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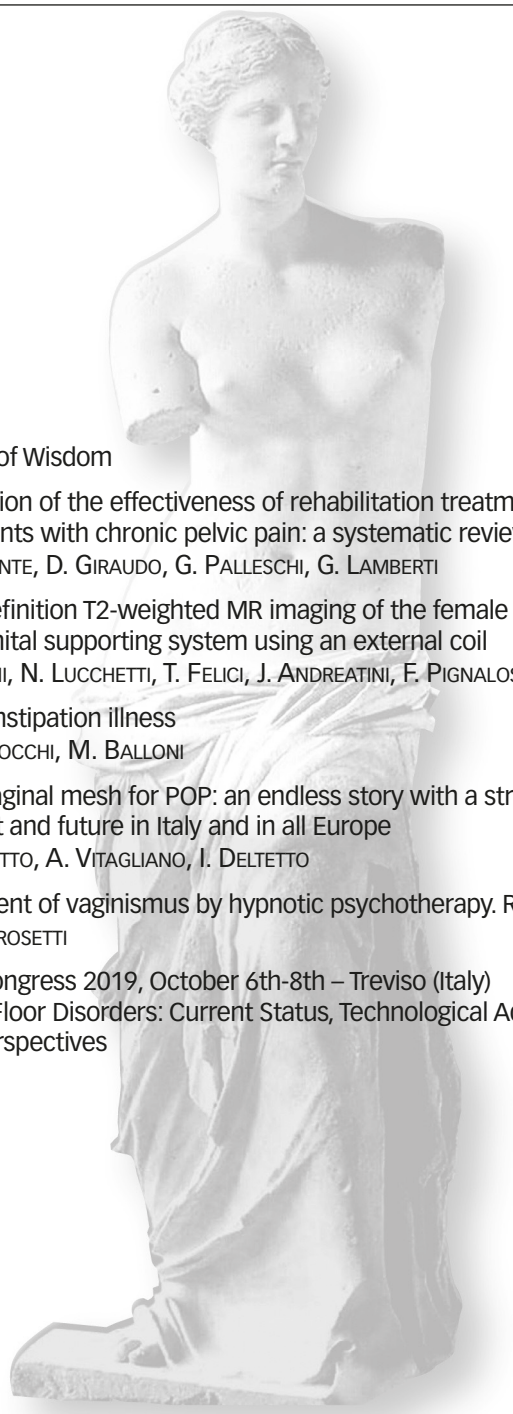

Contents

'Taxe Perçue' 'Tassa Riscossa' - Padova C.M.P.
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Surgical technique adaptable to the individual anatomy for the treatment of female stress incontinence with

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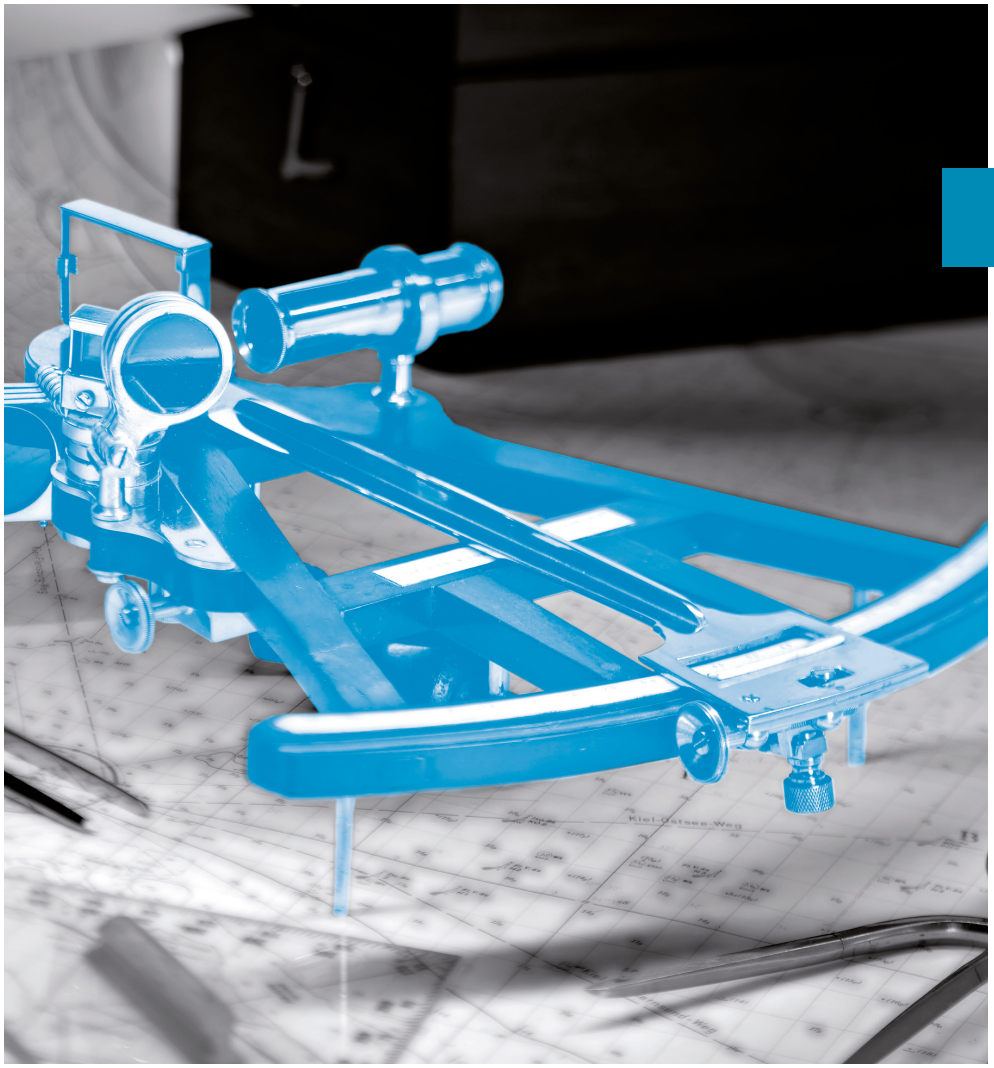

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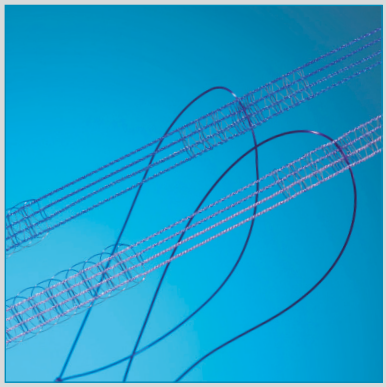

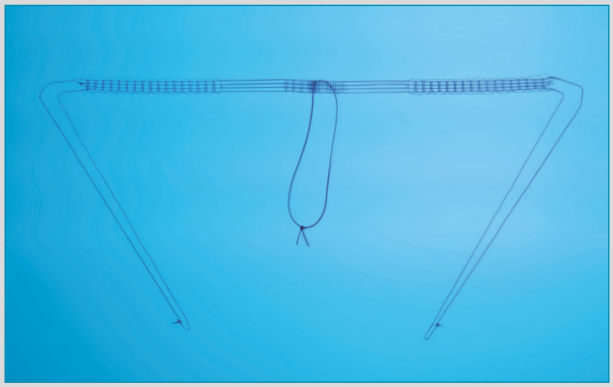

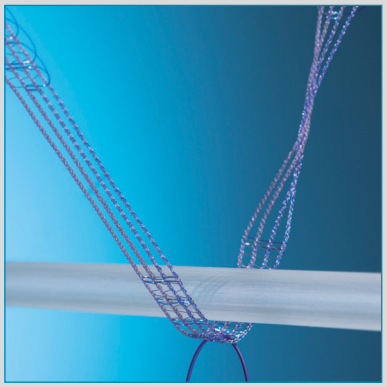

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Editorial

The September issue is an important one for the journal and as well for what it means in the *science of pelviperineology*: it is edited for the 12th ISPP Congress of the International Society of Pelviperineology, an event to which we attribute multiple meanings.
Thanks to the support of the ISPP Scientific Board, of the local University Hospital well represented by the co-president Giulio Santoro, to the sponsors, and to the scientific national and international societies involved in the pelvic floor, this conference is definitely the full expression of the multidisciplinary and interdisciplinary spirit of pelviperineology, a branch of medicine that deals holistically with all the complex and fascinating components of that part of our body.
The journal contains a *supplement* with the abstracts of the congress and of the numerous workshops, where a central role in this overall and future-oriented vision is represented by the Integral Theory. For this we have requested contributors from the dedicated workshop to distil some of their thoughts in a short pithy resume as *Words of Wisdom*. We hope to present in Pelviperineology journal from time to time this new feature designed by Peter Petros.
As the presentation of the scientific program states, the chosen theme of the congress is *Current status, technological advances and perspectives*. We have the ambitious aim to provide not only a consensus on the management of pelvic floor disorders, according to the evidence-based medicine and the international guidelines, but to look forward considering which are the perspectives of the new technologies. For this reason many experts in the field of the pelvic floor from Italian and international societies have been involved into an open debate during the round tables representing a fundamental opportunity to the growth of what is becoming a real new *specialty* as evidenced by the multiplication of pelvic floor specialist centers in the most advanced countries around the world. This leads to an editorial of this journal, still named "Journal of Coloproctology", in 1990 when we invented the word *perineology* foreseeing and hoping for it an interesting future.
The approach to the pelvic floor belongs to urologists, gynecologists, colorectal surgeons, gastroenterologists, physiatrists, obstetricians, nurses, physiotherapists, psychologists, radiologists, sexologists, andrologists: a patient-centered vision is obviously needed and is being accepted. All these figures are represented in the Treviso meeting as well as they are in this journal, which is the voice of ISPP.
Aims of ISPP are to realize Masterclasses, Fellowships, the *School for the Pelvic Floor Surgeon*, as well as to develop technology partnership with all the interested Companies in this field.
Research and education are the basis of the progress in science. Many functions and dysfunctions of the pelvic floor commonly met in the everyday life are still mysterious, as Darren Gold states in his Word of Wisdom, and a great effort is needed to improve our knowledge.

Professor Giuseppe Dodi
Editor in Chief Pelviperineology

Words of Wisdom

Knowing what you don't know

DARREN GOLD dandjgold@gmail.com

Einstein said, "Any fool can know. The point is to understand." The perpetual problem with pelvic organ dysfunction is that the lack of understanding of normal physiology has hampered progress in the management of these conditions for well over a century. How we empty our bladder and bowel and also maintain continence is still considered a mystery. The most significant breakthrough came in 1990 with the advent of the mid-urethral sling, that was based on a new and still controversial understanding of stress incontinence and pelvic organ function. It revolutionised the management of stress incontinence and became one of the most studied operations in the history of surgery. It was adopted by almost all practising urogynaecologists and is still considered the gold standard. It introduced the use of prosthetic materials as standard practice for the management of stress incontinence.
The problem was that very few understood how the midurethral sling (MUS) restored the continence mechanism, but once they knew how to do it there was no going back. Unfortunately, the lack of understanding of its mechanism of restoring continence led to personal modifications, a misunderstanding of the role of prosthetic material in the management of these conditions and what was later to be known as the 'mesh disaster'. The largest group to lose in this tale of woe are women themselves. They have lost their trust in all forms of prosthetic reconstructive surgery and many will refuse to have surgery, remaining incontinent and miserable.
We must take stock and start again. We must rebuild from the ground up by understanding the normal mechanisms of bowel and bladder emptying and continence and relearn our anatomy and reassess our understanding of physiology in order to appreciate how these mechanisms may be restored by surgical techniques that are based on this understanding. The knowledge is there. It is not too late, but time is running out.

Understanding the Integral Theory- what do we need to know?

PETER PETROS pp@kvinno.com

The Integral Theory System (ITS) uses functional anatomy to explain how nerves, ligaments, muscles work holistically for organ support, bladder, bowel function and dysfunction. Ligament laxity due to collagen defect is the weak point in the system and the basis of the ITS diagnostic and management system.
Bladder and bowel have only two modes, open or closed, involuntary, controlled by closure or opening reflexes. Oppositely-acting directional muscle forces, fig1, contract against pubourethral and uterosacral ligaments to close urethral and anal tubes (continence), open them (evacuation), and stretch the organs sufficiently to prevent stretch receptors from firing off prematurely to activate the opening reflexes (micturition, defecation). Damaged ligaments weaken these muscle forces, so they cannot adequately close outlet tubes (incontinence) open them, (evacuation difficulties) or stretch organs sufficiently to control evacuation reflexes (urge incontinence). Reinforcing weakened ligaments with tensioned tapes reverses the cascade of events to cure up to 90% of organ prolapse, plus symptoms, bladder, bowel, chronic pelvic pain.

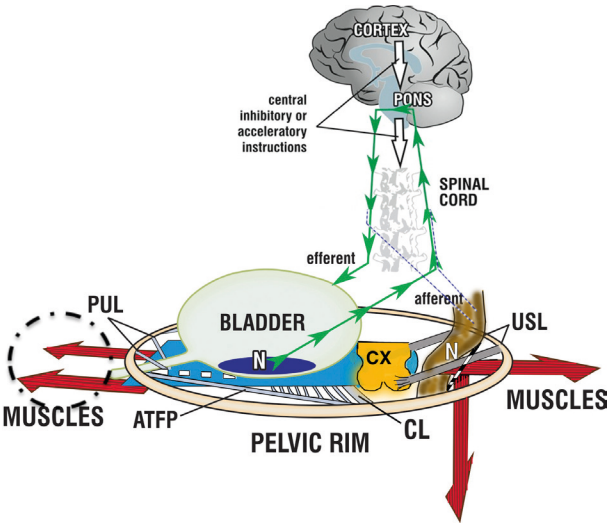


Fig 1. Binary control of bladder & bowel. Schematic 3D sagittal view. System in normal closed mode. Like a trampoline, the organs are stretched and balanced by 3 opposite vector forces (arrows), contracting against PUL (pubourethral ligaments) and USL (uterosacral ligaments). Afferent impulses from stretch receptors 'N are reflexly suppressed cortically (white arrow). When required, the cortex activates the defecation and micturition reflexes: the forward muscles relax, pubococcygeus for urethra (broken circle), puborectalis for anus (not shown); this allows the posterior muscles (arrows) to unrestrictedly open out the posterior wall of anus and urethra (broken white lines) just prior to bladder/ rectal evacuation by smooth muscles contraction (spasm). If PUL or USL are loose, the muscles contracting against them (arrows) weaken. Urethra/ anus cannot be closed (incontinence), opened (emptying problems) or organs stretched to support 'N', ('urge incontinence).

Lax connective tissue and chronic pelvic pain - pathophysiology and treatment

KLAUS GOESCHEN klaus.goeschen@googlemail.com

There is a strong interrelationship between chronic-pelvic-pain and pelvic-organ-prolapse (POP). Recent results of the PROPEL study, submitted for publication from Liedl et al, show that preoperatively two thirds of all POP-patients had relevant-pain-complaints (RPC). According to Martius there are two pathways for pain-transmission: 1) A short mechanical way to the plexus sacralis: Deficient suspending ligaments or insufficient support from pelvic floor lead to increased tension against the plexus sacralis. This causes pain symptoms in the back: low-dragging abdominal pain or deep-sacral backache.
2) A long visceral way via spinal cord to the brain transmitted through the paired Ganglia Frankenhäuser, located in the parametrium 2cm bilaterally to the cervix. Pressure or tension on it causes pain particularly in the middle and/or front area of the pelvis. These pains radiate mainly to the anterior and lateral abdominal wall, the inguinal region and the thighs.
Deficient suspending ligaments generates pain symptoms as follows: 1) utero-sacral-ligaments (USL) = back-pain, 2) cardinal-ligaments (CL) = back-pain, 3) perineal-body = middle/ back-pain, 4) arcus-tendineus-fascia-pelvis = middle/front-pain, 5) pubo-urethral-ligament (PUL) = middle/front-pain.
Deficient support from pelvic floor generates mainly pain in the pelvic center.
Why is this differentiation important for therapy? In all cases lax connective tissue is responsible for pain formation! These patients can be pooled into three groups:
1) Patients with intact pelvic floor, but damaged ligamental suspension.
2) Patients with damaged pelvic floor but sufficient ligaments.
3) Patients with a combination of both.
This differentiation has important therapeutic consequences and allows explanations for different cure-rates after vaginal or abdominal surgery.
1) If USL and/or CL are exclusively damaged this problem can be solved vaginally with posterior IVS/TFS or abdominally by cervico/vagino sacropexy.
2) + 3) In case of pelvic-floor-damage only restoration of the base is sufficient, if necessary in combination with ligament-repair. In my opinion this can only be done vaginally. Abdominal surgery provides no access for damaged muscle layer or membrane repair and does not recreate the natural axis of the vagina. In contrast, this procedure creates an abnormal vertical inclined vaginal axis. Fixation of vaginal apex to the promontorium pulls the uterus forwards and opens the Douglas cavity. Intraabdominal pressure can now push the Ganglion Frankenhäuser downwards generating more pain than before.
Conclusion: Due to the fact that deficient connective tissue is mainly responsible for prolapse induced organic lumbosacal pains an isolated damage of ligaments represents an exception. In the majority of cases, pains are the consequence of both, insufficient support and suspension.

Cure of bedwetting by squatting-based pelvic floor exercises

ANGEL FERNANDEZ-GARCIA, PETER PETROS agarciafernandez00@gmail.com

We hypothesized that day/night wetting was caused by loose ligaments/muscles failing to control inappropriate activation of the micturition reflex (Integral Theory). Furthermore, the reflex pelvic muscles and ligaments could be strengthened using squatting-based exercises. An RCT was conducted over 4 months on 48 children, mean 7.6 ± 2.5 years, 34 fe-

males, 14 males, attending Instituto Integral de Piso Pélvico Cordoba Argentina. Initially, the study had two arms, 10 squats, 10 bridge exercises twice daily (n=24) against placebo, running 50 metres twice daily (n=24). Groups randomly assigned, each trial step blinded.
The eligibility for the trial was daytime urine leakage and night-time bedwetting. Exclusion: refusal to sign consent forms. Recruitment was between 1.9.2018 to 2.2.2019. The assessment was by intention to treat. The criterion for cure was complete dryness.
At the 1st review at 4 weeks, 12/24 from the treatment group reported total cure of wetting, but there was zero effect from the placebo group. The placebo arm was immediately terminated by the Ethics Committee and all 24 children were transferred to the treatment arm. The trial now comprising all 48 children was carried out to termination at 4 months. The primary outcome was: 41/48 (86%) children cured of *both* daytime/nightime enuresis ($p<0.001$). Two children discontinued. There were no adverse events. Secondary outcomes were concomitant cure of constipation, fecal incontinence, urinary retention as predicted by the Theory.
Conclusions. Weak muscles/ligaments allow premature activation of stretch receptors and micturition reflex to cause day/night wetting. Squatting stimulates new collagen production; Treatment available to poorest nations.
This is a very simple method which appears to work very well. Clearly our results need to be validated by other studies. If to be used on an individual basis, we advise that diligent adherence to exercises is required for 4 months.

Simulated operations – a mechanical test for Integral Theory predictions

ALFONS GUNNEMANN gunnemann@gmail.com

Simulated operations are a substantial diagnostic tool for decision making in urogynecology to predict outcome of operative interventions. According to the Integral Theory, the simulated operation restores anatomy by mimicking the effect of a surgical intervention. Once a preliminary diagnosis is made, the zone of damage can be validated (or not) by 'simulated operations'.
Simulated operations are a technique which can give the surgeon an understanding of the contribution of each connective tissue structure in each zone to continence. The surgeon supports the connective tissue structures in each of the three zones with his small finger, a forceps or a tampon (pessary), using patient sensory control (percentage diminution of urge), or direct observation (percentage diminution of urine loss with coughing) as criteria.
From 01/2012 till 04/ 2019 we applied the technique of simulated operations evaluation before 867 urodynamic examinations in a standardized manner: the patient always empties her bladder right before the examination. During cystoscopy objective residual volumes are noted, the bladder pathology is described than the bladder is filled up to the sense of urge measuring the capacity at the same time. A cough test is applied in a lying position with mirror demonstration for the patient. The first simulated operation is applied by unilateral pressure applied with the forefinger immediately behind the pubic symphysis (the site of the pubourethral ligament 'PUL'). It controls urine loss on coughing, and restores urethrovesical geometry to normal.
Next step is a vaginal examination with vaginal ultrasound revealing and documenting vaginal pathology and condition of the urethral and anal sphincter.
In patients with cystoceles (frequent and often neglected cause of recurrent infections in urology) a special temporary pessary made of foam rubber is inserted to mimic the situation of a corrected cystocele. The patient keeps it for several hours and reports the effect.
In a classic SUI, the effect of the unilateral pressure is in our findings 92 % with a complete reduction of urine loss on coughing.
The applied tampon pessary was lost immediately by 17 % of the patients due to a large prolapse not properly being reduced by the size of the tampon. Urge symptoms were reported to improve in 35 % immediately and in 48 % during the hours to follow. Bladder voiding was reported to be significantly better in 61 %. Nocturia was significantly improved by 68 %– as long as the tampon was tolerated overnight.
Simulated operations are a simple and easy way to predict the success of a pelvic floor surgery and give valuable insight of the sides of repair to relief symptoms to the surgeon. They provide direct instant proof of the Integral Theory's predictions.

Safety and short term outcomes of a new truly minimally-invasive mesh-less and dissection-less anchoring system for pelvic organ prolapse apical repair

ADI Y. WEINTRAUB, MASHA TSIVIAN, JOERG NEYMEYER, YONATAN REUVEN, MENAHEM NEUMAN, ALEX TSIVIAN adiyehud@bgu.ac.il

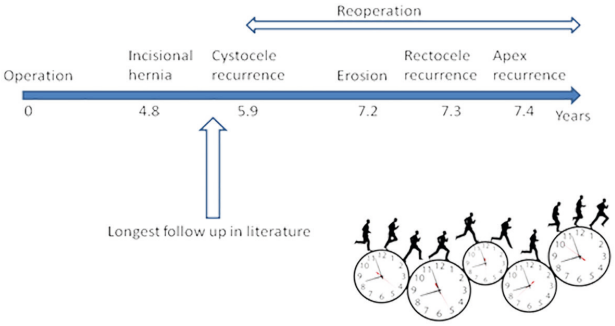
A prospective study was conducted using the NeuGuide™ device system for pelvic floor apical repair. All surgeries were performed using the same surgical technique. The primary effectiveness outcome was centro-apical pelvic floor prolapse by POP-Q after six months. The primary safety outcome was intraoperative and early post-operative complications and adverse effects after six months. A standardized questionnaire (UDI-6) to assess quality of life at entry and during follow-up visits was used. Patients were followed-up and evaluated six weeks, three months and six months following surgery. All statistical analyses were performed using the SPSS, software version 22.0. Two-sided p-value of <0.05 was considered significant.
Results: Ten women were enrolled to the study. The mean age of the study population was 63.8±12.0 years. Five had a previous hysterectomy and 2 had stress urinary incontinence symptoms. During surgery six patients had a concurrent colporrhaphy. There was no injury to the bladder, rectum, pudendal nerves, or major pelvic vessels and no febrile morbidity was recorded. At six months no cases of centro-apical recurrence were noted. Patients were found to be satisfied with the procedure and had favorable quality of life scores. Using the UDI-6 questionnaire an improvement, in all domains was seen. Moreover, although the small sample size improvement in urge and overflow incontinence related domains was demonstrated to be statistically significant.
This new NeuGuide™ device allows rapid and safe introduction of a suspending suture through the sacrospinous ligament and makes sacrospinous ligament fixation easy to perform, while avoiding dissection and mesh complications.

