Stress incontinence

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ABBREVIATIONS

1. SUI - Stress urinary incontinence
2. UUI - Urge urinary incontinence
3. MUI - Mixed urinary incontinence
4. OSUI - Occult stress urinary incontinence
5. PGII - The Patient Global Impression of Improvement
6. PGIS - Patient Global Impression of Severity
7. UTI - Urinary tract infection
8. PPV - Positive predicted value
9. PVR - Postvoid residual
10. AHCPR - Agency for Health Care Policy and Research
11. EMG - Electromyography
12. US - Ultrasonography
13. PTR - Pressure transmission ratio
14. CNS - Central nervous system
15. BMI - Body mass index
16. MMPI - Matrix metalloproteinase inhibitor
17. FDA - Food and Drug Administration (of the united states)
18. POP - Pelvic organ prolapse
19. SNRI - Serotonin–norepinephrine reuptake inhibitor
20. PVS - Pubovaginal sling
21. MMK - Marshall Marchetti Krantz
22. MUS - Mid-urethral sling
23. TVT - Tension free vaginal tape
24. TVT-O - Tension free obturator tape
25. MPP - Modified Pereyra Procedure

CONTENTS

1. ABSTRACT

Title: Stress incontinence

Author: Or Azoolay

Stress urinary incontinence (SUI) is an involuntary loss of urine, that occurs in response to elevation of the intra-abdominal pressure. Patients usually complain of urine leakage when they cough, laugh, or sneeze. When considering stress incontinence, and urinary incontinence in general, it is important to understand that it is considered a social, hygienic and medical problem, that can cause depression, seclusion and isolation and consequently a decrease in quality of life.

In the past, the clinical evidence-based knowledge on urinary incontinence was limited due to many reasons, such as non-advanced diagnostic criteria and investigation methods, conservative society that tends to hide and ignore gynecological pathologies, and many more.

Nowadays, thanks to studies and clinical trials, more and more medical useable data is collected. Different methods for assessment, that simplify the evaluation process in order to achieve quick and inexpensive diagnosis, are become more accessible to the patients. In addition, the treatment becomes more specific, in terms of addressing each of the incontinence types individually, and therefore provides the patient a proper therapeutic management.

Even though there is a plenty of therapeutic solutions that can be applied in the management of urinary incontinence, many women patients still do not receive a proper diagnosis and treatment, despite the fact that urine leakage is a treatable problem, that can be etiologically treated (unlike pads or frequent urination). Unlike other medical conditions, urinary tract pathologies, and gynecological pathologies in general, are still considered as shameful and held in secret by many patients. As medical professionals, we need to know how to approach these patients sensitively, as well as to address this problem and provide the best solution individually to each patient. By proper medical education of both the patients and the medical staff, it is possible to achieve better understanding of the condition, and therefore to minimize the stigma; which is beneficial for patient-doctor communication, as well as for the management process. When dealing with urinary incontinence, it is important to deal with the stigma as well, using proper evidence-based education. That way, we can ensure quicker and cheaper diagnosis process and treatment, as well as better quality of life for the patients.

Key words: stress urinary incontinence, intra-abdominal pressure, diagnosis, treatment, stigma, urine leakage, gynecological pathologies

2. SAŽETAK

Titula: Stresna Inkontinencija

Autor: Or Azoolay

Stresna urinarna inkontinencija (SUI) je nenamjeran gubitak urina, koji nastaje kao odgovor na povišenje intra-trbušnog tlaka. Pacijenti se obično žale na curenje urina kad kašlju, smiju se ili kihaju. Kada se razmatra stresna inkontinencija i urinarna inkontinencija općenito, važno je razumjeti da se ona smatra socijalnim, higijenskim i medicinskim problemom koji može uzrokovati depresiju, osamljenost i izolaciju te posljedično pad kvalitete života. U prošlosti kliničko znanje o urinarnoj inkontinenciji je bilo ograničeno iz mnogih razloga, kao što su ne napredni dijagnostički kriteriji i metode ispitivanja, konzervativno društvo koje sakriva i zanemara ginekološke patologije i mnoge druge. Danas, unaprijedena klinička ispitivanja prikupljaju se sve više i više medicinski korisnih podataka. Različite metode procjene koje pojednostavljuju postupak evaluacije kako bi se postigla brza i jeftina dijagnoza. Uz to, tretman postaje specifičniji u pogledu obrade svake vrste inkontinencije pojedinačno, te pacijentu se pruži pravilno terapijsko upravljanje. Iako postoji mnoštvo terapijskih rješenja koja se mogu primijeniti u liječenju urinarne inkontinencije, mnoge pacijentice još uvijek ne dobivaju odgovarajuću dijagnozu i liječenje. SUI je curenje urina koji se može etiološki liječiti (za razliku od jastučića ili učestalog mokrenja). Za razliku od ostalih medicinskih stanja, patologije mokraćnog sustava i ginekološke patologije općenito još uvijek smatraju sramotnima i mnogi pacijenti drže te informacije u tajnosti. Kao ljecnici, moramo znati pristupiti ovim osjetljivim pacijentima i pružiti najbolje rješenje pojedinačno svakom pacijentu. Pravilnim medicinskim obrazovanjem pacijenata i medicinskog osoblja je potrebna za postići bolje razumijevanje stanja, a samim tim stigmu svesti na minimum, što je korisno za komunikaciju izmedu pacijenta i liječnika. Kada se bavite urinarnom inkontinencijom, važno je rješavati i simptome i stigmu, koristeći odgovarajuću edukaciju utemeljenu na dokazima. Na taj način možemo osigurati brži i jeftiniji postupak dijagnoze i liječenja, kao i bolju kvalitetu života pacijenata.

Ključne riječi: stresna urinarna inkontinencija, intra-abdominalni tlak, dijagnoza, liječenje, stigma, curenje urina, ginekološke patologije

3. INTRODUCTION

Urinary incontinence is defined as involuntary loss of urine. The condition affects many women and men all over the world. Even though this condition is common and influences the lives of so many people, many patients do not receive any treatment. The reasons for not getting a proper treatment vary greatly, and include inappropriate diagnostic management, cultural differences, and many others. As part of the therapeutic process, and the management of urinary incontinence, it is important to evaluate the specific incontinence type that the patient suffers from, in order to provide the patient with the most effective and beneficial treatment.

There are several types of urinary incontinence: stress, urge, mixed and overflow.

Stress urinary incontinence (SUI) is the defined as involuntary, sudden loss of urine secondary to increased intra-abdominal pressure, in the absence of a detrusor contraction. Physical activities that precipitating SUI include laughing, sneezing, straining, coughing or exercising. The patient may describe the loss of urine as leaking, dripping or flooding; along with complaints of frequency, urgency and dysuria. The loss of urine due to SUI is bothersome and affects negatively the patient's quality of life [1,2,3].

The prevalence of urinary incontinence increases gradually during young-adult life, has a peak around middle age, and then steadily increases in the elderly [4].

When comparing SUI to urge or mixed urinary incontinence, we can see that the main characteristics associated with stress incontinence are: brief, small amount of urinary loss, corresponds to stress and events such as coughing or laughing (which increase the intra-abdominal pressure); as well as upright and sitting position, but rarely when the patient is supine. Unlike stress incontinence, urge and overflow incontinence are not associated with a specific position, nor exacerbated by external or internal stimuli or specific event [4].

Although urinary incontinence is significantly more frequent in women, the condition occurs in both sexes. There is some overlap in pathophysiology between sexes, but the condition in men is often a consequence of prostatic pathologies (e.g. benign prostatic hyperplasia, prostatic cancer); or from damage to the urinary tract and continence mechanisms during prostate cancer therapy (e.g. surgery, radiotherapy) [5]. This is in contrast to the etiology of stress incontinence in women, which is associated with abnormal transmission of pressure in the pelvic region, as well as loss of urinary sphincter integrity. The etiology of SUI in women will be discussed further under "etiology" section in this thesis.

4. EPIDEMIOLOGY

Even though urinary incontinence is well known for decades, it is still hard to conclude a proper prevalence rate that is correct and conclusive to all countries and ethnical groups.
The range of reported prevalence for urinary incontinence of all subtypes is broad (5-72%), with median prevalence of 27.6% for female urinary incontinence [6,7].
This variation among studies is observed between countries, as well as within countries.
This is probably a result of the differences in cultures and the perception of urinary incontinence and willingness to report, as well as methodological differences (e.g. differences in phrasing and definitions used among the questionnaires, administration methods, etc.).

The prevalence of female urinary incontinence is increasing with age, and we can see from different studies that the association between urinary incontinence and age is well defined [6, 8]. Among all available studies, the age-specific incidence is less than 2 per 1000 women which are less than 40 years of age, but the incidence increases with age [8]. For example, in the study "*Urinary incontinence incidence: quantitative meta-analysis of factors that explain variation*" [8], it was shown that 41% of women older than 40 years of age, will have urinary incontinence, and up to 77% of elderly women in nursing homes will have urinary incontinence.
In another longitudinal study in Norway [9] which was held in 1995-1997, and then again in 2006-2008, they have found an increase of 16% in prevalence of urinary incontinence between the two-time period.

