
Evaluation and management of female urinary incontinence

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Introduction: Urinary incontinence (UI) is a common condition in all demographics of women and consists of stress UI (SUI), Urgency UI (UUI), and mixed UI (MUI). Treatment includes lifestyle modifications, medical treatment, and surgery depending on the type of UI and severity of symptoms. This review is an update on the evaluation and management of UI in women.

Materials and methods: This review article covers the evaluation and management options for UI in women and includes the most recent guidelines from the American Urological Association (AUA) as well as recently published literature on the management of UI.

Results: Any evaluation of UI should include a thorough targeted history and physical, and counseling

for treatment should consider patient goals and desired outcomes. For both SUI and UUI, behavioral therapy and lifestyle modifications are effective first line treatments. Patients with UUI can benefit from medical therapy which includes anticholinergics and β 3-agonist medications, as well as neuromodulation in treatment refractory patients. SUI patients may further benefit from mechanical inserts which prevent leaks, urethral bulking agents, and surgical treatments such as the mid urethral sling and autologous fascial pubovaginal sling.

Conclusions: Treatment of UI in women requires a graded approach that considers patient goals and symptom severity, beginning with lifestyle and behavioral modifications before progressing to more aggressive interventions.

Key Words: urinary incontinence, stress urinary incontinence, urgency urinary incontinence, mid urethral sling, autologous fascial pubovaginal sling

Introduction

Urinary Incontinence (UI) is common across all demographics of women and is characterized by the involuntary loss of urine. UI can be divided into three subtypes: stress urinary incontinence (SUI), urgency urinary Incontinence (UUI), and mixed urinary incontinence (MUI). Risk factors for UI include age, race/ethnicity, body mass index (BMI), parity, smoking, diabetes, and hysterectomy.¹ Data from a national survey of women in the United States shows that 49.6% of women report having some form of UI.² When broken down by subtype, 49.8% of that group have SUI, 34.4% have MUI, and 15.9% have UUI. Longitudinal studies have reported the

incidence of SUI to range from 4%-11% per year, and recent estimates for the United States estimate that the number of women with UI will increase from 18 million in 2010 to 28.4 million in 2050.³⁻⁵

Idiopathic overactive bladder (OAB) is considered a symptom complex as opposed to a single, discrete disease.⁶ The prevalence of OAB in women in the United States has been estimated to be as high as 43%.⁷ It is defined by urinary urgency, where UUI may occur but is not necessarily present, with no signs of urinary tract infection (UTI) or other obvious underlying pathology (i.e. neurogenic bladder). Urgency can also be accompanied by urinary frequency and nocturia. Urinary frequency is defined as urination that occurs more often than the normal interval. Nocturia is the interruption of sleep in order to void one or more times. UUI results when there is involuntary loss of urine associated with urgency.

SUI is the most common manifestation of UI, being found in about 50% of women with symptoms of

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UI.⁵ SUI is defined by the involuntary loss of urine in response to physical exertion or sudden increase in intraabdominal pressure that is generated during such activities as sneezing or coughing.

UI places a considerable medical, psychosocial and economic burden on patients.^{8,9} Because of this, an understanding of screening, evaluation, and treatment of UI is essential in any clinical practice to adequately address the growing demographic of UI patients. This article will review the evaluation and management of female urinary incontinence including the initial evaluation and considerations for treatment.

Initial evaluation of the UI patient

The pathophysiology of UI can broadly be divided into issues of urine storage and emptying.¹⁰ Therefore, it is critical to elicit the exact nature of UI symptoms the patient is experiencing to properly manage them. The initial evaluation of any suspected UI should always begin with a thorough history and physical exam.¹¹ A focused history should include the type of incontinence, duration, severity, bother, previous evaluation/testing, and prior treatments. Having the patient log a voiding diary is an important tool to assess for drinking habits, voiding volumes, frequency of void, daytime and nighttime urinary output, and episodes of incontinence. Diaries should be 3 days in length.¹² The physical portion should include BMI, a pelvic exam, and an objective demonstration of SUI with a full bladder. Helpful exams to elicit SUI are the cough test or Valsalva maneuver. The genitourinary exam should also assess for peri-urethral cysts, urethral hypermobility, and prolapse. Post void residual (PVR) assessment and urinalysis (UA) to evaluate for UTI or microhematuria should also be included in an initial evaluation. Routine urine culture is not necessary unless there are symptoms to suggest UTI or a positive dipstick. In most cases, a thorough history and physical exam are sufficient to diagnose the subtype of incontinence.^{13,14}

