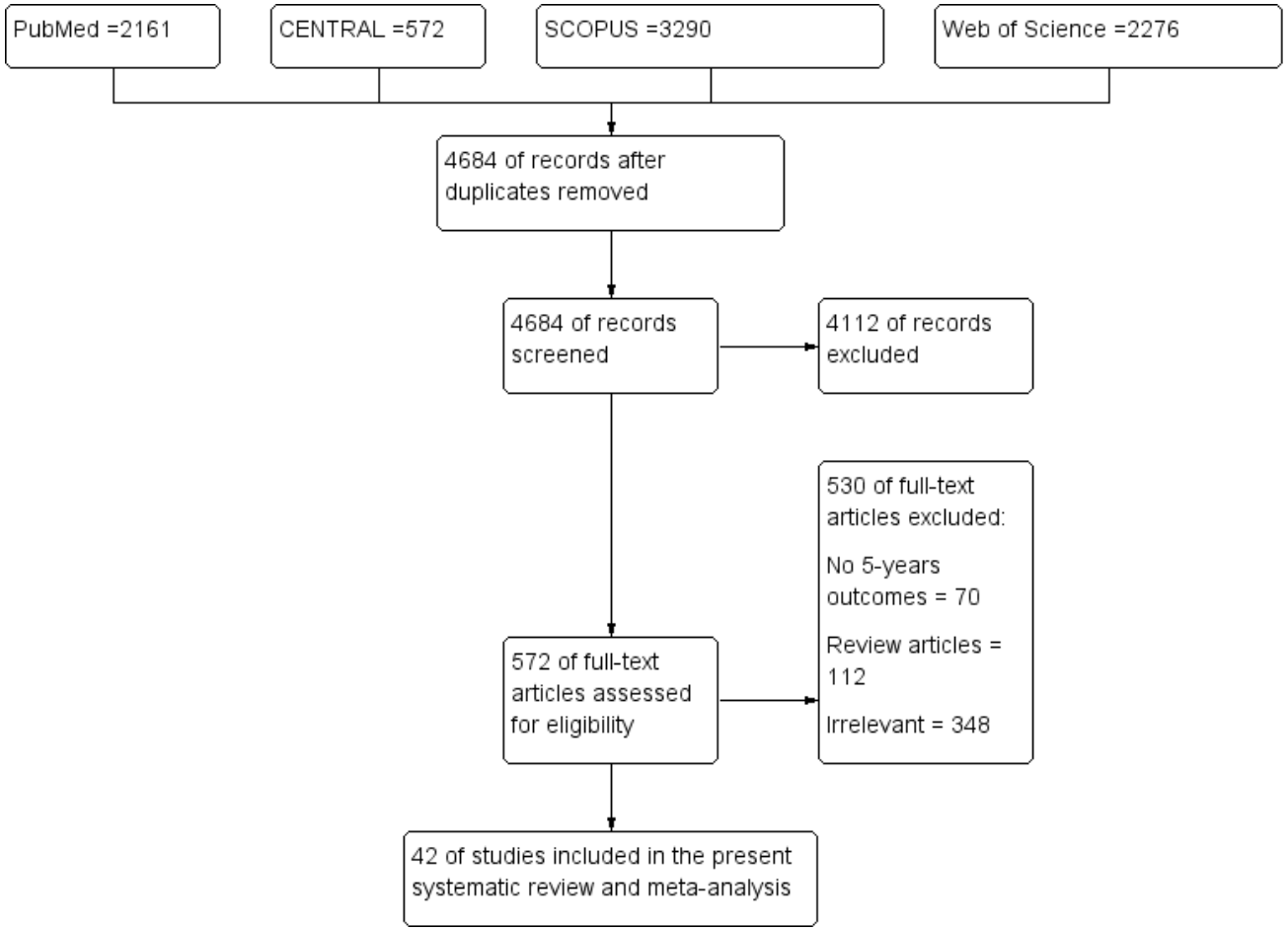


Figure [1]: PRISMA Flowchart

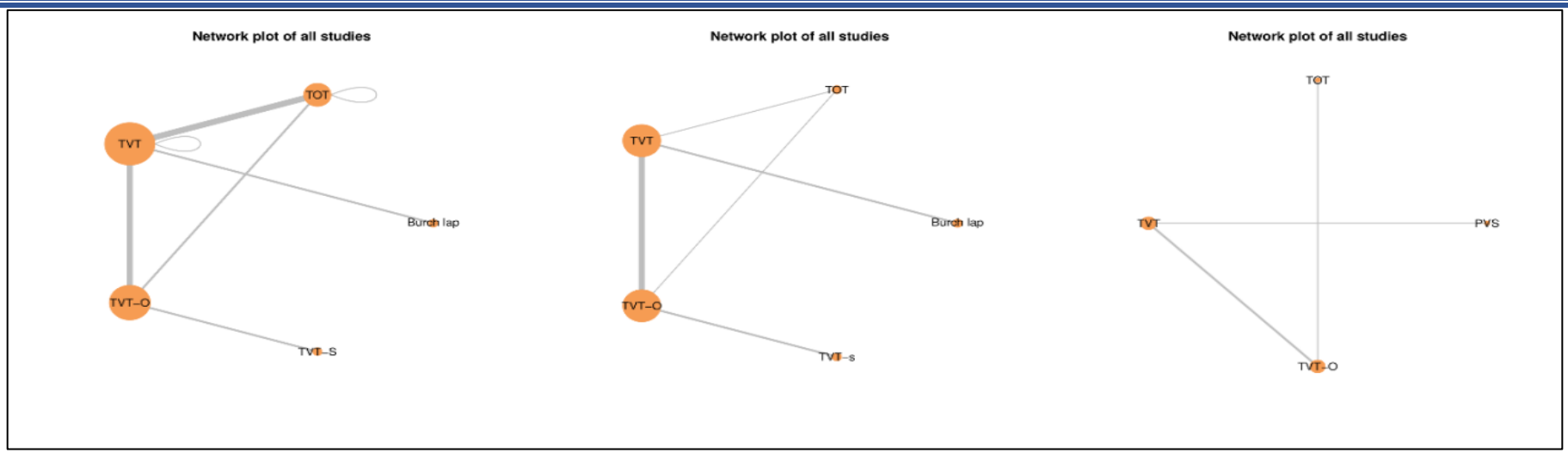
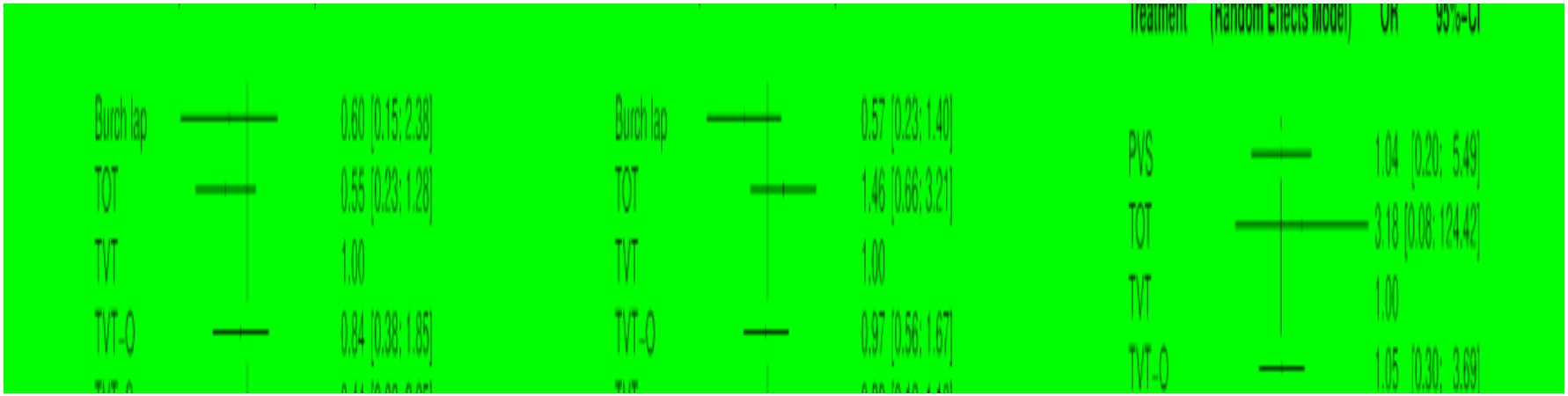


Figure [2]: Network graph for [a] subjective cure rate, [b] objective cure rate, and [c] repeated surgery



Figure[3]: Network meta-analysis for [a] subjective cure rate, [b] objective cure rate, and [c] repeated surgery

