Dr. Tanja Hülder, Frauenklinik/Beckenbodenzentrum, KSSG

VAGINALE NETZE NACH DER FDA-WARNUNG – WO STEHEN WIR HEUTE?

Inhalt

- Pelvic organ prolapse
- Operative Therapieoptionen
- FDA-Warnung
- Aktuelle Literatur
- Zusammenfassung
- In eigener Sache

Epidemiologie

Obstet Gynecol 1997

Epidemiology of Surgically Managed Pelvic Organ Prolapse and Urinary Incontinence

AMBRE L. OLSI ... OM, MD,
JOYCE C. COLL

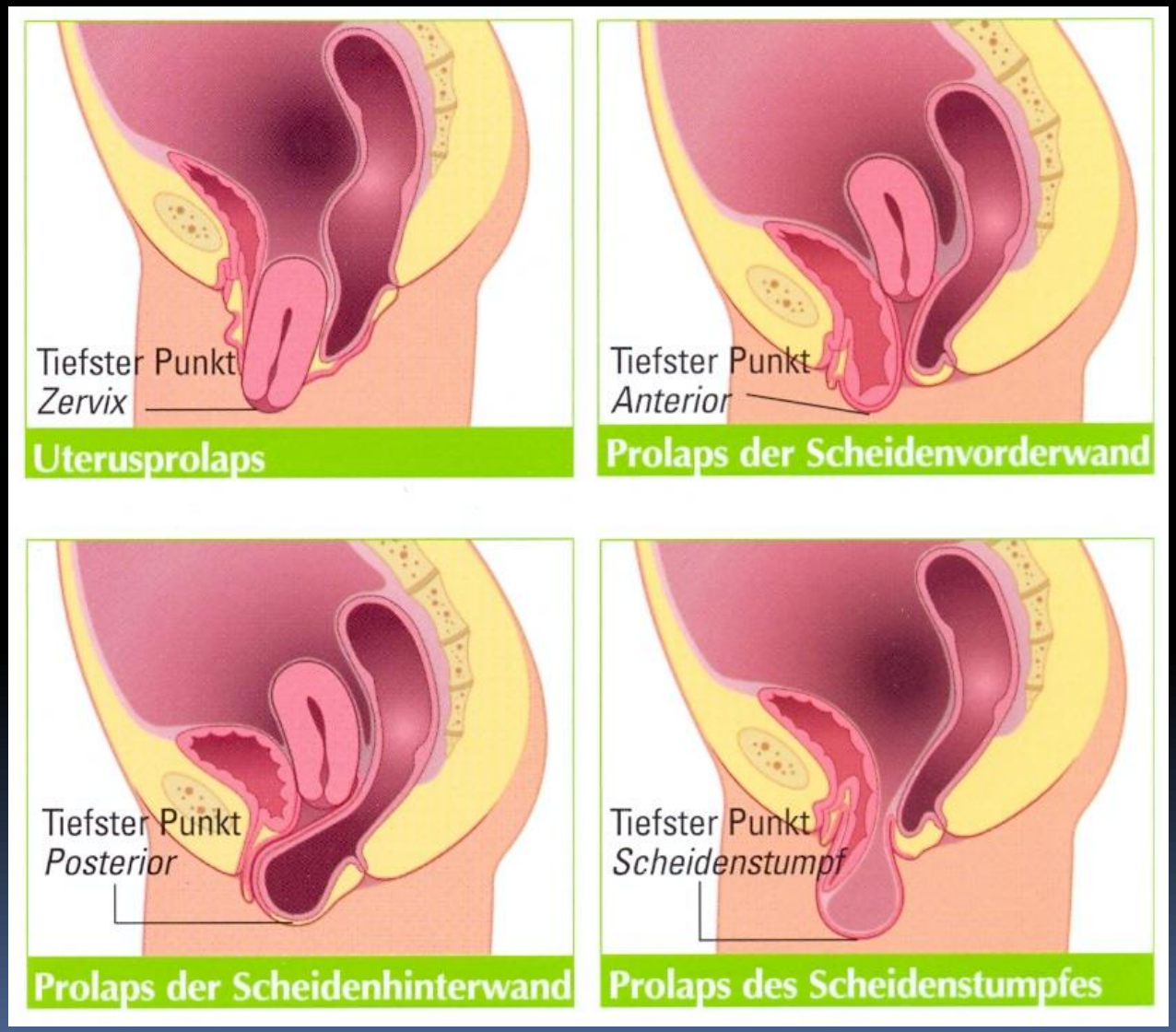
Table 8. Mean Time Intervals Between Prior Procedures

Prior procedures	*n*	Years
Hysterectomy not for prolapse–1st POP UI	115	19.3
1st POP UI–2nd POP UI	107	12.5
2nd POP UI–3rd POP UI	33	4.6
3rd POP UI–4th POP UI	11	3.2
4th POP UI–5th POP UI	2	1.5

POP UI = Pelvic organ prolapse and/or urinary incontinence.

