INVITED REVIEW

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# New insights into the pathogenesis of (urgency) urinary incontinence

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## ABSTRACT

Urinary incontinence is a chronically progredient condition that usually begins around in the early forties of life with urine leakage after coughing or sneezing [stress urinary incontinence (SUI)]. Several years later the patients realize that after the feeling of urge to void they may lose urine when waiting too long [urgency incontinence, (UUI)]. The etiology of UUI is unknown. However, previous studies have shown that these patients with UUI could regain continence by the surgical tensioning and elevation of the vagina and the attached trigone of the bladder and the urethra. That effect was achieved by the surgical replacement of the uterosacral ligaments (USL) by laCESA or laVASA according to the Integral Theory by Petros. An additional suburethral tape led to overall continence rates (CR) in between 56% and 87% of these patients. Multivariate analyses revealed that the CR in patients younger than 60 years were significantly higher CR than in the older patients. The CR after a trans-obturator tape (TOT); however, was independent of the age at surgery. It has been hypothesized that this development of incontinence is caused by declining estrogen levels especially peri- and postmenopausally. All patients were suffering from UUI. The diagnosis and the age at menopause were evaluated in the context of personal interviews. In all patients with UUI, the vagina was elevated and tightened in the longitudinal axis laparoscopically by substituting the USL with polyvinylidene fluoride-structures of defined identical length (laCESA, laVASA). If that did not lead to continence, a suburethral tape (TOT 8/4) was inserted some months later. Between 2010 and 2022, 326 patients with UUI underwent the surgical replacement of the ligaments. After previous SUI they had developed UUI after menopause. Patients who got estrogen or estrogen/gestagen combinations before menopause became incontinent only after they had discontinued their hormonal treatment. In total, between 67% and 87% of the patients became continent after surgery. According to decades of life the CR after tensioning the vagina by laCESA/laVASA were between 46% and 58% in 50-year-old patients decreasing to 16% and 20% in patients older than 70 years. An additional TOT 8/4 led to continence in between 43% and 40% of the still incontinent patients irrespective of the age. In all patients urinary incontinence started premenopausally as SUI and progressed to UUI after menopause. This continuous worsening of UUI during the years after menopause was probably caused by the estrogen deficiency. The USL, the vagina and the trigone of the bladder express estrogen receptors indicating that their physiological function is dependent on estrogen. Declining estrogen levels lead to a hypo-estrogenic loss of elasticity leading to laxity, particularly in the USL the vagina and the adherent trigone of the bladder. The decreasing CR after tensioning of the vagina by laCESA/laVASA with increasing age can be interpreted as a consequence of the loss of elasticity caused by the longer duration of estrogen deficiency especially in the trigone of the bladder. Patients with perimenopausal hormone replacement therapy (HRT) only became incontinent when they stopped HRT. That observation warrants further investigations.

**Keywords:** Urgency urinary incontinence; OAB; CESA; VASA; hypo-estrogenic tissue remodeling; hormone replacement therapy

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## INTRODUCTION

Urinary incontinence (UI) is a chronically progredient condition that usually begins around in the early forties of life with urine leakage during coughing or sneezing [stress urinary incontinence (SUI)]. Several years later the patients realize that after the feeling of urge to void they may lose urine when waiting too long [urgency incontinence (UUI)]. In the beginning of UUI patients can still reach the toilet "dry" if they go immediately after the urge to void, however, within few years the time intervals shorten until loss of urine becomes uncontrollable. That has significant impact on the quality of private and social life.

The etiology of UUI is unknown. Therefore, there is no specific therapy for UUI and current treatments are aimed to reduce symptoms.[1]

In 1997, however, a chance observation in operative oncological gynecology demonstrated that even patients with UUI could regain continence by the tensioning of the vagina.

During a posterior exenteration in a patient with cervical cancer invading the sigmoid the respective organs were resected, however, the bladder was preserved. In order to stabilize the bladder suspension, the upper wall of the vagina under the bladder remained inside. For further stabilization of the bladder the upper (abdominal) end of the vagina was fixed with a mesh (8x10 cm) to the promontory.

During postoperative (cancer) follow-up examinations, the patient reported that she had become continent after surgery, whereas she had been completely urinary incontinent before the exenteration and no treatment had helped her.

During the following years that stabilisation of the bladder after posterior exenteration was repeated in further six patients. Before surgery they al had been totally incontinent for several years and had been advised that there was no further treatment for them and they had to learn to live with the incontinence. All patients became continent after surgery.

The response of the patients was so enormous that it was decided to develop that surgery also for non-cancer patients with advanced UI.

The effect on restoring continence after posterior exenteration was interpreted as being due to the surgical elevation and tensioning of the vagina.

The urethra and the trigone of the bladder were the respective parts of the urinary system which were attached to the vagina.