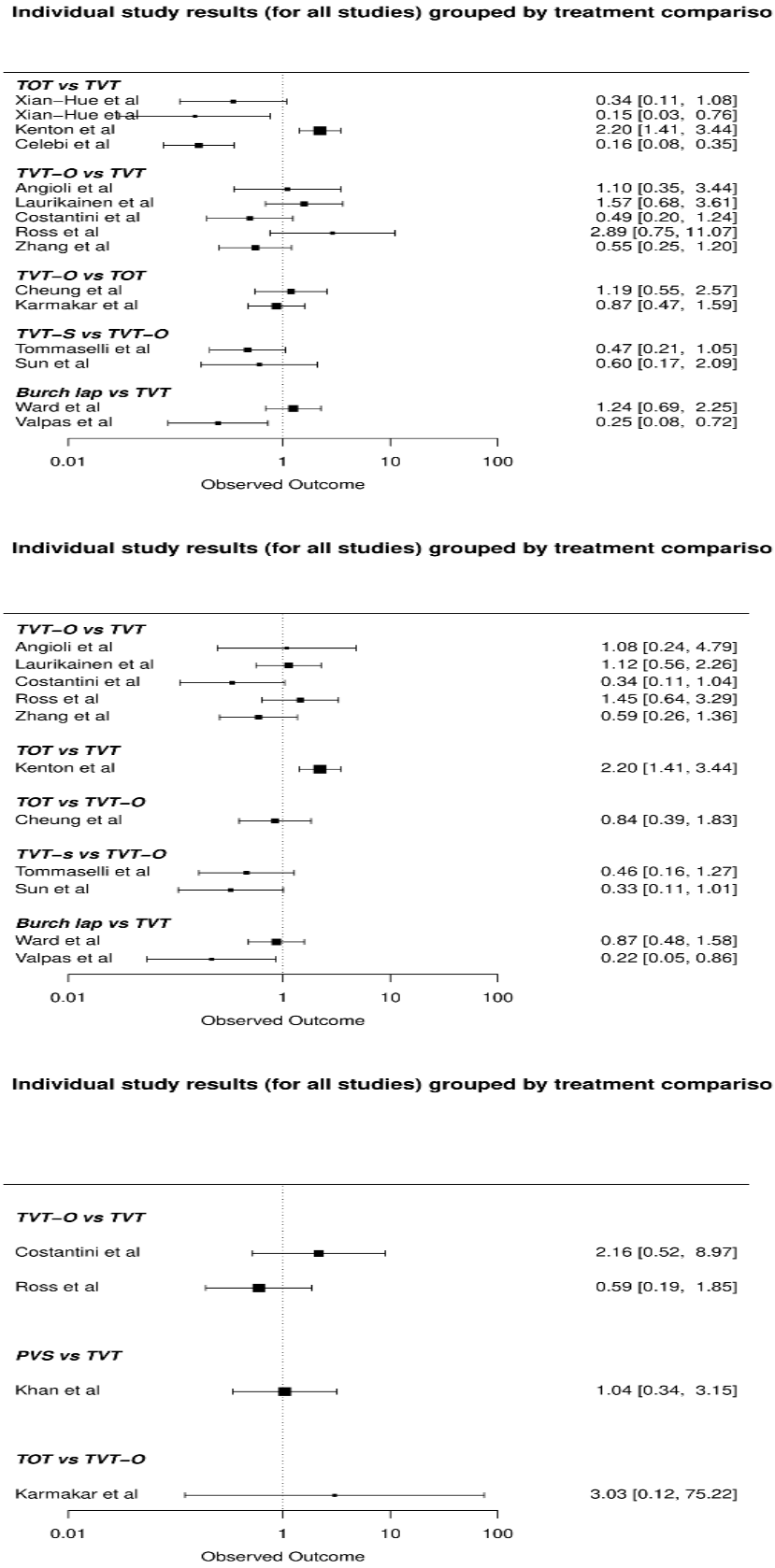


Figure [4]: Ranking probability for [a] subjective cure rate, [b] objective cure rate, and [c] repeated surgery

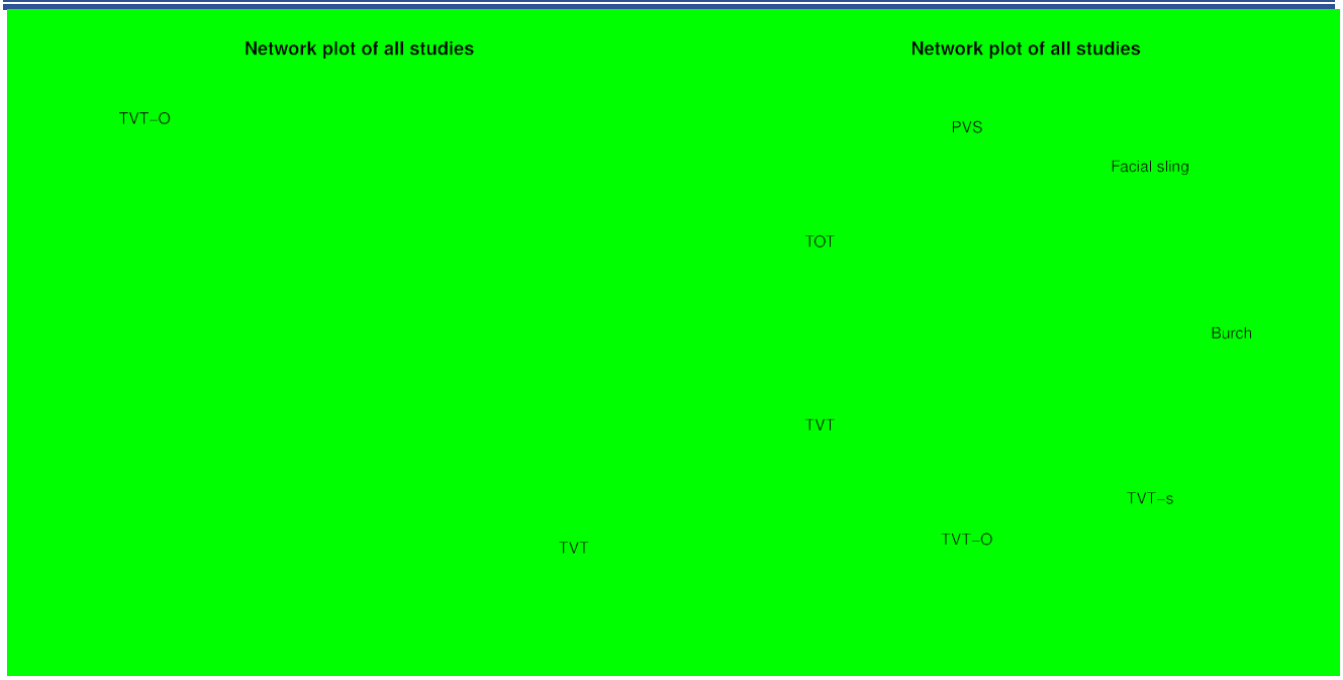


Figure [5]: Network graph for [a] storage symptoms and [b] voiding symptoms

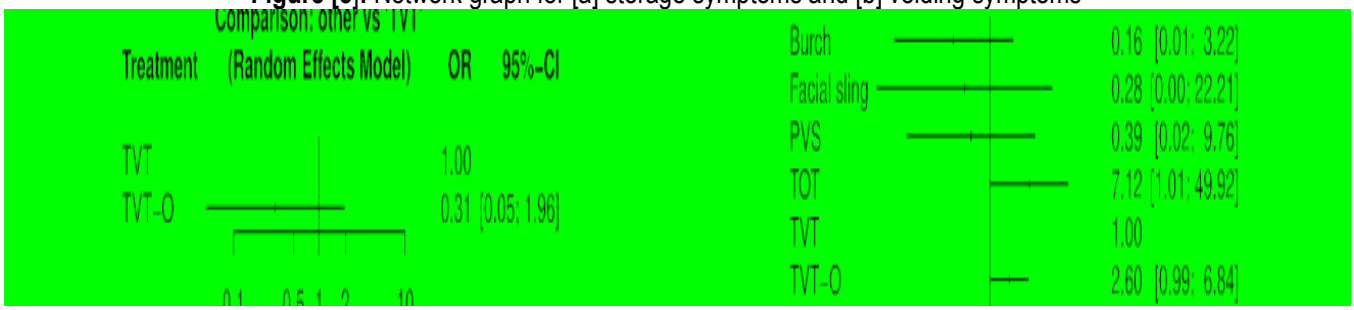


Figure [6]: Network meta-anlysis for [a] storage symptoms and [b] voiding symptoms

