Vol. 38 - N. 4
December 2019

Rivista Italiana di Colon-Proctologia
Founded in 1982

ISSN 1973-4905

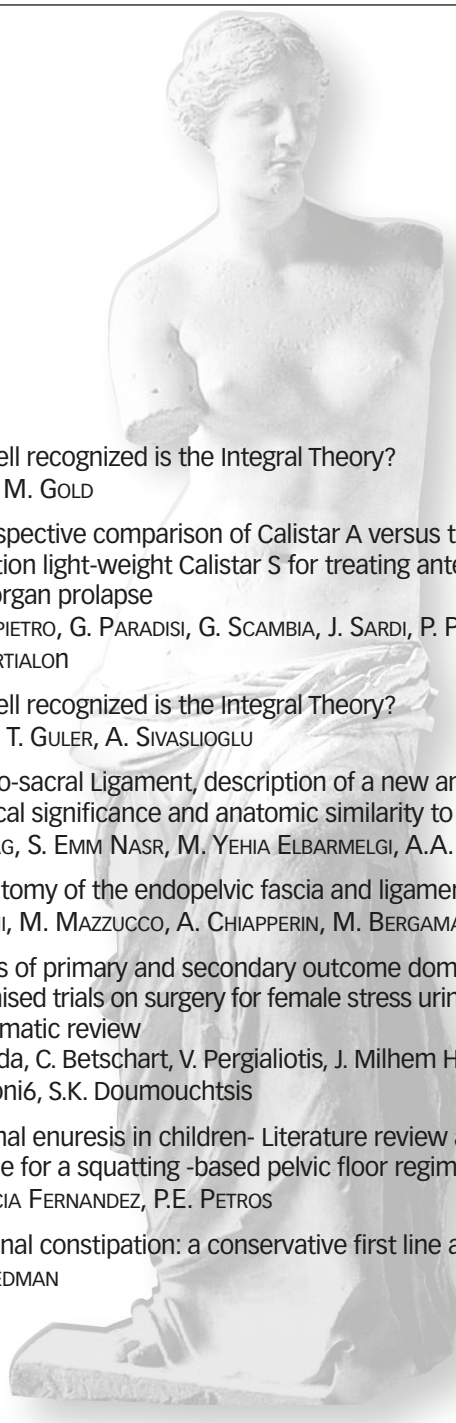
PELVIPERINEOLOGY

A multidisciplinary pelvic floor journal

www.pelviperineology.org

INSTRUCTIONS FOR AUTHORS

The manuscripts including tables and illustrations must be submitted to Pelviperineology only via the Isubmit system **www.isubmit.it**. This enables a rapid and effective peer review. Full upload instructions and support are available online from the submission site.
In **http://www.pelviperineology.org/pelviperineology_authors_instructions.html** please find the updated guidelines for the Authors.

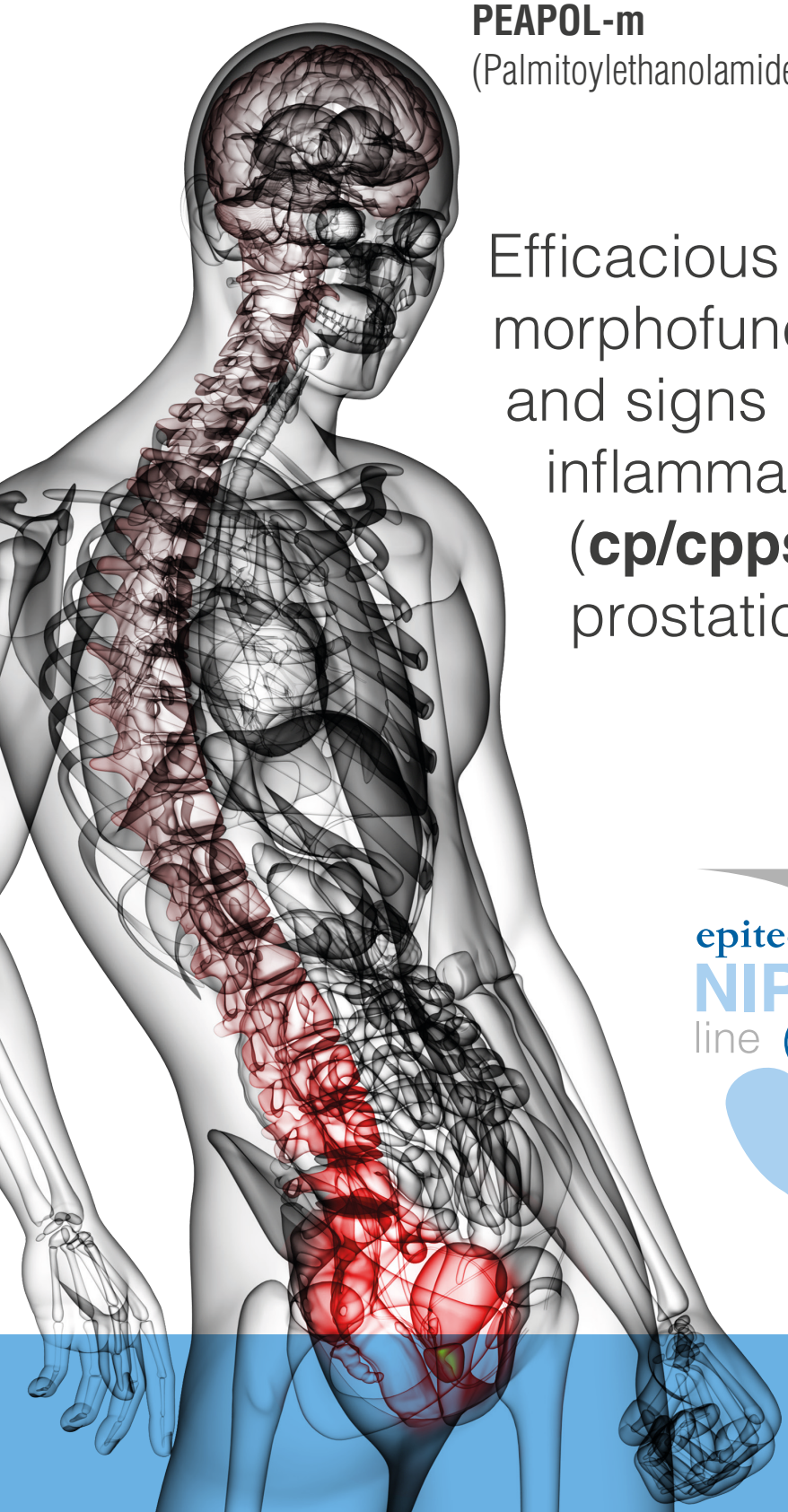


Contents

'Taxe Perçue' 'Tassa Riscossa' - Padova C.M.P.
Poste Italiane s.p.a.
Spedizione in Abb. Post. - 70% - DCB Padova

pelviprost®

PEA-um
Ultramicronized Palmitoylethanolamide 400 mg
PEAPOL-m
(Palmitoylethanolamide co-micronized with Polydatin) 440 mg



Efficacious control of morphofunctional symptoms and signs in case of chronic inflammatory prostatitis (**cp/cpps**) and benign prostatic hyperplasia.

epitech NIP line

Packaging 20 tablets

epitech group
www.epitech.it

Vol. 38

N. 4

December 2019

Rivista Italiana di Colon-Proctologia
Founded in 1982

PELVIPERINEOLOGY

A multidisciplinary pelvic floor journal

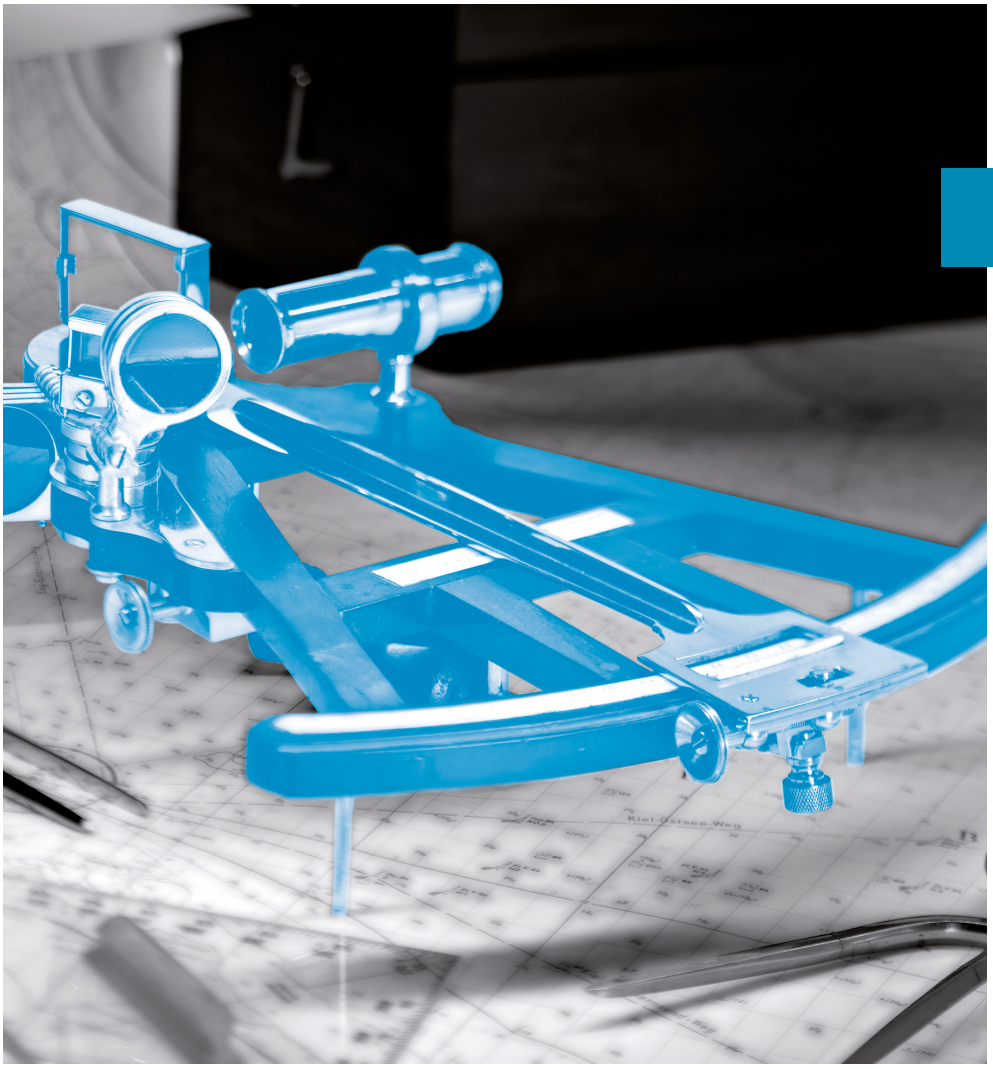
www.pelviperineology.org

Official Journal of the: International Society for Pelviperineology (www.pelviperineology.com)
Associaciòn LatinoAmericana de Piso Pelvico
Perhimpunan Disfungsi Dasar Panggul Wanita Indonesia
The Israeli Society of Urogynecology and Pelvic Floor
Romanian Uro-Gyn Society
Pelvic Reconstructive Surgery and Incontinence Association (Turkey)

Editorial Office: Benito Ferraro, Luisa Marcato
e-mail: benito.ferraro@sanita.padova.it - luisa.marcato@sanita.padova.it
Quarterly journal of scientific information registered at the Tribunale di Padova, Italy n. 741 dated 23-10-1982 and 26-05-2004
Editorial Director: Giuseppe Dodi. The journal is property of the International Society for Pelviperineology

Surgical technique adaptable to the individual anatomy for the treatment of female stress incontinence with

SERASIS® JK-Tape®



Advantages

extra slim tape for incontinence surgery

suitable for urethras of all lengths and mobility

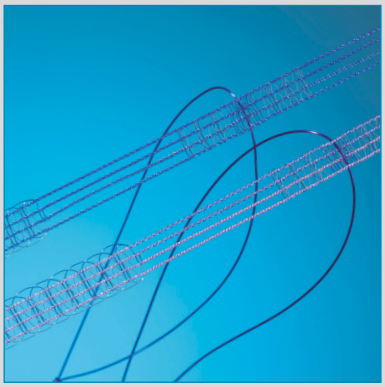
anatomically adapted geometry

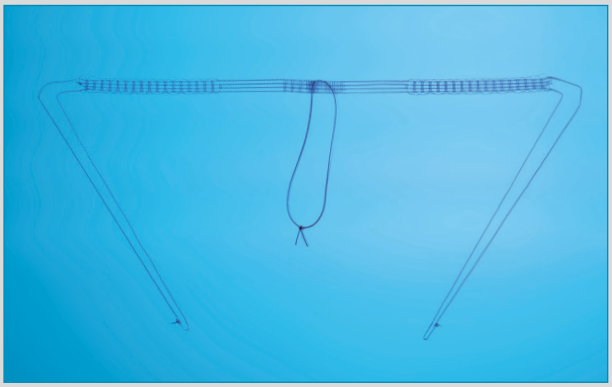
adjustability

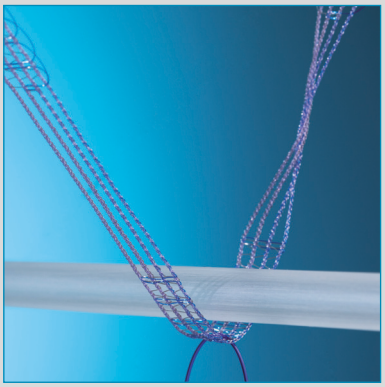
lies reliably flat beneath the urethra, thanks to buffer zones

reduces the risk of a ‘tethered tape’

keeps its shape under tension







SERAG WIESSNER

SERAG-WIESSNER GmbH & Co. KG
Zum Kugelfang 8 - 12
95119 Naila/Germany

+ 49 9282 937-0
+ 49 9282 937-9369

info@serag-wiessner.de
www.serag-wiessner.de

Editorial

How well recognized is the Integral Theory?

DARREN M. GOLD

Colorectal Surgeon, Senior Lecturer in Surgery, St Vincent's Clinical School, UNSW, Sydney, Australia

In the article by Kilic, Guler and Sivaslioglu, the authors make an astute observation and ask a compelling question. In fact, from my own reading other journals such as the International Urogynecology Journal and Neurourology and Urodynamics frequently publish papers that unwittingly confirm the Integral Theory. The answer to this question, as to why the Integral Theory is still unrecognized after 30 years since its original publication[1], lies in the work of Leon Festinger[2] and his theory of cognitive dissonance published over 60 years ago.

In the scientific world, cognitive dissonance refers to the feelings of discomfort that occur when an individual's understanding are in conflict with new discoveries and research, or when new information that is contrary to their beliefs is presented to them. People like consistency. Doctors are certainly no exception. They are comfortable with the assurance that their values and beliefs have always been correct. They always want to act in ways that are in line with their beliefs. When their long held beliefs are challenged, or when their behavior is not aligned with their beliefs, this creates an uncomfortable disagreement (dissonance).

Science and medicine is replete with examples of where cognitive dissonance has delayed the acceptance of numerous discoveries, sometimes for years, often for decades and on occasions for centuries. The most well-known example is Copernicus heliocentric system for the planets, which placed the sun at centre of our planetary system rather than the Earth. It took over 150 years to accept this observation despite the fact that much research during that period would have confirmed it. But how do we deal with such dissonance?

Perhaps the simplest way to resolve dissonance between opposing beliefs is simply to change our beliefs. This would quickly and effectively take care of any dissonance. However, if the accepted belief is fundamental and important such action is unlikely. Although this is the simplest option for resolving dissonance it is not the most common and certainly the most difficult.

A more complex yet more common method of resolution, is to change the way we view/remember/perceive our current beliefs in order to make them fit, eliminating the dissonance. In other words we "rationalize" our actions.

Such is the understanding of the mid-urethral sling; the Integral Theory and the well demonstr6ated three-directional movements of urethral closure challenging the accepted and still taught pressure based theories, even though these movements are repeatedly demonstrated[3]. The success of the MUS is simply rationalised to "fit" with pressure theories despite evidence to the contrary[4,5]. Dissonance, in the absence of anything else to "fit" driving other aspects of the Integral Theory to be ignored and vehemently rejected.

Eventually the Integral Theory will be accepted. There is no choice. Unfortunately, the successful champion for this change has not yet been born.

REFERENCES

1. Petros PE and Ulmsten UI. An integral theory of female urinary incontinence. Acta Obstet Gynecol Scand Suppl, 1990. 153: p. 7-31.
2. Festinger L. A theory of cognitive dissonance, Evanston, IL: Row &Peterson, 1957
3. Gold DM and Ende D. Re: Correlations between Sonographic and Urodynamic Findings after Mid Urethral Sling Surgery: L. Wen, KL Shek, N. Subramaniam, T. Friedman and HP Dietz J Urol 2018; 199: 1571–1576. The Journal of urology, 2018. 200(6): p. 1379-1381.
4. Constantinou CE and Govan DE. Contribution and timing of transmitted and generated pressure components in the female urethra. Prog Clin Biol Res, 1981. 78: p. 113-20.
5. Kamo I, Kaiho Y, Miyazato M et al., Two kinds of urinary continence reflexes during abrupt elevation of intravesical pressure in rats. Low Urin Tract Symptoms, 2009. 1(s1): p. S40-s43.

Correspondence:
dandjgold@gmail.com

Original article

A retrospective comparison of Calistar A versus the second-generation light-weight Calistar S for treating anterior and apical pelvic organ prolapse

AGUSTIN SAMPIETRO[1], GIANCARLO PARADISI[2], GIOVANNI SCAMBIA[2], JUAN SARDI[3], PAULO PALMA[4], CASSIO RICCETTO[4], PASCAL MOURTIALON[5]

[1] *Faculty of Medicine, University of Buenos Aires, Buenos Aires, Argentina*
[2] *Catholic University of Sacred Heart, Rome, Italy*
[3] *British Hospital, Buenos Aires, Argentina*
[4] *University of Campinas (UNICAMP), Campinas, Brazil*
[5] *Provence Gynecologie, Hôpital Privé de Provence, Aix en Provence; Clinique de Vitrolles, France*

Abstract: Introduction: Pelvic organ prolapse (POP) repair with synthetic mesh has low recurrence and good anatomical correction. The new-generation meshes may provide better outcomes than meshes with greater superficial density. This multicenter study aimed to evaluate the outcomes of POP repair using Calistar S (CaS; 44 g/cm^2) versus Calistar A (CaA; 16 g/cm^2). *Methods:* Data from women with anterior and/or apical POP repaired with either CaA (n=91) or CaS (n=126) between January 1, 2011 and April 30, 2017 were retrospectively analyzed. The primary endpoint was the overall response based on Barber's criteria. Secondary endpoints were anatomical correction and patient-reported outcomes assessed with the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12) and Pelvic Floor Disability Index (PFDI-20). Adverse events were recorded. Minimum follow-up was 6 months. *Results:* Barber's criteria for cure were met by 75 (82%) in the CaA group and 114 (90%) in the CaS group (p=0.0806). Anatomical correction was significantly improved in both groups from a median POP-Q stage of 3 preoperatively to 1 postoperatively (p<0.0001 in both groups). Quality of life (measured by the PISQ-12 or PDFI-20) showed similar significant improvements from baseline in both groups. De novo overactive bladder only occurred in the CaA group (p=0.0121), and urinary tract infection, mesh exposure, and de novo stress urinary incontinence were significantly more frequent in the CaA group than the CaS group. Rare adverse events (only one case per event) occurred in the CaA group. *Conclusion:* Ultra-light-weight CaS is safer and achieves a similar success rate compared with heavier-weight CaA.

Keywords: Ultra-light-weight mesh; Transvaginal approach; Pelvic organ prolapse; Anterior and/or apical prolapse

INTRODUCTION

Pelvic organ prolapse (POP) is a major concern affecting the life quality of millions of women, with a reported prevalence of 3–6% when defined by symptoms[1] and 50–97% when based on vaginal examination[1,2]. The etiology of POP is multifactorial, with many risk factors associated with sustained episodes of increased intra-abdominal pressure (such as pregnancy, vaginal delivery, heavy lifting, chronic coughing, and constipation) and others related to a decrease in tissue quality (such as hysterectomy, previous continence or prolapse surgery, menopause and estrogen levels, and collagen abnormality)[3,4].

The lifetime risk of undergoing one surgery for POP is approximately 11%[5]. Surgery is generally indicated for severe cases that are non-responsive to conservative management such as lifestyle interventions, physical therapy, and pessaries[6]. Almost 30% of patients require a new surgical treatment after the first procedure for POP repair, progressively reducing the resolution of the problem and increasing the costs related to the treatment of this condition[7,8]. The high failure rates of native tissue repair led to the introduction of various allograft materials and repair systems that offered lower failure rates[9,10]. It is broadly accepted that POP surgical repair with the use of synthetic meshes is associated with lower recurrence rates and good anatomical correction compared with native tissue repair[9]. However, safety concerns related to the transvaginal approach used for POP repair with synthetic meshes have increased the scrutiny of clinical data to better understand the benefit/risk ratio for this type of surgery. POP surgery management trends were greatly affected by safety notices published by the FDA in 2008 and 2011[11]. Subsequently, health regulatory agencies worldwide have increased the requirements for the approval and use of such POP repair devices, and the use of transvaginal meshes has been withdrawn by some agencies, such as the Australian Therapeutic Goods Administration in 2017 and the FDA in 2019.

A 2016 Cochrane review stated that mesh repair might not be associated with a high benefit/risk ratio for primary surgery, although the use of synthetic mesh may be appropriate in cases with a relatively high risk of recurrence[12]. However, the lack of robust evidence means that extreme caution must be exercised when POP repair is performed with synthetic mesh; care must be taken during patient selection, and surgeons must undergo training regarding the use of specific devices. These strategies are important in improving the safety profile of POP repair with meshes while retaining the good anatomical outcomes that this method achieves. Additionally, new research is focused on intrinsically improving POP repair devices to minimize the complications associated with the materials and surgical techniques; efforts are being made to reduce the amount of material that is implanted in the pelvic floor area in an attempt to decrease the risks of foreign body reaction, infection, and mesh exposure. Ultra-light-weight meshes are considered to lower the risks of infection and erosion. The use of this newer generation of meshes, mainly via the transvaginal approach, may provide better safety outcomes than the previous meshes with greater superficial density[13,14]. However, high-level evidence data on the use of lighter meshes is still lacking, regardless of the compartment in which they are intended to be used[15,16].

The objective of this retrospective study was to evaluate the outcomes of two similar mesh products that each contain a different amount of material; this information may be used in the design of future prospective trials.