It was therefore hypothesized that the stretching and elevation of the vagina in the longitudinal axis must have increased the closing pressure at the meatus internus. Beside the longitudinal stretching of the trigone the elevation of the vagina took the trigone out of the maximum pressure area in a more vertical axis when standing (Figure 1).[2]

Several different surgical techniques were established for sacropexy but none was recommended for treatment of UUI. Therefore, it was decided to develop a new surgical procedure imitating the effects of the mesh in posterior exenteration.

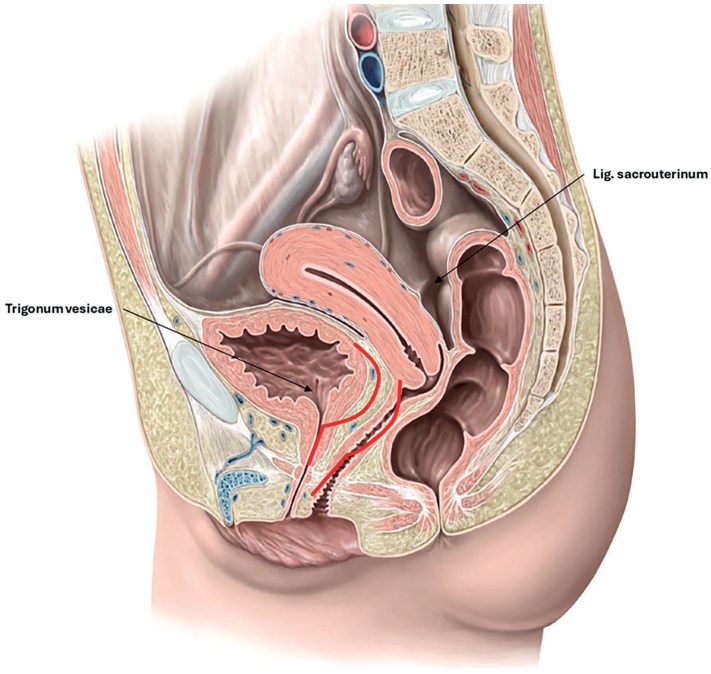


**Figure 1.** Hypothetical assumptions about how the anatomy of the trigonum vesicae and the anterior vaginal wall change with the descent of the uterosacral ligament (USL) and the anterior vaginal wall with the trigone of the bladder and the area of the meatus internus urethrae (red lines). The tensioning of the USL will restore the normal anatomical position

The main problem during that development phase was to find the best places for fixation of the tapes. The fixation at the sacrum led to a constriction of the sigmoid while the fixation on the back of the symphysis led to a limitation of the bladder volume.

The solution of that problem was found in the "bridge allegory" by Petros.

In 1993, Petros and Ulmsten[3] had presented that example in the "Integral Theory". They compared the position of the bladder and urethra on the vagina with a bridge which was hold up by the ropes of pillars in the front and in the back. The "rope" in front below the urethra was the pubourethral ligament (PUL) and the ropes holding the street on the back were the uterosacral ligaments (USL).[3]

They proposed that UI was based on an impaired function ("laxity") of the PUL and USL ligaments and probably not a neurological disorder.[4,5] That implied that continence is based on the normal physiological anatomical function of these ligaments.

The replacement of the PUL with suburethral tapes was so effective to cure SUI that it became recommended in all guidelines for treatment of SUI.[6]

It was hypothesized that the replacement of the USL could than probably cure UUI. Therefore, it was decided to replace the left and right USL by tapes.[7]

The respective tapes were placed in the peritoneal fold of the USL and sutured to the vaginal stump and below the promontory (vagino-sacropexy). According to the previously used mesh the length was about 9 cm. Since the method should also be possible in patients with uterus it was decided that in these patients the anatomical attachment of the vagina at the cervix should remain untouched. Therefore, instead of a total hysterectomy a supracervical hysterectomy was performed and the tapes sutured to the stump (cervico-sacropexy).[8]

According to the previous experiences in the patients who were totally incontinent before posterior exenteration it was expected that all patients with UI would become continent after cervico- or vagino-sacropexy.

In 1996 a laparotomy to implant alloplastic tapes as replacement of the USL for the treatment of UUI was massively criticized. Therefore, the Ethical Committee of the University of Erlangen, Germany, agreed that these operations could only be done in patients who had signed the informed consent agreement together with a notary. Furthermore, the operations should only be done in patients younger than 65 years as previous experiences were based on patients <65 years at exenteration.

After 20 patients an intermediate analysis should be performed.

When the USL were replaced by the tapes it was realized that after the first 20 patients only 11 patients became continent again. They either reported that they were totally continent or that nothing had changed at all after the operation ("all or nothing"-effect).

According to the previous experiences that was unexpected.