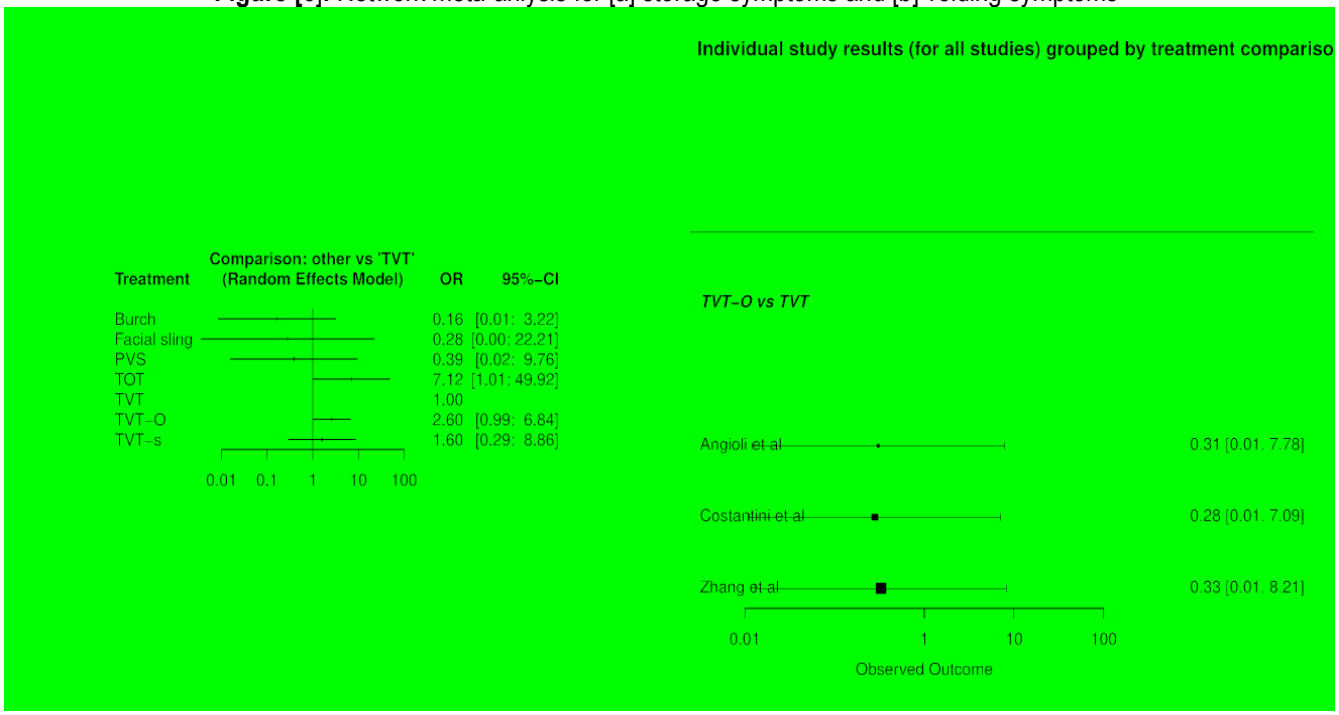


Figure [7]: Ranking probability for [a] storage symptoms and [b] voiding symptoms

DISCUSSION

Although there is a plethora of evidence about the efficacy and safety of surgical modalities for SUI, the published literature still lacks high-quality evidence about the long-term outcomes of these modalities[28, 29]. Thus, we conducted the present meta-analysis to investigate the long-term outcomes of MUS, Burch colpo-suspension, PVS, SIMS, anterior colporrhaphy with Kelly's plication, bulking agents, and laser therapy in the treatment of SUI. Our ranking analysis demonstrated that TVT and TOT achieved the highest objective and subjective cure rates at long-term follow-up, as compared to other included interventions. As, both modalities were associated with the lowest rate of need for revision surgery and the highest improvement in storage/voiding lower urinary symptoms, as compared to other included interventions, and the rates of pelvic hematoma were the least in TVT and TOT as well.

MUS is a commonly performed, minimally-invasive, procedure for the management of SUI that has the advantage of high cure rates [up to 94%] [9] and low risk of postoperative complications, including visceral injuries and retention[11]. The procedure is based on passing of a small band of an artificial mesh into either the retropubic space [known as tension-free vaginal tape, TVT] or through the obturator foramen [known as trans-obturator tape, TOT [outside- in] or TVT-O [inside-out] [30]. The short-term efficacy of MUS appears to be well-established with a large number of systematic reviews and meta-analyses confirming its safety and efficacy [31,32].

Recently, authors have evaluated the long-term outcomes of MUS in the setting of SUI; for example, a previous meta-analysis on eleven RCTs concluded that the MUS [whether TOT or TVT] exhibited acceptable levels of cure rate and safety profile on long-term follow-up among women with SUI [33]. Similar findings were reported by Giovanni et al., meta-analysis [34].

On the other hand, Burch urethropexy, firstly introduced in the early 1960s, was previously considered as the best treatment option for SUI, before the introduction of newer modalities; the technique of Burch urethropexy depends on the suspension of Cooper's ligament via open or laparoscopic approaches [13]. According to a previous Cochrane review, Burch urethropexy achieved a short-term cure rate of 75-90% [35, 36].

Another option for SUI is PVS, which is usually reserved for severe cases due to technical complexity and associated risks of postoperative complications and seroma [14].

As recently demonstrated by Imamura et al. [29], the comparative efficacy of these modalities is still largely unknown. In the present network meta-analysis, we found that TVT and TOT achieved the highest objective and subjective cure rates at long-term follow-up, as compared to other included interventions.

Our findings are in line with short and medium-term results reported by Imamura et al. [29], in which the MUS achieved higher cure rates than other procedures. However, these findings should be interpreted with caution as there is scarcity in the published reports assessing long-term outcomes of other modalities, especially PVS and laser therapy.

