Laursen SH[1], Hansen SG[2], Taskin MB[3], Chen M[4], Wogensen L[5], Nygaard JV[4], Axelsen SM[1]. ***Electrospun nanofiber mesh with connective tissue growth factor and mesenchymal stem cells for pelvic floor repair - long-term study***

[1]Department of Gynaecology and Obstetrics, Aarhus University Hospital, Denmark, [2]Department of Medicine, Soenderborg Hospital, Denmark, [3]Leibniz Institute of Polymer Research Dresden, Max Bergmann Center of Biomaterials Dresden, Germany, [4]Department of Biological and Chemical Engineering - Medical Biotechnology, Aarhus University, Denmark, [5]Deans Office Health, Aarhus University, Denmark

Purpose: We aim to develop a safe mesh-based approach to pelvic organ prolapse (POP) using biodegradable meshes with growth factor and stem cells. With this study we wish to investigate the long-term outcome in aging tissue.

Methods: In an abdominal repair model, electrospun meshes made from polycaprolactone (PLC) with connective tissue growth factor (CTGF) and stem cells were implanted in a group of elderly and heavier female rats. Averagely, the meshes were removed 53 weeks after implantation. Mesh areas were evaluated for collagen mRNA by qPCR, collagen protein by Western blotting, for the histological appearance, and for the biomechanical properties. Results were compared to results from a previous study on a group of younger rats having the same mesh implanted for 24 weeks.

Results: The 53-week group differed from the 24-week group in: 1) a decrease in collagen III in the 53-week group, 2) a strong reduction in foreign body giant cells response in the 53-week group, and 3) altered histological appearance in the 53-week group. We found comparable biomechanical properties between the two groups, despite the mean tissue stiffness, which was higher, although not significantly, in the 53-week group. Lastly, we were still able to identify mesh components 53 weeks after implantation.

Discussion: Our study shows that a mesh-based approach with CTGF-coated electrospun PCL meshes with stem cells exhibit sufficient support, no mesh-related complications and biocompatibility longterm in a rat abdominal repair model. However, our study groups were heterogenic and small. Moreover, the rat abdominal repair model is different from POP pathology in women, and the meshes was not fully degraded at the time of evaluation. Therefore, further evaluation in a larger animal with POP-like pathology over an even longer period is needed. Still, our use of older and heavier rats in this study try to mimic post-menopausal women, the major group to undergo pelvic floor repair. Altogether, the positive findings in our study might lead the way for safer mesh-based approaches for pelvic organ prolapse.

Christoffersen T[1], Kornholt J[1], Riis T[1], Sonne DP[1], Sonne J[1], Klarskov N[2]. ***Effect of reboxetine and citalopram on anal opening pressure: A randomized, double-blind, placebo-controlled crossover study in healthy women***

[1]Department of Clinical Pharmacology, Bispebjerg and Frederiksberg Hospital, [2]Department of Gynecology and Obstetrics, Herlev and Gentofte Hospital

Background and objectives: Drugs that enhance the anal sphincter function constitute a potential pharmacological treatment strategy for fecal incontinence. Anal acoustic reflectometry (AAR) is a new method to assess anal sphincter function, which has shown ability to detect pharmacologically induced changes in the anal opening pressure (AOP). The aim of this study was to assess the effect of citalopram (selective serotonin reuptake inhibitor) and reboxetine (noradrenaline reuptake inhibitor) on AOP in healthy females.

Materials and methods: In a randomized, double-blind, placebo controlled three-period crossover study in 24 healthy women, we measured AOP during rest and squeeze with AAR after a single dose of citalopram (40 mg), reboxetine (8 mg) or placebo. AOP was measured at estimated time of peak plasma concentration of the study drugs. The washout period was at least 8 days.

Results: There were no dropouts and no serious adverse events. Most frequent adverse events were nausea, disturbed sleep, dizziness and headache. Compared with placebo, reboxetine increased resting AOP with 23.4 cmH_2O (95% CI 15.1-31.6, p<0.001) and squeezing AOP with 23.4 cmH_2O (95% CI 14.6-32.2, p<0.001). Citalopram did not increase the AOP significantly compared with placebo (3.9, 95% CI -4.1-12.4, p=0.4 [during rest] and 4.2 95% CI -4.9-12.7, p=0.5 [during squeeze].

Conclusion: Single dose reboxetine 8 mg increased the placebo-corrected AOP significantly, suggesting that reboxetine or other noradrenalin reuptake inhibitors may be efficacious in the treatment of fecal incontinence. However, clinical trials in patients with fecal incontinence are needed to evaluate the potential clinical benefit.