Additional evaluation may be considered in the diagnosis of UI in situations where the initial assessment does not provide a diagnosis, or those with abnormal urinalysis, elevated PVR, failure of prior anti-incontinence surgery, or high-grade pelvic organ prolapse (POP). Cystoscopy and/or urodynamic testing (UDS) should not be performed in an otherwise standard patient. It may be appropriate to perform cystoscopy in patients with concern for lower urinary tract abnormalities. Patients with a history of anti-incontinence surgeries, mismatch between subjective and objective measures, significant voiding dysfunction, elevated PVR, MUI with a substantial

urgency component, or neurogenic lower urinary tract dysfunction may undergo UDS.¹⁴ Other forms of UI which should be mentioned for completeness' sake but will not be reviewed in depth in this article include overflow incontinence, continuous incontinence, and insensible incontinence.

UII treatment

Once a proper history and physical have been performed and OAB/UII has been identified, patients should be educated about the normal physiology of voiding. Treatment goals for OAB/UII should be discussed with the patient and aimed at improving patient quality of life. It is important that treatment outcomes should be addressed up front as this has been shown to improve adherence.¹⁵

According to the AUA/SUFU guidelines on treatment for non-neurogenic OAB, first-line treatment is behavioral therapy.^{16,17} Behavioral therapies pose no risk to patients and should be offered to all as they have been shown to improve UI outcomes compared to no treatment.¹⁸ Possible interventions include bladder training, fluid intake modification, pelvic floor muscle training (PFMT), and biofeedback. Patients should be advised to reduce intake of bladder irritants such as caffeine, alcohol, acidic/citrus liquids, and artificial sweeteners. Bladder training is intended to help patients increase the interval between voiding as well as increase bladder capacity. Patients can perform timed voiding and utilize techniques like Kegels to suppress urgency.

Second-line treatments involve pharmacologic therapy of the bladder.^{16,17} There are two drug classes: anticholinergic and β -agonist medications. Anticholinergics (also known as antimuscarinics) block the muscarinic receptors in the bladder which facilitate the voiding phase of urination by contracting the detrusor smooth muscle. β -agonists target the storage phase by enhancing relaxation of detrusor smooth muscle. Currently there are eight approved medications on the market in the United States, Table 1.^{19,20}

A systematic review of anticholinergics has found them to be comparably efficacious and safe, but with varying side-effect profiles.²¹ Common side-effects include dry mouth, dry/itchy eyes, constipation, blurred vision, dyspepsia, and impaired cognitive function. Extended-release formulations can offer a more favorable side-effect profile as there is less risk of dry mouth compared to their immediate-release counterpart.²² Anticholinergic medications are contraindicated in patients who have previously

TABLE 1. List of medications for overactive bladder

Trade name	Generic name	Class
Vesicare	Solifenacin	Anticholinergic
Toviaz	Fesoterodine	Anticholinergic
Sanctura	Tropium	Anticholinergic
Detrol	Tolterodine	Anticholinergic
Enablex	Darifenacin	Anticholinergic
Ditropan	Oxybutynin	Anticholinergic
Myrbetriq	Mirabegron	β 3-agonist
Gemtesa	Vibegron	β 3-agonist

exhibited high sensitivity to this medication class, narrow angle glaucoma, gastroparesis, and cognitive impairment. Of note, recent studies have also shown an association between anticholinergic medications and increased brain atrophy, dysfunction, and clinical decline.²³ Anticholinergic medication adherence is a known issue with up to 89% of patients reporting either unmet treatment expectations and/or tolerability as the reason for discontinuation.^{15,24}

β 3-agonists have shown similar efficacy to anticholinergics but offer a different side-effect profile.²⁵ Mirabegron side-effects include headaches, nasopharyngitis, and elevated systolic blood pressure. It is contraindicated in patients with uncontrolled hypertension. Mirabegron is metabolized by cytochrome P450 CYP3A4, as well as CYP2D6, so there is a risk of drug-drug interactions.²⁶ Approved by the FDA in 2020 following the results of the EMPOWUR trial, Vibegron is the second and newest medication in the β 3-agonist class.²⁷ Unlike mirabegron, it is metabolized independently from CYP3A4, 2D6, and 2C9 and less likely to cause drug-drug interactions. It is also not associated with an increase in systolic blood pressure. An important factor that will also impact the choice of pharmacologic agent is drug cost and insurance coverage.