Treatment failure and recurrence are major concerns during surgical management of SUI, previous reports demonstrated that nearly 4% of women require reoperation for recurrent SUI on long-term follow-up, with substantial variations in the reported recurrent rate amongst different modalities [37].

The use of MUS is thought to be associated with a considerable risk of reoperation as synthetic mesh may be exposed in the long-term and need removal; besides, the use of a mesh may lead to chronic pain and voiding dysfunction [30].

The risk of recurrence, in women undergoing MUS, was reported to be significantly higher in obese women, diabetic patients, women with a history of SUI surgery, and mixed UI [38]. However, in a recent long-term follow-up study [median follow-up was 13 years] that recruited 3280 women with SUI, the rate of reoperation after MUS was low and the use of MUS was considered safe in this regard [39].

Other systematic reviews demonstrated similar findings [33, 34]. In the present study, we demonstrated that the MUS was associated with the least risk of reoperation, as compared to other procedures.

The use of laser therapy has tremendously expanded to involve many gynecological conditions. In the setting of SUI, the concept of laser therapy stems mainly from the well-known association between SUI and collagen defect; a cumulative body of evidence exhibited that women with SUI had significantly lower expressions of collagen type I and III [40].

Laser therapy can thermally induce neo-collagenesis, elastogenesis, neoangiogenesis, and fibroblast recruitment in the nearby skin and pelvic floor tissue [17, 18].

Initial reports showed promising short-term results of Er: YAG laser in the management of SUI, the laser achieved significant improvement in the symptomatic burden of stress urinary incontinence and quality of life of the affected women [41, 42].

The Er: YAG laser showed similar findings on medium-term follow-up [43].

In a 2019 review, the authors concluded that laser therapy is effective, minimally-invasive, modality for short-term improvements in SU I[44].

In the present review, we could not identify any published reports about the long-term outcomes of laser therapy; thus, well-designed studies with long-term follow-up is needed to characterize the efficacy of laser therapy on the outcomes of SUI. Anterior vaginal repair [anterior colporrhaphy] is a surgical approach through the vagina. The vaginal mucosa below the urethra is dissected, ending just in front of the cervix. One to three sutures [often referred to as Kelly sutures] are placed in the peri-urethral tissue and the pubocervical fascia to support and elevate the bladder neck. Excess vaginal tissue is removed and then the dissected area is closed. A wide variety of techniques and modifications have been described, including Bologna procedure, Kelly-Kennedy, Marion Kelly, diaphragmplasty, vaginal urethrocystopexy, cystocele repair and Kelly plication [45].

Previously, it was reported that Kelly bladder neck plications for treatment of latent or concurrent SUI are not effective at the time of anterior repair, and are therefore no longer recommended [22]. However, limited evidence indicates that the anterior vaginal repair has increased risks for repeated surgery for incontinence than after other technique [45].

In this analysis, we could not pool the outcomes of the anterior vaginal repair due to limited data; however, the reported success and recurrence rates of this technique are not encouraging, especially at the long-term follow-up.

While the present systematic review has the advantages of comprehensive search of databases, we acknowledge the presence of some limitations. The pooled estimates of the network meta-analysis model were inconsistent in all pooled outcomes, suggesting wide variations in methodology of the included studies, definitions of studied outcomes, and duration of follow-up

. We could not investigate the impact of these factors in the pooled outcomes due to limited data of various subgroups amongst the included studies. Besides, the quality of the included studies was low-to-moderate, which further lower the confidence in the obtained evidence. The scarcity in the number of published reports regarding the 5-years outcomes of some modalities, such as PVS and laser therapy, is another limitation.

In conclusion, MUS appears to be the most effective and safe procedure for SUI at long-term follow-up. Our network meta-analysis demonstrated that TVT and TOT achieved the highest objective and subjective cure rates at long-term follow-up, as compared to other included interventions.

In addition, both modalities were associated with the lowest rate of need for revision surgery and the highest improvement in storage/voiding lower urinary symptoms. However, these findings should be interpreted with caution as there is scarcity in the published reports assessing long-term outcomes of other modalities, especially PVS and laser therapy. Further, high-quality, evidence is still needed.

Acknowledgements: None

Funding: None

Conflict of Interest: The authors declare that they have no conflict of interest.

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Appendix (1): Supplementary file shows the results of quality assessment of included trials