MATERIALS AND METHODS

Study design and hypotheses

The present study was an international, multicenter, post-market, open, non-randomized, retrospective analysis carried out in participating tertiary referral centers in Italy, France, Argentina, and Brazil (ClinicalTrials.gov identifier: NCT03715803).The target population was defined by the inclusion criteria as all adult women (> 18 years old) with an initial diagnosis of at least a stage 3 anterior and/or apical POP (defined using the POP-Q System) with or without

stress urinary incontinence (SUI) who had undergone POP repair surgery with either Calistar A (CaA; Promedon, Argentina) or Calistar S (CaS; Promedon, Argentina) as primary surgical treatment or to correct recurrent POP after a previous surgical intervention occurring between January 1, 2011 and April 30, 2017 in the participating centers; all included patients had at least a 6-month postoperative follow-up. Exclusion criteria included recurrent vaginal infection, chronic colorectal disease (e.g. chronic nonspecific ulcerative colitis, diverticulitis, diverticulosis, Crohn's disease, irritable bowel syndrome, familial polyposis), the presence of any coagulopathy, impairment of the immune system or any condition that would compromise recovery, prior irradiation, and chronic pelvic pain. The sample size was determined by the application of the eligibility criteria over the study period, and was therefore not statistically calculated.

The study hypothesis was that the use of the CaS system (consisting of an ultra-light-weight mesh) provides a comparable therapeutic effect and has a superior safety profile compared with the CaA system (a device with a heavier-weight mesh).

The primary effectiveness endpoint was the patient overall response based on Barber's criteria for cure: lowest POP-Q stage < 0 (no points beyond the hymen), no subjective adverse symptoms (absence of vaginal bulge), and no re-treatment or interventions for 1 year after the POP repair procedure[17]. The secondary effectiveness endpoints were the objective assessment of anatomical correction based on the validated POP-Q system, and patient-reported outcome measurements as assessed with validated questionnaires such as the Patient Global Impression of Improvement (PGII), Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12), and Pelvic Floor Disability Index (PFDI-20), depending on the record availability at each participating center. The safety endpoint was defined as the record of any peri- and/or postoperative adverse event or complication associated with the use of the devices under evaluation. Other variables that were analyzed included the follow-up duration, intraoperative blood loss, surgical procedure time, number of recurrent prolapses defined by the cure criteria based on the POP-Q system, and number of cases requiring reintervention.

Device description

oth devices under evaluation involve the same indications for use, surgical approach, and fixation methods. They are indicated to surgically treat anterior and apical prolapses via a single-incision vaginal approach, with fixation points at the SSL and obturator internus muscles. The surgical kits consist of the polypropylene implant (mesh with multipoint fixation columns on the anterior arms), a retractable insertion guide (RIG) to facilitate fixation maneuvers (the CaS comes with two different RIGs), and three polypropylene tissue anchoring systems (TAS), which are harpoon-like anchors for SSL fixation at DeLancey's Level I, as depicted in Fig. 1 and Fig. 2. The CaS kit also includes a knot pusher that can be used when suturing the anchored TAS to the implant. The main difference between the CaS and CaA systems is the amount of material contained in each implant. Whilst the superficial density of CaA mesh is 44 g/cm^2, the newer generation low-weight mesh in CaS is 16 g/cm^2. In addition, CaA provides mid-urethral support that can be used to treat concomitant SUI; a feature that is not present in CaS.

Surgical technique

The surgical procedures for each of the two meshes were very similar. Briefly, a single incision was made on the anterior vaginal wall under local or regional anesthesia. The incision began at the bladder neck for CaS and at the middle portion of the urethra for CaA, and extended to the cervix or the apex in both cases. Blunt bilateral dissection was performed toward the ischial spine until the SSL was identified. The first TAS was loaded into the RIG (using the appropriate RIG for CaS) and anchored at the anterior face of the SSL, 2.5 medial to the ischial spine. A second identical SSL fixation was done for the contralateral SSL, and the suture threads connecting the TAS were kept outside the incision for the posterior step. Afterwards, the same RIG (for CaA) or the smaller RIG (for CaS) was connected to one of the multipoint fixation columns and anchored at the obturator internus muscle, and the process was repeated on the other side. As a result, the middle portion of the anterior aspect of the implant rested below the bladder neck (for CaS) or the mid-urethra (for CaA), imposing no mechanical tension on the upper tissues (tension-free approach). The implant was secured in place with two absorbable sutures placed over the bladder neck (for CaS) or over both sides of the mid-urethra (for CaA). At this point, the TAS suture threads were passed through the tiny holes on the corresponding posterior arms of the implant. When the threads were passed through on each side, care was taken to leave at least 5 mm between the entry points of the threads to enable the creation of a double sliding knot. Before placing the posterior arms onto the SSL, two additional absorbable sutures were placed to fix the implant to the remnants of the cardinal ligaments or the pericervical ring. Anterior and apical prolapse reduction was achieved by moving the implant towards the SSL, using the double sliding knots created on the posterior arms. For the CaS system, the knot pusher was used to facilitate the sliding of the knot towards the SSL. The implant was placed in a free-tension fashion, and the excess mesh at the mid-posterior part (dome shape) was trimmed. Finally, the vaginal incision was closed in a routine manner.

Data collection and statistical analyses

Medical records from the gynecological/urogynecological unit of each participating center were screened to identify the cases that met the eligibility criteria. Once the cases were identified, data were transferred from the center records to the investigation case report forms for standardization and anonymization. Statistical analyses were performed with InfoStat Software (National University of Cordoba, Cordoba, Argentina)[18]. Continuous variables were initially checked for normality using the Shapiro-Wilks test. Hypothesis testing for normally distributed samples was completed with paired-sample t-testing (pre- vs postoperative values within a group) and independent sample t-testing (comparisons between different groups at the same study timepoint). For non-normally distributed samples, the analog non-parametric versions were used (Wilcoxon signed rank test and Mann-Whitney U test, respectively). For categorical variables, chi-square tests were used (proportions difference). The significance level was set at 0.05 for all comparisons.

RESULTS

Two-hundred-and-seventeen patients met the eligibility criteria, comprising 91 in the CaA group and 126 in the CaS group. Baseline clinical and demographic data did not significantly differ between the groups (Table 1). However, compared with the CaA group, the CaS group tended to have a higher incidence of previous pelvic surgeries (37 (41%) patients in the CaA group and 25 (20%) in the CaS group) and a lower incidence of previous POP surgical interventions (16 (13%) in the CaS group and four (4%) in the CaA group).

Intraoperative and follow-up data are summarized in Table 2. The CaA and CaS surgical procedures involved similar mean operation times (70 and 66.5 min, respectively). No simultaneous hysterectomies were performed at the time of Calistar implantation in either group, whereas concomitant anti-incontinence surgery was more common in the CaS group than

Table 1. Demographic and baseline clinical data.

	CaA group (n=91)	CaS group (n=126)	p value
Age [years], mean (SD)	*62 (9)*	*62 (8)*	*0.6471*
BMI [kg/m^2], median (range)	*26 (17–38)*	*26 (20–40)*	*0.3728*
Diabetes, n (%)	*6 (7)*	*11 (9)*	*0.6183*
Smoking, n (%)	*11 (12)*	*12 (10)*	*0.6559*
Parity, median (range)	*2 (0–10)*	*2 (0–7)*	*0.2101*
Prior hysterectomy, n (%)	*16 (18)*	*14 (11)*	*0.2314*
History of pelvic surgery, n (%)	*37 (41)*	*25 (20)*	*0.0008*
Prior prolapse surgery, n (%)	*4 (4)*	*16 (13)*	*0.054*
PISQ 12, median (range) [n]	*0 (0–5) [21]*	*0 (0–13) [17]*	*0.2876*
PFDI 20, median (range) [n]	*31 (0–91) [28]*	*19.5 (0–52) [30]*	*0.1103*

the CaA group (p=0.0006). Regarding intraoperative complications, there were only a few cases of blood loss and only one case of bladder injury in the CaS group (Table 2).
The median postoperative follow-up duration was significantly longer in the CaA group than the CaS group (24 months vs 12 months, p<0.0001). Compared with the CaA group, more women in the CaS group reported being sexually active in the postoperative period (p=0.0005).

According to the primary effectiveness endpoint (Barber's criteria), both devices performed similarly, with no statistical difference between groups. The criteria for cure were met by 75 (82%) patients in the CaA group and 114 (90%) in the CaS group (p=0.0806). Anatomical correction as measured by the POP-Q system showed statistically and clinically significant differences in both groups from a preoperative median POP-Q stage of 3 at baseline to a postoperative POP-Q

Table 2. Surgical procedure and follow-up data.

	CaA group (n=91)	CaS group (n=126)	p value
Surgical procedure			
Operative time [min], median (range)	70 (30–120)	66.5 (35–240)	0.9124
Concomitant hysterectomy, n (%)	0	0	1
Concomitant anti-incontinence surgery, n (%)	10 (11)	33 (26)	0.006
General postoperative data			
Sexually active subjects, n (%)	37 (41)	68 (54)	0.0005
Follow-up [months], median (range)	24 (6–64)	12 (6–36)	<0.0001
Intraoperative adverse events, n (%)			
Blood loss > 200 ml	1 (1.2) [n=84]	2 (2.4) [n=126]	1
Bladder injury	0	1 (0.8)	1
Postoperative adverse events, n (%)			
Pain	6 (7)	6 (5)	0.7649
Mesh erosion	10 (11)	5 (4)	0.0577
Mesh shrinkage	2 (2)	0	0.1747
Recurrence of prolapse	16 (18)	14 (11)	0.2314
Reoperation for prolapse	2 (2)	2 (2)	1
Retention	4 (4)	1 (1)	0.1639
Overactive bladder	5 (5)	0	0.0121
Urinary tract infection	12 (13)	1 (1)	0.0002
Dehiscence	1 (1)	0	0.4194
Mesh exposure	8 (9)	2 (2)	0.0187
Enuresis	1 (1)	0	0.4194
Stress urinary incontinence	4 (4)	0	0.0297
Mixed urinary incontinence	1 (1)	0	0.4194
Nocturnal urgency	1 (1)	0	0.4194
Hematoma	3 (3)	1 (1)	0.3115
Hemorrhage	1 (1)	0	0.4194
Dyspareunia*	3 (8.1)	3 (4.4)	0.663
Granuloma	1 (1)	0	0.4194
Enterocele	1 (1)	0	0.4194
Renal tumor	1 (1)	0	0.4194

Table 3. Objective anatomical correction (POP-Q system) at final follow-up.

	CaA group			CaS group			CaA group vs CaS group	
	Preoperative, median	**Postoperative, median**	**p value (*)**	**Preoperative, median**	**Postoperative, median**	**p value (*)**	**Preoperative p value (**)**	**Postoperative p value (**)**
POP-Q stage	*3*	*1*	*<0.0001*	*3*	*1*	*<0.0001*	*0.4185*	*0.0024*
Aa	*3*	*-2*	*<0.0001*	*3*	*-2*	*<0.0001*	*0.6362*	*0.0486*
Ba	*4*	*-3*	*<0.0001*	*3*	*-3*	*<0.0001*	*0.3258*	*0.036*
C	*1*	*-7*	*<0.0001*	*2*	*-7*	*<0.0001*	*0.8048*	*0.5619*
GH	*4*	*3*	*<0.0001*	*4*	*4*	*<0.0001*	*0.6087*	*0.4099*
PB	*2*	*3*	*<0.0001*	*2*	*3*	*<0.0001*	*0.0881*	*0.025*
TVL	*8*	*8*	*0,875*	*8*	*8*	*0,0638*	*0.0685*	*0.9495*
Ap	*-1*	*-2,5*	*<0.0001*	*-1*	*-3*	*<0.0001*	*0.059*	*<0.0001*
Bp	*-2*	*-3*	*<0.0001*	*-2*	*-3*	*<0.0001*	*0.0623*	*<0.0001*
D	*-3*	*-8*	*<0.0001*	*-3*	*-8*	*<0.0001*	*0.1746*	*0.4281*

Table 4. Quality of life questionnaire findings.

	CaA group			CaS group			CaA group vs CaS group	
	Preoperative, median	**Postoperative, median**	**p value (*)**	**Preoperative, median**	**Postoperative, median**	**p value (*)**	**Preoperative p value (**)**	**Postoperative p value (**)**
Patient Global Impression of Improvement	---	*5*	---	---	*5*	---	---	*0.4258*
PISQ-12	*0*	*0*	*0.0038*	*26*	*0*	*0.0082*	*<0.0001*	*0.2876*
PDFI-20	*116.6*	*30.85*	*<0.0001*	*32*	*19.4*	*<0.0001*	*<0.0001*	*0.0868*

stage of 1 (p<0.0001 in both groups). The only individual POP-Q measure that did not significantly change from baseline was the total vaginal length. The comparative analyses showed no significant differences between the CaA and CaS groups in the POP-Q stage or individual POP-Q points at baseline. In contrast, the postoperative data showed that the CaS group had a significantly superior POP-Q stage and was superior in the individual Aa, Ba, Pb, Ap and Bp POP-Q points compared with the CaA group. Details of these comparisons are shown in Table 3.

Questionnaires measuring patients' subjective impressions were also analyzed. In both groups, women considered their quality of life to have improved significantly from baseline after the surgery when measured by either the PISQ-12 or the PDFI-20 (Table 4). Both questionnaire results showed similar tendencies when comparing the CaA and CaS groups. At baseline, the CaS group had significantly higher median PISQ-12 scores (26 vs 0, p<0.0001) and lower PDFI-20 scores (32 vs 116.6, p<0.0001) than the CaA group. However, the postoperative questionnaire results did not significantly differ between the two groups.

There were some statistical differences between the two groups regarding postoperative adverse events (Table 2). De novo overactive bladder (OAB) was only seen in the CaA group (p=0.0121). Other complications that were significantly more frequent in the CaA group than the CaS group were urinary tract infection, mesh exposure, and de novo SUI. Mesh exposure was more common in the CaS group than in the CaA group (p=0.0187). Rare adverse events (only one case per event) also occurred in the CaA group, including vaginal dehiscence, enuresis, urge incontinence (mixed), nocturnal urgency, hematoma, hemorrhage, granuloma, and an enterocele.

DISCUSSION

This retrospective study evaluated mid-term follow-up data from women who underwent surgical POP repair using one of two transvaginal meshes. The two devices were similar in terms of surgical approach and surgical instruments, type of implanted material, and anatomical landmarks for mesh fixation. The main difference between the two meshes was the amount of implanted material and knitting pattern. CaS is manufactured with less material than CaA, and is considered an ultra-light-weight mesh. Both groups showed significant improvements from baseline in anatomical correction and patient-reported outcomes. Postoperatively, the CaS group had statistically better anatomical correction (based on the POP-Q stage) than the CaA group, but both groups had similar success rates in accordance with Barber's criteria. The clinical significance of these findings is discussed in the following paragraphs. The quality of life questionnaires showed that there were similar significant subjective improvements postoperatively within both groups. However, the quality of life significantly differed between the two groups at baseline.

The surgeons who performed the operations in the present study were all highly-trained in POP repair techniques and had little experience with CaA when they first used it. The surgical techniques and surgical instruments used for CaA and CaS are almost identical. Surgeons learned to master this technique and became familiar with the device by using CaA, as it was the first product to be launched. This chronological mismatch meant that the surgeons underwent more training for the specific technique and type of device for the CaS system than for the CaA system. There were no differences between groups regarding operation time and intraoperative complications. However, a surgeon with little experience caused one major intraoperative complication in the CaS group. A patient with a very atrophic vagina incurred a bladder injury during the dissection. This injury was resolved with raffia of the lesion and probe insertion for 10 days, and did not result in any long-term complications.

The success rate according to Barber's criteria was similar in the CaA and CaS groups (82% and 90% for the CaA and Cas groups, respectively). A previous prospective study evaluat-

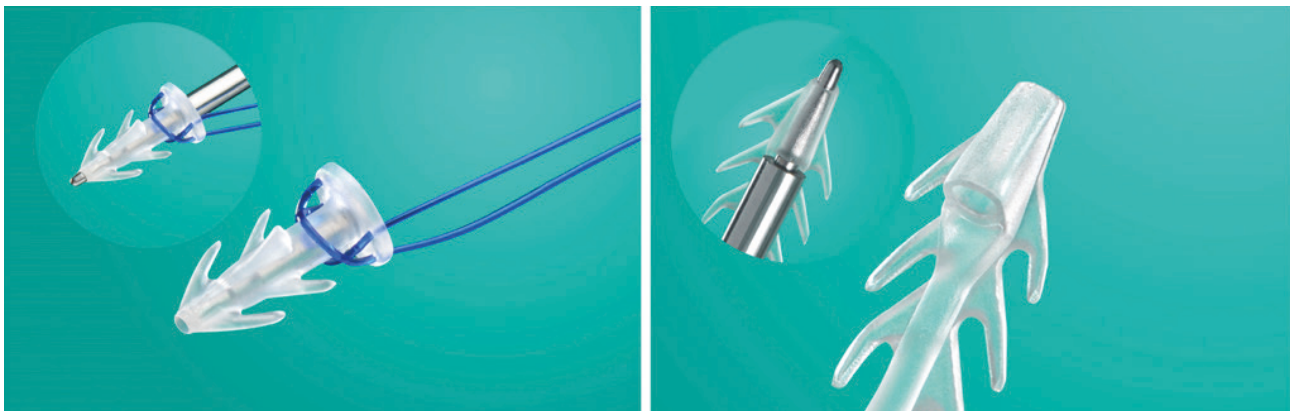


Figure 1. Left image: Tissue anchoring system for SSL fixation. Right image: Multipoint fixating columns for anterior fixation.
In both images, the pictures enclosed in the circles show the anchoring devices loaded on the surgical instrument (retractable insertion guide).

ing CaA reported a success rate of 88.7% during a median follow-up of 12 months [range 6–24 months] with the criterion for success defined as a Ba point of less than -1 cm[19]. Furthermore, a retrospective analysis with a mean follow-up of 18 months reported that CaA achieved an objective operative efficacy of 94% (POP-Q anterior stage 0 or I) and a subjective efficacy of 91% (no vaginal bulge symptoms)[20]. The first results for CaS were presented at the 69th Annual Congress of the German Society of Urology in 2017, showing a patient satisfaction rate of 95% in 154 women. These previous studies show that the success rates of CaA and CaS are comparable, although the success criteria differed among the studies, with more stringent criteria used in the present study. In general, the anatomical outcomes are less optimal than the subjective outcomes, and so it is encouraging to see good anatomical and patient-reported outcomes.

In terms of anatomical correction, CaA and CaS showed an identical median postoperative POP-Q stage (stage 1), although the postoperative POP-Q stage significantly differed between groups (p=0.0024). From a clinical perspective, the clinical perception of the elasticity of the anterior wall of the vagina suggests that there was less retraction of the mesh in the CaS group than the CaA group, but this requires further exploration, possibly with ultrasound. Recent reviews and meta-analyses report that the use of transvaginal meshes is associated with lower rates of recurrence, awareness of prolapse, and repeat surgeries than native tissue repairs[12,15]. In the present study, the CaA and CaS groups did not significantly differ in recurrence or repeat surgeries, with lower rates than those reported in previous reviews.

A recent publication from the PROSPECT study cast doubt on the superiority of meshes over native tissue repair[21]. The PROSPECT study is one of the most recent analyses of the comparative use of meshes and native tissue repair, and is a large, well designed RCT that adds valuable high-level evidence[21]. The PROSPECT study found no apparent benefits of transvaginal meshes or biological grafts when compared with native tissue repair,[21] which contrasts with the conclusions of the Cochrane Reviews[12,15]. The large number of surgeons involved in the PROSPECT study and the freedom for each surgeon to choose the mesh/surgical technique give a fair representation of the users and devices[21]. However, this comes at the expense of being able to evaluate the performance of specific devices when used by comparable users. It can be assumed that at least some mesh kits were used in the PROSPECT study, and this may have impacted the standardization of surgical techniques, which again represents a situation of compromise between representativeness and specificity. The PROSPECT study also showed no large increase in complications associated with mesh repair versus native tissue repair,[21] suggesting that the learning curve associated with mesh devices may be small. Moreover, the PROSPECT study did not evaluate operative times, and evidence shows that the use of mesh kits decreases the operative time compared with native tissue repair.

Regarding the safety of surgical POP repair, the four adverse events that had lower incidences in the CaS group than in the CaA group in the present study were SUI, OAB, urinary tract infection, and mesh exposure. In-depth analysis of the lower incidence of SUI in the CaS group than the CaA group is inappropriate for two reasons. First, CaS was not designed to concomitantly treat SUI, and second, simultaneous anti-incontinence surgeries were more frequently performed at the time of prolapse repair in the CaS group than in the CaA group. Therefore, the larger number of SUI repairs per-

Figure 2. Left image: Calistar S kit (implant, surgical instruments, and tissue anchoring system).

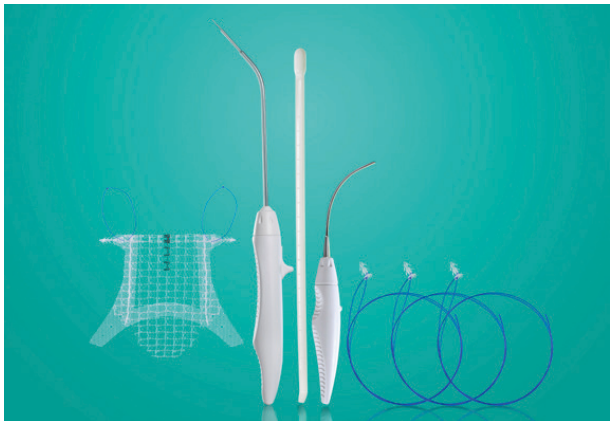
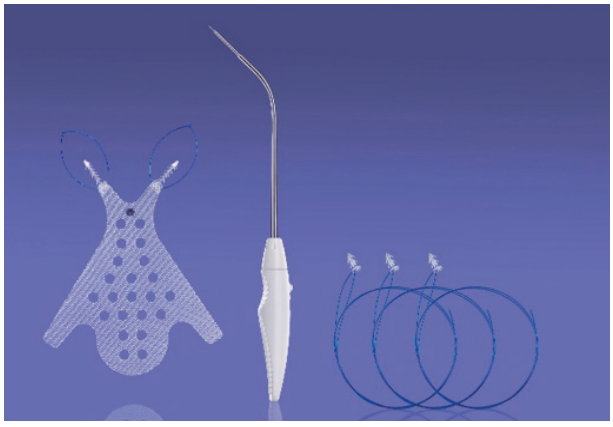


Figure 2. Right image: Calistar A kit (implant, surgical instrument, and tissue anchoring system).



formed in the CaS group may be masking the real impact of the mesh in reducing baseline SUI. In addition, the lack of data regarding preoperative SUI prevented comparison with the postoperative incidences of SUI within each group. However, the present findings show that a device used to treat both incontinence and prolapse simultaneously does not achieve the same efficacy as that achieved by the treatment of each issue via separate procedures. If we assume that the CaS and CaA groups had a similar prevalence of SUI preoperatively, all patients in the CaA group were then treated for SUI, while only those in the CaS group that actually had SUI were treated. Thus, the results favored selective treatment via two separate approaches over 100% treatment via the same approach.