According to studies, it is estimated that the prevalence of urinary incontinence, along with other pelvic abnormalities, organ prolapse and fecal incontinence, will increase in the future.
The estimation is that in the U.S., the number of women who suffer from urinary incontinence will increase from 18.3 million in 2010, up to 28.4 million in 2050 [10].

According to meta-analysis that includes 48 studies, the prevalence of urinary incontinence is 16% in women under the age of 30 and 29% among women between the ages 30 to 60 years.
When comparing the prevalence of stress incontinence to other types of incontinence (urge and mixed), we can observe a different prevalence rates among the different types.
The same meta-analysis shows a prevalence of 78% for stress urinary incontinence, 51% for urge urinary incontinence, and 29-36% for mixed urinary incontinence [11].

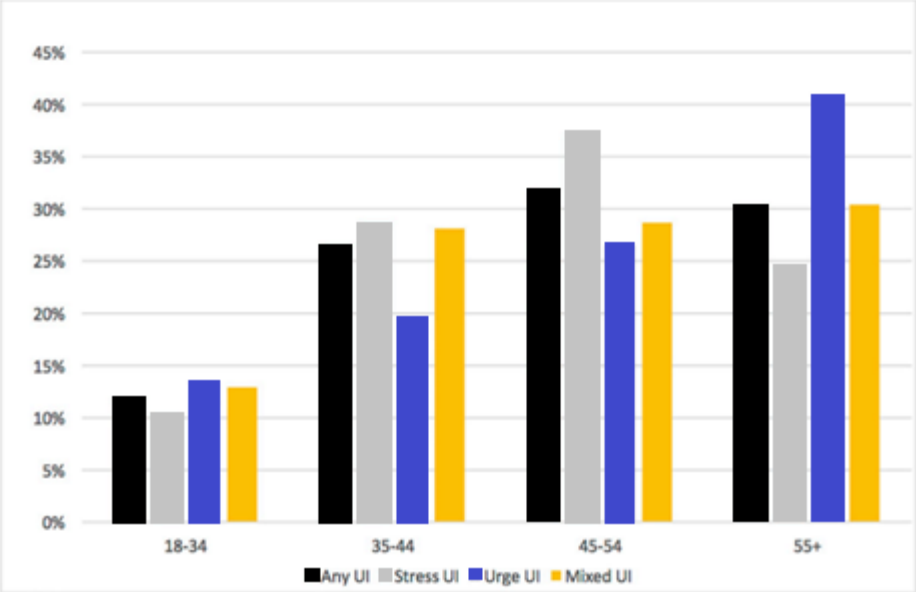

Figure 1. The prevalence of urinary incontinence types according to age groups.
Modified from the study "*Urinary incontinence and its relation to delivery circumstances: A population-based study from rural Kilimanjaro, Tanzania*" [12].

In the figure above [12] that is based on a study from rural Kilimanjaro (Tanzania), we can observe that the prevalence of stress urinary incontinence (SUI) peaks between the 4th and the 5th decades of life (ages 45-55), and later on decreases (above the age of 55). The prevalence of mixed (MUI) and urge urinary incontinence (UUI) continuously rises throughout life.
Also, it is shown that urge urinary incontinence is predominant after the age of 55, while stress urinary incontinence is predominant at the ages 30 to 50.

Stress urinary incontinence is still considered as a stigma in most populations.
The stigma is not only associated with urinary incontinence, but also noticed with other urinary tract pathologies that cause frequency and urgency [13].
This fact, can influence the results and creates a respondent bias in observational studies [14].
Therefore, most of the reliable information comes from general health, system-based questionnaires that also include questions that related to other body systems; and not from surveys specific for urinary incontinence or urinary system pathologies [15].
It is important to mention, that such studies exist in the U.S. and developed European and Asian countries, but less readily available for developing countries.

Also, data from different studies regarding the association of urinary incontinence and ethnicity was different; some studies have shown a higher prevalence of urinary incontinence in white women (Caucasian), while other studies have shown similar prevalence among women with different ethnicities [14,16].

In several studies in the U.S., it was shown that stress urinary incontinence is more common in white women, compared to African American or Asian-American women [14, 17].

This result, can also be related to the fact that non-white women (predominantly from Hispanic ethnicity) show the least willingness to share information concerning their urinary tract symptoms, and tend to keep the SUI symptoms in secret [13].

According to the "*Establishing the Prevalence of Incontinence (EPI)*" study, only 17% of the women of black ethnicity reported about urinary incontinence, in comparison to 34% of women of white ethnicity that reported symptoms. In the same study, it was also mentioned that there was no difference in the risk factors (15 risk factors) between the two racial groups [18].

It is also important to mention, that even though stress urinary incontinence is a common condition among women all over the world, a study on this topic showed that only 60% of women with incontinence sought treatment [19], a phenomenon that can be related to the embarrassment that those patients feel regarding their condition, or the stigma.

5. ETIOLOGY

The pathophysiological explanation behind stress incontinence is still considered to be theoretical [20]. In the past, many theories were suggested in order to establish a proper diagnosis and treatment methods for stress urinary incontinence, and incontinence in general.

Nowadays, thanks to newer studies and methods of investigation, several theories have suggested different explanations for the problem, that are based on several aspects of the anatomy and physiology behind normal continence:

5.1. Urethral hypermobility

Urethral hypermobility results from inability of the urethra and bladder neck to completely close against the anterior vaginal wall [21]. Under increase in the intra-abdominal pressure, a urethral closure failure will enhance urethral mobility and urine leakage. There are several pathophysiological etiologies behind urethral hypermobility, such as insufficient support of the urethra and bladder neck by the pelvic floor muscles, as well as lack of functional suppurative vaginal connective tissue [21]. The loss of urethral support can be associated with many factors, including chronic high pressure (chronic cough, obesity or heavy lifting), trauma, and childbirth (especially vaginal delivery). More detailed explanation about the different risk factors that are associated with the pathophysiology behind SUI, can be found under the risk factors section later in this thesis.

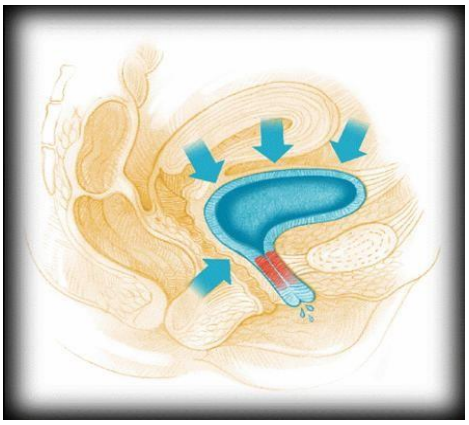

Figure 2. An illustration of urethral hypermobility.

5.2. Pressure transmission and anatomical support

Under normal physiological settings, an increase in the intraabdominal pressure will be transmitted equally to the bladder and urethra. Equal pressure transmission will reduce the pressure burden from specific anatomical parts, and prevent the urine leakage [20]. In addition, the pelvic muscles (levator ani muscle) and the vaginal connective tissue function to support the lower urinary tract against increased intra-abdominal pressure. In stress urinary incontinence, a weakening of the levator ani muscle or lack of suppurative connective tissue, will result in urine leakage [20].

In order to identify the specific mechanism of SUI, studies were focused on understanding the pressure transmission ratio, and its effect on the different anatomical parts of the urinary system. According to the pressure transmission ratio equation, the pressure transmission ratio (PTR) is the ratio of the change in urethral pressure (Pura) to the change in vesical pressure (Pves) associated with a cough, expressed in percentage [22]. From that information we can conclude that a reduction in the PTR (below 100%) is associated with reduced pressure in the urethral sphincter during increase in intra-abdominal pressure, an effect that cause urinary leakage.

According to Bump and colleagues [23], who have investigated the pressure transmission mechanism, the pressure transmission ratios of less than 90% in the level of the proximal aspect of the urethra, had a sensitivity of 97%, and positive predicted value of 98% for urodynamic stress incontinence. The same study also identifies that most (if not all) of the women who experience SUI symptoms, had proximal urethral PTR of less than 90%, with result specificity value of 56%.

That result, supports the fact that decreased level of PTR is highly related to stress urinary incontinence symptoms [22, 23], hence lower PTR equals to higher risk for SUI.

5.3. Urethral integrity and urethral sphincter pressure

Under normal physiological conditions, the urethra is supported by the pubourethral ligaments, the vagina, tendinous arch of pelvic fascia, and the levator ani muscle [20].

Those structures, help to maintain a proper urethral support, hence proper urethral closing pressure. Under pathological conditions, reduced urethral support, along with increased abdominal pressure will result in urine leakage [20].

As part of a research that has been conducted in order to understand the mechanism behind SUI, and the connection between urethral pressure decline and SUI symptoms, the concept of “urethral sphincter

deficiency" was proposed by the "*Agency for Health Care Policy and Research*". As part of the study, several "intrinsic urethral sphincter deficiency" risk factors were suggested and identified [24].