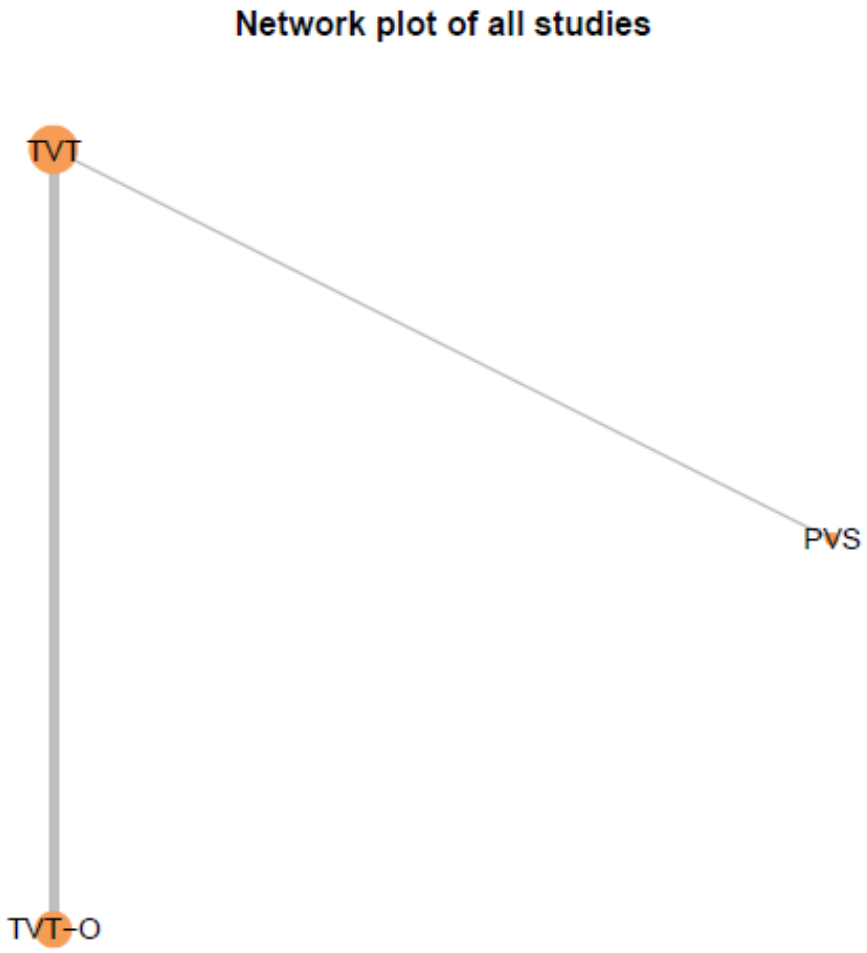
3. Ward et al. 2008	**Risk of Bias**	**Quotations**
Random sequence generation (selection bias)	low risk	"Randomization was computer generated using blocks of four and six."
Allocation concealment (selection bias)	low risk	"Researchers randomized participants via a tele-phone system, which allocated trial identification number and treatment group."
Blinding of participants and personnel (performance bias)	High risk	"Owing to differences between the procedures in incision, anesthesia, and catheterization, it was not possible to blind investigators or participants to the treatment allocation."
Blinding of outcome assessment (detection bias)	Unclear risk	Not described.
Incomplete outcome data (attrition bias)	High risk	"The reasons for missing data at 5 years were: due to investigator withdrawal—that is investigators elected not to take part in the 5-year extension to the study (21 TVT and 17 colposuspension), loss to follow up (40 and 39) and patient withdrawal (11 and 11)."
Selective reporting (reporting bias)	Low risk	"All outcome of interest were reported."
Other bias	High risk	"This study was supported by a grant from Ethicon Ltd who also provided materials and additional support to collaborating centres."
4. Angioli et al. 2010	**Risk of Bias**	**Quotations**
Random sequence generation (selection bias)	low risk	"Patients were randomly allocated to the TVT or TVT- O procedure using a predetermined, computer-generated randomisation code."
Allocation concealment (selection bias)	low risk	"Patients were randomly allocated to the TVT or TVT- O procedure using a predetermined, computer-generated randomisation code."
Blinding of participants and personnel (performance bias)	High risk	"The study was not blinded."
Blinding of outcome assessment (detection bias)	Low risk	Not described.
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Low risk	"All outcome of interest were reported."
Other bias	Unclear risk	
5. Sivaslioglu et al. 2012	**Risk of Bias**	**Quotations**
Random sequence generation (selection bias)	Low risk	"patients were randomly allocated by computer Program for a TOT or TFS operation. Each group included 40 patients."
Allocation concealment (selection bias)	Low risk	"patients were randomly allocated by computer Program for a TOT or TFS operation. Each group included 40 patients."
Blinding of participants and personnel (performance bias)	High risk	"Single blinded."
Blinding of outcome assessment (detection bias)	High risk	"Single blinded."
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	low risk	All outcome of interest were reported.
Other bias	Unclear risk	
6. Laurikainen et al. 2014	**Risk of Bias**	**Quotations**
Random sequence generation (selection bias)	low risk	"The women were randomized into groups using a computer-generated random allocation in a 1:1 ratio in balanced blocks of four."
Allocation concealment (selection bias)	low risk	"The women were randomized into groups using a computer-generated random allocation in a 1:1 ratio in balanced blocks of four."