Third line treatments for OAB include various forms of neuromodulation such as peripheral tibial nerve stimulation (PTNS), sacral neuromodulation (SNS), and chemodenervation via onabotulinumtoxinA.^{16,17} PTNS and SNS are both forms of neuromodulation that have been described in the literature since the 1980s.^{28,29} PTNS involves stimulation of the tibial nerve which is a mixed motor and sensory nerve innervated by L4-S3 roots. Electrical stimulation of the posterior tibial nerve causes retrograde neuromodulation of the bladder and pelvis floor which shares common innervation from the sacral nerve plexus. Stimulation is delivered via a battery powered stimulator connected 34 gauge needle electrode inserted above the medial malleolus.³⁰ Treatment involves 30 minute weekly sessions for 12 weeks. Maintenance therapy is once a month. Absolute contraindications to PTNS include pregnancy and presence of a pacemaker or defibrillator. Relative contraindications include peripheral neuropathy, peripheral edema, and neurogenic bladder. Complications of treatment are minimal but consideration must be given to the time commitment required by the patient.

Sacral neuromodulation (SNS) for OAB has been FDA approved since 1997 and there are currently three devices on the market, Table 2.^{31,32} It involves direct stimulation of the S3 nerve root of the sacral nerve plexus that modulate the reflexes influencing the bladder, urinary sphincter, and pelvic floor.³³ It is a two staged procedure that requires an initial temporary lead placement to check for at least 50% improvement in patient symptoms. After this has been confirmed, the second stage of the procedure involves surgically implanting a permanent pulse generator. During the procedure, proper S3 lead placement is confirmed by observing bellows of the perineum and plantar flexion of the big toe. Complications from the procedure include device infection which would require explantation and loss of efficacy due to lead migration. Contraindications, like for PTNS, include pregnancy and presence of a pacemaker or defibrillator. It should be noted that anti-coagulation

TABLE 2. Sacral neuromodulation devices

Device	Size	MRI compatibility	Battery life
InterStim	14 cm ³	Head 1.5T	4-5 years
InterStim Micro	2.8 cm ³	Full Body 1.5T + 3T	15 years (rechargeable)
Axonics r-SNM	5.5 cm ³	Head 1.5T + 3T Full body 1.5T	15 years (rechargeable)

must be held in the peri-operative setting. Patients should also be advised that the device will require battery replacement for the generator over time.

OnabotulinumtoxinA (BTX-A) was first FDA approved for neurogenic OAB in 2011.³⁴ Following successful Phase 2 and 3 clinical trials, BTX-A was FDA approved in 2013 for idiopathic OAB at a recommended dose of 100 units.³⁵⁻³⁷ Its mechanism of action is inhibiting acetylcholine release from pre-synaptic cholinergic junctions which results in chemodenervation and reduced muscle contractility and possibly reduced afferent input.³⁸ Treatment can be performed in the office with local anesthesia or in the operating room with sedation with either a flexible or rigid cystoscope.³⁹ A UA should be performed prior to procedure to rule out UTI. Patients should also have a baseline PVR and be followed up with a PVR after procedure to check on incomplete bladder emptying. The treatment effects usually last for 6 months before requiring retreatment. Complications of the procedure include UTI, hematuria, urinary retention, and systemic weakness. In the case of urinary retention, patients should be advised about the possibility of requiring clean intermittent catheterization (CIC) if they are unable to void following the procedure.

