Vol. 30 - N. 2
June 2011

Rivista Italiana di Colon-Proctologia
Founded in 1982

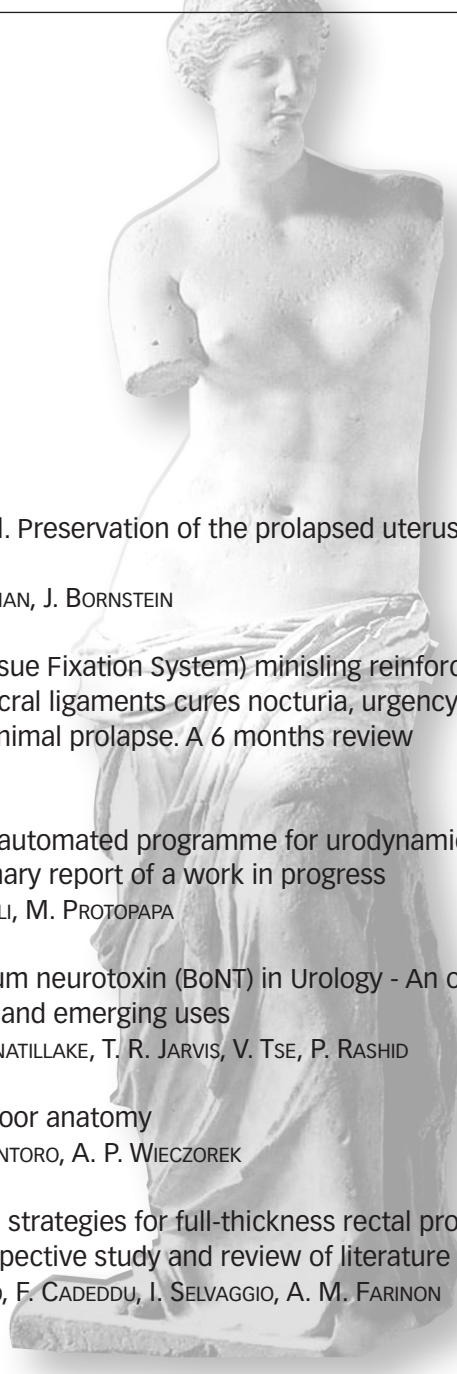
ISSN 1973-4905

PELVIPERINEOLOGY

A multidisciplinary pelvic floor journal

ANNOUNCEMENT

Pelviperineology is open access in the web. In 2010 **www.pelviperineology.org** and **www.pelviperineologia.it** have been visited over 100.000 times. Some printed copies of the journal are distributed free by sponsors. If you wish to receive all issues of the printed journal, unless this is provided by your scientific society, send your name and full postal address to **subscriptions@pelviperineology.org**, and pay a 30,00 € yearly fee to the **Integrated Pelvis Group** via Paypal account (see the instructions in the website **www.pelviperineology.org**).



Contents

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

Why?

PSYLLOGEL® fibra

In case of...

... Constipation, Hemorrhoids, Pelvic floor diseases.

The most natural way to promote, restore and maintain **regularity**.

Psyllium is the strongest natural dietary fiber for promoting regularity and supporting benefits overall health. Psyllium has low fermentation; this gel provides lubrication that facilitates propulsion of colon contents and produces a stool that is bulkier and more moist.

AVAILABLE IN THE TASTES:

Red orange | Strawberry | Lemon tea | Cocoa | Vanilla

PSYLLOGEL® fibra
The leader in **psyllium fiber 99% purity**.

Informations reserved to the doctors and pharmacists
IN PHARMACY

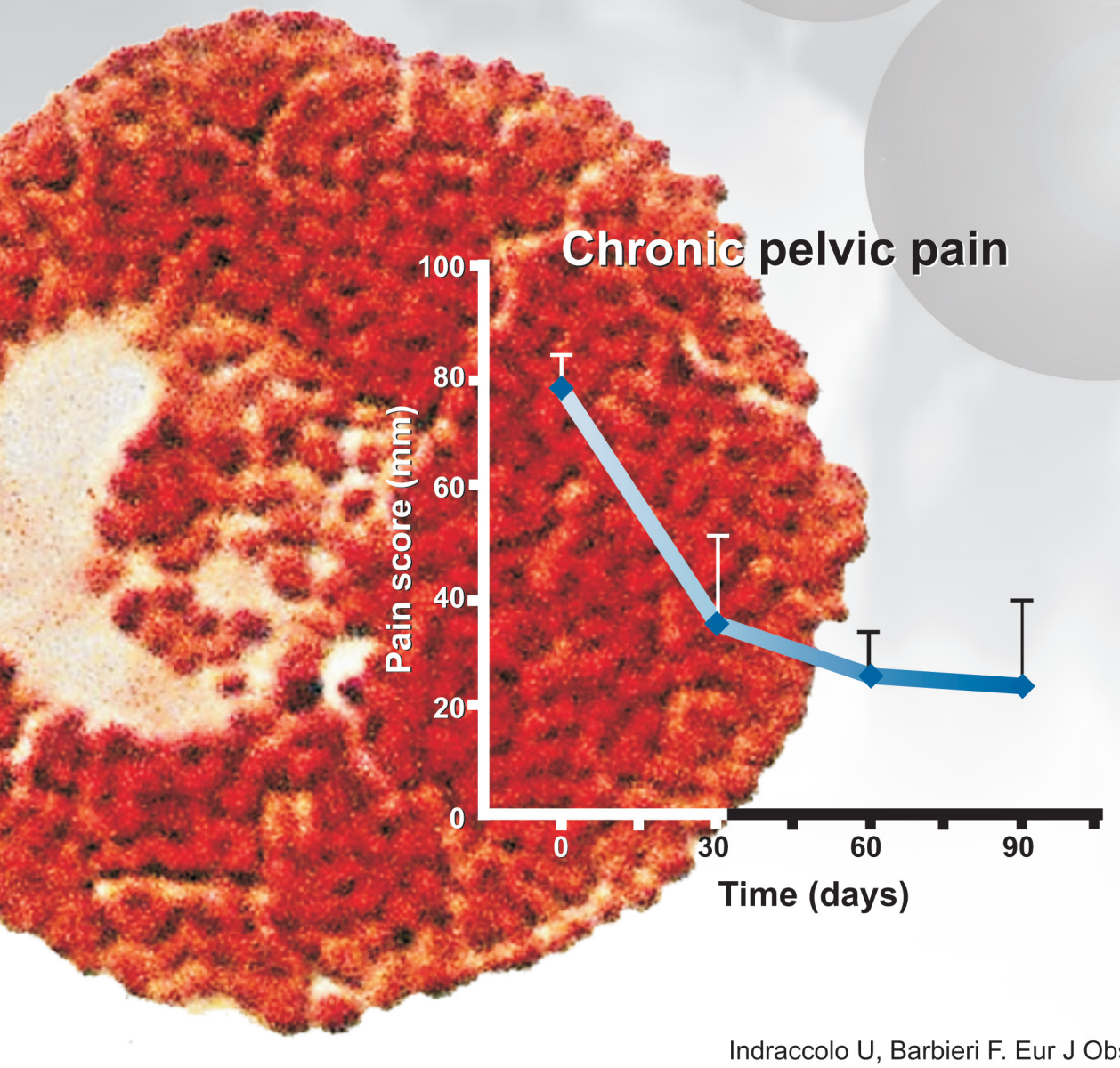
NATHURA SRL - Tel. +39 0522 865464 - www.nathura.com - nathura@nathura.com
UNI EN ISO 9001:2008 QUALITY MANAGEMENT SYSTEM CERTIFIED BY CERTIQUALITY

NATHURA®
Nutrizione Scientifica

Pelvilen®

(Palmitoylethanolamide + Polydatin):

a novel approach to pelvic pain



Indraccolo U, Barbieri F. Eur J Obstet Gynecol (2010)

epitech group SRL

Via Luigi Einaudi, 13
35030 Saccolongo (PD)
Italy
tel +39 049 8016784
fax + 39 049 8016759
info@epitech.it
www.epitech.it

epitech
Pelvic System
project

Vol. 30
N. 2
June 2011

Rivista Italiana di Colon-Proctologia
Founded in 1982

PELVIPERINEOLOGY

A multidisciplinary pelvic floor journal

www.pelviperineology.org

Official Journal of the: International Society for Pelviperineology (www.pelviperineology.com)
(the former Australasian Association of Vaginal and Incontinence Surgeons)
International Pelvic Floor Dysfunction Society
Pelvic Reconstructive Surgery and Incontinence Association (Turkey)
Perhimpunan Disfungsi Dasar Panggul Wanita Indonesia
Romanian Uro-Gyn Society

Editorial Office: Enrico Belluco
c/o Clinica Chirurgica 2 University of Padova, 35128, Padova, Italy
e-mail: **editor@pelviperineology.org**
Quarterly journal of scientific information registered at the Tribunale di Padova, Italy n. 741 dated 23-10-1982
Editorial Director: Giuseppe Dodi
Printer "Tipografia Veneta" Via E. Dalla Costa, 6 - 35129 Padova - e-mail: info@tipografiaveneta.it

ISPP ANNUAL SCIENTIFIC MEETING

www.pelviperineology.com

INTERNATIONAL PELVIPERINEOLOGY CONGRESS

SYDNEY, AUSTRALIA
OCTOBER 6-9, 2011

COCKLE BAY WHARF

DOCKSIDE - DINNER

DOCKSIDE - THEATRE

PLENARY SESSIONS

CADAVER WORKSHOPS
1. Slings and roundabouts (American Medical Systems)
2. Sacral Neuro-Modulation (Medtronic)

SPECIAL SYMPOSIA
In faecal incontinence and male urinary incontinence
Urology, coloproctology, gynaecology

PELVIPERINEOLOGY
Emphasising the multi-disciplinary approach to the assessment and treatment of pelvic pathology

Following the Annual General Meeting of AAVIS in Vienna last September AAVIS has become the International Society for Pelviperineology. The change of name reflects the fact that AAVIS has evolved into an international and multidisciplinary pelvic floor society. Once again we will be holding our Annual Scientific Meeting and International Pelviperineology Congress. The venue for the meeting is Dockside Convention Centre at Darling Harbour in Sydney with special Cadaver Workshops at Macquarie University. Plenary sessions will be held at Dockside on October 7th and 8th 2011 with workshops at Macquarie on October 9th. Social activities will include a welcome cocktail party on Thursday 6th October and a conference dinner on Friday 7th October.

Editorial

Preservation of the prolapsed uterus in pelvic surgery

(Presented at the 12th Annual AAVIS/ISPP Scientific Meeting, 2010, Vienna)

- *Is uterine prolapse an (absolute) indication for vaginal hysterectomy?!*
- *Is vaginal hysterectomy an (essential) part of pelvic floor reconstruction?!*
- *Is the uterus an innocent victim?*
- *Are we performing vaginal hysterectomies only because we were trained to?*
- *Hysterectomy is a complication related operation*
- *Hysterectomy mutilates physiologically the patient*
- *Hysterectomy defects the endo-pelvic fascia integrity and makes the pelvic floor vulnerable*
- *Hysterectomy impairs the pelvic floor blood supply, increasing the risk of vaginal mesh exposure*
- *Preservation the Uterine isthmus provides the benefit of recruiting the cervical ring and the attachments to it's ligaments for reinforcement*

Pelvic organ prolapse (POP) herniation concept: *POP is actually bulging of viscera through weakened pelvic floor and vaginal walls. Terms used to describe the pelvic organ prolapse in general, and particularly post hysterectomy vaginal vault prolapse could be easily replaced by simply stating the specific herniation process. Cystocele and urethrocele are then herniation of the anterior compartment of the pelvic floor. Uterine, uterine cervix and post-hysterectomy vaginal vault prolapse are all central pelvic floor herniation and enterocele, rectocele and perineal body tear are herniation of the posterior compartment of the pelvic floor. Endorsement of this approach improves the understanding of the underlying process and points to the appropriate therapeutic tools elected for cure, based on the knowledge accumulated regarding hernia repair at other regions of the human body.*

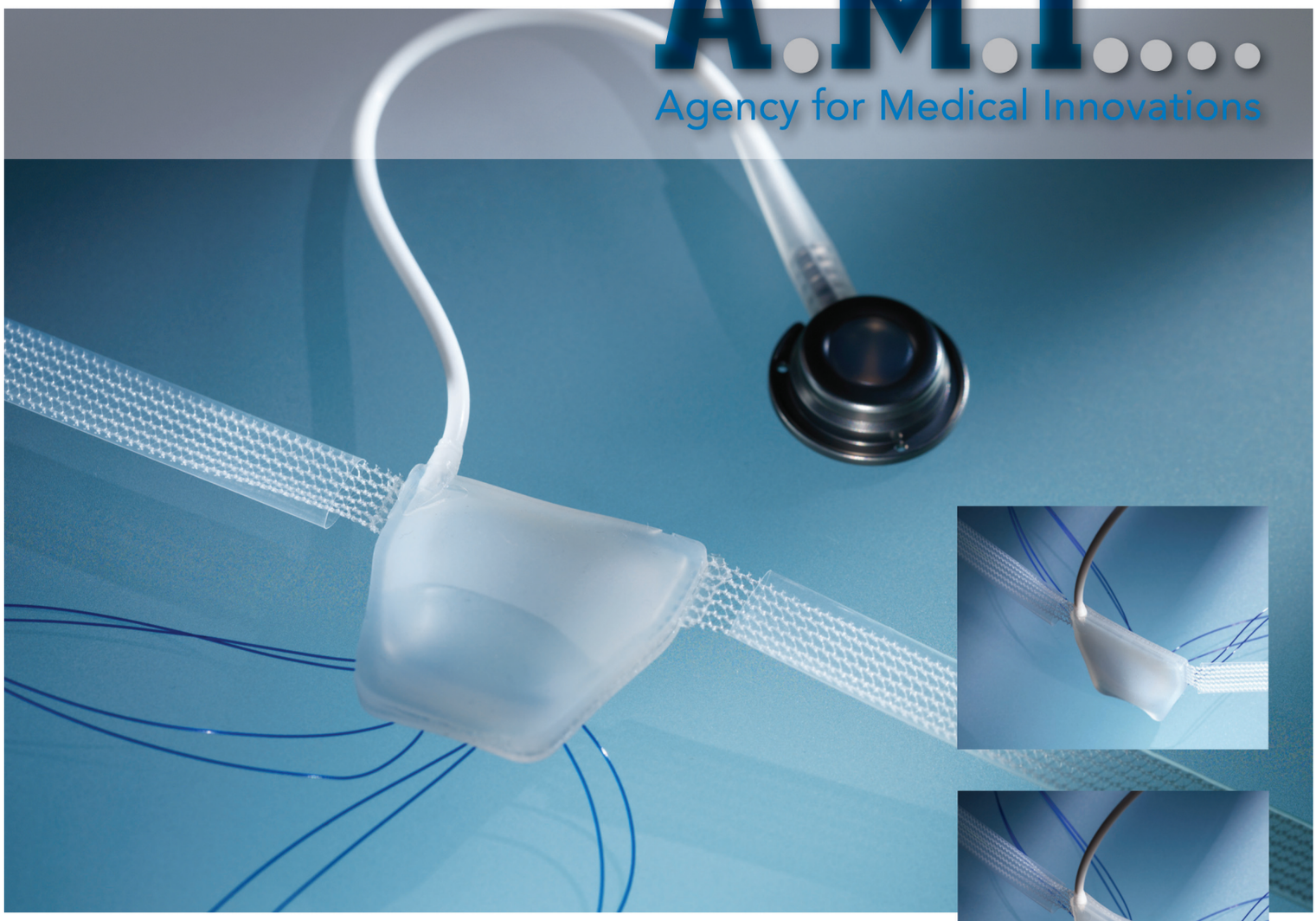
POP reconstruction architectural design: *comprehensive pelvic floor anatomic-functional approach should be based upon solid long lasting suspension of the vaginal vault apex to well establish pelvic sustained structures. Among such are the ATFP (Arcus Tendineus Fascia Pelvis) and the SS (Sacro-Spineous) ligament. The first lays along the lateral border of the levator ani muscles, from the inferior pubic ramus and the obturator membrane anteriorly to the iscial spine posteriorly and the second connects the iscial spine to the sacrum. Another anchoring option is the pre-sacral fascia, which longitudely covers the sacral vertebra and provides a solid structure which might serve as a suspensory point to secure the vaginal apex to. Attaching the vaginal vault to one of these ligaments will yield a long lasting apical support, permitting restoration of the impaired pelvic floor and organs functions. Some advocates the pre-sacral fascia, as it is easily reached via the peritoneal cavity, either by laparotomy or by laparoscopy, while others are against because of relatively high rates of intra and post operative bleeding potential, prolapse recurrence and difficult vaginal access. The ATFP, being relatively easily accessed via vagina is elected by some for vaginal vault support, and others will go for the SS ligament, saying this is the most stable pelvic structure, hence providing the best and longest standing support. Deep pelvic dissection, wider than for the ATFP, is necessary for reaching the SS. The cardinal and the utero-sacral ligaments are other potentially usable supportive pelvic anchoring points, yet not easily identified and often obscure. Unfortunately, there is no comparative data to guide any evidence based decision making regarding the preferred pelvic supportive connective tissue, rather than experts opinions.*

Post hysterectomy vaginal vault prolapse versus repair of vaginal vault prolapse while the uterus is in situ: *the un-removed uterus offers the surgeon solid central pelvic encoring points such as the cervical ring or the uterus itself. These organs might then both be attached to various solid structures at the pelvic side-walls, as the SS, sacro-uterine, ATFP or the pre-sacral ligaments. Being connected to the cervico sacral, cardinal and cervico-pubic ligaments provides the spared cervical ring extra sustainability for the pelvic floor, arising out of recruitment these web architecture structures to the pelvic reconstruction. This perspective challenges the widely endorsed practice of reflective appointment for vaginal hysterectomy with any uterine prolapse diagnosis, trained at many centers and performed routinely around the globe. Solid data regarding the question whether should the prolapsed uterus be removed are not available currently. Yet, some level 2 evidence supports the preservation of the prolapsed uterus or the uterine cervix at least, potentially guiding a change with the common attitude of automatic indication towards vaginal hysterectomy whenever POPS is present. The direct disadvantages of hysterectomy regarding pelvic floor reconstruction are the damages to the endo-pelvic fascia integrity, vasculature, blood supply and innervation and the deprivation of the advantage of using the cervical ring and the web of connected ligaments for providing extra strength to the pelvic floor architecture. All these are extremely important for maintaining further pelvic floor sustainability and functions. Performing hysterectomy concomitantly with mesh pelvic floor reconstruction increases significantly the risk of post operative mesh vaginal exposure and the need for further operative intervention to cure this complication. Not rare is the occurrence of vaginal shortening after hysterectomy, to such degree that impairment of sexual intercourse. Except of the negative influence on the pelvic floor structure and functions, entails vaginal hysterectomy many operation related complication, some of are health and life threatening, and it might also physiologically mutilate the disregarded hysterectomized patient's body image and self esteem. Minimally invasive novel methods for the treatment of menorrhagia, endometrial polyps and uterine myomas as well as increasing public awareness against preventable hysterectomies lead towards preservation of the prolapsed uterus.*

MENAHEM NEUMAN, JACOB BORNSTEIN
[1]*Urogynecology, Ob-Gyn, western Galilee hospital, Nahariya, Israel*
mneuman@netvision.net.il

A.M.I.®

Agency for Medical Innovations



The first adjustable transobturator system for male urinary incontinence.

ATOMS by A.M.I.®

- **Easy, firm attachment without fasteners or screws**
  The mesh tapes are positioned around the inferior pubic bone and secured to the cushion with the sutures

- **Long-term fine-tuning without surgical intervention**
  Patient-specific adjustment of the cushion pressure can be made at any time via the port

A.M.I. GmbH . Im Letten 1 . 6800 Feldkirch . Austria . t +43 5522 90505 0 . f ext. 4006 . info@ami.at . **www.ami.at**

Original article

TFS (Tissue Fixation System) minisling reinforcement of uterosacral ligaments cures nocturia, urgency, frequency, even with minimal prolapse. A 6 months review

STEFANO DATI

IP1D Chirurgia Uroginecologica Ospedale Policlinico Casilino - Roma

Abstract: *Background*: Nocturia is said to have no known cause or treatment. The aim of the study is to help 12 patients with severe nocturia, urgency and frequency given no other hope of cure by minimally invasive surgical reinforcement of damaged uterosacral ligaments. Exclusion criteria: patients with other pelvic symptoms such as stress incontinence. *Materials and methods*: Twelve patients with frequency, urgency, nocturia of serious entity, with POP-Q stage 1, without prior hysterectomy or stress urinary incontinence, were selected for the study. Median age was 63.2 years (37-81), BMI 27.8 (19-44), parity 2.1. Posterior TFS minisling operation with transvaginal access was performed to reinforce the uterosacral ligaments. *Results*: Mean operating time was 15′, with no intra/perioperative complications, and mean hospitalization time 2 days. Review at 3 and 6 months with the ICIQ-N QoL questionnaire showed average score reductions from 7.8 to 2.7 for frequency and 7.2 to 1.9 for nocturia. The score for the OAB questionnaire reduced from 17.6 to 9.8. The cure-rate of symptoms was 62.5% for frequency, 75% for nocturia, and 66.7% for urgency, with no age-related differences. *Conclusions*: The use of the TFS has allowed us to verify, albeit on short follow-up, that this mininvasive procedure can also be applied solely towards the resolution and/or improvement of symptoms which limit the QoL in patients with severe symptoms of nocturia, frequency and urgency without major POP. It is therefore applicable to elderly patients, even with tissues of poor quality.

Key words: Nocturia; Urgency; Frequency; TFS; Posterior Sling; Integral Theory.