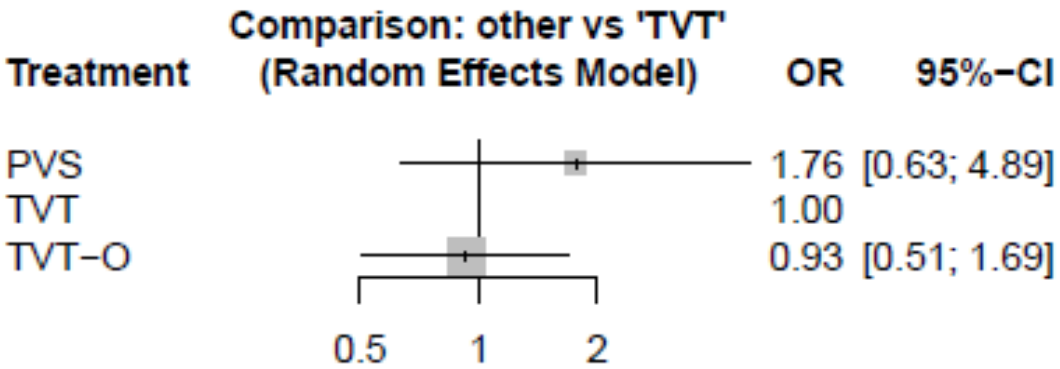
Blinding of participants and personnel (performance bias)	High risk	"Single blinded."
Blinding of outcome assessment (detection bias)	High risk	"Single blinded."
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Low risk	All outcome of interest were reported.
Other bias	Unclear risk	
7. Costantini et al. 2015	**Risk of Bias**	**Quotations**
Random sequence generation (selection bias)	Low risk	"Candidates were prospectively randomised, by means of a predetermined computer-generated randomisation code, to the retropubic route (TVT) or the transobturator route (TOT)."
Allocation concealment (selection bias)	Low risk	"Candidates were prospectively randomised, by means of a predetermined computer-generated randomisation code, to the retropubic route (TVT) or the transobturator route (TOT)."
Blinding of participants and personnel (performance bias)	High risk	"Single blinded."
Blinding of outcome assessment (detection bias)	High risk	"Single blinded."
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	low risk	All outcome of interest were reported.
Other bias	Unclear risk	
8. Khan et al. 2015	**Risk of Bias**	**Quotations**
Random sequence generation (selection bias)	Low risk	"Randomisation was achieved using a computer generated randomisation schedule for each centre and each individual surgeon."
Allocation concealment (selection bias)	Unclear risk	"Not described."
Blinding of participants and personnel (performance bias)	Unclear risk	Unclear risk
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear risk
Incomplete outcome data (attrition bias)	Low risk	"The assessment was carried out on the intent-to-treat (ITT) population."
Selective reporting (reporting bias)	Low risk	All outcome of interest were reported.
Other bias	Unclear risk	
9. Kenton et al. 2014	**Risk of Bias**	**Quotations**
Random sequence generation (selection bias)	Low risk	"Women were randomly assigned with the use of a permuted-block randomization schedule, with stratification according to clinical site."
Allocation concealment (selection bias)	Unclear risk	"Not described."
Blinding of participants and personnel (performance bias)	Unclear risk	"Not described."
Blinding of outcome assessment (detection bias)	Unclear risk	"Not described."
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	low risk	All outcome of interest were reported.
Other bias	Unclear risk	
10. Ross et al. 2016	**Risk of Bias**	**Quotations**
Random sequence generation (selection bias)	Unclear risk	"Randomisation was performed using a list generated by the study statistician (using permuted blocks and stratified by the surgeon)."
Allocation concealment (selection bias)	Unclear risk	"Not described."
Blinding of participants and personnel (performance bias)	Low risk	"The surgical team and patients were blinded to the next treatment assignment."
Blinding of outcome assessment (detection bias)	Unclear risk	"Not described."
Incomplete outcome data (attrition bias)	Low risk	"The assessment was carried out on the intent-to-treat (ITT) population."
Selective reporting (reporting bias)	Low risk	All outcome of interest were reported.
Other bias	Unclear risk	

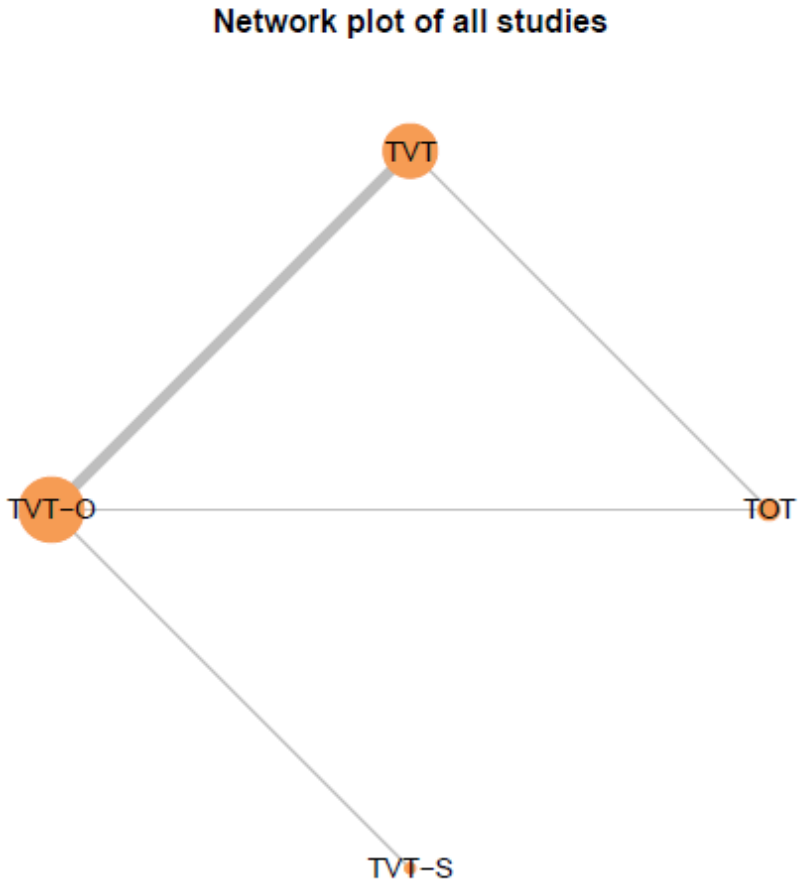
11. Tommaselli et al. 2015	**Risk of Bias**	**Quotations**