If the patient has failed the first three lines of therapy, the guidelines allow for augmentation cystoplasty and urinary diversion as a last resort.^{16,17} The goal of treatment is to disrupt coordinated detrusor contractions, increase bladder capacity, and create a low-pressure urinary storage system. Patients undergoing the procedure must also be willing to do CIC. However, with the advent of neuromodulation and BTX-A treatments, augmentation cystoplasty has become less frequently utilized.⁴⁰ Complications include revision, metabolic acidosis (from use of ileum), stone formation, and UTI.

SUI treatment

When starting treatment for SUI, non-surgical options should be considered before more aggressive interventions where it is appropriate. In general, SUI can be managed in a graded approach that includes measures such as lifestyle modifications and vaginal inserts before progressing to urethral bulking agents and then surgical measures such as the synthetic mid urethral sling (MUS) or the autologous fascial pubovaginal sling.

Lifestyle modifications

As with UUI, lifestyle modifications are often an effective first line treatment in the management of

SUI. These include behavioral therapy and pelvic floor muscle therapy (PFMT), and weight loss. PFMT is considered a mainstay of treatment for SUI, in some cases showing up to 70% improvement in symptoms across all age groups.⁴¹ A meta-analysis conducted by Dumoulin et al demonstrated that PFMT can improve symptoms of SUI, reducing the frequency of leakage and the amount of urine voided. Moreover, it is a cost-effective treatment with a low risk for adverse effects, making PFMT an attractive first line therapy for the motivated SUI patient.⁴²

Vaginal devices

Another non-surgical treatment for SUI entails introducing devices into the vaginal canal which exert a mechanical force on the urethra, in turn increasing urethral outlet resistance. This includes continence pessaries, vaginal inserts, and urethral plugs. The few studies which describe these interventions suggest they are an effective means of maintaining urinary continence, though their effectiveness can be reduced by previous UI surgery or anatomic variations among patients such as wide urethra or decreased bladder capacity.^{43,44}

Bulking agents

Bulking agents are a form of injection treatment which combat SUI through improved coaptation of the proximal urethra, thus increasing outlet resistance. These are an effective treatment, though long term data for their effectiveness is scant.¹⁴ The most common site of injection for bulking agents is the submucosa of the proximal urethra through either the periurethral or transurethral approach. The two classes of bulking agents are particulate agents (solid microparticles in a liquid or gel carrier), and non-particulate agents (homogenous gel). The composition of the microparticulate material in such agents includes polyacrylamide, calcium hydroxylapatite, polydimethylsiloxane, and carbon coated zirconium beads.⁴⁵ Bulking agents may represent an appropriate treatment in patients who have restricted surgical options, however, they are associated with a high rate of treatment failure and may therefore require multiple administrations to maintain symptom relief.^{46,47}

Mid-urethral sling (MUS)

MUS is a surgical procedure for SUI with either a retropubic or transobturator approach. The retropubic approach features the insertion of two needles which are passed through the retropubic space from the vagina

to the abdomen or from the abdomen to the vagina (top down and bottom up) and has a success rate between 51%-81%.¹⁴ There is no difference in outcomes between the approaches. The transobturator approach avoids entering Retzius' space and was introduced in response to the complication profile associated with the retropubic approach. In this approach, the sling is inserted into a horizontal plane underneath the middle of the urethra between the two obturator foramina.⁴⁸ The transobturator approach has a success rate between 43%-95% in follow up studies of up to 5 years.¹⁴

In long term analysis of these two approaches, patients treated with the transobturator approach experience less urinary urgency, negative quality of life impact, and sexual dysfunction compared to the retropubic approach. However, the transobturator approach resulted in a lower 5-year success rate compared to the retropubic approach.⁴⁹

While complication rates for MUS placement are low, they must be considered as with any surgery. Some of the more common complications included bladder perforation with a retropubic MUS, reoperation for persistent SUI, urinary retention requiring sling incision, pelvic hematoma, infection, vaginal mesh erosion, and postoperative groin pain. The retropubic approach and the transobturator approach have differing adverse event profiles, with the retropubic approach having a higher rate of bladder perforation and problems with voiding, while the transobturator approach having lower long-term efficacy and increased groin pain.⁴⁸