Laparoscopic sacrocolpopexy (LSCP) – a personal long-term experience

PETER VON THEOBALD vontheobald@gmail.com

We have published a retrospective monocentric single operator series of 80 laparoscopic sacrocolpopexies performed for genital prolapse, according to the double mesh technique at the unit of Gynecology of the University Hospital of Caen between January 1993 and December 2002.
The procedures have all been performed by me using the same surgical technique. Laparoscopic Burch colposuspension was almost systematically performed between 1993 and 2000. Later, TVT was used but only in case of objective stress urinary incontinence (SUI).
All the patients were directly contacted by and by mail and underwent examination by an independent gynecologist, 11 to 20 years after the operation. Long term results are finally good according to satisfaction index and QoL questionnaires. But 25% of patients had to be re operated average 5 to 8 years after first procedure, mainly for recurrent cystocele. This means that the results published in most series with a follow up between 1 to 3 years are truly overoptimistic. (figure 1). Pre-existing large cystocele is a risk factor for anterior compartment recurrence. In this case, vaginal repair with mesh should be discussed. Long term complication rate is low but some complications may be severe. As complications occur after a long period, the complication rate is also underestimated in literature. Some complications, like incisional hernia, are never mentioned in series despite a known incidence of more than 3.5 % after 3 years.

Figure 1. Timeline for average occurrence of recurrences and complications



Development of the midurethral sling

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The discovery of the midurethral sling (also known as the tension-free vaginal tape "TVT") began in 1986 with two unrelated observations: pressure applied unilaterally at the midurethra controlled urine loss on coughing; implanted Teflon tape caused a collagenous tissue reaction. It was hypothesized that the pathogenesis was collagen deficiency in the pubourethral ligament (PUL)which attaches to the middle part of the urethra. It was also hypothesized, that a strip of tape inserted exactly in the position of the PUL would create new collagen to reinforce the PUL.
In 1987, Mersilene tape was implanted retropubically in 13 large dogs, with the aim of creating an artificial collagenous pubourethral neoligament. Extensive testing showed that the operation was safe and effective. In 1988–1989, human testing was carried out (n=30).Mersilene tape cured 100 % of stress and mixed incontinence with a sling in situ; however, there was simultaneous recurrence of the two symptoms in 50 % on sling removal. X-rays showed no elevation of the bladder neck.
In 1990–1993, collaboration with Ulf Ulmsten took place. This led to a permanently implanted tape at PUL. It was found that polypropylene was the ideal material for implantation. In 2003, the neoligament principle was applied as an adjustable "mini sling" , initially to reinforce PUL for cure of stress urinary incontinence, then later to arcus cardinal ligaments for cure of transverse defect cystocele, ATFP for central cystocele, then uterosacral ligaments for cure of uterine prolapse, then perineal body for cure of rectocele and descending perineal syndrome. It was found that symptoms such as urgency, nocturia, chronic pelvic pain, obstructive defecation syndrome (ODS), and fecal incontinence were frequently cured or improved by repair of these ligaments.

Retropubic tissue fixation system tensioned mini-sling carried out under local anesthesia cures stress urinary incontinence and intrinsic sphincter deficiency: 1-year data

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We retrospectively studied a total of 96 intrinsic sphincter deficiency patients treated with the tissue fixation system midurethral sling at Yokohama Motomachi Women's Clinic from 2006 to 2015. We evaluated intraoperative and 1-year postoperative results. Regarding the cure rate, we divided patients into three groups: (i) patients with maximum urethral closure pressure <20 and Valsalva leak point pressure <65 combined (n = 17); (ii) patients with maximum urethral closure pressure <20 (n = 55); and (iii) patients with Valsalva leak point pressure <65 (n = 47).
The median age was 63 years (range 38–89 years). The median operating time including local anesthesia was 24 min (range 12–55 min) and median blood loss was 5.0 mL (range 3–69 mL). All operations were day surgery under local anesthesia. Postoperative pain was minimal. All patients were discharged the same day. There were no intraoperative complications except one bladder perforation. There were no tape rejections. The 1-year postoperative cure rates were: 88.2% among patients with maximum urethral closure pressure <20 and Valsalva leak point pressure <65, 90.9% for patients with maximum urethral closure pressure <20, and 85.1% among patients with Valsalva leak point pressure <65.
Conclusions: The tissue fixation system midurethral sling operation is a simple, safe and effective operation for older women with intrinsic sphincter deficiency, and it can be carried out under local anesthesia.

Review

Evaluation of the effectiveness of rehabilitation treatment in patients with chronic pelvic pain: a systematic review

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Abstract: Introduction: Chronic pelvic pain refers to persistent or recurrent pain, perceived in the structures related to the male or female pelvis. Because of its complex aetiology, there is no one therapy that can be recommended, but guidelines propose a multimodal treatment approach that makes use of the skills of various health figures, including physiotherapists. *Aim:* To evaluate the effectiveness of rehabilitation treatment in patients suffering from CPP, in terms of reducing pain symptoms, improving the quality of life and addressing associated psychological symptoms. *Materials and Methods:* A systematic review was conducted using the online databases Pubmed, PEDro and Cochrane, including only RCTs in English with full-text availability, concerning rehabilitation treatment in subjects with CPP. The methodological quality of each article was evaluated using the PEDro *Scale*, and the risk of bias using *Cochrane collaboration's tools for assessing risk of bias*. Results: Of the 996 studies analysed, only 10 articles (420 participants) met the inclusion criteria. In all of the studies, when compared with baseline, post treatment outcomes showed significant reduction in pain symptoms. The same result was obtained with respect to quality of life and psychological symptoms, where these were examined (5/10). A comparison of treatments failed to show a statistically significant superiority of physiotherapy intervention. *Conclusions:* The small number of studies and the critical internal methodological issues identified, make it impossible to reach definitive conclusions. New RCTs are therefore needed to validate the effectiveness of rehabilitation treatment in patients with CPP.

Keywords: Chronic pelvic pain; Rehabilitation; Multimodal treatment; Physiotheraphy; Physical theraphy

INTRODUCTION

Over the years, associations related to a number of medical disciplines, proposed various definitions of chronic pelvic pain (CPP). The differences in definitions proposed concern not only the duration or precise location of the pain, but also other characteristics such as persistence or cyclicity, the sex of affected patients, the possible presence of associated symptoms and the possibility of identifying a triggering cause.

Probably the most complete definition of chronic pelvic pain was provided by the *International Association for the Study of Pain* (IASP)[1], later taken up by the Association of European Urologists (UAE)[2]. Chronic pelvic pain is therefore defined as "persistent or recurrent pain, perceived in structures related to the male or female pelvis, often associated both with cognitive, behavioural and sexual consequences and with other symptoms that suggest urinary, sexual, intestinal, gynecological and pelvic floor dysfunctions."

Therefore, CPP can be perceived in both sexes but must have a precise location and duration. It must be located in the pelvis or in the associated structures, such as the anus, testicles, the penis or the vulvar area. To fall into the definition of "chronicity", the pain must be continuous or recurrent for at least 6 months if it is of peripheral origin, or linked to a persistent nociceptive stimulus; or independent of the duration of symptoms if it is of central origin, or associated with sensitization in the central nervous system (CNS).

Findings arising from epidemiological studies are difficult to implement and interpret due to a lack of consensus in scientific literature on the definition of CPP, and absence of adequate education and information for both patients and therapists. As a result, the prevalence of CPP is underestimated[3,4].

From the aetiopathological point of view, the pain can be divided into conditions caused by a known pathology (such as neoplasms or infections) and those where medical causes have been excluded and are of unknown origin.

The focus of current studies has moved from a search for triggering causes to identifying factors that predispose and maintain chronic pain. The foremost predisposing factors are of genetic[5] and cognitive-psychological[6] origin, while the maintenance of pain is caused by pathophysiological changes in nervous tissue[7]. Regardless of any peripheral damage, these changes may manifest clinically with functional alterations at a visceral level and with the amplification of the perception of painful stimuli (hyperalgesia), up to the point where pain is felt even in the absence of a stimulus (allodynia). Physical symptoms can be further exacerbated by affective, cognitive and behavioural variables.

On a diagnostic and therapeutic level there is no "*gold standard"*. The diagnosis is often based on the exclusion of known pathologies, and many treatments have been proposed as cures, from alternative medicine to surgery, from physiotherapy to phytotherapy.

Despite this variety, the lack of clarity of the aetiopathological mechanisms underlying CPP, the treatment is often unsatisfactory and limited to reduction of the symptoms. Currently, the increasing attention paid to the concomitant causes of CPP has been reflected in a new multimodal and multidisciplinary approach.

Within the multidisciplinary team, an important role belongs to the physiotherapist. Various studies have shown that patients affected by CPP, when compared to healthy controls, present altered parameters not only at the musculoskeletal level, but also at postural, respiratory and motor level[8,9].

Furthermore, in addition to the clinical description of the various sub-categories of CPP provided by the ICS, the evidence seems to support the hypothesis that independent of the causes and origin of CPP, some common associated signs may be present, such as "tenderness" and "*trigger points"* in the pelvic muscles.

Although the presence of the physiotherapist is now commonly accepted within this therapeutic team, the evidence supporting the effectiveness of physiotherapy is not yet clear. The purpose of this study is to find the best scientific evidence concerning the effectiveness of rehabilitation treatment in patients with CPP. Through a systematic review of literature, of all randomized controlled trials focused on the management of chronic pelvic pain, the effects of reha-

bilitation treatment was evaluated – whether therapy was provided in association with, or without other types of therapy, and through analysis compared to non-treatment, placebo or other types of conservative interventions.
To define the efficacy of treatment, the data analysis focused on the reduction of pain symptoms, improvement in quality of life and of the associated psychological symptoms.

MATERIALS AND METHODS

Criteria for considering studies within this review

The following criteria were used in selecting studies for this review:
- **Population**: Subjects included men and women, suffering from chronic pelvic pain, included in the dual meaning of symptom or illness in itself). In the first case, only articles that explicitly stated the persistence of symptom for at least 6 months were included; in the second case, *trials* were included that classified the patient as suffering from "*chronic pelvic pain syndrome"* or one of its sub-categories, regardless of the duration of the symptoms.
- **Intervention**: Patients subjected to rehabilitation treatment of safe physiotherapy competence, in association with or without other conservative treatments, such as pharmaceutical or psycho-therapeutic interventions.
To avoid misunderstanding, only those techniques that the ICS defines as belonging to pelvic floor physiotherapy were included: "physical activity, cognitive-behavioural therapy, bladder training, training of bowel habits, training of muscles (resistance, power) and coordination, *biofeedback* and electrical muscle stimulation"[10].
While falling within the Pubmed index as *"physical therapy* modalities", treatment modalities such as electromyographic biofeedback, *percutaneous* electrical stimulation in the posterior tibialis, *Pilates* and other procedures whose relevance in Italy is still controversial were excluded.
- **Control**: Patients not undergoing treatment / undergoing a placebo / or other type of conservative treatment.
- **Outcome**: In this review the outcomes considered in the single studies were not used as an inclusion criterion.
Primary outcome: effectiveness of rehabilitation treatment in terms of pain reduction.
Secondary outcomes: treatment efficacy in terms of improvements in psychological symptoms and quality of life.
- **Studies**: Randomized controlled trials, reported in English, with full text availability, without any time limitations.
Other exclusion criteria were:
- Studies appearing in more than one research (duplicates)
- Studies not relevant to the objective under consideration
- Studies concerning pathologies other than CPP.

Sources of information and research strategy

The research was conducted using the electronic databases Pubmed, PEDro and Cochrane. Medical Subject Headings (MeSH) used included "*pelvic pain"* and "*physical therapy modalities"* and other keywords such as "*chronic pelvic pain*", "*physical therapy*", "*physiotherapy*", "*rehabilitation*".
Here are the search strings used for each database:
1) Pubmed: ("*chronic pelvic pain"* or "*pelvic pain"* [MeSH]) and ("*physical therapy modalities"*; [MeSH] or "*physical therapy"* or *physiotherapy* or *rehabilitation*)
2) Cochrane: ("*chronic pelvic pain*" or "*pelvic pain*") and ("*physical therapy modalities*" [MeSH] or "*physical therapy*" or *physiotherapy* or *rehabilitation*)
3) Pedro: "*pelvic pain"*.
The last bibliographic search was carried out on 31 August 2017.
On the basis of reading the title and the abstract of the articles identified, the articles not in line with the inclusion criteria were systematically excluded. The hierarchy used to exclude articles was the following:
- Articles that are not in English or Italian
- Articles whose study design was not a "*randomised controlled trial"*;
- Articles that did not relate to chronic pelvic pain or in which the definition of chronic pelvic pain did not conform/ comply with that used by the IASP.
- Articles that did not relate to rehabilitation treatment
- Articles which, although proposing rehabilitation treatment, had not been designed to evaluate the effectiveness of the intervention
- Articles published more than once
- Articles of which full text is not available
Once the potentially useful abstracts were identified, these same inclusion criteria, in this same order, were used to skim full text articles.

Data extraction process

To guide the extraction process of the variables of interest a table was created (Tab. 1) in which, for each article, the following features are reported:
- Study (citation of the first author, year of publication)
- Characteristics of the sample (number, gender, pathology investigated)
- Type and method of treatment carried out on the sample group
- Type and method of intervention carried out on the control group
- Types of outcomes assessed
- Evaluation scales adopted
- Short summary of the results obtained.
In the results, particular importance was given to data relating to the measurement of pain, quality of life and associated psychological symptoms.

Data Processing

The risk of *bias* was assessed through the "*Cochrane risk of bias assessment* tool" an assessment tool that allows a systematic collection of data related to 6 possible *biases*: randomisation and hiding the allocation (*selection bias*), staff and patient blindness (*performance bias*), blindness of the evaluators (*detection bias*), display of the results of all participants (*attrition bias*), display of all the results obtained (*reporting bias*) and other *biases*. For each domain, the risk of *bias* was judged low, high or unclear, if the available information was insufficient to provide an assessment.
The methodological quality was evaluated through the *Pedro scale*, a scale composed of 10 questions related to the internal validity of the processing: the higher the final score, the better the methodological quality. In fact, each *item* is assigned a score of 1 if the criterion is explicitly satisfied or 0 if the criterion is not met or if the data are not clear enough in this regard.

RESULTS

According to the recent guidelines for conducting a good systematic review (PRISMA statement) the flow chart should be displayed and commented on in the results, but if there is a question of fluidity and synthesis it could be included in the part concerning materials and methods.
The different phases of study selection have been reported in the flow chart (Fig. 1).
The research within the Pubmed, PEDro and Cochrane databases produced 771, 90 and 135 results respectively, for a total of 996 articles. The first *screening*, carried out by applying the filter by language and type of article, allowed us to identify 231 RCTs in English. The second *screening* was

TAB. 1 :Data extraction of articles related to "standard" physiotherapy. **CP/CPPS** = chronic prostatitis / chronic pelvic pain syndrom. **IC/PBS** =interstitial cystitis / chronic pelvic pain syndrome **CPP** = chronic pelvic pain. **BPS** =painful bladder syndrome. **PVK** = Vestibulodynia. **NIH – CPSI tot** = National Institutes of Health Chronic Prostatitis Symptom Index **VAS** = Visuo-analalogic Scale of pain; **BDI** = Beck Depression Inventory; **SAI – Y** = State Anxiety Inventory Y; **GRA**= Global Rate assessment; **ICSI** = Interstitial Cystitis Symptoms Index; **ICPI** = Interstitial Cystitis Problem Index; **ICSI** = Interstitial Cystitis Problem Index; **SF12** Short form 12; **FSFI** = Female Sexual Function Index; **FSQ** = Female sexual quotient; **PUF** = Pelvic Pain and Urinary Urgency Frequency Patient Symptom Scale; **NRS** = Numeric Rating Scale; **GUPI** = GenitoUrinary Pain Index; **SHIM** = Sexual Health inventory for men; **MPQ** = Mcgill pain questionnaire; **PCS** = Pain Catastrophizing scale; **CSQ** = Coping scale questionnaire.

Study	Population	Intervention	Control	Outcome	Evalutation scales	Results
Giubilei et al (2007)	N = 103 (52-51) Men CP/CPPS	Aerobic exercises (EA) (1h x 3/weeks x 18 weeks)	Stretching and general mobility exercises (1 h. 3/weeks x 18 weeks)	Pain Urological symptoms Quality of Life Psychological symptoms	NIH – CPSI tot NIH – CPSI subscore VAS SAY – Y BDI	76 subjects analyzed. In both groups, all parameters evaluated, except for urinary symptoms, improve significantly. Significant difference in pain and QoL improvement in EA group compared to control.
Haugstad et al (2008)	N = 40 (20 – 20) Women CPP	Gynecological therapies + Mensendieck Somatocognitive Therapy	Gynecological therapies (tips + drugs)	Pain, Motory functions Psychological symptoms	VAS Mensendieck performance test (posture, movement, walking, sitting position, breathing). GHQ30	37 subjects analyzed. Only in group 1 significantly improve pain and motor functions and psychological symptoms. These results are maintained at a distance of 9 months.
FitzGerald (2012)	N = 81 (39 – 42) Women IC/PBS	Myofascial treatment™ (1h/weeks x 10 tratt. In 12 weeks)	Global therapeutic massage (GTM) (10 x 1h, in 12 weeks)	Perceived improvement by the pt Pain Urological symptoms Sexual symptoms Quality of life	GRA Likert scale for pain, urgency and voiding frequency Voiding diary ICSI ICPI SF12 FSFI FSQ	Symptomatic improvement (GRA> 5) in 59% of patients with TM and in 26% with MTG (p = 0.0012). All the parameters evaluated in both groups improve, without statistically significant differences in the two groups
FitzGerald et al (2013)	N = 47 (23 – 24) Men(23), Women (24) CP/CPPS o IC/PBS	Myofascial treatment™ (1h/weeks x 10)	Global therapeutic massage (GTM) (1h/weeks x 10)	Perceived improvement by the pt Pain Urological symptoms Sexual symptoms Quality of life	Per IC/PBS: GRA Likert scale for pain, urgency and voiding frequency ICSI ICPI SF12 (physical and mental) FSFI CP/CPPS: GRA ICSI, ICPI NIH – CPSI tot NIH – CPSI subscore SHIM	Significant difference in the improvement of symptoms perceived by the patient (GRA> 5) between the two groups: 57% of the TM patients and 21% of the MTG patients. Pain improves significantly after treatment, quality of life does not.
Goldfinger et al (2016)	N = 20 (10 – 10) Women PVK	Various physiotherapy techniques (FT) (1.5h x 10)	Cognitive behavioral therapy (CBT) (1.5 h x 10)	Pain during sexual intercourse Physical symptoms Psychological symptoms Perceived improvement by the pt	NRS mean during sexual intercourse and in 5 different anatomical sites % of painful and non-painful sexual intercourse % of activities that cause vulvar pain MPQ (sensory and affective) FSFI – R PCS CSQ Self assessment scale of impovemente (1-6)	Miglioramento significativo del dolore e dei sintomi psicologici in entrambi i gruppi, mantenuti anche al follow up (6mesi). Miglioramenti significativi della funzione sessuale solo nei pz CPT. No differenze significative tra i gruppi.
Bond et al (2017)	N = 9 (5-4) Women BPS	Trattamento Miofasciale ™ (15 min/sett x 6) + PMFT a casa da soli (7/sett x 12) + Therapeutic Wand (3/sett x 12)	Trattamento miofasciale ™ (15 min/sett x 6 sett) + PFMT a casa da soli (7g/weeks x 12 weeks)	Pain Urological symptoms Quality of life	VAS ICSI NRS for pain on palpation ICPI PUF GUPI	Clinically significant improvements in both groups for all assessed outcomes. 6 weeks, in the sample group, clinically relevant difference in ICSI and ICPI compared to the control group.

carried out using the reading of the title and the abstract: 182 articles were discarded because they were judged to be irrelevant to the research objective. In particular, 87 did not concern chronic pelvic pain and 95 described non-physiotherapy treatments.

In the remaining 48 articles, there were 22 duplicates and in 3 articles the full-text was not available and they were excluded. The 26 remaining trials were read in their entirety. A further 13 articles were excluded while the remaining 10 were included in the systematic review.