INTRODUCTION

In a recent review,[1] Van Kerrebroek et al stated that "Unlike other LUTS (lower urinary tract symptoms), nocturia has a specific and detrimental effect on the sleep period, and when ≥2 voids per night are experienced, it is associated with various sequelae including reduced QoL and productivity, and increased morbidity and perhaps mortality. Many sources suggest that nocturia is associated with chronic medical illness, but little evidence demonstrates that successful treatment of these conditions results in normalization of nocturia. It is likely that more than one contributory factor is responsible for nocturia, and management ought to better reflect this multifactorial pathophysiology. Indeed, traditional perspectives assuming nocturia to be part of the OAB or BPE symptom complex may have helped to propagate the misconception that therapy for these conditions is sufficient to improve nocturia. In reality, improvements in nocturia with anticholinergics, alpha blockers and/or 5 alpha reductase inhibitors have been consistently disappointing. Antidiuretic therapy may represent a more tailored approach to management for many nocturia patients, given the high rates of nocturnal polyuria reported. Combination therapy may be required. Further high quality research on pathophysiology, management and patient-reported outcomes with treatment is needed to augment existing limited data." The authors discuss the relationship between diabetes insipidus and nocturia, its treatment with Desmopressin, but warn of the failure, indeed, hazard of such treatment in other cases of nocturia. Another perspective is provided by the Integral Theory,[2] that nocturia is part of the "posterior fornix syndrome",[2] a grouping of symptoms deriving from the posterior zone of the vagina (figure 1). The Integral Theory which has an integrated and dynamic anatomic approach to pelvic floor dysfunction, is based on the principle that the organs are suspended by bands, maintained in suspension by ligaments connected and straightened muscle forces acting in turn in the opposite direction to the ligaments, determining the form and resistance (analogy of suspension bridge). A deficiency of ligaments and bands undermines the pelvic floor structural integrity by altering the balance of muscular tensions. The Visual Diagnostic Algorithm, (figure 1), represents the clinical expression of the Integral Theory. It visually depicts the correlation between symptoms and connective tissue damage (bands/ligaments). The algorithm identifies ligament damage in 3 different anatomical areas. Therefore, the importance of an accurate diagnosis, to locate the damaged structure, is the prerequisite for the choice of the surgical site-specific options for ligament repair offered by the TFS (Tissue Fixation System) tape, on the basis of the principle that the "restoration of shape (structure) leads to the restoration of function".[3] According to the theory, structural deficit of ligaments of the rear zone (uterosacral ligaments 'USL') allows excessive descent of the bladder base during filling, providing an early stimulus on the bladder base stretch receptors. At night, in the supine position, the uterosacral ligaments become an important support system for the filling bladder, (figure 2). The afferent impulses travel to the pontine centre of urination, to activate the micturition reflex (voiding reflex), eluding the cortical inhibitory closure mechanism "C", (figure 2).[3] The patient experiences this as symptoms of urgency, frequency, nocturia ("posterior fornix syndrome"). The TFS minisling (Tissue Fixation System), through 2 small polypropylene anchors and the attached tape, when inserted into the uterosacral ligaments[4] and then tensioned, uniquely restores the position and tension of the uterosacral ligaments, allowing the pelvic muscles to now effectively tension the vagnal membrane during the day (urgency,frequency control) and at night (nocturia control). The polypropylene tape reinforces the linear strength with the deposition of collagen, "neoligament formation".[5]

Background to the study. A tertiary referral urogynecological clinic in Rome. Only patients with severe symptoms of nocturia, urgency and frequency, who had only minimal prolapse, who had failed conventional drug therapy, and who had been advised that they had no hope of cure with existing conventional therapy, were selected for the study. On the basis of results from a previous study which reported high cure rates for nocturia, frequency and urgency,[4] and that the proposed intervention (TFS posterior sling)

was a minimal operation with few reported complications, it was recommended to patients that they had a reasonable hope for longer term cure with this procedure, with minimal if any sequelae if it failed.

Inclusion criteria. Patients with severely affected quality of life due to their symptoms of nocturia, urgency and frequency, who had only minimal prolapse.

Exclusion criteria. Patients with other pelvic symptoms such as stress incontinence, fecal incontinence.

Aim of the study. The primary goal of our preliminary study, was to help those patients with severely affected quality of life due to their symptoms of nocturia, urgency and frequency, patients who were given no other hope of cure. A secondary aim was to challenge the Integral Theory's prediction that nocturia was mainly a result of damaged uterosacral ligaments.

Written informed consent was obtained from all the study participants. No Ethics Committee approval was required for the studies as the TFS had already been approved by the Hospital Board as a standard surgical procedure. The principles outlined in the Declaration of Helsinki were followed.

MATERIALS AND METHODS

Between January 2009 and June 2010, we selected 12 patients from our Urogynecological Clinic who after full urogynecological work-up, complained of at least 2 of the triad of symptoms frequency, urgency, nocturia said to originate from the posterior vaginal fornix[4] of serious entity, with POP-Q staging 1 (Aa-2, Ba-2, C-6, Ap-2, Bp-2) and in the total absence of stress urinary incontinence (subjective/objective/urodynamic). Median age was 63.2 years (37-81), BMI 27.8 (19-44), parity 2.1.[1-4] None of the 12 patients had been subjected to hysterectomy. According to the Visual

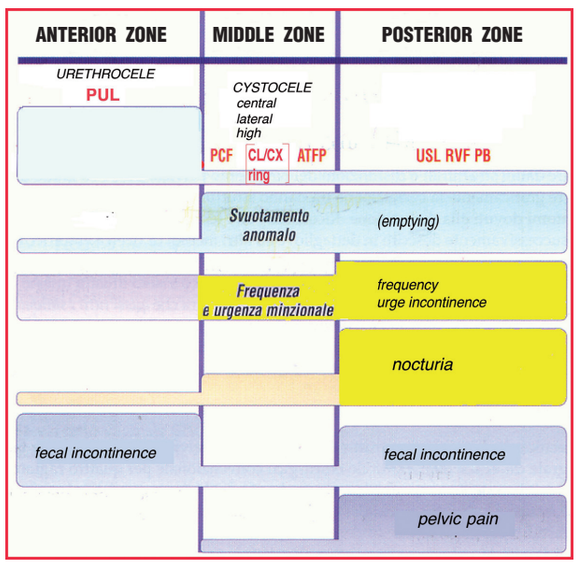


Figure 1. – Visual diagnostic algorithm. Symptoms are related to ligamentous laxity in 3 zones of the vagina. The areas in yellow denote the basis for diagnosing that the origin of the frequency, urgency and nocturia symptoms addressed in this study was from damaged uterosacral ligaments. The red letters below the prolapses denote the ligaments which can be repaired by the TFS: PUL, pubourethral ligament; PCF, pubocervical fascia; CL/CX ring, the cardinal ligament/cervical ring complex; ATFP, Arcus Tendineus Fascia Pelvis; USL,uterosacral ligament; RVF, rectovaginal fascia; PB, perineal body. Adapted from Pelviperineology[6] by permission.

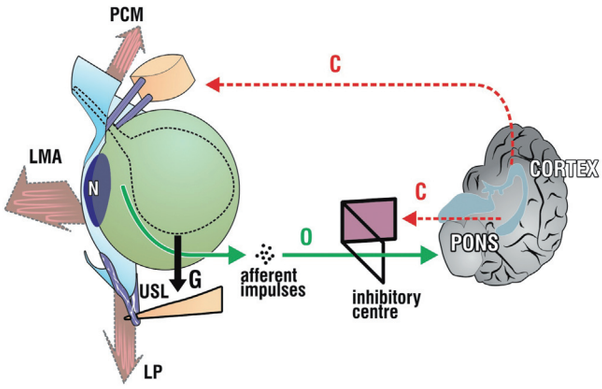


Figure 2. – Mechanical origin of nocturia- patient asleep. Pelvic muscles (arrows) are relaxed. As the bladder fills, it is distended downwards by gravity G. If the uterosacral ligaments (USL) are weak it continues to descend until the stretch receptors 'N' are stimulated, activating the micturition reflex once the closure reflex 'C' has been overcome. Printed by permission.[3]

Diagnostic Algorithm, clinical symptoms reported (frequency, urgency, and nocturia) were related to structural damage of the connective tissue of the rear area.[6] According to the psychometric validated questionnaire ICIQ-N QoL,[7] the average score was 7.8 for frequency and for nocturia 7,2. This was severely impairing the quality of life; the questionnaire OAB score average for urgency was s.f.=17.6. On full urodynamic examination, 9 of the12 patients had hyperactivity of the detrusor with reduced compliance and CVF < 280 ml. Of 12 patients symptoms frequency was present in 8, nocturia in all, and urgency in 9.

The patients have undergone intravenous antibiotic prophylaxis with ceftazidime + metronidazole, and the procedure was performed under spinal anestesia.

Posterior TFS minisling operation with transvaginal access was performed.[8] A transverse incision 2,5 cm. long was made in the apex 2 cm. from the cervix, to facilitate the identification of 2 uterosacral ligaments with Allis forceps. The apex was stretched towards the introitus to stretch the uterosacral ligaments, and one finger was placed in the rectum to identify them. A tunnel approximately 4 cm long was now made with fine scissors angled 30° to the vertical through the ligaments. The TFS surgical applicator was placed into the channel angled 30° to the vertical, and pushed so as to penetrate the ligament approximately 2 cm distal to its insertion into the sacrum. This protocol avoids the ureter which is supero-medial, and the rectum also. Pressing the applicator button releases the 1st anchor which is then checked for grip by pulling it gently. The procedure is repeated on the contralateral side, and holding the applicator firmly, grip of the 2nd anchor is also tested, exercising traction on the tape. Redundant tape is then cut, and the fascia overlying the tape is approximated with a No1 Vicryl suture. The tape is lightweight, and is specially knitted from polypropylene monofilament fibrils. It is macro-porous and non-stretch, and it forms an artificial neoligament.

RESULTS

The average operating time was 15′. There were no intra/perioperative complications, no ureteric/rectal perforations, no abscesses/haematomas, and no postoperative buttocks pain. The mean hospitalization time was 2 days. Review at 3 and 6 months with the ICIQ-N QoL question-

naire showed an average score = 2.7 for patients treated for frequency and 1.9 for those treated for nocturia . The score of the OAB questionnaire was 9.8. The cure-rate of the symptoms was 62.5% for frequency, 75% for nicturia, and 66.7% for urgency. The results of the questionnaires did not reveal any age-related differences.

DISCUSSION

In a previous study on TFS surgical reinforcement of the uterosacral ligaments,[4] 28 of the 67 patients who had only minimal prolapse reported high rates of cure with major pelvic symptoms such as urgency, frequency, nocturia, abnormal emptying, pelvic pain and fecal incontinence.

Other investigators have confirmed that all these symptoms can be cured/improved by a posterior sling.[9-13] However, the wide diversity of such symptoms stated to be cured/improved, made it difficult for our team to challenge the full array of "posterior zone" symptoms, fig1, in the tightly controlled way which science demands. The prediction that nocturia, urge incontinence and frequency were ultimately said to be different clinical expressions of a normal but prematurely activated micturition reflex,[14,15] gave us the opportunity for a simple tightly controlled clinical trial, that if we could repair the uterosacral ligaments, we could repair the function, and its clinical manifestations (nocturia, urge incontinence and frequency) in this severely affected group of patients. The emergence of the Tissue Fixation System (TFS) gave us the correct surgical (and ethical) tools to attempt both goals. The TFS is a very minimal technique with very few reported short or long-term complications. It directly reinforces specific ligaments, in this study, the uterosacral ligaments, and it tensions the lax vaginal membrane, a critical part of the stated pathogenesis.[2-4] Questions remain about the longer term prospects for cure. Shull et al.[16] observed in 1992 that herniations, usually in other parts of the vagina, occur in up to 38% of patients following vaginal surgery. Therefore we could predict that some patients may present with recurrence of urgency in the future, as urgency may be caused by any zone in the vagina, for example, a subsequent cystocele. The longer term results for nocturia may possibly be more encouraging. At least for apical/uterine prolapse surgery using the TFS posterior sling, the results reported are 86% cure at 3 years.[8] The perspective from our clinic is that subsequent symptoms or prolapse are bound to occur in some, perhaps many patients, given the deterioration of collagen/elastin with age,[3] but they can be potentially addressed using the same TFS method for connective tissue repair, albeit applied in another part of the vagina.

CONCLUSION

The use of the TFS minisling in the treatment of nocturia, frequency and urgency as part of the posterior fornix syndrome symptoms has allowed us to verify, albeit on an initial causal basis, and short follow-up, that the severity of symptoms is not related to the magnitude of prolapse, and that this minimally invasive procedure can also be applied solely towards the resolution and/or improvement of symptoms which limit the QoL, in patients without major POP. It is therefore applicable to elderly patients, even with tissues of poor quality. It is our hope that this study will be a catalyst for not only further studies on urgency and nocturia in females, but also to test other predictions of the theory, such as pelvic pain, abnormal emptying, and idiopathic fecal incontinence, all major causes of debility in the aged.

REFERENCES

1. Van Kerrebroeck P, Dmochowski R, FitzGerald M, Hashim H, Norgaard P Robinson D and Jeffrey Weiss J. Nocturia Research: Current Status and Future Perspectives, Neurourol. Urodynam. 2010; 29:623-628.
2. Petros PE & Ulmsten U. An Integral Theory and its Method, for the Diagnosis and Management of female urinary incontinence. Scandinavian J of Urol 1993; Supp 153:1-93.
3. Petros PE. Chapter 2. The Anatomy and Dynamics of Pelvic Floor Function and Dysfunction, 14-47. In: The Female Pelvic Floor. Function, Dysfunction and Management, According to the Integral Theory. Heidelberg: Springer, 2004.
4. Petros PE, Richardson PA. TFS posterior sling improves overactive bladder, pelvic pain and abnormal emptying, even with minor prolapse. A prospective urodynamic study. Pelviperineology 2010; 29: 52-55 .
5. Petros PE & Ulmsten U and Papadimitriou J. The Autogenic Neoligament procedure: a technique for planned formation of an artificial neo-ligament. Acta Obstetricia et Gynecologica Scandinavica, 1990; Supp 153:43-51.
6. Petros PEP The Integral Theory System, a simplified clinical approach with illustrative case histories. Pelviperineology 2010; 29: 37-51.
7. Abrams P, Avery K, Gardener N, Donovan J on behalf of the ICIQ Advisory Board, The International Consultation on Incontinence Modular Questionnaire: www.iciq.net. The Journal of Urology 2006; 1063-1066
8. Petros PE Richardson PA. A 3 year follow-up review of uterine/vault prolapse repair using the TFS minisling. RANZJOG 2009; 4: 439-440.
9. Sivaslioglu AA, Gelisen O, Dolen I, Dede H, Dilbaz S, Haberal A. Posterior sling (infracoccygeal sacropexy): An alternative procedure for vaginal vault prolapse. Australian and New Zealand Journal of Obstetrics and Gynaecology 2005; 45: 159-160.
10. Farnsworth BN. Posterior intravaginal slingplasty (infracoccygeal sacropexy) for severe posthysterectomy vaginal vault prolapse. A preliminary report on efficacy and safety. Int Urogynecol J Pelvic Floor Dysfunct 2002; 13: 4-8.
11. Inoue H, Sekiguchi Y, Kohata Y, SatonoY, HishikawaK, Tominaga T, and Oobayashi M. Tissue Fixation System (TFS) to repair uterovaginal prolapse with uterine preservation: A preliminary report on perioperative complications and safety J. Obstet. Gynaecol 2009; 2: 346–353 .
12. Abendstein B, Brugger BA, Furtschegger A, Rieger M, Petros PE. Role of the uterosacral ligaments in the causation of rectal intussusception, abnormal bowel emptying, and fecal incontinence,a prospective study. Pelviperineology 2008; 27:118-121.
13. Abendstein B, Petros PE, Richardson PA. Ligamentous repair using the Tissue Fixation System confirms a causal link between damaged suspensory ligaments and urinary and fecal incontinence. Pelviperineology 2008; 27:114-117.
14. Petros PE, Ulmsten U. Bladder instability in women: A premature activation of the micturition reflex. Neurourology and Urodynamics 1993; 12: 235-239.
15. Petros PE. Is detrusor instability a premature variant of a normal micturition reflex? Lancet 1997; 9060: 1255-6.
16. Shull BL, Capen CV, Riggs MW and Kuehl TJ Preoperative and postoperative analysis of site specific pelvic support defects in 81 women treated with sacrospinous ligament suspension and pelvic reconstruction. J Obstet Gynecol 1992; 166: 1764-71.

Correspondence to:
STEFANO DATI
Via Tolmino 12
00198 Roma
e-mail: stefanodati@virgilio.it

Original article

A semi-automated programme for urodynamic diagnosis: preliminary report of a work in progress

GIANCARLO VIGNOLI (*), MASSIMO PROTOPAPA (**)

(*) Urodynamics and Urogynecological Unit, Casa Madre Fortunata Toniolo, Bologna, Italy
(**) HC ITALIA srl, Milan, Italy

Abstract: A semi-automated computer diagnostic programme, titled *UDS ASSISTANT*, that can be used by physicians and medical professionals has been devised. The algorithms were developed basing on reference publications (ie, ICS standardization of terminology, ICI reports, Good urodynamic practice) and some urodynamic textbooks (Abrams' Urodynamics, Chapple's Urodynamics made easy, Nitti's Pratical Urodynamics). The programme assists the examiner in making a urodynamic diagnosis from the data recorded during the examination. Data are currently entered manually by the examiner, but after a large-scale validation of the method, we don't exclude a totally automated diagnosis through a direct post-processing of the traces. The software may be an important diagnostic aid for those who are not particularly expert in urodynamics. Furthermore, basing the diagnosis on objective criteria of an algorithm sheet more than on subjective interpretation of traces, it may reduce the inter- and intra-observer variability that is one of the main restrain of current urodynamic investigation.

Key words: Urodynamics; Diagnostic software; Computer-assisted diagnosis.

INTRODUCTION

In recent years the role of urodynamics in the assessment of lower urinary tract dysfunctions has become contentious.[1,2] Urodynamics is not an esoteric concept of limited applicability to be confined to the "ivory towers". Urodynamics may be questioned, but its basic principles are simple and in most cases it doesn't need complex mental efforts. However, some recent reports indicated that most of the time the personel carrying out urodynamics have little understanding of what the recordings mean.[3,4] The need of developing a urodynamics curriculum for urology residents has been recently addressed by some publications.[5,6] Indeed, in the Author's experience, there are instances of recordings still being sent to the equipment manufacturer for their interpretation! In cardiology the automatic interpretation of ECG is in use by at least 40 years and most of the electrocardiographs in current use are equipped with a diagnostic software with significant advantages for doctors and/or technicians who deal with more than hundred ECG tracings every day.[7,8,9] A urodynamic diagnostic software may be a useful tool to the beginners or where a doctor is not easily available, a situation quite common in a urodynamic lab. Furthermore, even among experts, interpretation of the tests is not always straightforward, resulting in a high intra- and inter-interpreter variability. The rigid criteria of the diagnostic algorithms should reduce the subjective interpretation of the tracings thereby reducing the inter-observer and intra-observer variability.

MATERIALS AND METHODS

The UDS ASSISTANT diagnostic software, developed by the second Author, is a Windows based program designed in Borland Delphi. The system acts as a black board in the sense that when faced with input data it gives an answer.[10] It's a unique file providing to install itself and generating all the service files. That means the software is able to recreate itself and all the files and parameters that could be accidentally deleted from the computer by the user. In addition the software checks automatically all the available update release. The software has been developed taking the criteria of ECG automated diagnosis programs as a model. In cardiology, the first automated ECG programs were developed in the 1970s, and improved in accuracy during the 1980s and 1990s. Today most currently commercial models incorporate these programs with significant improvement in relationship between user and the device. Technically, there is not much difference between an ECG and an urodynamic tracing (Fig. 1). In ECG the digital signal resulting from heart "electrical" activity are processed by a series of specialized algorithms to derive conclusions, interpretation and diagnosis. In UDS-ASSISTANT software "pressure "signal resulting from bladder and urethral activity and electrical signal resulting from pelvic floor muscle activity are processed through the most widely accepted algorithms developed in literature for the specific underlying pathology to make the more predictable diagnosis. Analyzed LUT dysfunctions include female and male incontinence, male

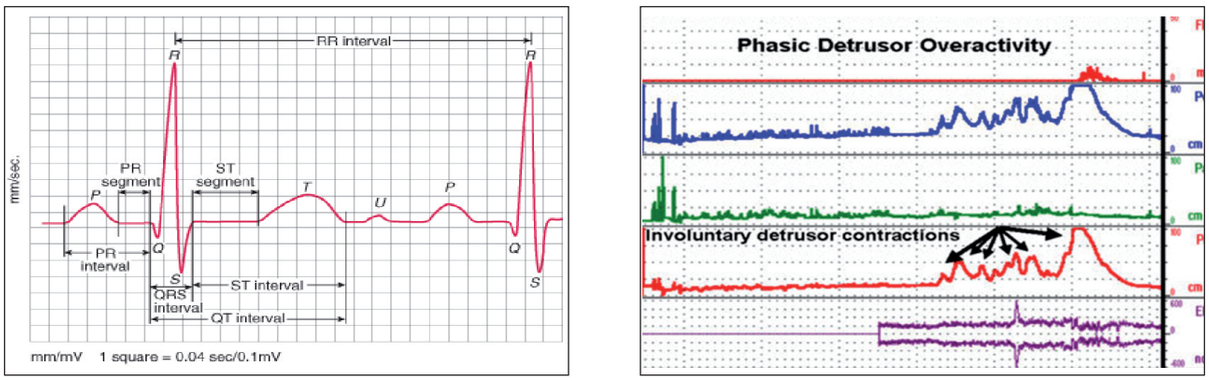


Figure 1. – "Electrical " spikes and segments of ECG, and "pressure" spikes (involuntary contractions) and segments (FSV, NDV, SDV, etc) of a cystometry trace.

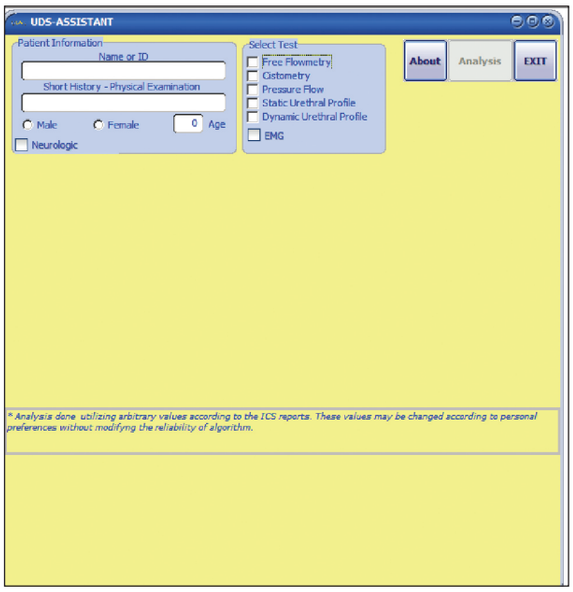


Figure 2. – The display of the software.