Autologous fascial pubovaginal sling

An autologous pubovaginal sling procedure utilizes autologous fascia lata or rectus fascial tissue to recreated the periurethral support.¹⁴ This procedure has been shown to be an effective and durable long term treatment option, with a success rate between 85%-92%.⁵⁰⁻⁵² Because of this, AFPS may be an attractive option in patients who had a previous mesh complication or placement failure, prefer to avoid mesh, or are high-risk for poor wound healing.¹⁴ The SISTEr trial compared AFPS to a Burch colposuspension and found that an autologous pubovaginal sling was a more effective treatment overall and had a lower retreatment rate.⁵³ A systematic review by Fusco et al reported that patients undergoing an autologous pubovaginal sling had similar short term cure rates when compared to patients who had MUS, though pubovaginal sling patients were more likely to have postoperative storage lower urinary tract symptoms. Complication profiles were otherwise similar between pubovaginal slings and MUS.⁵⁴

Conclusions

UI is a prevalent condition that affects nearly half the female population in the United States. While not a life-threatening condition, it can significantly reduce patient quality of life. Determining the type of UI and level of bother to the patient are critical. The work up must always include a thorough history and physical, UA, and PVR. Appropriate adjunct tests can be utilized if the diagnosis is still not certain. Advanced therapies should only be used when needed. Education and advocacy remain cornerstones of treatment since it can they establish treatment expectations, improve adherence, and increase patient satisfaction. □

References

1. Danforth KN, Townsend MK, Lifford K, Curhan GC, Resnick NM, Grodstein F. Risk factors for urinary incontinence among middle-aged women. *Am J Obstet Gynecol* 2006;194(2):339-345.
2. Dooley Y, Kenton K, Cao G et al. Urinary incontinence prevalence: results from the national health and nutrition examination survey. *J Urol* 2008;179(2):656-661.
3. Irwin DE, Milsom I, Chancellor MB, Kopp Z, Guan Z. Dynamic progression of overactive bladder and urinary incontinence symptoms: a systematic review. *Eur Urol* 2010;58(4):532-543.
4. Rortveit G, Subak LL, Thom DH et al. Urinary incontinence, fecal incontinence and pelvic organ prolapse in a population-based, racially diverse cohort: prevalence and risk factors. *Female Pelvic Med Reconstr Surg* 2010;16(5):278-283.
5. Reynolds WS, Dmochowski RR, Penson DF. Epidemiology of stress urinary incontinence in women. *Curr Urol Rep* 2011;12(5):370-376.
6. Artibani W. Diagnosis and significance of idiopathic overactive bladder. *Urology* 1997;50(6A Suppl):25-32; discussion 33-35.
7. Coyne KS, Sexton CC, Vats V, Thompson C, Kopp ZS, Milsom I. National community prevalence of overactive bladder in the united states stratified by sex and age. *Urology* 2011;77(5):1081-1087.
8. Hampel C, Artibani W, Espuña Pons M et al. Understanding the burden of stress urinary incontinence in europe: a qualitative review of the literature. *Eur Urol* 2004;46(1):15-27.
9. Margalith I, Gillon G, Gordon D. Urinary incontinence in women under 65: quality of life, stress related to incontinence and patterns of seeking health care. *Qual Life Res* 2004;13(8):1381-1390.
10. Rahn DD, Roshanravan SM. Pathophysiology of urinary incontinence, voiding dysfunction, and overactive bladder. *Obstet Gynecol Clin North Am* 2009;36(3):463-474.
11. Aoki Y, Brown HW, Brubaker L, Cornu JN, Daly JO, Cartwright R. Urinary incontinence in women. *Nat Rev Dis Primers* 2017;3:17042.
12. Nambiar AK, Bosch R, Cruz F et al. EAU guidelines on assessment and nonsurgical management of urinary incontinence. *Eur Urol* 2018;73(4):596-609.
13. Holroyd-Leduc JM, Tannenbaum C, Thorpe KE, Straus SE. What type of urinary incontinence does this woman have? *JAMA* 2008;299(12):1446-1456.
14. Kobashi KC, Albo ME, Dmochowski RR et al. Surgical treatment of female stress urinary incontinence: AUA/SUFU guideline. *J Urol* 2017;198(4):875-883.