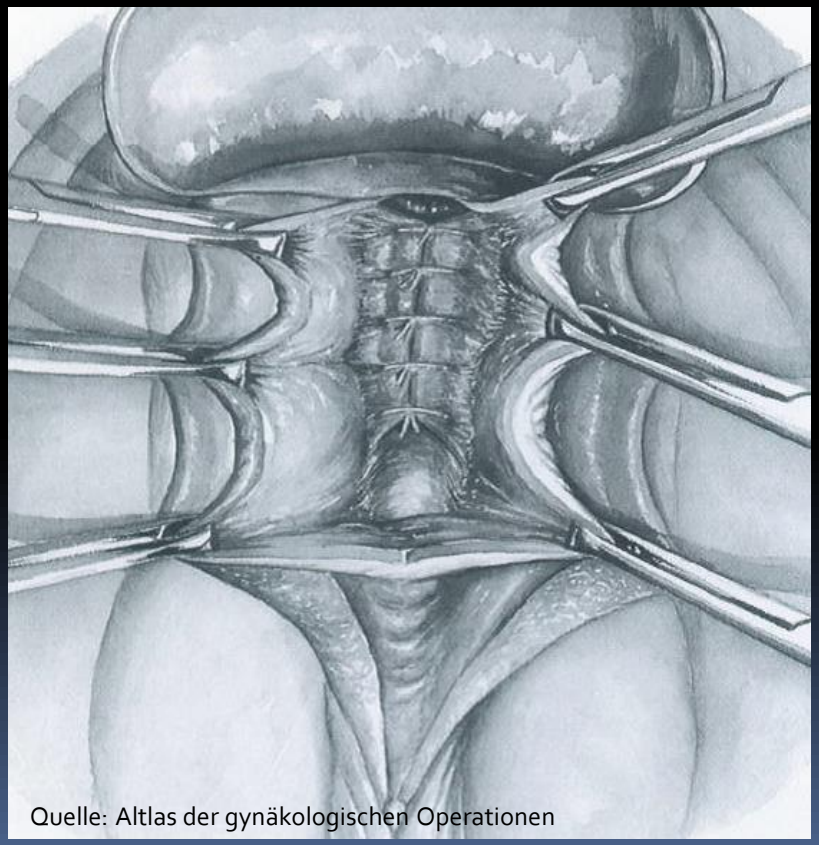
Results: ... with advancing age. T ... gle operation for prolapse or incontinence by age 65 was 11.1%. Most patients were older, postmenopausal, parous, and overweight. Nearly half were current or former smokers and one-fifth had chronic lung disease. Reoperation was common (29.2% of cases), and the time intervals between repeat procedures decreased with each successive repair.

Die Kompartimente



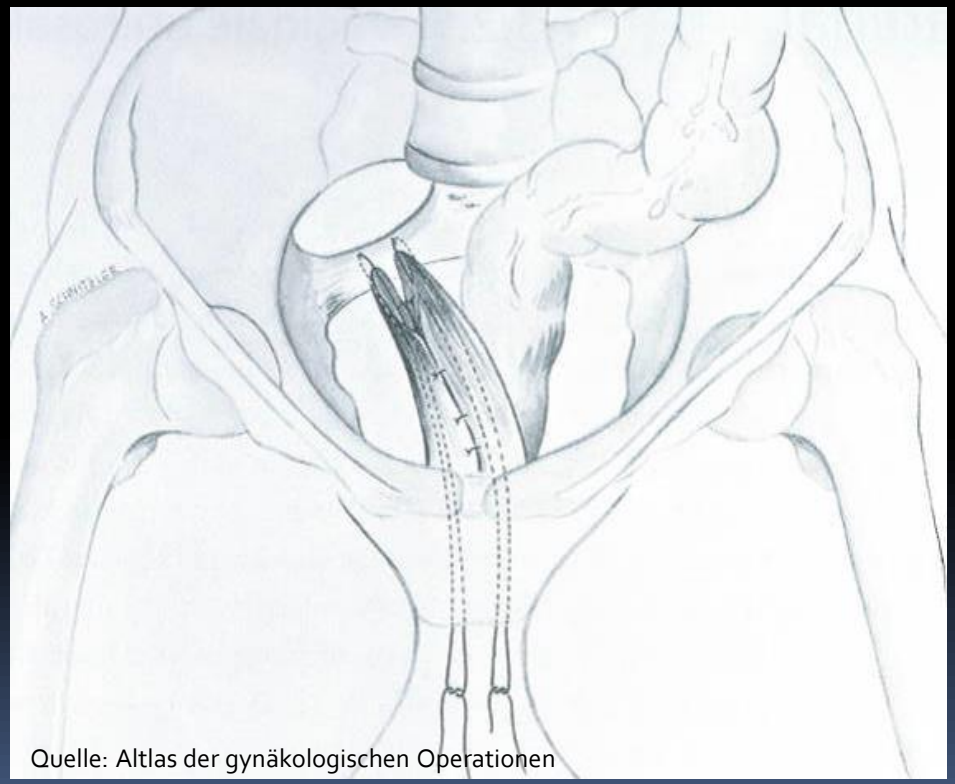
Konventionelle Verfahren

«Raffungen»