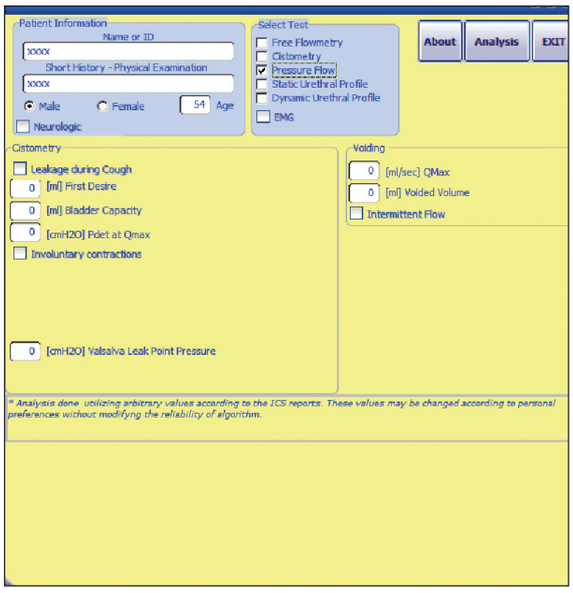
and female obstruction, urgency, neurogenic bladder and voiding disorders in pediatric age. Algorithms have been realized utilizing the statements and recommendations of the most authoritative Guidelines on urodynamics:

1. ICS *(International Continence Society) Reports*[11,12]
2. IUGA/ICS Joint Report on the Terminology for Female Pelvic Floor Dysfunction[13]
3. ICCS *(International Childrens Continence Society)* Terminology Document[14]
4. ICI *(International Consultation on Incontinence) Reports*[15-18]
5. Good Urodynamic Practice[19]

In addition three basic textbooks of urodynamics have been consulted:

1. Abrams: Urodynamics[20]
2. Nitti: Pratical Urodynamics[21]
3. Chapple: Urodynamics made easy[22]

In situations poorly defined by the literature, the choice of reference values was made on personal experience. The figure 2 shows the software display.



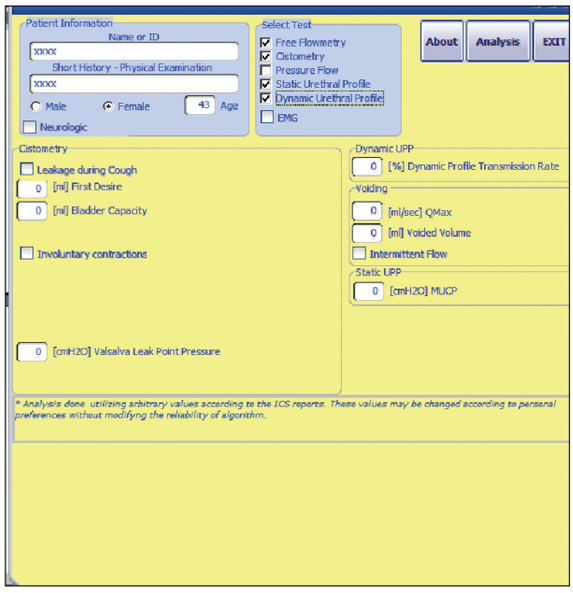


Figure 3. – Single test and pressure/flow analysis.

On the left, the ID of the patient including age, sex and a short clinical history is indicated. On the right, the list of urodynamic tests. To facilitate office urodynamics, the analysis has been devised both for single tests and for pressure/ flow studies. Once selected the test, a series of boxes to be filled out with data of the traces is displayed (Fig. 3). Likely ECG signals that are conditioned at starting of the procedure to remove noise, correct base level variations etc, a quality control procedure is accomplished by UDS-software at the beginning of pressure/flow study asking the examiner to check the proper strain gauges calibration by verifying that the difference between Pabd and Pves should no greater than 6 cm H20 (Fig. 4). A specific box identifies the neurologic patient, likewise ECG in patient with cardiac pacemaker. Urodynamics in neurologic patient has some special features including terminology that is different from that used in the non-neurologic patient (Fig. 5). After filling the boxes with the requested values, a click on the analysis button activate the display of the report that includes row data on the top, and the results of automated interpretation below (Fig. 6). Below we report the rationale of diagnostic algorithms utilized in the analysis of each test.

Male flowmetry

The International Continence Society has standardized certain objective measurements to be recorded during uroflow measurement, including flow pattern, voided volume, maximum flow rate (Q_{max}), voiding time, and time to maximum flow . However, flow pattern, Qmax, and volume voided generally are regarded to be the most clinically useful for both screening and following patients. Because uroflow is partly dependent on volume voided, uroflowmetry nomograms are useful in distinguishing normal from abnormal flow rates. Since males show a significant decline in flow rate with age, the software utilizes Siroky nomogram for men under 55, and Bristol nomogram for men over 55.[23,24,25]

Voided volume should be at least 150ml and preferably 200 ml. For voided volume lower than 150 ml (correspondingly less in children: 50 to 100 ml) a warning indicate the voiding pattern has to be interpreted with caution for possible erroneous result due to inadequate voided volume and suggest to repeat the test. Intermittent flow may be due to abdominal straining to overcome a BOO or may indicate a

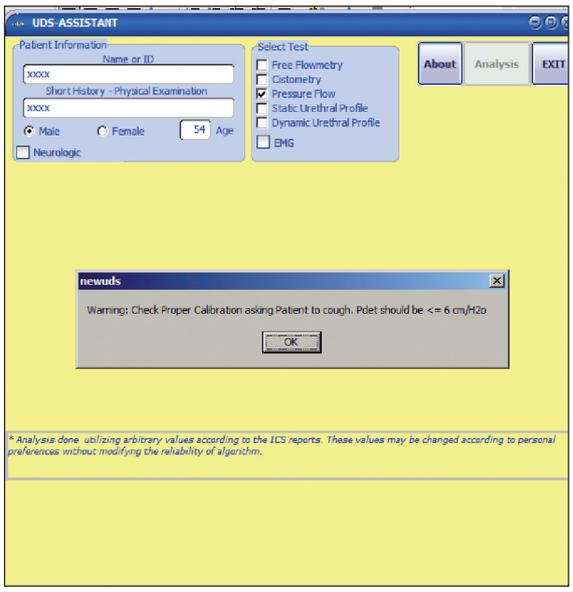


Figure 4. – Quality control procedure before starting pressure/flow study.

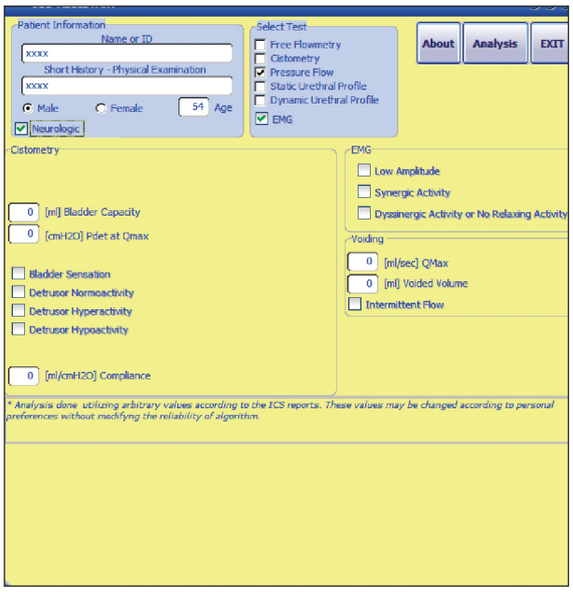


Figure 5. – Pressure/flow study in neurologic patient.

poorly contractile detrusor or a dysfunctional voiding in pediatric age or in younger adults. With an intermittent flow, a second warning indicate the need of a pressure/flow study for a better definition of the finding. In adults the free flowmetry predictive value is also reported, in order to reduce the need of pressure/flow study according to Limm and Abrams: if the Qmax is below 10 ml/the chance of the patient to have a bladder outlet obstruction is 90%; if the Qmax is 10 ml/s to 15 ml/s the incidence of obstruction falls to 71%; if the Qmax is over 15 ml/s the chance of obstruction is 50% (high pressure/high flow system).[26]

Female flowmetry

Unlikely male, female doesn't show statistically significant variations in urine flow rate with respect to age, parity or first versus repeated voiding. The 10th centile of the Liverpool Nomogram for the maximum urine flow rate has been considered to be the most useful discriminant for a final urodynamic diagnosis of voiding difficulties in females.[27]

Uroflowmetry in pediatric age

Urine flowmetry togheter with ultrasound assessment of residual urine is by far the most common procedure in pediatric urodynamic practice. The results of the examination decide whether the child requires an invasive urodynamic investigation. Two aspects are particularly significant in a child flow curve: maximum flow and the shape of the curve.

Maximum flow (Qmax)

In studies of normal children a linear correlation has been found between the square of maximum flow (Qmax) and voided volume. If the square of Qmax (ml per second^2 is equal to or exceeds voided volume in ml, the recorded maximum flow is most probably within the normal range.[28]

Mean Qmax is higher in girls than in boys probably due to girls' shorter urethra. Recently nomograms in centile forms have been reported both for girls and boys under 14 yrs of age for a wide range of voided volume.[29] These nomograms have been utilized in our software for automated analysis of flow in children.

Flow curve shape

A child with organic outlet tract obstruction often has a low amplitude flow curve, that is a plateau-shaped curve. Similarly this may be the case when there is a tonic sphincter contraction during voiding. However, more commonly sphincter overactivity during voiding is seen as sharp peaks and troughs in the flow curve, that is labelled as an irregular or "staccato" flow curve. With a "staccato" flow curve a warning indicate the possibility of dysfunctional voiding inviting the examiner to proceed to a pressure/flow study with patch EMG.

Residual urine

Measurement of post-void residual urine is the current complement of uroflowmetry for evaluating voiding dysfunction. However, threshold values delineating what constitutes an abnormal PVR are poorly defined. The pro-

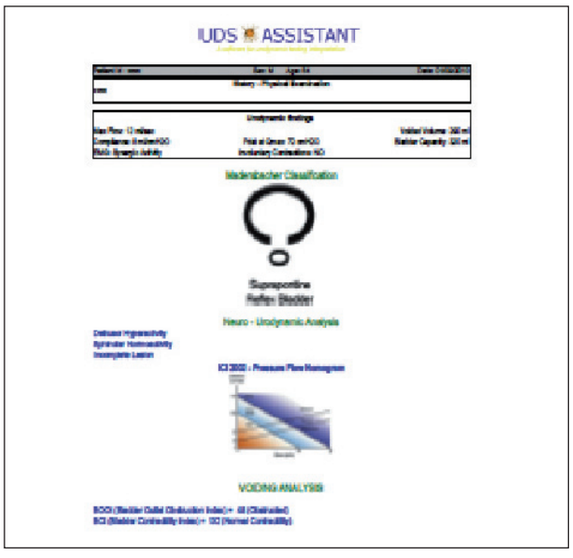


Figure 6. – Sample of a final diagnostic report in neurogenic patient.

gramme take into account only large PVRs (> 200ml) with a warning indicating that values greater than 200 ml may be associated with an increased risk of urinary retention, upper urinary tract dilation and renal insufficiency.[30,31]

Cystometry

Cystometry is mostly interpretative. The investigator should approach cystometry with a clear principle in mind, namely that "the role of urodynamics is to reproduce the patient symptoms". This means there should be a continuous dialogue between the investigator and the patient through the examen. This concept is particularly important when assessing the sensation the patient experience during cystometry.[32,33] Bladder storage function should be assessed in terms of bladder sensation, detrusor activity, bladder compliance and bladder capacity. Furthermore the urethra should be assessed in term of competency through cough (urodynamic stress incontinence) and strain (Valsalva leak point pressure). The failure to store urine during the filling phase may be either a result of an abnormal (overactive or oversensitive) detrusor or an abnormal (i.e. too weak) sphincter complex. In mixed incontinence the two situations coexist.

The software analysis considers the following data: FSF (first sensation of filling); cystometric capacity; involuntary detrusor contractions spontaneous or on provocation; compliance, espressed as increase in bladder volume per centimetre of water increase in pressure (ml/ cm H20). In the normal bladder the change in pressure from empty to full should be less than 10 cm H20 giving a figure for normal compliance of greater than 40 ml/cm H20; urine leakage through the external meatus during cough; VLPP at 200 ml of filling.[34]

Overactive bladder is diagnosed in presence of significant detrusor overactivity, subjectively observed by the examiner. There has been considerable confusion over the objective definition of DO with some investigators labelling patients as having DO if there is an increase of pdet greater than 15 cm H20 during filling. However, the ICS standardization document of 1988 made it clear that DO is characterised by phasic contractions (pressure rise and fall) whithout specifying a minimum change in pdet. Waves of an amplitude of less than 5 cm H20 are difficult to detect using most modern urodynamic equipments.[35] However, it is undoubtedly true that low pressure DO waves (5 cm H20 – 15 cm H20) can produce troublesome symptoms of urgency particularly in women. Bladder hypersensitivity is diagnosed in presence of an early first sensation of filling and an early first sensation to void (usually < 100ml) which persist into normal and strong desire without concomitant phasic detrusor contractions. Bladder capacity is less than 250ml Reduced compliance is diagnosed when the pressure at cystometric capacity is greater than 10 cm H20. Urodynamic stress incontinence is diagnosed when urine leak from the external meatus is observed when the patient raises her intra-abdominal pressure in the absence of a detrusor contraction. IDS is diagnosed when VLPP at 200 ml of filling is lower than 60 cmH20. A VLPP greater than 90 cm H20 is usually associated with pure uretral hypermobility. VLPP values between 60 and 90 cm H20 form a grey area in which hypermobility and ISD usually coexist. If the patient does not leak a bladder cause for the leakage should be considered. The two stressors (cough and Valsalva) differ physiologically with regard to the rate and nature of the rise in pressure. Although higher abdominal pressures can be achieved with cough, the Valsalva LPP is better controlled and less variable.[36] Generally, cough LPP is used for patients who do not leak during Valsalva LPP measurement. The programme takes into account both values.

Pressure/flow studies

Conventional urodynamics is able to provide information on both filling and voiding phases of micturition cycle. This is achieved by measuring bladder and abdominal pressure with real-time computational determination of detrusor pressure by using the formula $pdet = pves - pabd$. The accurate measurement of pdet is entirely dependent on the accuracy with wich pabd and pves are measured. The 2002 ICS report says that after derivation, pdet is 0 cm H20 to 6 cm H20 in 80% of cases. As previously said, before starting the pressure/flow study, quality control is ensured by a warning that ask the examiner to check that pdet is under 6 cm H20. The pressure-flow relation is much better defined in men than in women. In male patients the diagnosis of BOO is made by plotting the maximum flow rate (Qmax) against detrusor pressure at Qmax (pdet Qmax) into the ICS nomogram which is derived from Abrams-Griffiths, LPURR and URA nomograms.[37] BOO is also calculated without reference to nomogram utilizing the equation:
BOOI (Bladder Outlet Obstruction Index) = $pdetQmax - 2\ Qmax$

If the BOOI is greater than 40 then BOO exist; if it is below 40 then no definite BOO exists. Under 20 patient is unobstructed. In addition the software analyzes the detrusor contractility utilizing the equation: BCI (Bladder Contraction Index) = $pdetQmax\ -5\ Qmax$

A BCI of greater than 150 suggests strong contractility, whereas less than100 is poor. BCI 100-150 is the normal range. The definitions and nomograms that are used to describe BOO in men do not apply to women, since men and women have unique micturitional characteristics. There is a distinct lack of consensus relating to the use of urodynamic assessment in the interpretation of voiding dysfunction in women. There are universally accepted nomograms for men with outflow obstruction[38,39] but there remain various different urodynamic criteria for women.[40-44] Recent attempts have been made to simplify and clarify them, such as the nomogram proposed by Blaivas and Groutz in 2000. [45] but standardization is still awaited. Nevertheless, voiding phase of female patient is analyzed through the Groutz-Blaivas nomogram. The nomogram includes 4 zones: unobstruction, mild, moderate, severe obstruction BOO is defined as free Qmax < 12 ml/ s combined with pdet Qmax > 20 cm H20. In according to the Authors, given the difficulty in performing uroflowmetry with a catheter in place and the fact that there was a significantly higher flow rate in the same woman without the catheter, we chose to use a non-invasive flow rate in the nomogram. Also, because they found no statistical difference in pdetQmax in obstructed versus unobstructed patients, we choose pdetmax as the pressure parameter. This enables analysis also in patients with urinary retention. Unlike male, detrusor contraction strength is not assessed in women. However, since an inadequately contracting detrusor may be related to post–operative voiding problems, the addition of pressure/ velocity plots described by van Mastrigt and Griffiths[46] and provided by some urodynamic equipments may be worthwhile.

Female static & dynamic profilometry

Urethral function tests represent a dark area of urodynamics.[47] Urethral hypermobility and intrinsic sphincteric deficiency probably falls in a bell-shaped distribution across stress incontinence populations; so that most cases of stress incontinence have some degree of both types of pathology. [48] Static and dynamic profilometry are the cur-

rent urodynamic tests to assess both intrinsic urethral tone and the urethral support.

Static profilometry

Static profilometry assess the functional status of the urethra by measuring the pressure throughout the urethral length.[49] Proponents believe it gives an indication of the severity of SUI and usually equate a maximal urethral closure pressure (MUCP) below 20 cmH_2O, with ISD. Values greater than 20 cm H20 but lower than the hypothetical normal MUCP may indicate a hypofunctional urethra.[50] MUCP in female is closely dependent on age and decreases by 15 cm H20 per decade starting from 90 cm H20 at 25 yrs.[51,52] This concept is summarized in a simple formula, proposed by the SIFUD (*Societe Francophone d'Urodinamique*) several years ago, to calculate the theoretical normal MUCP of each woman.

MUCP = 110 minus age

Example: a woman of 72 yrs should have a theoretical MUCP of: 110-72=38 cmH20

The values between 20 and 38 cmH20 indicate a possible "hypofunctional" urethra

The values under 20 cm H20 indicate a possible ISD

Dynamic Profilometry

In women with a normal mechanism of support, increases in abdominal pressure during coughing are transmitted to the proximal three quarters of the urethra with urethral pressures exceeding intravesical pressures. The lack of such pressure transmission to the urethra indicates a poor supporting mechanism. The PTR (Pressure Transmission Ration) is calculated as follow: PTR = urethral pressure rise during stress maneuvers/intravesical pressure rise x 100. The PTR in normal women tend to be greater than 90. Values under 90% are diagnosed as defect in support. A pressure transmission ratio value less than 90% in the proximal half of the dynamic profile had a sensitivity of 97%, a specificity of 56%, an abnormal predictive value of 53%, and a normal predictive value of 97%.[53]

Male profilometry

Male profilometry has limited clinical relevance as a diagnostic tool for bladder outlet obstruction, because it doesn't reflect the dynamic behaviour of the urethra during micturition. Conversely, it may be used to evaluate the degree of sphincter lesion after radical prostatectomy and to follow spontaneous recovery. Several papers reports the multifactorial origin of incontinence after radical prostatectomy: ISD is present in 2/3 of cases, sphincter and bladder dysfunction coexist in 1/3, isolated bladder dysfunction is less 10%, while BOO due to anastomotic stricture is present in 2.7-20% of the cases.[54-58] Quantification of sphincteric damage became important after the introduction of sling surgery in alternative to AUS, since sling surgery appears to be efficacious only in mild to moderate cases of incontinence. There are controversies about the assessment of sphincteric function after radical prostatectomy. Although VLPP has not been shown to correlate with severity of incontinence.[59] MUCP appears to be a more useful measurement in the post-RP population. MUCP in incontinent patients has been reported significantly lower than in continent patients.[60] Basing mostly on personal experience, the software algorithm describes three incontinent sub-groups:

1. MUCP between 60 and 80 cm H20 suggesting a mild sphincteric weakness.
2. MUCP between 40 and 60 cm H20 suggesting a moderate sphincteric weakness.
3. MUCP under 40 cm H20 suggesting a severe sphincteric weakness.

Urethral profilometry and dysfunctional voiding

The ICS has defined dysfunctional voiding as an intermittent and / or fluctuating flow rate due to involuntary intermittent contractions of peri-urethral striated muscle during voiding in neurologically normal patients. In male the pattern, that has been called also "pseudodyssinergia" seems to account for 35% of bladder outlet obstruction especially in young adults.[61] In female dysfunctional voiding is quite common in painful bladder and related pelvic floor syndromes.[62] Obviously, the "gold standard" for diagnosing the disorder is the pressure/flow study with EMG. Is not infrequent, however, to observe in office practice the performance of flowmetry followed by cystometry and urethral profilometry. In presence of an interrupted free flow and with an MUCP exceeding 10 cm H20 the normal age-dependent MUCP value in the female and a fixed value of 120 cmH20 in male, a pressure/flow study with EMG is warranted. The latter usually evidentiate a poor relaxing sphincter with mild – to moderate obstruction in female and equivocal obstruction with underactive detrusor in male.

Neurogenic bladder

Urodynamic diagnosis in neurogenic bladder follows special features (terminology, sensation, compliance) in a condition similar to ECG in the patient with a pacemaker. As previously said, the software provide a specific algorithm for neurogenic patient. Neurogenic bladder dysfunction may be due to: dysfunction of the detrusor, dysfunctions of the sphincter, and a combination of both

When one suspect neurogenic bladder, a pressure/flow study with EMG becomes mandatory. Two types of information can be obtained from EMG: a simple indication of muscle behaviour, the so-called kinesiological EMG, or an electrical correlation of muscle pathology.[63] During urodynamic investigation a kinesiological EMG is usually obtained. Sphincter activity may be: synergic, dyssinergic or non-relaxing and low-amplitude. Synergic activity indicates a progressive increase of EMG activity during filling of the bladder (guarding reflex) followed by by a timely relaxation of the pelvic floor during voiding. Dyssinergic *or* non-relaxing activity indicates an increase of EMG activity during voiding (sometimes the activity may result unmodified or "waxing and waining"). Low amplitude EMG indicates a reduced electrical activity both during filling and voiding phase. The finding may indicate a peripheral denervation of the muscle for which a neurophysiological approach, through a needle EMG and oscilloscope, is recommended in the final report. Correspondingly, detrusor function may be: normo-, hyper-, hypo-active. The patterns of detrusor- sphincter function reported in the boxes of the display identifies eight types of neurourodynamic diagnoses , according to Madersbacher: [64]

– supra-pontine reflex bladder (detrusor hyperactivity-synergic EMG activity)
– spinal reflex bladder (detrusor hyper activity-dyssinergic or non-relaxing EMG activity)
– sub-sacral lesion (detrusor hypoactivity-low amplitude EMG)
– lumbosacral lesion I (detrusor hyperactivity-low amplitude EMG)
– lumbosacral lesion II(detrusor hypoactivity-dyssinergic or non-relaxing EMG activity)
– intra-pelvic lesion I (detrusor hypoactivity-synergic EMG activity)

– intra-pelvic lesion II (detrusor normoactivty-dyssinergic or non-relaxing EMG activity)
– intra-pelvic lesion III (detrusor normoactivity-low apmlitude EMG activity).