There were no cases of OAB in the CaS group, while five (5%) patients in the CaA group developed OAB. If we focus only on the mesh weight, the reason for this higher incidence of OAB in the CaA group than the CaS group may be that the bladder irritation increases in tandem with the mesh weight, resulting in a higher incidence of OAB after POP repair using CaA compared with CaS. However, if the differences between CaA and CaS in the mesh shape and placement are also considered, it can be hypothesized that some patients have subclinical obstructive alterations encountered during concomitant urinary incontinence surgery, which may increase the incidence of OAB. Furthermore, it is possible that larger postmictional residues in the CaA group than in the CaS group favor the occurrence of urinary tract infection, as demonstrated by the occurrence of only one case in the CaS group and 12 cases in the CaA group.

Mesh exposure is one of the major concerns associated with the use of transvaginal meshes, due to potential adverse effects such as pain and infection, and the potential need for corrective surgeries. The group that received the lighter mesh (CaS) had significantly fewer cases of mesh exposure than the CaA group; this may be initial confirmation of the real benefit of using less material in the implant. The likelihood of mesh exposure is proportional to the area of tissue–material contact. Cases with less mesh material in contact with tissue experience less interaction between the two surfaces, resulting in a dose-response relationship between the amount of mesh used and subsequent erosions and other complications requiring repeat surgery[22].

The present data must be interpreted in the context of the limitations of the study. This was a retrospective study that compared data from surgeries that were not performed within the same timeframe; the CaA procedures were started a long time before the first CaS cases. This issue had an impact on the level of surgeon training in the specific surgical technique used for these devices. Additionally, the available data only enables mid-term follow-ups of differing durations between the two groups.

CONCLUSION

Both CaA and CaS have a similar design and are inserted using a similar technique, and so the greatest differences between the two devices are the mesh surface density and knitting pattern. We hypothesized that the lighter mesh would have a better safety profile and similar success rate than the heavier mesh. The present retrospective study provides initial data to confirm this hypothesis, as CaS performed similarly to CaA in terms of effectiveness but caused less adverse events. Prospective studies are necessary to confirm this hypothesis, but the present study provides valuable information on the safety and effectiveness of these two devices.

REFERENCES

1. Barber MD, Maher C. Epidemiology and outcome assessment of pelvic organ prolapse. Int. Urogynecol. J. 2013; 24: 1783–90
2. Chow D, Rodríguez LV. Epidemiology and prevalence of pelvic organ prolapse. Curr. Opin. Urol. 2013; 23: 293–8
3. Vergeldt TFM, Weemhoff M, IntHout J, Kluivers KB. Risk factors for pelvic organ prolapse and its recurrence: a systematic review. Int Urogynecol J. 2015; doi:10.1007/s00192-015-2695-8
4. Ismail SI, Bain C, Hagen S. Oestrogens for treatment or prevention of pelvic organ prolapse in postmenopausal women. Cochrane Database Syst. Rev. 2010; CD007063 doi:10.1002/14651858. CD007063.pub2
5. Olsen A, Smith V, Bergstrom J, Colling J, Clark A. Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. Obstet. Gynecol. 1997; 89**:** 501–506
6. Moore K et al. Adult conservative management. in Incontinence (eds. Abrams P, Cardozo L, Khoury , Wein A J) 1175–1195 (ICUD-EAU, 2013).
7. Clark A L, Gregory T, Smith V J, Edwards R. Epidemiologic evaluation of reoperation for surgically treated pelvic organ prolapse and urinary incontinence. Am. J. Obstet. Gynecol. 2003; 189: 1261–1267
8. Weber AM, Walters MD, Piedmonte MR, Ballard LA. Anterior colporrhaphy: A randomized trial of three surgical techniques. Am. J. Obstet. Gynecol. 2001; 185: 1299–1306
9. Altman D, Väyrynen T, Engh M E, Axelsen S, Falconer C. Anterior Colporrhaphy versus Transvaginal Mesh for Pelvic-Organ Prolapse. N. Engl. J. Med. 2011; 364: 1826–1836
10. dos Reis Brandão da Silveira S *et al*. Multicenter, randomized trial comparing native vaginal tissue repair and synthetic mesh repair for genital prolapse surgical treatment. Int. Urogynecol. J. 2015;26: 335–342
11. Skoczylas L C, Turne LC, Wang L, Winger DG, Shepherd JP. Changes in prolapse surgery trends relative to FDA notifications regarding vaginal mesh. Int. Urogynecol. J.2014;25: 471–7
12. Maher C et al. Transvaginal mesh or grafts compared with native tissue repair for vaginal prolapse. 2016; Cochrane Database Syst. Rev. doi:10.1002/14651858.CD012079
13. Moore RD, Lukban JC. Comparison of vaginal mesh extrusion rates between a lightweight type i polypropylene mesh versus heavier mesh in the treatment of pelvic organ prolapse. Int. Urogynecol. J. Pelvic Floor Dysfunct. 2012; 23: 1379–1386
14. Lensen E, Withagen M, Kluivers K, Milani A, Vierhout M. Comparison of two trocar-guided trans-vaginal mesh systems for repair of pelvic organ prolapse : a retrospective cohort study. Int Urogynecol J 2013; doi:10.1007/s00192-013-2098-7
15. Maher C. et al. Surgery for women with anterior compartment prolapse. 2016; Cochrane Database Syst. Rev. doi:10.1002/14651858.CD004014.pub6
16. Maher C. et al. Surgery for women with apical vaginal prolapse. Cochrane Database Syst. Rev. (2016). doi:10.1002/14651858. CD012376
17. Barber, M. D. et al. Defining success after surgery for pelvic organ prolapse. Obstet. Gynecol. 2009; 114: 600–609
18. Di Rienzo, J. A. et al. InfoStat versión 2016. (2016).
19. Palma PCR et al. Treatment of Anterior Vaginal Wall Prolapse Using Transvaginal Anterior Mesh With Apical Fixation: A Prospective Multicenter Study With up to 2 Years of Follow-up. Int. Neurourol. J.2018; 22: 177–184
20. Rogowski A. et al. Efficacy and safety of the Calistar and Elevate anterior vaginal mesh procedures. Eur. J. Obstet. Gynecol. Reprod. Biol. 2019; 239: 30–34
21. Glazener CM et al. Mesh, graft, or standard repair for women having primary transvaginal anterior or posterior compartment prolapse surgery: two parallel-group, multicentre, randomised, controlled trials (PROSPECT). Lancet (London, England) 2017; 389: 381–392
22. Chughtai B et al. Association between the amount of vaginal mesh used with mesh erosions and repeated surgery after repairing pelvic organ prolapse and stress urinary incontinence. JAMA Surg. 2017; 152, 257–263

ACKNOWLEDGMENTS AND DISCLOSURES

We thank Kelly Zammit, BVSc, from Edanz Editing (www.edanzediting.com/ac), for editing a draft of this manuscript. None of the authors have any financial issues or conflicts of interest to disclose.

Correspondence to:

Agustin Sampietro E-mail: asampietro@live.com.ar

Review

How well recognized is the Integral Theory?

DERYA KILIC[1], TOLGA GULER[1], AKIN SIVASLIOGLU[2]

[1]*Department of Obstetrics and Gynecology, Pamukkale University, Denizli, Turkey*
[2]*Department of Obstetrics and Gynecology, Mugla Sitki Kocman University, Mugla, Turkey*

Abstract: *Background, hypothesis and aim:* The Integral Theory (IT) is a universal, ligament-based theory of pelvic floor function and dysfunction which encompasses organ prolapse, bladder, bowel and chronic pelvic pain dysfunction. The aim was to systematically analyse the applicability of the Integral Theory System (ITS) to publications in a pelvic floor journal. *Methods*: We chose a journal Pelviperineology journal www.pelviperineology.org (PPJ) which encompasses all aspects of the Integral Theory System's reach: Urology, Gynecology, Coloproctology, Perineology. We scanned every publication in PPJ over a two year period to check the applicability of the ITS to the paper in hand. *Results:* An analysis of manuscripts published in Pelviperineology journal (Volume 36 and 37), only 29 clinical research articles were included as being suitable for analysis. Among the 29 clinical research articles, only 11 (37.9%) mentioned IT and/or related articles as a reference. However, according to evaluation of the clinical papers with respect to the concordance with IT predictions, 26 (90%) manuscripts were regarded as being consistent with IT predictions. *Conclusions*: Our review indicates consistency with the Integral Theory in 90% of clinical papers, though almost 2/3 of these authors did not seem to be aware of the theory. Why? We can only speculate. One reason may the difficulty in accepting that pathogenesis for bladder and bowel dysfunctions comes not from the organ itself, but from weak ligaments inactivating the opening and closure muscles which act on the ligaments.

Keywords: Integral Theory; Pelvic floor; Incontinence; Pelvic pain; Ligaments

INTRODUCTION

The Integral Theory (IT) is a ligament-based theory which has been presented as a universal theory of pelvic floor function and dysfunction[1]. The first commercial application of the midurethral sling (MUS), the TVT, was based on the IT. The Integral Theory System (ITS) is a management system which includes a ligament based diagnostic and surgical system[2] and a squatting based pelvic floor system[3]. In its 2018 iteration, the Integral Theory states that pelvic organ prolapse (POP), chronic pelvic pain, and bladder and bowel dysfunction are mainly caused by collagen/elastin deterioration in 5 main suspensory ligaments and their vaginal attachments[2]. The Integral Theory explains cure for POP, bladder and bowel dysfunction via the dual function of the ligaments: i.e., their role in pelvic organ suspension and as insertion points for three oppositely acting muscle forces. Lax ligament insertion points weaken muscle forces so they cannot adequately close the urethral or anal tubes (incontinence), evacuate them (constipation, bladder emptying problems), or tension the bladder and rectum sufficiently to prevent inappropriate activation of the micturition and defecation reflexes by peripheral stretch receptors (urinary and fecal urge incontinence)[2].

And relationship of symptoms to POP; The pictorial diagnostic algorithm accurately indicates which ligaments are damaged[1,2].

The aim of this review is to explore

1. The applicability of the Integral Theory System (ITS) to publications in a standard pelvic floor journal.
2. Whether the publications which qualified as "applicable" actually recognized the theory.

METHODS

We chose a journal which encompasses all aspects of the Integral Theory System's reach, Urology, Gynecology, Coloproctology, Pelviperineology journal www.pelviperineology.org (PPJ). We scanned every publication in PPJ over a two year period to check the applicability of the ITS to the paper in hand.

RESULTS

An analysis of manuscripts published in last 2 years of the pelviperineology journal (Volume 36 and 37) revealed overall 49 publications. With respect to the applicability of Integral Theory (IT), only 29 clinical research articles were included as being suitable for analysis[6-34]. Besides these clinical data, 6 more manuscripts were regarded as opinion and/or hypothesis which though consistent with the Theory, were not included.

Among the 29 clinical research articles, only 11 (37.9%) mentioned IT and/or related articles as a reference. The country of origin of the authors was analysed (Table 1).

When the type of the clinical data was analyzed, retrospective papers were the most common type (n=11, 37.9%) followed by prospective non-randomized studies (n=9, 31%), cross-sectional (n=6, 20.7%) and case reports (n=3, 10.3%). All articles presenting clinical data were evaluated, critically analyzed and the presented data in them were summarized in Table 2.

The number of participants in these manuscript ranged between 1

Table 1. Origin of country with respect to the correspondence of the authors per paper

Name of the country	Number of the correspondence	%
Australia	9	23
Israel	6	15.3
Italy	5	12.8
Brasil	5	12.8
Germany	2	5.1
Belgium	2	5.1
France	2	5.1
Venezuela	2	5.1
Other (S. Africa, Poland, Tanzania, Ethiopia, Argentina, Japan)	6 (one for each)	15.4

Table 2. Analysis of the content of the clinical data

Parameter	Number of manuscripts that evaluated and/or presented such data	%
Focused on Lower Urinary Tract function	19	65.5
Focus on pelvic organ prolapse	6	20.7
Focus on bowel function	10	34.5
Focus on chronic pelvic pain	13	44.8
Sexual function evaluated	3	10.3
Tethered vagina evaluated	2	6.9
Obstetric injury evaluated	2	6.9
Stress urinary incontinence data presented	15	51.7
Urge incontinence data presented	11	37.9
Urinary evacuation problems presented	8	27.6
Anal incontinence data presented	9	31
Bowel evacuation problems presented	10	34.5

and 1143, making a total of 4961 individuals. In three of the manuscripts, these individuals also included males.
A validated patient evaluation questionnaire was used in 11 (37.9%) manuscripts. Quality of life evaluation was performed in 11 papers (not all the same manuscripts where a questionnaire was used). According to the diagnostic modalities used, one (3.4%) paper presented Q-tip test results, 5 (17.2%) used pad test, 5 (17.2%) used valsalva leak test, 7 (24.1%) used POP-Q, 2 (6.9%) used pelvic floor sonography, and 6 (20.7%) used urodynamic evaluation. Surgical results comprised the presented data in 10 of the manuscripts (34.5%). Of these, 6 evaluated mesh use and 4 evaluated repair without any mesh implementation.
According to evaluation of the clinical papers with respect to the concordance with IT predictions, 26 (90%) manuscripts were regarded as being consistent with IT predictions. For the 6 papers that were regarded as opinion/hypothesis, 3 of them were accepted to be consistent with the predictions of IT. The 3 clinical papers that were not applicable with IT were evaluated in detail. One was a retrospective and two were prospective non-randomised studies. One included male data and the number of the participants in this paper was between 16 and 55. None of these non-applicable papers were related to surgical data. In other words, all manuscripts presenting surgical data (n=10) were found to be consistent with the predictions of IT.

DISCUSSION

It is now almost 30 years since the IT was first published. We conclude that even though the most widely performed operation for SUI, the midurethral sling, (estimated 5,000,000 operations to date), is based on the IT, the IT itself was still not widely quoted in our review. Only half of the papers which qualified for inclusion mentioned the IT, even though the content of 90% of the papers examined was consistent with the IT or its predictions.
Everything in medicine is based on some sort of theory. The Burch Colposuspension was based on elevating the proximal urethra above the pelvic diaphragm into the "pressure transmission zone" where the pressure could be "equalized". "Detrusor overactivity" is thought to arise from some problem in the detrusor muscle, hence its treatment with drugs which suppress detrusor activity.
There are two universal pelvic floor theories in the literature, the Petros Integral Theory[1] and the Swash Unifying Theory[4]. Swash et al published "A unifying concept of pelvic floor disorders and incontinence" in 1985. Based on nerve conduction and other studies, Swash et al demonstrated that childbirth in patients who presented with urinary and fecal incontinence, the nerve supply to pelvic muscles was often damaged during childbirth[4]. The Integral Theory is a musculo-elastic theory where muscles contract against suspensory ligaments to open and close the urethral and anal tubes. Loose ligaments invalidated the 3 directional forces which open and close these tubes and control the evacuation reflexes[1]. Different from the Swash Unifying Theory, the Integral Theory from day 1 has demonstrated surgical cure of symptoms by ligament repair. The best known example is the midurethral sling (MUS) which cures stress urinary incontinence (SUI) by pubourethral ligament repair with a tape. The Swash theory cannot explain cure of SUI by a MUS operation, nor the results of [5].
Ligament or muscle? In a blinded histological/ surgical trial, 45/47 patients undergoing midurethral sling showed histological evidence of severe muscle damage, yet 89% were cured of their stress urinary incontinence (SUI) the day after surgery. It was concluded that ligament damage (pubourethral) was more important than muscle damage in the pathogenesis of SUI[5].
The discussion of how theories can be validated or invalidated, become dominating or discarded are the province of the philosophy of science and are outside the scope of this paper. One validated example is said to be sufficient to invalidate a theory; the more radical a theory, the longer it takes to be accepted.

CONCLUSIONS

Our review indicates consistency with the Integral Theory as regards content of most clinical papers (90%), though almost 2/3 of these authors did not seem to be aware of the theory, even though most likely a majority would use the midurethral sling operation which is based on the Theory.
We can only speculate at reasons for this discrepancy, the principal one being the inevitable difficulties encountered by a clinician in trying to come to grips with a completely foreign concept, a different paradigm, one where the pathogenesis for bladder and bowel dysfunction comes not from the organ itself, but from weakness in the suspensory ligaments of the pelvis.

REFERENCES

1. Petros PE & Ulmsten U. An Integral Theory of female urinary incontinence. Acta Obstetricia et Gynecologica Scandinavica. 1990;69:7-31.
2. Bernhard Liedl, Hiromi Inoue, Yuki Sekiguchi, et al. Update of the Integral Theory and System for Management of Pelvic Floor Dysfunction in Females. European J of Urology. 2017;17:100-108.
3. Skilling PM,·Petros PE. Synergistic non-surgical management of pelvic floor dysfunction: a second report. Int Urogynecol J Pelvic Floor Dysfunct. 2004; 15:106-110.
4. Swash M, Henry MM, Snooks SJ. A unifying concept of pelvic floor disorders and incontinence. J Royal Soc Med 1985;178:906-908.
5. Petros PE, Swash M, Kakulas B. Stress urinary incontinence results from muscle weakness and ligamentous laxity in the pelvic floor. J. Pelviperineology 2008;27:107-109.
6. AndrettaE, Masin A , Zuliani C, Mariotti G, Sciarra A. Does sacral nerve modulation work on simultaneous bladder and rectal dysfunctions? Pelviperineology 2017;36:53-59.
7. Giraudo D, Gozzerino F, Lamberti G, et al. Urodynamic evaluation before and after continuous intrathecal Baclofen infusion (ITB) in patients unresponsive wakefulness syndrome and minimally conscious state. Pelviperineology 2017;36:60-62.
8. Messelink B. A new method to evaluate the part of stress in pain: injection of dextrose 5% (neural prolotherapy) on acupuncture points corresponding to the stellate, coeliac and mesenteric ganglions. A pilot study. Pelviperineology 2017;36:67-70.
9. Browning A, Williams G, Petros P. Prevention and cure of post vesico-vaginal fistula repair incontinence by insertion of skin graft in the bladder neck area of vagina. Update on hypothesis and interim report. Pelviperineology 2017; 36:9-11.
10. Giraudo D, Gozzerino F, Antoniono E, Lamberti G. Anal incontinence and severe acquired brain injury: a retrospective study of 347 rehabilitation inpatients. Pelviperineology 2017;36:13-16.
11. Mazzariol O, Palma P, Souto S. Impact of apical prolapse surgical correction on the quality of life of women. Pelviperineology 2017;36:21-23.
12. Teixeira T, Re Go A, Filho C, et al. Quality of sexual life of women with urinary complaints in reproductive age and after menopause. Pelviperineology 2017;36:41-44.
13. Ghazaleh Rostaminia G, Javadiann P , O'boyle A. Parity and pelvic floor dysfunction symptoms during pregnancy and early postpartum. Pelviperineology 2017;36:48-52.
14. Petros P, D Med Sc, FRCOG, FRACOG, CU. Severe chronic pelvic pain in women may be caused by ligamentous laxity in the posterior fornix of the vagina. Pelviperineology 2017;36:71-73.
15. SekiguchicY, Inoue H, Liedl B, et al. Is Chronic Pelvic Pain in the female surgically curable by uterosacral/cardinal ligament repair? Pelviperineology 2017;36:74-78.
16. Skilling PM, MB ChB (St And.). Pelvic floor exercises according to the Integral Theory - strengthening the 3 directional muscle forces improves chronic pelvic pain, bladder & bowel dysfunctions. Pelviperineology 2017;36:79-83.
17. Goeschen K, Gold DM. Surgical cure of chronic pelvic pain, associated bladder & bowel symptoms by posterior sling in 198 patients validates the Pescatori Iceberg principle of pelvic symptom co-occurrence. Pelviperineology 2017;36:84-88.
18. Zarfati D, Petros P. The Bornstein Test- a local anaesthetic technique for testing uterosacral nerve plexus origins of chronic pelvic pain. Pelviperineology 2017;36:89- 91.

19. Sommariva M, Schievano C, Saleh O. Micronized palmitoylethanolamide reduces bladder chronic pelvic pain due to different etiologies and improves bladder functions. Pelviperineology 2017;36:92-96.
20. Tiecher JTA , Palma PCR, Ricetto CLZ. Is there a correlation between simulated operations, urodynamics (vlpp) and urethral mobility? Pelviperineology 2017;36:99-103.
21. Aharoni A, Mamet Y, Agranat AA. Efficacy of vaginal and laparoscopic sacrocolpopexy (VLSCP), a dual approach to utero-vaginal prolapse, compared with laparoscopic sacrocolpopexy (LSCP) alone. Pelviperineology 2017;36:113-114.
22. Chrysostomou A, Jacobson H, Chrysotomoun M. An assessment of the functional outcome and quality of life before and after trans-obturator tape surgery for stress urinary incontinence. Pelviperineology 2017;36:116-121.
23. Pinango-Luna S, Petros P. Questionnaire validation may not validate- a critical analysis. Pelviperineology 2017;36:122-124.
24. Martinho N, Botelho S, Nagib A, et al. The effects of pelvic floor and transverse abdominal muscles? maximal voluntary contractions on pelvic floor ultrasound biometric parameters in women with stress urinary incontinence: preliminary results. Pelviperineology 2017;36:125-128.
25. Johns S, Jantos M, Baszak-Radomanska E, Galenson S. Age related comorbidities in chronic urogenital pain. Pelviperineology 2017;37:20-24.
26. Baumfeld Y, Weintraub AY, Yaniv SS, Spiegel E, Yohay Z, Elharr D, Yohay D. Characteristics, risk factors and outcomes of deliveries complicated with obstetrical anal sphincter injury. Pelviperineology 2017;37:35-38.
27. Beco J, Antolak S, Seidel L, Albert A. Pelvic trauma and pudendal syndrome (post-traumatic pudendal syndrome). Pelviperineology 2017; 37:42-48.
28. Levin M. Pathohysiology and diagnosis of descending perineum syndrome in children. Pelviperineology 2017;37:52-56.
29. Pucciani F. Descending perineum syndrome: pathophysiology of fecal incontinence. Pelviperineology 2017;37:57-63.
30. Barbier V, Duperron C, Delorme E. Evolution of the TOT OUT/IN technique: retropubic TOT. Morbidity and 5-year functional outcomes. Pelviperineology 2017;37:74-77.
31. Chill HH, Olek M, Yahya RH, Karavani G, Shveiky D. Validation of the patient global impression of improvement questionnaire to the Hebrew language. Pelviperineology 2017;37:78-79.
32. Andrey K, Yagel Y, Khashper A, Sheizaf B, Yohay D, Weintraub AY. A slow growing pelvic actinomyces related abscess in a premenopausal patient mimicking genito-urinary malignancy - Case report and literature review. Pelviperineology 2017;37:80-82.
33. Reid RI. A 20 year experience of microsurgical removal of the Bartholin?s glands for refractory vulvodynia. Pelviperineology 2018; 37:83-87.
34. Palma P, Cassio Ricetto C, Andrade DL, Zocco MZ. Urethrolysis and Martius flap graft for recurrent urinary stress incontinence with fixed urethra. Pelviperineology 2018;37:88-89.