However, according to the "bridge allegory" of the Integral Theory holding ropes at both sides of the bridge are necessary to hold up the street (achieve continence). Therefore, it was decided that in those patients who remained incontinent after the USL replacement (posterior pillar) the anterior pillar (PUL) should also be replaced by a suburethral tape.

It was expected that after the suburethral tape the SUI symptoms would disappear but the urgency symptoms would remain. However, after the trans-obturator taped (TOT) 4 of the 9 incontinent patients after cervico- or vaginosacropexy became continent and they reported that the stress as well as the urgency symptoms had disappeared ("all or nothing"). Five patients remained incontinent.

It was unexplained why patients remained incontinent after both surgeries. It was assumed that this was caused by the different personal data as birth rates, body weight or other factors. However, it could not be excluded that this was caused by the imprecisely defined length of the tapes, the inherent elasticity of the material of the intra-abdominal tapes, and different tensioning of the suburethral tapes.

## METHODS

Therefore, it was decided to standardize the surgical procedures as far as possible.

The exact length of the USL was unknown. Therefore, anatomical measurements were performed during examinations of corpses in the pathology. Considering the postmortal change of tissue the length of the USL was calculated between 8.5 and 9.5 cm.

Due to the uniform dimensions of the bony pelvis in women, it was possible to develop USL polyvinylidene fluoride-implants of identical length for all patients (Dynamesh-CESA: 9.3 cm, Dynamesh-VASA: 8.8 cm, Dahlhausen, Köln, Germany).[9] The fixation points of the implants (structures) on the sacrum and the vagina or cervix were also precisely defined and marked on the structures (Figures 2, 3).[10]

These standardized operations were named "CESA" or "VASA".

Furthermore, the placement of the TOT was described as "tension-free". The standardization of that description was tested in several studies by placing HEGAR-pins with different

diameters in the urethra and between the urethra and the tape. It turned out that the combination of a HEGAR 8 in the urethra and a HEGAR 4 between the urethra and the tape led to best results without narrowing of the urethra (TOT 8/4).[11]

The most important aspect of studies applying new treatments (medical or surgical) is the comparability of the same indication and the same treatment. Only when all patients had the same symptoms of UUI and got the identical treatment the results could be compared between patients and analysed.[12]

The way to define UUI had changed during the years from a previous diagnosis made by urodynamics to a diagnosis based on the subjective symptoms.

For the definition of UUI the questionnaire of the International Continence Society was used and adapted for the purposes of the study.[13] The definition of urgency UI was mainly based on the question of how patients react on the feeling of urgency while watching the news on TV. Two groups were separated: Those who could wait until the weather forecast or even longer were defined as continent.

Patients who had to go immediately because otherwise they lost urine on the way to the toilet were defined as "urgency urinary incontinent".

All patients were asked to determine the age at which they realized that they lost urine short after the urgency sensation (UUI).

The clinical results were controlled in interviews and documented in questionnaires during follow-up examinations.

Besides the usual clinical examinations, the patients were also examined vaginally in standing position, because they were not incontinent when they were in lying position.