The risk factors are separated into three main categories [22]:

- Congenital: including CNS dysfunctions or lesions, smooth muscle disorders, and striated muscle disorders.
- Acquired: including childbirth, surgical therapy, radiation therapy, CNS lesions, peripheral neuropathies and chronic catheter drainage.
- Other: including aging and reduced estrogen levels.

It is also important to mention, that the two risk factors that have been supported the most by data, are surgical procedures of the pelvis, and older age [25].

Nowadays, newer investigations and studies search for the relation between urethral sphincter dysfunction and SUI symptoms. By using a probe, it is possible to conduct a continues measurements for studies, of the urethral closing pressure, and the cross-section of different anatomical parts of the urethra (proximal, mid, distal) [26].

6. RISK FACTORS

In order to establish a proper algorithm for diagnosis and treatment methods and improving the quality of life for patients, intensive research on the pathophysiology of SUI had been conducted [3]. As part of those studies, the researchers have been trying to identify the risk factors that contribute to the development and escalation of SUI, and other pelvic floor pathologies, such as other urinary incontinence types, pelvic organ prolapse and fecal incontinence as swell [3]. Over the years, many risk factors were suggested in order to support the etiological theories behind SUI.

One of the leading studies that analyze the risk factors associated with pelvic floor dysfunction, is a study that has been conducted by Bump and Norton [27]. As part of the study, Bum and Norton divided the pelvic floor dysfunction risk factors into several categories, in order to understand their contribution to the symptoms development.

This division of risk factors is called "*The model for the development of pelvic floor dysfunction in women*", and includes five categories [27] (some risk factors can be under more than one category):

- Predispose factors: including gender, racial, neurologic, collagen, muscular, cultural and environmental.
- Incite factors: including childbirth, nerve damage, muscular damage, radiation, tissue disruption and radical surgery.
- Promote factors: including constipation, occupation, recreation, obesity, surgery, lung disease, smoking, menstrual cycle, infections, medications and menopause.
- Intervene factors: including behavioral, pharmacologic, devices and surgical.
- Decompensate factors: including aging, dementia, debility, disease, environment, medications.

Even though the model is well organized and summarizes the risk factors that contribute to SUI development in a meaningful way, the model is based on expert opinion, and its support by epidemiological and clinical data is limited [27]. It is also important to mention that none of the factors in this model have been studied in a longitudinal fashion in a representative study [27]. Some of the risk factors in this model are still not fully understood, or without a proper proof for actual relation to SUI; while some are reasonably confident, including aging, obesity, smoking, pregnancy and vaginal delivery [3].

6.1. Age

It is well supported by clinical evidence, that age is a risk factor for pelvic floor dysfunction in general, and for SUI as well [28]. Many theories were suggested to explain this phenomenon, including low estrogen level post menopause, and anatomical changes in the pelvic floor associated with aging [29].

According to the "*Norwegian Epidemiology of Incontinence in the County of Nord-Trøndelag (EPINCONT) group*", there is a clear relation between increase in prevalence of SUI and advancing age [28,3]. As part of their research, they conducted a community-based cohort study, in which only women younger than 65 were participated, that checked the relation between urinary incontinence and age, vaginal delivery, and caesarian sections. According to their results, along the risk associated with the form of delivery (vaginal delivery vs caesarian section), there was also a relationship between SUI symptoms and age groups [28].

As part of the discussion section in their study, the researchers compared the percentage of women who suffered from urinary incontinence symptoms, according to their age groups (started from the age of 20, until the age of 64).

From their results, we can learn that the percentage of women with any urinary incontinence symptoms was lower for younger ages. For example, 10.2% for age group 20-24, 14.3% for age group 25-29, and 18% for age group 30-34. When considering older age groups, the researchers noticed increase in the percentage of women with symptoms, with reporting number of 23.8% for age group 40-44, 28.4% for age group 45-49, and 29.3% for age group 50-54. From those results, we can see a clear relation between specific age groups (45-55 years of age) and urinary incontinence symptoms [28]. It is also important to mention that there is a decline in the prevalence of the symptoms after the age of 55 (22.7% for ages 55-59, and 16.1% for ages 60-64), a result that was also supported by other studies [12,28].

6.2. Obesity

High BMI value is associated with urinary incontinence symptoms as well. There are several theories that explain the pathophysiological mechanism of obesity in urinary incontinence [3].

One of the studies that investigate the relationship between obesity and urinary incontinence is "*Norwegian EPINCONT Study".* The study tries to establish a correlation between urinary incontinence and high BMI, cigarette smoking, alcohol drinking and physical activity. According to the results, there is a high correlation between urinary incontinence symptoms and high body max index. The study also has found a link between urinary incontinence, heavy smoking and tea drinking [30].

Other studies also suggested pathophysiological explanations for obesity as a risk factor. Some suggested that there is an increase in intra-abdominal pressure due to obesity, which increases the risk of urinary leakage [31], and others suggested β3-adrenergic receptor mutation that simultaneously affects both insulin sensitivity and β3-mediated detrusor muscle relaxation [32].

6.3. Childbirth

The correlation between pregnancy and childbirth to SUI is clinically well defined [29]. This correlation can be explained by damage to the pudendal nerve during the labor, muscular damage and direct damage to the surrounding tissue [27]. As part of some studies, it was well defined that different modes of delivery will affect differently the risk for SUI.

According to the study "*Urinary incontinence after vaginal delivery or cesarean section*" [28], who studied the correlation between SUI symptoms and different modes of delivery (vaginal delivery and caesarian section), the correlation does exist. When comparing the percentage of women suffer from SUI symptoms from all ages, the results are 4.7% for no deliveries, 7% for caesarian section, and 14.7% for vaginal delivery. When comparing the results according to specific age groups, for the ages 40-49 (the age group with the highest percentage according to the results of this study), we can see a percentage of 9.4% for no deliveries, 9% for caesarian sections, and 17.2% for vaginal. From those results, it is possible to conclude that caesarian section works as a protective factor against SUI symptoms development.

Some researchers suggested that the protective effect is related to less damage to the pudendal nerve and the levator ani muscle during caesarian section in comparison to vaginal delivery [29].

6.4. Cigarette smoking

According to several studies, there is a correlation between cigarette smoking and SUI symptoms. "*The Norwegian EPINCONT Study*" [30] has shown that both previous and present cigarette smoking is associated with SUI, but only for women who smoke more than 20 cigarettes per day. It is also important to mention that according to the study, it was found that the correlation was stronger between smoking to mild to moderate SUI symptoms, whereas severe incontinence was weakly associated with smoking.

Another study [33] that supports the EPINCONT's study results, also claims that there is a strong statistical relationship between both previous and present cigarette smokers, and urinary incontinence. It was also noted that smoking increases the risk for both stress incontinence and urge incontinence.

6.5. Genetics

Both SUI symptoms, and genito-vaginal prolapse, are influenced by genetics [34]. According to a study that investigated this relationship, the relative risk to have SUI symptoms or prolapse, was five times higher for a siblings of SUI patients [34]. It was also noted, that the inheritance pattern was of dominant type.

Another study that investigated the relationship between genetics and bladder neck mobility, has shown a significant correlation between the patient genome and the phenotype of the bladder neck, and especially the bladder neck mobility [35].

From these studies, we can see that a certain genetic information can also increase the risk of SUI and prolapse, a fact that becomes more and more supported by different studies and researches.

6.6. Ethnicity

As was shown before in the epidemiology section of this thesis, ethnicity is also a risk factors for SUI. One of the studies that investigated this relationship is "*Race as a predictor of urinary incontinence and pelvic organ prolapse*" [36]. 183 African Americans and 132 Caucasians have participated, and asked for urinary incontinence symptoms, pelvic organ prolapse or both.

According to their results, the risk factors of urinary incontinence differ significantly among African-American and Caucasian women. Racial differences in risk factors and prevalence of incontinence subtypes may be of great importance for the diagnosis and prevention of urinary incontinence [36].

Another research that studies this risk factor, compared urinary incontinence among white (causation), African-American, Asian and Hispanic women [37]. As part of the study, a urodynamic data has been collected from the patients in the urogynecology clinic, during a period of 10 years. The researchers collected data on 195 women of Hispanic ethnicity, 95 women of white (Caucasian) ethnicity, 66 women of Asian ethnicity, and 59 women of African-American ethnicity. The data that were collected was complete history of the patients, physical examination, and urodynamic testing.

According to the results of the study, the women from African-American ethnicity had the highest urethral closing pressure, in comparison to women from other races. According to these results, the study concludes that women of African-American ethnicity are less likely to have SUI symptoms. The study also notes that even though African-American women are less likely to have SUI, they are at higher risk to have detrusor muscle instability in comparison to women from the other racial groups [37].

6.7. Hysterectomy

The link between urinary incontinence symptoms and hysterectomy was well studied. Different researches try to find the relation between the two, in order to develop a better understanding that can be practically used. Several pathophysiological mechanisms were suggested, including disruption of the endopelvic fascia, uterosacral-cardinal ligament support and local nerve supply during hysterectomy, which impairs the pelvic floor [29]. Nowadays, many studies try to address the mechanism of this risk factor in a practical clinical manner, and test if there are any differences between different approaches of hysterectomy procedure.