DISCLOSURE STATEMENTS
There was no conflict of interest. The authors of the publication did not receive any financial support by any grant/research sponsor.

Correspondence:
Derya Kilic, Camlaralti Mahallesi, 6095 Sokak 11, Kinikli 20180
Denizli - Turkey
deryakilic.md@gmail.com

Original article

Prostato-sacral Ligament, description of a new anatomy in males, its clinical significance and anatomic similarity to female anatomy

AHMED FARAG[1], SAHAR EMM NASR[1], MOHAMED YEHIA ELBARMELGI[1], AMAL A. FARAG[1], PETER PETROS[2]

[1] *Kasralainy faculty of medicine, Cairo University.*
[2] *University of NSW. Professorial Department of Surgery*

Abstract: *Background and Aim*: The uterosacral ligament (USL) has become an increasing focus of interest in terms of its use for surgical support in the management of pelvic organ prolapse. Description of an equivalent ligament in males is lacking. Our aim is to describe a new Ligament in males which was found during rectal resection using the trans-anal Total mesorectal excision "Ta TME" which we called Prostato-sacral ligament and its clinical significance. *Methods*: The Transanal Total Mesorectal Excision "TaTME" technique was done in 46 patients from January 2017 till April 2018 for rectal resection. The group included 27 males and 19 Females "Age range = 31 - 72 years , Mean= 34.13 years. In the present work we describe a new ligament in males – which we encounter during the operation- that has the same anatomic orientation to the female anatomy. *Results*: Histologic studies revealed the musclo-tendinous structure of the newly described ligament with abundant blood vessels, elastic fibers and nerves with great similarity to female Utero-sacral ligament. It forms a very important landmark for rectal resection using the new TaTME approach. It can also explain the cause of chronic pelvic pain as a striking similarity to female utero-sacral ligament was noticed. *Conclusion*: To the best of the authors' knowledge this is the first time for this ligament to be described and histologically studied in the Literature. The Surgical and medical significance had been discussed.

Keywords: Ligament; Pelvis; Pain; Utero-sacral; Prostato-sacral; Transanal; TME

What this paper add to literature?
This research add to the literature a description of a new ligament in male pelvis which we called Prostato-sacral ligament with a striking similarity to female anatomy (Utero-sacral ligaments). This ligament is suggested as a landmark of the proper dissection plane during Ta TME and can explain chronic Pelvic pain in males.

INTRODUCTION

The Uterosacral ligament (USL) has become an increasing focus as it has been used with different surgical techniques for support in the management of pelvic organ prolapse [1–2]
There are a lot of variations in the description of the anatomy of USL in the published literature. The main point of controversy is the proximal attachment and whether it is connected to the sacrum [3–5] or attached to the sacrospinous ligament and the coccygeus[6].
Some authors [3,5] distinguish between the USL and the so-called cardinal ligament (CL). Other authors[1, 7] refer to that as the less defined term "uterosacral-cardinal ligament complex".
In the surgical literature the USL is described as a dense, strong band of connective tissue. However, these non condensed ligamentous structures were not demonstrated in the cadaveric and histological studies histological studies[7].
In males, a sacrogenital fold was described as a continued tissue to the upper ends of the seminal vesicles and the bladder; on either side of the rectum it forms the pararectal fossa, which varies in size to accomodate the distension of the rectum. Anterior to the rectum the peritoneum forms the rectovesical excavation, which is limited laterally by peritoneal folds extending from the sides of the bladder to the rectum and sacrum. These folds are known from their position as the rectovesical or sacrogenital folds. However this was considered not a true ligament but just a peritoneal fold[8].
Aim of work: In the present work we describe a real ligament which we named the Prostato-Sacral ligament as a male equivalent to the female utero-sacral ligament, based on our findings during the new technique of Trans-anal Total Mesorectal incision "Ta TME" and the value of such ligament as an important landmark for proper circumferential resection margin for rectal cancer during such new procedure.

PATIENTS AND METHODS

The transanal total Mesorectal "Ta TME" technique was done in 46 patients from January 2017 till April 2018 for rectal resection. The group included 27 males and 19 females. During the operation biopsies where taken from the newly described ligaments and microscopic histological examination was done using Using H&E stains, Masson's trichrome collagen stain, Orcein elastic stain and modified Palmgren's method for nerve fibres and this is compared to the known description of female Utero-sacral ligament or uterosacral-cardinal ligament complex described in literature.

RESULTS

Age distribution ranges from 31 to 72 years. Mean age was 34.13 years.
This study ends up into 27 male patients and 19 female patients inserted in this study. Among the 27 male patients who are the group of main interest 24 patients were operated upon for mid and low rectal cancer. They had had a Laparoscopic Trans Abdominal – Trans Anal approach, "LATA approach"[9]. Two patients had had Proctocolectomy with Ileo-anal pouch anastomosis, one for familial adenomatous polyposis and one patient for Ulcerative Colitis with high grade dysplasia. Another case had advanced Rectal Polyp with high Intra-epithelial neoplasia, which couldn't be removed endoscopically.
Six cases among the male cancer patients had an intersphincteric resection before proceeding to the Ta TME of the resection. Patients with FAP and UC had anal mucosectomy for 4 cm before proceeding with Ta- TME.
We used the technique of TaTME [9] during the anterior and posterior dissection guided by the Denonvillier's fascia between the rectum and prostate in males and between the rectum and posterior vaginal wall in females anteriorly. Posteriorly we used the Waldeyer's fascia as a posterior limit of our rectal resection avoiding injury of such fascia in order to avoid subsequent massive bleeding from the presacral plexus of veins.
Laterally we used the technique described by Mike[10] to see the parietal pelvic peritoneum and go up into the pelvis until we meet the dissected pelvic planes which were dissected laparoscopically until we divide the so-called lateral ligaments of the rectum while visualizing and preserving the hypo-gastric nerves on both sides.
As we connect the lateral planes that have developed transanaly with the anterior plane, we could visualize the uterosacral ligaments (USL) on both aspects of the midline i.e with the vagina in-between the USLs (Figure 1 a) and a similar ligament in ma-

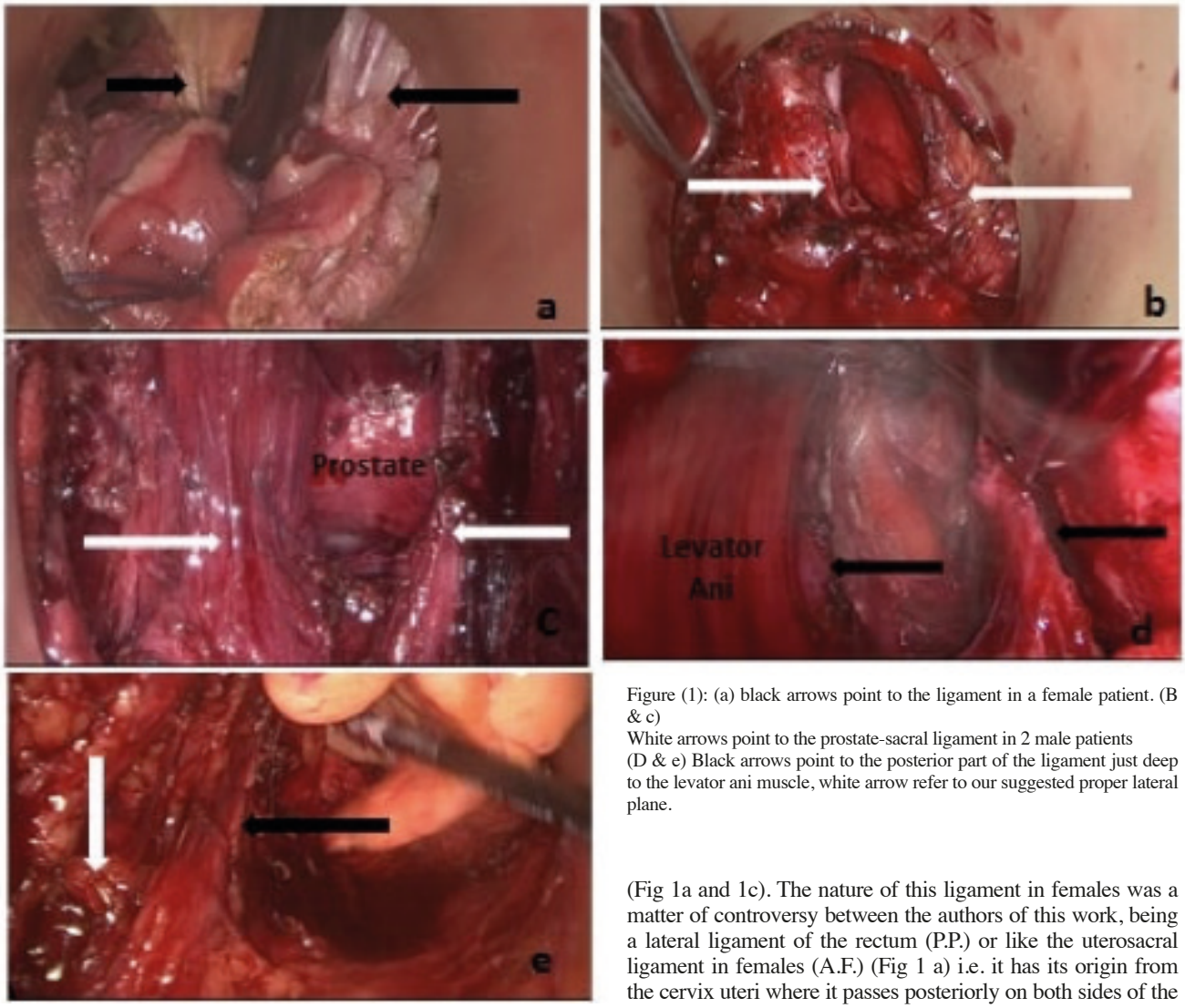


Figure (1): (a) black arrows point to the ligament in a female patient. (B & c)
White arrows point to the prostate-sacral ligament in 2 male patients
(D & e) Black arrows point to the posterior part of the ligament just deep to the levator ani muscle, white arrow refer to our suggested proper lateral plane.

les with the prostate between them in males. (Fig 1 b)
This ligament looked to be attached to the prostate on both sides of the prostatic sulcus in most of the cases (25 cases) (Fig 1 b), and to come directly from the pubis without being attached to the prostate in only 2 cases. (Figure 1 c)
Connecting the posterior dissection plane with the lateral dissection planes shows the posterior part of the USL in females and its equivalent ligament in males as it approaches the sacrum at the S 3-4 level (Fig 1d and Fig 1e). In between the anterior and posterior parts of both ligaments, the ligaments are fused with the fascia propria of the rectum on both sides before both become thinned out as they leave the fascia propria of the rectum on their way to their posterior attachment.
Specimens from the studied ligament were obtained during Ta-TME & fixed in 10% buffered formula saline for 5 days and then processed for preparation of paraffin blocks. Preparation of 6 μm paraffin sections were done. These sections were stained by H&E, Masson's trichrome collagen stain, Orcein elastic stain and modified Palmgren's method for nerve fibres (Fig 2) in paraffin-embedded material [11]. The biopsies revealed collagen bundles, with scarred smooth muscle fibers and scattered blood vessels, a lot of Elastin and nerve fibers. This has a great similarity to Utero-sacral ligament (USL) or the "uterosacral-cardinal ligament complex" described in females.

DISCUSSION

In the present work we describe a new ligament in the male which has the same anatomic orientation to the female anatomy (Fig 1a and 1c). The nature of this ligament in females was a matter of controversy between the authors of this work, being a lateral ligament of the rectum (P.P.) or like the uterosacral ligament in females (A.F.) (Fig 1 a) i.e. it has its origin from the cervix uteri where it passes posteriorly on both sides of the rectum before gaining its posterior attachment, which is still a matter of controversy[1-7].
In males it starts on both sides of the median sulcus of the prostate (Fig 1b) in 25 out of the studied 27 patients (92.6%). In the remaining 2 male patients "7.4 %" (Fig 1c), it arises from the conjoined ischio-pubic ramus without obvious attachment to the prostate. In all the studied 27 patients, and in all the female patients, the ligament passes lateral to the rectum being fused with the lateral margin of the mesorectum before leaving it as it thins out to be attached posteriorly similar to the uterosacral ligament (Fig 1d and Fig 1e).
Histologic studies revealed its Musclo-tendinous structure with abundant blood vessels, elastic fibers and nerves (Fig 2).
The Significance of such ligament is many folds, including dividing the inner pelvic space "the TME holly plane" into an innermost plane between the 2 ligaments which includes the rectum and mesorectum an outer part lateral to this ligament. However the dissection medial to this ligament would be very close to the lateral circumferential margin of the TME plane and will not connect easily with the proper TME medial plane developed by abdominal dissection as the dissection proceed from below upwards in the TA-TME technique. The proper dissection plane has to be developed lateral to the prostatosacral ligament in males and the uterosacral ligament in females between those ligaments and pelvic fascia (Fig 1e) taking both the ligaments medially and the fascia laterally, as the landmarks for the proper TME plane which will connect the dissection plane from below with the proper TME holly plane developed abdominally.

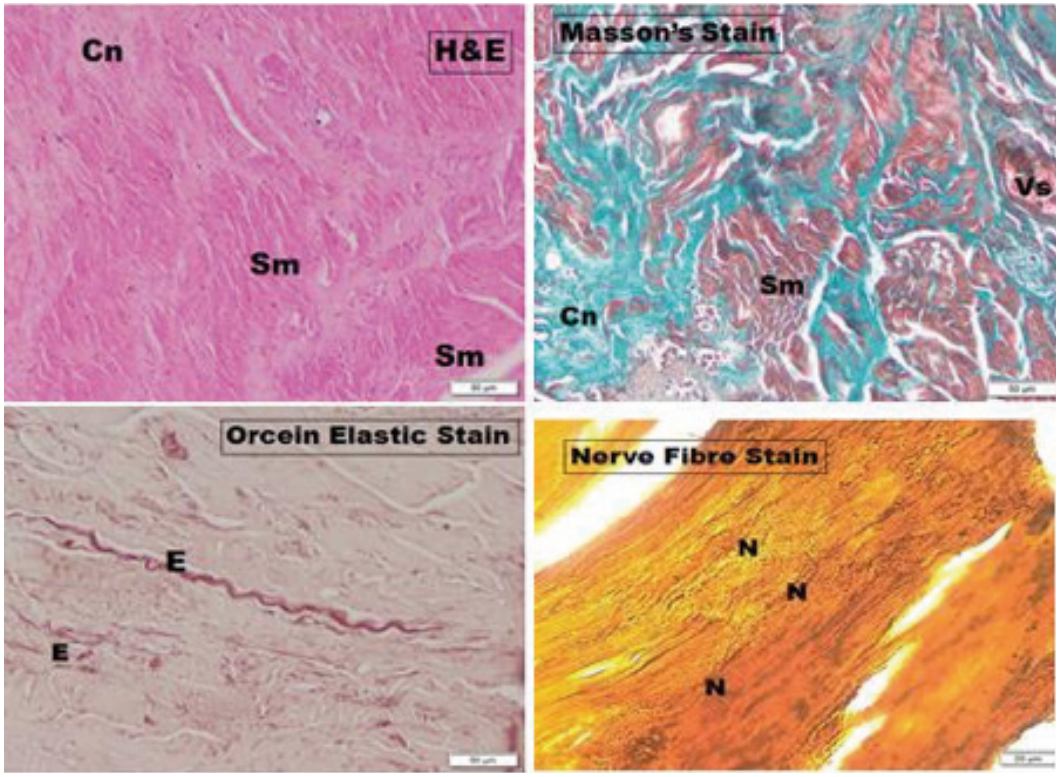


Figure (2): Histologic studies in a male revealed its Musclo-tendinous structure
With abundant blood vessels, elastic fibers and nerves, Using H&E Masson's trichrome collagen stain, Orcein elastic stain and modified Palmgren's method for nerve fibres.

Failure to see such ligaments and dividing them as part of the radical resection of the rectum may jeopardize the lateral circumferential resection margin.

In addition the ligament may play an important role in fixation of the rectum in normal controls and its repair can be done as a treatment of rectal prolapse as is used in females for uterine and vaginal prolapse[1-2].

Another important application is that the laxity of such ligament may be the cause of chronic pelvic pains in males an equivalent situation to cases of chronic pelvic pains due to laxity of such ligament in females, where the repair of such a ligament have been adopted to treat such pains in females[13].

In conclusion, to the best of the authors' Knowledge this is the first time for this ligament to be described and histologically studied in the literature and it represents a very important landmark for rectal resection using the new Ta-TME approach. It can also explain the cause of chronic pelvic pain as a striking similarity to female anatomy was noticed.

REFERENCES

1. Dwyer PL, Fatton B. Bilateral extraperitoneal uterosacral suspension: a new approach to correct posthysterectomy vaginal vault prolapse. Int Urogynecol J 2008; 19:283–292
2. Fatton B, Dwyer PL, Achtari C, Tan PK. Bilateral extraperitoneal uterosacral vaginal vault suspension: a 2 year 2009
3. Buller JL, Thompson JR, Cundiff GW, Sullivan LK, Schön, Ybarra MAS, Bent AE. Uterosacral ligament: description of anatomic relationships to optimize surgical safety. Obstet Gynecol 2001; 97(6):873–879
4. Blaisdell FE. The anatomy of the sacro-uterine ligaments. Anat Rec 1917; 12:1–42.
5. Campbell R. The anatomy and histology of the sacrouterine ligaments. Am J Obstet Gynecol 1950; 59:1–12
6. Umek WH, Morgan DM, Ashton-Miller JA, DeLancey JOL. Quantitative analysis of uterosacral ligament origin and insertion points by magnetic resonance imaging. Obstet Gynecol. 2004; 103(3):447–451
7. Ramanah R, Parratte B, Arbez-Gindre F, Maillet R, Riethmuller D. The uterosacral complex: ligament or neurovascular pathway? Anatomical and histological study of fetuses and adults. Int Urogynecol J 2008; 19:1565–1570
8. Henry Gray (1825–1861). Anatomy of the Human Body. 1918. http://www.bartleby.com/107/pages/page1154.html
9. Buchs NC, Nicholson GA, Ris F, Mortensen NJ, and Hompes R: Transanal total mesorectal excision: A valid option for rectal cancer? World J Gastroenterol. 2015 Nov 7; 21(41): 11700–11708. PMCID: PMC4631971. PMID: 26556997
10. Makio Mike. Laparoscopic Colorectal Cancer Surgery. Operative Procedures Based on the Embryological Anatomy of the Fascial Composition. By Igaku-Shoin Ltd., Tokyo Japan. 2012
11. Suvarna S.K, Layton C, Bancroft JD. Bancroft's theory and practice of histological techniques . 7th edition Churchill Livingstone Elsevier , 2013:187-358.
12. Braun, NM, Theobald PV. Chronic Pelvic Pain Caused by Laxity of the Uterosacral Ligaments: Are the Posterior Fornix Syndrome and the Allen– Masters Syndrome Synonyms? Pain Medicine. 2016; 17 (2): 370–371,https://doi.org/10.1111/pm/pme.12876
13. Petros PE Severe Chronic Pelvic Pain in Women May Be Caused By Ligamentous Laxity in the Posterior Fornix of the Vagina Aust. NZ J Obstet Gynecol 1996; 36: 3: 351-4.

DISCLOSURE STATEMENTS

Acknowledgement goes directly to Cairo University which completely funded this study.

The study was approved by the Research Ethics Committee of Cairo University.

All authors declare that they do not have any financial and personal relationships with other people or organizations that could inappropriately influence (bias) their work.

Correspondence:
dr.yeho@yahoo.com

Original article

MR anatomy of the endopelvic fascia and ligaments in males

VITTORIO PILONI[1], MATTEO MAZZUCCO[2], ANDREA CHIAPPERIN[2], MATTIA BERGAMASCO[2]

[1]Radiologist, MD; [2]Technician
Diagnostic Imaging Centre Affidea, Monselice (Padova), Italy

Abstract: *Aim* To describe the characteristics of the connective supporting system at MR imaging and its clinical impact. *Materials and Methods* The imaging series of three hundred and fifty four consecutive men submitted to pelvic MRI between April 2012 and November 2019, were systematically reviewed for evidence of any linear hypointense structure consistent with the connective system as seen on the axial, sagittal and coronal planes using the T 2-weighted pulse sequence. *Results* In the anterior compartment, the fundiform ligament, the puboprostatic ligaments and the suspensory penis ligaments were recognized most frequently (100 %, 87.5 % and 70 %, respectively); in the middle compartment, the neurovascular bundle contained in the posterior triangular prostatic corner, the peritoneal reflection running over the bladder and suspending the seminal vesicles and the Denonvilliers fascia were see in 55.9 %, 42.6 % and 40.9 % of cases. Besides all, the typical H-shaped morphology of the sacro recto vescicolo genito pubic fascia characterized the endopelvic fascia of the posterior compartment in up to 77.9% of cases, closely resembling the features of the sacro uterine ligaments. *Conclusions* As it occurred in the case of female patients, MRI proves to be the imaging modality of choice to depict the anatomy of the connective tissue. This have a potential impact on the early detection of pathological processes (tumor staging and recurrence, abscess location and spread) as well as on the pathophysiology of functional disorders.

Keywords: Endopelvic fascia; Male pelvis; Magnetic Resonance Imaging; Mesorectal fascia; Denonvilliers fascia; Sacro recto vesico genito pubic fascia

INTRODUCTION

Over the past 20 years, numerous contributions have been published concerning the tudy of the endopelvic fascia in the female population, both from an anatomical and imaging point of view[1-5]. On the contrary, those were scarce for the same structure in males and limited to the interest in the anatomy involved in total mesorectal excision surgery after rectal tumor removal[6-8], prostatic cancer staging and periprostatic tissues following radical prostatectomy[9-13], or the retropubic space after inguinal hernioplasty[14].