Christoffersen T[1], Kornholt J[1], Riis T[1], Sonne DP[1], Sonne J[1], Klarskov N[2]. ***Effect of single doses of citalopram and reboxetine on urethral pressure: a randomized, double-blind, placebo- and active-controlled three-period crossover study in healthy women***

[1]Department of Clinical Pharmacology, Bispebjerg and Frederiksberg Hospital, [2]Department of Gynecology and Obstetrics, Herlev and Gentofte Hospital

Background and aim: Urethral closure function is essential for urinary continence in women and decreased urethral pressure is associated with stress urinary incontinence (SUI). For decades, the effects of serotonergic drugs on central neural control of urethral closure have been investigated and discussed. Epidemiological studies suggest that use of selective serotonin reuptake inhibitors, such as citalopram, is associated with SUI. However, literature findings are conflicting. This study aimed to evaluate citalopram's effect on opening urethral pressure (OUP) in healthy women.

Material and methods: A randomized, double-blind, placebo- and active-controlled, crossover study in 24 healthy women. On three study days, which were separated with eight days washout, the subjects received single doses of either 40 mg citalopram, 8 mg reboxetine, or placebo. At estimated time of peak plasma concentration of the study drugs, OUP was measured with urethral pressure reflectometry under both resting and squeezing condition of the pelvic floor.

Results: Compared to placebo, citalopram increased OUP by 6.6 cmH_20 (95% confidence interval [CI] 0.04-13.1, p=0.048) in resting condition. In squeezing condition, OUP increased by 7.1 cmH_20 (95% CI 1.3-12.9, p=0.01). Reboxetine increased OUP by 30.0 cmH_20 in resting condition compared to placebo (95% CI 23.5-36.5, p<0.001), and 27.0 cmH_20 (95% CI 21.2-32.8, p<0.001) in squeezing condition.

Conclusion: Citalopram increased OUP slightly compared to placebo suggesting that SSRI is unlikely to induce or aggravate SUI. Conversely, reboxetine induced a substantial placebo-corrected increase in OUP. Further research might explore the clinical benefit of reboxetine in treatment of women with both depression and SUI.

Juhl C[1], Bjørk J[1], Glavind K[1]. ***Treatment of stress urinary incontinence with polyacrylamide hydrogel (Bulking) in an office setting: patient perspectives.***

[1] Dep. of gynecology and obstetrics, Aalborg University Hospital, Denmark.

Introduction: Office setting (OS) provides the opportunity for surgeons to perform specific procedures more efficiently than in a day case operating theatre (OR). Consequently, health care systems are interested in altering surgical services from OR to OS. The impact on patient's satisfaction is more challenging to estimate. Bulking procedure (BP) is an intervention for urinary stress incontinence. It was originally performed in the OR in general anesthesia (GA) or sedation. Today, the procedure is mostly done in local anesthesia and the opportunity to alter the setting from OR to AS became possible. The aim of this study was to assess patient satisfaction with the change from OR to OS.

Methods: From 15th of September 2020 to 1st of June 2021, 115 women underwent BP in the OS. Follow-up three months post-surgery for quality assurance is mandatory. Concurrently to the routine post-surgery follow-up, the OS experience was assessed. Results: A total of 95.6 % (110/115, $P<0.001$) preferred the BP being performed in the OS. Reasons were: simple/accessible and short waiting time 61.8% (68/110), less nervousness 42.7% (47/110) and felt safer 44.5% (49/110). On a Visual Analogue Scale (VAS) from 0 to 10, 37.4% (43/115) considered short waiting time important with VAS 10, and 81.7% (94/115) rated short waiting time ≥ VAS 5.

Conclusions: The OS provides a patient friendly and comfortable place for the BP and is generally preferred by the patient over the OR. Important for the preference is the accessibility and minimal waiting time. The OS is therefore both convenient and efficient for surgeon and patient.

Aagesen AH[1,2], Klarskov N[1,2], Gradel KO[3,4], Husby KR[1,2]. ***Pelvic Organ Prolapse as a result of Hysterectomy on Benign Indication – A National Matched Cohort Study***

[1]Dept of Obstetrics and Gynecology, Copenhagen University Hospital – Herlev and Gentofte, Copenhagen, Denmark, [2]Dept of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark. 3Center for Clinical Epidemiology, Odense University Hospital, Odense, Denmark, [4]Research Unit of Clinical Epidemiology, Dept of Clinical Research, University of Southern Denmark, Odense, Denmark

Background: Hysterectomy on benign indications is a frequent procedure but increases the risk of pelvic organ prolapse (POP) surgery. POP reduces life quality and lifetime risk of surgery is 18,7%. This study wishes to investigate POP-surgery after hysterectomy and address how parity influences this as well as which compartments are affected.