Random sequence generation (selection bias)	Low risk	"Patients were randomly allocated by means of a randomization list generated by a computer with blocks of 6 to undergo either TVT-O or TVT-Secure hammock approach."
Allocation concealment (selection bias)	Low risk	"Patients were randomly allocated by means of a randomization list generated by a computer with blocks of 6 to undergo either TVT-O or TVT-Secure hammock approach."
Blinding of participants and personnel (performance bias)	High risk	"Single blinded."
Blinding of outcome assessment (detection bias)	High risk	"Single blinded."
Incomplete outcome data (attrition bias)	Low risk	"The assessment was carried out on the intent-to-treat (ITT) population."
Selective reporting (reporting bias)	Low risk	All outcome of interest were reported.
Other bias	Unclear risk	
12. Valpas et al. 2015	**Risk of Bias**	**Quotations**
Random sequence generation (selection bias)	low risk	"Women were randomized into the groups by using a computer-generated random allocation in a ratio of 1:1 in balanced blocks of 40 for each participating center."
Allocation concealment (selection bias)	Unclear risk	"Not described."
Blinding of participants and personnel (performance bias)	High risk	"No blinding was possible."
Blinding of outcome assessment (detection bias)	High risk	"No blinding was possible."
Incomplete outcome data (attrition bias)	Low risk	"Women with missing data or lost to follow-up were regarded as treatment failures in the ITT analysis."
Selective reporting (reporting bias)	Low risk	All outcome of interest were reported.
Other bias	Unclear risk	
13. Zhang et al. 2016	**Risk of Bias**	**Quotations**
Random sequence generation (selection bias)	Low risk	"The patients were enrolled by study surgeons at the outpatient department and were allocated to the TVT or TVT-O group according to random assignments sealed in an envelope."
Allocation concealment (selection bias)	Low risk	"The patients were enrolled by study surgeons at the outpatient department and were allocated to the TVT or TVT-O group according to random assignments sealed in an envelope."
Blinding of participants and personnel (performance bias)	High risk	"The surgeons and patients were not blinded to the treatment."
Blinding of outcome assessment (detection bias)	Unclear risk	"Not described."
Incomplete outcome data (attrition bias)	Low risk	"The assessment was carried out on the intent-to-treat (ITT) population."
Selective reporting (reporting bias)	Low risk	"All outcome of interest were reported."
Other bias	Unclear risk	
30. Brubaker et al, 2012	**Risk of Bias**	**Quotations**
Random sequence generation (selection bias)	High risk	"Method of randomization hasn't been mentioned."
Allocation concealment (selection bias)	Unclear risk	"Not described."
Blinding of participants and personnel (performance bias)	Unclear risk	"Not described."
Blinding of outcome assessment (detection bias)	Unclear risk	"Not described."
Incomplete outcome data (attrition bias)	Unclear risk	
Selective reporting (reporting bias)	Low risk	All outcome of interest were reported.
Other bias	Unclear risk	
33. Karmakar et al. 2017	**Risk of Bias**	**Quotations**
Random sequence generation (selection bias)	Unclear risk	"Method of randomization hasn't been mentioned."
Allocation concealment (selection bias)	Unclear risk	"Not described."