Quelle: Altlas der gynäkologischen Operationen

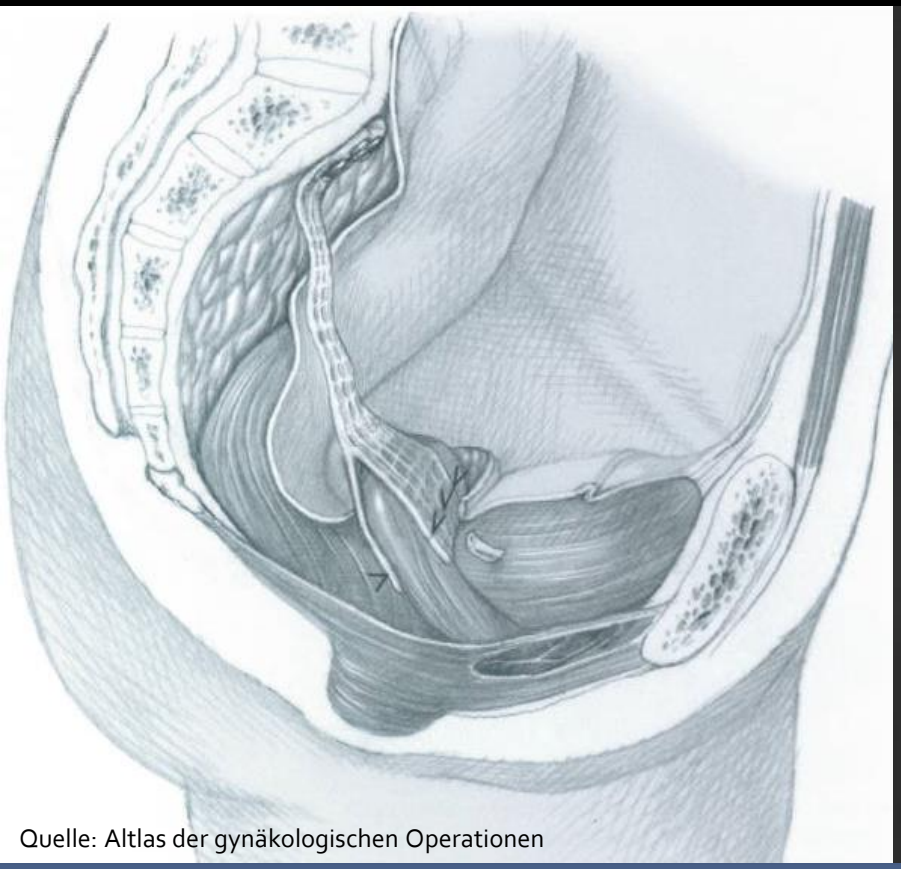
Sacrospinale Fixation



Quelle: Altlas der gynäkologischen Operationen

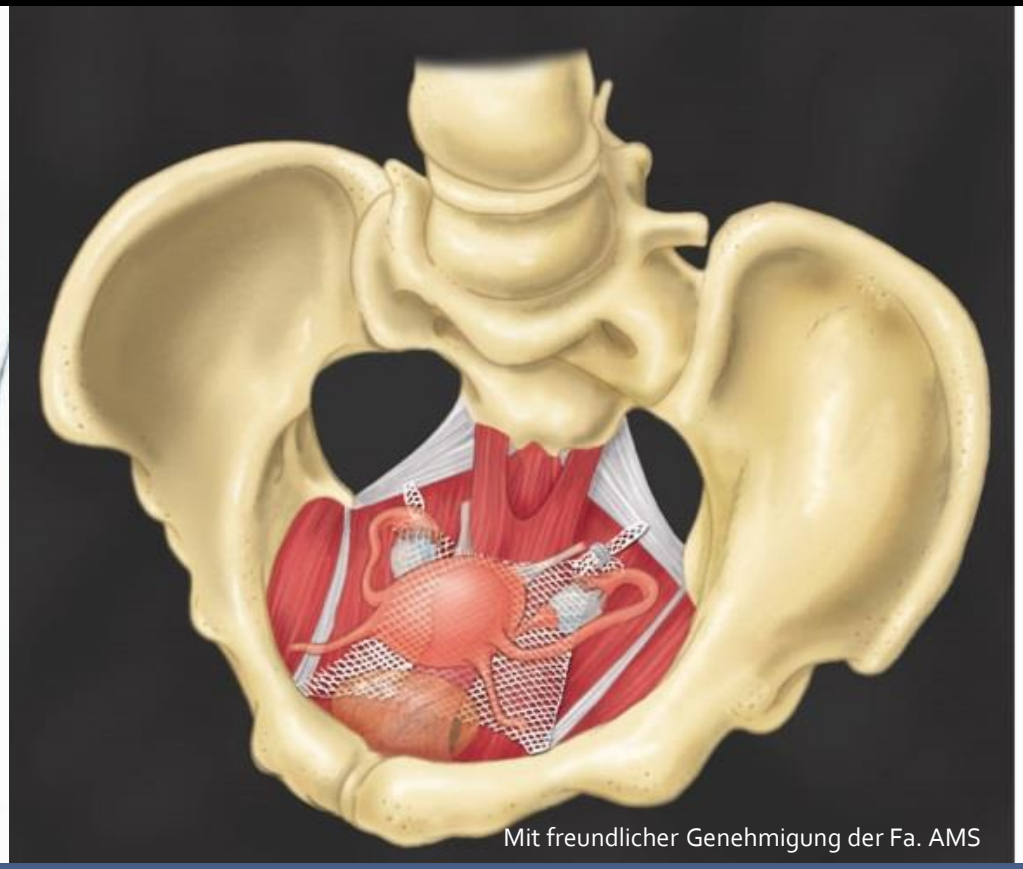
Verfahren mit Mesh

Sacrocolpopexie



Quelle: Altlas der gynäkologischen Operationen

Vaginale Netze

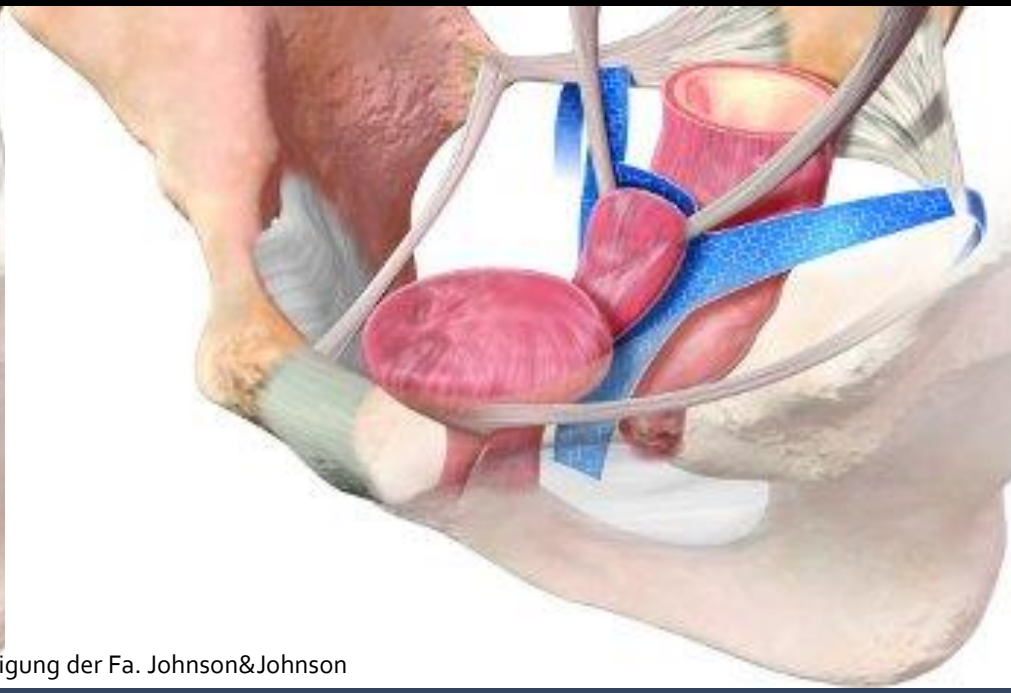


Mit freundlicher Genehmigung der Fa. AMS

Transobturatorische Netze

Bsp. Prolift anterior®

Bsp. Prolift posterior®

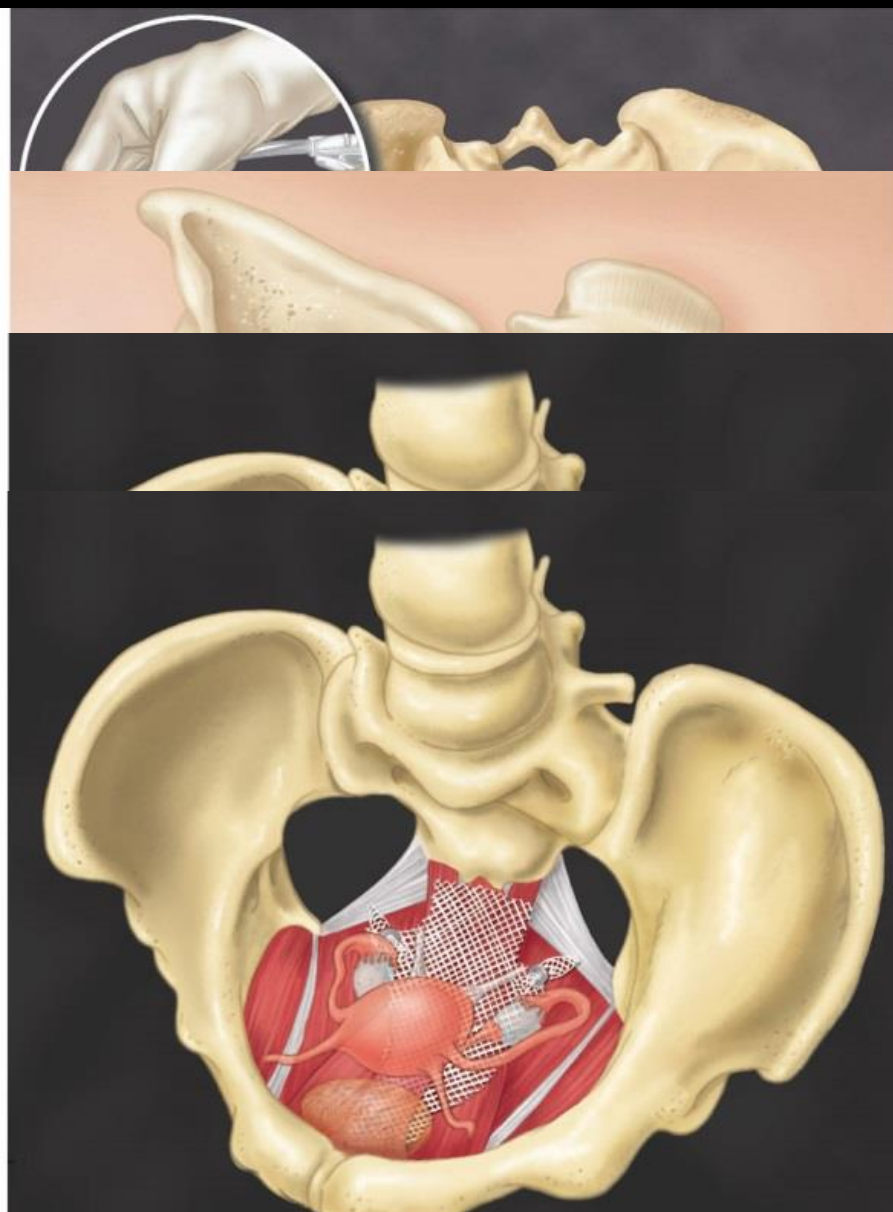


Mit freundlicher Genehmigung der Fa. Johnson&Johnson

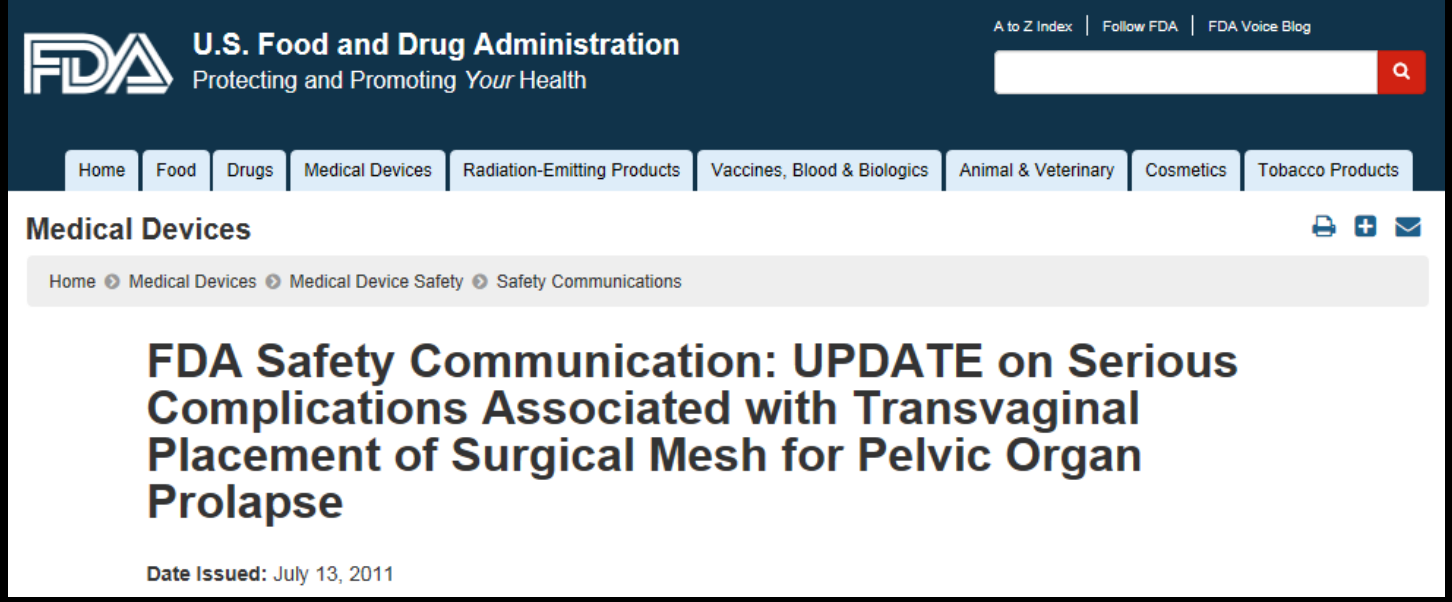
Single incision Netze

Bsp. Elevate®

- Insertion der apikalen Netzarme
- Insertion der ventralen Netzarme
- Lage anteriores Netz
- Lage posteriores Netz



Mit freundlicher Genehmigung der Fa. AMS



- TVM beinhaltet Risiken, die für trad. Verfahren nicht zutreffen
- KSP scheint niedrigere Risiken für Meshkomplikationen zu haben als TVM
- Kein Beweis, dass bei apikalem oder posteriorem Repair ein TVM zusätzlichen Nutzen bringt
- TVM bringt besseres anatomisches Outcome bei anteriorem Repair, dies muss aber keine besseres subjektives Outcome bedeuten

Reaktionen

Int Urogynecol J (2012) 23:5–9
DOI 10.1007/s00192-011-1581-2

DEBATE: TRANSVAGINAL MESH FOR POP – THE RECENT FDA UPDATE