In an attempt to fill the void, we hereby report our experience concerning the anatomical features of the endopelvic fascia, as seen on magnetic resonance imaging, in a wide range of male patients referred to our diagnostic unit for a number of pathologies other than those mentioned above[15]. All this, in the supposition that their fascial system was intact or, at most, was affected by minor changes only. Over time, however, the need for taking care of even minimal abnormality/variant during the reporting phase, has lead us to gradually change our view of male pelvic fascia and ligaments until the point of considering their relevant possible role also in the development of functional disorders, sexual dysfunctions and chronic pelvic pain syndromes. As such, the goal of the paper is two-fold, as follows: firstly, to fill the existing gap of knowledge which is still present in the medical literature with regard to the characterization of the pelvic connective structures as a whole; secondly, to stimulate readers interpreting pelvic floor pathologies and dysfunctions in males under the new perspective of the anatomical defects of the connective tissues that sustain them.

MATERIALS AND METHODS

The pelvic MR imaging series of three-hundred and fifty-four consecutive men (mean age 53.2±6.1 yr, range 16-83 yr) referred to our unit between March 2012 and November 2019 were systematically reviewed. Reasons for the examination included voiding dysfunctions, obstructed defecation syndrome and rectal prolapse, ano-perianal fistula disease, sexual dysfunctions, and chronic pelvic pain. All MR imaging examinations were developed on a 1.5-T, horizontally oriented, whole-body system (Philips, Multiva model, The Netherland) using a TORSO XL SENSE four-element, flexible wraparound surface coil. No bowel preparation or intravenous antispasmodic agents were used. However, patients were encouraged to empty their rectal ampulla early in the morning of the examination date by a spontaneous bowel movement and were asked to void their bladder in the toilette room just before imaging. Regardless of the presenting symptoms, which led us to tailor the MR imaging protocol to the singular case, a fast localizer scout scan (TFE T1 pulse sequence, TR 8 ms, TE 5 ms, FA° 25, thickness 15.0 mm, number of images 5-to-11) was acquired first which served to mark the boundaries of the region of interest (ROI); then, sagittal, axial and coronal T2-weighted turbo spin-echo (TSE) acquisitions of the pelvis were performed in all cases with the following technical settings: TR, range 3649–4656 ms; TE, 100 ms; flip angle, 90°; section thickness, 4 mm; intersection gap, 4 mm; reconstruction matrix, 576 and 3-4 averages; echo train length, 16; FOV, 280-350 mm; acq.time, 3:00- 3:44 min; total number of images, 35. The field of view extended from the testes (bottom level) to the upper margin of the iliac crest (upper level) and from the sacrococcygeal spine (backward) to the anterior margin of the abdominal wall (forward) so as to include all relevant anatomy (fat recesses and connective supporting structures, prostate gland and seminal vesicles, distal gut and the urinary bladder, testes and the fixed portion of penis). Image analysis of each scan plane was focused, besides all, on evidence of any linear, low- intensity-signal condensation of the connective tissue consistent with one of the pelvic supporting structures, as reported by previous articles[16-21] or by Atlas and Text-book of Human Anatomy. With regard to the subdivision of pelvic spaces into compartments[22, 23], owing to the partial overlap of bladder base with the prostate and the more complex topographical anatomy of male pelvis, the classic subdivision adopted in the females was revised, as follows: the anterior compartment included the external genitalia and the retropubic space, taking the anterior aspect of prostate as its backmost boundary; the middle compartment comprised the entire prostate and the seminal vesicles, while the posterior compartment extended back from here to the sacrococcygeal spine (Fig. 1) . The frequency with which the various anatomical components of the endopelvic fascia could be consistently recognized as distinctive structures in the three compartments was recorded. Although beyond the scope of the current study, the analysis of images included also routine linear measurements (list of tool bar options, putting the cursor on "Annotation Toos" and selecting "ruler") of (1) the vertical distance (mm) of bladder neck, prostate base, seminal vesicles and rectal floor from a reference line drawn horizontally tangent to the inferior border of the symphysis pubis; and (2) the levator hiatal anterior/posterior and transverse diameters (mm); and area (cm^2).

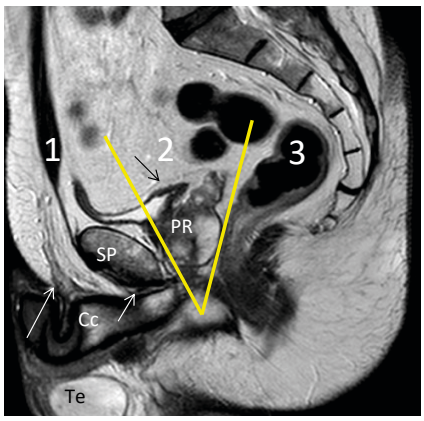


Figure 1- Midsagittal T 2-w TSE MR image of the male pelvis for subdivision into three compartments by two planes (yellow lines) tangent the anterior and posterior aspect of the prostate, respectively: 1= anterior; 2= middle; 3= posterior; SP = symphysis pubis; Cc = corpus cavernosum; Te = testis; thin black arrow= supra bladder peritoneal reflection; long white arrow= fundiform ligament; short white arrow = suspensory ligament of penis.

RESULTS

Anterior Compartment

On median and paramedian sagittal MR sections, the fundiform ligament of penis was the most frequently identifiable connective structure (100% of cases) among those located superficially inside the anterior compartment. It appears as a hypointense fibroelastic sheat which originates from the linea alba of the lower abdominal wall 5 cm above the symphysis pubis and is seen to fade into fan branches when reaching the dorsal aspect of penis (Fig. 2); thereafter it splits in two bundles that adhere to the penis fascia and merge on its ventral surface to join the scrotal septum. More deeply and back to it, the suspensory ligament of penis is also visible (70%) as a short, robust 2-mm thick, quadrangular shaped structure of low-signal-intensity which attaches the dorsal aspect of penis to the lower border of pubic bone. Inside the abdominal cavity, on the axial MR images, the retropubic, subvesical prostatic space (Retzius space) was occupied in 87.5 % of cases by an intricate latticework system of linear structures (see Fig.1) showing low-intensity signal which are thought to represent the combination of the puboprostatic/pubovesical ligaments, the anterior urethral connective support, the dorsal vein of penis and some smooth muscle fibers, as part of the detrusor apron.

Less frequently (31 and 16.6 % of cases, respectively), thanks to the background of the hyperintense prevesical adipose tissue, just behind the posterior aponeurosis of the rectum abdominis muscle, the median and lateral umbilicovesical ligaments are seen (Fig. 3) as a long, tapering hypointense structure which arises from the apex of the antero-superior bladder wall, In favourable conditions, i.e. adequate amount of intraabdominal fat, no crowded or overlapping bowel loops, and empty bladder, the thin linear hypointense image of the visceral peritoneal reflection could be depicted in up to 42.6 % of cases. It is seen to arise from the posterior transveralis fascia and course parallel over the superior bladder wall continuing back and holding in suspension the apex of seminal vesicles (see Fig. 1).

Middle Compartment

The outer layer of the prostate gland tissue was seen to assume a continuous contour appearance (mimicking a true capsule) of low- signal- intensity, consistent with the so called prostatic fascia. Posterolaterally, depending on where the contour meets the neurovascular bundle, a triangular space of hyperintense signal intensity (fat) containing thin hypointense structures (nerves and vessels) was visible in 55.9 % of cases. At the point of contact with the posterior surface of the seminal vesicles, the peritoneal reflection fuses

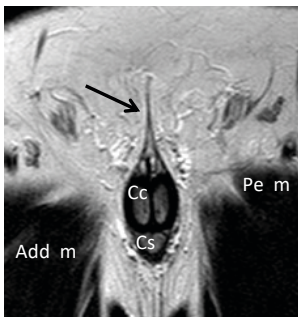


Figure 2- Coronal T 2-w TSE MR image taken at the level of the anterior abdominal wall with arrow pointing at the fundiform ligament: Add m = adductor muscles; Pe = pectineus muscle; ; Cc = corpus cavernosum; Cs = corpus spongiosum

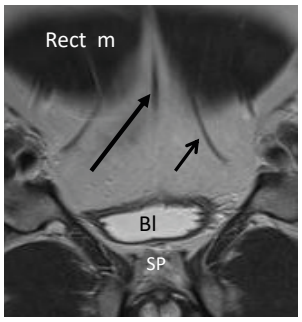


Figure 3 Coronal T2-w TSE MR image taken behind the symphysis pubis (SP), at the level of the rectum abdominis muscle (Rect m) showing the median (long arrow) and the lateral umbilico vesical ligaments (short arrow).

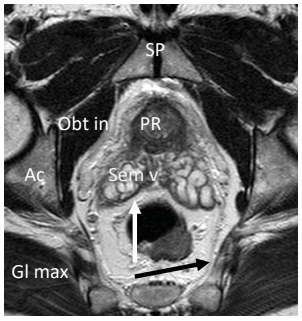


Figure 4- Axial oblique T 2–w MR image taken at the level of the acetabulum (Ac) showing the Denonvilliers fascia (white arrow)) as a reinforcement of the hypointense posterior margin of the seminal vesicles (Sem ves). SP= symphysis pubis; Gl max = gluteus maximus muscle; Obt in = obturator internus muscle.

with the endopelvic fascia and the fibromuscular stroma of the prostate to give origin to the Denonvilliers fascia which appears as low-intensity-signal linear reinforcement of the posterior prostate contour (Fig. 4).

Posterior Compartment

The three rectal wall layers of different signal intensity reported in the literature (the inner low-intensity mucosa, the intermediate high-intensity submucosa, and the outer low-intensity circular and longitudinal muscle separated by the high-intensity myenteric plexus) were visualized only rarely, probably due to inadequate rectal cleansing and/or residual fecal material. Similarly, short linear or undulated low-signal condensations arising from the outer margin of the rectal wall at the 12, 6, 3 and 9 o clock position, could only occasionally (22.8 %) be observed which were

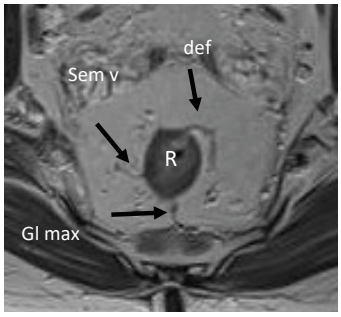


Figure 5 Axial T 2-w MR image of the posterior and lateral rectal ligaments (arrows) which are seen in contrast to the hyperintense perirectal fat. R= rectum; Gl max = gluteus maximus muscle; Sem ves = seminal vesicles; Def = deferent ducts.

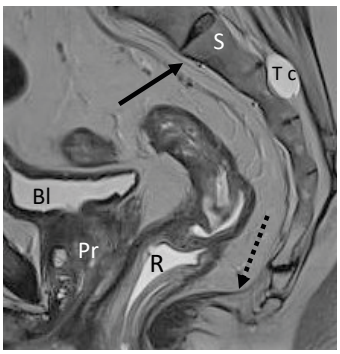


Figure 6 Midsagittal T2-w MR image of the posterior compartment for evidence of the presacral space: note the presacral fascia (blak arrow) and the Waldeyers fascia (dotted arrow). Bl = bladder; Pr = prostate; R = rectal ampulla after evacuation of contrast (acoustic gel); S= sacrum; Tc = Tarlov cyst.

interpreted as the anterior, posterior or lateral rectal ligaments, respectively (Fig. 5). Conversely, the high-intensity perirectal fat surrounded by the low-signal-intensity of the mesorectal fascia were consistently seen in the vast majority of cases (up to 96%). In the prerectal space, the thin linear condensation of the peritoneal reflection, after suspending the apex of the seminal vesicles, is distinctly seen to continue dorsally and pass over the anterior aspect of the rectal ampulla dividing the supra from the infra mesorectal portion of distal gut. The sagittal MR images are also most suited to depict the retrorectal space (Fig. 6), which contains the presacral fascia (71.7%), the Waldeyer fascia (80%) and the mesorectal fascia (between 81.9 and 96 %). A new feature in over 77% of cases was the evidence of two bilateral and symmetrical low-signal- intensity linear condensations (Fig. 7 and 8) which are slightly concave toward the internal side of pelvic cavity and are seen to arise from the anterior aspect of the sacral spine. They course laterally to the mesorectal fascia in a symmetric fashion and connect the anterior aspect of the sacral spine on both sides to the posterior margin of the seminal vesicles, mimicking the shape of the female utero sacral ligaments. From here, they continue forward along the inner surface of the pelvic side wall and fuse with the prostatic fascia being sometimes continuous also with the Denonvilliers fascia to form a "H-shaped" configuration and were interpreted as the so called "sacro-recto-vescico-genito-pubic fascia". A complete summary of the results of MR imaging studies relative to the visualization of the pelvic connective support system in males is presented in Table 1.

DISCUSSION

As expected, MRI has proved more effective than any other imaging diagnostic tool for depicting the connective tissues and ligaments of male pelvis, as it occurred in the case of women. This,

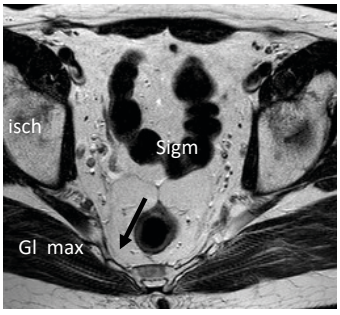


Figure 7 Axial T 2-w MR image taken at the level of the ischiatic bone showing the typical appearance of the sacro recto-vesico genito pubic fascia (arrow). Gl max = gluteus maximus muscle; Isch = ischiatic bone; Sigm = sigmoid colon.

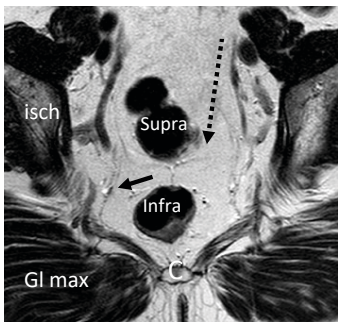


Figure 8 Coronal T 2-w MR image taken at the level of the "H-shaped" morphology of the endopelvic fascia (short arrow) joining the peritoneal reflection (long dotted arrow) which separates the supra from the infra mesocolic rectum

thanks to its superior contrast resolution and multiplanar capabilities which make MRI unique to visualize even minimal anatomical detail and variant. The routinary utilization of sagittal, coronal and axial planes combined with high-resolution, T2-w pulse sequences gave us a complete and detailed spatial representation of the male pelvic anatomy, quite similar to that obtained in the female population. More precisely, the depiction of ligaments and fascia as low-signal-intensity linear structures has become consistently feasible and easily identifiable, according to their anatomical position. In particular, it's worth noting how useful has been tilting the scan plane, taking the long axis of the anal canal as reference, for revealing unknown features of the connective support system. Not by chance, the two most important innovations highlighted by this study, never reported earlier to our knowledge, concern the dense lattice network of connective structures seen in the retropubic space and the bilateral, symmetric linear hypointense condensations of the sacro-recto-vesico-genito-pubic fasciae which connect the sacrococcygeal spine to the pubic bone. Such structures in turn, seem to act as a sort of scaffold which securely anchor the internal organs to the pelvic side wall. In addition, in the posterior compartment the single most striking observation has been the arcuate linear hypointense stripe arising from the posterior aspect of the seminal vesicles which closely resemble the feature of the female uterosacral ligaments.

Table 1 Proportion of visualized connective structures at MRI of male pelvis by compartment and scan plane (n° = 354)

Comp	Observed structure	Scan Plane					
		Sagittal		Axial		Coronal	
		N°	%	N°	%	N°	%
Anterior	Fundiform ligs	354	100			354	100
	Suspensory penis ligs	240	70			112	31.6
	Umbilico vesical ligs						
	Median	110	31			156	44
	Lateral					58	16.3
	Puboprostatic ligs	310	87.5	299	84.4		
	Peritoneal reflection (supra vesical)	195	55			99	27.9
Middle	Peritoneal reflection			96 27.1			
	Denonvilliers fascia	145	40.9	115	32.4	98	27.6
	Neurovascular bundle			198	55.9	117	33
	Peritoneal reflection (seminal vesicles)	151	42.6			120	33.8
Posterior	SRVGP fascia			250	70.6	276	77.9
	Rectal ligs			81	22.8	64	18.07
	Mesorectal fascia	290	81.9	310	87.5	340	96
	Presacral fascia	254	71.7	170	48		
	Waldeyer fascia	284	80.2				

Note SRVGP = Sacro recto vesico genito pubic fascia; Comp= Compartment

Now turning the attention of readers to the issue of the potential clinical impact of the study, there is no doubt that having such an effective imaging tool as MRI to depict the anatomy in vivo, may be used to improve the diagnosis and localization of relevant pathological processes, including tumor spread and recurrence, and complex fistula-in-ano disease. Aside from this, the depiction in exquisite details of the connective support system, is also promising for a new interpretation of the functional disorders of pelvic floor in males, whose reports are increasingly frequent in the clinical practice and deserve more attention.

Further progress can be anticipated in the future from studies comparing the results of imaging tools with those of techniques for the analysis of anatomical samples so as to add better certainty to the diagnosis of pathological entities still in search for definition.

REFERENCES

1. Fritsch H, Hotzinger H Tomographical anatomy of the pelvis, visceral pelvic connective tissue, and its compartments. Clin Anat 1995; 8:17–24
2. Chou Q, DeLancey JOL A structured system to evaluate urethral support anatomy in magnetic resonance imaging. Am J Obstet Gynecol 2001; 185: 44-50
3. Tunn R, DeLancey JOL, Quint EE Visibility of pelvic organ support system structures in magnetic resonance images without and endovaginal coil. Am J Obstet Gynecol 2001; 184: 1156-1163 .
4. Kim J K, Kim Y J, Choo M S, Cho K S The urethra and its supporting structures in women with stress urinary incontinence: MR imaging using an endovaginal coil. AJR 2003; 180: 1037- 1044
5. DeLancey JOL, Kearney R, Chou Q, et al. The appearance of levator ani muscle abnormalities in magnetic resonance images after vaginal delivery. 2003; 101:46-53
6. Brown G, Richards CJ, Newcombe RG et al. Rectal carcinoma: thin-section MR imaging for staging 1n 28 patients. Radiology 1999; 211: 215-222
7. Brown G, Kirkham A, Williams GT et al. High resolution MRI of the anatomy important in total mesorectal excision of the rectum. Am J Roentgenol 2004;182:431–439
8. Hadfield MB, Nicholson AA, Mc Donald AW, et al. Preoperative staging of rectal carcinoma by magnetic resonance imaging with a pelvic phased array coil. Br J Surg 1997; 84: 529-531
9. Myers RP, Cahill DR, Devine RM, et al. Anatomy of radical prostatectomy as defined by magnetic resonance imaging. J Urol 1998; 159: 2148-2158
10. Myers RP Practical surgical anatomy for radical prostatectomy Urol Clin North Am 2001; 28 (3): 473-490
11. Kiyoshima K, Yokomizo A, Yoshida T et al. Anatomical features of periprostatic tissue and its surroundings: a histological analysis of 79 radical retropubic prostatectomy specimens. Jpn J Clin Oncol 2004; 34 (8): 463-468
12. Benoit G, Boccon-Gibod L, Steg A Anatomical study of total cystoprostatectomy. Eur Urol 1985;11(4): 228-232
13. Raychaudhury R, Cahill D Pelvic fascia in urology. Ann R Coll Surg Engl. 2008; 90:633-637
14. Ansari MM Retzius space: not a single anatomic entity. New insights, simplified and illustrated in a laparoscopic study during TEPP hernioplasty for inguinal hernia. Ann Int Med Dent Res 2017; 4(1):63-67
15. Piloni V, Bergamasco M, Chiapparin A Quantification of the levator ani hiatus enlargement by magnetic resonance imaging in males and females with pelvic organ prolapse. J Vis Exp (JOVE) 2019; 58534: 1-9
16. Hricak E, Williams RD, Sping DB et al. Anatomy and pathology of the male pelvis by magnetic resonance imaging AJR 1983; 141: 1101-1110
17. Sattar AA, Noel JC, Vanderhaeghen JJ, et al. Prostate capsule: computerized morphometric analysis of its components. Urology 1995; 46(2):178-181
18. van Ophoven A, Roth S The anatomy and embryological origins of the fascia of Denonvilliers: a medico-historical debate. J Urol 1997; 157(1):3-9
19. Kourambas J, Angus DG, Hosking P, et al. A histological study of Denonvilliers' fascia and its relationships to the neurovascular bundle. Br J Urol 1998; 82(3):408-410
20. Aigner F, Zbar AP, Ludwikowski B, et al. The rectogenital septum: morphology, function, and clinical relevance. Dis Colon Rectum 2004; 47(2):131-140
21. Raychaudhuri B, Cahill D Pelvic fasciae in urology Ann R Coll Surg Engl 2008; 90(8):633-637
22. Myers RP, Cahill DR, Kay PA et al. Puboperineales: muscular boundaries of the male urogenital hiatus in 3D magnetic resonance imaging. J Urol 2000; 164:1412–1415
23. Mikuma N, Namagawa M, Morita K et al. Magnetic resonance imaging of the male pelvic floor. The anatomical configuration and dynamic movement in healthy men. Neurourol Urodyn 1998; 17:591–597

DISCLOSURE STATEMENTS

There was no conflict of interest on the publication of the study.

Correspondence:

Vittorio Piloni, MD

Diagnostic Imaging Centre, Affidea, Iniziativa Medica, via Rialto 14, Monselice (Padova) Italy

Email: vittorio.piloni@ libero.it

Original article

Analysis of primary and secondary outcome domains reported in randomised trials on surgery for female stress urinary incontinence. A systematic review

MARIA-PATRICIA RADA[1,2], CORNELIA BETSCHART[3], VASILIOS PERGIALIOTIS[4], JORGE MILHEM HADDAD[5], GABRIELE FALCONI[6], STERGIOS K. DOUMOUCHTSIS[1,4,7,8]
CHORUS, an International Collaboration for Harmonising Outcomes, Research and Standards in Urogynaecology and Women's health (i-chorus.org)

[1] *Department of Obstetrics and Gynaecology, Epsom & St Helier University Hospitals NHS Trust, United Kingdom*
[2] *2nd Department of Obstetrics and Gynaecology, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania*
[3] *Department of Gynecology, University Hospital of Zurich, Zurich, Switzerland*
[4] *Laboratory of Experimental Surgery and Surgical Research N S Christeas, Athens University Medical School, Athens, Greece*
[5] *Department of Obstetrics and Gynaecology, Urogynaecology Division, Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil*
[6] *Department of Obstetrics and Gynaecology, San Bortolo Hospital, Vicenza, Italy*
[7] *St George's University of London, London, United Kingdom*
[8] *The American University of the Caribbean School of Medicine*

Abstract: *Introduction*. Published randomised controlled trials (RCTs) on surgery for female stress urinary incontinence (SUI) evaluated the efficacy and safety of different surgical options using a variety of outcomes and outcome measures. Our objective was to perform a systematic review of the primary and secondary outcomes, analyse their selection in different RCTs and evaluate research choices and priorities. *Methods*. A literature search was conducted using Embase, Medline and Cochrane databases. The primary and secondary outcomesreported across trials were analysed. We grouped different outcomes into domains (categories). *Results*. One hundred twenty-five RCTs, which enrolled 20757 women, were included in this study. A total of 4 primary and 7 secondary outcome domains were reported. The most prevalent primary outcome domain involved cure rates, being reported by 86.2% of the included RCTs. Complication rates had the highest prevalence among secondary outcome domains, being reported by 71% of RCTs. Sample size calculations were performed in approximately two thirds of studies that used 1 primary outcome and in an even smaller fraction of studies that reported 2 primary outcomes. *Conclusions*. A variation in selection of different primary and secondary outcomes as well as domains was confirmed. Complications may have been underreported as the majority of trials were potentially underpowered to evaluate complication rates.