In addition to neurourodynamic diagnosis, voiding phase is analyzed through A-G nomogram in male and Groutz-Blaivas nomogram in female to evaluate the presence or absence of a mechanical obstruction. The absence or presence of sensation during filling account for a complete versus incomplete neurogenic lesion.

RESULTS

One hundred urodynamic studies were retrospectively reanalyzed using the software. The diagnosis done by an urodynamicist was compared with that resulting from the software analysis. Data were inserted in the program blindly, for example, without knowing the diagnosis. Seventy-six exams were considered as routine investigation, while twenty-four were classified as a difficult cases. Difficult cases were considered male patients undergone several endoscopic operations (TUIP, TURP, re-do) for suspected bladder outlet obstruction and female patients undergone several anti-incontinence surgeries. Examiner skill was classified as high (expert urodynamicist), average (residents), poor (clinician not specifically involved in urodynamics). Only eighty-eight exams were eligible for reanalysis since twelve traces were discarded for technical inadequacy (poor calibration, infusion pump oscillations in UPP measurement, loss of detrusor line during voiding) in spite of examiner diagnosis. Diagnostic agreement between software and examiner diagnosis is reported in Table I. Overall, the correspondence between the two diagnoses was observed in 54.5% of the cases. Discrepancies were observed in 45.5% of the studies. As expected, diagnostic agreement was lower in complicated cases, mostly due to initial wrong diagnosis. Examiner skill was not a discriminating factor in resident diagnoses, probably because younger people strictly follow the available guidelines. In general, however, there was evidence of an unwillingness to follow existing standardization recommendations. In addition, poor facility with urodynamics was an important factor in the questionable diagnosis of the clinicians, since most of them had already planned an "unmodifiable surgical solution" despite the urodynamic traces. The best diagnostic agreement (90%) was seen in the sub-group of patients with neurogenic bladder dysfunction. Although in neurogenic bladder each individual patient may have a unique pattern of lower urinary tract dysfunction and require an individual management plan, the site of the lesion gives an indication of the likely pattern of the dysfunction. In this sub-group the only two discrepancies in diagnosis were seen during the spinal shock period, that software failed to recognize. In male LUTS diagnostic agreement was seen in 50% of the patients. Discrepancies were due mostly to missed diagnosis of detrusor underactivity (4/18: 22%) and poor-relaxing external sphincter(14 /18: 77%). In our opinion there is a tendency in the clinician to underestimate the problem of detrusor underactivity in favour of bladder outlet obstruction, while the diagnosis of poor- relaxing spincter is almost never done. In female incontinence diagnostic agreement was seen in 37.5% of the cases. Discrepancies were present in the quantification of ISD (12/20: 60%) and in the diagnosis of bladder hypersensitivity (8/20: 40%), the latter being classified as overactive bladder in most of the cases. This was not surprising, since it is well known that both urethral function assessment and detrusor dysfunction evaluation are considered the "dark-grey zones" in current urodynamic investigation.

TABLE 1. – Diagnostic agreement between software and examiner diagnosis in 88 selected LUT dysfunctions.

LUT dysfunction	N° pts	Diagnostic agreement	%
Female incontinence	32	12/32	37.5
Male BOO	36	18/36	50
Neurogenic bladder	20	18/ 20	90
Overall	88	48/88	54.5

DISCUSSION

Urodynamics is a series of more or less agreed-upon clinical tests to assess the function and dysfunction of lower urinary tract. According to this definition urodynamics is the only way of understanding why people are continent or incontinent. Urodynamics is the pivotal link between basic science on the one hand and the clinical reality on the other. Therefore it occupies a central place in the consultation. At present however there is a limited objective evidence for the clinical utility of urodynamics. According to Griffiths such a surprising conclusion could have, among others, at least two possible explanations:

1 any given symptom group have similar underlying pathophysiology requiring similar treatment, and so there is no need to differentiate them by urodynamics

2 current treatments are so non-specific and non-quantitative that underlying dysfunction is unimportant. Treatment works equally well or poorly in any case.

Beside these consideration, there is however a strong suspicion, based on expert opinion, that urodynamics is often done poorly, both in accomplishing the examination as well as in interpreting the traces. Recent experience from the central monitoring of multicentre studies[65,66] suggested that the quality of urodynamic results was often compromised because there is no quality control. In one large trial up to 38% of the traces were rejected during a central review.[67] Such high rates of rejection suggested that quality control was a problem in several urodynamic units, and this led to the development of the International Continence Society guidelines on Good Urodynamic Practice (ICS GUP). Furthermore, to improve this situation, the ICS tried to establish standards for proper training and certificate programs for urodynamics. In a competency-based approach to teaching UDS, five measurable components were defined: terminology and theory, setting up the study, running the study, interpreting the study, and reporting UDS.[69] Several papers have been published in the last years on quality control in urodynamics.[68-71] None of them however deal specifically with traces interpretation. Computer-aided diagnosis is a widely accepted procedure that supports the doctor's interpretations, particularly if the experience and skill in a specific field is less than optimal. Many studies demonstrate that the use of computer software to partly or fully make a differential diagnosis improve the quality of care by reducing medical errors.[72,73,74] The urodynamic algorithm imitate the step-by-step reasoning that expert urodynamicists were assumed to use when they analyze the traces. This is particularly useful since often we tend to solve most of our problems using fast, intuitive judgments rather than the conscious, step-by-step deduction. It was particularly impressive to see that in some cases the software reported a diagnosis that was totally unexpected. After a re-evaluation of the patient the working diagnosis was modified. The display may be an useful track for a good urodynamic practice, since the examiner is forced to consider all significant aspects of the traces. Data are currently entered manually by the examiner, but a direct process of the traces, like the

ECG stripe, is not technically difficult. The solution of "diagnostic machine", however, would distort the current approach of the software, that is a structured guide to urodynamic tests. In urodynamics a basic principle often missed is that any urodynamic parameter must be "correctly" interpreted" and "intelligently" evaluated. That means that any incongruence of software urodynamic diagnosis with clinical picture should act as a red flag and imply a more detailed evaluation. Conversely, the overall reliability and significance of each urodynamic test in clinical practice has nothing to do with the software. We perfectly know that many tests have several short comings, but we assumed that they are the best in current use.

The better agreement between software and examiner diagnosis was observed in neurogenic patients except in spinal shock phase. During spinal shock, bladder filling is accompanied by an elevation of resistance in the bladder neck area, with a concomitant increase of pressure in the external sphincter zone but without a simultaneous increase of the electromyographic activity. These results indicate an increased sympathetic activity in the smooth muscle component of the entire urethra.[75] Analyzing only the detrusor and sphincter activity in a set-up of pressure/flow study despite the patient inability to void, the software fail to recognize this activity and the subsequent diagnosis is "subsacral lesion-complete". A good accordance between software and examiner diagnosis was observed in male outlet obstruction. The wide use of nomograms makes highly reproducible the diagnosis of male outlet obstruction. A recent report indicated that urodynamics has good reproducibility when looking at the BOOI (bladder outlet obstruction index) and BCI (bladder contraction index), indicating that a second study is not necessary in most patients and one investigation is sufficient for an accurate diagnosis on which treatment options can be based.[76] However, classify the male patients with symptoms of lower urinary tract (LUT) dysfunction ''only'' on the basis of prostate enlargement is a limited view of the problem.

Results of a recent study indicated that LUTS in male can result from a complex interplay of pathophysiologic features that can include bladder dysfunction and bladder outlet dysfunction such as benign prostatic obstruction or poor relaxation of the urethral sphincter. About one third of men with LUTS who were older than 55 years of age had benign prostatic obstruction. Patients younger than 55 years old were more likely to have poor relaxation of the urethral sphincter as a likely cause of LUTS. [61] In clinical practice a poor relaxing sphincter is rarely acknowledged. A typical finding is that of a patient 55 years old undergone TUIP, TURP, and TURP re-do by different surgeons for a suspected bladder outlet obstruction due, in fact, to a poor relaxation of the urethral sphincter.

Most of conflicting results in female incontinence were related to the distinction between ISD and urethral hypermobility and to the assessment of combined detrusor dysfunction. Currently, there is no adequate consensus on how to diagnose SUI or categorize the disorder in terms of the two principal postulated pathophysiological mechanisms; intrinsic sphincter deficiency (ISD) and urethral hypermobility. These represent extremes of a spectrum, and coexist in the vast majority of patients. Recent reports indicate that mid-urethral sling may be equally effective in both conditions (77,78). However, it is clear from other reports that the appropriate diagnosis of SUI poses many challenges, both in the need to clarify the role of the relative components of ISD and hypermobility, which appear to exist across a spectrum, and to determine their influence on treatment outcome.[79,80]

Likewise, CMG is an essential part of the diagnostic evaluation of incontinent female, both in defining underlying pathophysiology of a mixed incontinence and directing treatment. In spite the ICS Revision of Terminology (2002) that abolished the distinction between sensory and motor urgency, recent evidence indicates urothelium as sensory function and sensory hypersensitivity may be causative of frequency and urgency unrelated to a detrusor overactivity.[81,82] The software make a clear distinction between hypersensitivity and OAB ,but probably the latter should be further re-defined according to the type of detrusor contractions, for example phasic and terminal,[83] and warning time that may account for brain control.[84] Last but not least, the programme may have a role also among expert urodynamist by reducing the inter- and intra-observer variability of urodynamic diagnosis. Urodynamics provide in essence a subjective interpretation of an objective evaluation .This account for short-long-term variability of urodynamic diagnoses and for inter-observer variability. Considerable efforts have been made in recent years to improve the standards and comparability of urodynamics worldwide.[85,86,87] In spite of rules and recommendations of ICS and other reference groups, it is interesting to see that experienced urodynamists failed to agree on the interpretation of urodynamic recordings in several situations. Recently some reports on the development of an objective method to assess bladder filling sensation during cystometry have been published.[88] Likewise, extensive objective methods of assessment of urodynamic tracings are strongly warranted by several experts. The step-by-step analysis of the programme may be an useful tool for interpreting the traces utilizing the same criteria. A multicenter study in under way to verify this goal. As indicated in the title the software is a work in progress. Some modifications have been already planned. The most significant is the introduction of a range value instead a single value.

The range should include a test retest variation of 10-15% for various parameters (volume, pressure, or flow), which can be regarded as the physiological variation of UDS.[89]

Furthermore, values chosen according to the experience of the Author, mostly related to urethral hyper- and hypoactivity, should be verified by others. However, it is our belief that the values can be changed according to personal preferences without modify the reliability of the algorithm.

CONCLUSION

Despite limitations, urodynamic studies remain the primary method of evaluating lower urinary tract complaints. Latest reports indicates urodynamic evaluations are fast becoming routine in the office environment (with only complicated cases referred to specialty centers) due to increasing demand of medical justification for surgical procedures.[90] The dictum "bladder is an unreliable witness" is now around 30 years old, but probably it's time that urodynamics is no longer complicated or cumbersome. In this scenario, urodynamic diagnostic software promise to be an useful technical support to the examiner who seeks assistance in interpreting urodynamic testing results and applying this to their practice. In principle, the software does not add anything new but simply collect the data in a structured way to coin a correct diagnosis according to the literature. This approach has at least two advantages: the first is to improve the performance of the inexperienced urodynamist, the second is to encourage the practice of urodynamics by making it easy.

REFERENCES

1. Brucker B, Jaffe W. Urodynamics to guide surgical therapy in LUTS/BPH. Current bladder dysfunction report 2009; 4: 53-60.
2. Lemack G. Use of urodynamics prior to surgery for urinary incontinence: how helpful is preoperative testing? Indian J Urol 2007; 23: 142–147.
3. Renganathan A, Cartwright R, Cardozo L et al. Quality control in urodynamics: analysis of an international multicenter study. Neurourol Urodyn 2009; 28: 380-4.
4. Sullivan J, Lewis P, Howell S et al. Quality control in urodynamics: a review of urodynamic traces from one center. BJU Int 2003; 91: 201-7.
5. Mueller ER, Kenton K, Scarpero HM, et al. Urodynamics curriculum for urology residents (UCUR) Neurourol Urodyn 2008; 27: 137. Poster 22.
6. Scarpero H. Creating taxonomy and assessing proficiency in urodynamic education of the urologyresident. Neurourol Urodyn. 2008; 27: 137. Poster.
7. Caceres CA, Hochberg HM. Performance of the computer and physician in the analysis of the electrocardiogram. Am Heart J 1970; 79: 439-443.
8. Drazen E, Mann N, Burun R et al. Survey of computer assisted electrocardiography in the United States. J Electrocardiol 1988; 21: Suppl: S98-S104.
9. Willems J, Abreu-Lima C, Arnaud P et al. The diagnostic performance of computer programs for the interpretations of the electrocardiograms. NEJM 1991; 25: 1767-1773.
10. Lennart Ljung, System Identification. Theory for the user, Prentice -Hall, 1987.
11. Abrams P, Cardozo L, Fall M, et al. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. Neurourol Urodyn 2002; 21: 167-178.
12. Sand P, Dmochowsky R. Analysis of The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. Neurourol Urodyn 2002; 21: 167-178.
13. Haylen DE, Ridder, Freeman et al. IUGA/ICS on the terminology for female floor dysfunction. Standardization and terminology Committees IUGA & ICS, joint IUGA/ICS Working group on female terminology. Neurourol Urodyn 2010; 29: 4-20.
14. ICCS *(International Childrens Continence Society)* Terminology Document. J. Urol, 2006;176: 314-324.
15. Griffiths D et al. Dynamic testing. In: *Third International Consultation on Incontinence*, 2005 edition, pp. 585-674. Paris: Health Publication Ltd, 2005.
16. Rosier P, Gajewsky J, Sand P et al. The International Consultation on Incontinence 2008.-Committee on «Dynamic Testing»; for Urinary Incontinence and Fecal Incontinence. Part 1: Innovations in Urodynamic Techniques and Urodynamic Testing for Signs and Symptoms of Urinary Incontinence in Female Patients. Neurourol Urodyn 2010; 29: 140-145.
17. Rosier P, Szabo L, Capewell A et al. The International Consultation on Incontinence 2008.-Committee on «Dynamic Testing»; for Urinary Incontinence and Fecal Incontinence. Part 2: Urodynamic Testing in Male Patients with Symptoms of Urinary Incontinence, in Patients with relevant Neurologic Abnormalities, and in Children and in Frail Elderly with Symptoms of Urinary Incontinence. Neurourol Urodyn 2010; 29: 146-152.
18. Madersbacher et al: Conservative management in neuropathic urinary incontinence. In : *Third International Consultation on Incontinence*, 2005 edition, pp 697-754. Paris: Health Publication Ltd, 2005.
19. Schafer W, Abrams P, Liao L, et al. Good urodynamic practices: uroflowmetry, filling cystometry, and pressure-flow studies. Neurourol Urodyn 2002; 21: 261-274.
20. Abrams P, Urodynamics, Third Edition, Springer-Verlag London Limited 2006.
21. Nitti V. Pratical Urodynamics, W.B. Saunders Co, 1996.
22. Chapple C, Mac Diarmid S, Patel A. Urodynamics made easy. Elsevier. Third Edition. Churchill Livingstone, 2009.
23. Siroky M, Olssen C, Krane R. The flow rate nomogram I Development. J Urol 1979; 122: 665-668.
24. Siroky M, Olssen C, Krane R. The flow rate nomogram II Clinical correlations. J. Urol 1980; 123: 208-210.
25. Kadow C, Howells S, Lewis P et al. A flow rate nomogram for males over the age of 50. Proceedings of the 15th Annual Meeting of the International Continence Society, London 1985, 138-139.
26. Limm C, Abrams P. The Abrams-Griffiths Nomogram. World J Urol 1995; 13: 34-39.
27. Haylen B, Parys B, Anyaegbunam W et al.Urine flow rate in males and females urodynamic patients compared with Liverpool nomogram. Br. J Urol. 1990; 65: 483-487.
28. Szabo L. and Fegyvernski S. Maximum and average flow rates in normal children: the Miskolc nomograms. Br J Urol, 1995; 76: 16.
29. Kajbafzadeh A, Yazdi C, Rouhi O et al. Uroflowmetry nomogram in Iranian children aged 7 to 14 years BMC Urology 2005, 5: 3.
30. Gray M. Urinary retention. Management in acute care setting. Part 1. Am J Nurs 2000; 100: 40-47.
31. Gray M. Urinary retention. Management in acute care setting. Part 2. Am J Nurs 2000; 100: 36-43.
32. Blaivas JG. Techniques of evaluation. In Neurourology and urodynamics: principles and practice Edited by S.VYalla, EJ McGuire, A Elbadawi, et al New York: McMillan pp 155-198, 1988.
33. Wyndaele J. Normality in urodynamics studied in healthy adults. J Urol 161: 899-902.
34. Zimmern, Nager, Albo et al. Interrater reliability of filling cystometrogram interpretation in a multicenter study. J Urol 2006; 175: 2174-5.
35. Abrams P, Blaivas JG, Stanton S et al. ICS Standardization of Terminology of Lower Urinary Tract Function 1988. Scand J Urol Nephrol, 1988; Supp 114: 5-19.
36. Peschers U, Junt K, Dimpfl T. Differences between cough and Valsalva leak-point pressure in stress incontinent women. Neurourol Urodyn 2000; 19: 677-681.
37. Abrams P. Bladder outlet obstruction index, bladder contractility index and bladder voiding efficiency: Three simple indices to define bladder voiding function. Brit J Urol 1999; 84: 14-15.
38. Abrams PH, Griffiths D. The assessment of prostatic obstruction from urodynamic measurements and from residual urine. Br J Urol. 1979; 51: 129-134.
39. Schafer W. The contribution of the bladder outlet to the relation between pressure and flow rate during micturition. In: Hinman F Jr, Boyarsky S, editors. Benign Prostatic Hypertrophy. New York, NY: Springer Verlag; 1983. pp. 470-496.
38. Farrar DJ, Osborne JL, Stephenson TL, et al. A urodynamic view of bladder outflow obstruction in the female: factors influencing the results of treatment. Br J Urol. 1976; 47: 815-822.
39. Bass JS, Leach GE. Bladder outlet obstruction in women. Problems in Urology. 1991; 5: 141-154.
40. Massey JA, Abrams PA. Obstructed voiding in the female. Br J Urol. 1988; 1: 36-39.
41. Chassagne S, Bernier PA, Haab F, et al. Proposed cut-off values to define bladder outlet obstruction in women. Urology. 1998; 51: 408-411.
42. Lemack GE, Zimmern PE. Pressure flow analysis may aid in identifying women with outflow obstruction. J Urol. 2000; 163: 1823-1828.
43. Defreitas GA, Zimmern PE, Lemack GE, Shariat SF. Refining diagnosis of anatomic female bladder outlet obstruction: comparison of pressure-flow study parameters in clinically obstructed women with those of normal controls. Urology. 2004; 64: 675-679.
44. Nitti VW, Tu LM, Gitlin J. Diagnosing bladder outlet obstruction in women. J Urol. 1999; 161: 1535-1540.
45. Blaivas JG, Groutz A. Bladder outlet obstruction nomogram for women with lower urinary tract symptomatology. Neurourol Urodyn. 2000; 19: 553-64.
46. Van Mastright R, Griffiths D. Clinical comparison of bladder contractility parameters calculated from isometric contractions and pressure/flow studies. Urology 1987; 29: 102-106.
47. Chapple CR, Wein AJ, Artibani W, et al. A critical review of diagnostic criteria for evaluating patients with symptomatic stress urinary incontinence. BJU Int 2005; 95: 327-334.
48. Patel A, Chapple C. Urodynamics in the management of female stress incontinence-which test and when? Curr Opin Urol 2008; 18: 359-364.