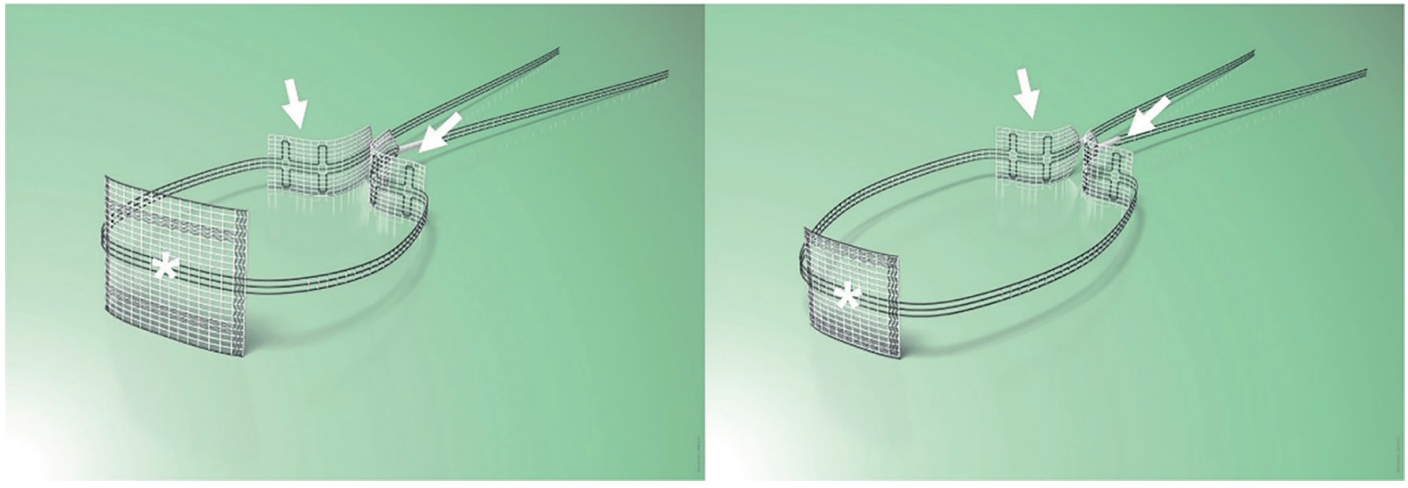

**Figure 2.** CESA and VASA structures. The arrows point to the suture sides on the sacral bone. The anterior part with the asterisk is fixed either on the cervix (left photo) or on the vaginal stump (right photo). Thereafter, the "arms" of the structure replacing the uterosacral ligament (USL) –the part between the fixation sides– are pulled through the peritoneal fold of the USL towards promontory. The CESA ligament is 0.5 cm shorter than the VASA ligament

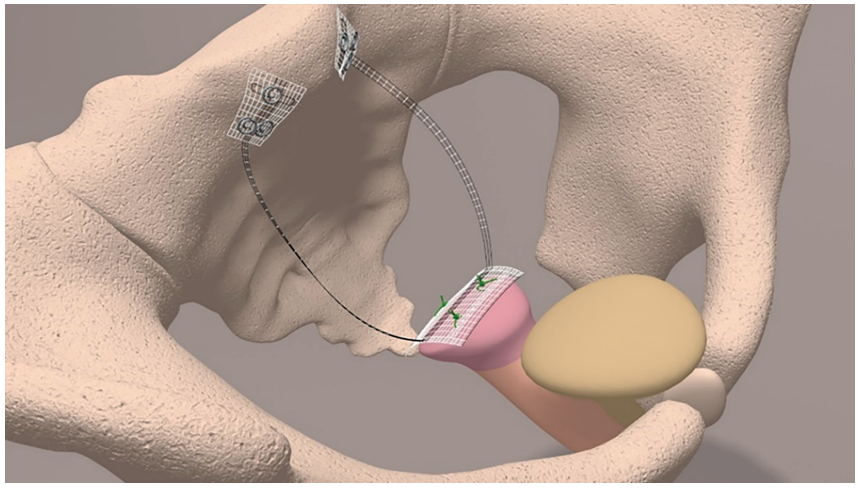

**Figure 3.** Schematic representation of the CESA structure *in situ*. Fixation of the structure to the cervical stump and the "uterosacral ligament arms" to the promontory. The fixation sides are marked on the structure

Patients were interviewed about their family history of incontinence, especially about her mother. Additionally, patients were asked about her age at menopause and if they had hormone replacement therapy (HRT) and for how long.

However, it had already been noticed in a previous Clinical Phase 1 study that several patients, even patients with mixed urinary incontinence (MUI), became continent just after CESA or VASA and did not need a TOT anymore.[7] Therefore, it was decided to begin treatment with the abdominal part (laCESA, laVASA) and add the vaginal part (TOT 8/4) three months later if needed.[7,14,15]

The study was approved by the Ethical Committee of the University of Köln, Germany. The age limitation for surgery (<65 years) and the signing of the informed consent by a notary were cancelled.

## RESULTS

Since 2010, 326 patients with UUI who failed conservative treatments were operated by CESA or VASA in a clinical Phase II study (since 2016 laparoscopically: laCESA or laVASA).[15]

All patients reported that UI had begun with urine loss during coughing or sneezing or another comparable stress between the ages of 40 and 45 years (SUI).

All patients described the UI as a continuous development from SUI to UUI – never the other way round (first UUI then SUI).

Most patients experienced menopause at the age of 50 years.

After menopause or cessation of ovarian function, patients made the experience that after the urge to void they sometimes lost urine before reaching the toilet. After about 2 to 4 years, they experienced urine loss already upon standing up from a chair or on the way to the toilet (UUI).

During the digital examination in the standing position in all patients a slight prolapse of the vaginal wall in the suburethral and the sub-bladder part of the vagina was felt.

Patients who got estrogen or estrogen/gestagen combinations (HRT) before menopause became incontinent only after they had discontinued the HRT, some of them only between the ages of 60 and 70 years.

97% of patients reported that their mother also had UUI. As far as they knew that was probably at the same age when their own incontinence began.

The overall CR after laCESA was 39% and after laVASA 33%.[14] The additional TOT led to continence in between 35% and 45% of the remaining incontinent patients.[14] That led to overall continence rates (CR) between 67% and 87% in these patients (Figures 4, 5).