Keywords: Stress urinary incontinence; Randomised controlled trials; Surgical interventions outcomes; Core outcome sets

INTRODUCTION

Surgical interventions are therapeutic options for women suffering from SUI when other non-surgical measures have failed[1]. These procedures may provide short and long-term benefits, improving the patient's quality of life[2] and reducing the costs on resources used for incontinence management or "routine care"[3]. Given the fact that various interventions are available for the same condition, choosing the appropriate intervention to treat women with SUI can be challenging. Recently, the National Institute for Health and Care Excellence (NICE) guidelines recommended an active involvement of women in the therapeutic choice by providing a patient decision aid tool[1]. Most guidelines base their recommendations on published research, with RCTs being considered to carry a high level of quality of evidence.

Gaining understanding into the choices of outcomes collected and reported in RCTs on interventions for SUI in women will add weight on interpreting the study findings on safety and efficacy of various surgical modalities. However, researchers have reported many different outcomes in RCTs, making data synthesis challenging. Consistency in the selection and definition of primary and secondary outcomes is essential to address this issue. Recently, a greater attention has been paid to the way in which surgical interventions are delivered in RCTs[4] and comparisons between the outcomes presented in study protocols and the actual reported outcomes have been evaluated as part of quality assessment of RCTs. Outcomes' discrepancies are not uncommon in research on surgical interventions and raise concern about what clinical trials conclude, running the risk of poorly-informed treatment options[5]. Recent efforts have focused on establishing a minimum set of outcomes, termed a 'core outcome set'[6] for various conditions[7-10], including pelvic floor disorders[7, 11, 12] in order to address the high variability in outcome reporting.

Combining and comparing different studies' results would be facilitated following a harmonization of study designs. Robust data from high quality meta-analyses could inform clinical practice better and contribute to the provision of better care to women.

Objective

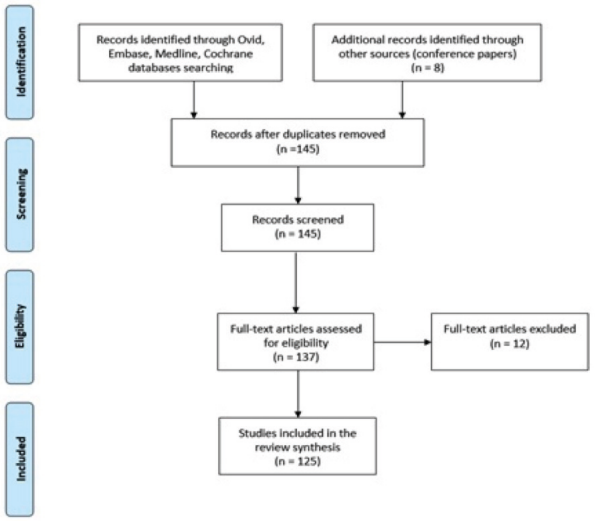
Our objective was to perform a systematic review of the literature, on RCTs on surgical interventions for SUI and evaluate the selection of the primary and secondary outcomes in these studies. Following data collection, we aimed to analyse the selected and reported outcomes in order to understand the research priorities and criteria for the study designs and contribute to the process of developing a core outcome set in the area of female stress urinary incontinence.

METHODS

Protocol and registration

This study is part of a wider project led by CHORUS, an International Collaboration for Harmonising Outcomes, Research, and Standards in Urogynaecology and Women's Health (i-chorus.org)[13], aiming to develop, disseminate and implement a Core Outcome Set for SUI, which has been prospectively registered with the Core Outcome Measures in Effectiveness Trials (COMET) initiative[14] (registration number 981). Ethical approval for this study was not required, as this study was a systematic review. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) were consulted during the conduct of this review.

Figure 1. Diagram showing study search methodology (according to PRISMA flowchart)



Eligibility criteria

RCTs published in English or in different languages for which English translation was available, evaluating surgical interventions related to female SUI were eligible for inclusion in this study for primary and secondary outcomes analysis. Non-randomized, quasi-randomized, observational studies, systematic reviews and meta-analyses were excluded from this study.

Information sources

A comprehensive literature search was conducted searching Embase, Medline databases and the Cochrane Central Register of Controlled Trials (CENTRAL) from inception to May 2019. Relevant studies were searched using the following MeSH terms: 'stress urinary incontinence' and 'surgical interventions' and 'randomised controlled trials'.

Study selection

The process for article selection was completed in consecutive steps that included deduplication of articles, reading of titles, abstracts and texts (when needed) to evaluate for potential eligibility and retrieval of full texts in case of assumed eligibility and reading it in full text. Snowballing of references of full texts was also performed to minimize the possibility for potential article losses. A summary of the article retrieval process is provided in Figure 1.

Data collection process

The data collection was conducted by 2 researchers independently. Verbatim primary and secondary outcomes reported by the studies included were identified and entered into an inventory for further analysis. The outcomes that shared similar definitions were then grouped and entered into the inventory. Also, an inventory of the types of surgical interventions for female SUI evaluated in the RCTs included was created. Some trials compared different techniques of the same procedure, this aspect being reflected in the percentage of the procedures out of the total number of interventions.

Figure 3. Frequency of primary outcome domains reported by RCTs evaluating surgical interventions for SUI

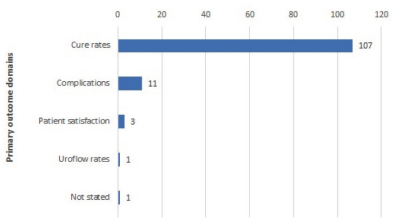
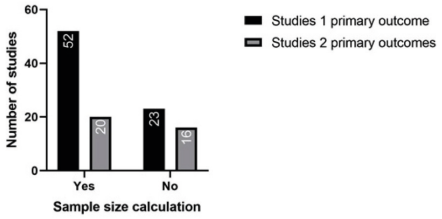


Figure 2. RCTs that reported that sample size calculation was performed vs RCTs that reported that sample size calculation was not performed



The number of surgical interventions and primary and secondary outcomes reported by each trial was assessed and recorded and their frequency was calculated. Descriptive statistics were used to present these data.

RESULTS

Study selection

A total of 125 RCTs (appendix 1), which enrolled 20,757 women, were included in this study according to the methodology presented in Figure 1[15]. Sixty two percent of articles that reported one primary outcome and 48% of articles that reported two primary outcomes performed a sample size calculation (Figure 2). In 14 RCTs it was not stated if sample size calculations were performed or the full texts were not available.

The surgical interventions evaluated in the included RCTs are presented in table 1. TVT was the most studied procedure, the percentage of RCTs that studied that procedure summarizing more than the other interventions all together.

Each trial reported a specific number of outcomes. Most RCTs (66.4%) reported only 1, 32.7% reported 2, while only 1 RCTs did not specify any primary outcome. Secondary outcomes showed a greater heterogeneity, between 0 and 6 primary or secondary outcomes being reported by each trial. Most RCTs (38.4%) reported only 1, followed by 28,7% of RCTs which reported none, 12% reported 3, 8.7% reported 4, 5.6% reported 2, 4% reported 5 and 2.4% reported 6 secondary outcomes, respectively (Table 2).

Outcomes were grouped into outcome domains to classify broad aspects related to the interventions. Four different primary outcome domains and 7 secondary outcome domains were identified across the included trials. The outcome domains, ordered based on their frequency of use across trials, are shown in figures 3 and 4.

Of the 124 included studies, 107 (86.26%) reported primary outcomes that were classified in cure rates domain. More precisely, 39 RCTs (31.4%) reported a composite of subjective and objective cure rates, 37 (29.8%) reported objective

Figure 4. Frequency of secondary outcome domains reported by RCTs evaluating surgical interventions for SUI

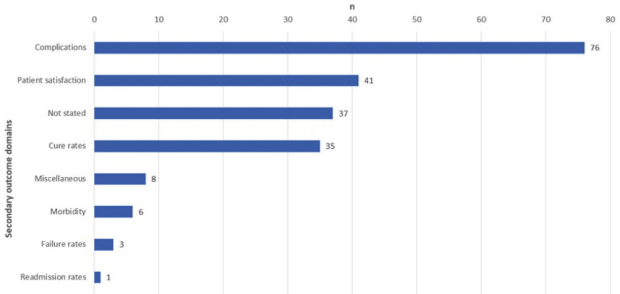


Table 1. Types of surgical interventions evaluated by RCTs

Intervention	Number of times a procedure was evaluated in a RCT	% of total interventions
Retropubic sling	131	50.90%
Transobturator tape	63	24,5%
Bulking	30	11,6%
Single incision minisling	19	7.30%
Colposuspension	14	5,4%

cure rates only, 21 (16.9%) reported subjective cure rates only and 10 (8.06%) reported cure rates of unspecified type. Eleven (8,8%) RCTs reported primary outcomes that were classified in complications domaindomanin. Outcomes reporting domains reflecting patient satisfaction and failure rates, were reported less frequently as primary outcomes, between 2 and 3 times each (Figure 3). One of the included RCTs did not state any primary outcome.

The most frequently reported secondary outcomes were grouped into the complications domain. Seventy one percent of outcomes for which the outcome measures included the necessity of further operative procedures over time, SUI symptoms, number of catheterisations/day fell under this domain. In 42.05% of RCTs, the secondary outcomes were not specified. Based on their frequency, the following categories of secondary outcome domains were patients' satisfaction and cure rates with their corresponding percentages of 46.5%, 39.7%, respectively. The remaining secondary outcomes: miscellaneous, morbidity, failure rates and readmission rates were used between 1 and 8 times each (Figure 4).

DISCUSSION

The choice of primary outcome in a RCTs is of paramount importance as the power calculations for sample sizes are based on this outcome. Equally, the selection and reporting of secondary outcomes is essential as the study may be underpowered to detect true differences between different interventions. It is suprising that a significant number of trials did not report sample size calculation at all. Given the importance of sample size calculation and the other arbitrary power parameters of a study, one assumes that a significant amount of data is not necessarily based on an adequate sample size to draw definitive conclusions and, thus, information may be misleading for current clinical practice.

Our review analysed the selection and reporting of primary and secondary outcomes reported by 125 RCTs. As expected, in the absence of a robust and standardized reporting system, a variety of outcomes were reported by researchers to evaluate surgical procedures for SUI in women[16]. While a composite of objective and subjective cure rates was the most frequently used primary outcome, the complication rates were the most prevalent secondary outcomes across the trials included.

The Consolidated Standards of Reporting Trials (CONSORT) statement suggested that only 1 primary outcome should be used in RCTs[17]. In line with this recommendation, most trials (66.4%) that were included in our analysis reported only 1 primary outcome. However, about one third of the trials reported 2 different primary outcomes.

The heterogeneity related to the number of outcomes appeared even greater in the case of secondary outcomes. Most trials (38.4%) reported a single secondary outcome, while the other two thirds have either not reported any secondary outcome or have reported between 2 and 6 outcomes.

Table 2. Number of selected primary and secondary outcomes per RCTs

Number of selected primary outcomes per RCT	n
0/not stated	(0.8%) 1/125
1	(66.4%) 83/125
2	(32.8%) 41/125
Number of selected secondary outcomes / RCT	
0/not stated	(28.7%) 36/125
1	(38.4%) 48/125
2	(5.6%) 7/125
3	(12%) 15/125
4	(8.7%) 11/125

We recently conducted a systematic review on outcome reporting in RCTs on surgical interventions for female stress incontinence[18]. This is a secondary analysis that focuses on specific choices of primary and secondary outcomes in RCTs. Researchers conducting RCTs very rarely report power calculations of secondary outcomes[19], in most cases the power calculations of each study being solely based on the chosen primary outcomes. Therefore, an outcome's position and prioritization in RCTs should not be overlooked.

An obvious trend that results from the analysis of these data is that most researchers tend to report a single primary and secondary outcome, respectively. However, there is still a lack of reporting-wise uniformity, making any analysis difficult and therefore limiting the ability of research to inform clinical practice.

The Core Outcome Measures in Effectiveness Trials (COMET) Initiative recommended the use of 'core outcome sets' (COS) with the purpose of improving the comparability between trials[20]. COS represent 'agreed standardised sets of outcomes' that constitute 'the minimum that should be measured and reported in all clinical trials of a specific condition'[21]. Apart from COS, clearly defined outcomes and definitions of success or failure are compulsory for interpreting the results of different studies[22]. Given the researcher's tendency to select the outcomes that have the greatest success rates, misleading conclusions may be drawn when multiple outcomes are reported in trials. This selective reporting bias may have as a consequence provision of unreliable evidence to guide clinical practice[23].

In our study, we observed that the primary outcomes tended to focus more on cure rates as opposed to the secondary outcomes, which were particularly focused on complication rates. The quality of these outcomes is directly related to the outcome measures that have been used. It is indeed argued whether an objective cure rate measured by a pad or cough test, for example, represents an appropriate tool because of different standardization measures of these tests encountered across trials[24, 25]. Subjective cure rates are measured based on patient's perception and specific questionnaires were developed to allow quantification. Considering these facts, it appears obvious that it is difficult to achieve a high degree of outcome accuracy.

Our study raises awareness of what is being reported by trials and highlights the heterogeneity in outcome selection in RCTs. A methodology limitation should be taken into account when interpreting the findings of this research. Only data from RCTs were included in this study and therefore a wider assessment of outcomes on surgical interventions for SUI in non-randomised studies was not possible, given that the outcomes reported by other types of research or papers

written in other language than English were not included in the analysis. This study did not aim to investigate what determined the choice of specific outcomes by the researchers who designed the RCTs. Qualitative studies might provide additional insights and help to understand researcher's preference and approach towards outcome reporting. Involvement of patients in study design might help in the process of selection of outcomes that are relevant, engaging a more diverse perspective[26].

CONCLUSIONS

The findings of our study showed that most trials reported only 1 primary and 1 secondary outcome, being in accordance with CONSORT statement. A variation in selection of different primary and secondary outcomes as well as domains was confirmed.

Sample size calculations were performed in approximately two thirds of studies that used 1 primary outcome and in an even smaller fraction of studies that studied 2 primary outcomes and therefore the studies may be underpowered to detect true differences between various interventions.

FUNDING

No funding was received for this study.

REFERENCES

1. National Guideline A. National Institute for Health and Care Excellence: Clinical Guidelines. Urinary incontinence and pelvic organ prolapse in women: management. London: National Institute for Health and Care Excellence (UK) Copyright (c) NICE 2019.; 2019.
2. Tennstedt SL, Litman HJ, Zimmern P, Ghetti C, Kusek JW, Nager CW, et al. Quality of life after surgery for stress incontinence. International urogynecology journal and pelvic floor dysfunction. 2008;19(12):1631-8.
3. Subak LL, Goode PS, Brubaker L, Kusek JW, Schembri M, Lukacz ES, et al. Urinary incontinence management costs are reduced following Burch or sling surgery for stress incontinence. American journal of obstetrics and gynecology. 2014;211(2):171.e1-7.
4. Blencowe NS, Brown JM, Cook JA, Metcalfe C, Morton DG, Nicholl J, et al. Interventions in randomised controlled trials in surgery: issues to consider during trial design. Trials. 2015;16(1):392.
5. Fleming PS, Koletsi D, Dwan K, Pandis N. Outcome discrepancies and selective reporting: impacting the leading journals? PloS one. 2015;10(5):e0127495.
6. Kirkham JJ, Gorst S, Altman DG, Blazeby JM, Clarke M, Tunis S, et al. Core Outcome Set-STAndardised Protocol Items: the COS-STAP Statement. 2019;20(1):116.
7. Pergialiotis V, Durnea C, Elfituri A, Duffy J, Doumouchtsis SK. Do we need a core outcome set for childbirth perineal trauma research? A systematic review of outcome reporting in randomised trials evaluating the management of childbirth trauma. BJOG : an international journal of obstetrics and gynaecology. 2018;125(12):1522-31.
8. Nielsen KK, O'Reilly S, Wu N, Dasgupta K, Maindal HT. Development of a core outcome set for diabetes after pregnancy prevention interventions (COS-DAP): a study protocol. Trials. 2018;19(1):708.
9. Dadouch R, Faheim M, Juando-Prats C, Parsons J, D'Souza R. Development of a Core Outcome Set for Studies on Obesity in Pregnant Patients (COSSOPP): a study protocol. 2018;19(1):655.
10. Viau-Lapointe J, D'Souza R, Rose L, Lapinsky SE. Development of a Core Outcome Set for research on critically ill obstetric patients: A study protocol. Obstetric medicine. 2018;11(3):132-6.
11. de Mattos Lourenco TR, Pergialiotis V, Durnea C, Elfituri A, Haddad JM, Betschart C, et al. A systematic review of reported outcomes and outcome measures in randomized controlled trials on apical prolapse surgery. International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics. 2019;145(1):4-11.
12. de Mattos Lourenco TR, Pergialiotis V, Duffy JMN, Durnea C. A systematic review on reporting outcomes and outcome measures in trials on synthetic mesh procedures for pelvic organ prolapse: Urgent action is needed to improve quality of research. 2019;38(2):509-24.
13. An International Collaboration for Harmonising Outcomes R, and Standards in Urogynaecology and Women's Health,. Developing a core outcome set for female pelvic floor disorders 2017 [cited 2019 30 June]. Available from: https://i-chorus.org/projects/developing-a-core-outcome-set-for-female-pelvic-floor-disorders-urinary-incontinence-pelvic-organ-prolapse-childbirth-perineal-trauma-and-pelvic-pain-syndromes.
14. Core Outcome Measures in Effectiveness Trials (COMET) Initiative. 2011 [cited 2019 30 June]. Available from: http://www.comet-initiative.org/.
15. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ (Clinical research ed). 2009;339:b2700.
16. Clarke M. Standardising outcomes for clinical trials and systematic reviews. Trials. 2007;8:39.
17. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. BMJ (Clinical research ed). 2010;340:c332.
18. Doumouchtsis SK, Pookarnjanamorakot P, Durnea C, Mudiaga Z, Elfituri A, Haddad JM, et al. A systematic review on outcome reporting in randomized controlled trials on surgical interventions for female stress urinary incontinence. A call to develop a core outcome set. BJOG : an international journal of obstetrics and gynaecology. 2019.
19. Jakobsen JC, Ovesen C, Winkel P, Hilden J, Gluud C, Wetterslev J. Power estimations for non-primary outcomes in randomised clinical trials. BMJ open. 2019;9(6):e027092.
20. Williamson P, Clarke M. The COMET (Core Outcome Measures in Effectiveness Trials) Initiative: Its Role in Improving Cochrane Reviews. The Cochrane database of systematic reviews. 2012(5):Ed000041.
21. Williamson PR, Altman DG, Bagley H, Barnes KL, Blazeby JM, Brookes ST, et al. The COMET Handbook: version 1.0. Trials. 2017;18(Suppl 3):280.
22. Lim R, Liong ML, Leong WS, Yuen KH. Which outcome measures should be used in stress urinary incontinence trials? BJU international. 2018;121(5):805-10.
23. Page MJ, McKenzie JE, Kirkham J, Dwan K, Kramer S, Green S, et al. Bias due to selective inclusion and reporting of outcomes and analyses in systematic reviews of randomised trials of healthcare interventions. The Cochrane database of systematic reviews. 2014(10):Mr000035.
24. Simons AM, Yoong WC, Buckland S, Moore KH. Inadequate repeatability of the one-hour pad test: the need for a new incontinence outcome measure. BJOG : an international journal of obstetrics and gynaecology. 2001;108(3):315-9.
25. Carmel ME, Deng DY, Greenwell TJ, Zimmern PE. Definition of Success after Surgery for Female Stress Incontinence or Voiding Dysfunction: An Attempt at Standardization. European urology focus. 2016;2(3):231-7.
26. Rolfe DE, Ramsden VR, Banner D, Graham ID. Using qualitative Health Research methods to improve patient and public involvement and engagement in research. Research involvement and engagement. 2018;4(1):49.

Correspondence:
mpr1388@gmail.com

Original article / Short review

Nocturnal enuresis in children- Literature review and anatomical rationale for a squatting -based pelvic floor regime

ANGEL GARCIA FERNANDEZ*, PETER E. PETROS**

** Universidad Nacional de Córdoba Argentina*
*** University of Western Australia*

Abstract: *Aim* To analyse whether the squatting-based pelvic floor regime based on the Integral Theory System would assist children with nocturnal enuresis. *Methods* A literature review and an analysis of the anatomical rationale for a squatting-based regime was made with regard to an RCT between two groups, a squatting-based regime based on the Integral Theory System and a placebo. CONSORT were guidelines to be followed as regards randomization, blinding and independent assessment of results. Statistically, it was determined that 48 patients would give 90% power with a CI of 95% allowing a 9% placebo effect. *Results and conclusions* The literature review of existing practice revealed no insights which could influence the proposed study. The origin of bed-wetting was said to be essentially unknown. Analysis of the xrays, however, confirmed that the squatting-based regime of the Integral System would act on the same pubourethral and uterosacral ligaments which are repaired surgically using tapes, and which give high cure rates for bladder, bowel and chronic pelvic pain dysfunctions. It was also reasoned that the main difference between adults and children with reference to the Integral Systems's pelvic floor regime was that children are in a collagen formation mode, which should reinforce the ligaments in a better way than in adults, with superior results to those obtained already in premenopausal adult women.

Keywords: Nocturnal enuresis; Squatting; Integral theory; Pelvic floor regime.

INTRODUCTION

Enuresis or "wet bed" syndrome represents an important percentage of the daily consultation of the pediatrician and the pediatric urologist. It is estimated that between 15 and 20% of children at 5 years of age wet the bed. [1]

Nocturnal enuresis was rarely mentioned in the old literature, given the little importance that was then assigned to the sufferings of children.

Probably the first reference to enuresis was published in Ketham's Fasciculus Medicinae, a text of general medicine and one of the first medical books produced by the printing press in Venice in 1491: "Enuresis is the involuntary emission of urine during sleep".)