Characteristics of the included studies

10 RCTs were included: Montenegro et al. 2015[8]; Fitzgerald et al. 2013[11], de Bernardes et al. 2010[12]; Fitzgerald et al. 2012[13]; Bond et al. 2017[14]; Giubilei et al. 2007[15]; Lamina et al. 2008[16]; Haugstad et al. 2008[17], Goldfinger et al. 2016[18];

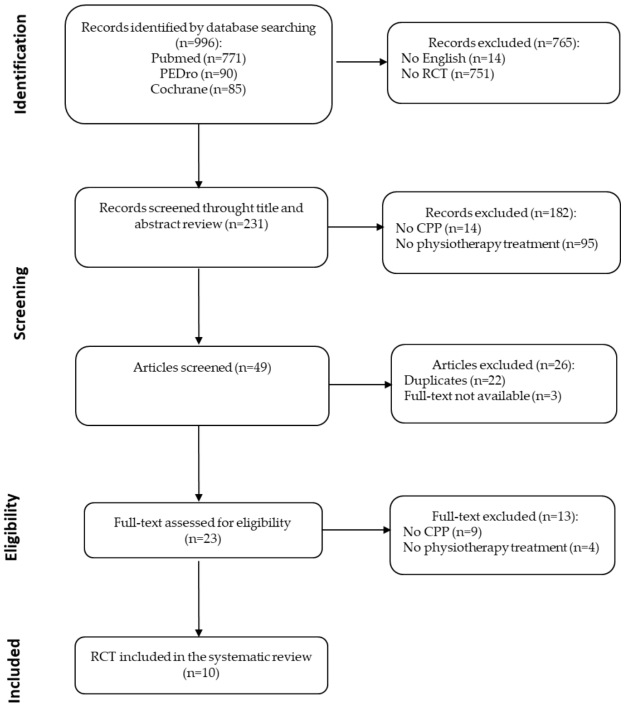


Fig. 1. Flow chart

Lamina et al. 2011[19].
Study design and setting: All included studies are RCTs, only one is a crossover. All were conducted in one clinic, except for two multi-centre studies (Fitzgerald 2013). The countries of origin of the trials are varied: two studies are set in the USA, two in Nigeria, two in Brazil while the remaining three studies were conducted respectively in Italy, Canada, Norway.
Patient characteristics: A total of 420 patients were included, 198 (47.1%) were part of the sample group and 222 (52.9%) in a control group. Only in one study relating to 40 subjects the sex of the patients is not specified. Of the remaining 360 participants, 150 (39.5%) are men and 230 (60.5%) women.
Types of interventions: All proposed interventions are individual and not in a group.
The therapy is exclusively physiotherapy in eight studies while the rest involve a combination with other types of interventions (drugs).
In eight studies the comparison was made between two groups, in the other two the comparison was made between three groups.
The proposed interventions can be classified into three large groups, including "standard" physiotherapy treatment (Tab. 1), the use of physical therapies (Tab. 2) and the combination of these two interventions (Tab. 3).
In the six articles in which the "standard" treatment was tested, the methods were as follows: myofascial treatment (2), myofascial treatment and pelvic floor exercises associated with the use of an intravaginal therapeutic rod (1), aerobic exercises (1), combination of various physiotherapy techniques (1), somatocognitive therapy (1).
The physical means considered were TENS (1), intravaginal electrical stimulation (1) and short-wave diathermy (1). Only one article included the effect of combining a manual therapy (manual ischemic compression) with a physical medium (TENS).
The types of interventions proposed for the control groups are also variable and include non-physiotherapy conservative therapies.
Other characteristics and their range of variability are indicated below:
- Frequency (daily → weekly)
- Duration of the single session (20 minutes → 90 minutes)
- Duration of the entire rehabilitation program (4 weeks → 18 weeks).
Only two studies show data relating to a follow-up evaluating therapy outcomes, respectively evaluated after six or nine months.

Data Processing
Method quality of the included studies
The method quality was analysed using the PEDro scale. On the scale from 0 to 10 the average score obtained was 5.7, in a range between 4 and 7.
As summarized in Table 3, all the articles satisfy the first and ninth criteria (in fact we are in the presence of RCT). The first criterion concerns randomization in determining which of the included subjects should be part of the experimental group and which of the control group; while the ninth concerns the statistical comparison between the two groups.
The tenth criterion, relating to the description of measures of both size and variability for at least one of the main objectives, is also unanimously satisfied. The second criterion concerns hiding the allocation of the subjects to the groups: only in two studies is it satisfied since the assignment to the experimental group or to the control group took place

TAB. 2: Data extraction of articles related to physical media. **CP / CPPS** = chronic prostatitis / chronic pelvic pain syndrome. **CPP** = chronic pelvic pain. **PID** = pelvic inflammatory pathology. **TENS** = trancutaneous electrical nerve stimulation; **SWD** = short wave diathermy; **NIH – CPSI** = National Institutes of Health Chronic Prostatitis Symptom Index **VAS** = Visuo-analalogic Scale of pain

Study	Population	Intervention	Control	Outcome	Evalutation scales	Results
Lamina et al (2008)	N = 24 (8 – 16) Men CP/CPPS	TENS + antibiotics (20 min. 5/weeks x 4 sett)	2 control groups: - analgesics + antibiotics - placebo + antibiotics	Pain	- NIH – CPSI(pain score only)	Significant improvement in pain in the TENS group compared to the other two groups. There is no significant difference between the two control groups
Bernades et al (2010)	N = 26 (13 – 13) Women CPP	Intravaginal electrical stimulation (10 x 30 min. 2/ weeks)	Placebo stimulation (10 x 30 min. 2/ weeks)	Pain	VAS (0-10)	Intravaginal electrical stimulation significantly improves pain
Lamina et al (2011)	N = 40 (13 – 27) chronic PID	SWD + antibiotics + analgesics placebo (SWD: 20 min x 15 treatment every other dayi)	2 control groups: SWD placebo + antibiotics + placebo analgesics SWD placebo + antibiotics + analgesics	Pain	VAS (0-10)	32 subjects analyzed. Pain in the sample group improves statistically compared to the other two groups.

TAB. 3: Data extractions of the articles related to the combination of "standard" physiotherapy and physical means. **CPP** = chronic pelvic pain. **BPS** = painful bladder syndrome. **PID** = pelvic inflammatory pathology. **PVK** = Vestibulodynia. **TENS** = trancutaneous electrical nerve stimulation; **SWD** = short wave diathermy; **NIH – CPSI tot** = National Institutes of Health Chronic Prostatitis Symptom Index **VAS** = Visuo-analalogic Scale of pain; **BDI** = Beck Depression Inventory; **SAI – Y** = State Anxiety Inventory Y; **GRA**= Global Rate assessment; **ICSI** = Interstitial Cystitis Symptoms Index; **ICPI** = Interstitial Cystitis Problem Index; **ICSI** = Interstitial Cystitis Problem Index; **SF12** Short form 12; **FSFI** = Female Sexual Function Index; **FSQ** = Female sexual quotient; **PUF** = Pelvic Pain and Urinary Urgency Frequency Patient Symptom Scale; **NRS** = Numeric Rating Scale; **GUPI** = GenitoUrinary Pain Index; **SHIM** = Sexual Health inventory for men; **MPQ** = Mcgill pain questionaire; **PCS** = Pain Catastrophizing scale; **CSQ** = Coping scale questionaire.

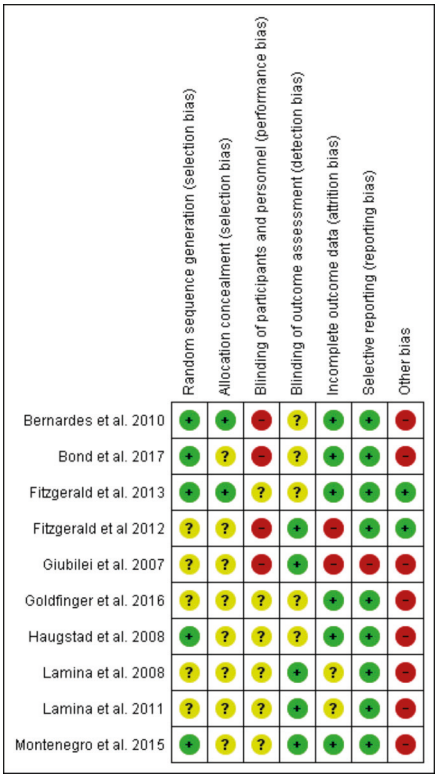
Study	Population	Intervention	Control	Outcome	Evalutation scales	Results
Montenegro et al (2015)	N = 30 (15 – 15) Women CPP + abdominal trigger point	Manual ischemic compression (CIM) after 30 min of TENS (1/sett x 4 weeks)	Anesthetic injections (IA): Lidocaine 2 mL 0.5% (1/weeks x 4 weeks)	Pain	VAS Algometer (kg / cm ^ 2) for threshold and pain tolerance in trigger points	Significant improvement (ΔVAS> 50%) in IA units, compared to the PCs treated with the CIM. Results maintained at follow up (2 months). No significant differences in the variations of Tolerance and threshold to pain but in group 1 they improved only in the short term, while in group 2 they progressively improve

through an opaque closed envelope; in the 8 remaining studies this feature is not specified, therefore it was not possible to assign the score.
The third item concerns the comparability between the two groups at time zero, i.e. before the start of treatment, as regards the main prognostic factors. This criterion is satisfied even if the comparison was made using a descriptive analysis that refutes clinically significant differences. In the case of chronic pelvic pain, the most important prognostic factors are the demographic and clinical characteristics: these factors were comparable in five trials. In four cases a quantitative analysis was made, in the other case the comparison was made in a descriptive manner. In the remaining four trials: two report the data without showing the statistical analysis, one does not report the statistical comparison of the patient age data (TENS) and another states that there are statistically significant differences in terms of pain intensity.
The fourth and fifth criteria concern the blindness of the participants and the therapist respectively. No RCT was conducted in double blind. Two studies report the blindness of the subject and one the blindness of the therapist.
The evaluator's blindness, confirmed by point six, is reported by five studies.
The seventh criterion was met by seven trials since these reported in the second follow-up data relating to more than 85% of the subjects initially randomized in the two groups.
The requirements of the eighth criterion were met by five studies: in one of these all subjects received treatment, in the remaining four the data related to excluded subjects were also included in the analysis.

Bias risk assessment

The bias risk assessment was conducted using the "*Cochrane collaboration's tools for assessing risk of bias*". The judgment on the risk of *bias* of each article and the reasons that led us to this choice are defined in the table above. The summary of the data obtained is presented graphically in and described below:
- *Selection bias* (generation of the randomization sequence and concealment of the allocation): In 5 studies neither the information on the modality with which the randomization was carried out nor that relating to hiding the allocation are specified, so that both the risks of *bias* are not clear. Three studies are at low risk of *bias* regarding the generation of the randomization sequence but the risk is not clear for the hiding of the allocation. Two studies are at low risk of *bias* for both criteria.
- *Performance bias*: The risk of *bias* cannot be determined in five trials. The five remaining studies were judged to be at high risk of *bias* due to lack of blindness of therapists, patients or both.
- *Detection bias*: five studies did not provide the data necessary to provide an opinion. So they were judged to be at risk of unclear *bias*. The other five trials specify how the evaluator is external to the trial and / or does not know the allocation of the patients, so the risk of *bias* was judged low.
- *Attrition bias*: Six trials were judged to have a low risk of *bias* because all the participants concluded the treatment and were analyzed, or in the case of patients lost at follow-up, the missing data were considered in the analysis. Three trials report a high percentage of patients lost at follow-up and do not carry out an analysis by (intention to treatment? – not sure what is meant here), therefore the risk of *bias* was considered high. One study does not report data on the number of patients who completed the trial, therefore it was judged to be at risk of unclear *bias*.
- *Reporting bias*: all the studies, except one, report data re-

Tab. 4.
Risk of bias summary.



lating to all the outcomes that were initially assessed. So in nine articles the risk of *bias* was judged low and in one high.
- Other *bias*: Eight articles were judged to be at high risk of *bias*

Of the eight articles at high risk of *bias*: one trial was interrupted early, in another study the interventions are partly overlapping, in the other five RCTs the main critical points are the lack of the sample size, the lack of analysis of the main factors of baseline risk or non-homogenous nature of these characteristics.
In the remaining two articles no other sources of *bias* were identified, therefore they were judged to be low risk.

Effectiveness of the intervention
Primary outcome: Pain
All studies evaluated the effect of treatment in terms of reduction of pain symptoms.
The rating scales used are different: the most commonly used was the VAS (Visual Analogue Scale), proposed alone in five studies and in one study in association with the NIH-CPSI part (National Institutes of Health Chronic Prostatitis Symptom Index) relating to pain, a validated questionnaire, specifically for chronic prostatitis / chronic pelvic pain syndrome. Four articles used other assessment tools: two the Likert pain scale, one the NRS (Numeric Rating Pain scale) and another one the domain of pain of the NIH - CPSI.
The results obtained in each study are shown below:
- A rehabilitation program consisting of aerobic exercises has proven to be more effective in reducing pain (both in terms of VAS and NIH-CPSI score) compared to a training programme involving stretching exercises and general mobility;
- Mensendieck's somatocognitive therapy in addition to a standard gynaecological treatment produced significant improvements in terms of VAS, while in the group subjected exclusively to standard gynaecological treatment these improvements were not significant. Data relating to the inter-group comparison are not reported;
- Two trials compared myofascial treatment with a global therapeutic massage, and evaluated both interventions using the Likert pain scale: in the first case there were no statistically significant differences between the two groups; this result was also confirmed by the second study but in this case significant improvements emerge after treatment only in group 1;
- In a trial where pain is assessed through the sensory domain of the McGill Pain Questionnaire (MPQ), the significant improvements were only reported in the group undergoing physiotherapy, but there were no statistically significant differences with respect to a psycho-therapeutic approach (cognitive behavioural therapy) ;
- There are no clinically relevant differences in terms of VAS and NRS from the addition of an intravaginal therapeutic wand to a rehabilitation protocol but both approaches resulted in clinically relevant changes in pain perception;
- The combination of TENS and manual ischemic compression of trigger points proved less effective than local anaesthetic injections.
- Transvaginal electrical stimulation significantly reduced the VAS, compared to placebo stimulation;
- In one study, the effectiveness of TENS in the reduction of VAS was evaluated by comparing 3 groups of patients who, in addition to antibiotic therapy, received TENS, analgesic drugs or placebo analgesic All groups improved significantly after treatment but posteriori analyses refuted differences between group 2 and group 3 and demonstrated the superiority of the TENS group when compared to other therapies.

A similar approach was used to evaluate the efficacy of short-wave diathermy (SWD): 3 groups of patients in addition to antibiotic therapy received the SWD and placebo analgesics, placebo SWD and placebo analgesics, placebo SWD and analgesics. Group 1 showed better results than other interventions.

Secondary outcome: Quality of life
Quality of life was evaluated in five studies through generic evaluation scales such as General Health Questionnaire 30 (GHQ-30) or specific evaluation scales, such as the NIH - CPSI (Chronic Prostatitis Symptom Index) quality of life subscore and the ICPI (Interstitial Cystitis Problem Index). Giubilei et al (2007) demonstrated the efficacy of a rehabilitation programme consisting of aerobic exercises: the NIH - CPSI quality of life subscore improves significantly, both within the group, before and after treatment, and when compared to a placebo programme of stretching exercises and general mobility. In the study conducted by Fitzgerald et al (2012), there were no statistically significant differences in ICPI in the comparison between myofascial treatment and global therapeutic massage. This same comparison was repeated in a sample of men and women in a 2013 study. In women the evaluation was conducted through the ICPI and the Short Form 12 (SF12); both indices statistically improve only in the group subjected to myofascial treatment but there are no inter-treatment differences. The results of the study conducted by Haugstad et al. (2008) comparing outcomes of a group subjected to standard gynecological treatment and a group in which somatocognitive physiotherapy treatment was also combined, showed no improvement in terms of GHQ30 in any of the participants of the two groups.
Bond et al (2017) verified that the addition of an intravaginal therapeutic wand to a myofascial rehabilitation programme provides clinically relevant improvements in terms of ICPI compared to myofascial treatment alone.

Secondary outcome: Psychological symptoms
Psychological symptoms were assessed in five studies. The first trial, using the BDI (Beck Depression Inventory (BDI) and the State Anxiety Inventory Y (SAI – Y), evaluates for depression and anxiety respectively: both aerobic exercises and stretching exercises and general mobility, statistically improved anxiety and depression scores but no differences emerge between the two groups. The study by Goldfinger et al[18] compared various physiotherapy interventions with cognitive-behavioural and psycho-therapeutic therapy. The participants in the two groups show significant improvements on the Pain Catastrophizing scale (PCS) and in the Coping Scale Questionnaire (CSQ), which they maintained at follow-up, but the univariate analysis of the variance shows no difference between the two interventions. Patients treated with standard gynaecological therapy, at nine months apart, did not significantly improve in the psychological domains of General Health questionnaire (GHQ-30) as opposed to patients who additionally received somatocognitive therapy; furthermore, the differences between the two groups were statistically different.
In two studies in which the same intervention were proposed (myofascial treatment vs global therapeutic massage), the effects on psychological symptoms were evaluated through the mental domain of the SF12. In the first case there were no statistically significant differences between the two groups. In the second case, neither of them resulted in significant improvements and no differences emerged between the two groups.

DISCUSSION

Summary of the evidence

In the guidelines of the main associations, the role of physiotherapy is of primary importance in the management of chronic pelvic pain, especially when the disorder is associated with the presence of musculoskeletal or myofascial changes.

To assess the scientific evidence supporting this approach, we included within this systematic review the RCTs that evaluated the efficacy of rehabilitative treatment in patients with chronic pelvic pain.

Of the 996 studies analyzed, only 10 (420 participants) met our inclusion criteria**.** The variety of treatments offered, the frequent association with other types of therapy, the differences in the method of administration (in terms of frequency, duration of the single session and of the entire treatment) and in the assessment scales, did not allow for a quantitative analysis.

To provide a realistic estimate of the effect of the treatment, before analysing the effectiveness of the various treatments proposed, the quality of the internal methodology was evaluated in the various articles and the presence of any systematic errors, labeled as *biases*. The tools that allowed us to evaluate these features were the PEDro scale and the Cochrane risk of bias assessment tool, respectively.

From these analyses, various critical issues emerged: information on the quality of methodology is often poor or unclear. The greatest ambiguity in relation to data emerged in the randomization (both in the nature of the randomization sequence and in the concealment of the allocation) and in the blindness of the subjects involved (patients, therapists and evaluators), therefore it was often not possible to clearly determine the relative *bias* (selective *bias*, performance *bias* and detection *bias*). Greater clarity has emerged in the data relating to the number of randomized subjects actually treated and to the number of outcomes assessed and actually reported: the risk of the respective *bias* (*attrition bias* and reporting *bias*) is low overall. In 8 studies other *biases* emerged due to the absence or non-homogenous nature of the *baseline* data and / or the absence of the sample size.

We carried out a qualitative summary of the estimation of the effects of rehabilitation treatment not only in terms of reduction of pain symptoms but also in terms of improvement of psychological symptoms and quality of life, given the frequent association of these with chronic pelvic pain disorders.

To make summarizing easier, it is possible to divide the investigated treatments in the 10 trials into 3 large groups:

- Six trials concern "standard" physiotherapy (which includes manual myofascial techniques, pelvic floor relaxation exercises, teaching of self-treatment strategies ...);
- Three trials related to rehabilitation based on the use of physical means (electrical stimulation, diathermy and TENS)
- One trial investigated the combination of these two approaches (TENS and manual ischemic compression).

All studies concerning standard physiotherapy proposed an estimate of the effect of rehabilitation on pain, as perceived by the patient. In all cases there was an improvement in pain symptoms and in 4 of the 6 studies analyzed, the improvement was statistically significant. Even in the controls, there was a more or less significant improvement in pain. From the comparison between groups, only one of the studies, that of Giubilei et al[15], showed significant superiority of physiotherapy treatment with regard to the other treatments with which it was compared.

Five of the six trials analysed also assessed psychological symptoms and quality of life; for these outcomes the improvement trend, although homogeneous, is not always statistically significant.

In studies related to physical media, the results highlight the superiority, in this case always statistically significant, of such intervention compared to placebo or non-treatment. However, in these studies, the effect of treatment on psychological symptoms and quality of life was not evaluated

In the only article concerning the combination of standard physiotherapy and physical means the outcomes were not taken into consideration. As regards pain, on the other hand, the comparison between the association of these techniques with medical therapy produced an unfavourable result for physiotherapy treatment.

Limits

This revision has some limitations: the search uses only 3 online databases, albeit significant (Pubmed, Cochrane and PEDro). Within these databases it was not possible to find the full-text of 3 articles considered particularly interesting based on reading the abstract. Another limit could be the search string used: due to the terminology used to define chronic pelvic pain and its subgroups, the search strings used may not have allowed the inclusion of relevant studies defined by terms such as "persist pain" or "chronic myalgia".

CONCLUSIONS

Clinical practice and existing guidelines attribute an important role to physiotherapist in the management of chronic pelvic pain. Studies published in current literature regarding the effectiveness of rehabilitation treatment are scarce (10 RCTs) and present with a range of critical methodological issues, the chief of which is the methodological importance of blinding of therapists and patients.

In terms of efficacy, with regard to pain, the RCTs in which the rehabilitation intervention is compared with the placebo provided the most evidence. When physiotherapy treatment is compared with other conservative interventions, while improvements emerge within each of the groups considered, there are no significant differences between the approaches, suggesting that the supremacy of one intervention cannot be asserted over the other.

From the available data it is not yet possible to estimate the effect of treatment on psychological symptoms and quality of life

In light of what has been observed, it is difficult to hypothesise how to reorganize the therapeutic approach from a purely physiotherapy point of view to chronic pelvic pain.

Current innovations in the classification and distribution of chronic pelvic pain syndromes allow the drafting of more specifically sectoral algorithms. The diagnostic-therapeutic algorithms may in the near future, have a specific path based on the sector (section?) of the pelvis "involved" and make not only the diagnostic framework easier but also the therapeutic effect better. There is no doubt that an early diagnosis, and its correctness, are essential prerequisites for therapeutic success, even if it may not always be global, improves the patient's quality of life while preserving organ function, whenever possible. This result is utopian if the patient is not framed within a path (pain team) in which the multidisciplinary aspect allows each of the players (medical specialists, nurses, midwives, rehabilitation therapists) to have a precise role at the right moment in the treatment and, above all, enable follow-up. There is no doubt that scientific progress in each of the medical disciplines, can contribute to defining the clinical picture, help delineate the etiology of chronic pelvic pain, and ensure improvements from a physiotherapy point of view. For this reason further investigations are desirable. This analysis has shown how difficult it

is to determine the most adequate tools for measuring symptoms and, above all, to evaluate the effectiveness of therapies. The possibility of having clear parameters that allow us to predict the results of a proposed therapeutic approach still appears a long way off. Research in this area still needs to make a greater effort, just as a better understanding of the patho-physiological mechanisms is necessary in order to be able to combine, where possible, drug therapy with the immense rehabilitative effort.

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CORRIGENDUM

In the article "On collagen, ageing and surgical treatment options following commercial kit withdrawals- a critical analysis", Authors B. ABENDSTEIN, D. SHKARUPA, P. PETROS, Pelviperineology 2019; 38:58-60, the correct caption of Figure 3 is: Scarring "tethers" LP and LMA to overcome oppositely acting PCM vector during straining (arrows): indicates the imperative of an elastic zone at ZCE so as to allow the vector closure forces to operate independently.