49. Jarvis GJ, Hall S, Stamp S, et al. An assessment of urodynamic investigation in incontinent women. BJOG 1980; 87: 873-96.
50. Lose G, Griffiths D, Hosker G, et al. Standardization of urethral pressure measurement: report from the Standardisation Sub-Committee of the International Continence Society. Neurourol Urodyn 2002; 21: 258-260.
51. Madersbacher S, Pycha A, Schatzl G et al. The aging lower urinary tract: a comparative urodynamic study of men and women.Urology 1998; 51: 206-12.
52. Pfisterer M, Griffiths D, Schaefer W et al. The effect of age on lower urinary tract function. A study in women. J Am Geriatr Soc 2006; 54: 405-12.
53. Bump RC, Copeland WE, Hurt WG et al. Dynamic urethral pressure/profilometry pressure transmission ratio determinations in stress-incontinent and stress-continent subjects. Am J Obstet Gynecol 1988; 159: 749-55.
54. Porena M, Mearini E, Mearini L et al. Voiding dysfunction after radical retropubic prostatectomy: more than external urethral spnicter deficiency. Eur Urol 2007; 52: 38-45.
55. Groutz A, Blaivas J, Chaikin D et al. The pathophysiology of post-radical prostatectomy incontinence: a clinical and video urodynamic study. J Urol 2000, 163: 1767-70.
56. Ficazzola M, Nitti V. The etiology of post-radical prostatectomy incontinence and correlation of symptoms with urodynamic findings. J Urol 1998; 160. 1317-20.
57. Kundu S, Roehl K, Eggener S et al. Potency, continence and complications in 3477 consecutive radical retropubic prostatectomies. J Urol 2004; 172: 2227-31.
58. Kao T, Cruess D, Garner D et al. Multicenter patient self- reporting questionnaire on impotence ,incontinence and stricture after radical prostatectomy. J Urol 2000; 163: 858-64.
59. Comiter C, Sullivan M, Yalla S. Correlation among maximal uretral closure pressure, retrograde leak point pressure and abdominal leak point pressure in men with post-prostatectomy stress incontinence. Urology 2003; 62: 75-8.
60. Kielb S, Clemens J Comprehensive urodynamics evaluation of 146 men after radical prostatectomy. Urology 2005; 66: 392-396.
61. Kuo HC. Videourodynamic analysis of pathophysiology of men with both storage and voiding lower urinary tract symptoms. Urology 2007; 70: 272-6.
62. Kim SH, KimTB, Kim SW et al. Urodynamic findings of the painful bladder syndrome/interstitial cystitis: a comparison with idiopathic overactive bladder. J Urol 2009; 181: 2550-4.
63. Homma Y et al. Urodynamics. In: 2 nd International Consultation on Incontinence, 2002 edition, pp. 346-347. Paris: Health Publication Ltd, 2002.
64. Madersbacher H et al. Conservative management in neuropathic urinary incontinence In: 2 nd International Consultation on Incontinence, 2002 edition, pp 699-754. Paris: Health Publication Ltd, 2002.
65. Schafer W, delaRosette JJMCH, Hofner K, et al. The ICS-BPH study: pressure flow studies, quality control and initial analysis. Neurourol Urodyn 1994; 13: 491-2.
66. Lewis P, Abrams P. Urodynamic protocol and central review of data for clinical trials in lower urinary tract dysfunction. BJU Int. 2000; 85 (Suppl 1): 20-30.
67. Lewis P, Howell S, Shepherd A, Abrams P. Urodynamic interpretation. guidance not guesswork. 28th Annual Meeting of the International Continence Society. Jerusalem, 1998.
68. Nager C, Albo M, Fitzgerald M et al. A process for the development of multicenter urodynamic studies. Urology 2007, 69. 63-68.
69. Ellis-Jones J, Swithinbank L, Abrams P. The impact of formal education and training on urodynamic practice in the United Kingdom: A survey. Neurourol Urodyn 2006; 25: 406-10.
70. Sullivan J, Lewis P, Lowell S et al. Quality control in urodynamics: a review of urodynamics traces from one center. BJU Int 2003; 91: 201-207.
71. Sriram R, Ojha H, Farrar D. An audit of urodynamic standardization in the West Midland .UK. BrJU Int 2002; 90: 537-9.
72. Liao LM, Schafer W. Effects of retrospective quality control on pressure-flow data with computer-based urodynamic systems from men with benign prostatic hyperplasia. Asian Journal of Andrology 2007; 9: 771-780.
73. Leaper D, Horrocks J, Staniland J et al. Computer-assisted diagnosis of abdominal pain using "Estimates "provided by clincians. BMJ 1972; 4.350-354.
74. Peldschus K, Herzog P, Wood S et al .Computer-aided diagnosis as a second reader. CHEST 2005; 128: 1517-1523.
75. Gilbert F, Astley S, Gillan M et al. Single reading with computer – aided detection for screening mammography. NJM 2008; 359: 1675-1683.
76. Rossier A, Fam B, Di Benedetto M. Urodynamics in spinal shock patients. J Urol 1979; 122: 783-87.
78. Hashiom H, Elhilali M, Bjerklund Johansen T et al. ARIB 3004 Pressure Flow Study Group. The immediate and 6-mo reproducibility of pressure-flow studies in men with benign prostatic enlargement. Eur Urol. 2007; 52: 1186-93.
79. Ghezzi F, Serati M, Cromi A et al. Tension-free vaginal tape for the treatment of urodynamic stress incontinence with intrinsic sphincteric deficiency. Int Urogynecol J Pelvic Floor Dysfunct 2006; 17: 335-9.
80. Miller JJ, Botros SM, Akl MN, et al. Is transobturator tape as effective as tension-free vaginal tape in patients with borderline maximum urethral closure pressure? Am J Obstet Gynecol 2006; 195: 1799-1804.
81. Chen HY, Yeh LS, Chang WC, et a Analysis of risk factors associated with surgical failure of inside-out transobturator vaginal tape for treating urodynamic stress incontinence. Int Urogynecol J Pelvic Floor Dysfunct 2007; 18: 443-447.
82. Guerette NL, Bena JF, Davila GW. Transobturator slings for stress incontinence: using urodynamic parameters to predict outcomes. Int Urogynecol J Pelvic Floor Dysfunct 2008; 19: 97-102.
82. Yamaguchi O, Honda K, Nomiya M et al. Defining overactive bladder as hypersensitivity. Neurourol Urodyn 2007; 26 (6 Suppl): 904-7.
83. Haylen BT, Chetty N, Logan V et al. Is sensory urgency part of the same spectrum of bladder dysfunction as detrusor overactivity? Int Urogynecol J Pelvic Floor Dysfunct 2007; 18: 123-8.
84. Flisser A, Walmsley K, Blaivas J. Urodynamic classification of patients with symptoms of overactive bladder. J Urol 2003; 169: 529-33.
85. Dasgupta R, Kavia R, Fowler C. Cerebral mechanisms and voiding function. BJU Int. 2007, 99: 731-34.
86. Nager, Albo, Fitzgerald. Process for development of multicenter urodynamic study. Uology 2007; 69: 63-7.
87. Hermieu JF. Recommendations for the urodynamic examination in the investigation of non-neurological female urinary incontinence Progr Urol 2007; 17 (Suppl 2) 1264-84.
88. Heesakkers JP. The role of urodynamics in the treatment of lower urinary tract symptoms in women. Curr Opin Urol 2005; 15: 215-21.
89. Craggs MD. Objective measurement of bladder sensation: Use of a new patient-activated device and response to neuromodulation. BJU Int 2005; 96: 29-36.
89. Kortmann BB, Sonke GS, Wijkstra H, et al. Intra- and inter-investigator variation in the analysis of pressure-flow studies in men with lower urinary tract symptoms. Neurourol Urodyn 2000; 19: 221-32.
90. Winters J. Urodynamics in 2009. Utilization, education and best practices. Are they aligned? ICS 39th Annual Meeting, S. Francisco, 2009.

Correspondence to:

Dr. GIANCARLO VIGNOLI
Via S. Giorgio 3, 40121 Bologna, Italy
Email: vignoli.g@tiscali.it
phone: + 39 051223205

Review

Botulinum neurotoxin (BoNT) in Urology - An overview of current and emerging uses

AYESHA KARUNATILLAKE,[1] THOMAS R JARVIS,[2] VINCENT TSE,[3] PREM RASHID[4]

[1]*Rural Clinical School, University of New South Wales, Port Macquarie Base Hospital.*
[2]*Department of Urology, Port Macquarie Base Hospital, New South Wales.*
[3]*Department of Urology, Concord Repatriation Hospital, Sydney, New South Wales*
[4]*Department of Urology, Port Macquarie Base Hospital and University of New South Wales, Rural Clinical School*

Abstract: *Background:* Botulinum neurotoxin (BoNT) is produced by the anaerobic organism *Clostridium Botulinum*. BoNT has increasingly diverse uses in medicine due to its ability to relax muscles by inhibiting the release of acetylcholine. There are now a number of established and emerging uses for BoNT. *Objective:* This article provides an overview of the current therapeutic uses of BoNT in urology. *Discussion:* BoNT is now used in the treatment of a number neurogenic and non-neurogenic lower urinary tract disorders. The efficacy of BoNT, combined with its low risk profile, makes it a promising alternative when conservative medical therapies fail and surgical management is not appropriate. At present the use of BoNT in urology is '*off label*'. It is anticipated that within the next 12 months, the United States Food and Drug Administration (FDA) will approve BoNT use in neurogenic bladder overactivity.

Key words: Botulinum neurotoxin (BoNT); Urologic disease; Neurogenic bladder; Benign prostatic hyperplasia; Pelvic pain

INTRODUCTION

Botulinum neurotoxin (BoNT) is produced by the anaerobic bacteria *Clostridium Botulinum*. The toxin was first discovered in 1897.[1] Although scientists recognized the ability of BoNT to block nerve transmission in 1949, it was not until the 1980s that the toxin was used in a clinical setting. Produced within the cytosol of the bacteria, BoNT is released as a polypeptide chain. It consists of a light (50kDa) and heavy (100kDa) chain linked by a disulphide bond.[2] The structure of BoNT is pivotal to its ability to act on the cholinergic neuromuscular junction.[3] There are seven serotypes of BoNT, each produced by a distinct strain of the bacteria. Designated type A, B, C1, D, E, F or G, each BoNT serotype has individual characteristics. However, only types A (Botox®, Allergan, Inc., CA, USA; Dysport, Ipsen Ltd, Berkshire, UK) and types B (Myobloc®, Elan Pharmaceuticals, Inc., Princeton, NJ, USA) are commercially available.[4] In urology, type A BoNT is most commonly used.

MECHANISMS OF ACTION

BoNT exerts its clinical effects of paralysis by preventing the release of acetylcholine at the cholinergic nerve terminals. The key cellular steps leading to the inhibition of neurotransmitter release are binding, translocation and cleavage.[5]

The heavy chain of BoNT binds to a specific receptor on the parasynaptic nerve terminal (Figure 1). The BoNT/receptor complex is then endocytosed into the nerve terminal. The light chain is translocated into the cytosol where it is able to cleave one or two of the pre-synaptic proteins (Figure 2).[2] These proteins are responsible for the docking and release of vesicles containing neurotransmitters.[6] It is the cleavage of these pre-synaptic proteins (SNAP 25) that results in the inability for acetylcholine to be released and exert its action (Figure 3).[7] Eventually the light chain within the cytosol deteriorates, allowing turnover of parasynaptic vesicles.[7] The effects of BoNT tend to last from 3 to 12 months.[8]

INDICATIONS

Neurogenic bladder

Detrusor sphincter dyssynergia

Detrusor sphincter dyssynergia (DSD) was the first and remains the most common urologic application of BoNT.[8] DSD has been defined as a detrusor contraction concurrent with an involuntary contraction of the urethral and/or periurethral striated sphincter muscle (rhabdosphincter), which prevents adequate voiding. The impact of DSD can be significant and is associated with a substantial burden of disease.[9] The management of DSD relies heavily on clean intermittent self-catheterisation (CISC). Patients unable to perform CISC require an alternative means to decrease outlet resistance.[10] In addition, low functional bladder capacity may mean that very frequent CISC is required and/or leakage may be difficult to prevent. Whilst other surgical procedures have been used, they are associated with significant complications including bleeding and stricture disease.[8,11] BoNT injections into the external sphincter are most useful in tetraplegics where clean intermittent self-catheterisation is often impossible and in whom one wants to avoid long-term catheterisation as a means of drainage due to risks of inherent catheter-related problems.

BoNT injections into the external sphincter can be performed by either a transurethral or transperineal approach. The former approach is more common. BoNT is injected transurethrally via a cystoscopic needle at the level of the striated sphincter.[12] Transperineal BoNT injections are performed by inserting a spinal needle on each side of the urethral meatus in women 10 and it requires electromyographic (EMG) guidance.[8, 10]

Over the past 20 years, a number of small prospective studies have evaluated BoNT therapy in DSD. In 1998 Petit et al. demonstrated success rates as high as 88%, with a reduction of residual urine by more than 50%.[13] The success of BoNT in DSD has been echoed by the other studies.[12, 14] BoNT therapy is safe, reversible and effective, making it a valuable treatment option in DSD.

Neurogenic Detrusor overactivity

Neurogenic Detrusor overactivity (NDO) is involuntary detrusor contraction due to a neurological condition, often resulting in incontinence.[15-16] NDO may be due to conditions such as spinal cord injuries, multiple sclerosis and spina bifida.[17] This condition is often managed by anticholinergic medications, however these drugs are not effective in all individuals with NDO and are associated with a number of side effects.[18]

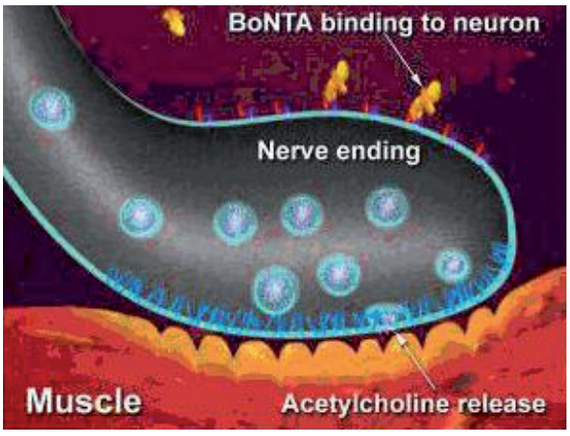


Figure 1. – BoNT Mechanism of Action - Binding.

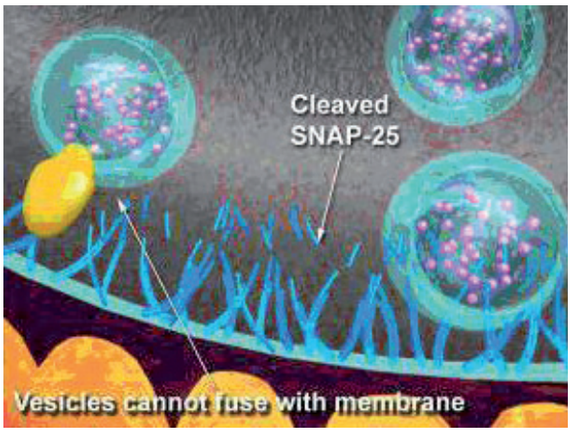


Figure 3. – BoNT Mechanism of Action – Cleavage.

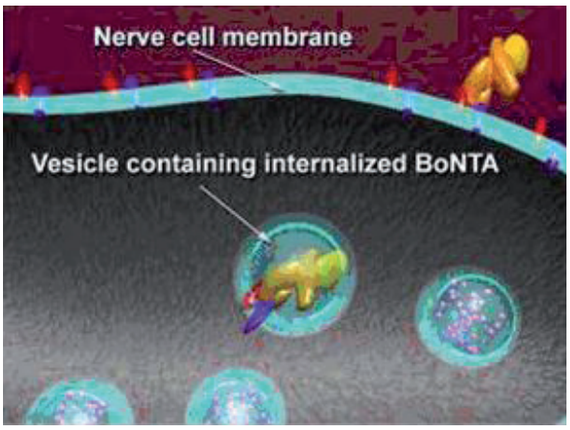


Figure 2. – BoNT Mechanism of Action - Translocation.

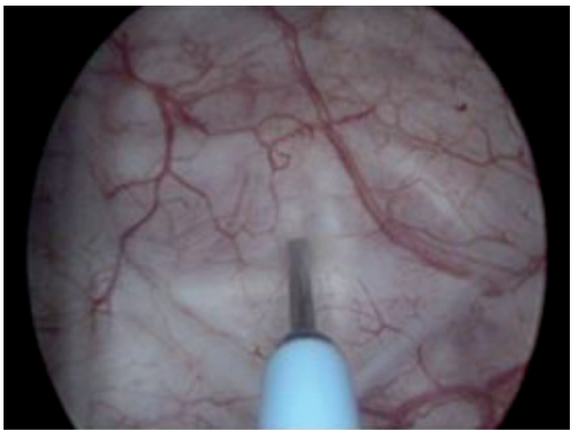


Figure 4. – BoNT injection under cystoscopic guidance into the bladder.

Multiple injections into the detrusor muscle or sub endothelial layer of the bladder can be performed using a cystoscope through which a long thin injection needle can be passed (Figure 4).[8] Most doctors perform 10-30 injections and the urinary trigone is generally avoided.[10]

The largest prospective study to date found that 73% of the 200-person cohort maintained complete continence 12 weeks after treatment.[19] In 2007, a review of clinical evidence by Dmochowski and Sand reported a continence rate between 50-90% in NDO after BoNT therapy.[17] Patient satisfaction was also deemed to be high in those with NDO treated with BoNT therapy.[17] It is anticipated that within the next 12 months, the United States Food and Drug Administration (FDA) will approve BoNT use in neurogenic bladder overactivity.

Non-neurogenic Lower Urinary Tract Dysfunction

Non-Neurogenic (Idiopathic) Detrusor Overactivity

Idiopathic detrusor overactivity (IDO) is represented often by involuntary detrusor contraction during bladder filling where no defined cause is found. It often causes overactive bladder (OAB) symptoms of urgency, frequency and/or nocturia, with or without urge incontinence. 16 For individuals with idiopathic OAB, traditional management options such as solifenacin (Vesicare™), oxybutinin (Ditropan™, Oxytrol™), tolterodine (Detrusitol™), or darifenacin (Enablex™) are not always effective or well-tolerated.[20]

BoNT is often administered as a day-surgery procedure, in a similar fashion to patients with neurogenic detrusor overactivity, except doses are often lower to prevent side effects, such as temporary urinary retention which may require a period of clean intermittent self-catheterisation or indwelling urethral catheterisation. All potential injection candidates are made aware of this risk during the informed consent process.

A number of cohort and randomised control trials (RCT) have been carried out in the last 10 years to assess the success of BoNT in refractory idiopathic OAB. Continence rates in the cohort studies ranged from 33-91% in patients treated with BoNT.[17] The combined result of three RCTs found the individual treated BoNT had 3.88 fewer episodes of incontinence compared with the placebo group and had an improved quality of life.[21-24]

Benign prostatic hyperplasia

Benign prostatic hyperplasia (BPH) is due the proliferation of transitional zone prostate tissue that results in enlargement and clinically manifests as lower urinary tract symptoms (LUTS). The gold standard therapy in BPH is considered transurethral resection of the prostate (TURP), however 15-25% of men who undergo this procedure have a poor long-term outcome.[25] BoNT has been found to relieve the symptoms produced by BPH by varying degrees.[25-27]

BoNT may be administered to the prostate by one of three routes; transurethral, transrectal or transperineal.[25-28] The transrectal approach is performed using transrectal ultrasound (TRUS) guidance.[29]

Current studies have demonstrated a 34-86% decrease in prostate volume at first follow-up.[28-29] The mechanism of action of BoNT in BPH is not fully understood. It is thought to relate to the toxins ability to relax smooth muscle and increase apoptotic activity in the prostate.[29-30] It may be useful in the drug-refractory patient group where TURP is contraindicated (e.g. in anaesthetically unfit patients). While BoNT therapy has the ability to reduce prostate size and BPH symptoms, larger randomised clinical trials are required before the clinician knows which patient groups are suitable for it to be considered in everyday clinical practice.

Pelvic Pain

The use of BoNT in the treatment of pelvic pain is still emerging, however the anti-noceptive mechanism of the toxin is not entirely understood.[15] BoNT therapy in the symptomatic treatment of interstitial cystitis has been explored in two small cohort studies with varying outcomes. Smith et al, found 69 % of patients experienced a decrease in symptoms such as pain, urinary frequency and nocturia; while the second study reports that there was no significant improvement in pain.[31-32] In 2000, Zermann et al. found a decrease in pain severity in 82% of male subjects with chronic pelvic pain syndrome (CPPS) after BoNT treatment into the perisphincteric area.[33] BoNT has also been shown to reduce pelvic pain and pressure in women with pelvic floor hypertonicity,[34] which is a condition associated with CPPS in its presentation. The evidence to support the analgesic effects of BoNT is promising but limited. Further studies are required before BoNT can be used in the routine treatment of pain-related urological conditions.

CONTRAINDICATONS

BoNT therapy is contraindicated in individuals who have a peripheral neuropathy (e.g. amyotrophic lateral sclerosis) or pre-existing disease of the neuromuscular junction.[10] BoNT treatment should be avoided during pregnancy, when breastfeeding and when taking medications that interfere with neuromuscular transmission (e.g. aminoglycosides).[10, 35]

TABLE 1. – Unwanted effects of BoNT.

Local	Systemic
Urinary retention	Decreased sensitivity
Haematuria	Dysphagia
Haematoma	Respiratory compromise
Urinary tract infection	Generalised weakness
	Diminished sensation
	Death

TABLE 2. – Summary of BoNT therapy in Urology

Benefits	Risks /Limitations
Clinical effects last a number of months	'Off Label' applications of the drug
Low risk profile	Rare but lethal side effects
Minimally invasive route of delivery	Repeated use may lead to sensitisation
Improved quality of life	Long term safety has not been
Improves symptom in a numbe of urological conditions	Limited high power clinical evidence

UNWANTED EFFECTS

BoNT therapy is considered safe, however it may be associated with a number of adverse effects (Table 1).

Local

BoNT injections have been associated with transient urinary retention, haematuria, local haematomas and an increased risk of urinary tract infections.[22, 35]

Systemic

Systemic effects are rare, as it requires the migration large quantities of BoNT into the blood stream. The lethal BoNT dose is considered 2000-3000 units, well above the therapeutic dose of 150-300units used in lower urinary tract dysfunction.[10] Repeated BoNT treatments may lead to the formation of neutralising antibodies that may reduce the efficacy of the toxin.[32] Other rare potential systemic effects include dysphagia, respiratory compromise, short term generalised weakness and diminished sensation.

CONCLUSION

BoNT has been shown to have a number of diverse urological applications, with new uses still emerging. At present, clinical evidence has demonstrated that BoNT is effective, safe and improves the quality of life in a number of conditions (Table 2). With respect to OAB, at the present time, BoNT should be reserved for anti-cholinergic-refractory cases only. Further robust clinical evidence is required before it can be used as a first line or standard treatment. Current research now focuses on better patient selection to maximise efficacy, improving and standardising injection protocols, and even less invasive delivery methods (e.g. bladder instillation with liposome-encapsulated BoNT). Due to its efficacy, low risk profile, duration of action and minimally invasive route of delivery, BoNT should surface in the very near future to become an integral part of the armamentarium in the treatment of a number of drug-refractory lower urinary tract conditions to improve quality of life.