One of the studies that was concerned with this issue is a study from Denmark [38]. The study tried to find if there are any differences between total hysterectomy to sub-total hysterectomy outcomes, regarding urinary incontinence symptoms. As part of their research, the researchers collected data by data collection procedures and questioners, during a time period of one year.

According to the results of that study, a significantly smaller proportion of women had urinary incontinence one year after total abdominal hysterectomy (9%) compared with subtotal abdominal hysterectomy (18%) [38]. Form these results, we can learn that not only the hysterectomy itself is a risk factor for developing SUI symptoms, but the hysterectomy approach as well.

6.8. Collagen abnormalities

In order to achieve proper scientific data on the topic, that will be used clinically later on, studies have been searching for the correlation between collagen matrix abnormalities, SUI and pelvic organ prolapse [29].

Several factors were suggested as the reason for collagen abnormalities, including: elevated plasma and tissue collagenases and elastases, elevated MMPI, abnormal collagen synthesis and abnormal high collagen degradation [29].

A study concerning collagen abnormalities, has collected data on women with Ehlers-Danlos syndrome, in order to test the relationship between the disease and SUI symptoms [39]. As part on the study, 41 adult women who were diagnosed with Ehlers-Danlos syndrome, came to the clinic and were evaluated by the researchers (gynecologic history, physical examination, urodynamic testing, and physical therapy evaluation). According to the results, 59% of the women reported urinary incontinence symptoms, and 29.3% of the women reported organ prolapse. In addition, 27% reported endometritis, 57% reported dyspareunia, and 44% reported previous hysterectomy.

From this data, the researchers concluded that the prevalence of urinary incontinence is higher among women with Ehlers-Danlos syndrome than in normal population, a fact that should be taken into account when examining a patient with Ehlers-Danlos syndrome later during the clinical work [39].

6.9. Hormone replacement therapy

The correlation between HRT and urinary incontinence symptoms was well studied. The effect of estrogen on the urethra, can be related to the fact that the urogenital tract is full of estrogen receptors. The effects of estrogen include elevation of urethral blood flow, increase in the sensitivity of α-adrenergic receptor, increase in the urethral closing pressure and improvement of cellular maturation of the bladder, trigone and urethra [29,40].

A recent research that studies the correlation between HRT and urinary incontinence, has compared the effects of oral and vaginal estrogen therapy on the lower urinary tract in postmenopausal women with prior hysterectomy [41]. As part of that study, 57 women who are post hysterectomy and post-menopausal, received oral or topical estrogen, once a day. It is important to note, that the study was randomized (the decision who will get oral or topical therapy was random), and prospective. The data that has been collected includes measurements of the E2 levels, urine analysis, pelvic examinations, introital color Doppler ultrasonography (US), and personal interviews using the Bristol Female Lower Urinary Tract Symptoms Questionnaires [41]. The researchers collected the data at the beginning of the study, and again after 3 months.

According to their results, the subjects reported significantly less symptoms of urinary frequency and nocturia. Even though there was no significant change in the incidence of urinary incontinence (both stress and urge), an improvement of the stress urinary incontinence symptoms was reported by 72.6% of the oral estrogen group, and 60% of the topical estrogen group. From these results, the researchers concluded that the use of estrogen in the treatment of SUI and overactive bladder is beneficial. The study also suggested that the explanation for the results, involves an increase in the urethral blood flow around the bladder neck and mid-urethra [41].

7. DIAGNOSIS AND EVALUATION

In the management of stress incontinence, or urinary incontinence in general, it is important to gain as much information as possible.

A major concern in dealing with urinary incontinence, is that in many cases, the embarrassment can prevent the patient from sharing the information needed to establish a proper diagnosis. When preforming a detailed evaluation, a “sensitive ear” is needed, to search for the specific clues that can lead us to the correct diagnosis.

7.1. INITIAL EVALUATION

When assessing a patient with urinary incontinence symptoms, the initial step is to evaluate the existence of incontinence, and to rule out any other organic or non-organic causes, that can be related to urinary leakage symptoms.

7.1.1. History taking and comprehensive questioning

It is important to achieve as much information as possible about the nature the urinary leakage, in order to choose the proper diagnostic exams later on. When assessing a patient with urine leakage, a proper history taking is important, in order to evaluate the relevant risk factors that can be associated with the patient's symptoms, such as diabetes, obesity, organ prolapse, bowel leakage or neurological conditions [42,1]. As part of the initial evaluation, specific questions need to be asked, in order to diagnose the type of urinary incontinence that the patient suffers from.

By understanding the nature of each incontinence type, a symptomatic evaluation can be useful for diagnosis. In the table below, the main characteristics of urinary incontinence are presented, each type of incontinence has a different set of characteristics.

	Characteristics of chief complaint	Urine leakage volume	Urge to urinate prior to the leakage
Stress incontinence	Urine loss when coughing, sneezing or laughing	Small or large	No
Urge incontinence	Frequent urine loss that keeps the patient up at night or worsens after taking a diuretic	Small	Yes
Overflow incontinence	Urine leakage related to change in position or activity. Can be related to voiding difficulties (urinary hesitancy, slow flow, and nocturia)	Small or large	Varies

Table 1. Characteristics of chief complaint of different urinary incontinence types. Modified from the article "*Evaluation of females with urinary incontinence*" [42].

In order to help the physician to diagnose the incontinence type (stress, urge, mix or overflow) and prevent misdiagnosis, three short standardized questionnaires (3IQ) are available [42].

As part of a study [43] from 2004 that assessed the accuracy of a simple questionnaire to categorize the types of urinary incontinence in women, 301 women patients (older than 40, mean age 56) have been evaluated with the 3IQ questionnaire. The results of the study are presented in the table below.

	Sensitivity (true positive)	Specificity (true negative)	Positive likelihood ratio
Stress urinary incontinence	0.86 (CI, 0.79 to 0.90)	0.60 (CI, 0.51 to 0.68)	2.13 (CI, 1.71 to 2.66)
Urge urinary incontinence	0.75 (95% CI, 0.68 to 0.81)	0.77 (CI, 0.69 to 0.84)	3.29 (CI, 2.39 to 4.51)

Table 2. The results of the study. Modified from the article *"The sensitivity and specificity of a simple test to distinguish between urge and stress urinary incontinence"* [43].

According to the results, the researchers concluded that the 3IQ questionnaire is a simple, quick, and noninvasive tool, with an acceptable accuracy to identify the type of incontinence from which the patient suffers (i.e. urge, stress incontinence) and may be appropriate tool to use in primary care settings [43].

As part of the questioning process, evaluation of eating and drinking habits, as well as medications, is of great importance.

According to a study [44] from 2017, there is a relationship between eating and drinking habits and urinary incontinence symptoms. The study has conducted a literature review based on a systematic search, and it was found out that there is a correlation between the amount of fluid intake and incontinence symptoms, as well as the type of beverages consumed (e.g. caffeine, alcohol, carbonated beverages, are all associated with urinary incontinence symptoms) [44].

7.1.2. Quality of Life Questionnaires

As part of a complete evaluation, an assessment of the patient's quality of life is needed in order to understand what is the most beneficial treatment. For that evaluation, several quality of life questionnaires are available [42]:

- International Consultation on Incontinence Questionnaire
- Kings Health Questionnaire
- Pelvic Floor Distress Inventory
- Pelvic Floor Impact Questionnaire
- The Patient Global Impression of Improvement (PGII)
- Patient Global Impression of Severity (PGIS)

7.1.3. Uro-gynecological physical examination

The use of physical examination as part of SUI evaluation is not usually indicated, and reserved for specific circumstances (atypical symptoms, diagnostic uncertainty, or failure of initial treatment strategies). When examining the patient, it is important to evaluate atrophy of the vagina and pelvic muscle rigidity, and to look for pelvic masses and any sign of pelvic organ prolapse beyond the level of the hymen. Neurologic evaluation (limited evaluation of lower-extremity strength, reflexes, and perineal sensation) is usually not needed, unless the incontinence is of new and sudden onset [42,1].

7.1.4. Urine analysis

Should be performed for all patients with urinary incontinence symptoms, as part of the initial evaluation. In any case of hematuria or UTI suspicion during the screening process, a urine culture is also indicated [42,1].

7.1.5. Urination (voiding) diary

There are different formats of voiding diaries, that can be found in the literature or in online sources. The diary can provide additional information that the patient forgot to report during the initial diagnostic process. The main benefits of using voiding diary are: assessment of the relation between urine leakage and fluid intake, information about the bladder capacity, the time interval that the patient can reasonably wait between voids (will be used for bladder training), as well as measurement of the severity of the condition [42,1].

Blank Diary

Date	**Drink**		**Urine**		**Leakage**		
Time	Type	How much (mls)	Volume of Urine (mls)	How Urgent 0-3 3= most urgent	Leakage with Urgency	Leakage with activites	Pad change

Figure 3. An example of voiding diary. Modified from the website *IUGA your pelvic floor*, who provide information for patients.