Original article

High definition T2-weighted MR imaging of the female uro- genital supporting system using an external coil

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Abstract: Aim To provide evidence of the imaging features of such anatomic structures. *Materials and Methods* The imaging series of sixty-eight consecutive nulliparous females (mean age 51.5 ±4.2 yrs, range 18-72 yrs) who underwent pelvic MR examination between April 2017 and June 2019, were reviewed. With no history of lower urinay tract symptoms (LUTs), evacuation dysfunctions or pelvic organ prolapse, clues for the examination included: known or suspected pudendal nerve neuropathy and ano-perianal sepsis. Patients with prior surgery for prolapse repair, partial or total hysterectomy and pelvic reconstruction for neonatal congenital anomalies were excluded. MR images were analyzed for evidence and imaging features of ligaments connecting the urethra, uterus and vagina to the internal boundaries of levator ani hiatus and pelvic side walls. The optimal scan plane for their identification and the frequency with which the various ligaments could be recognized as a distinctive anatomic structure were calculated. *Results* The axial MR images proved most informative (diagnostic yield as high as 89%); however, tilting the scan plane obliquely, perpendicular to the long axis of the anal canal improved the visibility of some structures in over half the cases. Three groups of ligaments supporting the female urethra were recognized, as follows: the periurethral ligaments (87%), running ventrally to the urethra; the paraurethral ligaments (60%), originating at the two and ten o'clock position of the urethra's outer border, respectively; and the pubourethral ligament (57%), hammock-like structure in close contact with the posterior aspect of the urethra. On the same plane, the vagina appeared as a three-layer structure showing different morphology in the upper (horizontal line), middle (H-shaped) and lower third (U-shaped) with faint, low intensity signal lateral attachments seen only occasionally (< 20 %) inside the paracolpium. The parametrium was seen in different proportions as low signal intensity condensations, showing linear (uterosacral and round ligaments, 68% and 96%, respectively), reticular (cardinal ligaments, 81%), or wide fold feature (broad ligaments, 35%), connecting the sides of the uterus to the walls and floor of the pelvis. Finally, the perineal body was better visualized on sagittal than on axial images (only 22%) as a hypointense pyramidal structure between the posterior labial commissure and the anal verge.
Conclusions MRI allows precise characterization of most relevant female urogenital supporting structures. In case of pathology, it can be used to guide surgeons and researchers to develop new focal-defect repair techniques.

Keywords: Magnetic resonance imaging; Female pelvis; Urethral support system; Parametrium and paracolpium; Endopelvic ligaments

INTRODUCTION

Clinical evaluation of women presenting with voiding dysfunctions, urogenital prolapse and sexual complaints is often difficult and imaging techniques are more and more frequently involved to obtain objective data on the status of pelvic anatomy and relationship among various structures. During the last two decades, the prevailing interest of clinicians and researchers has been focused on the assessment of the visceral fascia which covers the pelvic organs and provides their attachment to the side walls. Despite the plethora of references in the literature, however, there is still little objective information on that sheet of fascia that extends longitudinally and lines the walls of the pelvis giving origin to a number of linear condensations of connective tissue called ligaments. In particular the supporting system of the female pelvis, a term used to describe a composed of collagenous, elastic fibers and smooth muscle cells that provides stability to the bladder neck, urethra, vaginal canal and uterus, is still in search of final definition. Magnetic resonance imaging (MRI), the most powerful diagnostic tool available today, is particularly suited to the scope and we hereby report the results of our current experience with the study of female pelvic anatomy which, hopefully, will contribute to improve the knowledge of this relevant structure.

MATERIALS AND METHODS

Patient population

Between April 2017 and June 2019, sixty-eight consecutive nulliparous females (mean age 51.5 ±4.2 yrs, range 18-72 yrs) with no symptoms of voiding or evacuation dysfunctions, pelvic organ prolapse nor fecal incontinence, were enrolled into the study. Clues for MRI examination included chronic pelvic pain from known or suspected pudendal neuropathy and ano-perianal sepsis. Patients with prior surgery for prolapse repair, partial or total hysterectomy and pelvic reconstruction for neonatal congenital anomalies were excluded.

Imaging protocol

All MR imaging studies (NL, TF, JA, FP) were performed on a 1.5 T scanner (Siemens; Aera model, phased array external coil, Germany). For the examination, with no need for prior rectal cleansing nor intravenous contrast administration, patients are asked to void just before imaging, so as to have their bladder empty; then, they are placed in the supine position on the diagnostic table. For the assessment of perianal sepsis and fistulas, a modified 3 mm wide rubber catheter is positioned intra-anally to act as marker and subsequent acquisition of pelvic images in the true midcoronal and midaxial (oblique) planes taken parallel and perpendicular, respectively, to the long anal axis. In case of suspected pudendal nerve neuropathy, a cardiac gating, peripheral optic device called PPU (peripheral pulse unit) is employed which is applied at the extremity of the 2nd finger of right hand so as to obtain images directly or indirectly involved in the phenomenon of blood pulsatility.

Imaging technique

At the beginning, a localizer scout scan is performed in the three planes (HASTE pulse sequence, TR/TE 3.83/1.92 ms, FA° 54-70, slice thickness 6-7 mm, FOV 400 mm, two averages, matrix 256 x 156, total images 14-20) to mark the boundaries of the region of interest (ROI). The field of view extends from the anal verge (bottom level) to the upper margin of the iliac crest (upper level) and from the sacrococcygeal bone (backward) to the anterior margin of the pubic bone (forward) so as to include all relevant anatomy.Then, the pelvic anatomy is depicted in the midsagittal plane, using the turbo spin-echo (TSE) T2-weighted pulse sequence (TR/TE 3880/91 msec, FA° 150, slice thickness 4 mm, FOV 260, one average, matrix 384 x 384, FOV, 350 mm; scan time 4.33 min; total images 36). Thereafter, taking the

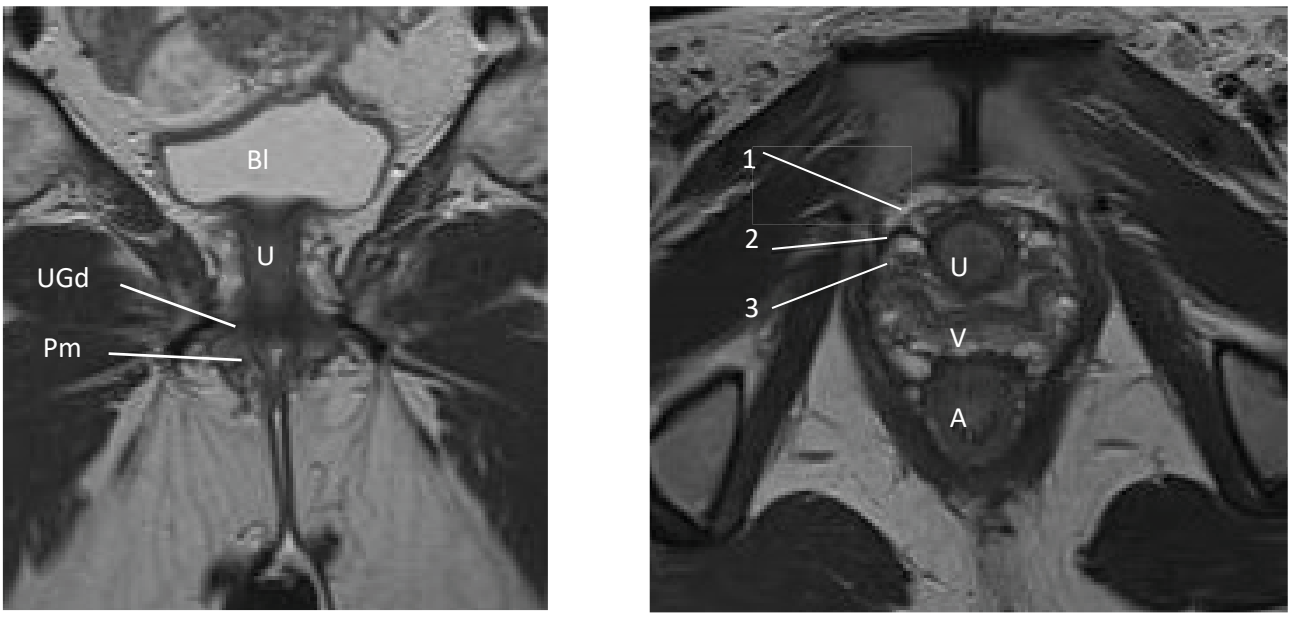

Figure 1 MR anatomy of female lower urinary tract and supporting structures.
(a) Coronal T 2-weighted image taken at the level of bladder neck and urethra showing the horizontal, 4 mm-thick, low signal intensity stripe of the **urogenital diaphragm** (UGd) and the triangular- shaped **perineal membrane** (Pm).
(b) Axial T 2- weighted MR image showing the **periurethral ligament** (1) coursing ventrally to the urethra, the **paraurethral ligament** (2) arising at the 10 o' clock position from the outer border of the urethra, and (3) the horizontal **pubourethral ligament**. Bl= bladder; U= urethra; UGd= urogenital diaphragm; Pm= perineal membrane; V= vaginal canal; A= anal canal.

intra-anal marker as reference, the sequence is repeated with use of the same parameters in the true midcoronal and midaxial (oblique) planes taken parallel and perpendicular to the long axis of the anal canal, respectively. At this point, the short tau inversion recovery (STIR) pulse sequence (TR/TE 2800/29 msec; TI, 150 msec; FA° 150°; slice thickness 3 mm, FOV 380, one average, matrix 245x 320, scan time 2.48 min, total images 40) is employed in patients referred for fistula-in-ano disease, while the TSE T2-W double inversion recovery (IR), fat sat (FS) dark blood (DB) pulse sequence is used in those with suspected pudendal neuropathy. Finally, regardless of the clue, a straight axial TSE T2 weighted series is also obtained in all patients.

Figure 2 Coronal T 2-weighted MR image taken at the level of symphysis pubis. Note the thin linear, low signal intensity structure of the **round ligament** coursing vertically in oblique manner through the labia major. RAm= rectum abdominis muscle; Sp= symphysis pubis; Lm= labia major; R lg = round ligament.

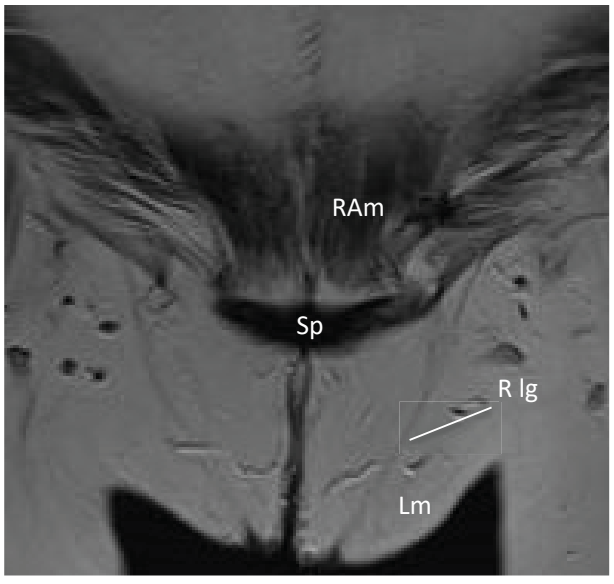

Image analysis

All examinations are taken to a viewing station and systematically reviewed (V.P.) and analyzed with regard to the urethral and genital ligaments according to the basic criteria described by Kim JK et al[1], and Tunn R. et al.[2] , as reported in a previous report[3]. In addition, the method of Chou Q. et al.[4] was employed to systematically analyze the location and identity of various supporting structure for proper differentiation of anatomic variations from abnormalities. In particular, the criteria for assignment of integrity of ligaments included the following: (a) tightness along the entire length; (b) no discontinuity or fluttering; (c) visibility at the expected site. Quantification of the levator ani hiatus anterior/posterior and transverse diameters (mm) and area (cm^2) is beyond the scope of the present paper. Readers interested in the issue are referred to a recent article by us[5].

RESULTS

The axial MR images were the most informative (see Table 1). On the other hand, a combination of coronal, axial and sagittal scans were found necessary for proper depiction of the lower urinary tract anatomy and support system (Figure 1). With regard to the genital organs, the **round ligaments** were the most frequently recognizable structures (up to 96% of cases) originating at the uterine horns as low signal intensity structures in the parametrium, exiting the pelvis via the deep inguinal ring, then passing through the inguinal canal and terminating on to the labia majora (Figure 2). At the other end of the spectrum, the **pubocervical ligaments, i.e.** collagen containing structures connecting the side of the cervix to the pubic symphysis, were seen only rarely as distinct structures on MR images. The **broad ligaments,** resulting from the double layer of peritoneum that, after covering the uterus anteriorly and posteriorly, comes in direct contact with itself on the sides, appeared in only 35% of cases as wide folds of peritoneum that connects the sides

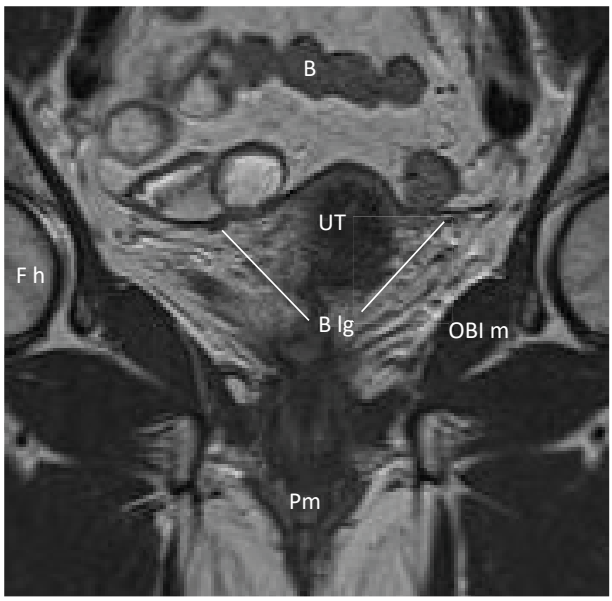

Figure 3 Coronal T 2- weighted MR image obtained at the level of femoral heads: after covering the uterus, the double layers of peritoneum come into contact one to another on the sides to produce the 3-mm thick linear appearance of the **broad ligament**. Note the wing-like feature of the ligament connecting the uterus to the pelvic side walls. B= bowel; UT= uterus; OBI m = obturator internus muscle; Pm= perineal membrane; B lg= broad ligament; Fh= femoral head.

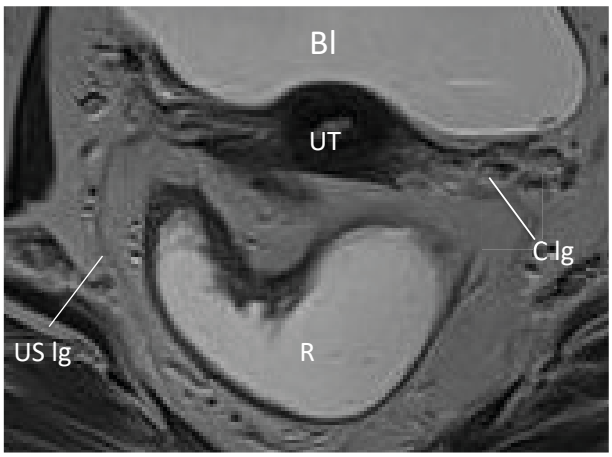

Figure 4 Axial T 2_ weighted MR image showing the reticulo-troncular feature of the **cardinal ligament** as opposed to the thin, curvilinear appearance of the **uterosacral ligament** travelling toward the anterior aspect of sacral bone. Bl= bladder; UT= uterus; R= rectum; US lg= uterosacral ligament.

of the uterus to the walls and floor of the pelvis (Figure 3). Conversely, the **cardinal ligaments** (or **Mackenrodt's ligament**,) were seen in 81-85% of cases as reticular or troncular shaped structures containing fibrous tissue and blood vessels, located at the base of the broad ligament which attach the cervix to the lateral pelvic wall by means of the fascia of the obturator internus muscle. The **uterosacral ligaments** (or **recto-uterine ligaments**) were identified (68% of cases) as linear, low signal intensity structures containing considerable amount of fibrous tissue and non-striped muscular fibers which travel from the upper part of the cervix to the anterior aspect of the sacrum (Figure 4).

As described in details in a previous report [3] the vaginal canal appeared as a three-layer structure showing high signal intensity in the center (mucous or secretion), and two, 3-mm thick layers of low-to-intermediate signal layers on both sides (walls). On axial MR images, its morphology was consistently seen as a linear, horizontally oriented structure in the upper third, H-shaped in the middle and U-shaped in the lower third.

Also, three categories of urethra's support system, were observed , as follows: the periurethral and paraurethral ligaments (83%) at the level of the proximal third of the urethral length, as a curvilinear hypointense structure coursing ventrally and as a triangular-shaped structure originating at 2-and 10- o' clock position from the outer margin of the urethra, respectively; and the pubourethral ligament (58%) seen at the half of urethra length as a hammock-like structure in close contact with its posterior margin (Figure 1b). Finally, other relevant structures belonging to the support system which were consistently depicted included the sacrospinous ligaments, the sacrotuberous ligaments, the perineal body and the perineal membrane (Table 1).

Table 1 Visibility of urogenital support system at MRI by scan plane (n=68)

Compartment	Scan plane			
	Axial		Coronal	Sagittal
	Straight	Oblique		
Anterior				
Arcuate lg	68 (100%)	68 (100%)	68 (100%)	-
Periurethral lg	59 (87%)	57 (84%)	8 (12%)	-
Paraurethral lg	41 (60%)	47 (69%)	-	-
Pubourethral lg	39 (57%)	44 (65%)	2 (3%)	-
Perineal membrane	-	-	68 (100%)	-
Middle				
Round lg	46 (68%)	43 (63%)	65 (96%)	-
Broad lg	-	-	24 (35%)	-
Cardinal	55 (81%)	58 (85%)	4 (6%)	-
Uterosacral	46 (68%)	47 (69%)	-	-
Pubocervical	-	-	-	-
Perineal body	-	15 (22%)	-	66 (97%)
Posterior				
Sacrospinous	68 (100%)	68 (100%)	51 (75%)	-
Sacrotuberous	68 (100%)	68 (100%)	61 (90%)	68 (100%)

Note: Numbers in parenthesis are percentages; lg: ligament

DISCUSSION

Thanks to its superior contrast tissue resolution and panoramicity, magnetic resonance imaging (MRI) is unanimously considered today as unsurpassed modality in the diagnosis of pelvic pathology. More specifically, the advantage of MRI over ultrasonography, its current major competitor, relies on the ability to display in exquisite details all the components of pelvic anatomy, including fat tissue recesses, the connective network, fascial attachments and condensations, i.e., ligaments. Undoubtedly, the adoption of rigorous imaging protocols and multiplanarity, combined with the well known multiparametric capabilities and lesser operator dependence, make the MRI modality unique for depiction of the endopelvic fascia, which is considered by researchers the key factor for characterization of both, organic and functional pathology.

This was largely confirmed by the present study which highlighted how frequently (see Table 1) the various supporting structures of female lower urinary tract and genital organs could be recognized at best using a conventional scan system and coil with no need for additional costs or expensive devices. Contrary to what could have been expected, however, not every existing structures of the supporting system found a match with a distinctive MR feature — as it occurred with the pu-

bocervical ligaments, for example — , despite their recognized relevance and well known anatomic location. Similarly, not all the anatomic structures visualized on MR images could necessarily be considered clinically relevant. Besides all the above, two issues deserve special consideration and should be brought to the attention of the reader, as follows: first of all, the efficacy of tilting the scan plane in obtaining better visualization of some anatomic structures, such as the pubourethral ligaments, should be emphasized. Secondly, and most important, the overt difficulty encountered by the examiner when establishing the threshold beyond which an unusual appearing morphology of a structure should be considered as an anatomic variation rather a clear abnormality, cannot be overlooked.
At present, the only way to assign the judgement of presence or absence of any abnormality relies on the frequency with which a single structure is visualized in a given location with a given shape. Obviously, better certainty can only be expected from further studies on larger series including nulliparous and parous subjects[6], as well as investigation comparing MR features with anatomic samples. Hopefully, the information yielded by the present study will stimulate researchers to develop new surgical procedures for focal defect-repair techniques.

CONCLUSIONS

The integrity of the urethral support system and that of female genital organs can be assessed noninvasively in living individuals using conventional 1.5 T MR scanner and external coil with no need for contrast administration. Although important individual variation can be encountered, recognizing the same structure with the same shape in the same anatomic site remains the basis for the diagnosis of normal vs. abnormal condition in singular cases. The technique described in this article seems ideally suited to be adopted in a standardized fashion in the clinical practice. Perspectively, its routine use after vaginal delivery may be suggested so as to distinguish those women requiring simple pelvic floor rehabilitation from surgical repair.

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Disclosures statements
There was no conflict of interest, informed patient consent was obtained, and the study was approved by the local ethical committee. The authors of the publication did not receive any financial support by any grant/research sponsor.

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Multidisciplinary UroGyneProcto Editorial Comment

To improve the integration among the three segments of the pelvic floor, some of the articles published in *Pelviperineology* are commented on by **Urologists, Gynecologists, Proctologists/Colo Rectal Surgeons or other Specialists**, with their critical opinion and a teaching purpose. Differences, similarities and possible relationships between the data presented and what is known in the three fields of competence are stressed, or the absence of any analogy is indicated. The discussion is not a peer review, it concerns concepts, ideas, theories, not the methodology of the presentation.

Anatomist... The breakthrough in the imaging of female uro-genital supporting system

The role of the imaging in the modern medicine is crucial to provide evidence of the features of such anatomic structures. Clinical evaluation of women presenting with voiding dysfunctions, urogenital prolapse and sexual complaints is often difficult and imaging techniques are more and more frequently involved to obtain objective data on the status of pelvic anatomy and relationship among various structures. There are a lots of papers in the literature about the female urogenital supporting system, but few objective information on that sheet of fascia that extends longitudinally and lines the walls of the pelvis giving origin to a number of linear condensations of connective tissue called ligaments. De Caro et al in 1998 (Morphometric analysis of the fibroadipose tissue of the female pelvis. J Urol 1998; 160: 707-13) concluded after a morphometric analysis of the fibroadipose tissue of the female pelvis that it has the function to sustain the pelvic viscera and it is based on the descriptions of connective condensations forming visceral fascia (rectal, cervicovaginal and vesical fascia) and ligaments. The possibility to see these structures with MRI it would become very important in the planning of surgery at the pelvis, helping the surgeons in the correct surgical identification of the anatomic structures and in monitoring the healing processes in the post-surgery and in the follow-up. Therefore, it is revolutionary relearn our anatomy and to be able to see with the unsurpassed MRI in the diagnosis of pelvic pathology.