KEY POINTS

- BoNT exerts clinical effects: paralysis and analgesia
- Shown to be beneficial in a range of urological conditions, especially overactive bladder (OAB)
- BoNT has a low risk profile
- BoNT therapy should be considered when standard treatments fail

Conflict of interest: A/Prof Prem Rashid has been a visitor to the American Medical Systems (AMS) US manufacturing facility undertaking a cadaveric dissection clinic and observed operative procedures by high volume implant urologists affiliated with AMS during that time. He also has acted as a consultant for Coloplast, Astra Zeneca, Ipsen, Hospira and Abbott pharmaceuticals, as well as, the Neotract Corporation. He was a Preceptor in Advanced Laparoscopic Urology with Professor Inderbir S. Gill, (then) Head of the Section of Laparoscopic and Robotic Surgery and Chairman, Glickman Urological Institute, Cleveland Clinic Foundation via a 2006 grant from the Australasian Urological Foundation. No commercial organization initiated or contributed to the writing of the article (apart from providing images for use where indicated).

REFERENCES

1. Erbguth FJ. From poison to remedy: the chequered history of botulinum toxin. Journal of Neural Transmission. 2008; 115(4):559-65.

2. Montecucco C, Schiavo G. Structure and function of tetanus and botulinum neurotoxins. Quarterly Reviews of Biophysics. 1995; 28(04):423-72.
3. Schurch B, Schmid DM, Stöhrer M. Treatment of Neurogenic Incontinence with Botulinum Toxin A. New England Journal of Medicine. 2000; 342(9):665-.
4. Leippold T, Reitz A, Schurch B. Botulinum Toxin as a New Therapy Option for Voiding Disorders: Current State of the Art. European Urology. [doi: DOI: 10.1016/S0302-2838(03)00250-1]. 2003; 44(2):165-74.
5. Sahai A, Khan M, Fowler C, Dasgupta P. Botulinum toxin for the treatment of lower urinary tract symptoms: A review. Neurourology and Urodynamics. 2005; 24(1):2-12.
6. Dolly JO, Aoki KR. The structure and mode of action of different botulinum toxins. European Journal of Neurology. 2006; 13:1-9.
7. Humeau Y, Doussau F, Grant NJ, Poulain B. How botulinum and tetanus neurotoxins block neurotransmitter release. Biochimie. [doi: DOI: 10.1016/S0300-9084(00)00216-9]. 2000; 82(5):427-46.
8. Moore C, Rackley R, Goldman H. Urologic applications of botox. Current Bladder Dysfunction Reports. 2006; 1(2):99-103.
9. Ku JH. The management of neurogenic bladder and quality of life in spinal cord injury. BJU Int. 2006; 98:739–45.
10. Smith CP, Chancellor MB. Emerging role of botulinum toxin in the management of voiding dysfunction. The Journal of Urology. [doi: DOI: 10.1097/01.ju.0000127725.48479.89]. 2004; 171(6, Part 1):2128-37.
11. Rajkumar GN, Conn IG. Botulinum toxin: a new dimension in the treatment of lower urinary tract dysfunction. Urology, 2004; 64(1):2-8.
12. Jost WH, Naumann M. Botulinum toxin in neuro-urological disorders. Movement Disorders. 2004; 19(S8):S142-S5.
13. Petit H WL, Gaujard E, Le Breton F, Ferrière JM, Lagueny A, Joseph PA BM. Botulinum A toxin treatment for detrusor-sphincter dyssynergia in spinal cord disease. Spinal Cord. 1998; 1998; 36:91–94.
14. Phelan MW, Franks M, Somogyi GT, Yokoyama T, Fraser MO, Lavelle JP, et al. Botulinum toxin urethral sphincter injection to restore bladder emptying in men and women with voiding dysfunction. The Journal of Urology. [doi: DOI: 10.1016/S0022-5347(05)66438-5]. 2001; 165(4):1107-10.
15. Rajkumar GN, Conn IG. Botulinum toxin: a new dimension in the treatment of lower urinary tract dysfunction. Urology. [doi: DOI: 10.1016/j.urology.2004.03.007]. 2004; 64(1):2-8.
16. Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, et al. The standardisation of terminology in lower urinary tract function: report from the standardisation sub-committee of the International Continence Society. Urology. [doi: DOI: 10.1016/S0090-4295(02)02243-4]. 2003; 61(1):37-49.
17. Dmochowski R, Sand PK. Botulinum toxin A in the overactive bladder: current status and future directions. BJU International. 2007; 99(2):247-62.
18. Reitz A, Schurch B. Intravesical therapy options for neurogenic detrusor overactivity. Spinal Cord. 2004; 42(5):267-72.
19. Reitz A, Stöhrer M, Kramer G, Del Popolo G, Chartier-Kastler E, Pannek J, et al. European Experience of 200 Cases Treated with Botulinum-A Toxin Injections into the Detrusor Muscle for Urinary Incontinence due to Neurogenic Detrusor Overactivity. European Urology. [doi: DOI: 10.1016/j.eururo.2003.12.004]. 2004; 45(4):510-5.
20. Nygaard I. Idiopathic Urgency Urinary Incontinence. New England Journal of Medicine. 2010; 363(12):1156-62.
21. Brubaker L, Richter HE, Visco A, Mahajan S, Nygaard I, Braun TM, et al. Refractory Idiopathic Urge Urinary Incontinence and Botulinum A Injection. The Journal of Urology. [doi: DOI: 10.1016/j.juro.2008.03.028]. 2008; 180(1):217-22.
22. Anger JT, Weinberg A, Suttorp MJ, Litwin MS, Shekelle PG. Outcomes of Intravesical Botulinum Toxin for Idiopathic Overactive Bladder Symptoms: A Systematic Review of the Literature. The Journal of Urology. [doi: DOI: 10.1016/j.juro.2010.02.009]. 2010; 183(6):2258-64.
23. Flynn MK, Amundsen CL, Perevich M, Liu F, Webster GD. Outcome of a Randomized, Double-Blind, Placebo Controlled Trial of Botulinum A Toxin for Refractory Overactive Bladder. The Journal of Urology. [doi: DOI: 10.1016/j.juro.2009.01.117]. 2009; 181(6):2608-15.
24. Sahai A, Khan MS, Dasgupta P. Efficacy of Botulinum Toxin-A for Treating Idiopathic Detrusor Overactivity: Results From a Single Center, Randomized, Double-Blind, Placebo Controlled Trial. The Journal of Urology. [doi: DOI: 10.1016/j.juro.2007.01.130]. 2007; 177(6):2231-6.
25. Chuang Y-C, Chiang P-H, Huang C-C, Yoshimura N, Chancellor MB. Botulinum toxin type A improves benign prostatic hyperplasia symptoms in patients with small prostates. Urology. [doi: DOI: 10.1016/j.urology.2005.04.029]. 2005; 66(4):775-9.
26. Maria G, Brisinda G, Civello IM, Bentivoglio AR, Sganga G, Albanese A. Relief by botulinum toxin of voiding dysfunction due to benign prostatic hyperplasia: results of a randomized, placebo-controlled study. Urology. [doi: DOI: 10.1016/S0090-4295(03)00477-1]. 2003; 62(2):259-64.
27. Kuo H-C. Prostate botulinum A toxin injection--an alternative treatment for benign prostatic obstruction in poor surgical candidates. Urology. [doi: DOI: 10.1016/j.urology.2004.10.077]. 2005; 65(4):670-4.
28. Park DS, Cho TW, Lee YK, Lee YT, Hong YK, Jang WK. Evaluation of Short Term Clinical Effects and Presumptive Mechanism of Botulinum Toxin Type A as a Treatment Modality of Benign Prostatic Hyperplasia. Yonsei Med J. 2006; 47(5):706-14.
29. Chuang YC, Giannantoni A, Chancellor MB. The potential and promise of using botulinum toxin in the prostate gland. BJU International. 2006; 98(1):28-32.
30. Goldstraw MA, Kirby RS, Dasgupta P. The role of botulinum toxin in benign prostatic hyperplasia. BJU International. 2006; 98(6):1147-8.
31. Smith CP, Radziszewski P, Borkowski A, Somogyi GT, Boone TB, Chancellor MB. Botulinum toxin a has antinociceptive effects in treating interstitial cystitis. Urology. [doi: DOI: 10.1016/j.urology.2004.06.073]. 2004;64(5):871-5.
32. Frenkl TL, Rackley RR. Injectable neuromodulatory agents: botulinum toxin therapy. Urologic Clinics of North America. [doi: DOI: 10.1016/j.ucl.2004.09.005]. 2005; 32(1):89-99.
33. Zermann DH, Ishigooka M, Schubert J, Schmidt RA. Perisphincteric Injection of Botulinum Toxin Type A. European Urology. 2000; 38(4):393-9.
34. Jarvis SK, Abbott JA, Lenart MB, Steensma A, Vancaillie TG. Pilot study of botulinum toxin type A in the treatment of chronic pelvic pain associated with spasm of the levator ani muscles. Australian and New Zealand Journal of Obstetrics and Gynaecology. 2004; 44(1):46-50.
35. Smith CP, O'Leary M, Erickson J, Somogyi GT, Chancellor MB. Botulinum Toxin Urethral Sphincter Injection Resolves Urinary Retention after Pubovaginal Sling Operation. International Urogynecology Journal. 2002; 13(3):185-6.

Correspondence to:

VINCENT TSE, MD
Consultant Urologist
Department of Urology
Concord Hospital, Sydney
New South Wales, Australia
e-mail: vwmtse@gmail.com

Book review

As announced in the Editorial by Bruce Farnsworth (Pelviperineology 2011; 30:5) this is the first of a series of articles highlighting the different sections of the book "Pelvic Floor Disorders, Imaging and a Multidisciplinary Approach to Management" edited by G.A. Santoro, P. Wieczorek, C. Bartram, Springer Ed, 2010.

Pelvic floor anatomy

GIULIO A. SANTORO[1], ANDRZEJ P. WIECZOREK[2]

[1]*Pelvic Floor Unit, I° Department of Surgery, Regional Hospital, Treviso - Italy*
[2]*Department of Pediatric Radiology, University of Lublin, Poland*

The *first section* of the book "Pelvic floor disorders - Imaging and Multidisciplinary Approach to Management" is entitled "Pelvic Floor Anatomy" and consists of five chapters describing the detailed anatomy of female pelvic floor, its physiology and patophysiology as well as neural control.

In the first chapter "*State of the Art: Pelvic Floor Anatomy*" J. O. L DeLancey and S. A. Shobeiri describe the functional anatomy of the pelvic floor in women especially highlighting supportive function of muscles and fasciae for pelvic organs and changes in their structures with the presence of prolapse. The female pelvis is naturally divided into anterior, posterior and lateral compartments, and its bottom is formed by levator ani muscles. Pelvic organs support system is multifaceted including the perineal membrane, the endopelvic fascia, and the levator ani muscles. The support of uterus and vagina differs in various regions: the upper-third of the vagina and the cervix (1st level) has relatively long suspensory fibers, attached vertically; mid-portion of the vagina (2nd level) has more direct attachment laterally to the pelvic wall and the most caudal portion of the vagina (3rd level) is attached directly to the surrounding structures and the elevator ani muscle and the perineal membrane are important supportive structures in this level. Damage in level 1 results in uterine or vaginal prolapse of the apical segment, while damage in levels 2 and 3 cause anterior and posterior vaginal wall prolapse. Various combinations of these defects are responsible for diversity of clinical problems.

The authors describe very precisely the anatomy and morphology of each of these supportive structures correlating their function with histological and patophysiological studies. Separate subdivision of this chapter provides information about levator ani muscles anatomy. There are three major components: iliococcygeal muscle, pubovisceral muscle and puborectalis muscle. The anatomical characteristics, origins and insertions of these muscles are also precisely described. The opening between levator ani muscles through which pelvic organs pass, forms the levator hiatus and its part ventral to the perineal body is called urogenital hiatus. The levator ani tonic activity keeps the hiatus closed by compressing the urethra, vagina and rectum to the pubic bone and pulling the pelvic floor upwards. This constant action eliminates any opening within the pelvic floor preventing prolapse to occur. Damage to the levator ani muscles caused by nerves or connective tissue damage will result in prolapse. Authors highlight the role of endopelvic fascia, which in the case of the levator ani damage, is the last supporting structure of pelvic organs preventing the prolapse to develop for short periods of time. The interaction between pelvic floor muscles and endopelvic fascia maintains the "flap valve" configuration in the pelvic floor lessening ligaments tension.

The second chapter "*The Integral Theory: A Musculoelastic Theory of Pelvic Floor Function and Dysfunction*" by Peter Papa Petros and Michael Swash, provides information about accurate diagnosis and surgical treatment for pelvic floor symptoms, such as: urinary and fecal incontinence, pelvic pain and defecation difficulties, basing on the Integral Theory. The authors explain essential concepts of this theory. The essential statement is that pelvic organs are suspended by four suspensory ligaments and are controlled by neurologically coordinated muscle forces contracting against these ligaments. Any laxity of these suspensory ligaments might hamper muscle forces resulting in organ prolapse or dysfunction in organ closure or opening causing incontinence or evacuation symptoms, respectively. Thus, to perform a successful reconstructive surgery, knowledge about which ligament is affected is required (Figure 1).

According to integral theory, an accurate diagnosis of ligaments laxity could be made with the use of symptom-based algorithm and three zones (anterior, middle, posterior compartments) examination system. Some symptoms are zone specific, however some of them may occur due to the damage in at least two compartments (e.g. fecal incontinence in the anterior and posterior zones, urge incontinence in all three zones). In such cases, coexisting symptoms and vaginal digital examination should be involved to diagnose and confirm the site of damage. Once it is done, proper surgery, which aim is to reconstruct affected ligaments with the use of propylene tapes, could be performed.

The third chapter entitled "*Pathophysiology of the Pelvic Floor: Basic Physiology, Effects of aging, and Menopausal Changes*" written by Dee E. Fenner and Yvonne Hsu describes etiologic risk factors and associations contributing to pelvic floor disorders such as vaginal parity, ageing, hormonal status, pelvic surgery, collagen diseases and depression. Many of these relationships are poorly understood, moreover, various pelvic floor disorders may be explained by different etiological risk factors or pathophysiological mechanisms. For example, vaginal parity predisposes to developing pelvic organ prolapse, while urinary incontinence has got many other risk factors with equal or greater influence including obesity and ageing. Differences found in women with prolapse suggest that biochemical changes in the connective tissue may play and important role in prolapse, however these studies are unable to explain the sequence of prolapse progression. Thus, it is not defined whether alterations in connective tissue lead to prolapse or are a response to the mechanical effects of prolapse. Electromyographic (EMG) studies of women with pelvic floor disfuctions, including prolapse and incontinence, found changes consistent with motor unit loss or failure of central activation. It has been confirmed that vaginal delivery con-

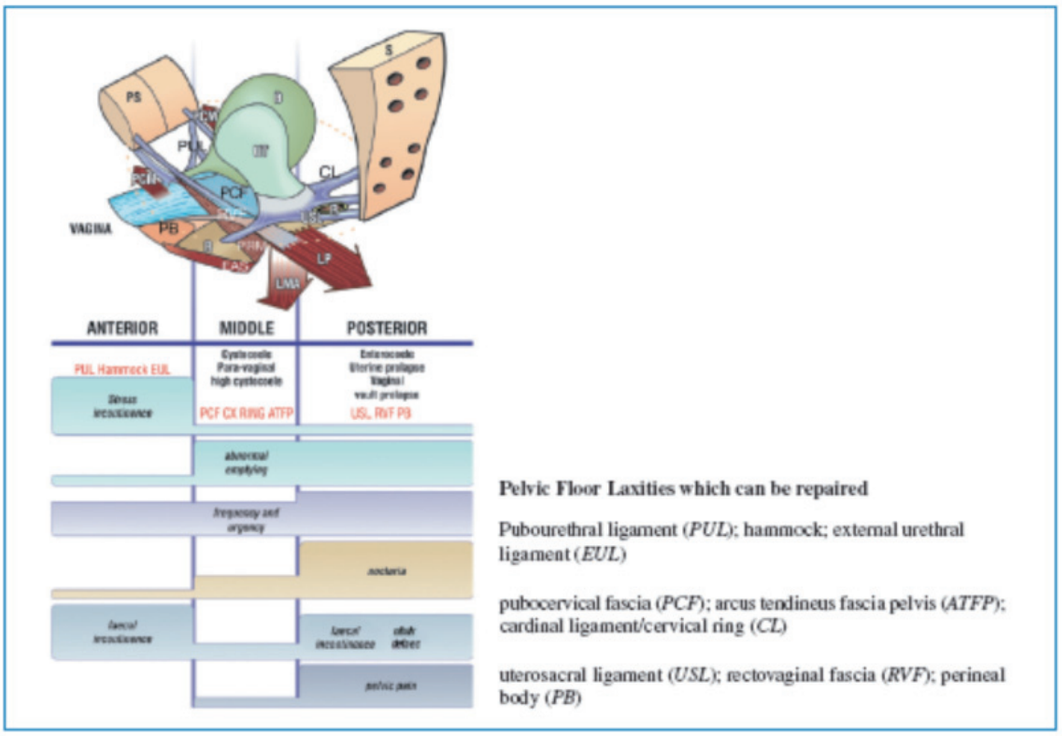


Fig. 2.8 The pictorial diagnostic algorithm schematically indicates the sites of connective tissue defects (laxities of ligaments or fascias), which can be repaired by surgery, and the association of each zone with symptoms of pelvic floor dysfunction. The area of the symptom rectangle indicates the estimated frequency of symptom causation in each zone. Anterior zone: external meatus to bladder neck; middle zone: bladder neck to anterior cervical ring; posterior zone: posterior vaginal wall from the cervix to the perineal body. *B*, bladder; *EAS*, external anal sphincter; *LMA*, longitudinal muscle of the anus; *LP*, levator plate; *PCM*, pubococcygeus muscle; *PS*, pubic symphysis; *R*, rectum; S, sacrum; *UT*, uterus

Figure 1. – The Integral Theory: A Musculo-elastic Theory of Pelvic Floor function and dysfunction.

fers a four-to eleven-fold higher risk of prolapse that increases with parity. The structural components that include the pelvic floor musculature, connective tissue condensations and fibromuscular walls of the pelvic viscous work together to provide pelvic organ support. When components of pelvic support and their relations to each other have been identified, we will be able to understand how disruptions result in failure and the resulting sypmtoms. Investigations into the biochemical processess are lacking. It has been proven however, that hormonal replacement therapy (HRT) clinically does not improve urinary incontinence and may in fact promote symptoms and increase severity of incontinence. In contrast, HRT may protect from developing POP. Much work is needed at the molecular, cellular, and clinical levels to understand the mechanisms and associations between HRT, ageing, and the impact of vaginal birth on pelvic floor disfunctions.

The fourth chapter "*The Pelvic Floor: Functional Concepts and Neurocontrol*" by Michael Swash includes the rewiev of the development of current ideas of pelvic floor function. The importance of understanding motor control mechanisms of pelvic floor responsiveness in health and disease is an underlying theme of the response to all forms of treatment in pelvic floor disorders. This is an adaptive response based on the capacity of the system to respond when there is significant functional damage. The author underlines that the pelvic floor should be concidered as a holistic functional entity, rather than three separate anterior, middle, and posterior perineal systems or structures. Continence and evacuation of feces and urine are under the control of the will, and therefore of the brain. The necessity to initiate evacuation, however, is almost always triggered by sensory input from the bladder or lower colon and rectum, indicating a need to switch from storage to evacuation. When the pelvic floor is dysfunctional, whether beacuse of stretch injury to ligaments, or beacuse of denervation-induced weakness to the pelvic floor musculature, or as a result of direct injury during childbirth, the central nervous system (CNS) is capable to adapt the action of the weakened muscular system to maintain function, even when the damage to the effector is quite severe.

Biofeedback has been propounded as a treatment for fecal incontinence. The technique utilizes several methods involving feedback from EMG signals of pelvic floor muscle activity in order to "teach" the subject how better activate and control these muscles. In mild dysfunctional states, it can be quite effective.

Much has been learned in recent years, however a full understatnding of the effects of weakness in specific muscular systems, and of the effects of loss of elastic resistance in pelvic floor ligaments, is not yet accomplished. The compensatory capacity of the CNS to modulate pelvic floor function is also not yet well understood. Inly a full knwoledge of this capacity will enable appropriate and testable procedures to be develloped. Much progress has been made, but there is much more to be learned.

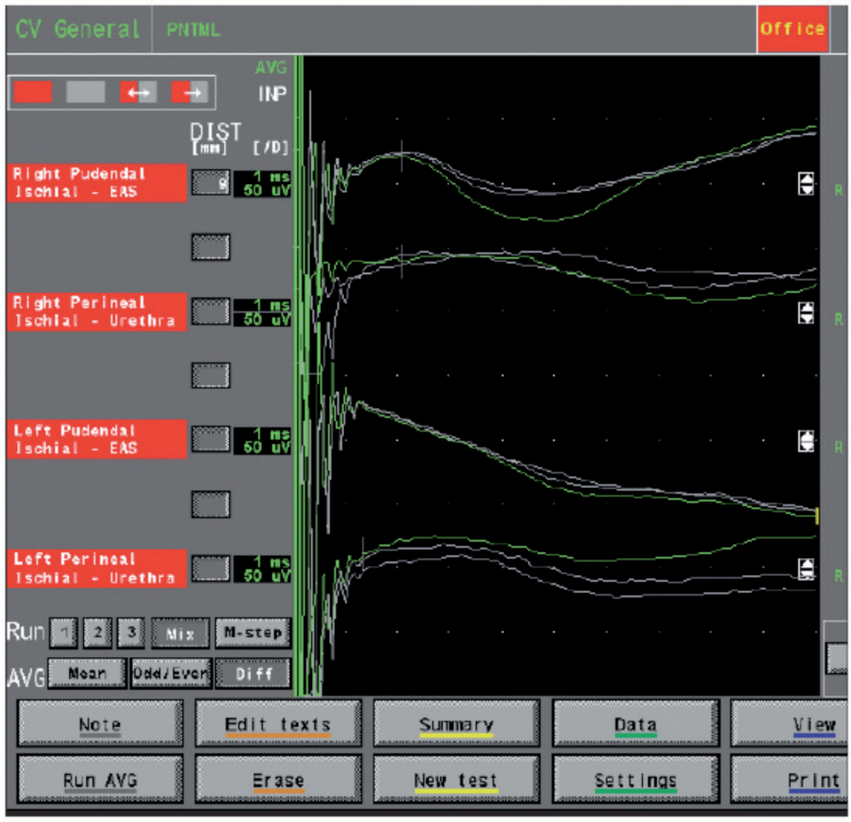


Fig. 5.4 PNTML and PeNTML. Stimulus is applied with the St Mark's electrode. A two-channel system allows for simultaneous recording of CMAP latency at the anal (PNTML) and urethral (PeNTML) sphincter. Typical small-amplitude responses are seen. Occasionally, due to the short latency, there is no return to "baseline" after the shock artifact prior to the onset of the CMP, making measurement difficult

Figure 2. – Typical waveform from pudendal (PNTML) and perineal (PeNTML) nerve conduction studies with simultaneous recording of CMAP (compound muscle action potentials) latency at the anal and urethral sphincters.