Time to rethink: an evidence-based response from pelvic surgeons to the FDA Safety Communication: "UPDATE on Serious Complications Associated with Transvaginal Placement of Surgical Mesh for Pelvic Organ Prolapse"

Miles Murphy · Adam Holzberg · Heather van Raalte · Neeraj Kohli · Howard B. Goldman · Vincent Lucente · on behalf of the Pelvic Surgeons Network

Reaktionen

- Entwicklung Meshmarkt
  - Rückzug grosser Firmen vom Markt
  - Verwendung vaginaler Meshes in den USA und Ländern, die sich an den USA orientieren ↓
  - Gleichzeitig Sacrocolpopexie ↑

Aktuelle Literatur

Int Urogynecol J (2012) 23:5–9
DOI 10.1007/s00192-011-1581-2

DEBATE: TRANSVAGINAL MESH FOR POP -

The purpose of this response is to demonstrate that TVM is an important tool in our surgical armamentarium that may be the best option in some cases. From our vantage point, it appears that the FDA has presented a biased view of TVM among all POP repair procedures because of the current reporting mechanisms in place.

Time to rethink: an evidence-based response from pelvic surgeons to the FDA Safety

"Mesh used in transvaginal POP repair introduces risks not present in traditional non-mesh surgery for POP repair"

The UPDATE lists the following complications that have been reported to the FDA for TVM: mesh erosion, pain, infection, bleeding, pain during intercourse, organ perforation, and urinary problems. These risks do exist, and any patient who is considering a TVM surgery should be aware of them. However, they should also be aware that with the exception of mesh erosion, these are all risks of traditional nonmesh surgery as well. This statement implies that there are multiple risks of TVM that do not exist with traditional repairs. This is not accurate and is misleading to the public.

Erosion

Few specialists in the treatment of POP would argue that there are not some clinical scenarios (i.e., severe or recurrent prolapse) in which some type of graft-based repair is beneficial—whether that be done in a transvaginal or transabdominal approach. Across the board, the risk of mesh erosion might be higher with TVM; but in two large, multicenter trials conducted by surgeons who perform the index surgery on a regular basis, the results of the abdominal and vaginal approach are quite similar. In the TVM trial that randomized over 400 subjects, 3.2% had undergone a procedure to correct mesh erosion at 12 months [19]. In a well-known RCT of 322 women undergoing ASC, the erosion rate at 12 months was 4.3% (the number

Aktuelle Literatur

Surgical management of pelvic organ prolapse in women (Review)

Maher C, Feiner B, Baessler K, Schmid C

THE COCHRANE COLLABORATION®

nd Urodynamics 27:3–12 (2008)

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002/14651858.CD004014.pub3
ey & Sons, Ltd.