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Uro-gynecol... This is a brilliant paper. The MRI figures provide some excellent insights into the ligamentous attachments of the organs to the skeleton. I have no criticisms of this paper. I would point out, though, that the cardinal ligament has an important reflection onto the anterior cervical ring which is not mentioned. This is evident just below the broad ligament in fig 3.

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Gyn... The Integral Theory says that there are 9 pelvic connective structures (pubourethral ligaments\PUL, external urethral ligaments\EUL, suburethral hammock, pubocervical fascia PCF, arcus tendineous fascia pelvica\ ATFP, cervical ring, uterosacral ligaments\USL, rectovaginal fascia\RVF, perineal body\PB) whose damage is responsible for symptoms (pain, nocturia, urgency, etc.) and signs (prolapses and incontinence) that characterize the functional diseases of the pelvic floor. The impairment of these anatomical sites would be responsible for syndromic pictures even in the absence of important degrees of genital prolapse. In fact, in the etiopathogenesis of fecal incontinence, also the ligaments of the anterior compartment appear to be involved (EUL, hammock, PUL), while symptoms such as pelvic pain and nocturia involve structures of the posterior compartment (USL, RVF, PB). Piloni's proposal is quite interesting as the anatomical evaluation obtained by MRI would allow to correlate the symptomatology referred to an objective description of the site of impairment of ligaments and fasciae. The re-evaluation with post-operative imaging, in the same patients, with an adequately long follow-up, and in a sufficiently large number of cases, would allow to verify, in vivo, the tissue reactions "caused" by the inserted polypropylene tapes (TFS) responsible for the creation of neo-ligaments and the possible improvement of the symptomatology.

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Proctol... According to the Integral Theory (IT) the intriguing relationships between the three pelvic compartments allow the treatment of fecal incontinence with the creation of neoligaments in the anterior pelvis (B.Abenstein. Pelviperineology 2008; 27: 114). With slings surgery, IT has achieved global success in SUI. Although there are significant clinical reports from pelvic reconstructive surgery centers in Germany, Austria, Japan, widespread skepticism surrounds IT interpretations about the physiopathology of conditions such as some forms of constipation and anal incontinence and the treatments offered with TFS. It is vital that in order to overcome such resistance and consequently provide for a therapy that at present has very poor alternatives, to document the damage of the different ligaments and the possible improvement after the appropriate surgical therapy. The work of Piloni corresponds to this need, i.e. to demonstrate the ligamentous structures by means of pelvic MR and provides us with a sort of atlas of normal anatomy in which the MR must clearly show the five main structures: pubo-urethral, uterosacral, cardinal ligaments, arcus tendineous, perineal body.

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Review and medical hypothesis

The constipation illness

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Abstract: Constipation is commonly described as a variety of symptoms including infrequent bowel movements and/or rectal evacuation disorders. Hard stools, excessive straining, bloating and abdominal pain are frequently associated. The several clinical pictures resulting by their combination are mostly due to a primary disturbance of colonic propulsion and/or obstructed rectal emptying, but the chronicity of these initially functional disturbances induce structural changes in the recto-colonic tract (such as dilatation, dolicocolon, rectal prolapse, rectocele, hemorrhoids): constipation turns so in a condition of illness where primary and secondary disorders, functional and organic alterations are not no more clearly detachable and therapeutic priorities are a real challenge for primary care physicians and specialists. The recent knowledges indicate a pivotal role for the gut microbiota in the pathophysiology of colonic dysfunction underlying constipation, contributing to make it is a real "systemic" illness, and not a disorder of an organ, given that the impressive consequences which intestinal dysbiosis has on the Enteric, Autonomic and Central Nervous Systems.

Keywords: Chronic constipation; Intestinal microbiota; Colonic motility; Fecal microbiota transplantation

DEFINITION AND CLINICAL PICTURE

Constipation is traditionally defined as a symptom, not a disease, but today it is preferred to define it as a condition of suffering, an illness, a set of symptoms and clinical signs, which the patient can arrive in several ways to[1,2]. These ways are very different between themselves, but all of them converge towards a precise Syndrome defined by two clinical pictures. The first is characterized by a rarity and a reduced perception of the evacuative stimulus, followed by an easy defecation, after all satisfactory, even if frequently with the expulsion of small and hard stools. Apart from the long interval between two defecations, however spontaneous and normal, there are no other disorders, which clearly distinguishes this form of constipation from the symptomatic disorders that are typical of Irritable Bowel Syndrome (IBS): abdominal pain, swelling and abdominal distension, loss of appetite, difficult digestion and discomfort[3,4].

The second "scenario" of constipation is instead characterized by a remarkable association of symptoms: first of all a difficult expulsion, with the perception of an obstacle to the discharge of stools, for which an intense "strain" and need to exercise an excessive abdominal pressure are required. Moreover, sometimes manual maneuvers for supporting stool expulsion are necessary, often with a residual sensation of not having completed bowel emptying. Although this is even more true if stools are scarce and hard, this picture may be present even if the fecal consistency is regular or even fluid. The two clinical pictures often succeed one another, usually the latter is added over time to the first, or they add up and alternate in the short term, creating the most diverse and complicated situations, also in relation to therapeutic attempts (laxatives, drugs, supplements, diets, etc.) which are carried out by patients[5].

These altered defecation dynamics, the first identified as *Slow Transit Constipation* (STC), the second as *Disordered Defecation* (DD), are then associated with all those conditions that define IBS, above mentioned, in a way that a certain clinical and consequently pathophysiological distinction between the two pathological syndromes, constipation and IBS, is neither possible nor useful for therapeutic purposes. Further symptoms and signs may be associated, such as evidence of abnormal shape and stool (thin, "blocky", fragmented, smelly), perineal pain, evidence of rectal prolapse or bleeding during and/or after defecation. It should also be considered that these two forms of constipation are further complicated by wrong patient behaviors rather than intestinal dysfunctions: people who think that defecation should be forced after lack of perception of the urge to evacuate for 48, 36, or even only 24 hours, use a whole series of measures to induce it (laxatives ingestion; positioning on the toilet trying to expel feces; introduction of suppositories or enemas), thus upsetting what would otherwise have been a regular interval between a spontaneous defecation and the next one. Other people would like to confine defecation at certain times of the day, when toilet is available at home, so that it does not happen during office hours, or for similar reasons: they position themselves on the toilet without having perceived any "need to evacuation" feeling, and "try" to defecate. In the very likely event of a failure or a shortage of intestinal emptying, they seek for treatment because they consider themselves suffering from constipation. This behavior is very often adopted to try to reduce bloating, meteorism or abdominal distension. It is clear that these behaviors, alone or superimposed on a real existing STC or DD, create such complex clinical pictures that their analysis requires an anamnestic investigation, mostly incompatible with the normal times of a medical examination, even in a specialized context. However, the lack of understanding of all the dynamics underlying the condition of constipation reported to the doctor, almost invariably affects the effectiveness of any treatment, even a surgical one, that is prescribed.

ETIOLOGY

As far as the etiopathogenesis of constipation is concerned, it is advisable to immediately clear the field of those situations where evacuation disorders are secondary to an intestinal disease whose onset may occur also, or only, with these conditions: tumors, complications of Diverticular Disease, inflammatory colitis, Celiac Disease and other pathological entities. The suspicion that bowel disturbances are a consequence of these pathologies may easily arise because, in addition to constipation, other symptoms and clinical signs, defined as "alarm features" are present, such as anemization, weight loss, stool blood in absence of anal pathologies, asthenia, fever, and alterations in laboratory test. "Acute" constipation, which suddenly appears in individuals with earlier regular and satisfactory evacuation habits, should be managed as potentially secondary to the above causes and therefore an appropriate diagnostic investigation should be performed[6]. Even when constipation is chronic, it may be secondary to other pathologies, first of all to drug consumption. The intake of opioids, calcium antagonists, adrenergic agonists, dopaminergics, tricyclic antidepressants, neuroleptics and chemotherapeutic agents is often burdened by the progressive appearance of defecation disorders. Moreover, metabolic and hormonal disorders (hypercalciemia,

hypopotassiemia, etc.) can cause constipation.
The role of neurological pathologies is also very important: severe constipation can easily be classified as a consequence of a spinal or brain injury, due to trauma, hemorrhage, inflammation, and more[7]. On the contrary, other neurological diseases can be the basis of constipation in a decidedly more subtle way: it is not so rare to find of a pathology such as Spina Bifida occulta, tethered cord syndrome and, more generally, pathologies of the cauda equina and sacral region (e.g. Currarino syndrome) after years and years during which the patient, as a rule in the pediatric age, but, from personal experience, even in adult age, reported a constipation which was particularly severe and refractory to any treatment[8,9].
The appearance of constipation in young women can be for many years the first and only disorder of Multiple Sclerosis, a disease that is then recognized when the typical neurological symptoms appear or are associated with disorders of a "neurogenic bladder": retention and/or urinary incontinence[10]. Even the great neurodegenerative diseases such as Parkinson's or Alzheimer's are almost invariably characterized by constipation, both with aspects of STC and DD[11,12].
It should not be forgotten that diseases of the nerve ganglia of the intestinal wall, such as the congenital Hirschsprung's disease and the Idiopathic Intestinal Pseudo-obstruction (which instead arises later in life), may cause defecation disorders which are sometimes really difficult to identify.
However, all forms due to a clearly identifiable etiology represent a minority of all constipation pictures: in order to have exact percentages, a distinction by age, sex and comorbidity should be performed, which goes beyond the objectives of this article. Anyway, there is consensus that in most cases constipation does not have a known cause, therefore it is classified as primitive or, better, as Functional Constipation, where "functional" means that an intestinal dysfunction is present and, at least at the current state of knowledge, it cannot be related to a verifiable anatomic-pathological picture, or to "markers" of morphological or biochemical alterations affecting the digestive tract or other organs[3]. However, there are precise observations that even in these forms it is possible to find anomalies, either structural that concern the cellular composition of the Enteric Nervous System (ENS), or neuro-humoral such as alterations of neuromediators and substances that influence the regulation of the motility of the colorectal colon: the problem is, however, that anomalies are never present in all forms of functional constipation, so that, on the one hand, the number of those with unknown etiopathogenesis is narrowed, and, on the other hand, it is possible to state that constipation is a Syndrome, almost never a Disease, but certainly an Illness.

PATHOPHYSIOLOGY

Constipation is always a consequence of a dysfunction of the colon and rectum, given the transit time in the stomach and small intestine is measured in hours, compared to that in the large intestine in days. In a nutshell, we can identify two mechanisms that characterize the dysfunction of the colon at the basis of constipation: on the one hand a deficit, an inefficient propulsive motility of the colon that provides mixing and transport of endoluminal contents (gas and fecal material) and ensures the cyclic filling of the rectum - let's call it *colonic dysmotility*; on the other hand, an alteration of the complex sensory-motor dynamics that presides over the complete emptying of rectum, sigmoid and descending colon, which we call *obstructed defecation*. The Central Nervous System (CNS) acts in the modulation of both mechanisms. Colonic dysmotility involves the *Autonomic* Nervous System (*ANS*), the Enteric Nervous System (ENS) and the smooth muscle of the colon, while the efficiency of evacuation is guaranteed by the peripheral somatic innervation of the striated diaphragm musculature, the abdominal wall, the pelvic floor including its myo-fascial structure and the anal sphincters.
Colonic Dysmotility is characterized by the reduction/absence of peristaltic contractions with propulsive effect of the colon: recent studies have found alterations of the complex regulation mechanisms of the ENS, a real "second brain" that is located in the intestinal wall and whose complexity, for the number of neurons and integrations between them, is comparable to the brain[13]. Technical and ethical difficulties prevent us from conducting studies on healthy and sick people to understand the relationships between the anomalies identified in ENS functioning, and the behavior of contractility of the bowel muscles seen in patients with constipation, but there is no doubt that the abnormal transport of the endoluminal content through the colon, which is often long and twisted, plays a causal role in many constipations[14-17].
Only recently, thanks to the works by the Australian group directed by the physiologist Marcello Costa, it has been possible to understand that propulsion in the large bowel is consequence of two neural mechanisms. The first is the content-indipendent spontaneous colonic migrating motor complexes that occurs cyclically. The second is a content-dependent, adaptable mechanism controlled by the mechanical activation of enteric neural activity. Mechanosensory enteric neurons (located in the myenteric plexus) have essential mechanosensitive nerve endings in the circular muscle. Distension or stretch of the colon activates these sensory neurons to initiate polarized neural pathways that result in oral contraction and anal relaxation. These pathways do not require the mucosa but can be modulated by sensory nerve endings that project into the mucosa[18]. Enteric neural circuity can efficiently propel content with a wide range of physical properties. This content-dependent activity can be modified in terms of force of contraction and speed of propulsion depending upon consistency and volume of the colonic contents[19]. In others words, bolus size and its consistency affects propulsion speed suggesting that propulsion is not a simple reflex, according to the classic theory about intestinal peristalsis[20], but rather a more complex process involving an adaptable neuromechanical loop[21]. Consistency depends on the degree of fluidity of the intraluminal colonic contents, which in turn depends on the degree of absorption of fluids along the gut. But consistency is due also by the dry-component of the formed stools, and this is for the 60-80% composed by alive microbial cells originating from the microbiota that dwell in the colon[22].
Based on recent revised estimates, the *human microbiota* comprises approximately 10^{13} prokaryotes (bacteria and archaea), as well as fungi and viruses with a contribution of 0.5 kg of the average adult's body weight, but with an extraordinary metabolic capacity, far exceeding that of human beings[23-26]. Of all these microbial components, bacteria have been the most thoroughly studied, but it is become increasingly clear that trans-kingdom interactions are just as important in influencing health and disease[27]. Many if not all human cell structures coexist with a more or less rich microbiota: organs as the lung, or the bladder, not to mention the fetus, which until a few years ago were considered examples of "sterile structures and systems", in fact turned out to have their own microbiota, and in many cases some of their pathologies have been associated with alterations of its composition. That applies for example to all recent works that describe the role of urinary microbiota in urinary tract and gynecological dysfunction[28-30]. Not discounting a number of shortcomings in the available studies, even blood does not seem to be excluded[31], whereas the only exception,

to date, is represented by the CNS. There is no doubt, however, that the microbiota residing in our gastrointestinal tract is the hub upon which the modulation not only of all intestinal functions, but also of other organs, depends, including the CNS, even at the level of its "higher" functions such as mood and ideation. Harboring around 10-100 trillion prokaryotic cells at density of 10^{11} to 10^{12} cells/mL, the human gastrointestinal tract is one of the most complex microbial ecosystem on the planet Earth, comprising only a few phyla (Firmicutes and Bacteroidetes) but hundreds of species, thousands of strains, and millions of bacterial genes with specific assemblies for each subject, like fingerprints. Added to this is the high degree of plasticity, i.e. the microbiota ability to change in response to several endogenous and exogenous factors, such as age, diet, geography, lifestyle, intake of drugs and host inflammation[32].
So, when a relevant impoverishment of the microbial biomass occurs in the large bowel, that significantly influences colonic propulsion capacity. It should be noted that the action of fibers and prebiotics is not due to a "mass" effect resulting from a recall of water produced by the polysaccharide molecules of which they are made up, but their action, which favors evacuation derives from the fact that they constitute the main metabolic substrate for the colon microbiota, that, as we have seen, the biomass which constitutes the dry weight of the feces[33]. Moreover, colonic dismotility may be the direct consequence of intestinal dysbiosis, independently by change in the intraluminal content volume, because function and neuroplasticity of the Enteric Nervous System are influenced directly by colonic microbiota: butyrate may affect neurochemical coding of myenteric neurons and the contractile activity in the rat colon upon long-term exposure. We can speculate that reduced concentration of butyrate in the gut lumen, inducing alterations in cholinergic neurons of myenteric plexus, is only an example among many how colonic motility can be influenced by microbiome imbalance[34].
In summary, for the same "contractile" capacity of the bowel, when the content is made up of scarce and fluid fecal material, the efficiency of the oro-aboral transit is profoundly different, if compared to a voluminous content with pasty consistency. It can be said that *an empty colon has no motor activity* and this is very important for explaining many cases of constipation in patients where disturbances of defecation came after profound imbalance in diet habit or antibiotic consumption. Intestinal evacuation, contrary to urination, which is necessary to eliminate metabolic products that would otherwise be harmful and toxic for the body, is nothing but the mechanism, necessary but not sufficient, to maintain a balance of microbiota that dwells and develops in our gut, as a result of a real production process, a sort of "anaerobic bioreactor" contained particularly in the large bowel. It follows that the primary objective of every therapy for constipation is certainly to achieve defecation but not *di per sè*, but as a way of rebalancing the ecosystem in the intestinal lumen[35]. In an our study, we demonstrated that in a population of patients with severe functional constipation it was enough to restore a regular colonic content using a symbiotic product for improving defecation disturbances[36].
An efficient intestinal evacuation requires a total coordination between effort and relaxation of the pelvic floor muscles and anal sphincters. It is not surprising to verify how is frequent a disorder of this area when considering that the ability to control bladder and bowel emptying is the last function that the Homo Sapiens "cub" learns: children start walking and talking before being able of avoiding micturition and defecation at inappropriate times and before diaper weaning. Acquiring this ability means having the encephalic and medullary centers of both the CNS and the ANS well organized in order to control the same muscle-fascial structures of the abdominal wall and of the pelvic floor, so that they can first be effective at "retaining", containing urine, feces of various consistency, gas, and then efficient at expelling them at chosen times, thus ensuring a complete emptying.
An *Obstructed Defecation* can derive from a paradoxical contraction of the puborectalis muscle and/or an abdominal-perineal dyssynergia, so that the pressure increase indispensable to expel is not achieved; or it can derive from structural alterations that mechanically hinder the expulsion of fecal content: a bulging of the wall of the rectum (rectocele), a pathological descent of the perineal plane, or a rectal prolapse or intussusception are the conditions that hinder efficient evacuation, sometimes up to completely prevent it. Hence derives the need to "open" the way to the expulsion of fecal content with suppositories, enemas, manual maneuvers and the assumption of particular postures. Continuous vicious circles exist between functional and structural alterations, so that the onset of one worsens the second and so on.

ASSESSMENT

A meticulous clinical history and a proctological evaluation, better if complete with an anoscopy, make it possible, in most cases, to gather all necessary elements for a correct framing of the constipation form. The execution of a rectal exploration, first digital and then with a disposable rectoscope, without any preparatory cleaning, is very useful in these cases because it allows to identify the presence of feces in the rectum: knowing the time from the last evacuation, it can be deduced if the rectal coprostasis is a consequence of incomplete emptying, if this has happened in a short time. Or it can signal a problem of visceral sensitivity if the last evacuation has taken place previously, at a considerable distance, and the presence was not perceived by the patient.
The clinical and anamnestic evaluation is sufficiently precise when the "alarm" symptoms/signs mentioned above are not present. In the presence of one or more signs, a specific clinical and laboratory diagnostic pathway is necessary to exclude the aforementioned pathologies and other possible organic causes of the evacuative disorder.
Other forms of investigation that allow acquiring further elements of distinction between the physiopathological mechanisms at stake in a constipation are certainly the *defecography* and the *ano-rectal manometry*[4,5,37]. They provide useful elements only if carried out by expert operators and according to specific execution protocols which, unfortunately, are almost never the "standard" ones in Radiology and Gastroenterology units, not dedicated to this pathology. A clear example is the ano-rectal manometry performed with a technique that does not allow recording the pressure increase that occurs in the upper rectum during the abdominal pressure, the evacuative effort. The lack of this element does not allow recognizing and classifying the type of dissynergic defecation[38]. Other investigations are the rectal balloon expulsion test and the perineal and anal sphincter electromyography, but the same applies: they provide useful elements only in expert hands and when the indication is very clear.
Investigations such as the study of the intestinal transit time using radiopaque markers are not of widespread use because their clinical value depends on the technique used, on a documented bowel diary and on the inclusion in a very specific therapeutic program.

PHARMACOLOGIC THERAPIES FOR CONSTIPATION

Supplements, drugs, devices, dietary schemes, behavioral indications, rehabilitation programs, psychological treatments or treatments with water could fill up an endless list.

Perhaps no other condition boasts as many "cures" as constipation. Many of these approaches have never been subjected to a rigorous scientific evaluation, but are spread by word of mouth about constipation therapy and, maybe even more, about desperate search for solution, since defecation disorders, along with scarcity of integrated, competent and dedicated responses by public hospital facilities, may cause such an incredible impairment of Quality of Life[2].

The medical "arsenal" is very wide, even if restricted to products and devices supported by evidence of effectiveness. Certainly macrogol 3550 or 4000 products are useful: at high doses to resolve "blocks" and important fecal retentions; in small doses to guarantee optimal fecal consistency and easy evacuation[39,40]. Also the stimulant laxatives are useful: picosulphate, senna products, cascara, etc. may effectively stimulate the propulsion of the colon[41]. However, entrusting the solution of constipation exclusively to these drug intake does not make sense, but their use can be beneficial and irreplaceable, when in combination with other strategies. It is difficult to understand why laxatives from herbalist's shops, markets, or "natural" product stores, are preferred to the products which are proposed by pharmacies and so subjected to strict tests of tolerability, definition of the right dose and reliability of the preparation technique. The alleged "naturalness" of the non-pharmacy product often hides big problems of bioavailability, purity, dose-dependent efficacy, presence of additives and other substances with counterproductive effects.

There are also products based on soluble dietary fiber (psyllium derivatives, glucomannans and many others): the axiom that constipation equals fiber deficiency and, therefore, requires a diet rich in fruit, vegetables and bran supplements, has never been true and is nourished only by common myths[42], although there is no doubt that these treatments can have positive effects in many forms of constipation, particularly when an impoverishment of colon microbiota occurs so compromising a regular "stool production", as we have already discussed. The same goes for products based on alive bacteria, the probiotics, and prebiotics such as FOS, inulin and others. Systematic review and meta-analysis still struggle for finding clear evidence of efficacy of probiotics in chronic constipation[43], but this may be due to the methodological approach of the studies since the rationale for its benefic action is too strong. The best is probably their combination with other strategies (laxatives, prokinetic drugs). It is already possible to distinguish between the different types of probiotics, mono-strain products and mixtures of various microorganisms, and to define the dose administration and their ability to colonize the digestive tract, according to the pathology, e.g. constipation , diarrhea, inflammatory disease, visceral pain etc.[44,45].