The fifth chapter entitled "*Clinical Neurophysiology of the Pelvic Floor*" by W. Thomas Gregory and Kimberly Kenton focuses on electrodiagnostic testing of the pelvic floor, which is becoming increasingly common in clinical pelvic medicine and pelvic floor research. Clinically, it can be used with history, physical examination, and urodynamic testing to aid in the disgnosis of certain pelvic floor disorders and to determine if a central or peripheral neurologic problems exist. Electrodiagnostic testing is also emerging in studies investigating the etiology of pelvic floor disorders. A basic understaning of the principles and techiques used in electrodiagnostic medicine is essential for reconstructive pelvic surgeons. However, most pelvic surgeons will never have the skills or expertise to perform pelvic floor neurophysiologic testing. According to authors a multidisciplinary teams including urogynecologic, urologic and colorectal surgeons, phychatrist, neurologist, and physical therapists are imperative if we are going to improve our understanding of pelvic floor disorders and improve treatment outcomes.

Much of our current understanding of the etiology of pelvic floor disorders has come from both nerve conduction studies and EMG of the pelvic floor muscles in women with stress incontinence, fecal incontinence or pelvic organ prolapse. We understand that surgery can affect pelvic innervation, the relationship between vaginal childbirth and pudental neuropathy has been also confirmed. The degree of denervation and pelvic floor injury can be measured. Such measurements have some correlation with clinical outcomes, but further research refining techniques and establishing normative electrodiagnostic parameters for the urethral sphincter, anal sphincter, and levator ani are imperative. Pelvic floor electrodiagnostic studies may aid in the clinical diagnosis of some pelvic floor disorders and help to predict outcomes of incontinence surgery. However, further confirmatory studies are necessary.

Correspondence to:
Dr G.A. SANTORO
Chirurgia Generale 1
Ospedale regionale Cà Foncello
31100 Treviso Italia
e-mail: gasantoro@ulss.tv.it

Original article

Surgical strategies for full-thickness rectal prolapse: a retrospective study and review of literature

GIOVANNI MILITO, FEDERICA CADEDDU, IVANA SELVAGGIO, ATTILIO M FARINON

University Hospital Tor Vergata, Rome, Italy

Abstract: Purpose**:** Treatment of rectal prolapse is extremely challenging; both perineal and abdominal approaches have shown significant limitations: considerable incidence of postoperative constipation after both laparotomic or laparoscopic rectopexies; long operative time and anastomotic leakage risk after resection-rectopexy; Delorme transrectal excision requires surgical skills and is associated with high anal stenosis and recurrence rate; finally, levatorplasty is often ineffective. Methods**:** We retrospectively reviewed our experience of the period 2004-2009: 89 constipated patients with rectal prolapse were treated using transperineal procedures in 28 cases and through transabdominal approaches in 61 cases. Furthermore, a literature review was performed using the National Library of Medicine's Pubmed Database; articles reporting on treatment of rectocele both with transperineal procedures and abdominal rectopexy were examined. Results**:** Out of 89 constipated patients, 16 underwent Delorme procedure with a mortality rate of 1.4% morbidity of 5.2% and recurrence rate at 5 years of 9.2%; 12 patients underwent Altemeier procedure with similar results but lower recurrence rate (1% at 5 years). Sixty-one patients underwent abdominal rectopexy with mesh: 25 patients were treated according to Orr Loygue technique with similar results but lower recurrence rate (2.5% at 5 years) and 36 were operated on according to Wells technique with similar mortality and recurrence rate but postoperative defecation impairment in 20% of patients. Conclusions**:** In summary, predicting which patient will benefit from surgical intervention remains a challenge. An effective method of patient selection based on an accurate morpho-functional assessment and patient performance status examination would optimize the outcome. In our experience, basically, we use transanal/perineal procedures to treat rectocele, and rectal prolapse in elderly, high risk patients and abdominal operations to treat of rectal prolapse and enterocele in young patients.

Keywords: Rectal prolapse; Transperineal procedure; Rectocele; Enterocele; Rectopexy

INTRODUCTION

Rectal prolapse is defined as a protrusion of the rectum beyond the anus. Full-thickness rectal prolapse should be distinguished from mucosal prolapse in which there is protrusion of only the rectal or anal mucosa.[1-3]

Aetiological factors include lax and anatomic condition of the muscles of the pelvic floor and anal canal, abnormally deep pouch of Douglas, weakness of both internal and external sphincters, lack of normal mesorectum and finally weakness of lateral ligaments.[3-6]

Constipation is associated with prolapse in 30% to 70% of patients, with chronic straining, sensation of anorectal blockade, need of digital evacuation. In addition 60% of patients have coexisting incontinence due to the stretching of the anal sphincters caused by the prolapse and due to the impaired rectal compliance.

Regardless of the therapy chosen, matching the surgical selection, i.e. physical examination, defecatory history, endoscopy, manometry and colonic transit studies, is essential for the correct management of the patients.[5-6]

A complete colonoscopy is useful to test for organic colonic pathologies anorectal manometry and defecating proctography to confirm rectal prolapse and to test for outlet dysfunction or associated rectocele. A colonic transit study can be helpful for those patients who give a history of severe constipation and in whom the surgeon may be considering a resection-rectopexy.

Regarding the treatment, patients who gain no relief from dietary modification and biofeedback therapy should be offered surgery.

Surgical therapy is aimed to correcting the prolapse, restore the continence and prevent constipation or impaired evacuation with acceptable mortality and recurrence rates. There are many procedures described for the treatment of rectal prolapse, that can be divided into abdominal or perineal approaches. The perineal approaches have been reserved to the frail and elderly patients, given that general anesthesia and laparotomy can be avoided; whereas the abdominal approaches are thought to provide a more effective repair with a lower recurrence rate.

More recently, laparoscopic surgery has emerged as an effective tool for the treatment of rectal prolapse because no specimen is removed and no anastomosis is required. Previous trials have suggested that laparoscopic surgery has many short term advantages over open surgery, including less pain and scarring, shorter hospital stay and faster recovery. In this retrospective study we reviewed our experience with 89 constipated patients presenting with rectal prolapse surgically treated using both transperineal and open abdominal approaches. In addition a review of literature was performed to point out the surgical strategies and outcomes for the treatment of rectal prolapse.

MATERIALS AND METHODS

Between January 2004 and December 2009, 89 constipated patients after medical treatment failure, were evaluated and surgically treated at the Division of General Surgery of the Department of Surgery, Tor Vergata University Hospital, Rome. All the patients underwent a pre-treatment evaluation, which included history of previous gynaecological, urological, or ano-rectal surgery and symptoms, clinical examination, anorectal manometry, anoscopy, colonic transit test and defecography. In some cases transanal ultrasound, pelvic MR, colpo-entero-defecography and colonoscopy were performed in order to evaluate concomitant bowel diseases.

Anorectal manometry was performed at rest, after voluntary contraction (ie, the maximal voluntary increase above the resting tone) and during straining. At defecography, resting state, voluntary and maximum contraction of the sphincter and pelvic floor muscles, and straining during defecation were recorded. Rectal emptying was also assessed. X-ray films were taken in each position and dynamic assessment of the defecation was also obtained.

All patients were operated on by the same senior surgeon (G.M.). Written informed consent had been obtained from all the subjects after a full explanation of the procedure.

Regarding the surgical technique both perineal (Delorme and Altemeier procedures) and abdominal approaches (Wells and Orr Loygue procedures) were used according

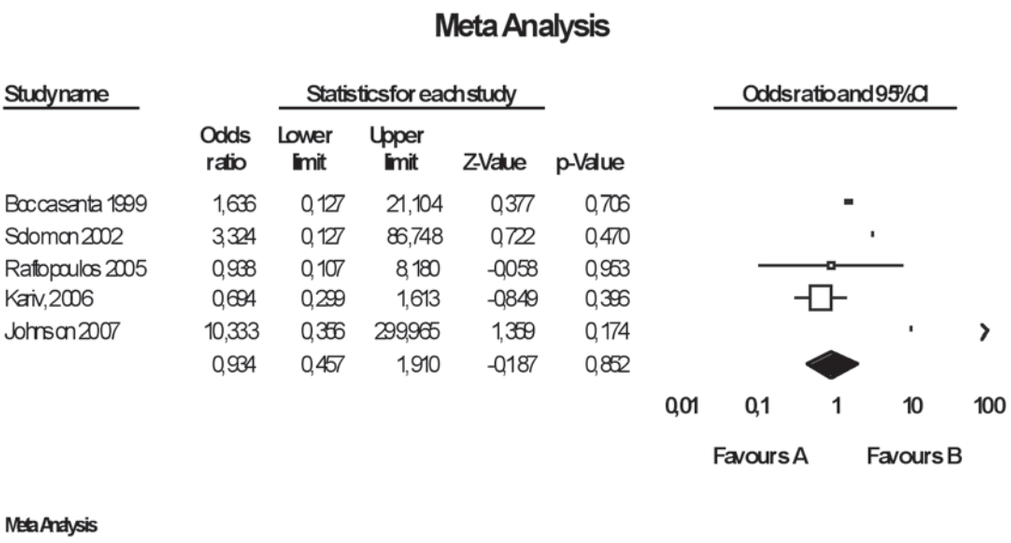


Fig. 1a – Meta-analysis of trials comparing open and laparoscopic approach. Forest plot of recurrence. Random model. Salked 2004 and Baker 1999 have been excluded because of lack of data.

to the clinical presentation and performance status of each patient.

Patients were clinically assessed at the first follow up visit up to 7 days after the operation. Subsequently they were followed up every 15 days for the first 2 months and then at 6, 12, 24 and 36 months

Demographic data, faecal continence and complications were recorded. Degree of continence was scored according to the Wexner continence score. The quality of life was evaluated using SF-36 questionnaire. During follow up visits all patients were submitted to clinical examination of the perineum, rectum and vagina, digital exploration and anoscopy.

RESULTS

Twenty-eight patients were treated using transperineal procedures and 61 through transabdominal approaches.

Sixteen patients (10 males 6 females, average age 72 years, range 58-94) underwent Delorme procedure with a mortality rate of 1.4%, morbidity of 5.2% and recurrence rate at 5 years of 9.2%. No constipation worsening was recorded. Continence improvement was recorded in 47% of patients. The follow up ranged between 6 and 60 months.

Twelve patients (4 males 8 females average age 63 years range 48-79) underwent Altemeier procedure with a mortality rate of 1.9%, morbidity of 6% and recurrence rate at 5 years of 1%. No constipation worsening was recorded. The follow up ranged between 6 and 60 months.

Sixty-one patients underwent abdominal rectopexy with mesh. Twenty-five patients (16 males 9 females, average age 46 years, range 38-79) were treated according to Orr Loygue technique with a mortality rate of 2%, morbidity of 6.2% and recurrence rate at 5 years of 2.5%. Constipation was cured in 61% of patients in absence of worsening. Continence improvement was recorded in 58% of patients. The follow up ranged between 5 and 57 months.

Thirty-six patients (20 males 16 females, average age 61 years, range 52-86) were operated on according to Wells technique. The mortality was 3%, the morbidity 8% and recurrence rate at 5 years of 3%. Constipation worsening was recorded in 6 patients. Continence improvement was recorded in 55% of patients. The follow up ranged between 7 and 55 months.

DISCUSSION

The management of rectal prolapse is still a challenge with no clear predominant treatment of choice. The procedures described for the treatment of rectal prolapse can be divided into abdominal or perineal approaches.

Perineal approaches

Perineal procedures for rectal prolapse include the

TABLE 1 – Results reported in literature of suture rectopexy

Authors	Year	N Pts	Procedure	Continence improvement %	Constipation improvement %	Recurrence N (%)	Follow-up (months)
Carter[10]	1983	32	SR	NS	NS	1 (3)	144
Novell[11]	1994	32	SR	15 (+)	31(-)	1 (3)	47
Graf[12]	1996	53	SR	36(+); 12(-)	30(+); 27(-)	5 (9)	97
Khanna[13]	1996	65	SR	75(+)	83(+)	0	65
Briel[14]	1997	24	SR	67(+)	NS	0	67
Llyanage[15]	2009	81(70)	SR+ resection	81(+)		5 (7)	2-47*

N Pts: number of patients; SR: suture rectopexy; NS: not stated;* weeks

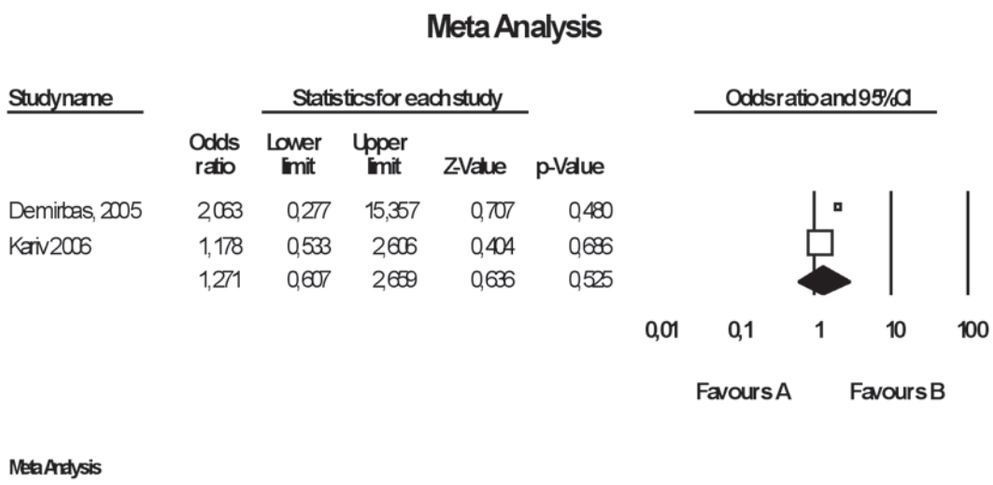


Fig. 1b – Meta-analysis of trials comparing open and laparoscopic approach. Forest plot of incontinence Random model. Salked 2004, Baker 1997, Boccasanta 1999, have been excluded because of lack of data. Johnson 2007, Solomon 2002 reported data in a way not suitable for meta-analysis.

STARR, the Delorme and the Altemeier operations. They are indicated in case of old, high risk patients presenting with II III degree prolapse.

The STARR procedure consists of transanal resection of the distal rectum by double stapler. According to the indications of SICCR it should be performed in extremely selected patients with low rectoceles up to 3 cm, small and low fascial defects in absence of enterocele, sigmoidocele, puborectalis dyssinergia and motility disorders.[7] Although some clinical series reported improvement rate over 80% after STARR procedure, different authors reported serious complications such as rectal bleeding, sepsis, rectovaginal fistula, urgency and faecal incontinence.[8]

The Delorme procedure includes mucosal stripping of the rectum, followed by plication of the muscle layers. It is indicated in high risk elderly patients presenting with prolapse up to 3-4 cm in absence of diverticulosis.

In line with our results, in literature mortality ranges between 0% and 4% and recurrence ranges between 4% and 38%. Continence improvement up to 67% has been reported in absence of postoperative constipation worsening. Factors associated with failure of the Delorme procedure include faecal incontinence, chronic diarrhoea, and major perineal descent (>9 cm on straining).[9]

The Altemeier procedure, or perineal rectosigmoidectomy, is a full-thickness resection of the rectum with coloanal anastomosis. It is indicated in high risk elderly patients presenting with II III degree prolapse and II degree sigmoidocele. Similar to our series, the reported overall mortality rates ranged from 0% to 5% and recurrence rates

TABLE 2 – Results reported in literature of mesh rectopexy

Authors	Year	Procedure	N Pts	Continence improvement %	Constipation improvement %	Recurrence N (%)	Follow-up (months)
Penfold[16]	1972	Post Mesh	101	22	NS	3 (2.97)	48
Morgan[17]	1972	Post Mesh	150	42	58	3 (2)	36
Notaras[18]	1973	Post Mesh	19	NS	NS	0	84
Launer[19]	1982	Ripstein	54	41	0 (10 worsening)	6 (11.1)	64
Holmstrom[20]	1986	Ripstein	108	37	0 (17 worsening)	4 (3.7)	83
Roberts[21]	1988	Ripstein	135	78	69	13 (9.6)	41
Novell[22]	1994	Post Mesh	31	3	0 (48 worsening)	2 (6.4)	47
Keighley[23]	1984	Post Mesh	100	64	NS	0	24
Tjandra[24]	1993	Ripstein	142	18	0	10/142	50
Galili[25]	1997	Post Mesh	37	NS	NS	1 (2.7)	44
Yakut[7]	1998	Post Mesh	48	NS	0	0	38
Aitola[26]	1999	Post Mesh	96	26	24	6 (6.2)	78
Schultz[27]	2000	Ripstein	69	20 (10 worsening)	37 (8 worsening)	1 (1.4)	82
Mollen[28]	2000	Post Mesh	18	NS	0	0	42
Winde[29]	1993	Ripstein-Corman	47	23	17	0	51

Post: posterior; NS: not stated.

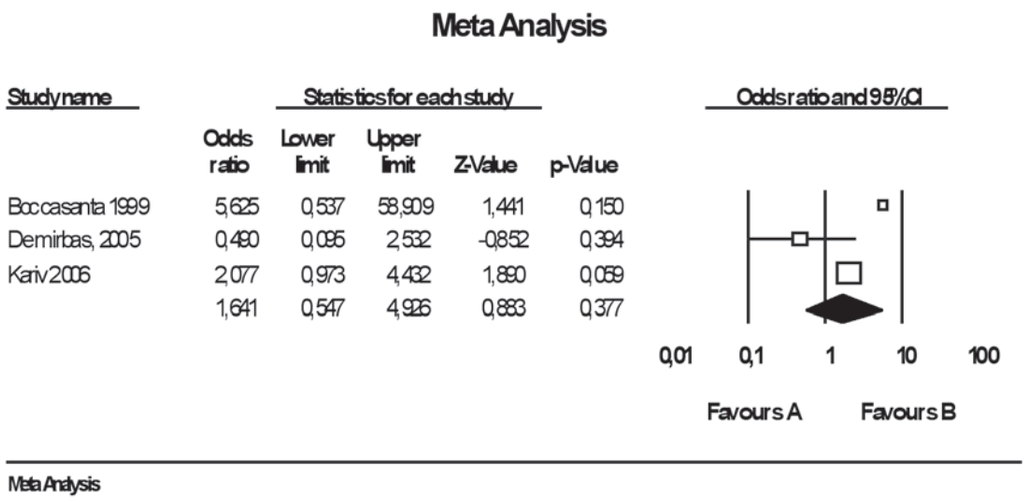


Fig. 1c – Meta-analysis of trials comparing open and laparoscopic approach. Forest plot of constipation. Random model. Salked 2004, Baker 1999, Raftopoulos 2005, have been excluded because of lack of data. Johnson 2007, Solomon 2002 reported data in a way not suitable for meta-analysis.

from 0% to 16%[9]. The postoperative course is generally uneventful. Potential complications include anastomotic bleeding, pelvic sepsis and, although uncommon, anastomotic dehiscence. This procedure can be combined with plication of the levator ani muscle, to reduce continence impairment reported up to 90%. Since recurrence probably reflects inadequate resection, care must be taken to mobilize the entire redundant rectum and to perform the anastomosis within the pelvis.

Abdominal approaches

Many transabdominal techniques have been proposed for rectal prolapse. These procedures require fixation of the rectum to the sacrum, by either a suture or mesh. An anterior resection or sigmoid colectomy is often added to the procedure. Suture rectopexy consists of rectum fixation to presacral fascia by interrupted sutures. In the Wells procedure after the rectal mobilization a mesh is inserted between the sacrum and the rectum and fixed to sacral promontory and lateral rectal wall. The Ripstein procedure is an anterior 360º rectopexy. The Orr-Loygue rectopexy consists of anterolateral rectum fixation with double mesh. The results of suture and mesh rectopexy in literature are shoed in table 1[10-15] and 2.[16-29]

The addition of sigmoid resection to rectopexy (Frykman Goldberg procedure) combines the advantages of mobilisation of the rectum, sigmoid resection and rectum fixation. Most series used resection plus suture rectopexy. Besides this, few authors performed resection plus posterior mesh rectopexy.[7,30-35]

Concerning the results of Wells procedure in literature, mortality rates ranged from 0% to 3% and recurrence rates were reported between 0% and 6%. Improvement in continence occurred up to 75%, but there was a variable response of constipation.[7,16-19,22,23,25,26,28] Accordingly in our series we reported constipation worsening in 20% of patients and recurrence rate at 5 years of 3%. Besides this, continence improvement was recorded in 55% of patients.

Regarding the results of resection+ rectopexy in literature, mortality rate ranges between 0% and 6.7% with an associated recurrence rate of 0%-5% (table 3).[30-35] There was an overall improvement both in continence and in constipation. Discussion about the mesh fixation, i.e. posterior or anterior approach, is still ongoing; in addition, the optimal material or suture to be used for fixation is still unclear.

Besides this, constipation is a major functional problem for patients with rectal prolapse with conflicting results and worsening of constipation reported up to 40% of patients.[9] The only theme that seems clear from literature is that postoperative constipation after rectopexy is not completely understood. Actually, the constipation may be obstructive (bowel intussusception into the rectum, enterocele, puborectalis dissynergia) or secondary to colonic dysmotility. Postoperative constipation may be due to colonic dysmotility from denervation, division of the lateral rectal ligaments, and sigmoid kinking secondary to rectal mobilization. Several authors suggested to preserve lateral ligament in order to improve both constipation and continence.[9,36] The left colon and rectum receive retrograde innervations through the lateral ligaments; thus, lateral

TABLE 3 – Results in literature of rectopexy plus resection

Authors	Year	N Pts	Procedure	Continence improvement %	Constipation improvement %	Recurrence N (%)	Follow-up (months)
Watts[30]	1985	80	SR+ Res	78	NS	2 (2.5)	48
Tjandra[31]	1993	18	SR+ Res	11	56	NS	50
Deen[32]	1994	10	SR+ Res	90	NS	0	17
Huber[33]	1995	42	SR+ Res	44	18	0	54
Kim[34]	1999	176	SR+ Res	55	42	9	98
Husa[35]	1988	48	SR+ Res	90	56	4 (8.3)	51,6

SR: suture rectopexy; Res: resection; N Pts: number of patients: NS: not stated.