7.2. CLINICAL TESTS

Will serve as a complimentary diagnostic tool, after the initial clinical evaluation. Clinical test can be useful if the physician did not receive a proper diagnosis, in cases of misdiagnosis, to confirm a diagnosis, or in case of abnormal recurrence.

7.2.1. Bladder stress test

Simulates the accidental release of urine (urinary incontinence) that may occur when coughing, sneezing, laughing, or exercising. As part of the test, the patient is asked to stand with a comfortably full bladder. the physician will examine the urethra, and will ask the patient to preform Valsalva maneuver or cough, in order to increase the intra-abdominal pressure. In case of SUI, the physician will notice urine leakage from the urethra [42,1]. The bladder stress test is very useful and reliable, and has high positive predictive value (PPV) according to studies.

One of the studies [45] on that topic, has noted that a positive cough stress test (or bladder stress test) has a PPV of 55% for detecting pure SUI and 91% for a mixed condition (SUI plus additional diagnosis).

7.2.2. Measurement of the postvoid residual (PVR) urine volume

Even though it is not measured during the initial SUI assessment, the PVR is very useful in case of urinary retention or overflow, as well as misdiagnosis during the initial evaluation, and failure of initial treatment [42]. The PVR is evaluated, by measuring the remaining urine in the bladder shortly after a voluntary void; this can be accomplished through ultrasound (trans-abdominal or trans-vaginal US examination), bladder scan, or by directly measuring the urine volume drained by a urinary catheter (the *gold standard*) [46]. It is very important to measure the PVR as quickly as possible. Waiting of more than 10 minutes after voiding can provide a non-accurate PVR value, and impact the diagnostic process [46]. The indications for PVR measurement are: patients with neurologic abnormality, any symptom or history of detrusor dysfunction, symptoms of severe constipation, resurrect UTI, any obstruction of the urinary bladder, pelvic organ prolapse beyond the hymen, diabetes mellitus with peripheral neuropathy, new sudden onset of incontinence symptoms after surgical treatment of incontinence, or any use of medications that suppress detrusor contractility or increase sphincter tone [42]. According to the AHCPR guidelines, a PVR urine volume of less than 50 ml is considered as adequate bladder emptying, and PVR urine volume of more than 200 ml is considered as inadequate bladder emptying [47] (according to other sources it is 150 ml [42]).

7.2.3. Uro-dynamic examination

An invasive test, that can differentiate between stress, urge and mix urinary incontinence. In addition, by using the test, the physician can evaluate difficulties with bladder emptying as well as damage to the urethra sphincter muscle.

Even though the urodynamic examination is not always integrated in the diagnostic process, it is useful is certain cases: diabetic patients with urinary incontinence symptoms, any history or suspicion of neurologic abnormality that can be related to the urinary incontinence, and investigation of overflow incontinence symptoms. Is it also indicated when the diagnosis is unclear or when there is failure of the treatment, and further investigation is needed [42].

The test can be separated into single channel urodynamic testing, and multi-channel urodynamic testing.

- Single channel urodynamic testing - during the single channel testing, the patient is asked to urinate, and the volume is recorded. Afterwards, the physician inserts a urinary catheter, and the postvoid residual (PVR) urine volume is measured. Then, the bladder is filled (retrogradely), and the patient is asked to note when she feels the first sensation of her bladder being filled, when she has desire to urinate, and when she cannot hold the urine anymore. The volumes are calculated and used as part of the diagnostic process. The values that considered as normal (not pathologic) are 100–150 cc for first sensation, 250 cc for first desire to void, and 500–600 cc for maximum capacity [4].

- Multi-channel urodynamic testing - during the multi-channel testing, while one transducer is placed in the rectum or vagina (to measure the intra-abdominal pressure), another transducer is placed inside the urinary bladder. In addition, EMG pads are placed along the perineum. During this test, an uninhibited bladder contraction, and the entire pelvic floor can be documented [4].

Because the test is invasive and costly, it is not used initially during urinary incontinence evaluation [42]. In addition, studies have suggested that the urodynamic testing is not necessarily needed before surgical or non-surgical management because it may not affect the treatment outcomes [42,1].

7.3. REFERRAL TO UROLOGIST OR UROGYNECOLOGIST

A referral to urologist or urogynecologist will be indicated in the following circumstances [42,1]:

- Culture-proven recurrent UTIs (3 or more per year/ 2 or more per 6 months)
- Hematuria without UTI
- Failure of non-surgical or surgical method of treatment
- Neurologic condition
- Unclear diagnosis
- Chronic urinary catheterization or difficulty passing a catheter
- Suspected overflow incontinence, in addition to diabetes or neurologic condition

8. TREATMENT

The options for treating stress urinary incontinence are multiple and varied, and the treatment success varies greatly among the different methods. It is important to adjust the right treatment for each patient, according to the severity of her problem, with taking into account the adverse effects that can be related to the therapy.

Before starting the treatment, a complete evaluation is needed, in order to identify if there is another problem that causes the incontinence symptoms. In order to offer the most suitable treatment for the patient, different pathologies need to be excluded. As part of the physical examination and history taking, several questions need to be addressed, including [48]:

- Any abdominal or pelvic pain, that is associated with the urinary incontinence symptoms
- Hematuria (gross or microscopic) in the absence of UTI
- Any history of recurrent UTI, with positive culture
- New neurologic symptoms
- Suspicion for urinary fistula, or urethral diverticulum
- Chronic catheterizations
- Any difficulty passing urinary catheter
- Any sign of pelvic organ prolapses, below the level of the hymen
- Any history of pelvic surgery of pelvic radiation
- Persistently elevated postvoid residual urine volume

After exclusion of another pathology behind the urinary incontinence symptoms, more detailed investigation is needed to identify the specific type (stress, urge, mixed, overflow) and severity of the incontinence, as written in the diagnosis and evaluation part of this thesis.

When comparing different treatment methods, it is important to proceed in stepwise fashion in order to achieve the best quality of life for the patient, with minimum side effects following the treatment [48]. When discussing the different treatments available, classification is made according to the type of incontinence, and according to the approach itself (non-surgical or surgical).

8.1. INITIAL TREATMENT METHODS FOR URINARY INCONTINENCE

Initial treatment methods, are usually non-specific (can be beneficial for both stress or urge incontinence), and meant to help the patient to cope with her symptoms, before progressing to more specific treatment. According to the guidelines, the initial treatment needs to be evaluated for at least 6 weeks, before progressing to different more specific treatment methods.

In the cases of women who suffer from high BMI levels, it is advised to continue the conservative treatment for time period of 6 months [48].

The initial methods of treatment are discussed below.

8.1.1. Risk factors and lifestyle modifications

As presented in the risk factors section of this thesis, SUI have several risk factors that can affect the development and progression of symptoms. By identifying those risk factors, clinician can evaluate the risk of the patient, and can advise for proper risk factors reduction.

Example of a proper risk factor reduction, is weight loss, in the case of obese women. As explained before, studies [49] have shown a correlation between high BMI levels and SUI symptoms, and suggested that obesity can increase the prevalence of SUI. By advising the patient to reduce weight (e.g. using weight reduction programs and weight reduction groups) it is possible to improve the symptoms without proceeding to non-conservative methods of treatment.

Another example of risk factor modulation is smoking cessation. As previously mentioned, cigarette smoking is identified as a risk factor by several studies [30, 33]. by understanding the risk of smoking, cessation can potentially prevent further progression of the symptoms. As is with obesity, introduction of the patient to smoking cessation programs, can help the patient quite smoking, and therefore to reduce the risk of SUI, as well as other risks and complications associated with smoking.

8.1.2. Kegel exercise

The Kegel exercise, also known as pelvic floor exercises, consists of continuously contracting and relaxing the muscles of the pelvic floor.

According to the recent guidelines, the basic regimen consists of 3 sets of 8 to 12 contractions sustained for 8 to 10 seconds each, performed 3 times a day. Patients should try to do this every day and continue for at least 15 to 20 weeks [48, 50]. According to the "*Patient education: Pelvic floor muscle exercises*

(Beyond the Basics) [51]" an initial physical examination by a gynecologist is needed in order to isolate the specific muscle or muscle group that will be targeted for treatment. After evaluating the target muscle, the physician should advice the patient to perform the Kegel exercise, by contracting (squeezing), hold the contraction for 8-10 seconds, and then fully relax the pelvic floor. For better results, the patient needs to increase the contraction holding time later on, before the relaxation phase.

As part of one of the studies that investigate the effect of home-based Kegel exercises on women with SUI symptoms [52], a total of 90 women with stress and mix urinary incontinence, performed the Kegel exercise regimen, consisting of 10 sets of contractions/day; each set included 10 repetitions, for at least 8 weeks.

According to the study results, 68.4% of the women who had SUI, and 41.2% of the women who had MUI, reported improvement of their symptoms. The researchers concluded that home-based Kegel exercises (without physician supervision), have been found effective in women with SUI and MUI. It is important to mention, that the improvement was more prominent in women with SUI [52].