Other drugs such as prucalopride, linaclotide, and other more recently available ones, have powerful effects in stimulating peristalsis of the colon with different and more "physiological" mechanisms compared to laxatives[46-48]. When the constipation is based only on dysmotility, they are undoubtedly useful, while when obstructed defecation and dysbiosis are involved, they cannot solve the situation alone. Moreover, they are often abandoned due to fairly high costs, while they could be effective and decisive in combination with other products, so permitting to reduce them. If oral therapy is ineffective, many people with constipation often use enemas, rectoclysis, or colon hydrotherapy sessions[49]. Even these approaches are often not decisive, but they are undoubtedly useful to remove stagnant contents from the large intestine and to allow the colon to bear a poly-therapy specifically aimed at rebalancing the intestinal microbiota, which, in the early stages, may be burdened by swelling, pain, irregular evacuation frequency and persistent obstruction symptoms. These disorders lead the patient to suspend therapy before time, since the effects are possibly beneficial, but often unbearable, in the long term. Hence derives the usefulness of guaranteeing an "artificial" evacuation through different Trans Anal Irrigation (TAI) approaches that make use of sophisticated "constant and controlled positive pressure" systems: water is introduced by positive pressure, unlike the atmospheric one (as used for rectoclysis), not intermittently (as for enemas and washing syringes) and adapted to the single patient[50,51]. TAI with these devices, initially exclusive for patients with forms of constipation secondary to neurological pathologies, is proving to be useful also in the most severe functional forms and in forms arising after destructive operations of the pelvic organs[52].

WHAT ABOUT DIET, REHABILITATION OF PELVIC FLOOR, BIOFEED-BACK, SURGERY?

Patients are more and more confused about "nutrition", and so are the therapists who prescribe restrictions that are often unbearable and meaningless. As regards constipation *di per sè*, when not associated with the symptoms of other functional diseases, such as Irritable Bowel Syndrome, or allergies and intolerances well documented by laboratory and instrumental tests, the diet regime to follow is the *mediterranean diet*[53]. Eliminating components from our traditional diet, for fear of other pathologies (off with harmful fats!) or increasing others in the hope of relieving constipation (eat more fruit and vegetables!) results in an imbalance of the intestinal microbiota and an impoverishment of its richness and stability, with a higher prevalence of certain bacterial groups and pathological consequences, including constipation and abdominal discomfort: whenever this approach could be therapeutic for the same disorders?

Pelvic floor rehabilitation techniques and biofeedback, in experienced hands and for well-selected forms of constipation, are unquestionably useful[5]. The same applies to surgical operations aimed at resolving the pathologies that cause mechanical obstruction to stool passage and expulsion. There is no doubt indication for surgical repair in a woman with a rectal prolapse/intussusception or a large anterior rectocele, which formed over time after difficult childbirths, and after years of food errors and evacuation effort due to hard stools is correct. But also in this case, operation will not be so succeed if not preceded and followed by restoration of normal stool consistency and volume, since hard stools are expression of dysbiosis and dysmotility of the colon, as well as pathological stagnation in the sigmoid due to the incomplete evacuation.

In recent years doubts have arisen over the indication of major surgery, such as total colectomies or extensive resections, without any detailed documentation of ENS alterations. These interventions are usually a *last resort* when previous surgery was not useful.

It is probably too early for including the *Fecal Microbiota Transplantation* (FMT) among the therapeutic options for chronic constipation, even if this approach has been already tested[54]. We have seen that the human gut microbiota is not a mere assembly of microorganisms, but a highly organized integrated network of cells interacting intensely with each other as well as with the host, which could be thought of as an additional organ within the human body. Based on the available literature, the possibility of transferring this *organ* from a healthy individual, i.e. endowed with a high-diverse intestinal microbiota, to an individual whose microbiota is impoverished, unbalanced and unable to oppose the action of pathogens, has proved to be highly effective and statements on FMT indications, donor selection, preparation of

fecal material, clinical management and fecal delivery, and basic requirements for implementing an FMT centre are already well established[55,56]. The first and most documented clinical application of FMT is recurrent Clostridium difficile infections (rCDI) in which it is currently used as a last-resort treatment after failure of multiple courses of antibiotics[57], but beyond rCDI, FMT has been evaluated as a treatment option in a variety of gastrointestinal diseases, such as Inflammatory Bowel Diseases[58,59], non-alcoholic steatohepatitis, alcoholic hepatitis, hepatic encephalopathy[60,61]. The evidence that FMT can be useful in the treatment of disorders as Irritable Bowel Syndrome[62] and constipation is very interesting, confirming what we have discussed, i.e. in this disorder intestinal dysbiosis and altered interaction with gut mucosa are pivotal. Moreover, extremely interesting it is that manipulation of gut microbiota through FMT seems to be effective also in conditions outside the GI tract, such as autism and mood disorders[63] and the metabolic syndrome[64]. Since it is clear that intestinal dysbiosis may contribute to the pathogenesis of many diseases, FMT is increasingly being explored as a potential treatment that aims to optimize microbiota composition and functionality[65].

CONCLUSIONS

Constipation, it is a syndromic condition, not life-threatening unlike other diseases of the digestive system, such as cancer, inflammatory diseases, hepatitis, peptic ulcer, etc., but it causes suffering and undermines Quality of Life often more than these. It is common and burdened by entails huge social costs for treatments, examinations, hospitalizations and work capacity impairment, especially in countries with high standards of living. It recognizes a very complex etiopathogenesis in which both underlying pathophysiological mechanisms and therapeutic approaches - that are attempted, assumed and then abandoned, in inextricable cause-effect circles - play an equally important role. Constipation is not considered a significant health problem, so there are no specifically dedicated centers in Italian hospitals. In order to seek solutions, the patient has to contact a specialist, who, even if he/she is the right choice in terms of cultural knowledge and clinical experience, will hardly be able to work with a team that integrates all skills needed for diagnostics and a global approach to the patient with constipation illness.

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Review

Transvaginal mesh for POP: an endless story with a strong present and future in Italy and in all Europe

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Abstract: Vaginal vault prolapse is observed with increasing frequency in the era of increasingly aging populations. Various surgical techniques have been established, varying in performance, difficulty, outcomes and most importantly complications. A bilateral sacrospinous colposuspension technique (BSC) with a corresponding mesh prosthesis was developed using a direct I-Stitch fixation of the 38 microgram mesh from the vaginal apex or uterine cervix to the sacrospinous ligament or the parasacral tendinous region for the treatment of an anatomical central pelvic floor defect. As a minimally invasive approach with the potential for conservation of the uterus, this technique should be applicable to all age groups including the increasingly frequent elderly patient with significant co-morbidities.

Keywords: Pelvic organ prolapse; POP; Mesh; Fascial surgery; Women health; FDA; Urogynaecology

ONCE UPON A TIME…

Like all fairytales, this story will also have a happy ending. This article analyses the use and regulatory history of non-absorbable meshes implanted by vaginal way for the treatment of Pelvic Organ Prolapse (POP). The surgical mesh is a medical device used to provide additional support when repairing weakened or damaged tissue, most often made in polypropylene.

We will now outline a suite of guidelines and recommendations developed on the topic and we will assess its key strength and weakness points.

2016 COCHRANE REVIEW

In 2016, the Cochrane Library published a review of native tissue versus polypropylene absorbable meshes to determine the safety and effectiveness of surgery for anterior compartment prolapse[1]. The review found that 18% to 30% of women would be aware of prolapse after native tissue repair, versus only 13% of women after polypropylene mesh repair. Recurrent anterior compartment prolapse was more likely after native tissue repair compared with polypropylene mesh repair (RR 3.01, 95% CI 2.52 to 3.60; 16 RCT; 1976 women; I^2 = 39%; moderate-quality evidence), suggesting that if recurrent prolapse occurred in 13% of women after mesh repair, 32% to 45% would have recurrence after native tissue repair. Repeated surgery for prolapse, stress urinary incontinence or mesh exposure (composite outcome) was less likely after native tissue repair (RR 0.59, 95% CI 0.41 to 0.83; 12 RCT; 1,527 women; I^2 = 45%; moderate-quality evidence), suggesting that if 10% of women require repeated surgery after polypropylene mesh repair, 4% to 8% would do so after native tissue repair. For de novo stress urinary incontinence (SUI) and dyspareunia (de novo) there was few or no differences between groups (RR 0.54, 95% CI 0.27 to 1.06; 8 RCT; n = 583; I^2 = 0%; low-quality evidence).

FDA WARNINGS AND BOSTON SCIENTIFIC STUDIES

On January 5 2016, the FDA, after previous warnings since 2011[2], reclassified surgical mesh for transvaginal repair of POP into class III, and required submission of premarket approval (PMA) applications. The FDA mandated that premarket approval applications be filed by July 5 2018 for any surgical mesh marketed for transvaginal POP repair. Additionally, for women who had received transvaginal mesh for surgical repair of POP, routine check-ups and follow-up care were recommended, with no need to take additional action if they did not experience complications or symptoms. For women planning to have a mesh placed transvaginally for the repair of POP, the FDA recommended discussion of other treatment options with their doctor.

On April 16 2019, the FDA determined that the manufacturers Boston Scientific and Coloplast had not demonstrated reasonable assurance of safety and effectiveness for these devices. Due to this decision, no FDA-approved surgical mesh products for transvaginal repair of prolapse are currently available in the United States. Following these FDA changes, a literature review by Rizvi and Chughtai[3] aimed to look at the role of graft and mesh in vaginal surgery. They conducted a search for English-language articles published during 1997 to 2016, using MEDLINE, PubMed and United States National Library of Medicine databases, reviewing approximately 50 papers. The literature review provided a new insight regarding safety of mesh, demonstrating how polypropylene mesh is safe for vaginal surgery if used by experienced surgeons. The safety of mesh becomes compromised in the hands of commercial surgical kit providers, and therefore it was recommended all the new mesh tailored kits should undergo evidence-based trials to then be safely used worldwide. The FDA decision therefore seemed to be ill informed by not distinguishing between high-volume centers from low-levels ones, therefore overlooking the surgeons' level of experience. Furthermore, the negative attitude of the FDA stemmed from old generation meshes that do not share much with the modern ones except for the material, polypropylene. Cochrane itself stated in 2016 no recommendation can be made on current macroporous and ultralight meshes based on the current available reviews. This lack of clear direction is in turn reflected on patients, lawyers, and forensic doctors who never distinguish, often for opportunistic reasons, between the different available materials. Furthermore, the market seems to have failed to notice that the FDA did not impose any ban on the prolapse marketing in the USA, but simply requested additional studies from the two main companies marketing mesh in the USA, Coloplast and Boston Scientific. When these companies failed to comply and decided to exit the market due to urogynaecology representing a residual part of their revenues, this created a *de facto* unavailability of the devices in the country.

A recently published study by Boston Scientific[4] confirmed that in centres with high surgery volumes the results of the treatment with mesh are highly satisfactory. For Uphold Lite Vaginal Support System the percentage of anatomical success at three years was 83.3% compared with 73.8%

with native tissue repairs, particularly for the anterior compartment (97.6% vs 87.1%) and re-operations for prolapse (0.9% vs 3.7%). For apical compartment, the success rates are slightly lower than those of fascial surgery (95.2% vs 97.6%), as well as the subjective success rate (87.5% vs 92.6%) and a re-operation rate for mesh exposure of 1.3% by Altaman[5]. Nonetheless, even if safety and effectiveness remain higher with mesh compared to native tissue, Boston Scientific has renounced the American market due to the FDA lack of clear indications.

SCENHIR, 2017

In 2017 the Scientific Committee on Emerging and Newly Identified Health Risk (SCENHIR)[5] published an opinion on safety of surgical meshes used in urogynaecological surgery. This did not limit itself to the assessment of the current use of mesh, but also made recommendations. These included the idea that material properties, product design, overall mesh size, implantation route, patients' characteristics, associated procedures (e.g. hysterectomy) and surgeon's experience are aspects to consider when choosing appropriate therapy. The implantation of any mesh for the treatment of POP via the vaginal route was recommended to be considered only in complex cases in particular after failed primary repair surgery, and that for all procedures the amount of mesh should be limited where possible. A certification system for surgeons was promoted based on existing international guidelines and established in cooperation with the relevant European Surgical Associations. Therefore, SCENHIR 2017 stated no prohibition for use, but limited it to complex cases, including relapses, advanced cases, and patients at high risk of recurrence.

ICI, 2016

The International Consultation on Incontinence (ICI) in 2017[6] condensed the 2,000 pages of analysis of POP in a 20 pages summary, focusing on the meshes for the anterior compartment in the first surgery. The ICI considered the results from the Cochrane review, but also included additional studies which found much lower erosion rates, highlighting the contradictions in the FDA recommendations.

Newer lightweight transvaginal polypropylene mesh products have been introduced to decrease the complication rate, specifically mesh erosion. Among the ICI quoted studies, Altman et al[7] and similarly, De Tayrac et al[8] found in 79 women with grade 3-4 cystocoele an anatomic success rate of 95%, a satisfaction rate of 98% and a mesh exposure rate of 1.3% using a lightweight (28 g/m^2) polypropylene mesh (Surgimesh® Prolapse Xlight, Aspide Medical, France) at three years. Despite the current negative sentiment surrounding transvaginal meshes these newer lightweight meshes with very low rates of erosions require further evaluation.

GUIDELINE OF THE DGGG, SGGG E OEGG, 2016

In 2016 the German, Austrian and Swiss gynaecological societies developed guidelines for the treatment of POP[9]. These were based on the new generation of meshes with macropores >75µm and ultra-light, ≤32g/m^2, which also integrate the necessary apical fixation to the sacrospinous ligaments and are single-incision, avoiding the need for a transobturator insertion of the anchoring arms. From international studies on the treatment of anterior compartment defects, including studies not included in the Cochrane review in 2016, cumulative success rates of 93%, erosions of 8%, chronic pain and dyspareunia de novo of 7% were detected. The use of synthetic nets in the anterior compartment was therefore shown to reduce relapses of anatomical and subjective prolapse, even though no positive influence on quality of life was found.

Mesh use for the repair of posterior defect was considered appropriate as part of the guidelines, but not as a routine practice, as no supporting clinical studies are available. The extensive systematic review recommendations of these guidelines are based on an literature and practical experiences and evaluation of current literature and practical experiences in Germany, Austria and Switzerland. Interestingly, in the development of these guidelines the expert opinion of surgeons who perform mesh implantation was considered, representing an exception in the space.

CANADIAN GUIDELINE, 2017

The Canadian guidelines published in 2017[10] highlighted how better recurrence rates were achieved with the use of mesh compared to fascial surgery without improving the quality of life. It was not clearly outlined though whether the re-intervention for recurrence did in fact worsen the quality of life. However, 12% erosion rate was reported with meshes, very differently from what was obtained in other comparable recent studies. Finally, the use of local oestrogen were found not to protect from erosions, whereas smoking and hysterectomy were identified as risk factor for small versus extensive erosions, a discriminating element of gravity and therefore crucial in prolapses.

EUGA, 2017

The European Urogynaecology Association (EUGA)[4] in 2017 highlighted how current data suggest the use of non-autologous durable materials in surgery has well-established benefits, but also significant risks, which are specific to the condition and location they are used for. Exposure in the vagina, shrinkage, erosion into other organs and other various mesh-related complications have been described, including infection, chronic pain and dyspareunia. According to the EUGA, patients need to be aware of the alternative therapy and potential risks and complications of this therapy. Synthetic mesh for treating prolapse should be used only in complex cases with recurrent prolapse in specialist referral centres. These conclusions were largely developed based on the PROSPECT and PROSPERE trials, which, as outlined further in the article, contained significant bias.

NICE, 2019

The National Institute for Health and Care Excellence (NICE)[11] reiterated the public concern about the use of mesh procedures, though contradicting the position of the government and the NHS on the period of "high vigilance restriction". The NHS stated that some evidence of benefit was present with the use of mesh, but limitations were present in terms of long-term effectiveness and adverse effects. In particular, the true prevalence of long-term complications was considered to be unknown. The NHS recommends to promote informed preference and shared decision-making when a woman is considering a surgical procedure for pelvic organ prolapse. This position, very different from that expressed by NICE in 2017, has raised a degree of dismay in Great Britain[12], but it supports the use of vaginal meshes as a safe and effective device and procedure for the treatment of POP.

REACTION FROM UROGYNAECOLOGICAL WORLD: CHANGE.ORG PETITION, IUGA TOOL AND NICE BBC INTERVIEW

The role of mesh in pelvic prolapse surgery has been under critical debate. A petition named "Women's Health Physicians: Ensure Ethical and Fair FDA Mesh Research" promoted through change.org and sent to Ben Fisher, the Director of the FDA Division Urologic Devices, represented an interest-

ing way to support the mesh use and a movement supporting the fact that provide an efficient and effective treatment for complex or recurrent prolapse, able to preserve the uterus compared to procedures such as hysterectomy (change.org).
In response to the issues raised around mesh use, the FDA mandated 522 post-market studies. These studies were conducted with great effort, expense, and with an ethical understanding that the 3-year assessment described in the study protocols would provide the key outcomes required to answer clinical questions and determine the best regulatory decisions. The physicians involved in these studies believe that FDA action occurred primarily due to outside pressures, and that these factors will ethically compromise interpretation of the 522 trials. More than 6,500 physicians and advocates have made their voices heard by supporting this petition, but the voices of countless patients remain the most important untold part of the story, and these voices have remained largely silent. This can change, starting today.
Indeed, in May 18, 2019 the International Urogynaecological Association (IUGA) has launched "Have Your Say: Your Pelvic Floor Story" (https://www.yourpelvicfloor.org/your-pelvic-floor-story), a new online tool within the IUGA website inviting women to share their stories, maintaining the privacy but allowing for submission of video stories and public sharing, depending on a patient's personal comfort level. This can finally allow millions of successful outcomes to be accurately represented and reported.
Another interesting intervention in April 2019 in support of mesh was done by Anna Collinson and Jessica Furst in the BBC Victoria Derbyshire programme, reporting that "vaginal mesh ban can be lifted with changes". Controversial vaginal mesh implants can be offered again on the NHS in England, as long as certain conditions are met, according to the health watchdog NICE. Nonetheless, the NHS is not compelled to act on the guidelines - which are for England only - and the "pause" on vaginal mesh surgery remains in place.

FROM THE NEW YORK TIMES, JULY 14, 2019
"WOMEN WHO SUED MAKERS OF PELVIC MESH ARE SUING THEIR OWN LAWYERS, TOO"
A nearly decade-long legal battle over the harm inflicted on tens of thousands of women by surgically implanted pelvic mesh, totaling about $8 billion in settlements, is moving away from manufacturers and towards the lawyers who helped women bring their cases to court. Indeed, these women have started suing their lawyers, accusing them of improperly enriching themselves with excessive fees or stretching themselves too thin to properly handle the pelvic mesh cases.
A potential class action lawsuit filed in July 2019 in a state court in New Jersey contends that the 40% fee a group of law firms charged about 1,400 of their clients violated state law. The law caps fees in personal injury lawsuits at about 33%. A separate suit filed in federal court in Houston alleges that another group of firms took too many cases, missing filing deadlines for hundreds of women, potentially reducing the value of their claims against the mesh manufacturers to negligible amounts.
A half-dozen medical device manufacturers, including Boston Scientific and Johnson & Johnson, have agreed to pay billions of dollars to tens of thousands of injured women. But one of the most troubling aspects of the mesh cases involves pushing women to have the implants removed, a procedure that is sometimes necessary but can be rather complex, as the mesh is made of a fibre designed to bond with human tissues. In addition, the removal of the mesh in itself can become an exploitable profitable business. In June 2019, federal prosecutors in Brooklyn indicted a doctor and a consultant in a scheme to profit from removing mesh implants. A lawsuit filed in a federal court in Houston raised a similar issue, with three women contending that lawyers from Clark, Love & Hutson and several other Texas firms helped arrange for them to have costly removal procedures that would increase the value of the women's claims and lift the lawyers' fees.

PROSPECT AND PROSPERE STUDIES
When discussing the safety of mesh in pelvic prolapse, two studies are most often cited, namely PROSPECT[13] and PROSPERE[14].
PROSPECT (PROlapse Surgery: Pragmatic Evaluation and randomised Controlled Trials) was the evaluation of two pragmatic, parallel-group, multicentre, randomized controlled trials conducted in a mix of secondary and tertiary centres in the UK. This study, representing the largest RCT to date on mesh, shows no advantages of vaginal repair reinforcement with mesh material in terms of anatomical cure and improvement of quality of life with higher rate of post-operative complications in comparison to standard surgery. Due to these findings the Authors concluded mesh use should be avoided in the surgical treatment of primary anterior or posterior compartment prolapse, except for specific categories of women with high risk of prolapse-recurrence. However, the detailed characteristics of such patients are not clearly defined, generating various misleading interpretations of this key message.
Most importantly, despite the large number of patients included in the study and its rigorous randomization protocol, PROSPECT results are potentially influenced by different sources of bias deserving a thorough analysis in order to avoid misinterpretation of evidence. Among others, no distinction between anterior e posterior defects is used, nor a subgroup analysis conducted, too many patients with functional and less inclined to improvement defects are included, such as faecal incontinence and severe dyspareunia, type of apical prolapse repair is varied, possible concomitant hysterectomy is included, and no distinction nor subgroup analysis is conducted on the heterogeneity of meshes in term of weight, size and surgical placement.
In response to these significant sources of bias that were overlooked in the study, we drafted a letter to the editor of the Lancet journal, which was unpublished due to a delay in submission – and not due to its content – titled *"Mesh use for transvaginal prolapse surgery: real 'evils' or viable alternatives to standard repair?"*.
In this letter, we outlined how the interpretation of results could potentially be misleading due to the lack of adequate definition of the patient population. In addition, we outlined the significant sources of bias which were not addressed in the study, detailing how each of them could substantially impact the results of the study.
A single large study such as PROSPECT can hardly lead to conclusive recommendations regarding the superiority of standard vaginal repair in comparison to mesh repair, whose application is supported by more than 20 years of scientific research, particularly with its level of heterogeneity and bias.
The second study often cited when discussing mesh effectiveness is PROSPERE (PROSthetic PElvic organ prolapse REpair). This was a randomized controlled trial conducted in 12 French hospitals; the main objective of the study was to compare the morbidity of laparoscopic sacropexy with vaginal mesh for cystocele repair. Also this study has significant issues undermining the validity of its results.
As a response, Dr M. Bologna, Dr A. Vitagliano and Dr M. Cervigni of the Associazione Italiana di Urologia Ginecologica e del Pavimento Pelvico (AIUG) wrote a letter on behalf of the organization, published on European Urology and titled

"Is There Enough Evidence To Prove Higher Safety of Laparoscopic Sacropexy in Comparison to Vaginal Surgery for Cystocele Mesh Repair?"[15]. Quoting from the letter:
We read with interest the article by Lucot et al. The authors conducted a multicentre trial (PROSPERE) to compare 1-yr morbidity between laparoscopic sacropexy (LS) and vaginal mesh repair (VMR). In view of their results, the authors concluded that "LS is safer, sexual function is better preserved and it can be performed, whenever possible, as first-line surgical treatment for cystocele mesh repair".
We want to commend authors for their efforts in undertaking such a unique and much needed trial. Nevertheless, we feel it is important to point out some aspects of the PROSPERE that may help readers in a more cautious interpretation of the results.
First, as honestly recognized by the authors, they found a statistically nonsignificant result for the primary outcome of grade II or higher postoperative complications (p=0.088). As their study was adequately powered to detect a statistical difference for the primary outcome (but not for secondary ones), a fully substantiated conclusion would be that LS and VMR were similar in terms of grade II and higher postoperative complications[16].
Besides type II error in the analysis of secondary outcomes and error for intention-to.treat approach we were surprised to note that some specific grade III complications (umbilical abscess, vaginal polyp, macroscopic haematuria after 6 wk) were judged as being definitely correlated to VMR[17,18]. *But what is of serious concern is that inclusion of an umbilical abscess in calculation of VMR-related complications (Table 3 in Lucot's article*[14]*)may suggest an inadvertent shift of a patient from the original allocation group (LS) to the other one (VMR).*
Finally, the heterogeneity in mesh composition (polypropylene alone or combined with absorbable components), kits, and techniques for VMR (variable mesh dimension, with or without sacrospinous fixation), as well as the considerable number of LS requiring a conversion to the vaginal route (n=7) may have affected comparison between the groups in terms of severe complications. Nevertheless, the total number of events (n=12) would in any case have been insufficient to draw any firm conclusion about the safety of each technique[14].