Multivariate analyses revealed that the difference in the CR after laCESA and laVASA was dependent on the age of patients at surgery. Patients younger than 60 years had significantly higher CR than the older patients. The CR after a TOT; however, was independent of the age at surgery.[14]

Overall, between 76% (laVASA) and 87% (laCESA) of patients under 60 years of age regained continence by the replacement of the USL and a suburethral tape (TOT 8/4).

In older patients (older than 60 years at surgery) CR ranged between 56% and 67%.[14]

The CR after tensioning the vagina by laCESA/laVASA were between 46% and 58% in 50-year-old patients, however only between 16% and 20% in patients older than 70 years. That

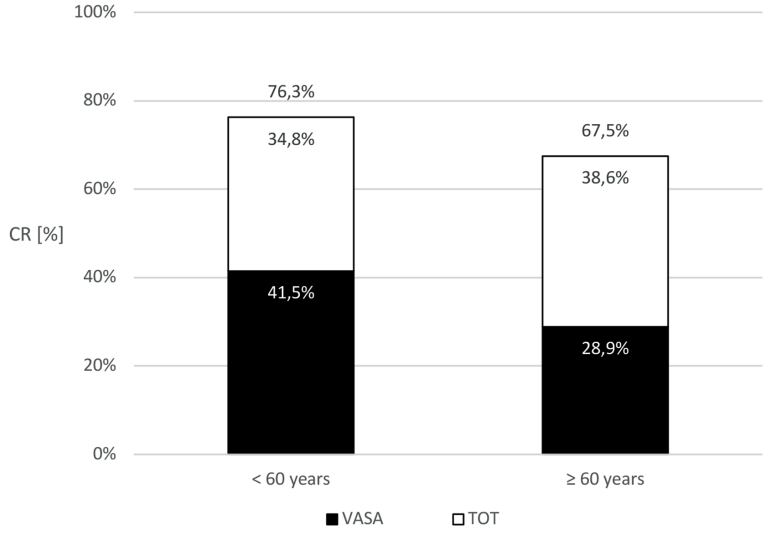


**Figure 4.** Continence rates (CR) after VASA and trans-obturator taped (TOT) 8/4 depending on the age at the time of surgery. The CR between <60 years and >60% were significant ($p$<0.01) for CESA-not for TOT 8/4

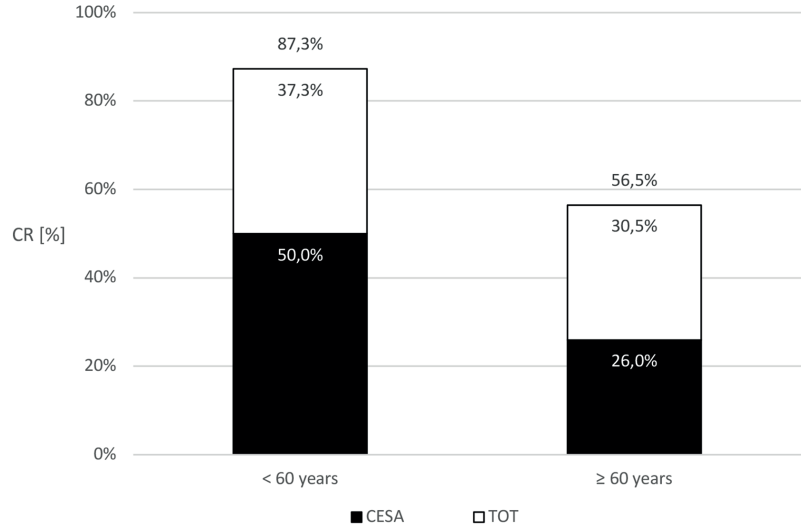


**Figure 5.** Continence rates (CR) after CESA and trans-obturator taped (TOT) 8/4 depending on the age at the time of surgery. The CR between <60 years and >60% were significant ($p$<0.01) for CESA-not for TOT 8/4

difference was statistically significant.[14] An additional TOT 8/4 led to continence in between 43% and 40% of the still incontinent patients irrespective of age at surgery.

The CR of an additional TOT 8/4 was between 40% and 43%.[14]

## DISCUSSION

The studies demonstrated that patients with UUI can get continent again after surgical replacement of the USL and PUL as predicted in the Integral Theory. It further demonstrated that the results of surgery in terms of CR were critically dependent on age of patients especially on the years after menopause.

### Surgery

The Integral Theory used the "bridge allegory" to explain the function of the ligaments for continence.[3] The vagina is held and tensioned by the ropes in front (PUL) and in the back (USL). The importance of the PUL for SUI had been shown impressively, however, the second aspect of the Integral Theory– the importance of the suspension of the vagina by the USL–was not pursued clinically.

However, the reason for this dysfunction of the ligaments especially the PUL leading to SUI and the occurrence in the early fourth decade of life remained unexplained.