Material and methods: This was a cohort study based on Danish registries. We identified women born from 1947 – 2000. Women who were hysterectomized on benign indication were matched 1:5 with a non-hysterectomized reference on age and calendar year. The women were followed from 1977-2018. We excluded women who emigrated had POP-surgery prior to their hysterectomy or had a gynaecological cancer diagnosed up till 30 days after hysterectomy. The risk of pelvic organ prolapse surgery after hysterectomy was calculated using Cox's regression adjusting for age, income, education, and parity.

Results: We included 80,444 hysterectomized women and 396,303 references. The cohort was followed for an average of 15 years. The risk of POP-surgery was significantly higher for hysterectomized women, HR 1.4 95% CI [1.3;1.5]. When analysed by compartment the risk of a posterior compartment prolapse was HR 2.2 [2.0;2.3] and risk of anterior compartment prolapse HR 1.1 [1.0;1.1]. The risk of subsequent POP-surgery increased with parity and were 40% higher in hysterectomised women for all parities compared to non-hysterectomized women.

Conclusions: The study showed an increased risk of POP following hysterectomy on benign indications. Risk of posterior compartment prolapse was highest and parity amongst hysterectomized further increased the risk of POP.

Husby KR[1,2], Gradel KO[3,4], Klarskov N[1,2]. ***Endometrial cancer after Manchester procedure: A nationwide cohort study***

[1] Department of Obstetrics and Gynecology, Herlev and Gentofte University Hospital, [2] Faculty of Health and Medical Sciences, University of Copenhagen, [3] Center for Clinical Epidemiology, Odense University Hospital, [4] Research Unit of Clinical Epidemiology, Department of Clinical Research, University of Southern Denmark

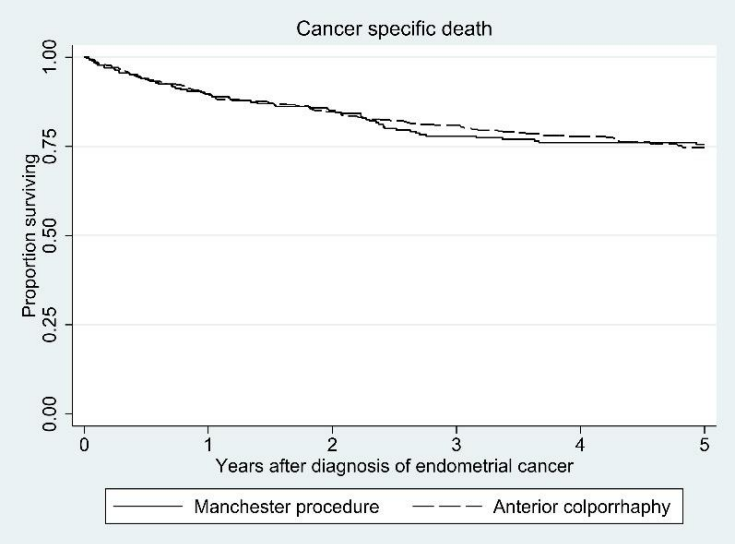
Background: The Manchester procedure (MP) may be the best way to treat uterine prolapse due to fewer recurrences compared to hysterectomy with suspension and sacrospinous hysteropexy. However, it is unknown how it affects the risk and prognosis of endometrial cancer.

The aim of this study was to investigate the risk and prognosis of endometrial cancer for women operated with MP compared to women operated with anterior colporrhaphy (AC).

Materials and methods: We conducted a historical cohort study based on the nationwide Danish registers. We identified all Danish women born 1947–2000 and living in Denmark during 1977–2018. We included women operated with MP during 1977–2018. Women operated with AC were included as reference group. We performed Cox regressions to analyze the risk of endometrial cancer and the risk of death. The models were adjusted for age, calendar year, income level, and parity. A Chi-Square test for trend was performed to compare the diagnostic stage for the two groups of women.

Results: This study cohort included 23,935 women operated with MP and 51,008 operated with AC. The adjusted hazard ratio (HR) for endometrial cancer was 1.00 [95% confidence interval (CI) 0.86-1.16] and the HR for cancer specific death was 0.86 [95% CI 0.65-1.15]. The Kaplan Meier survival curve for cancer specific death showed 5-year survival rates of 77% after Manchester and 75% after anterior colporrhaphy (fig). The stage of the cancer at time of diagnosis was not significantly different between the two groups (p=0.18).