However, when the symptom lasted until adolescence and maturity, the obvious social disconfort pressed to find a solution. In the Children's Book, Thomas Phaires discusses "urinating the bed**.**[2]"

Shakespeare's son-in-law, physician John Hall relates in a 1657 publication the cure of enuresis, of a 15-year-old boy by a homemade preparation in base to dried chicken and eggs every morning[3].

After millennia of darkness on the subject, during the last century, there has been a particular interest on the subject since the "wet bed" ceased to be considered more a domestic problem than a disease. Thus, different specialties considered the topic from their own unique point of view, particularly the psychologists and psychiatrists who see the problem of the wet bed as a behaviour disorder[4].

This concept still persists in popular belief although to a lesser extent. As early as 1937, Burns wrote in Growing Child: "... that the neurotic attitude of an enuretic child is an effect of enuresis rather than a cause".

The point of view of our modern urology estimates that enuresis should be considered in the broad context of voiding dysfunctions.

Neurophysiology and urodynamics of the lower urinary tract have contributed greatly to the knowledge of the process of urination and continence. The concept of complete elimination (evacuation) and its dysfunctions[5] add interesting data to our clinical knowledge.

The failure to awaken when the bladder is full is an obvious factor that was very well studied in the past decade, as well as the hormonal regulation of nocturnal polyuria[6].

Multiple publications deal with different aspects related to enuresis: decreased functional bladder capacity[7-9], the prevalence of micturition diurnal symptoms and bladder instability[10], ingenious alarm devices for the treatment of enuresis[11,12] and others.

Different classifications of enuresis were also proposed, taking as parameter one or the other aspect that make up this broad clinical spectrum called enuresis or wet bed. The most popularized classification is that of primary enuresis, when I never stop wetting the bed and secondary enuresis when an interval of at least 6 months passed dry. Other classifications recognize four etiological areas: psychological (environmental, emotional and as a consequence of the disorder, impact on their self-esteem), neurological (sleep disorders, DAHA, where enuresis appears with an important index in comorbidity)[13], hormonal (polyuria, disorders in the production of antidiuretic hormone) and functional urology (retentionist habit, voiding incoordination, overactive bladder)[14].

It is very important to mention the report of the Standardization Committee of the International Society for Pediatric Continence, which unifies the terminology in this area[15]. It defines enuresis as synonymous with intermittent nocturnal incontinence, there being ample evidence that children with enuresis they present symptoms of dysfunction of the urinary tract under different clinical, therapeutic and pathogenetically of children without these symptoms. For this reason, unequivocal classification is essential in two subgroups: monosymptomatic and non-monosymptomatic enuresis. The previous division based on the presence or absence of diurnal incontinence is only inadequate since other diurnal symptoms (constipation, urinary infection, etc.) may also be indicative of voiding dysfunction.

Another vision, based on the Integral Theory of Female Incontinence[16] proposed by Prof. Peter Petros of Sydney Australia. maintains that the enuresis could be conditioned by a congenital laxity of the ligaments, at the level of the ligaments that support the urethra.

EPIDEMIOLOGY. PREVALENCE OF NOCTURNAL ENURESIS

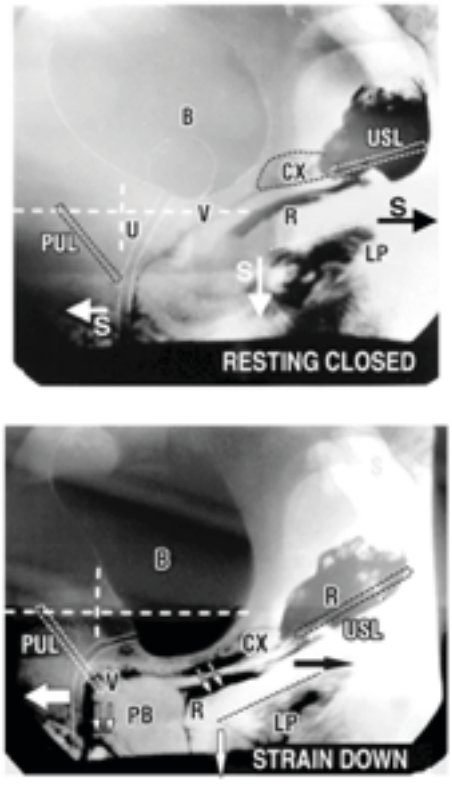
In a study on child development conducted by Feeham et

al in 1990, 1,139 children were born in a year in Dunedin, New Zealand, and 92% were followed 6 years later. It was found that primary enuresis remits with age with an annual rate of around 15%. At 7 years, the prevalence is significant since most children, now schoolchildren, add more problematic social consequences[17]. In this age, the prevalence is between 6 and 10%. The similarity of these prevalence rates in populations from all over the world is remarkable[18]. Jon Heron, published in May 2008 an interesting work on a cohort of 11,000 children in the United Kingdom, studying the trajectories of daytime incontinence and soiling (evacuation dysfunction syndrome) and its importance in understanding the development of urinary and fecal control and identify risk groups[19].

A study conducted by Hirasing in 1997 on the prevalence of wet bed in adults aged 18-64 years, on the other hand, is interesting. A total prevalence of 0.5% was found, referring to a large untreated population. Assuming a prevalence of enuresis of 8% at 7 years in boys, the results can be transferred and show that the risk of a child enuretic remains symptomatic for the rest of his life is 3%, if not treated during childhood, cited by Hjalmas et al in 2004)[20].

Night enuresis is a genetic and heterogeneous disorder. Genetic factors are important while environmental factors exert major modifying effects on the phenotype (21). Empirical family studies have repeatedly shown a high rate of affected children (39% if the father was enuretic, 23% of mothers and 46% of parents). Bakwin in 1973 showed that if a father was enuretic, children have a 40% chance of being. If both parents this figure rises to 70%[21].

Fig 1. Three directional muscle actions pull against pubourethral (PUL) and uterosacral (USL) suspensory ligaments Broken lines represent bony vertical and horizontal co-ordinates .
Radioactive dye has been inserted into the bladder "B", vagina "V", rectum "R" and levator plate "LP"
Upper xray image Three slow twitch muscle forces "S" maintain continence.
Lower xray image On straining, three fast twitch muscles pull forwards and backwards against the puborethral ligaments "PUL" (arrows) and downwards against the uterosacral ligaments "USL" (downward arrow). The downward vector pulls down the anterior border of LP to "kink" the urethra at bladder neck.



ETIOLOGY OF ENURESIS: GENETICS

Night enuresis is a genetic and heterogeneous disorder. Genetic factors are important while environmental factors exert major modifying effects on the phenotype[21]. Empirical family studies have repeatedly shown a high rate of affected children (39% if the father was enuretic, 23% of mothers and 46% of parents). Bakwin in 1973 showed that if a father was enuretic, children have a 40% chance of being. If both parents this figure rises to 70%[21].

Hypothesis

That a squatting based pelvic floor regime would help children with nocturnal enuresis (bed wetting).

The background to the hypothesis was Patricia Skilling's squatting -based pelvic floor regime which gave excellent results in studies in premenopausal women, Tables 1&2[22-24].

With reference to fig 1, squatting exercises strengthen the 3 involuntary muscles, m.pubococcygeus (forward arrow), m.levator plate (backward arrow) and m.longitudinal muscle of the anus (downward arrow), which in turn pull against the pubourethral ligaments (PUL) anteriorly and the uterosacral ligaments (USL) posteriorly, fig 1[25-27].

This contrasts markedly with the "squeezing-based" Kegel exercises which are based on voluntary upward contraction of the puborectalis muscle 'PRM' fig 2[26,27].

Why the Integral Theory System for pelvic floor rehabilitation was developed

It was evident from radiological studies[16], that the organ and muscle movements observed during Kegel exercises

Fig 2. Same patient as fig1. Broken lines represent bony vertical and horizontal co-ordinates .
Note how "squeezing" ('Kegel muscle') lifts all the organs upwards and forwards with reference to the bony co-ordinates.

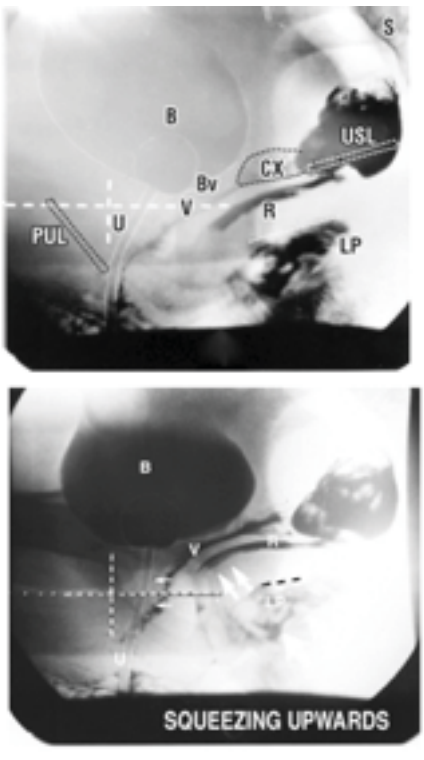


Table 2	
Fate of Individual Symptoms (n=78)	
condition	>50% improvement
stress incontinence (n=69)	57 (82%)
urge incontinence (n=44)	33 (68%)
frequency only (n=12)	10 (83%)
nocturia (n=32)	29 (90%)
pelvic pain (n=17)	13 (76%)

Table 1	
Fate of Individual Symptoms (n=60)	
condition	>50% improvement
stress (n=42)	78%
urge (n=39)	61%
frequency (n=53)	62%
nocturia (n=24)	75%
pelvic pain (n=20)	65%
leakage (n=50)	68%
bowel problems (n=28)	78%

(squeezing upwards) were very different from coughing and straining. It was evident that the pubourethral (PUL), and uterosacral ligaments (USL), were major insertions for the 3 directional muscle forces. It was already known that simultaneous surgical reinforcement of PUL by a midurethral sling, and USL by a posterior sling[25], gave high cure rates for symptoms of stress incontinence (SI), urgency, frequency, abnormal emptying, and chronic pelvic pain.
It was reasoned that using exercises such as squatting and straining would strengthen the natural closure muscles, and their ligamentous insertions, PUL and USL. It was also reasoned that if the Theory was valid, not only SI, but a much wider range of symptoms such as urgency, frequency, abnormal emptying, and pelvic pain should
also be curable simply by including squatting type exercises. Th is proved to be so. The methods and results of the 1st and 2nd applications of the Integral Theory System PFR[22-24] are detailed below in Tables 1&2.

PROPOSED METHODOLOGY

To follow the CONSORT guidelines with regards to randomization, blinding and independent assessment of the results. An RCT with two groups, experimental and placebo of 46 patients would give a power of 90% with confidence interval of 95% allowing a 9% placebo effect. The primary exercise regime (24 patients) would, as a minimum, be based on squatting, 10 times morning and evening, with adoption of a "squatting culture", encouraging the child to perform all its activities in the squatting position. The placebo group had 24 patients.
Assessment was to be with an independent doctor plus the signed testimony of the parent as to whether the child was dry or not at assessment at 4 months.

RESULTS AND DISCUSSION

The literature review of existing practice revealed no insights which could impact on the proposed study. The origin of bed-wetting was said to be essentially unknown. Analysis of the xrays, however, confirmed that the squatting-based regime of the Integral System would act on the same pubourethral and uterosacral ligaments which are repaired surgically using tapes, and which give high cure rates for bladder, bowel and chronic pelvic pain dysfunctions[27].
It was also reasoned that the main difference between adults and children with reference to the Integral Systems's pelvic floor regime was that children are in a collagen formation mode, which should reinforce the ligaments in a better way than in adults, with superior results to those in Tables 1&2.

CONCLUSIONS

The analysis was very positive for the initiation of a squatting based pelvic floor regime for children with nocturnal enuresis with prospects of a higher cure rate than that achieved in adults.

Conflicts

Peter Petros: Principal author of the Integral Theory
Angel Fernandez Garcia: None

REFERENCES

1. Moffat M. Nocturnal enuresis. Is there a rationale for treatement? Scan J Urol Nephol Suppl 1994;163: 55-67.
2. Phaires T. On pissing in the bed - and elsewhere. The Lancet 1977; 310: 1214-1215.
3. Hall J. Select Observations on English Eminent Persons in Desperate Diseases. Ed. James Cook. Printed by J.D.for Benjamin Shirley P.11, London, 1679.
4. Miller K. Concomitant non pharmacologic therapy in the treatment of primary nocturnal enuresis. Clinical Pediatrics 1993; (Special Edition): 2-37.
5. Bloom DA, Seeley WW, Ritchey ML, Mc Guire EJ. Toilet habits and continence in children: an opportunity sampling in search of normal parameters. J Urol 1993; 149: 1087-1090.
6. Moffatt MEK, Harlos S, Kirshen AJ, Burd L. Desmopressin acetate and nocturnal enuresis: how much do we know? Pediatrics 1993; 92: 420-425
7. Norgaard JP, Pedersen EB Djurhuus JC. Diurnal antidiuretic hormone levels in enuretics. J Urol 1985; 134: 1029-1031.
8. Hansen MN, Ritting S, Siggaard C, Kamperis K, Hvistendahl G, et al. Intraindividual variability in nighttime urine production and functional bladder capacity estimated by home recording in patients with nocturnal enuresis. J Urol 2001; 166 (6) 2452-2455.
9. Rushton Hl, Belman AB, Zaontz MR, Skoog SJ, Sihelnik S. The influence of small functional bladdler capacity and other predictors on the response to Desmopressin in the management of monosymptomatic nocturnal enuresis. J Urol 1996; 156 (suppl 2): 651-655.
10. Chandra M, Saharia R, Hill V, Shi Q. Prevalence of diurnal voiding syntoms and difficult arousal from sep in children with nocturnal enuresis. J Urol 2004; 172(1): 311-316.
11. Woo SH, Park KH. Enuresis alarm treatment as a second line to pharmacotherapy in children with monosymptomatic nocturnal enuresis. J Urol 2004; 171(6): 2615-2617.
12. Hvistendahl GM, Kamperis K, Rawashdeh YF, Ritting S, Djurhuus JC. The effect of alarm treatment on the functional bladder capacity in children with monosymptomatic nocturnal enuresis. J. Urol. 171 2004; (6): 2611-2614.
13. Astbury J,Orgill AA, and Bajuk B. Relatonship between two years behaviour and neurodevelopment outcome at five years of very low birthweight survivors. Developmental Medicine and Neurology 1987; 29 (3): 370-379.
14. García Fernández A, Palacio MM, Santo R, Llorens V,Abadía GP. Coordinated voiding resolves the symptoms of bladder instability in children. BJU 2000; 84 (suppl 4): 12-
15. Neveus T, von Gotard A, Hoebeke P,Hjalmas K, Bauer S. et al "The standardization of terminology of lower urinary tract function in children adolescents: Report from de Standardisation Committee of the International Children´s Continence Society. J Urol 2006; 176: 314-324.
16. Petros PE & Ulmsten UU An Integral Theory of female urinary incontinence. Acta Obstetricia et Gynecologica Scandinavica, 1990; Supplement 153; 69: 1-79.
17, Feehan M, McGee R, Stanton W, Silva PA. A 6 year follow-up of childhood enuresis: prevalence in adolescence and consequences for mental health. J Paediatr Child Health 1990; 26:75–9.
18. Lee SD, Sohn D, Lee JZ, Park NC, Chung MK. An epidemiological study of enuresis in Korean Children. BJU Internat 2000; 85: 869.

19. Heron J, Joinson C, Croudace T, von Gontard A. Trajectories of Daytime Wetting and Soiling in a United Kingdom 4 to 9-Year-Old Population Birth Cohort Study. J Urol 2008; 179(5): 1970-1975.
20. Hjalmas K, Arnold T, Bower W, Caione P, Chiozza LM, von Gontard A, et al. Nocturnal enuresis: an international evidence based management strategy J Urol 2004; 171(6): 2545- 2561
21. Hublin C, Kaprio J, Partinen M, Koskenvuo M. Nightmares: Familial aggregation and association with psychiatric disorders in a nationwide twin cohort Am J Med Genet/Neuropsychiatric Genetics, 1999; 88: 329-336
22. Petros PE and Skilling PM Pelvic floor rehabilitation according to the Integral Theory of Female Urinary Incontinence. First report, European Journal of Obstetrics & Gynecology and Reproductive Biology 2001; 94: 2, 264-269
23. Petros PE and Skilling PM The physiological basis of pelvic floor exercises in the treatment of stress urinary incontinence. Br J Obstet Gynaecol 1999;106:615-616
24. Skilling PM,·Petros PE Synergistic non-surgical management of pelvic floor dysfunction: second report. Int J Urogyne 2004; 15: 106-110
25. Petros PE and Ulmsten U Role of the pelvic floor in bladder neck opening and closure: I muscle forces. Int J Urogynecol and Pelvic Floor 1997; 8: 74-80
26. Petros PE and Ulmsten U Role of the pelvic floor in bladder neck opening and closure: II vagina. Int J Urogynecol and Pelvic Floor. 1997; l8: 69-73
27. Liedl B, Inoue H, Sekiguchi Y et al. Is overactive bladder in the female surgically curable by ligament repair? Cent European J Urol. 2017; 70: 51-57.

Correspondence

Prof. Dr. Angel Garcia Fernandez MD PhD
Universidad Nacional de Córdoba Argentina
agarciafernandez00@gmail.com

Review

Functional constipation: a conservative first line approach

MARILYN FREEDMAN PT, DPT, CAPP

Essential Physical Therapy
Great Neck, New York, USA

Abstract: Functional Constipation (FC) is a common bowel disorder leading to restricted activity and a reduction in health-related quality of life. It is usually managed initially by increasing liquid intake, increasing or balancing the intake of soluble and non-soluble fiber, or using over the counter or prescription laxatives. However, these interventions are often ineffective and fail to address the underlying pathophysiology contributing to this condition. The knowledge and skills of practitioners well versed in a range of neuromusculoskeletal, manual and motor coordination skills, are a necessary adjunct in diagnosing and treating FC. This article focuses on Chronic Functional Constipation, and the conservative role that neuromuscular diagnosis and treatment offers. It seeks to inform professionals about the value of implementing a neuromuscular behavioral approach in the treatment of functional constipation.

Keywords: Electrotherapy; Functional/chronic constipation; Neuromuscular; Physical therapy; Visceral mobilization

INTRODUCTION

Constipation is a common gastrointestinal (GI) problem and its prevalence in adults has been estimated at 16% worldwide (varying from 0.7% to 79%). It is more common in women than in men and more common with age progression[1]. A person with chronic constipation (CC) may experience infrequent bowel movements, hard, difficult to pass stools, incomplete bowel movements or straining.

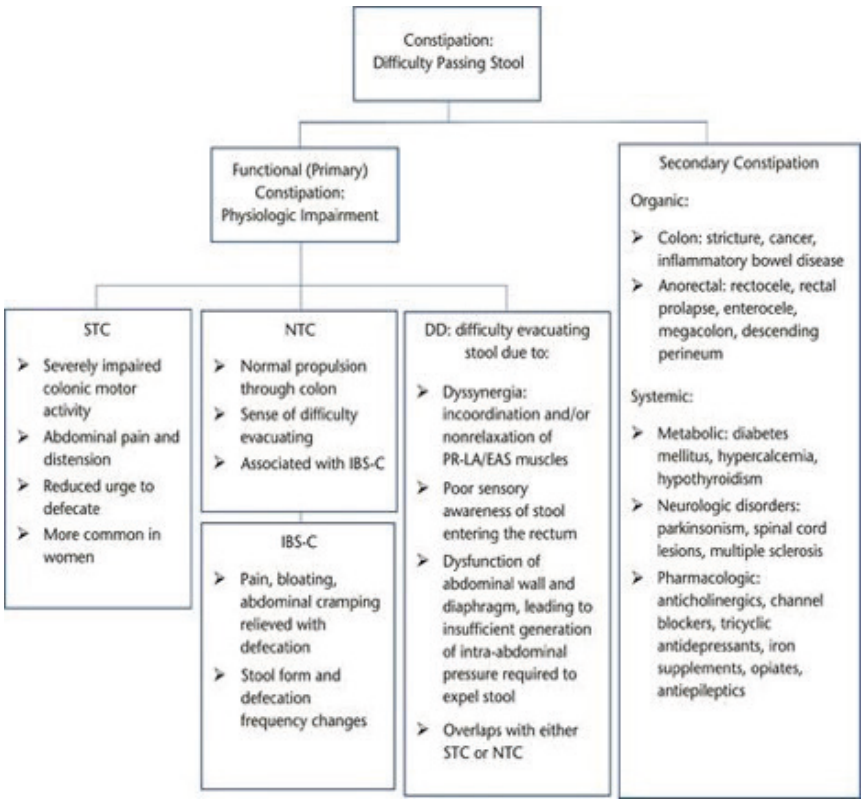
CC can be divided into two types[1,2]: primary constipation with functional impairment of colon and anorectal structures and secondary constipation related to disease or medications.

Figure 1 illustrates these two types of constipation and presents their characteristics and etiology.

Nerves and muscles help maintain continence until we decide to have a bowel movement. The pelvic floor muscles, together with anal sphincter muscles, must all relax in a coordinated way. At the same time the abdominal muscles and diaphragm need to work together to increase intra-abdominal pressure sufficiently in order to have a normal bowel movement. Failure of this to happen can lead to problems of constipation.

A survey of 100 patients with FC found that in nearly one-third (31%) of respondents the problem began in childhood. 29% appeared to have developed the problem after a particular event, such as pregnancy or injury. In the remaining 40% no cause was identified that may have brought on the condition. Within the same cohort, over half who developed the condition in adulthood reported the frequent or intermittent passage of hard stools. It may be that too much straining to expel hard stools over time is a factor leading to dyssynergic defecation. According to the Rome III diagnostic criteria, a diagnosis of functional constipation must include the presence of ≥2 of the following in at least 25% of defecations: straining, lumpy/hard stools, sensation of incomplete evacuation, sensation of anorectal obstruction or blockage, digital maneuvers to defecate, and <3 BMs per week. In addition, the diagnosis must include that loose stools are rarely present without use of laxatives, there are insufficient criteria for IBS, and the criteria must have been present for the past three months, with symptom onset at least six months prior to diagnosis. Although no one classification scheme fits all, these criteria appear to be widely accepted and provide a framework for further understanding. Functional constipation can be further divided into three general subgroups: normal transit constipation (NTC), slow transit constipation (STC), and defecation disorder (DD), as delineated in Figure 1.

Figure 1. Table outline of Chronic Constipation



GENERAL EXAMINATION

Treatment is based on a thorough evaluation of each patient. A patient's age and bio-psycho-social medical history need to be taken into account. Each patient is different, and treatment needs to be tailored to the individual.