Since all patients had the same symptoms of UUI and all had the same surgical procedures with structures of identical length sutured to the same defined anatomical sides the reason for failure to establish continence could be statistically analysed.

After meticulous statistical analyses it turned out that the only statistically important factor for CR after surgery was the age of the patients at surgery.[14]

The surgical elevation and tensioning of the vagina by laCESA or laVASA probably leads to the compression of the meatus (Figure 1). However, the number of patients who regained continence after laCESA or laVASA decreased significantly with increasing age after menopause.

That age dependency of CR was not observed after the suburethral tape (TOT 8/4). While a suburethral tape can cure SUI, this method alone is not capable of curing UUI. This observation strongly indicates that the effect of the suburethral tape is restricted to an area below the meatus internus which is not affected by decreasing estrogen levels. The results implicate that a suburethral tape (e.g., TOT) can probably only be effective for treatment of SUI and UUI as long as the trigone and the vagina are not submitted to the hypoestrogenic tissue remodelling and the USL are still intact.

### Age Dependence

UI usually begins around in the early forties of life with urine leakage during coughing or sneezing (SUI).

After menopause –at about 50 years of age– patients realize that if they wait too long after the urgency, they may lose urine before reaching the toilet (UUI).

This continuous development ("pathophysiological continuum") between the ages of 40 years to 55 years from SUI via MUI to UUI leads to the hypothesis of a common underlying etiology which is caused by biological changes during that phase of a woman's life.[16,17]

## Hormone Dependance

The progression from SUI to UUI (via MUI) after menopause led to the hypothesis that estrogens play a major role in that respect. That was first described by the North American Society of Menopause and the International Society for the Study of Women's Sexual Health.[16] That association between urgency and urgency UI is so close according to the opinion of these Societies that they put both forms of incontinence as symptoms of a common syndrome of menopause (genito-urinary syndrome of menopause). They conclude that urgency and UUI can be attributed to the decline of estrogens after menopause.[16,18] According to that hypothesis the respective important organs or structures important for continence must have estrogen receptors (ER).

It has been shown that ER are expressed in the uterus, the endometrium and the vaginal epithelium.[19] That could be explained by the norma menstrual cycle (Figure 6).[19,20]

However, ER were also found in comparable amounts in the trigone of the bladder and the urethral inner lining.[21]

On first view that seems incomprehensible what estrogens should exert in the bladder.

It is probably the ability of estrogens to form elastic hyaline structures which make them important for the trigone and the urethra. Elasticity is the ability to stretch and to contract. That elasticity is of crucial importance during pregnancy not only for the female genitalia but also for the female bladder.[21,22]

Beside the increase in uterine size during pregnancy the USL must increase their elasticity and length to hold the uterus during pregnancy and at birth. The elastic capacity of the vagina is enormous considering that until delivery the circumference of the vagina must stretch to approximately 38 cm for the passage of the child.[22] When the child during birth reaches the parts of the vagina where the bladder trigone is adherent, not only the vaginal wall must stretch but also the trigone of the bladder in order to prevent tearing of the bladder during the passage of the child's head. Finally, the urethra must also be able to stretch longitudinally during the child's exit out of the birth canal. Therefore, these structures also need to have ER.

During pregnancy, parallel to the child´s growth the concentrations of estrogens increase massively.[23] These increasing amounts of estrogen needed for uterine growth and the other mentioned anatomical structures until birth cannot be produced by the ovaries and therefore becomes a significant task of the placenta. The increase in estrogen levels during pregnancy, particularly in the last trimester, supports the assumption that estrogens are crucial for the aforementioned increase in tissue elasticity.[23,24]

It can be assumed that the declining levels of estrogens before menopause and the missing estrogens thereafter will lead to a loss of elasticity in all of these estrogen-sensitive tissues. That can lead to laxity or a shrinkage of the respective tissues.[3,18]

If UUI is generally based on estrogen deficiency and SUI and MUI have the same etiology than UI starts with the laxity of the PUL leading to SUI. That is in accordance with the "Integral