15. Schabert VF, Bavendam T, Goldberg EL, Trocio JN, Brubaker L. Challenges for managing overactive bladder and guidance for patient support. *Am J Manag Care* 2009;15(4 Suppl):S118-S122.
16. Gormley EA, Lightner DJ, Burgio KL et al. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline. *J Urol* 2012;188(6 Suppl):2455-2463.
17. Lightner DJ, Gomelsky A, Souter L, Vasavada SP. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline amendment 2019. *J Urol* 2019;202(3):558-563.
18. Balk E, Adam GP, Kimmel H et al. Nonsurgical treatments for urinary incontinence in women: a systematic review update. 2018. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK534625/>
19. Leron E, Weintraub AY, Mastrolia SA, Schwarzman P. Overactive bladder syndrome: evaluation and management. *Curr Urol* 2018;11(3):117-125.
20. Kayki-Mutlu G, Michel MC. A year in pharmacology: new drugs approved by the US food and drug administration in 2020. *Naunyn Schmiedeberg Arch Pharmacol* 2021;394(5):839-852.
21. Chapple CR, Khullar V, Gabriel Z, Muston D, Bitoun CE, Weinstein D. The effects of antimuscarinic treatments in overactive bladder: an update of a systematic review and meta-analysis. *Eur Urol* 2008;54(3):543-562.
22. Madhuvrata P, Cody JD, Ellis G, Herbison GP, Hay-Smith EJ. Which anticholinergic drug for overactive bladder symptoms in adults. *Cochrane Database Syst Rev* 2012;1:CD005429.
23. Risacher SL, McDonald BC, Tallman EF et al. Association between anticholinergic medication use and cognition, brain metabolism, and brain atrophy in cognitively normal older adults. *JAMA Neurol* 2016;73(6):721-732.
24. Benner JS, Nichol MB, Rovner ES et al. Patient-reported reasons for discontinuing overactive bladder medication. *BJU Int* 2010;105(9):1276-1282.
25. Huang CK, Lin CC, Lin AT. Effectiveness of antimuscarinics and a beta-3 adrenoceptor agonist in patients with overactive bladder in a real-world setting. *Sci Rep* 2020;10(1):11355.
26. Chapple CR, Cardozo L, Nitti VW, Siddiqui E, Michel MC. Mirabegron in overactive bladder: a review of efficacy, safety, and tolerability. *Neurourol Urodyn* 2014;33(1):17-30.
27. Staskin D, Frankel J, Varano S, Shortino D, Jankowich R, Mudd PN Jr. International phase III, randomized, double-blind, placebo and active controlled study to evaluate the safety and efficacy of vibegron in patients with symptoms of overactive bladder: EMPOWUR. *J Urol* 2020;204(2):316-324.
28. Staskin DR, Peters KM, MacDiarmid S, Shore N, de Groat WC. Percutaneous tibial nerve stimulation: A clinically and cost effective addition to the overactive bladder algorithm of care. *Curr Urol Rep* 2012;13(5):327-334.
29. Gajewski JB, Hassouna MM, Corcos J, Gray GJ, Tu LM, Dwyer N. The history of sacral neuromodulation in Canada. *Can Urol Assoc J* 2020;14(4):87-90.
30. Gaziev G, Topazio L, Iacovelli V et al. Percutaneous tibial nerve stimulation (PTNS) efficacy in the treatment of lower urinary tract dysfunctions: a systematic review. *BMC Urol* 2013;13:61.
31. Medtronic, Inc.; premarket approval of the interstim sacral nerve stimulation (SNS) system—FDA. notice. *Fed Regist* 1998;63(19):4457.
32. De Wachter S, Knowles CH, Elterman DS et al. New technologies and applications in sacral neuromodulation: an update. *Adv Ther* 2020;37(2):637-643.
33. Das AK, White MD, Longhurst PA. Sacral nerve stimulation for the management of voiding dysfunction. *Rev Urol* 2000;2(1):43-60.
34. Linsenmeyer TA. Use of botulinum toxin in individuals with neurogenic detrusor overactivity: state of the art review. *J Spinal Cord Med* 2013;36(5):402-419.