Cochrane 2013

apikaler Prolaps: anatomisches Outcome

Comparison: 1 Surgery for upper vaginal (vault or uterine) prolapse

Outcome: 5 Number of women with any prolapse (objective failure)

Study or subgroup	Method A n/N	Method B n/N	Risk Difference M-H,Fixed,95% CI	Risk Difference M-H,Fixed,95% CI
1 abdominal sacral colpopexy vs vaginal sacrospinous colpopexy (failed)				
Maher 2004	11/46	13/42		-0.07 [-0.26, 0.12]
2 abdominal sacral colpopexy vs vaginal sacrospinous colpopexy (not improved)				
Lo 1998	3/52	13/66		-0.14 [-0.25, -0.02]
3 abdominal sacral colpopexy vs vaginal McCall				
Braun 2007 abstract	0/23	2/24		-0.08 [-0.21, 0.05]
4 cadaveric fascia lata (Tutoplast) vs polypropylene (Trelex)				
Culligan 2005	14/44	4/45		0.23 [0.07, 0.39]
5 vaginal sacrospinous colpopexy vs posterior intravaginal slingplasty				
de Tayrac 2008	7/24	2/21		0.20 [-0.02, 0.42]
6 sacral colpopexy without colposuspension versus sacral colpopexy with colposuspension				
Brubaker 2008	58/132	50/117		0.01 [-0.11, 0.14]
7 uterosacral colpopexy versus vaginal polypropylene mesh				
Iglesia 2010	22/33	20/32		0.04 [-0.19, 0.27]
8 laparoscopic sacral colpopexy versus total vaginal polypropylene mesh kit				
Maher 2011	12/53	32/55		-0.36 [-0.53, -0.18]

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apikaler Prolaps: anatomisches Outcome

Comparison: 1 Surgery for upper vaginal (vault or uterine) prolapse

Outcome: 6 Number of women with recurrent vault/uterine prolapse (objective)

Study or subgroup	Method A n/N	Method B n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 abdominal sacral colpopexy vs vaginal sacrospinous colpopexy				
Benson 1996	1/38	5/42		0.22 [0.03, 1.81]
Maher 2004	2/46	8/43		0.23 [0.05, 1.04]
Subtotal (95% CI)	**84**	**85**		**0.23 [0.07, 0.77]**

Total events: 3 (Method A), 13 (Method B)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.00$, df = 1 (P = 0.97); $I^2 = 0.0\%$

Test for overall effect: Z = 2.37 (P = 0.018)

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apikaler Prolaps: Symptome

Comparison: 1 Surgery for upper vaginal (vault or uterine) prolapse

Outcome: 1 Number of women with prolapse symptoms (subjective failure)

Study or subgroup	Method A n/N	Method B n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 abdominal sacral colpopexy vs vaginal sacrospinous colpopexy					
Benson 1996	6/38	14/42		74.1 %	0.47 [0.20, 1.11]
Maher 2004	3/46	4/43		25.9 %	0.70 [0.17, 2.95]
Subtotal (95% CI)	**84**	**85**		**100.0 %**	**0.52 [0.25, 1.09]**
5 laparoscopic sacral colpopexy vs total vaginal polypropylene mesh					
Maher 2011	1/53	4/55		100.0 %	0.26 [0.03, 2.25]
Subtotal (95% CI)	**53**	**55**		**100.0 %**	**0.26 [0.03, 2.25]**

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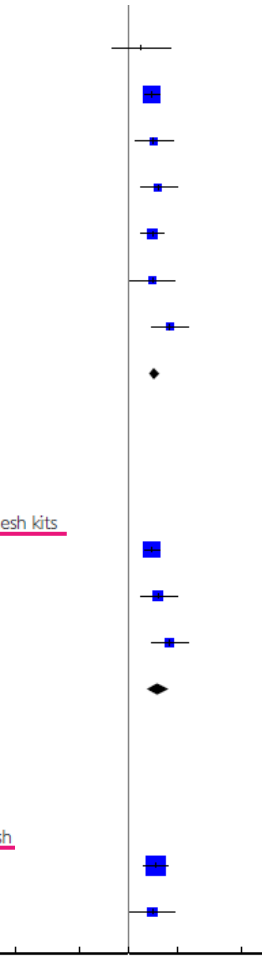
vorderes Kompartiment: anatomisches Outcome

Comparison: 2 One method of anterior prolapse repair versus another surgical method

Outcome: 6 Number of women with anterior prolapse / cystocele (objective failure)

14 anterior colporrhaphy versus any transvaginal polypropylene mesh				
Ali 2006 abstract	5/43	3/46	3.0 %	1.78 [0.45, 7.01]
Altman 2011	96/183	33/186	49.6 %	2.96 [2.11, 4.15]
Menefee 2011	14/24	5/28	7.6 %	3.27 [1.38, 7.75]
Nguyen 2008	20/38	5/38	7.5 %	4.00 [1.67, 9.55]
Nieminen 2008	40/97	14/104	19.4 %	3.06 [1.78, 5.27]
Sivaslioglu 2008	12/42	4/43	5.2 %	3.07 [1.08, 8.77]
Vollebregt 2011	33/51	5/53	7.7 %	6.86 [2.91, 16.18]
Subtotal (95% CI)	**478**	**498**	**100.0 %**	**3.23 [2.55, 4.10]**
Total events: 220 (Method A), 69 (Method B)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 4.26$, df = 6 (P = 0.64); $I^2 = 0.0\%$				
Test for overall effect: Z = 9.64 (P < 0.00001)				
15 anterior colporrhaphy versus commercial transobturator polypropylene mesh kits				
Altman 2011	96/183	33/186	55.0 %	2.96 [2.11, 4.15]
Nguyen 2008	20/38	5/38	22.3 %	4.00 [1.67, 9.55]
Vollebregt 2011	33/51	5/53	22.7 %	6.86 [2.91, 16.18]
Subtotal (95% CI)	**272**	**277**	**100.0 %**	**3.83 [2.34, 6.26]**
Total events: 149 (Method A), 43 (Method B)				
Heterogeneity: $Tau^2 = 0.08$; $Chi^2 = 3.43$, df = 2 (P = 0.18); $I^2 = 42\%$				
Test for overall effect: Z = 5.36 (P < 0.00001)				
16 anterior colporrhaphy versus self styled transobturator polypropylene mesh				
Nieminen 2008	39/96	12/104	76.3 %	3.52 [1.96, 6.32]
Sivaslioglu 2008	12/42	4/43	23.7 %	3.07 [1.08, 8.77]