ITALIAN DEBATE INSIDE THE AIUG

These studies and international controversies have sparked a debate within the Italian UroGynecological Association (AIUG). It all begun with a request to the 2019 National Congress of the AIUG in Lecce for the association to take a position on the issues and to assume responsibility of the use of mesh in Italy, bearing in mind that there were no significant reports of mesh related complications in the country. Many Italian surgeons use mesh in the first surgery for POP and, so far, the Italian Ministry of Health has not received reports of the danger of using vaginal meshes and therefore there are no limitations in their use.
On behalf of the Scientific Secretary, I put forward the request for a "Position Paper" from the AIUG Board which, although not bearing a legal medical relevance, certainly would have reassured all the doctors who use this therapeutic strategy, and provided support in front of the Health Directorates of the Hospitals and patients suffering from POP. The agreement was that if the majority had approved the Position Paper, this would be published on the AIUG Association website.
The Position Paper prepared together with forensic doctors reads as follows:
Italian doctors can use, even if not routinely, synthetic material meshes for treatment of genital prolapse by vaginal way in first and second surgery in patients with correct indication, recorded in the Data Base (SRD) AIUG, with specific and detailed informed consent and with meshes certified for the purpose.
This would have been a significant opportunity for the AIUG to be the spokesperson for a scientific community wishing to pursue a research for the best cure for our patients.
However, after the approval by the majority of the Board, the scientific secretary objected to the publication of the statement on the AIUG website, proposing a modification, by adding the following statement at the beginning of the Position Paper:
Despite the current international concerns about the use of synthetic mesh.
It was the belief of the proponents that otherwise the Position Paper would have exposed doctors to legal medical disputes.
All this has generated a discussion that involved 90 Italian gynaecologists and urologists, activating an interesting online debate according to a modern style of discussion in which the Aristotelian principle "Ipse dixit" ceases to be valid. For all I quote a reply by Dr. Daniela Viviani (Gynecology Department, Montecchio Emilia, IT):
I would like to express only one thought. I believe that the indecision is the less protective attitude from a medical-legal point of view. I also believe that those who enthusiastically supported F. Deltetto's initiative are professionals who, in their treated cases, in small or large numbers, related to prosthetic surgery, have not recognized all the dangers feared by the FDA. Perhaps in Italy those who "adventure" in prosthetic surgery have always done so after having acquired a good expertise in fascial surgery, with good reasons and with religious respect for the rules of prosthetic surgery. I therefore believe that we are ready to face any struggle for approving our Position Paper.
Other colleagues have asked for guidelines to be developed, others for a short paper to be submitted to the AIUG board. My personal position on the matter was summarised in a question I posed: does the AIUG want to defend surgeons or not?
In addition, we reported to the group that the 2017 German, Austrian and Swiss guidelines state that the vaginal meshes for prolapse can be used in first and second surgery with the correct indications, and therefore we would not be "adventuring" nor failing to recognize international trends and recommendations.
Some have questioned the validity of the online voting mechanism that was used to communicate the approval of the Position Paper by the Board. Nonetheless, this is routinely used to gather consent and it gives clear evidence of unbiased and unpressured personal opinions. Finally, the publication on the AIUG website is only a formal and transitory formalization of the support, as the European MDR of 2020 will clarify the European positioning on mesh use.
At this point in the discussion, a clarification on the words used was requested – not routinely, correct indication, registration on the SRD Data Base, as informed consent, CE certification.
A finalized Position Paper was developed, which became the flag of a group of 60 experts (Mesh Italian Skilled Surgeons) (MISS). The new Position Paper reads as follows:
The meshes in synthetic material can be used by skilled surgeons in vaginal surgery for the treatment of some situations of genital prolapse (degree equal to or greater than 3, lateral detachment, relapse prolapse or with risk factors for recurrence - collagen diseases, chronic bronchopneumopathy, physically heavy work , etc). The cases treated must be recorded in a certified Data Base, as a guarantee of the access procedures, the preoperative checks and the correct

follow up. The treatments must be preceded by the signing of the specific informed consent and precise information to the patients, with the of meshes certified for the purpose and with the CE mark.

The debate continued with the statement of someone that no one can "ban" a method if not the professionals. The important thing is "not to wait for Godot" as a Becket comedy. Others talk about "open source" medical dynamics.

In July 2019 an Opinion Statement was published on the AIUG website by the Scientific Commitee. This statement outlined a position that not only appears unfavourable towards meshes implantations, but it will also give a potential tool to forensic doctors in lawsuits when arguing against surgeons. This Opinion Statement was actually defined as the AIUG Scientific Committee positioning, rather than guidelines.

Some AIUG members promptly expressed their disagreement, particularly Dr Antonello Azzena (Gynaecology department, Conegliano Veneto, TV). He expressed specific reservations about the nine points the Opinion Statement. Following, an analysis of the 9 points and the criticisms:

1. Better anatomical results are reported with prosthetics, but no evidence of improved quality of life for the patients is shown - if it is true in the treatment of the anterior prolapse the anatomical results are superior with the synthetic vaginal mesh and the percentage of relapse with facial surgery is higher, we should consider improving how we evaluate quality of life for prolapse surgery, as it is clear the current questionnaires are not able to capture the nuances of this patients' quality of life.
2. Mesh-related complications are 10-15% and often not definitively treatable - it would be useful to once and for all specify what are the key complications included in such assessments, and to subgroup them by gravity. To affirm mesh-related complications are 10-15% of all cases only raises concerns in doctors, patients and ultimately forensic doctors; truth is that new generation meshes have complication rates of 2-5%, as reported in the numerous sources quoted above.
3. Based on the evidence, the transvaginal implantation of synthetic prosthesis as first-line treatment of vaginal prolapse mono- or pluricompartimental should be discouraged, in the absence of specific risk factors - this represent a misleading medical lexicon, not really affirming whether they can or cannot be used (as it was originally requested in the MISS Position Paper), simply offering a legal tool for those suing surgeons for malpractice. In addition, to affirm that specific risk factors (identified in Friedman et al[19] as weight, stage 3-4, familiarity, avulsion to elevation and width of vaginal hiatus) would then allow the use of meshes do not clarify the Committee position, as most prolapses expert surgeons treat with meshes are indeed a grade 3 or superior. Nonetheless, this seems not to represent a good enough reason, according to point 8.
4. The use of meshes can be useful and appropriate in patients with specific risk factors, but in the apical defects then transabdominal route is better - again, this statement does not really represent a clear positioning, as according to the previous point the use of meshes for patients with specific risk factors seems actually recommended. In addition, the claim that the transabdominal route is free of significant complications related to the prosthetic material, and therefore preferable, overlooks crucial aspects such as mesh erosion, and issues related to the surgical practice, operating time and type of anaesthesia. Patients should be informed of all risks, whereas it appears from the statement that the vaginal route is more risky.
5. The treatment of prolapse relapse represents an indication for the use of vaginal meshes if it includes adequate informed consent and adequate surgical skills of the operator - it seems curious how the statement affirms the centrality of expert surgeons for the good success of the implant procedures, but also how no expert surgeon opinion was not considered by the Scientific Committee, and rather the evidence from bias studies such as PROSPECT and PROSPERE was considered more informative.
6. Most mesh kits have an apical attachments mechanism, but the in the apical prolapse no difference is present between native tissues and prosthesis vaginal surgeries - this statement does not find grounds in the other guidelines, as outlined in this article. It is also necessary to understand what is the vaginal referred to, whether with suspension of the sacrospinous ligament or uterosacral ligaments, with device or without. Every surgery has specific complications and to flatly criticize the use of vaginal meshes without any specification only increases the level of confusion in the already murky guidelines environment. This point of the statement also affirms that in the multicompartimental defect the abdominal route has a clear efficacy with no significant complication rate, even though no bibliographic evidence is provided to support such statement.
7. Synthetic meshes should not be used for the treatment of the posterior segment, except for exceptional cases - the highly problematic posterior vaginal segment has not yet found a certain surgical solution. Nonetheless, to affirm the use of meshes should be avoided completely without considering the specific case highlights the prejudicial and unscientific attitude, which only considers the anatomic results ignoring the functional one.
8. New devices and new meshes - this point of the statement is quite ambiguous, as it argues that modern meshes are likely to improve performances, but at the same time it affirms their use must only be in the context of controlled clinical studies, approved by ethics committees. The AIUG Scientific Committee seems unaware of the current Italian landscape, where it is extremely hard to obtain approval from ethical committees, in particular for vaginal meshes. In addition, all meshes used in Italy have been approved by the European Union. Therefore, not only the Committee is not using the available literature to back its members, but it further weakens them in the face of legal medical disputes. Moreover, limiting the use of meshes to controlled clinical studies would significant damage the companies currently on the market, a damage they could potentially seek compensation for.
9. The AIUG is committed to create centres of excellence for the use of vaginal meshes - no clear definition of who will determine the criteria for an excellence centre, nor who will assess such centres. In addition, no mention is made on how the AIUG will ensure a fair competition for all the meshes available on the market, nor indication that the skill of the surgeons will be considered as a criteria in making the excellence assessment, despite the literature clearly indicating this as a crucial factor in ensuring meshes effectiveness and safety.

The message emerging from the AIUG Opinion Statement is that not only are meshes not necessary to correct the pelvic floor defects, but they are dangerous. The most worrisome aspect is the final table reported in the statement, which states how in first-line surgery, even with relapse risk factors, it is optional to use vaginal meshes. This would expose patients to the 36% relapse risk[19] associated with traditional fascial surgery, rather than with meshes, which carry a significant lower risk. In this case, it would be much more

appropriately recommended to use meshes, as per point 4.
In addition, given all meshes have been approved for use, therefore previously assessed for safety and effectiveness, why should we limit their use in controlled clinical studies, rather than making them available to patients in need that would benefit from them?
Therefore, an open access debate including all key opinion leaders and expert professionals on the current guidelines would represent for us the best and most modern and scientific approach to debate the issue. The polypropylene meshes represent a great advancement in the care of our patients and we regret that some of us are now not using them only for fear of malpractices backlashes, even when used in the correct indications. It is for this reason that the AIUG must hear the voice of skilled experts on mesh implantation, by sharing the proposed Position Paper and modifying the Opinion Statement.
The question we should ask ourselves is what does the word *science* mean? During high school, I was passionate about physics and I remember a phrase by the great genius Richard Feyman, which has always been since then a guide in my life:
What is science? Science sometimes means a special method of discovering things; sometimes it means the set of knowledge that originates from the things discovered, but it can also mean all the new things that can be done using the acquired knowledge, or actually doing these things.
For us, a group of 60 colleagues who are passionate about surgery, who follow the debate and want to be at the forefront of the urogynaecology care, the only science is to look ahead using documentary evidence.
It is useful to clarify that when we talk about polypropylene, we mean all modern macroporous, light and ultra-light meshes[19-23]. Erosion is exceptionally rare and, when this happens, it is often due to implantation errors on the part of the surgeons. Today, no such thing as good polypropylene or bad polypropylene exists. There is a trend to believe that titanium coated propylene is the only safe option, even though this is happening in the absence of clinical studies that affirm its validity of safety and efficacy, evidence that does instead exist for the other polypropylene meshes.
Faced with the Anglo-Saxon world decisions it is necessary to react. This is a great scientific opportunity for the AIUG to be a driving voice in Europe, but the Opinion Statement, published on website, is not going in the right direction. The E.B.M. is obviously based on the evidence, but is there evidence that the current meshes are harmful? Certainly not as our Position Paper states.
But there is good news on the horizon. The European community regulation *"The medical device in Europe has less than one year until 26 May 2020, the Date of Application of the Medical Device Regulation (MDR - 745/2017)"* will come into practice in the next year. This regulation will allow the meshes currently used in Italy, as they all meet the biological criteria to be safely implanted.
As stated in the Position Paper by the Mesh Italian Skilled Surgeons (MISS), today it can therefore be affirmed that all polypropylene meshes with the CE mark have equal dignity of use, with equal and low risks of complications, when applied with expertise. Our wish is to be allowed to use the best available device to ensure the highest level of care for our patients. We are conscious that no surgery is free of complications, but also that most often these are caused by the surgical act in itself. The polypropylene meshes do not erode the tissues around them, except for when the vaginal wall is too thin for the procedure or the mesh is embedded above the pubocervical fascia.
A MISS study on prosthetic correction of anterior vaginal defects with different types of meshes, all in polypropylene, of low or ultra-low molecular weight currently available in Italy is underway, which is expected to shed some light on the issue and support our claims. This is an observational study involving more than 700 patients, with a mean follow-up of 18 months. The interim results already show that well applied meshes are a valid and safe surgical instrument and Italy is a vanguard country in their use, supporting the idea that POP surgery in 2019 must also be a vaginal mesh surgery. The data will be presented in October 2019 in Treviso, at the ISPP (International Society of PelviPerineology) world congress.
However in Europe the most important date will be 2020 MDR.

MDR EUROPE 2020: HARMONISATION OF STANDARDS FOR MEDICAL DEVICES

"The Medical Device Regulation (745/2017, to become applicable in May 2020)[24] is the most impactful legislative change for the medical devices sector since 1993, when the medical devices directive (93/42/EC) was published. Both legislative schemes follow the "New Approach" (NA) that was updated and replaced by the New Legal Framework (NLF) in 2007. The essence of the NA/NLF is that product regulations provide for general safety and performance requirements called "essential requirements" or "general safety and performance requirements", and that testable technical requirements addressing them are laid down in standards, developed jointly by all interested stakeholders. Those standards, following regulatory assessment, then become harmonized standards, are referenced in the Official Journal of the EU (OJEU) and thus provide for legal certainty for all stakeholders. Harmonized standards support the competitiveness of European industry, including small and

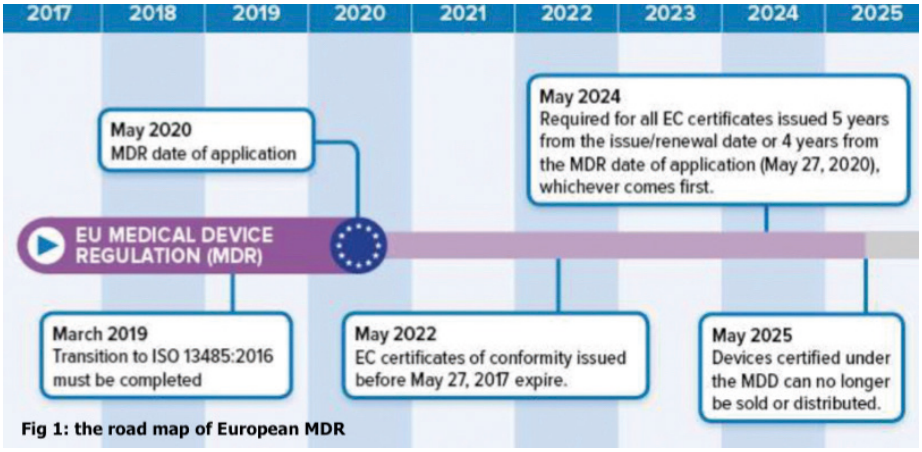

Fig 1: the road map of European MDR

medium enterprises as well as large global companies based in the EU and beyond" (Fig. 1).

CONCLUSIONS: "WHAT CAN WE LEARN FROM THE VAGINAL MESH STORY?"

What we can learn from the vaginal mesh story is effectively summarised in the abstract Karmaker and Hayward[25]:

The use of vaginal mesh in prolapse surgery has created enormous controversy and unprecedented media interest; it has become the most emotive topic in urogynaecology today. The US Food and Drug Administration 510(k) system allowed the proliferation of mesh products which were rapidly adopted by surgeons internationally. The importance of a firm understanding of the biomechanical properties of tissue and implants, surgical skill, patient selection, communication skills, informed consent, and high-quality research are all important lessons we can learn from the mesh story. These lessons need to be applied to all novel treatments in the field of urogynaecology and beyond.

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Review

Treatment of vaginismus by hypnotic psychotherapy. Review

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Abstract: Aim: To evaluate the level of knowledge of vaginismus in its psychological and sexual causes, the use of medical hypnosis as a therapeutic support, and to create an ad hoc hypnotic model for its treatment trough a grid comprising all dimensions used in the various researches considered in the literature. *Methods:* The review was performed by consulting the electronic Medline database (PubMed), DSM IV-TR and 5, Benini's biopsychosocial relational theories, and extracts abstracts data from various medical and sexology publications. *Results:* The vaginismic woman seems to present a psychobiological vulnerability, mainly triggered by hyperactivity of the emotional sphere and by a muscular hypertonus of the pelvic floor that influences the sexual sphere. The data support the idea of a general defensive reaction as a mechanism of involuntary muscular activity of the pelvic floor and a close connection between vaginismus, pelvic contraction, emotional motor system and biological anguishes of the reptilian mind. *Conclusions:* Further to the effectiveness of a multidisciplinary-approach in the treatment of vaginismus, hypnosis seems to have an impact in shortening therapy time, in pain management and anxiety reduction. According to Benini's approach, the cause of vaginismus is not identified in the fear of penetration but rather in the anguish of the reptilian mind.

Keywords: Hypnosis; Vaginismus; Psychotherapy; Sexual pain disorders; Emotional pelvic floor system

INTRODUCTION

Vaginismus affects the fertile female population in the percentage of 0.5-1%[1], and as many as 15-17%[2] of the population is treated for coital pain. This literature review is aimed to explore the psychological and sexual aspects of vaginismus, in order to build a protocol of functional and effective therapeutic interventions using hypnosis, an extremely flexible method for all health care providers.

METHODS AND MODELS OF STUDY FOR VAGINISMUS

The Medline database (PubMed) has been used searching the following keywords: "vaginismus", "hypnosis and vaginismus", "pain and vaginismus", "hypnosis and pain" "emotional motor system", "hypnosis and safe place", "innervation of the pelvic organs", taking into account Engel's biopsychosocial model[3], the definition and the criteria according to the DSM (Diagnostic and Statistical Manual of Mental Disorders), MacLean's Triune Brain model[4], and Benini's biopsychosocial relational psychology[5].

Engel's biopsychosocial model. It is a person-centred model, developed by Engel in 1977 based on the multidimensional conception of health submitted in 1947 by the WHO (World Health Organization)[6]. The model proposes to define health as a state of complete physical, mental and social well-being and not merely the absence of disease[3]. In this model all people are included in a network of biological, psychological and social relationships that influence health both in themselves and by interacting with each other. The importance of the genetic and biological factor is closely correlated with the psychological factor that takes into account the mental, emotional and spiritual dimension (dimensions that impact on the health) and with the social factor that includes systems such as family, community, culture, socio-economic status and the possibility of access to health care.

MacLean's Triune Brain. Paul MacLean formulated the theory of the "Triune Brain"[4], a brain made of three levels developed in the course of human evolution and presenting different characteristics. Reptilian or Primal Brain, the oldest, Paleomammalian or Limbic Brain, and Neomammalian, the most recent and advanced. The reptilian brain, which developed first, is positioned on the brainstem and includes the rachid bulb and the midbrain. Although human beings developed the subsequent brains during the period of their evolution, the former brain was not lost. Therefore, according to the tripartite division, the human being has three different mental levels, each one with its own characteristics. According to MacLean, the human mind has a *cellular memory* based on the memory of all the information received during its existence, stored and organized in order to interact with the internal and external world and to reach a state of adaptation. In a nutshell, the mind is composed of a biological cellular memory (*biological mind*), a psychological cellular memory (*psychological mind*), and a social cellular memory (*social mind*). Considering that the first task of the human being is to adapt to the environment (both physical, rational and social), the stored information is fundamental for the adaptation. The lack of adequate information therefore becomes the subsequent cause of anxieties and fears.

Benini's reptilian brain and biological mind. According to Benini theory, the *biological mind* deals with the primary survival needs as nutrition, hydration, sleep, thermoregulation, body care, disease care, movement, relaxation, play, sexuality, territory. Through its function each individual is able to satisfy the self-preservative needs that can be classified in terms of physical security (care and maintenance of the body) and environmental safety needs (search for safe environments). When a person perceives a danger that may jeopardize the integrity of her body, health or surrounding environment and at the same time is not able to adequately respond to the needs of self-preservation, some sentinels better defined as biological anguishes activate[5]. Their task is merely informative, to communicate to the person that the methods currently implemented are not effective and must be modified to restore a biological balance.