8.1.3. Pelvic floor physical therapy

Even though the Kegel exercise has been proven as beneficial in the treatment of SUI symptom, some women cannot perform it correctly. The reasons for this are vary, and can be related to inability to isolate the proper muscle, obesity that limits the patient's ability to perform the exercise, or even motivation [48]. By introducing the patient to physical therapy, the physician can be sure that the patient is supervised and properly guided when preforming the exercise, in order to achieve maximum beneficial effect from the treatment.

8.1.4. Biofeedback

The biofeedback method, is used with women who didn't manage to achieve a proper therapeutic gain with Kegel exercise, because they didn't succeed with isolation of the target muscle. During the biofeedback session, a sensor in inserted into the vagina. The sensor receives pressures, and transmits information in audible or visual feedback about the strength of pelvic floor contractions. Different versions of the biofeedback technology are available, and include abdominal and perineal electromyography (EMG) measurements, or electrical stimulation (placed inside the vagina or anus and promote muscle contractions by transmitting electric stimulations) [48].

One of the studies, that investigates the beneficial aspects of the biofeedback treatment, is presented in the article "*Feedback or biofeedback to augment pelvic floor muscle training for urinary incontinence in women*" [53]. The study tried to determine, whether there is any additive beneficial effect of biofeedback, on top of performing the Kegel exercise.

The study concluded, that there is an additional benefit with using biofeedback in addition to pelvic floor exercise, in women with SUI symptoms. Despite the successful results, the study also mentioned that further researches are needed, in order to differentiate whether it is the biofeedback that causes the beneficial effect or some other differences between the trial arms (such as more contact with health professionals) [53].

8.1.5. Vaginal weighted cones

Mostly useful for women who don't have time or ability to practice pelvic floor exercise, or biofeedback. The patient inserts a weighted cone into the vagina, and contract the pelvic muscles in order to hold the cone in place against gravity [48].

A study [54] (Randomized controlled trial) from 1998, investigated whether there is more benefit with pelvic floor exercise over vaginal weighted cone, in the treatment of stress urinary incontinence patients. As part of the study, 60 white (Caucasian) women, with a mean age of 56 years, have been treated for SUI symptoms for a time period of 12 weeks.

Under randomized separation, 30 women practiced pelvic floor exercise (once a week session), and 30 women practiced with the vaginal weighted cone (one session every 2 weeks).

According to the results of the study, improvement of the symptoms has been reported by 53% of the women who used the pelvic floor exercise, and 57% of the women who practiced with the weighted cone (it is important to mention that there was a withdrawal from treatment of 47% of the women from this group, so the actual percentage of women who have found the treatment beneficial is 50%). The researchers concluded that there is no difference in the results between practicing pelvic floor exercise and the vaginal weighted cone, in the treatment of SUI. They also added that even though it is useful, patients who are using the cone are less likely to adhere to treatment, and therefore not recommended over the Kegel exercise [54].

8.1.6. Bladder training (timed voiding)

Timed voiding, is usually beneficial in the treatment of urge incontinence, but can be also useful with SUI patients who have higher bladder volumes [48]. Bladder training takes time, and in order to achieve therapeutic level, the patient needs to use it for a time period of up to 6 weeks, and needs to practice out of home as well. In order to keep timed voiding as useful as possible, the physician needs to instruct the patient to void by the clock at regular intervals while awake, using the shortest interval between voids identified on the voiding diary as the initial voiding interval. When the patient can avoid leakage for one day using the initial urination interval, the time between scheduled voids is increased by 15 minutes. The intervals are gradually increased until the patient is voiding every three to four hours without urinary incontinence or frequent urgency [48].

In order to assess the benefit of bladder training in the treatment of urinary incontinence, the study "*Bladder training for urinary incontinence in adults*" [55] has been conducted. As part of the study, a data was collected from the Cochrane Incontinence Group trials register (January 2003). According to their results, bladder training is useful in the treatment of urinary incontinence, but the evidence for it is limited. They also added, that there is not enough data to conclude if bladder training is useful only in addition to another treatment, or as sole treatment method [55].

8.1.7. Topical vaginal estrogen

Topical vaginal estrogen, can be beneficial for both urge incontinence and stress incontinence, as well as for vaginal atrophy. It is used as method of treatment for women who are peri or post-menopausal, and can take up to three months in order to achieve therapeutic benefits [48]. The use of estrogen topically is possible in several methods of administration [48]:

- Topical estrogen cream – 0.5 gm two times a week (conjugated estrogen or estradiol).
- Estradiol tablet – 10 mcg two times a week.
- Estradiol ring – needs to be changed every three months.

A Cochrane review [56], that was published in 2003 and subsequently updated in 2009, assessed the effect of topical and systemic estrogen use in the treatment of urinary incontinence.

According to their results, there was an improvement using topical estrogen cream; as patients reported one to two fewer voids in 24 hours among women who treated with local estrogen. Also, less symptoms of urgency or frequency have been reported. It is important to mention, that the study also added that no data have been collected after the time period of the topical treatment, hence there is no information about the long-term benefits of the treatment. According to the study, the use of systemic estrogen is not

recommended as a long-term treatment, and needs to be limited because of the risk of endometrial and breast cancer, especially in those women with an intact uterus [56].

8.2. METHODS OF TREATMENT SPECIFIC FOR SUI

Are used if the initial treatment is not sufficient. The different methods can be classified as non-surgical or surgical. Non-surgical methods will be used initially, surgical approaches can be introduced in case of treatment failure [48].

8.2.1. Continence pessaries – pessaries, are devices made of plastic or silicone. In order to choose the most beneficial device for the patient, the physician needs to choose the proper pessary type and size according to:

- Concomitant organ prolapses, and their severity
- Presence or absence of a uterus
- Sexual activity
- The width of the mid-vagina (estimated)

Name of pessary	**Type of pessary**	**Used for the treatment of SUI**	**Used for the treatment of POP, stages 1-2**	**Used for the treatment of POP, stages 3-4**	**Needed to be removed before sexual intercourse**
Ring	Support Pessary	No	Highly recommended	Recommended	Not necessary
Lever (Smith, Hodge, Risser)	Support Pessary	No	Recommended	Least recommended	Not necessary
Gehrung	Support Pessary	No	Recommended	Least recommended	Not necessary
Incontinence ring	Support Pessary	Recommended	Highly recommended	Least recommended	Not necessary
Mer-land	Support Pessary	Recommended	Recommended	Least recommended	Not necessary
Gellhorn	Space-Occupying Pessary	No *According to other sources it is recommended [1]	Least recommended	Highly recommended	Not possible
Donut	Space-Occupying Pessary	No	Least recommended	Recommended	Not possible
Cube	Space-Occupying Pessary	No	Least recommended	Recommended	Highly recommended

Table 3. The different types of pessary devises. The table is based on a table from the article "*Pessary Use in Pelvic Organ Prolapse and Urinary Incontinence*" [57].

Before inserting the device, the patient needs to empty her urinary bladder (complete urination). The physician needs to insert the largest device that can fit comfortably, and needs to be able to fit a finger on each side of the device. After the insertion, the patient will be examined at supine and standing position, with and without Valsalva maneuver. After the initial examination is completed, the patient will be asked to sit on the toilet and perform Valsalva maneuver, for further assessment. If the devise fits properly, the physician will educate the patient how to remove and insert the device on her own, and will check that the patient can urinate when the pessary is inserted. The patient will need to come for a follow-up visit after 2-4 weeks [57]. For patients who are able to remove the device on their own, a weekly or even nightly removing and cleaning is recommended. If the patient cannot remove the pessary by herself, a gynecologist visits every 2-3 months is recommended [57].

One of the studies on that topic, has investigated the benefits of pessary use, in comparison to the conservative behavioral treatment [58]. As part of the study, 446 women who were diagnosed with stress incontinence, randomly assigned to use behavioral treatment, pessary treatment, or combined treatment. The patients have been evaluated after time period of 3 months.

According to the results, after 3 months, 40% of the women who used the pessary, and 49% of the women who used the behavioral therapy have reported improvement of their symptoms (according to the study, reported as "much better", or "very much better"), (P=.10). When asked about complete resolution of their symptoms, 33% of the pessary group, and 49% of the behavioral therapy group have reported positively (P=.006). In addition, when asked about satisfaction from the therapy, 63% of the pessary group, and 75% of the behavioral therapy group, have reported positively as well. (P=.02). It is also impotent to mention, that after time period of 12 months, both treatment groups had satisfaction of above 50%.

From these results, the researchers concluded that behavioral therapy have better satisfaction and more efficient then pessary treatment, after 3 months of treatment, but similar results after 12 months of treatment [58].

8.2.2. Pharmacological approach

According to the FDA, there is no formal approved pharmacological therapy for the treatment of SUI in women, hence, the use of pharmacotherapy in the case if SUI symptoms is off label [59].