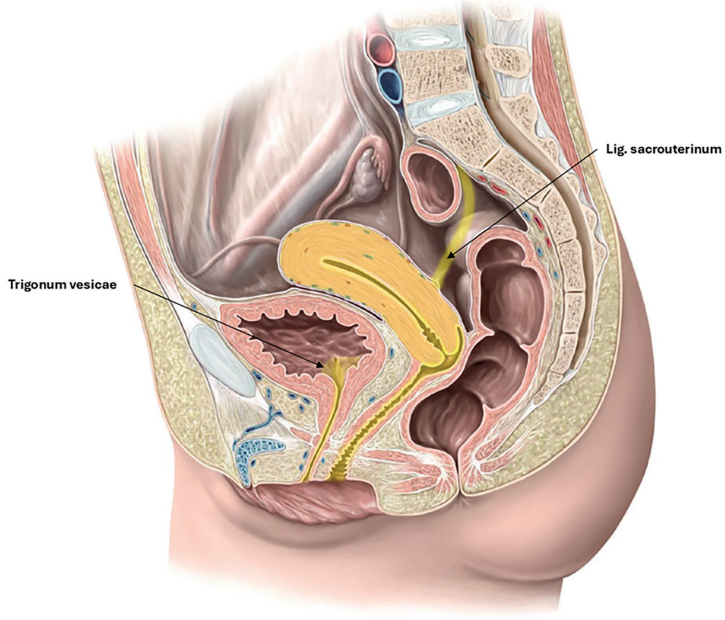


**Figure 6.** Distribution of estradiol receptors (ER) in the pelvis. ERs are primarily located in the uterosacral ligament, vaginal wall, endo-and myometrium, urethra, and trigonum vesicae

Theory". It seems reasonable to assume that the PUL and the lower trigone are (one of) the first genital structures affected by estrogen deficiency.[25]

With the increasing period of estrogen deficiency after menopause the elasticity of the trigone will continuously decrease leading to a laxity of the trigone which does not allow further stretching when the bladder fills. Therefore, the time interval between the sensation of urgency which is induced by the stretch receptors in the bladder wall and urine discharge also shortens continuously. The additional effect of the laxity of the USL will lead to a reduced suspension and a slight prolapse of the vagina. That laxity puts the meatus internus in a more horizontal axis especially when standing up (Figure 2). That assumption was confirmed by the clinical examination of the patient in standing position.

The hypothesis that estrogens are important for continence is supported by the observation that patients with HRT only became incontinent when they stopped HRT. Some of these patients stopped HRT at the age of 65 or 70 years. They remained continent until that age.

The reports in literature where no effect of HRT on UI was reported suffered from the fact that HRT only started after menopause when patients were suffering from menopausal symptoms.[25] Nevertheless, these studies demonstrate that the tissue remodelling after menopause is not reversible by estrogens. Therefore, HRT should be started at the first symptoms of SUI. If the patient accepts a suburethral tape in that situation it would be interesting to evaluate if the further development of continence/incontinence.

The "bridge allegory" of the Integral Theory led to the development of structures which replace the function of the ropes in front (PUL) and in the back (USL). The identical surgical procedures in every woman suffering from UUI allowed further insights in the etiology, pathogenesis and treatment of UI. The results obtained demand further scientific and clinical evaluation.

## CONCLUSION

UI is a genetically predisposed disorder. It follows a symptomatically and chronological sequence starting with SUI leading to UUI after menopause.

That pathogenesis is hypothetically caused by the decline of estrogen levels during the pre-, peri- and postmenopausal phases of life. UI is based on the uncontrolled loss of urine through the meatus internus of the bladder. The meatus is the lower angle of the trigone of the bladder, the area between the orifices of the ureters and the meatus internus of the urethra. The trigone is the only part of the bladder which expresses ER, indicating that estrogen is needed for the physiological function of the trigone. This physiological function is elasticity in order to stretch that part of the bladder during filling and to contract at the meatus when stress is exerted.

With decreasing estrogen levels, the elasticity diminishes what leads to laxity of the PUL and USL in the genetically predisposed women.

Furthermore, when the bladder fills, the trigone continuously loses its elasticity leading to an ever-shorter interval between urgency and urine loss.

The clinical consequence is uncontrolled loss of urine after the urge sensation (UUI).

UUI can surgically be cured by the standardized replacement of the lax USL by laCESA or laVASA and the replacement of the PUL by a TOT 8/4. However, the CR decrease significantly after menopause during each decade thereafter. That indicates that the postmenopausal hypoestrogenic tissue remodelling probably at the trigone cannot be reversed by these surgical procedures anymore.

It was an important observation that patients who had a previous HRT starting before menopause developed UUI only when they stopped HRT. Therefore, early estrogen substitution can probably prevent the tissue remodelling leading to UUI.

HRT should start at the same age as SUI started in the mother. HRT should be continued lifelong. The methods of application, preparation, or dosage of the estrogen should be studied in future clinical trials by gynecological endocrinologists.

## FOOTNOTES

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## DISCLOSURES

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## REFERENCES

1. JÄger W, Ludwig S, Neumann E, Mallmann P. Evidence of common pathophysiology between stress and urgency urinary incontinence in women. In Vivo. 2020; 34: 2927-32.
2. Jäger W, Brakat A, Ludwig S, Mallmann P. Effects of the apical suspension of the upper vagina by cervicosacropexy or vaginosacropexy on stress and mixed urinary incontinence. Pelviperineology. 2021; 40: 32-8.