TABLE 4 – Results of OPEN versus LAPAROSCOPIC APPROACH

Trial	Year	Study type	Type PTS	N PTS	Continence improvement N	Constipation improvement N	Recurrence N	Follow-up (months)
JOHNSON[39]	2007	Prosp NR	OPEN	5	GD	GD	1/5	17*
			LPS	15	GD	GD	0	
KARIV[40]	2006	Prosp NR	OPEN	86	19/56	30/56	11/86	59*
			LPS	86	17/56	20/56	15/86	
DEMIRBAS[41]	2005	Prosp NR	OPEN	17	3/11	411	0	36
			LPS	23	2/13	7/13	0	16
RAFTOPOULOS[42]	2005	Retrospec	OPEN	105	NS	NS	9/105	49
			LPS	11	NS	NS	1/11	
SOLOMON[43]	2002	Prosp RB	OPEN	19	NS	NS	1/19	23**
			LPS	20	NS	NS	0	
BOCCASANTA[44]	1999	Prosp NR	OPEN	13	NS	5/13	2/13	37*
			LPS	10	NS	1/10	1/10	26
BAKER[45]	1997	Retrospec	OPEN	10	NS	NS	NS	27
			LPS	8	NS	NS	NS	
SALKED[46]	2004	Retrospec Cohort	OPEN	20	NS	NS	NS	NS
			LPS	19				

NS: not stated; Retrospec: retrospective; Prosp: prospective; NR: not randomized; LPS: laparoscopic; GD: Grouped Data; RB: Randomized Blinded

ligament division during rectopexy has been suggested to denervate the rectum, causing postoperative constipation.[9] Accordingly, Nelson and coworkers in a recent Cochrane review on 12 trials and 380 patients, reported that division, rather than preservation, of the lateral ligaments was associated with less recurrent prolapse but higher post-operative constipation rate.[36]

The abdominal operations for rectal prolapse can all be performed laparoscopically. Laparoscopic rectopexy gained rapidly popularity given that it's simple, easy to perform and has several short term advantages, including less pain and scarring, decrease rate of wound hernias and bowel obstruction, shorter hospital stay and a more rapid recovery. Regarding the results reported in literature the mortality was 0% with recurrence rates up to 4%. The effect on continence and constipation depends on the type of operation performed.[9,36-38]

Laparoscopic versus open surgery

Three meta-analyses of comparative studies open versus laparoscopic surgery for rectal prolapse have been published in the literature. The results of these meta-analyses suggest that although the operative time is greater, laparoscopic surgery has many short term advantages over open surgery, including less pain and scarring, shorter hospital stay and faster recovery. There was no difference in recurrence rates or morbidity (the primary outcomes) between the two techniques.[36-38]

Recently, we meta-analysed the trials comparing laparoscopic versus open abdominal rectopexy (suture and mesh rectopexy with or without resection) with a focus on long term results.

Seventeen trials on open and laparoscopic rectopexy, including more than 1000 patients, were obtained from the literature research using the National Library of Medicine's Pubmed Database. Eight comparative studies, published between 1997 and 2007, matched the inclusion criteria, comparing laparoscopic and open rectopexy, with a follow up longer than 16 months. The median follow-up time of the studies ranged from 16 to 49 months (table 4).[39-46]

Our meta-analysis showed no significant difference in the recurrence rate between open rectopexy and laparoscopic rectopexy (OR, 0.934; 95 percent CI, 0.457-1.910; Z value = -0.187; $P = 0.852$) using random effect model (figure 1a).

Accordingly, most studies in literature showed that the recurrence rates for rectal prolapse after either laparoscopic or open surgery are lower than 10% and similar.[40]

Furthermore, we obtained no statistical significant difference regarding incontinence between open rectopexy and laparoscopic rectopexy (OR, 1.271; 95 percent CI, 0.607-2.659; Z value = 0.636; $P = 0.525$) using random effect modelling (figure 1b).

Actually, different mechanisms of fecal incontinence in patients with rectal prolapse have been claimed: pudendal nerve neuropathy, direct sphincter trauma from the rectal intussusception, chronic stimulation of the rectoanal inhibitory reflex, and impaired rectal sensation.[40]

Continence is restored after surgery, either open or laparoscopic, in a high percentage of patients with rectal prolapse.[9] The exact mechanism of continence restitution has not been firmly established. Suggested mechanisms include restoration of internal anal sphincter function, improved rectal compliance and anorectal sensation and finally it may be the effect of postoperative constipation that protects patients from incontinence.

Finally, our meta-analysis showed no statistical significance regarding constipation between open and laparoscopic rectopexy (OR, 1.641; 95 percent CI, 0.547-4.926; Z value = 0.833; $P = 0.377$) using random effect modelling (figure 1c).

Accordingly, previous comparisons between laparoscopic and open surgery failed to reveal significant long-term functional differences between the two groups with constipation worsening in up to 40% of patients.[9,36-38,40-46]

CONCLUSIONS

Predicting which patient presenting with rectal propose rectal prolapse and obstructed defecation will benefit from surgical intervention remains a challenge. Surgery should be considered only when conservative therapy fails and a careful patient selection is crucial to obtain a satisfactory outcome. As stated in the recent Cochrane Database System review on rectal prolapse[36], it is impossible to identify a gold standard of treatment. In our experience perineal approaches are preferred in elderly and high-risk patients and abdominal approaches are warranted in young and low-risk patients. Furthermore, laparoscopic rectopexy is associated with lower morbidity, faster convalescence and long term results similar to open approach in a referral centre for laparoscopic colorectal surgery.

REFERENCES

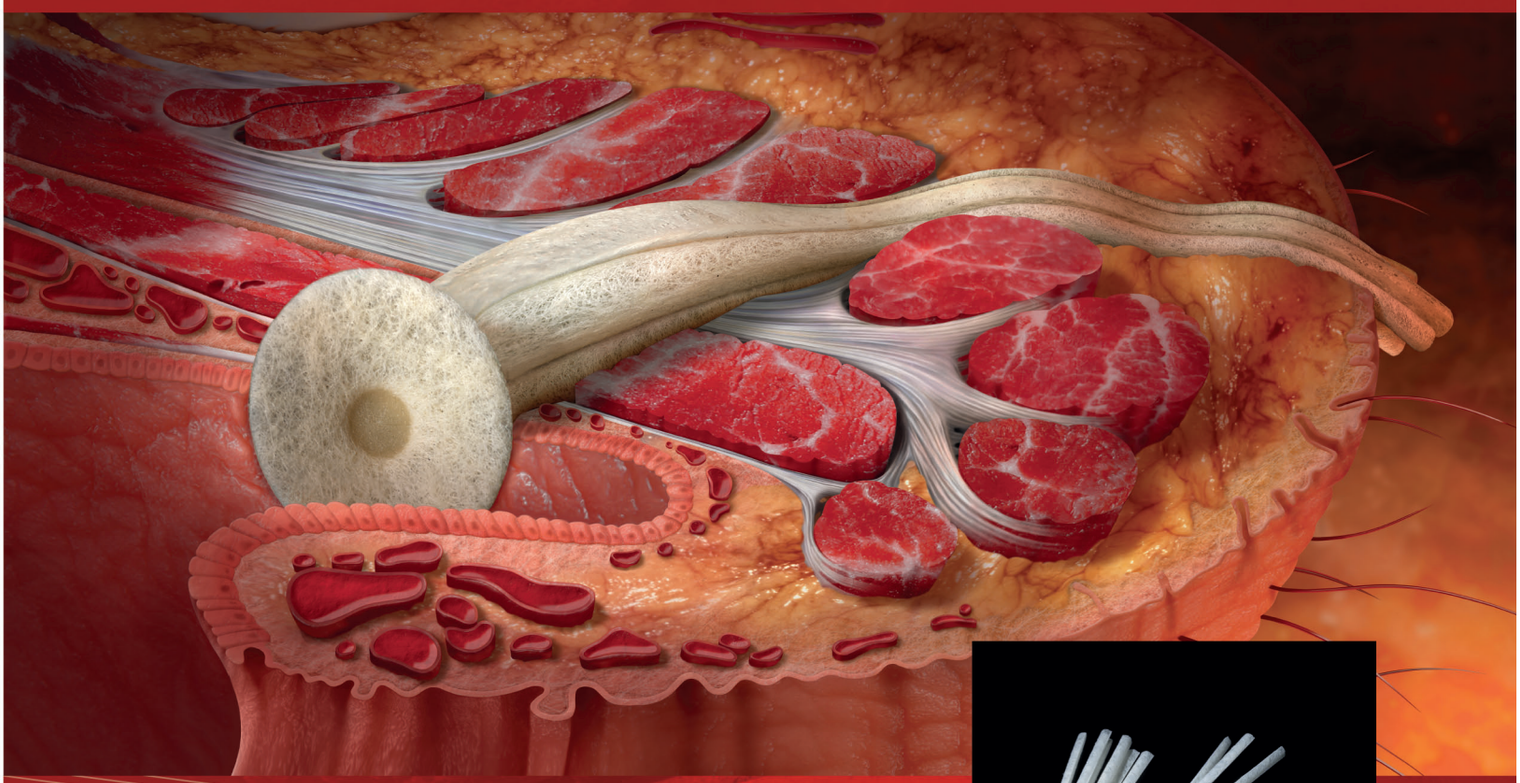
1. Jacobs LK, Lin YJ, Orkin BA. The best operation for rectal prolapse. Surg Clin North Am. 1997;77:49-70.
2. Felt-Bersma RJ, Cuesta MA. Rectal prolapse, rectal intussusception, rectocele and solitary ulcer syndrome. Gastroenterol Clin North Am. 2001;30:199-222.
3. Roig JV, Buch E, Alós R, et al. Anorectal function in patients with complete rectal prolapse: differences between continent and incontinent individuals. Rev Esp Enferm Dig. 1998;90:794-805.
4. Brodén B, Snellman B. Procidentia of the rectum: studies with cineradiography. Dis Colon Rectum. 1968;11:330-347.
5. Kuijpers HC. Treatment of complete rectal prolapse: to narrow, to wrap, to suspend, to fix, to encircle, to plicate or to resect? World J Surg. 1992;16:826-830.
6. Nicholls RJ. Rectal prolapse and the solitary ulcer syndrome. Ann Ital Chir. 1994;65:157-162.
7. Gagliardi G, Pescatori M, Altomare DF, Binda GA, Bottini C, Dodi G, Filingeri V, Milito G, Rinaldi M, Romano G, Spazzafumo L, Trompetto M; Italian Society of Colo-rectal Surgery (SICCR). Results, outcome predictors, and complications after stapled transanal rectal resection for obstructed defecation. Dis Colon Rectum 2008; 51:186-195
8. Pescatori M, Milito G, Fiorino M, Cadeddu F. Complications and reinterventions after surgery for obstructed defecation. Int J Colorectal Dis. 2009; 24: 951-959
9. Madiba TE, Baig MK, Wexner S. Surgical management of rectal prolapse. Arch Surg 2005;140:63-73.
10. Carter AE. Rectosacral suture fixation for complete prolapse in the elderly, the frail and the demented. Br J Surg. 1983;70:522-523.
11. Novell JR, Osborne MJ, Winslet MC, Lewis AA. Prospective randomised trial of Ivalon sponge versus sutured rectopexy for full-thickness rectal prolapse. Br J Surg. 1994;81:904-906.
12. Graf W, Karlbom U, Påhlman L, et al. Functional results after abdominal suture rectopexy for rectal prolapse or intussusception. Eur J Surg. 1996;162:905-911.
13. Khanna AK, Misra MK, Kumar K. Simplified sutured sacral rectopexy for complete rectal prolapse in adults. Eur J Surg. 1996;162:143-146.
14. Briel JW, Schouten WR, Boerma MO. Long-term results of suture rectopexy in patients with fecal incontinence associated with incomplete rectal prolapse. Dis Colon Rectum. 1997;40:1228-1232.
15. Liyanage CA, Rathnayake G, Deen KI. A new technique for suture rectopexy without resection for rectal prolapse. Tech Coloproctol. 2009 Mar;13(1):27-31.
16. Penfold JC, Hawley PR. Experiences of Ivalon sponge implant for complete rectal prolapse at St Mark's Hospital. Br J Surg. 1972;59:846-848.
17. Morgan CN, Porter NH, Klugman DJ. Ivalon sponge in the repair of complete rectal prolapse. Br J Surg. 1972;59:841-846.
18. Notaras MJ. The use of Mersilene mesh in rectal prolapse repair. Proc R Soc Med. 1973;66:684-686.
19. Launer DP, Fazio VW, Weakley FL, et al. The Ripstein procedure: a 16-year experience. Dis Colon Rectum. 1982;25:41-45.
20. Holmström B, Brodén G, Dolk A. Results of the Ripstein operation in the treatment of rectal prolapse and internal rectal procidentia. Dis Colon Rectum. 1986;29:845-848.
21. Roberts PL, Schoetz DJ, Coller JA, et al. Ripstein procedure: Lahey Clinic experience: 1963-1985. Arch Surg. 1988;123:554-557.
22. Novell JR, Osborne MJ, Winslet MC, Lewis AA. Prospective randomised trial of Ivalon sponge versus sutured rectopexy for full-thickness rectal prolapse. Br J Surg. 1994;81:904-906.
23. Keighley MR, Shouler PJ. Abnormalities of colonic function in patients with rectal prolapse and faecal incontinence. Br J Surg. 1984;71:892-895.
24. Tjandra JJ, Fazio VW, Church JM, et al. Ripstein procedure is an effective treatment for rectal prolapse without constipation. Dis Colon Rectum. 1993;36:501-507.
25. Galili Y, Rabau M. Comparison of polyglycolic acid and polypropylene mesh for rectopexy in the treatment of rectal prolapse. Eur J Surg. 1997;163:445-448.
26. Aitola PT, Hiltunen KM, Matikainen MJ. Functional results of operative treatment of rectal prolapse over an 11-year period: emphasis on transabdominal approach. Dis Colon Rectum. 1999;42:655-660.
27. Schultz I, Mellgren A, Dolk A, et al. Long-term results and functional outcome after Ripstein rectopexy. Dis Colon Rectum. 2000;43:35-43.
28. Mollen RM, Kuijpers HC, van Hoek F. Effects of rectal mobilization and lateral ligaments division on colonic and anorectal function. Dis Colon Rectum. 2000;43:1283-1287.
29. Winde G, Reers H, Nottberg H, et al. Clinical and functional results of abdominal rectopexy with absorbable mesh-graft for treatment of complete rectal prolapse. Eur J Surg. 1993;159:301-305.
30. Watts JD, Rotheberger DA, Buls JG, et al. The management of procidentia: 30 years' experience. Dis Colon Rectum. 1985;28:96-102.
31. Tjandra JJ, Fazio VW, Church JM, et al. Ripstein procedure is an effective treatment for rectal prolapse without constipation. Dis Colon Rectum. 1993;36:501-507.
32. Deen KI, Grant E, Billingham C, Keighley MRB. Abdominal resection rectopexy with pelvic floor repair versus perineal rectosigmoidectomy and pelvic floor repair for full-thickness rectal prolapse. Br J Surg. 1994;81:302-304.
33. Huber FT, Stein H, Siewert JR. Functional results after treatment of rectal prolapsed with rectopexy and sigmoid resection. World J Surg. 1995;19:138-143.
34. Kim D-S, Tsang CB, Wong WD, et al. Complete rectal prolapse: evolution of management and results. Dis Colon Rectum. 1999;42:460-469
35. Husa A, Sainio P, von Smitten K. Abdominal rectopexy and sigmoid resection (Frykman-Goldberg operation) for rectal prolapse. Acta Chir Scand. 1988 Mar;154(3):221-4.
36. Tou S, Brown SR, Malik AI, Nelson RL. Surgery for complete rectal prolapse in adults. Cochrane Database of Systematic Reviews 2008, Issue 4. Art. No.: CD001758.
37. Sajid M, Siddiqui M, Baig M. Open Versus Laparoscopic Repair Of Full Thickness Rectal Prolapse: A Re-Meta-Analysis Colorectal Dis. 2009 Apr 13
38. Purkayastha S, Tekkis P, Athanasiou T, et al. A comparison of open vs. laparoscopic abdominal rectopexy for full-thickness rectal prolapse: a metaanalysis. Dis Colon Rectum. 2005; 48: 1930-40
39. Johnson E, Stangeland A, Johannessen Ho, Carlsen E. Resection rectopexy for external rectal prolapse reduces constipation and anal incontinence. Scand J Surg. 2007;96(1):56-61.

40. Kariv Y, Delaney CP, Casillas S, et al. Long-term outcome after laparoscopic and open surgery for rectal prolapse: a case-control study. Surg Endosc. 2006;20:35-42.
41. Demirbas S, Akin ML, Kalemoglu M, Ogun I, Celenk T. Comparison of laparoscopic and open surgery for total rectal prolapse. Surg Today. 2005;35:446-452.
42. Raftopoulos Y, Senagore AJ, Di Giuro G, Bergamaschi R. Recurrence rates after abdominal surgery for complete rectal prolapse: a multicenter pooled analysis of 643 individual patient data. Dis Colon Rectum. 2005;48:1200-6.
43. Solomon M. Randomized clinical trial of laparoscopic versus open abdominal rectopexy for rectal prolapse. Br J Surg 2002; 89: 35–39.
44. Boccasanta P, Venturi M, Reitano MC, et al. Laparotomic vs laparoscopic rectopexy in complete rectal prolapse. Dig Surg. 1999;16:415-419.
45. Baker R, Senagore AJ, Luchtefeld MA. Laparoscopic assisted vs open resection: rectopexy offers excellent results. Dis Colon Rectum. 1995;38:199-201.
46. Salkeld G, Bagia M, Solomon M. Economic impact of laparoscopic versus open abdominal rectopexy. Br J Surg. 2004;91:1188-91.

Correspondence to:
Giovanni Milito
Department of Surgery
University Hospital Tor Vergata
Viale Oxford, 81
00133 Rome, Italy.
Phone +39.06.20902976
Fax +39.06.20902976
E-mail giovanni.milito@virgilio.it

A great fit

for anal fistula repair



PERFORMANCE by design

A revolutionary combination of proven material and patented design.

Introducing GORE BIO-A® Fistula Plug—the next generation of sphincter-preserving anal fistula repair.

GORE BIO-A® Fistula Plug combines a proven, synthetic bioabsorbable material with a patented design engineered to optimize operative success.

- Robust device placement
- Engineered to conform to the tract and reduce the potential for failure due to fall-out
- One configuration tailorable to fit most fistula shapes and sizes
- Proven 100% bioabsorbable scaffold facilitates tissue generation and healing

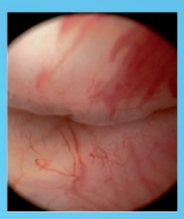
Insist on a great fit for anal fistula repair: GORE BIO-A® Fistula Plug.

GORE BIO·A® FISTULA PLUG

W. L. Gore & Associates, Inc. • Flagstaff, AZ 86004 • goremedical.com


DISPOSABLE
HYGIENIC
EASY TO HANDLE
SIMPLE TO USE
DO YOU NEED ANY MORE?
A COMPLETE PROGRAM
OF SYSTEMS AND INSTRUMENTS
FOR THE ADVANCED TECHNIQUES
IN COLOPROCTOLOGY
AND FOR PELVIC FLOOR DISEASES
sapimed S.p.A.
Alessandria - Italy
Tel. +39-0131-348109
Fax +39-0131-348383
info@sapimed.com
www.sapimed.com

DEXELL® SUI



DEXELL® - Implant for treatment of Stress Urinary Incontinence (SUI)

DEXELL is a sterile and viscous gel for the treatment of urinary incontinence caused by stress. It consists of a suspension of dextranomer microparticles and cross-linked hyaluronic acids of non animal origin. The cross-linked hyaluronic acid (Hylan gel) primarily functions as a means of transportation for the dextranomer microparticles which stimulate the connective tissue at the place of injection. Both the Hylan gel as well as the dextranomer microparticles of DEXELL are biodegradable and biocompatible.

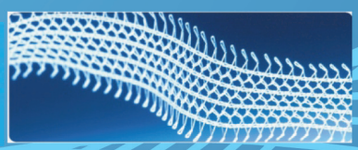
The treatment occurs with the assistance of the special DEXELL implantation system which is inserted into the urinary duct, and which provides a ready position for the hypodermic syringe. Through turning the funnel in a clockwise motion, the implant is then injected equally at four different

HYACYST®

HYACYST is a medical product that consists of a solution from highly purified hyaluronic acid of non-animal origin. It is use for the treatment of INTERSTITIAL CYSTITIS, RECURRENT BACTERIAL CYCTITIS and RADIATION INDUCED CYSTITIS. It is utilised as a sterile rinsing fluid with urothelial changes in the ureter, urinary bladder and the initial portion of the urethra.

HYACYST has no pharmacological effect on the tissue after introduction.

I-STOP®



SUBURETHRAL TAPE FOR THE TREATMENT OF FEMALE STRESS URINARY INCONTINENCE

The I-STOP is an innovative solution for the treatment of urinary incontinence.

The I-STOP Universal Sling incorporates the proven performance of polypropylene monofilament in a tape specifically designed for pelvic surgery. This unique tape, combined with a choice of needles, makes the I-STOP Universal Sling an ideal solution for virtually any surgical approach for Stress Urinary Incontinence (SUI) treatment in females including transvaginal, suprapubic and transobturator techniques. In addition, the I-Stop Universal Sling is proving to be a successful option for treatment of male SUI and pelvic organ prolapse.

Istem
MEDİKAL TIBBİ CİHAZ VE SANAYİ LTD.ŞTİ.

Mustafa Kemal Mahallesi, 2124 Sokak No. 25/1 06520 Ankara, Turkey
Tel: +90 312 219 53 85 Fax: +90 312 219 56 13
e-mail: istem@istemmedikal.com www.istemmedikal.com