Several medications are used as part of the therapy, including:

- Duloxetine (serotonin-norepinephrine reuptake inhibitor) – used in a case of combination of SUI with depression. The beneficial mechanism of SUI treatment is not completely understood.

A study on that topic, tried to determine whether SNRI is better than placebo in the treatment of women with SUI or mixed urinary incontinence, and which doses should be used. As part of the study, 3327 adults received duloxetine or placebo in randomized pattern, for a time period of 3 to 12 weeks [60]. According to the results, there was a significant improvement with the use of duloxetine (50% reduction of the symptoms during the treatment period). The researchers concluded that duloxetine treatment can significantly improve the quality of life of patients with stress urinary incontinence, but it is unclear whether or not benefits are sustainable [60].

- Phenylpropanolamine (Alpha-adrenergic agonist) – increases the contraction of the urethral smooth muscle. Not used anymore for SUI treatment, because of the side effects [48].

8.3. SURGICAL APPROACHES

Surgical approaches for the treatment of SUI, have been showing high cure rate, and proved as beneficial [48]. Nevertheless, the decision to choose surgery as the method of treatment needs to be based on certain criteria, in order to prevent unnecessary surgeries and complications.

Patients who are candidates for surgical treatment are [61]:

- Patients with failure of the non-surgical treatment - worsening or non-improving symptoms, after a trial of conservative treatment.
- Patients with occult SUI – the meaning of occult SUI, is the development of SUI symptoms, after correction of POP.
- Patients who don't want future pregnancies – both vaginal delivery and caesarian section can cause recurrence of the SUI symptoms. Higher recurrence rate was shown with vaginal delivery [62,61].

Surgical approaches for SUI can be divided into abdominal procedures (open or laparoscopic), vaginal procedures, and urethral bulking agents [1].

8.3.1. Abdominal procedures

Abdominal approach will be used in the case of large uterus that compresses the bladder, with no prolapse, or in the case of failure of vaginal procedure approach.

8.3.1.1. Pubovaginal sling (PVS)

Using the rectus muscle facia (most commonly used), facia lata or the vaginal wall, and replace it under the bladder neck.

The materials used for producing the sling can be autograft, allograft, xenograft, or synthetic prosthetic materials. The sling restores urethral resistance during stress maneuvers to prevent incontinence, while improving urethral coaptation at rest and allowing for spontaneous micturition [63].

A study from 2001 [64], asses the results of PVS method use, for women patients who suffer from SUI. As part of the study, A total of 67 patients with a mean age of 56 +/- 11 years, underwent pubovaginal sling surgery for simple sphincteric incontinence, and were prospectively followed for 12 to 60 months. According to their criteria, 67% of the patients were classified as cured and the remaining 33% were classified as improved [64].

There are several peri and post-operational complications that are associated with the PVS procedure [65]:

- Voiding dysfunction – the risk of voiding dysfunction includes de novo urge incontinence, as well as persistent postoperative urge. According to clinical data, the incidence of post-operative de novo urge incontinence is 3-30%, and the incidence of persistent urge is 10-33%. In addition, there is also a risk of urinary retention, with incidence of 2-12% (only 2-7% will need long term intermittent catheterization). Most voiding related adverse events associated with PVS can be managed conservatively with observation and medications, but some patients require additional interventions such as urethrolysis or sling division.
- Infections – there is a risk of infections after the PVS procedure. The risk of infectious cystitis is very high, with incidence rate of 92%. In addition, some patients can develop pyelonephritis (2%). The risk of wound infections is 22%.
- Vaginal, urethral or bladder erosions – the risk of erosions following PVS procedure is low. Erosions are highly associated with sling placement (76% of the cases are related to sling placement).

- Recurrent SUI – stress incontinence recurrence is a potential complication of any SUI treatment, including PVS. In that case, the patient can be treated with additional sling surgery or injection of bulking agents.

8.3.1.2. Burch colposuspension

As part of the operation, the surgeon will create a support of the bladder neck with stiches that are connected to the sides of the urethra and to the cooper's ligament on the posterior surface of the superior pubic ramus [1,61].

There are several peri and post-operation complications that are associated with the colposuspension procedure [66]:

- Bleeding – there is a risk of bleeding during and after the surgery. the risk of significant bleeding resulting in postoperative hematoma or transfusion events is around 2%. The bleeding is usually due to rupture of paravaginal veins when the surrounding fat pad is not fully cleared before suture placement.
- Bladder injury – there is a risk to cause bladder injury during the operation, with incidence of 0.4-9.6%. It is also important to mention, that it is more common in patients who have undergone prior pelvic surgery.
- Urethral injury – the risk for urethral injury is relatively low, with incidence of 0.2-2%.
- Infections – there is a risk of both UTI and wound infection.
  The incidence of UTI is 4-40%, while the incidence of wound infections is 4-10.8%.
- Voiding dysfunction – there is a high risk of voiding dysfunction after the colposuspension procedure. According to clinical data, post-operatively voiding dysfunction has incidence rate of 25%. Voiding dysfunction may have different presentations, including urinary urge, and urinary retention. The incidence of patients with retention that required long-term catheterization beyond 1 month is low, ranging from 0.7-7%. The incidence of patients with urge incontinence (de novo detrusor instability) is 3–8%.
- Dyspareunia and pelvic pain – the incidence of dyspareunia (difficult or painful sexual intercourse) after the colposuspension procedure is 2-4%. The incidence of pelvic pain (groin or suprapubic pain) is 2-6%.
- Postoperative enterocele – the risk of enterocele development is relatively high, with incidence of 12-17%.

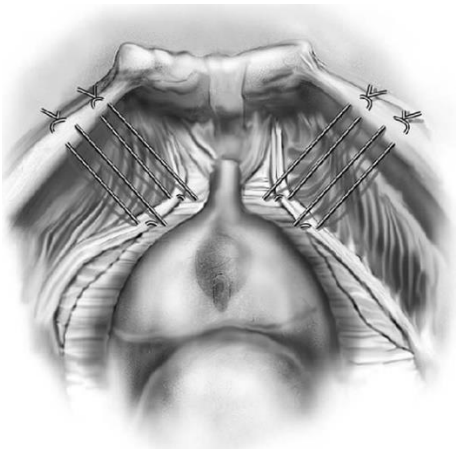

Figure 4. An illustration of the Burch colposuspension (from 1961)

8.3.1.3. Marshall Marchetti Krantz (MMK)

A type of retropubic colposuspension procedure, that has generally been an alternative to Burch colposuspension. As part of the operation, the surgeon creates elevation and fixation of the urethra (the anterolateral part) to the posterior pubic symphysis periosteum. Nowadays, this method is rarely used [1,61].

A study [67] from 2009, that studied the cure and failure rates for both Burch colposuspension and MMK procedures, included 46 trials involving a total of 4738 women patients. The patients were diagnosed with stress or mixed urinary incontinence, and have been treated with open retropubic colposuspension surgery. Afterwards, a data has been collected during time periods of 1 year and then after 5 years post operation. According to the results, the cure rate was 85 to 90% after the first year, and 70% after the fifth year. It is important to mention, that the study also concludes that failure was less common after Burch (RR 0.38 95% CI 0.18 to 0.76) than after the Marshall Marchetti Krantz (MMK) procedure at one to five-year follow-up [67].

8.3.2. Vaginal procedures

Will be used in the case of failure of abdominal surgical approach, if there is vaginal prolapse, or if abdominal surgery is contraindicated.

8.3.2.1. Mid-urethral sling procedures (MUS)

The use of mesh (made of polypropylene) that is placed under the middle part of the urethra. The mesh induces growth of collagen in that anatomical part over time. The use of urethral sling is the *gold standard* [1,61] for SUI treatment, with several benefits over the other surgical approaches, including: completion of the surgery in less than 30 minutes, no need for post-operational hospitalization or catheterization, short recovery time, and no post-operational pain [1].

- TVT- retropubic (tension-free vaginal tape) – inserted through the retropubic space. The main benefit of the use of TVT-retropubic is no bleeding from the medial branches of obturator vessels.
- TVT-O (tension-free obturator tape) – inserted through the vagina and the obturator foramen. The main benefit of the use of TVT-O is a decrease in the risk of bladder injury.

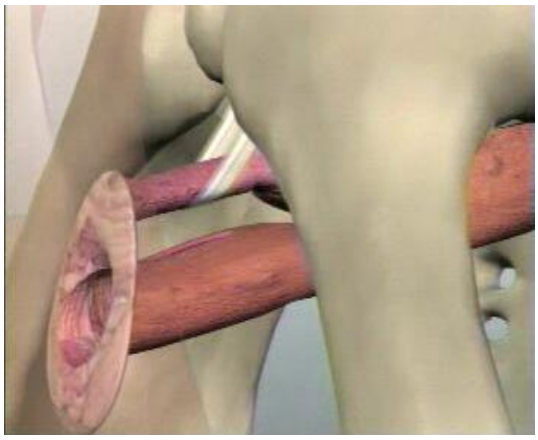

Figure 5. An illustration of the mid-urethral sling. The mesh is located under the middle part of the urethra.