Conclusions: MP did not alter the risk or prognosis of endometrial cancer.



Mørch EJ[1, 2], Perslev K[2], Wrønding T[3], Aabakke A[4, 5], Jangö H[2, 6]. *Counselling women with obstetric anal sphincter injury – risk of recurrence and the influence of mode of second delivery on subsequent anal incontinence – a systematic review and meta-analysis*

[1] Faculty of Health and Medical Science, University of Copenhagen, Denmark, [2] Department of Obstetrics and Gynecology, Herlev University Hospital, Borgmester Ib Juuls Vej 1, 2730 Herlev, Denmark, [3] Department of Obstetrics and Gynecology, Amager-Hvidovre Hospital, Denmark, [4]Department of Obstetrics and Gynecology, Copenhagen University Hospital - Holbæk, Denmark, [5] Department of Obstetrics and Gynecology, Copenhagen University Hospital - Nordsjælland – Hillerød, Denmark, [6] Department of Clinical Medicine, University of Copenhagen, Denmark

Introduction: Obstetric anal sphincter injury (OASI) is a severe complication of vaginal delivery. Up to 50% of women with OASI will experience anal incontinence at long-term. However, it is uncertain whether an elective cesarean section in the second pregnancy following OASI decreases the risk of anal incontinence. The objective of this study was to estimate the risk of recurrent OASI in a subsequent pregnancy after first delivery with OASI and to determine if mode of delivery in the subsequent pregnancy has an impact on development or worsening of anal incontinence.

Material and methods: Literature searches were made in PubMed, Cochrane and Embase in November 2021. One search regarded the risk of recurrent OASI, and the other regarded mode of delivery in women with a previous OASI and its effect on subsequent anal incontinence. Studies were screened and study quality was assessed using "SIGN – Methodology Checklist".

Results: Twelve studies (including 2 609 580 women) were included in the meta-analysis on risk of recurrent OASI. OASI in the first delivery increased the risk of recurrent OASI in the second delivery fivefold compared to women without previous OASI (OR 4.7 (95% confidence interval (CI) 3.7-5.7)). The overall risk of acquiring a recurrent OASI was 5.9% (95% CI 5.8-6.1%).

Four studies (including 2 160 women) were included in the meta-analysis assessing the effect of mode of subsequent delivery on anal incontinence. The risk of anal incontinence was non-significantly increased in women with a second vaginal delivery OR 1.2 (95% CI 0.9-1.5).

Conclusions: We found an increased risk of recurrent OASI in the second delivery for women with a previous OASI, compared to women without previous OASI. The risk of new onset or worsening of anal incontinence was not associated with mode of the second delivery. Women with previous OASI should be informed about the increased risk of recurrence and that elective cesarean section is not necessarily protective against anal incontinence.

Perslev K[1], Mørch EJ[2], Jangö H[1,2]. ***Increased risk of obstetric anal sphincter injury in women undergoing vaginal delivery after caesarean section: A systematic review and meta-analysis.***

[1] Department of Obstetrics and Gynecology, Herlev University Hospital, Herlev, Denmark. [2] Faculty of Health and Medical Science, University of Copenhagen, Denmark.

Objective: To evaluate whether there is increased risk of OASI in VBAC compared to primiparous women.

Background: There is increased focus on obstetric anal sphincter injury (OASI) and there are several well-established risk factors such as birth weight, instrumental delivery, and median episiotomy. Some studies have found increased risk of OASI in women delivering vaginally after a previous caesarean section (VBAC).

Metode: The results in this meta-analysis are based on a literature search performed PubMed, Embase, and Cochrane databases. All studies with data on both primiparous women and women undergoing VBAC were included. All included studies were evaluated using the "SIGN – methodology checklist" to verify if the quality was acceptable. This systematic review included 22 articles conducted in 11 countries over 19 years. Included studies were analysed using RevMan version 5.4.

Results: We found increased risk of OASI in the VBAC group; 8.2 % (95% CI 8.1-8.3) compared to 6.6 % (95% CI 6.5-6.6) in primiparous women. Correspondingly, the meta-analysis revealed increased risk for OASI in the VBAC group, OR 1.3 (95 % CI 1.1-1.4). Eight sub-analyses were conducted to evaluate the robustness of the main result and all found significantly higher risk of OASI in the VBAC group compared to primiparous women.

Conclusion: There is a significantly increased risk of OASI in women undergoing VBAC compared to primiparous women.