The anguishes of the biological mind. Biological anguishes can be considered guardians of survival. They activate to signal that the integrity and health of the body are at risk, and that the surrounding environment threatens to compromise the safety of the individual. These threats arise when the human being does not respond correctly to the demands of self-preservation, or when he is temporarily unable to do it because insurmountable obstacles arise between him and his needs for self-preservation. The *biological anguishes of fragmentation* activate when the body is in danger as in the case of environmental disasters, serious illnesses and accidents, malnutrition, violence, torture and poor care, or in all situations in which the individual is not able to satisfy the

physical security needs. Fragmentation anguish succeeds in triggering ancestral and violent defenses which strongly reactivate the animalistic part present in every human being, a part accustomed to the struggle for survival. The reemergence of the "animal part" allows the individual to endure hunger, cold and pain for longer. Strength and aggression increase to such an extent that he overcomes situations previously unthinkable and terrifying. In some cases, the activation of fragmentation anguish manages to save the human being, in others it can do nothing, in others it remains active even in absence of danger. In this last case, the anguish loses its adaptive meaning and turns from guardian into an aggressor leading the individual to perceive it as an enemy from which he must defend himself[7]. The biological anguishes of persecution activate when an individual perceives in his own living environment the presence of a danger that could damage his physical safety or that of the family, that is to say in all situations in which the human being is not able to meet his own security needs.

PAIN (Physical and psychological)

According to IASP's (International Association for the Study of Pain) "pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or otherwise described as such"[8]. According to Bunker[9] pain is "whatever the experiencing person says it is, existing whenever he says it". Pain has different dimension; it can be manifested with anxiety, mood disorders, depression, feelings of loneliness, incompleteness and inability to control the situation. The emotional consequences produced by pain can lead to the outcome of feelings such as: fear that pain can become uncontrollable, fear of dying, fear of losing mental or physical self-control, fear of losing one's social role, fear of losing one's autonomy. Fears, moods, feelings and the character of the person have the ability to influence, increasing or decreasing, the perception of pain. The brain areas that respond when we experience *physical* pain are the same areas that are also activated in case of *psychological*[10] pain. In particular, the areas involved are the anterior cingulate cortex and the anterior insula. Besedowsky[11] demonstrated that stress plays a significant role in the production of cortisol, a hormone able to suppress the response of the immune system. Pert[12] discovered the neuropeptides, molecules responsible for the transmission of information between the cells of the nervous system, the blood, the immune system and the intestine. The biological regulation systems interact, exchange information through neuropeptides one another, and are profoundly influenced by psychological states. Negative emotions produce a negative chemical change in the body[13].

EMOTIONAL MOTOR SYSTEM AND PELVIC FLOOR

The voluntary motor system does not have direct control of the pelvic organs, but rather, only some control of the striated muscles of the pelvic floor. The pelvic floor motoneurons are located in the nucleus of Onuf, which innervate all parts of the pelvic floor, including the external urethral sphincter and the external anal sphincter. Interestingly, the motor cortex cannot contract these muscles separately, but only as a unit. Furthermore, the motor cortex cannot continuously keep contracting the pelvic floor muscles, which means that a strong uncontrolled urge for micturition or defecation cannot be stopped for a long time, leading to urge-incontinence. The real control of the pelvic organs is through the emotional motor system. The emotional motor system also controls basic motor activities such as blood pressure, heart rate, respiration, and vocalization. An important role is played by the sympathetic and parasympathetic systems, the socalled autonomic motor systems as they cannot be controlled voluntarily by the emotional motor system. Fortunately, the sympathetic and parasympathetic motor systems are under very strong control of the emotional motor system in the brainstem and prefrontal cortex. The *sympathetic* system is especially activated when the individual has to immediately defend its existence (i.e. by fighting an aggressor or by flying from a dangerous situation [fight or flight]) or, reversely, when it has to catch animals to obtain food to survive). In contrast, the *parasympathetic* system is active in safe situations, when energy can be spent on motor activities such as eating, drinking, and digesting food. Also, the activities of the pelvic organs, such as micturition, defecation, and sexual activities, can take place only when the situation is safe. The individual eats food and digests it by activation of the stomach, duodenum, jejunum, ileum, and colon. The distal colon and *rectum* in the pelvis get rid of, as well as an important bacterial component, also the food that could not be digested. All these organs are activated by the parasympathetic system. The bladder is the pelvic organ that takes care of the urine produced by the kidneys. However, the *bladder* cannot empty itself from urine when the individual is in danger and the sympathetic system is active. In this context, the sympathetic fibers inhibit bladder contractions. The parasympathetic fibers also control the pelvic organs involved in *sexual behaviour* and the resulting pregnancy in women. The sacral parasympathetic motoneurons that innervate all the pelvic organs are specifically controlled by the so called Pelvic Organ Stimulating Center (POSC). The POSC in turn is controlled by the the periaqueductal gray (PAG) located in the mesencephalon (midbrain) the primary control center for descending pain modulation which receives, to be activated, instructions from higher brain levels such as the amygdala, bed nucleus of the stria terminalis, and various regions of the hypothalamus. The PAG also receives information regarding the situation of the individual from more rostral brain regions of which, in humans, the most important is the medial orbitofrontal cortex where it is decided whether the PAG can activate the POSC to start micturition, or defecation, or parturition or increase vaginal vasocongestion and lubrication. A possible reduction of PAG-POSC system activity causes absence of vaginal vasocongestion and lubrication[14].

VAGINISMUS

Definitions: «recurrent or persistent involuntary contraction of the perineal muscles surrounding the outer third of the vagina at attempt of penetration»[15], «whether or not associated with a variable degree of phobia of penetration»[16], «persistent or recurrent difficulty for the woman to accept vaginal penetration of the penis, a finger or an object, despite the woman's expressed desire to do it. There is often phobic avoidance and an anticipatory fear of pain. Anatomical abnormalities or other physical abnormalities must be excluded or treated»[17]. The vaginismus, from a psychoanalytic point of view, is symptom of conversion. Unresolved psychosexual conflicts are often seen as cause of the reaction: "women fear falling into the power of the man, being injured or exploded within by him. Under these circumstances, the vagina becomes in phantasy of biting organ which is going to render harmless the menacing penis"[18,19]. The physical *causes* of primary vaginismus, present from the beginning of the sexual life, are to be considered extremely rare. The main factor of "mechanical" obstacle to penetration can be connected to a particularly fibrous and rigid hymen (or cribrose or narrow) which fails to distend[20]. Other physical factors can be specific syndromes such as: Müllerian vaginal agenesis, typical of Rokitansky's syndrome, or acciden-

tal or provoked scarring in genital traumas with particular reference to infibulations associated with clitoridectomy[21]. Studies and electromyographic assessment of the levator muscle show how vaginismus can be a myogenic component that occurs with marked hypertonicity of the muscle itself with inversion of command[17]. Physical causes more frequently cause a spasm of the levator muscle that makes the coitus painful or impossible, a spasm that appears after a period of more or less normal relations, resulting in a secondary vaginismus, especially if there is also an acquired attitude of avoiding penetration[22].

Diagnostic criteria DSM (Diagnostic and Statistical Manual of Mental Disorders). Vaginismus and dyspareunia, often strictly associated but difficult to distinguish, have been incorporated into a single entry named *genito-pelvic pain/penetration disorder (GPPPD)*. The proposal to join them into a sole disorder arose from the real difficulty to differentiate these two disorders clinically. The DSM IV-TR[15] proposes a differential diagnosis between "Sexual dysfunction due to a general medical condition (dyspareunia due to physiological effects such as: insufficient vaginal lubrication, pelvic pathology due to vaginal or urinary infections, endometriosis, adhesions or vaginal scar tissue, vaginal atrophy post-menopause, fall in estrogen during breastfeeding, urinary tract irritation or infections, gastrointestinal disorders) and "Substance-induced sexual dysfunction" (dyspareunia caused, for example, by the use of fluphenazine, thioridazine and amoxapine). If dyspareunia is concomitant with one of the described dysfunctions and intrapsychic combined with interpersonal factors, a diagnosis of "Dyspareunia due to Combined Factors" will be proposed, if there are no dysfunctions due to general or substance-induced medical conditions, an evaluation of "dyspareunia due to psychological factors"[15] will be suggested. As opposed to the previous edition, the DSM-5[23] sexual dysfunction are no more included in the same category but in three distinct ones: *gender dysphoria, paraphilic disorders, sexual dysfunctions*.

DSM 5. Criteria. A) Lack or significant reduction in sexual desire/arousal due to at least three of the following problems: persistently or recurrently deficient (or absent) sexual/erotic fantasies and desire for sexual activity, reduced or no initiation of sexual activity, no response to partner's attempts, absent or reduced sexual excitement or pleasure during most sexual activity, absent sexual interest or arousal in response to sexual stimulation, absent or reduced genital or nonessential sensations during sexual activity.

B) Symptoms with six months requirement. The temporal characteristics must be evaluated, whether the disorder occurs at the beginning of the sexual-life (primary) or if it has appeared later, after a period of normal sexual function (secondary or acquired).

C) The problem causes clinically significant distress or impediments.

D) Sexual dysfunction is not better justified by another axis I* disorder. It is not due solely to the direct physiological effects of a substance or a general medical condition. In order to make a good diagnosis it is important to point out the contextual characteristics: the disorder could be of a generalized type, that is present in every situation even with possible different partners, or situational when it is limited to a partner or specific situations[24]. It is also important to assess the degree of stress ("distress") that arises as a result of the disorder[25].

In the DSM-IV **Axis I provides information about the following clinical disorders: anxiety, mood, somatoform, eating, psychotropic substance-related, dissociative, psychotic, sexual and gender identity (desire or arousal disorder, absent or early orgasm, dyspareunia, vaginismus, paraphilias like fetishism, pedophilia, masochism, sadism, voyeurism, exhibitionism).*

STUDY RESULTS

The literature review shows the efficacy of a *multidisciplinary model* in the treatment of vaginismus. The *biopsychosocial model* (BPS) is the basic structure for understanding whether a person is healthy or in illness; nevertheless this model has limitations: 1) cannot be considered scientific; 2) in the field of biological psychiatry, mental disorders derive from faulty biology; 3) the approach of "physicians" considers that the levels of biological, psychological and social analysis are or epiphenomena or can be completely reduced to the body. In fact, Ghaemi claims that the doctor who embraces the BPS model takes the serious risk of losing the limits of his knowledge and skills[26]. Biopsychosocial relational psychology assumes that mental illnesses reside in the ability of the three minds to communicate one another[4]. Critics believe that, assuming every mental disorder with a biopsychosocial model, there is the risk of increasing the gap between biology and psychology as if they were two separate fields in medicine. If a physical damage is considered exclusively from the biopsychosocial point of view, the treatment could be confused or have serious consequences. Some mental disorders can be explained by the biopsychosocial relational model but it is erroneously assumed that the model is applicable to any disease[26]. We can conclude that the biopsychosocial approach is very useful for health and health care in some situations. Pennebaker[27] stated that the perception of physical sensations is not based solely on peripheral receptor information. Situational signals seem to influence perception. Psychophysiological studies on sexual arousal in women have shown changes in the visibility of body sensations between and within subjects[28]. Van der Velde declares "we investigated the relationship between involuntary pelvic floor muscle activity during exposure to emotional film excerpts. We found an increase in pelvic floor muscle activity during threatening and sexually-threatening film excerpts[29]". From the neurobiological point of view, co-morbidity appears with various phobias and anxiety disorders[30]. At this point the vaginismic woman seems to present a neurobiological vulnerability, mainly triggered by the hyperactivity of the fundamental command emotion of anxiety/fear[31], which influences the sexual area with a specific psychosomatic penetration phobia[31]. This vulnerability could be reinforced due to other phobias (agoraphobia, acrophobia, claustrophobia, etc.)[20]. The data support the idea of a general defensive reaction as a mechanism of involuntary muscular activity of the pelvic floor[32]. The biopsychosocial relational model is a clear mean for comprehending the functioning of minds, which is easy to understand and use. According to this model the area which is activated in vaginismus is the reptilian brain, so we can no longer speak of anxiety as a signal of unread emotion or conflicting emotions, but of a signal of real danger which activates biological or primordial defenses. From the reading and the application of Benini's model, it is clear that the symptoms present in vaginismus can be phobic but the causes are deeper, stemming from the biological anguish. The term *anguish* should be used instead of the term *anxiety* when dealing with sexual dysfunctions, and technicians treating sexual dysfunctions should be aware they are not dealing with anxiety or phobia, but with an anguish of the reptilian mind. The *genito-pelvic pain/penetration disorder* is linked above all to Interest Disorder/Sexual Arousal[33]. It is to be underlined

Negative educational models and examples, ancient traumas (physical, emotional or sexual)[35]
Significant relationships; cultural or religious frustrations[36]
Over attachment to the mother figure, fear of defloration, fear of childbirth[31]
Current interpersonal difficulties, sexual dysfunction of the partner, inadequate stimulation and / or unsatisfactory emotional and sexual context[37]
List of all diseases including psychiatric disorders, side effects from taking drugs, substance abuse[34]
Desire and arousal disorders or genital arousal and dyspareunia[38]
Gynecological conditions: hormonal alterations, recurrent vaginitis, prolapse, endometriosis, natural or iatrogenic menopause [34]
Urological conditions such as recurrent cystitis, overactive bladder or urge, stress or mixed incontinence[21]
Diseases such as multiple sclerosis or pudendal nerve neuralgia[21]
Myalgia of the levator muscle and any manifestations of hypotone or hypertonus of the same[21]
Dysmetabolic disorders, among the main diabetes and cardiovascular symptoms[39]
Proctological disorders, constipation[34]

Table 1. Information and experiences to be collected in the history for the patient suffering from vaginismus. List of backgrounds checks for the construction of a survey tool.

that an accurate collection of the sexological history of the individual should be an integral part of the consultation, paying maximum attention to predisposing, precipitating and maintenance factors, both biological, psychosexual and relational, as they are factors that can certainly be an active and triggering cause of the disorder brought into gynecological (vulvar and vulvodynamic vestibulitis) and proctologyical (obstructive constipation, hemorrhoids, anal fissure) consultations[34]. The patient suffering from vaginismus must increasingly find acceptance on the part of doctors, pelvic floor rehabilitation technicians, psychotherapists and sexologists who, working with a team approach, can assess the vaginismus taking into account all aspects of the person's life, as suggested by Engel's biopsychosocial model. The patient should receive a diagnosis and a proper specialist referral. The more the patient is informed of all the factors involved in her own sexual disorders, the higher possibility of a reduction in treatment time, visible improvement of feelings of self-efficacy and decreasing of chronic illness risk, which leads to possible increase in comorbidity.

THE EFFICACY OF HYPNOSIS IN THE MEDICAL FIELD

Hypnotherapy has by now received numerous awards in the scientific field, in application disciplines, in the medical, psychiatric and psychotherapeutic fields. Studies on frequency analysis using EEG suggest a correlation between hypnotic susceptibility and theta frequency band and by the Yapko's school is highlighted that the brain of the subjects in hypnosis responds positively to the suggested experiences rather than to those actually perceived; biologically, the effects of hypnosis have been confirmed by modern imaging techniques and have shown changes in the activity of some regions of the subject's brain when suggestions in hypnosis are given[40].

Hypnosis has been found effective in many conditions: general and social anxiety[39], general phobias[39], anxiety and dental phobia in odontostomatology[39,41], post-traumatic stress disorders[39], depression[42], sleep disorders[43], eating disorders[44], obesity[45], anorexia[46], bulimia[47], sexual dysfunctions[48], acute and chronic pain[49], using the potentiality of the hypnotic analgesia[39], such as in the treatment of the fibromyalgia[39], rheumatoid arthritis[50], severe burn and childbirth pain[51,52], muscle tension headache[39], migraine[53], cancer pain and chemotherapy-induced nausea/vomiting[54], surgical and gastroenterological, dermatological invasive procedures[39,55], irritable bowel syndrome[56], psoriasis and alopecia areata[57], hypertension[39].

Hypnosis and pain. Hypnosis seems to have a good therapeutic impact in reducing therapy length and treating individual cases: the analgesic or antinociceptive effect of hypnosis is such as to reduce pain by at least 50%[39]. In a test with ischemic pain, researchers reported that highly hypnotizable subjects had an increase in pain tolerance of 113% versus a 26% increase in tolerance in poorly hypnotizable subjects[39] in reducing anxiety[58] and de-enhancing muscle rigidity. The study of the emotional motor system highlights the fundamental correlation between motor expression and psychological assumptions.

Hypnosis in female sexual dysfunctions. Hypnosis can help those suffering from sexual disorders either by accompanying the subject towards a greater awareness of the causes of dysfunction, or by providing a resolving therapeutic intervention. This, in fact, allows to face with the complex multifactorial system at the base of the disorder that often includes relational, physiological factors, false beliefs as well as any previous traumatic experiences[39,59,60].

The efficacy of hypnosis in vaginismus. Hypnotherapy provides an acceptable time and cost effective therapeutic tool that helps resolve vaginismus and improves sexual satisfaction in both spouses; although both behavior therapy and hypnotherapy were successful in treating vaginismus, hypnotherapy performed better than behavior therapy in reducing the level of the wife`s sex-related anxiety. In Pukal's[60] research 8 women suffering from vulvodynia were subjected to six hypnotherapy sessions through which different parameters have been investigated: pain reported during gynecological examinations, vestibular pain threshold and assessments about pain during sexual activity. The results reported a pain reduction during gynecological examinations and sexual activity resulting in increased satisfaction and improved sexual life in general. Meissner[61] reports the holistic approach of the Chinese Medicine and Hypnotherapy leading to a substantial pain reduction in patients affected by endometriosis, as well as an increased birth rate in patients refractory to conventional therapies. Fear and anxiety are of tremendous importance in the production and maintenance of a symptom. Vaginismus, as a reaction of avoidance of an anxiety-producing situation, is readily amenable to treatment by systematic desensitization. Fuchs[62] presented a study on the treatment of vaginismus by hypnotic desensitization with a case-controlled group: good results achieved in 16 out of 18 patients, no relapse or substitutions of symptoms occurred at 2 to 5 years follow-up. Overall, studies show that hypnosis can be a promising treatment for sexual disorders, as shown by data on patients with vulvodynia[63].

CONCLUSIONS

Despite the well documented beneficial aspects and methodological quality of many studies, the limited data on female dysfunctions, in particular concerning vaginismus as

the only variable, require further research on psychological interventions in relation to this disorder, using randomized and controlled designs and larger samples. The need arises to evaluate the *couple*, in addition to the social and relational aspects of the patient, as there is often an *inducer of the symptom*. As many as 32% of women's partners with vaginismus have sexual dysfunctions, such as desire disorder, premature ejaculation, erection disorders[64]. Studies on the use of hypnosis in vaginismus confirm its strong ability to reduce anxiety, reduce pain and relax muscles. An *intervention protocol* is needed that starts from an accurate *investigation* of the biopsychosocial dimensions, questionnaires and tests that measure the perception of physical and psychological pain only in this dysfunction, differentiating it from dyspareunia; and of a hypnotic *training* that deals step by step with the dimensions that characterize vaginismus. Furthermore, there is the need for a thorough study on the patients' ability to connect the body and emotional states restoring the dialogue between body and mind, a capacity present in each person evaluating how people can experience their emotions instead of using defenses such as rumination, avoidance or emotional freezing, and how hypnosis therapy can foster communication between the deep mind and the emotional motor system, and consequently manage painful states and muscle rigidity.

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DISCLOSURES

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Multidisciplinary UroGyneProcto Editorial Comment

To improve the integration among the three segments of the pelvic floor, some of the articles published in *Pelviperineology* are commented on by **Urologists, Gynecologists, Proctologists/Colo Rectal Surgeons or other Specialists**, with their critical opinion and a teaching purpose. Differences, similarities and possible relationships between the data presented and what is known in the three fields of competence are stressed, or the absence of any analogy is indicated. The discussion is not a peer review, it concerns concepts, ideas, theories, not the methodology of the presentation.

Behavioural med... The validity of the concept of "vaginismus" has been extensively questioned. The DSM has struggled to respond to criticisms challenging its validity as right fromits inception, vaginismus has been a descriptive term that lacked any scientific evidence. The DSM's spasm oriented diagnostic criteria and its listing of vaginismus together with dyspareunia as two separate pain disorders has confounded many researchers and clinicians. Studies utilizing surface electromyography have consistently failed to differentiate between normal controls and vaginismic women on the basis of muscle tension or spasm, thereby questioning the validity of DSM's classification system. What has been of interest is that the majority of "vaginismus" cases meet the diagnostic criteria of vulvodynia, a recognized form of chronic vulvar pain, under the classification of the International Society for the Study of Vulvovaginal Disease (ISSVD). When theory and conjecture is set aside, hypnosis as a form of relaxation may aid in reducing the severity of penetration related pain, but this is yet to be demonstrated.

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Urol... The close correlation between emotional motor system and pelvic floor is well known. In this context, vaginismus is the result of a skeletal muscular hyperactivity that is activated for pain relief. From a urological point of view, pelvic pain may cause not only vaginismus but also dysuria due to a failure to relax the external urethral sphincter, for the same reasons for which vaginismus is determined. In other words, very often vaginismus is not an isolated symptom but it may be also associated with dysuria and in some cases also with anal hypertonus. In these cases the hypnosis could determine a positive effect for the improvement of the vaginismus due to a reduction of the skeletal muscular hyperactivity of the pelvic floor with a consequent improvement of micturition, This condition in urology is more evident in *women* and is defined by some as *urethral syndrome*. In *males* the urethral syndrome is often confused with *prostate* hypertrophy or chronic infection.

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Gyn... In obstetrics, the "vaginismic women " have high rate of labor dystocia and perineal morbidity. Interesting, in women with sexual disorders there is an abnormal activation of Pelvic Organ Stimulating Center (POSC) that trigger the obstetric labor starting from pelvic floor modifications, by parasympathetic innervation. Indeed, to contain the fetal body during vaginal delivery, the pelvic floor muscles must stretch and slide each other in their three different layers of deepness (levator ani, deep trasversus and superficial trasversus perinei). In "vaginismic women" with such alteration of neuronal transmission, this process can be more difficult. The proven efficacy of hypnotherapy also in labor delivery, as in vaginismus can confirm the common origin of these muscular "dystocias ". It is interesting the couple approach with hypnotherapy in vaginismus, since it is not surprising that as many as 32% of vaginismic women's partners have sexual dysfunction, the author says.

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Proctol... Trying to cure a functional hypertonus of the internal and external sphincters (in the absence of painful lesions such as anal fissure), considering it as responsible of obstructed defecation, may produce iatrogenic damages. A basal pressures of 100 mmHg or more is high but it does not mean constipation, while the lack of sphincter inhibitory reflex in megarectum is a real internal sphincter problem. A non relaxing or paradoxically contracting external sphincter at straining in analogy with *vaginismus* has been initially defined *anismus*, or *inverted command* or sphincter *dyssynergia*. These conditions, the causes of which are not known, often suggest possible connections between viscera and emotions, and are cured by rehabilitation, in this way improving the difficult defecation if present. It is interesting to note that hypertonicity and dyssynergia are also highlighted in the so-called anodyspareunia in anal coitus in males and females.

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