Cochrane 2013

vorderes Kompartiment: Symptome

Comparison: 2 One method of anterior prolapse repair versus another surgical method

Outcome: 1 Number of women with prolapse symptoms (subjective failure)

5 anterior colporrhaphy vs armed transobturtor mesh				
Altman 2011	64/174	44/179	83.4 %	1.50 [1.08, 2.07]
Nieminen 2008	26/97	9/105	16.6 %	3.13 [1.54, 6.33]
Subtotal (95% CI)	**271**	**284**	**100.0 %**	**1.77 [1.32, 2.37]**
Total events: 90 (Method A), 53 (Method B)				
Heterogeneity: $Chi^2 = 3.54$, df = 1 (P = 0.06); $I^2 = 72\%$				
Test for overall effect: Z = 3.82 (P = 0.00013)				
9 anterior colporrhaphy versus any transvaginal polypropylene mesh				
Al-Nazer 2007	6/19	1/18	1.7 %	5.68 [0.76, 42.70]
Altman 2011	64/174	44/179	71.2 %	1.50 [1.08, 2.07]
Carey 2009	10/60	7/62	11.3 %	1.48 [0.60, 3.62]
Nieminen 2008	18/96	10/104	15.8 %	1.95 [0.95, 4.01]
Subtotal (95% CI)	**349**	**363**	**100.0 %**	**1.64 [1.24, 2.16]**
Total events: 98 (Method A), 62 (Method B)				
Heterogeneity: $Chi^2 = 2.04$, df = 3 (P = 0.56); $I^2 = 0.0\%$				
Test for overall effect: Z = 3.48 (P = 0.00050)				

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hinteres Kompartiment: anatomisches Outcome

Comparison: 3 One method of posterior prolapse repair versus another surgical method

Outcome: 2 Number of women with prolapse (objective failure)

Study or subgroup	Method A n/N	Method B n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 posterior vaginal colporrhaphy vs transanal repair (rectocele)					
Kahn 1999	1/24	1/33		12.3 %	1.38 [0.09, 20.90]
Nieminen 2004	1/15	6/15		87.7 %	0.17 [0.02, 1.22]
Subtotal (95% CI)	**39**	**48**		**100.0 %**	**0.32 [0.07, 1.34]**
Total events: 2 (Method A), 7 (Method B)					
Heterogeneity: $Chi^2 = 1.52$, df = 1 (P = 0.22); $I^2 = 34\%$					
Test for overall effect: Z = 1.56 (P = 0.12)					
2 posterior vaginal colporrhaphy vs transanal repair (enterocele)					
Kahn 1999	2/24	9/33		62.7 %	0.31 [0.07, 1.29]
Nieminen 2004	0/15	4/15		37.3 %	0.11 [0.01, 1.90]
Subtotal (95% CI)	**39**	**48**		**100.0 %**	**0.23 [0.07, 0.83]**
Total events: 2 (Method A), 13 (Method B)					
Heterogeneity: $Chi^2 = 0.40$, df = 1 (P = 0.53); $I^2 = 0.0\%$					
Test for overall effect: Z = 2.26 (P = 0.024)					
3 posterior vaginal colporrhaphy vs transanal repair (rectocele or enterocele))					
Kahn 1999	3/24	10/33		45.7 %	0.41 [0.13, 1.34]
Nieminen 2004	1/15	10/15		54.3 %	0.10 [0.01, 0.69]
Subtotal (95% CI)	**39**	**48**		**100.0 %**	**0.24 [0.09, 0.64]**
Total events: 4 (Method A), 20 (Method B)					
Heterogeneity: $Chi^2 = 1.59$, df = 1 (P = 0.21); $I^2 = 37\%$					
Test for overall effect: Z = 2.86 (P = 0.0043)					
4 posterior vaginal colporrhaphy vs posterior colporrhaphy with mesh reinforcement for rectocele					
Sand 2001	7/67	6/65		100.0 %	1.13 [0.40, 3.19]
Subtotal (95% CI)	**67**	**65**		**100.0 %**	**1.13 [0.40, 3.19]**

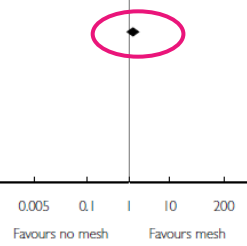
Cochrane 2013

Dyspareunie

Comparison: 6 No graft versus use of graft (synthetic mesh or biological graft)

Outcome: 14 De novo dyspareunia

Study or subgroup	No mesh n/N	Mesh n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 anterior and posterior colporrhaphy versus Anterior and posterior polypropylene Mesh overlay					
Carey 2009	13/60	11/62		23.3 %	1.22 [0.59, 2.51]
Withagen 2011	3/29	3/37		5.7 %	1.28 [0.28, 5.86]
Subtotal (95% CI)	**89**	**99**		**28.9 %**	**1.23 [0.64, 2.36]**
Total events: 16 (No mesh), 14 (Mesh)					
Heterogeneity: $Chi^2 = 0.00$, df = 1 (P = 0.96); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.63 (P = 0.53)					
2 native tissue repair vs mesh repair					
Al-Nazer 2007	10/23	0/21		1.1 %	19.25 [1.20, 309.49]
Allahdin 2008	3/9	3/12		5.5 %	1.33 [0.35, 5.13]
Altman 2011	2/101	8/110		16.5 %	0.27 [0.06, 1.25]
Carey 2009	13/60	11/62		23.3 %	1.22 [0.59, 2.51]
Iglesia 2010	3/14	1/11		2.4 %	2.36 [0.28, 19.66]
Nguyen 2008	4/26	2/22		4.7 %	1.69 [0.34, 8.38]
Sivaslioglu 2008	0/42	2/43		5.3 %	0.20 [0.01, 4.14]
Vollebregt 2011	2/21	3/20		6.6 %	0.63 [0.12, 3.41]
Withagen 2011	3/29	3/37		5.7 %	1.28 [0.28, 5.86]
Subtotal (95% CI)	**325**	**338**		**71.1 %**	**1.24 [0.80, 1.90]**
Total events: 40 (No mesh), 33 (Mesh)					
Heterogeneity: $Chi^2 = 10.03$, df = 8 (P = 0.26); $I^2 = 20\%$					
Test for overall effect: Z = 0.97 (P = 0.33)					
Total (95% CI)	**414**	**437**		**100.0 %**	**1.24 [0.86, 1.77]**
Total events: 56 (No mesh), 47 (Mesh)					
Heterogeneity: $Chi^2 = 10.03$, df = 10 (P = 0.44); $I^2 = 0\%$					
Test for overall effect: Z = 1.16 (P = 0.25)					
Test for subgroup differences: $Chi^2 = 0.00$, df = 1 (P = 0.99), $I^2 = 0.0\%$					