3. Petros PE, Ulmsten UI. An integral theory and its method for the diagnosis and management of female urinary incontinence. Scand J Urol Nephrol Suppl. 1993; 153: 1-93.

4. Arya NG, Weissbart SJ. Central control of micturition in women: brain-bladder pathways in continence and urgency urinary incontinence. Clin Anat. 2017; 30: 373-84.

5. Steers WD. Pathophysiology of overactive bladder and urge urinary incontinence. Rev Urol. 2002; (Suppl 4): S7-18.

6. Schultz-Lampel D. Die neue leitlinie harninkontinenz der frau" AWMF-register nr: 015-091 – das sollten sie wissen. J. Urol. Urogynäkol. 2023; 30: 15-24.

7. Jäger W, Mirenska O, Brügge S. Surgical treatment of mixed and urge urinary incontinence in women. Gynecol Obstet Invest. 2012; 74: 157-64.

8. Page AS, Page G, Deprest J. Cervicosacropexy or vaginosacropexy for urinary incontinence and apical prolapse: a systematic review. Eur J Obstet Gynecol Reprod Biol. 2022; 279: 60-71.

9. Bent AE, Ostergard DR, Zwick-Zaffuto M. Tissue reaction to expanded polytetrafluoroethylene suburethral sling for urinary incontinence: clinical and histologic study. Am J Obstet Gynecol. 1993; 169: 1198-204.

10. Ludwig S, Göktepe S, Mallmann P, Jäger W. Evaluation of different 'tensioning' of apical suspension in women undergoing surgery for prolapse and urinary incontinence. In Vivo. 2020; 34: 1371-5.

11. Ludwig S, Stumm M, Mallmann P, Jager W. TOT 8/4: a way to standardize the surgical procedure of a transobturator tape. Biomed Res Int. 2016; 2016: 4941304.

12. Stark M, Gerli S, Di Renzo GC. The importance of analyzing and standardizing surgical methods. J Minim Invasive Gynecol. 2009; 16: 122-5.

13. Hofmann R, Wagner U. Inkontinenz- und Deszensuschirurgie der frau. SpringerLink Bücher; Springer Berlin Heidelberg. Berlin: Heidelberg; 2015.

14. Jäger W, Päffgen A, Hagemeier A, Mallmann P. The surgical treatment of advanced urinary incontinence. Arch Obstet Gynecol. 2024; 5: 95-106.

15. Ludwig S, Morgenstern B, Mallmann P, Jäger W. Laparoscopic bilateral cervicosacropexy: introduction to a new tunneling technique. Int Urogynecol J. 2019; 30: 1215-7.

16. Portman DJ, Gass ML; Vulvovaginal Atrophy Terminology Consensus Conference Panel. Genitourinary syndrome of menopause: new terminology for vulvovaginal atrophy from the International Society for the Study of Women's Sexual Health and the North American Menopause Society. Menopause. 2014; 21: 1063-8.

17. Greendale GA, Lee NP, Arriola ER. The menopause. Lancet. 1999; 353: 571-80.

18. "The 2022 Hormone Therapy Position Statement of The North American Menopause Society" Advisory Panel. The 2022 hormone therapy position statement of The North American Menopause Society. Menopause. 2022; 29: 767-94.

19. Scharl A, Vierbuchen M, Graupner J, Fischer R, Bolte A. Immunohistochemical study of distribution of estrogen receptors in corpus and cervix uteri. Arch Gynecol Obstet. 1988; 241: 221-33.

20. Smith P. Estrogens and the urogenital tract. Studies on steroid hormone receptors and a clinical study on a new estradiol-releasing vaginal ring. Acta Obstet Gynecol Scand Suppl. 1993; 157: 1-26.

21. Blakeman PJ, Hilton P, Bulmer JN. Oestrogen and progesterone receptor expression in the female lower urinary tract, with reference to oestrogen status. BJU Int. 2000; 86: 32-8.

22. Brons JT, van Geijn HP, Bezemer PD, Nauta JP, Arts NF. The fetal skeleton; ultrasonographic evaluation of the normal growth. Eur J Obstet Gynecol Reprod Biol. 1990; 34: 21-36.

23. Hobson BM. Production of gonadotrophin, oestrogens and progesterone by the primate placenta. Adv Reprod Physiol. 1971; 5: 67-102.

24. Tal R, Taylor HS. Endocrinology of Pregnancy. 2021 Mar 18. In: Feingold KR, Ahmed SF, Anawalt B, et al. (editors). Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000–.

25. Palacios S, Castelo-Branco C, Currie H, et al. Update on management of genitourinary syndrome of menopause: a practical guide. Maturitas. 2015; 82: 308-13.

26. Easton BT. Is hormone replacement therapy (estrogen plus progestin) effective for the treatment of urinary incontinence in postmenopausal women? J Fam Pract. 2001; 50: 470.