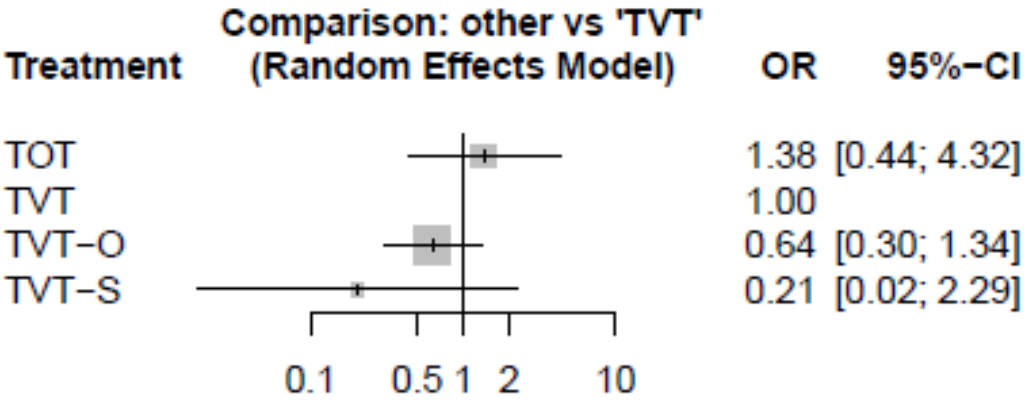
Blinding of participants and personnel (performance bias)	Unclear risk	“Not described.”
Blinding of outcome assessment (detection bias)	Unclear risk	“Not described.”
Incomplete outcome data (attrition bias)	Low risk	"All missing data were confirmed to be missing at random and were handled by multiple imputation and sensitivity analysis."
Selective reporting (reporting bias)	Low risk	All outcome of interest were reported.
Other bias	Unclear risk	
36. Shirvan et al. 2014	**Risk of Bias**	**Quotations**
Random sequence generation (selection bias)	Low risk	"Patients were randomly allocated by a predetermined computer-generated randomization code."
Allocation concealment (selection bias)	Low risk	"Patients were randomly allocated by a predetermined computer-generated randomization code."
Blinding of participants and personnel (performance bias)	Unclear risk	“Not described.”
Blinding of outcome assessment (detection bias)	Unclear risk	“Not described.”
Incomplete outcome data (attrition bias)	Unclear risk	“Not described.”
Selective reporting (reporting bias)	Low risk	All outcome of interest were reported.
Other bias	Unclear risk	
37. Zhu et al. 2007	**Risk of Bias**	**Quotations**
Random sequence generation (selection bias)	Low risk	"Women were allocated to the TVT or the TVT-O group by an SAS randomization schedule (SAS statistical software, Cary, SC, USA).”
Allocation concealment (selection bias)	Low risk	"Women were allocated to the TVT or the TVT-O group by an SAS randomization schedule (SAS statistical software, Cary, SC, USA).”
Blinding of participants and personnel (performance bias)	High risk	"Not blinded."
Blinding of outcome assessment (detection bias)	High risk	"Not blinded."
Incomplete outcome data (attrition bias)	Unclear risk	“Not described.”
Selective reporting (reporting bias)	Low risk	All outcome of interest were reported.
Other bias	Unclear risk	

Appendix (2): Network plots and random effects models






Network plot of all studies
TVT
TVT−O
TOT
TVT−S


Comparison: other vs 'TVT'
Treatment
(Random Effects Model)
OR
95%−CI
TOT
TVT
TVT−O
TVT−S
1.38 [0.44; 4.32]
1.00
0.64 [0.30; 1.34]
0.21 [0.02; 2.29]
0.1
0.5
1
2
10

International Journal of Medical Arts

https://ijma.journals.ekb.eg/
Print ISSN: 2636-4174
Online ISSN: 2682-3780