35. Dmochowski R, Chapple C, Nitti VW et al. Efficacy and safety of onabotulinumtoxinA for idiopathic overactive bladder: a double-blind, placebo controlled, randomized, dose ranging trial. *J Urol* 2010;184(6):2416-2422.
36. Nitti VW, Dmochowski R, Herschorn S et al. OnabotulinumtoxinA for the treatment of patients with overactive bladder and urinary incontinence: Results of a phase 3, randomized, placebo controlled trial. *J Urol* 2013;189(6):2186-2193.
37. Chapple C, Sievert KD, MacDiarmid S et al. OnabotulinumtoxinA 100 U significantly improves all idiopathic overactive bladder symptoms and quality of life in patients with overactive bladder and urinary incontinence: a randomised, double-blind, placebo-controlled trial. *Eur Urol* 2013;64(2):249-256.
38. Cruz F. Targets for botulinum toxin in the lower urinary tract. *Neurourol Urodyn* 2014;33(1):31-38.
39. Orasanu B, Mahajan ST. The use of botulinum toxin for the treatment of overactive bladder syndrome. *Indian J Urol* 2013;29(1):2-11.
40. Reyblat P, Ginsberg DA. Augmentation enterocystoplasty in overactive bladder: is there still a role? *Curr Urol Rep* 2010;11(6):432-439.
41. Price N, Dawood R, Jackson SR. Pelvic floor exercise for urinary incontinence: a systematic literature review. *Maturitas* 2010;67(4):309-315.
42. Dumoulin C, Cacciari LP, Hay-Smith EJC. Pelvic floor muscle training versus no treatment, or inactive control treatments, for urinary incontinence in women. *Cochrane Database Syst Rev* 2018;10(10):CD005654.
43. Brook G, Tessema AB. Obstetric fistula: the use of urethral plugs for the management of persistent urinary incontinence following successful repair. *Int Urogynecol J* 2013;24(3):479-484.
44. Farrell SA, Singh B, Aldakhl L. Continence pessaries in the management of urinary incontinence in women. *J Obstet Gynaecol Can* 2004;26(2):113-117.
45. Chapple C, Dmochowski R. Particulate versus non-particulate bulking agents in the treatment of stress urinary incontinence. *Res Rep Urol* 2019;11:299-310.
46. Gaddi A, Guaderrama N, Bassiouni N, Bechuk J, Whitcomb EL. Repeat midurethral sling compared with urethral bulking for recurrent stress urinary incontinence. *Obstet Gynecol* 2014;123(6):1207-1212.
47. Leone Roberti Maggiore U, Bogani G, Meschia M et al. Urethral bulking agents versus other surgical procedures for the treatment of female stress urinary incontinence: a systematic review and meta-analysis. *Eur J Obstet Gynecol Reprod Biol* 2015;189:48-54.
48. Ford AA, Rogerson L, Cody JD, Aluko P, Ogah JA. Mid-urethral sling operations for stress urinary incontinence in women. *Cochrane Database Syst Rev* 2017;7(7):CD006375.
49. Kenton K, Stoddard AM, Zyczynski H et al. 5-year longitudinal follow up after retropubic and transobturator mid urethral slings. *J Urol* 2015;193(1):203-210.
50. Athanasopoulos A, Gyftopoulos K, McGuire EJ. Efficacy and preoperative prognostic factors of autologous fascia rectus sling for treatment of female stress urinary incontinence. *Urology* 2011;78(5):1034-1038.
51. Chaikin DC, Rosenthal J, Blaivas JG. Pubovaginal fascial sling for all types of stress urinary incontinence: long-term analysis. *J Urol* 1998;160(4):1312-1316.
52. Morgan TO Jr, Westney OL, McGuire EJ. Pubovaginal sling: 4-year outcome analysis and quality of life assessment. *J Urol* 2000;163(6):1845-1848.
53. Albo ME, Richter HE, Brubaker L et al. Burch colposuspension versus fascial sling to reduce urinary stress incontinence. *N Engl J Med* 2007;356(21):2143-2155.
54. Fusco F, Abdel-Fattah M, Chapple CR et al. Updated systematic review and meta-analysis of the comparative data on colposuspensions, pubovaginal slings, and midurethral tapes in the surgical treatment of female stress urinary incontinence. *Eur Urol* 2017;72(4):567-591.