In order to study the therapeutic differences between the two approaches, a prospective randomized study [67] was conducted, in order to compare the cure rates and the complications. As part of the study, data about 164 patients have been collected, during a time period of 3 and 12 months. According to the results, the cure rates were similar for both approaches (88.9% for TVT, and 86.7% for TVT-O, P = 0.001), but the operative time was shorter for the TVT-O group. It is also important to mention, that the cure rate was higher in both groups, for patients with hypermobile urethra [68].

Another study [69] that is focused on the benefit rates of TVT, studied the post-operative results of 47 women with intrinsic sphincter deficiency, over different time periods (6, 12, 36, and 60 months post operation). The results of the study are presented in the table below.

	After 6 months	After 12 months	After 36 months	After 60 months
Completely satisfied	70%	72%	66%	57.4%
Improved urine control	18%	12%	20%	17.02%
No change in urine control	10%	7%	14%	25.5%

Table 4. The results of the study are presented in the table above, and include the satisfaction rates of the participants. Modified from the article "*Tension-free vaginal tape for surgical relief of intrinsic sphincter deficiency: results of 5-year follow-up"* [69].

Even though MUS procedure is considered safe, and associated with low complications rate, MUS procedures have the potential to cause several complications during the surgery, as well as during the post-operative period [70,71,72]:

- Bladder laceration or perforation – can occur following the needle passage during the operation. Bladder damage can be seen in 1-15% of the patients (the average perforation rate is 5%). The physician can minimize the risk, by emptying the bladder before the operation, and by providing finger guidance during needle passage through the retropubic space.
  The risk for bladder injury as well as for urethral injury is considerably lower (<1%) with the trans-obturator approach (TVT- O).
- Obstruction of the urethra – obstruction of the urethra can cause wide range of urinary problems and symptoms, including urge incontinence and urinary retention.
  The presentation depends on the level of obstruction. It is important to evaluate the patient post-operatively in order to identify any urinary problem. Some studies suggest that new onset (de novo) urge urinary incontinence symptoms can be seen in 10-30% of the patients, but despite the incidence rate, the intervention rate for these complications following midurethral slings is between 1% and 2% [70,72]. In cases of urinary retention caused by MUS procedure, catheterization beyond one week is necessary in 4–8% of patients following surgery [71].

- Recurrent SUI symptoms – can be related to many factors, including loose sling and placement of the sling in the wrong place. Recurrent SUI after sling procedure, can be seen in 5-10% of the patients. In order to prevent this complication, the cotton swab test and the bladder leak test can be performed (the bladder should leak moderately when filled with 500 mL of water).
- Vaginal and urethral erosions – can be related to the operation itself (incision), or to anatomical damage caused by the sling. Erosions are more commonly associated with synthetic sling materials (typically 4-30%), and can be seen with the use of PTFE (Gore-Tex®) polyester (Dacron® or Protegen), or silicone (InteMesh®). Erosions can be avoided by inserting a urinary catheter before the surgery, and by using non synthetic materials. If urethral erosion occurs, the tape can be removed endoscopically. It is recommended not to place another sling (even autologous) at the same time when erosion occurs.
- Hemorrhage – can be observed during, as well as after the surgery. In case of heavy bleeding, a direct pressure application is needed in order to reduce the bleeding, followed by identification and ligation (by sutures) of the bleeding vessels. Bleeding occurs in less than 1% of the procedures. The likelihood of hemorrhage is lower with the trans-obturator approach (TVT-O) in comparison to retropubic slings (TVT- retropubic).
- Sling infection and erosion – usually associated with the use of autologous, cadaver, and synthetic materials for the creation of the sling.
- Bowl perforation – a complication that is specific to TVT procedure. Can cause short and long-term sequelae, including peritonitis and bowl necrosis.

8.3.2.2. Bladder neck sling procedure

Also called proximal urethral sling. The sling is placed at the level of the proximal urethra and bladder neck. The surgery is performed under both vaginal and abdominal incisions. The sling is made of biologic or synthetic materials [73]. Bladder neck slings are mainly reserved for women in whom midurethral slings (MUS) are contraindicated or were unsuccessful. This is largely due to the decrease in morbidity and less voiding dysfunction associated with performing MUS [61].

8.3.2.3. Modified Pereyra Procedure (MPP)

An elevation of the paraurethral tissue is created, which is then connected to the abdominal wall. In that way, it creates an elevation of the ureterovesical angle.

As part of the study "*Retropubic cystourethropexy: a review of two operative procedures with long-term follow-up*" [74] who studied both MPP and MMK procedures, 252 women received the MPP treatment, and 490 women received the MMK treatment for SUI symptoms. According to the results in a time period of 17 years, the cure rates for both procedures were almost identical (93%) [74].

8.3.3. Urethral bulking agents

The use of bulking agents, is usually preserved for patients who are candidates for surgical treatment, but cannot tolerate, or prefer not to go into surgery. In addition, bulking agents can also be used in cases of recurrent SUI after previous surgical approach [61]. The synthetic materials (i.e. collagen), are injected into the urethral mucosa, and support the opening of the urinary bladder. the injections are made by the physician in the clinic. The treatment usually contains 2-3 injections in order to achieve therapeutic benefit [1].

Many materials are used as urethral bulking agents, including autologous fat, glutaraldehyde cross-linked bovine collagen, calcium hydroxylapatite, pyrolytic carbon-coated beads, polydimethylsiloxane, ethylene vinyl alcohol copolymer, dextranomer hyaluronic acid, and polytetrafluoroethylene [75].

According to studies, the reported cure rates for bulking agents are between 24.8% to 36.9% at 12-month follow-up [1,76]. From those rates, we can see that urethral bulking agents can provide a limited solution to SUI patients; hence they are less effective than other treatment methods.

8.4. MANAGEMENT OF OCCULT STRESS URINARY INCONTINENCE

Occult stress urinary incontinence (OSUI) is defined as the demonstration of SUI after pelvic organ prolapse (POP) reduction. The pathophysiological mechanism behind OSUI is only theoretical, and suggests that the herniated organ applies pressure on the urethra and prevents the urinary incontinence. Hence, when the POP resolves, nothing prevents the urine leakage, and urinary incontinence symptoms are observed [77].

According to studies, it is estimated that 80% of the women who have advanced POP, also have occult SUI [78].

Another study, that prospectively evaluated 24 continent women referred for evaluation of severe urogenital prolapse, found out that reduction of prolapse with a pessary unmasked sphincteric incontinence in 14 women (58%). The study concludes that pre-operative urodynamic evaluation with and without prolapse reduction is essential for making the correct diagnosis of masked stress incontinence in women with urogenital prolapse [79].

In order to avoid urinary incontinence symptoms after the correction of POP, it is important to evaluate the patient and to diagnose the potential risk for OSUI. The diagnosis can be made by stress testing with the prolapse reduced, or by pessary placement and pad testing. If OSUI is diagnosed or highly suspected, it is recommended to treat the incontinence (e.g. by SUI correction surgery, such as colposuspension or sling) in addition to the POP management. This regimen, can potentially prevent the development of urinary incontinence symptoms post-operatively, and can achieve better quality of life for the patient [77,78].

9. SUMMARY

Stress urinary incontinence is a uro-gynecological pathology that can affect women at different age groups. It is a sub type of urinary incontinence, along with urge, mixed and overflow. While urge incontinence mainly affects women at older ages (more than 55), stress incontinence effects women at younger ages, and can be related to many physiological and pathological factors. As part of the condition, there is urine leakage that is related to increase in the intra-abdominal pressure (lough, sneeze, cough), that can significantly affect the patient's quality of life, and influence her daily activities, as well as key decisions in life.

In the recent years, studies have suggested more clear and relevant etiological explanations for the mechanism of that pathology, as well as risk factors that can be related to the development, the progression and the prognosis of this condition. These evidence-based etiological explanations helped in the past, and will continue to help in the future, to establish better and more precise diagnostic and evaluation methods, that are used as a quick and cheap assessment tools for patients. By creating an evidence-based guideline for diagnosis, we can keep the assessment process easy and affordable as possible, in order to prevent mentally exhausting and unnecessary expensive investigation methods, that will create a financial burden on the patient, or government. By that, we can also spare the patients from going through unnecessary invasive procedures. And last but not least, to provide the most appropriate individual treatment, so they will be free of the inconvenient symptoms, and won't need to live with the embarrassment.

As part of the scientific development and studies on the topic, more and more specific etiological based methods of treatment are practiced in clinics. The ability to isolate the specific pathophysiological mechanism (e.g. muscular dysfunction, urethral closure dysfunction), helps the physicians to choose the most appropriate treatment approach for each patient, and to prevent unnecessary surgeries. As long as the first line of treatment is conservative and non-invasive (e.g. behavioral changes, pelvic floor exercise with Kegel exercise or biofeedback technology, voiding diaries, topical estrogen), the surgical approaches can be preserved for patients with a proper indication. By using newer and more clinically and study-based treatments (conservative as well as different surgical approaches), we can provide better quality of life for the patients, and help them to cope with the condition.

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