Fazit Cochrane 2013

- mittleres Kompartiment:
  - Gute Evidenz für abdominales Netz (LoE 1)
- Vorderes Kompartiment:
  - Gute Evidenz für vaginales Netz (LoE 1), bessere objektive und subjektive Ergebnisse als Colporrhaphie
- Hinteres Kompartiment:
  - Keine Evidenz für vaginales Netz (LoE 3)

FDA-Warnung

Was sagt die AUG dazu?

Expertenbrief No. 21

Kommission Qualitätssicherung
Präsident Prof. Dr. Daniel Surbek

Der Einsatz von Netzen bei Prolapsoperationen (Revidierte Version vom 20.August 2012)

Arbeitsgemeinschaft Urogynäkologie und Beckenbodenpathologie AUG
Autoren: G. Schär, A. Kuhn, A. Weil

Zulässige Aussagen aus den klinischen Studien

Bei **apikalem Deszensus** hat die Sakrokolpopexie Vorteile gegenüber der vaginalen Sakrospinalen Fixation betreffend Rezidiv-, Reoperations- und Dyspareunierate (1). Der Vergleich zwischen Sakrokolpopexie und totalem Mesh (totales Prolift) zeigt ebenfalls eine bessere objektive und subjektive Heilung und geringere Reoperations- sowie Komplikationsraten für die Sakrokolpopexie (8).

Im Vergleich zur Diaphragmaplastik weisen die vaginalen Netzkits bei **Zystozele** eine bessere objektive und subjektive Heilungsrate auf, jedoch zum Preis einer um 14% höheren Komplikationsrate (Blasenläsion 3%, Inguinalschmerzen 3% und Erosion 8%), während die Dyspareunierate keinen Unterschied aufwies (3). Withagen et al. verglichen ebenfalls Diaphragmaplastik mit Netzkit und fanden zwar bei der subjektiven Heilungsrate keine Unterschiede, jedoch signifikant häufigere Reoperationen wegen Rezidivdeszensus bei Frauen die mittels Diaphragmaplastik operiert wurden. Mit 17% war die Erosionsrate zudem in dieser Studie relativ hoch (4).

Bei der **Rektozele** ist sich die Fachwelt einig, dass im primären Fall die Rektozelenkorrektur mit einer Kolpoperineoplastik und ohne Levatornähte hohe Heilungsraten um 90% zeigt (1) und die Anwendung von Netzen nicht angezeigt ist, weil die Komplikationsrate von 6 bis 12% Erosionen (9) im Vergleich dazu nicht vertretbar ist. Netze sollten hier erst im Rezidivfall zur Anwendung kommen.

Take home message

- Vaginale Netze sind nicht die Lösung aller Beckenbodenprobleme, aber ein wichtiges Instrument und manchmal die beste Option
- Die Operateure sollten in der Meshtechnik gut geschult sein, vaginaloperative Erfahrung und ein gewisses case load haben
- Die verwendeten Netze sollten dem aktuellen Stand der Wissenschaft entsprechen (makroporös, monofilamentär)
- Die Neueinführung medizinischer Produkte braucht eine bessere Kontrolle und Nachweis von Studien

Ernst Bumm

OPERATION IST HANDWERK, INDIKATION IST WISSENSCHAFT.

In eigener Sache

BITTE UM IHRE UNTERSTÜTZUNG

Swiss clinical vaccine study in UTI patients
Phase I clinical trial

- CH-Biotec-Firma, GlycoVaxyn
- Innovativer Biokonjugat-Impfstoff gegen uropathogene *E.coli*
- 1 intramuskuläre Injektion für Langzeitschutz
- Ca. 10-12 CH-Zentren

A phase I clinical study, single blind, multi center and placebo controlled, will be performed with the *E.coli* bioconjugate tetravalent vaccine (EcoXyn4V) in healthy women aged between 18 and 70 years old with history of recurrent urinary tract infections. The aim of this Phase I study is to collect safety, tolerability and immunogenicity data, as well as to obtain a first indication of protection against RUTI with this precursor candidate vaccine. Higher *E.coli* UTI coverage is aimed to be reached with the final product that will include up to 10 most common serotypes of *E.coli*, and whose clinical evaluation will follow this first trial with the precursor tetravalent conjugate EcoXyn4V.

Zielpopulation

- Gesunde Frauen, 18-70 Jahre alt, mit rezidivierenden HWI und mindestens 1 Urikult-bestätigte ***E.coli***-Infektion (see GP letter)

- **Studienstart**: April/May 2014
- **Studiendauer**: 9 Mte
- **Visiten am Studienzentrum:**
  - 5 geplante Studienvisiten
  - ungeplante Visiten bei Auftreten HWI

- Entgelt: 900 CHF

Bitte kontaktieren Sie mich, wenn Sie geignete Frauen kennen: 071 494 18 76