Thoracoabdominal examination

should highlight respiration, particularly diaphragmatic, lower lateral and

posterior thoracic excursion. There can also be an imbalance of excursion from side to side. There is often impairment in people who have low back pain, sacro-iliac joint impairment or pelvic pain. Thoracic spine, rib mobility and static and dynamic postural habits are important to examine as they can affect chest wall kinematics and breathing patterns. This is essential to the intra-abdominal force production required to effectively expel a stool. A screen of the lumbar spine, pelvic ring, hip joints and core stabilizers will identify impairments that might impede proper toileting positioning. Assessment of myofascial tissues from T10 to thighs, including perineal and intrapelvic structures, will identify soft tissue impairments such as an inability to release or contract muscles functionally, and affected motor coordination. Diastasis recti (DR), which is primarily seen in women, especially during pregnancy or postpartum, can interfere with the patient being able to develop enough intra-abdominal pressure to be able to functionally expel a stool.

TREATMENTS

Initially patients stay on their medication schedule and are slowly weaned off it as they become more confident of their own ability to control their physiology. Dietary and liquid intake, as well as psycho-social and behavioural treatments are an important aspect, but will not be addressed here, as these have been well documented. There is, however, a paucity of research and information on the physical medicine protocols related to these treatments[3]. Outlined below are the neuro-muscular physical therapies that have been shown to be effective.

Management of FC should consider treatments that target neuromuscular impairments (sensory and motor coordination) and correct behaviors that are detrimental to overall health, including bowel function. Such an approach will consider other pelvic symptoms that co-exist in people with bowel disorders.

FC can be associated with dysfunctional activities of daily living (ADL). Three examples are: using a Valsalva mechanism to urinate; hovering over toilets; and delaying urination and/or bowel movements (BMs). These behaviors can interfere with the relaxation of pelvic floor and urinary sphincter muscles during micturition. Hovering over a toilet can lead to excessive straining during BMs and could contribute to the development of DD, as well as to urinary dysfunction and the prolapse of pelvic organs (POP)[4].

Respiration. The majority of patients suffering with FC are anxious, feel hopeless, are bloated and often in pain. They mostly use shallow, fast, upper chest breathing. Their diaphragmatic, lower lateral and posterior costal respiration is poor. Good excursion of the lungs, in combination with appropriate transverse abdominus muscle concentric and eccentric contraction provides a continual compression and release of abdominal contents, resulting in stimulation of the bowel. When this is combined with paradoxical pelvic floor respiration, a physiological set up for more optimal peristalsis occurs, and mega excursion of the bowel is minimized. Breathing retraining is best started in a hook lying position, and then progressed to sitting, standing and developing the ability to incorporate appropriately in all ADL.

Physiological Toileting Technique

The Israeli doctor Sikirov[5] tested this idea for a 2003 study published in *Digestive Diseases and Sciences*. He had several dozen patients defecate in each of three positions: sitting on a 16-inch-high toilet, sitting on a 12-inch-high toilet, and squatting over a plastic container. Sikirov found that, when squatting, subjects averaged 51 seconds to move their bowels, versus 130 seconds when sitting on a high toilet. Subjects were more likely to rate the squatting experience as easier. Figure 2 demonstrates an effective method of simulating a squatting position. Figure 3 demonstrates how this position assists in releasing the puborectalis muscle, increasing the ano-rectal angle, thus facilitating physiological passing of stool.

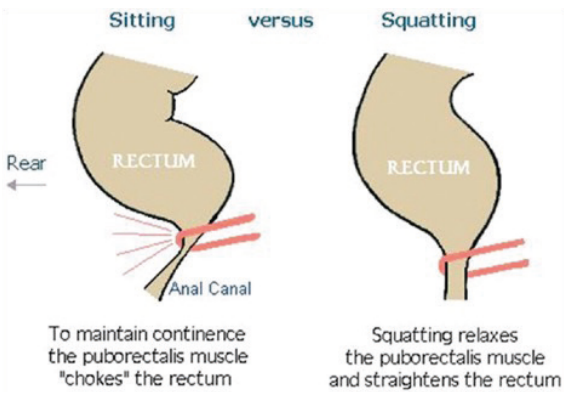
Figure 2. Toileting Posture

Today there are many commercially made devices to help increase hip and knee flexion while sitting on the type of pedestal toilets currently in use. However, something as simple as a small step stool, yoga blocks, or even large books placed under the feet work well. It is then advisable to lean forward from the hips, maintain a straight spine, and place forearms in a resting position on the thighs as shown in Figure 2.

Exercise. Few studies have examined the effects of physical exercise on colonic transit. As a clinician in this field, I have yet to find a client who did not benefit from some form of impact exercise and appropriate core strengthening during all ADL. This applies equally to patients who are challenged with conditions that make standing impossible. Patients with neurological symptoms where balance is affected, like Parkinson's Disease, Multiple Sclerosis, Cerebral Palsy, spinal cord injury or brain injury can be helped to sit on an exercise ball and bounce as this is a low impact activity.

Visceral Manipulation, also known as Abdominal Massage. Since 1999 there has been a growing number of studies demonstrating that abdominal massage can stimulate peristalsis, decrease colonic transit time, increase the frequency of bowel movements in constipated patients, and decrease the feelings of discomfort and pain that accompany them. There is also good evidence that massage can stimulate peristalsis in patients with post-surgical ileus. Individual case reports show that massage has been effective for patients with constipation as a result of a variety of diagnosed physiologic abnormalities, as well as in patients with long-term FC[6]. Figure 4A demonstrates an effective massage for the large bowel. It demonstrates using small circular clockwise

Figure 3. Postural change in anorectal angle



movements to stimulate and increase peristalsis in the ascending, transverse and descending colon. Figure 4B shows a firm stroking massage, known as the "I love you" massage. All strokes are repeated five times on an empty stomach. The I is for stroking down the descending colon. This is followed by the L (for Love) which is an upside down L stroked across the transverse colon from right to left, followed by a stroking down the descending colon and the U (for You) is an upside down U stroking up the ascending colon; across the transverse colon and down the descending colon (incorporating the entire large bowel). It is recommended for patients to perform this massage 3 times a day before meals as shown in Figure 4B.

Orthopedic Manual Therapy (OMT). OMT can be an effective treatment method for FC as it normalizes the colon transit time not only by lessening the symptoms of constipation but also by facilitating intestinal movements. Colon transit time is demonstrated in the following article: 30 subjects were measured before and after the interventions. 15 subjects were assigned to a Maitland OMT group, and 15 subjects were assigned to a dietary fiber group. The analysis of changes in colon transit time showed statistically significant differences in left colon transit time, rectosigmoid colon transit time, and total colon transit time for the OMT group. There were also statistically significant differences in rectosigmoid colon transit time and total colon transit time for the dietary fiber group. An analysis of group differences in the effects of OMT and dietary fiber intake showed that the former group achieved statistically significantly larger declines in rectosigmoid colon transit time and total colon transit time compared with the latter group[7].

Biofeedback. Biofeedback therapy has been shown to be effective by using neuromuscular training, assisted by visual, and verbal feedback. It is reported that > 70% of patients with gastrointestinal disorders eliminated symptoms through biofeedback therapy treatment. Biofeedback therapy is an efficient, multidisciplinary approach without adverse effects. It can be used during pregnancy or even with a patient who has cancer. The equipment is safe to use, as it only reads and records the patient's electromyographic activity. There is sensitive biofeedback equipment available using sophisticated hardware and software. A computer screen showing visual and auditory feedback assists the patient in learning the sensations associated with isolated pelvic muscle contraction and release, as well as learning what an effective bear down mechanism feels like. This is useful as an in-office treatment, as patient progress and statistical information can be saved and compared over time. A simpler unit is useful as a home trainer, so patients can practice what they have been taught in clinic[8].

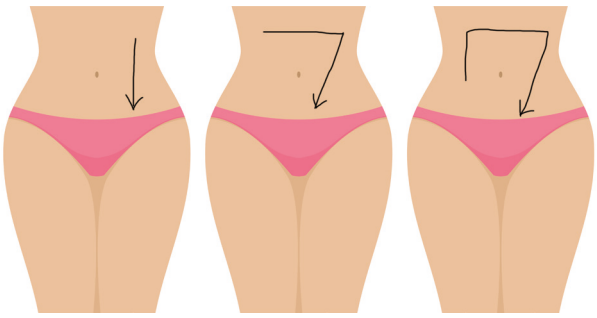


Figure 4B. I Love U Bowel Massage

During biofeedback therapy, either a sensor is placed in the anus or external sensors are placed on either side of the anus to give visual and auditory feedback of muscle function. Figure 5 demonstrates how a patient with paradoxical puborectalis contraction can learn how to relax their muscles when they bear down, in order to eliminate stool.

Alternatives to Biofeedback Therapy. There are also excellent non-technical and low-cost feedback methods.

1) A patient can *visualize* their perineum while in a physiological position to empty their bowel. A *yoga head stander* is ideal for this. The patient sits on the equipment, which has an opening in its seat that exposes the perineum. With a mirror placed under the equipment on the floor, the patient can clearly see their anal opening. A lighting source enhances visibility, and the patient is able to see their pelvic diaphragm function. Cueing facilitates contraction and relaxation of their pelvic diaphragm muscles. Patient observes what their bear down mechanism looks like, and how to train it.

2) The patient can use a *finger intra-anally* to monitor and train anal sphincter function.

3) Patients can be taught to effectively reverse outlet DD by inserting an *anal sensor*, mostly used for technical intra-anal biofeedback, into their anus, and expelling it gently against slight resistance from their finger. This maneuver can be repeated several times to retrain efficient stool emptying. Similarly, an *anal dilator*, which is flat at the end, like the *Milex* brand, is easier to use as it comes in different sizes.

Balloon-Assisted Training. Patients who are unable to sense when their rectum needs to be emptied can develop a mega-rectum, where the rectum is no longer able to contract and assist in bowel emptying. Using balloon

Figure 4A. Large Colon Massage

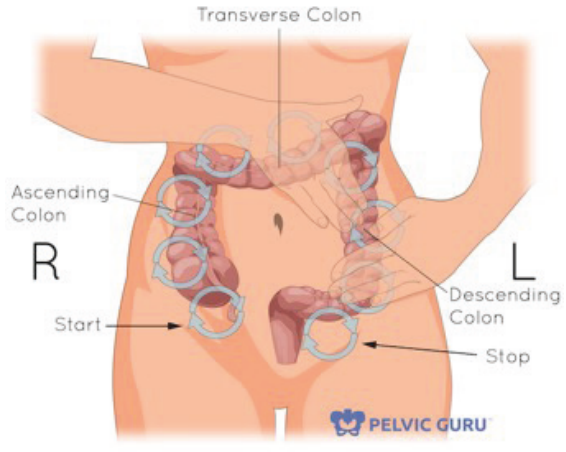
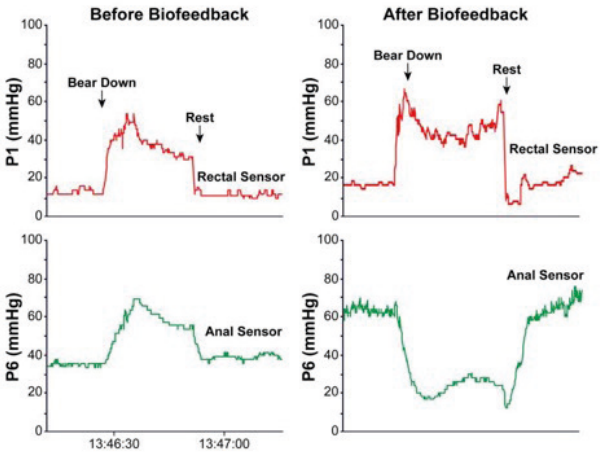


Figure 5. Biofeedback showing dyssenergic and functional pelvic muscle readings



training, a small, soft balloon is inserted into the rectum and is attached to a large syringe that will inject either water or air into the balloon, causing the balloon to enlarge within the rectum. This training technique provides feedback about the sensation of rectal filling, including the volume where the patient perceives urges to defecate. Over time the volume of water or air is diminished, so that patients learn to recognise earlier cues to empty.
Myofascial Trigger Point Release. A manual scan of a patient's myofascial tissue will quickly identify the areas of restriction in soft tissue. Initially, gentle rolling of the skin, or palpation of the superficial layer of abdominal and thoracic fascia and muscle will determine the areas that need release. Deeper palpation of the muscle tissue will reveal any tender trigger points, or fascial and muscle restrictions. Patients can easily be shown how to release these tissues. With CC there are three main findings:
1) Tight tissue over the area, which tends to be protective tightness. The areas of restriction are generally under the rib cage; diaphragm; superficial abdominal muscles; psoas and iliacus (which lies under the sigmoid colon.)
2) Scar tissue in all layers, including the greater and lesser omentum and mesenteries.
3) Loose low-tone tissue and muscle with no resistance or tone to assist in respiratory pumping motion, or ability to assist in increasing abdominal pressure to aid in stool evacuation.
Peri-Anal and Vaginal Splinting. Perianal pressure/splinting is a way to help move the stool out of a rectocele, so it can find the anal opening directly. Either (1) a patient's thumb or available commercial tool is inserted into the vagina (to support the posterior vaginal wall) or (2) a patient's forefinger and middle finger are placed on either side of anus (which is able to support a stretched perineum). There are times when both maneuvers are used simultaneously[9].
Interferential Current. Recent research has shown the efficacy of interferential current stimulation in the daily home treatment of children with CC. Four adhesive surface electrodes, two abdominal and two paraspinal produce two sinusoidal currents crossing the body. There is also a version that works anteriorly. Treatment is for up to three months. To date, only one open-label study has evaluated this technique in adults but it has shown encouraging results with an efficiency in 7/11 patients (63.6 %) in the number of stools, severity score of constipation and quality of life score[10].
Internal Anal Electrical Stimulation. Electrical stimulation therapy (EST) of the gastrointestinal tract has been used to treat gastric motor dysfunction since 1963. EST in the colon may be an alternative to conventional treatments, such as biofeedback and surgery. Most EST procedures are regarded as invasive but EST using an anal electrode is non-invasive. It has been shown to be successful in up to 60% of patients with fecal incontinence. It is a useful tool to treat ano-rectal hyposensitivity and useful in situations where patients are unable to generate a pelvic muscle contraction or release[11].

CONCLUSION

Patients diagnosed with FC need to be taught the biomechanics of defecation. Diet, fiber, liquid intake and exercise must be managed. Bowel massage, biofeedback, balloon training, electrical stimulation and interferential stimulation may be employed when necessary.
There are no adverse side effects to implementing a neuromuscular treatment approach for FC. It is inexpensive when compared to medical or surgical management and patients can usually become self-efficient in their own care after 4-6 treatments. It may save refractory patients from more invasive or radical procedures such as colostomies or surgery. This article advocates early referral to professionals familiar with a neuromuscular behavioural approach.

REFERENCES

1. Forootan M, Bagheri N, Darvishi M. Chronic constipation: A review of literature. Medicine (Baltimore). 2018;97(20):e10631. doi:10.1097/MD.0000000000010631. PubMed PMID: 29768326; PubMed Central PMCID: PMCPMC5976340.
2. George SE, Borello-France DF. Perspective on Physical Therapist Management of Functional Constipation. Phys Ther. 2017;97(4):478-93. Epub 2016/09/17. doi: 10.2522/ptj.20160110. PubMed PMID: 27634920.
3. Rao SS, Meduri K. What is necessary to diagnose constipation? Best Pract Res Clin Gastroenterol. 2011;25(1):127-40. Epub 2011/03/09. doi: 10.1016/j.bpg.2010.11.001. PubMed PMID: 21382584; PubMed Central PMCID: PMCPMC3063397.
4. George SE, Borello-France DF. Perspective on Physical Therapist Management of Functional Constipation. Phys Ther. 2017;97(4):478-93. Epub 2016/09/17. doi: 10.2522/ptj.20160110. PubMed PMID: 27634920.
5. Sikirov, D. Comparison of straining during defecation in three positions: results and implications for human health. Dig Dis Sci. 2003 Jul;48(7):1201-5. doi: 10.1023/A:1024180319005. PMID: 12870773
6. Sinclair M. The use of abdominal massage to treat chronic constipation. J Bodyw Mov Ther. 2011;15(4):436–445. doi: 10.1016/j.jbmt.2010.07.007.
7. Koo JP, Choi JH, Kim NJ. The effects of maitland orthopedic manual therapy on improving constipation. J Phys Ther Sci. 2016;28(10):2857-61. Epub 2016/11/09. doi: 10.1589/jpts.28.2857. PubMed PMID: 27821950; PubMed Central PMCID: PMCPMC5088141.
8. Forootan M, Bagheri N, Darvishi M. Chronic constipation: A review of literature. Medicine (Baltimore). 2018;97(20):e10631. doi:10.1097/MD.0000000000010631. PubMed PMID: 29768326; PubMed Central PMCID: PMCPMC5976340.
9. Apostolis C, Wallace K, Sasson P, Hacker MR, Elkadry E, Rosenblatt PL. Assessment of women with defecatory dysfunction and manual splinting using dynamic pelvic floor magnetic resonance imaging. Female Pelvic Med Reconstr Surg. 2012 Jan-Feb;18(1):18-24. doi: 10.1097/SPV.0b013e31823bdb98. PMID: 22453259; PMCID: PMC3707403.
10. Vitton V, Benezech A, Honore S, Sudour P, Lesavre N, Auquier P, et al. CON-COUR study: Interferential therapy in the treatment of chronic constipation in adults: study protocol for a randomized controlled trial. Trials. 2015;16:234. Epub 2015/05/28. doi: 10.1186/s13063-015-0752-8. PubMed PMID: 26012788; PubMed Central PMCID: PMCPMC4486681.
11. Jung KW, Yang DH, Yoon IJ, Seo SY, Koo HS, Lee HJ, et al. Electrical stimulation therapy in chronic functional constipation: five years' experience in patients refractory to biofeedback therapy and with rectal hyposensitivity. J Neurogastroenterol Motil. 2013;19(3):366-73. Epub 2013/07/23. doi: 10.5056/jnm.2013.19.3.366. PubMed PMID: 23875104; PubMed Central PMCID: PMCPMC3714415.

DISCLOSURES:

The author declares no conflict of interest, and no financial support by any grant or research sponsor.

Correspondence:

MARILYN FREEDMAN PT, DPT, CAPP
Essential Physical Therapy
Private Practice Owner
8 Bond Street, Suite 202,
Great Neck, NY 11021, USA
drfreedman@pelvicology.com

A MINIMALLY INVASIVE AND EFFECTIVE BRIDGE BETWEEN CONSERVATIVE THERAPY AND SURGERY FOR BOWEL INCONTINENCE

secca®

EFFICIENT
Performed in an outpatient setting

SAFE
Less than 1% complication rate*

EFFECTIVE
Up to 84% of patients experienced significant improvement*

QUICK RECOVERY
Return to normal activities in a few days

SECCA PATIENTS **84%** experienced significant improvement

Greater Quality of Life

Less than **1%** complications

MEDERI

Distributore esclusivo:

INNOVA medica SPA

DILAGENT®

Curative “exercises” for anal fissures, haemorrhoids, hypertonic muscles and postsurgical stenosis

DILAGENT is a **soft silicone** anal dilator.
It is indicated for the treatment of anorectal diseases caused by a hypertonic sphincter, namely anal fissures, haemorrhoids and painful spasms after surgical treatment of the anorectal segment. It is also effectively used in cases of postsurgical stenosis of the anal canal.

sapimed S.p.A.
www.sapimed.com

years after surgery. Int Urogynecol J Pelvic Floor Dysfunct 2005;16:447–54.
5. Lantzsch T, Goepel C, Wolters M, Koelbl H, Methfessel HD. Sacrospinous ligament fixation for vaginal vault prolapse. Arch Gynecol Obstet 2001;265:21–5.
6. de Ridder D. Should we use meshes in the management of vaginal prolapse? Curr Opin Urol 2008;18:377–82.
7. Dias FGF, Dias PHGF, Prudente A, Riccetto C. New strategies to improve results of mesh surgeries for vaginal prolapses repair--an update. Int Braz J Urol 2015;41:623–34.
8. Farnsworth BN. Posterior intravaginal slingplasty (infracoccygeal sacropexy) for severe posthysterectomy vaginal vault prolapse--a preliminary report on efficacy and safety. Int Urogynecol J Pelvic Floor Dysfunct 2002;13:4–8.
9. Petros PP. Medium-term follow-up of the intravaginal slingplasty operation indicates minimal deterioration of urinary continence with time. Aust N Z J Obstet Gynaecol 1999;39:354–6.
10. Feiner B, Jelovsek JE, Maher C. Efficacy and safety of transvaginal mesh kits in the treatment of prolapse of the vaginal apex, A systematic review. BJOG 2009;116:15–24.
11. Bjelic-Radisic V, Hartmann G, Abendstein B, Tamussino K, Riss PA. The posterior intravaginal slingplasty operation, Results of the Austrian registry. Eur J Obstet Gynecol Reprod Biol 2009;144:88–91.
12. Brubaker L, Cundiff GW, Fine P, et al. Abdominal sacrocolpopexy with Burch colposuspension to reduce urinary stress incontinence. N Engl J Med 2006;354:1557–66.
13. Barber MD, Brubaker L, Burgio KL, et al. Comparison of 2 transvaginal surgical approaches and perioperative behavioral therapy for apical vaginal prolapse, The OPTIMAL randomized trial. JAMA 2014;311:1023–34.
14. Barber MD, Brubaker L, Nygaard I, et al. Defining success after surgery for pelvic organ prolapse. Obstet Gynecol 2009;114:600–9.
15. Kraus P, Krofta L, Krčmář M, et al. Řešení sestupu tří kompartmentů pomocí syntetického implantátu a sakrospinózní fixace, Kohortová prospektivní studie s délkou follow-up pěti let [The results of five years follow-up prospective study of vaginal prolapse repaired by prolift total mesh surgery or sacrospinous fixation]. Ceska Gynekol 2017;82:277–86.
16. FDA. Urogynecologic Surgical Mesh: Update on the Safety and Effectiveness of Transvaginal Placement for Pelvic Organ Prolapse, 2011. (https://www.fda.gov/downloads/MedicalDevices/Safety/AlertsandNotices/UCM262760.pdf).
17. Dirk G. Kieback. Bilateral Sacrospineous Colposuspension (BSC) in the treatment of vaginal vault prolapse - description of a novel method. Pelviperineology 2019; 38:46-48

NOTES

Acknowledgements and disclosures

The authors report no conflicts of interest.

Correspondence to:

Dirk Kieback - St. Juergener Strasse 1-3 - Schleswig 24837 - Germany
E-mail: dirkkieback@hotmail.de