PROCEEDINGS OF THE 9th EURASIAN ANDROLOGY SUMMIT

25 - 26 April 2014

St. Petersburg / Russia

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TÜRK
ANDROLOJİ DERNEĞİ
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Dear Colleagues,

It is a great pleasure inviting you to the **9th Annual Eurasian Andrology Summit** which will be organized in St. Petersburg, Russia, 25-26th of April 2014.

The Eurasian Andrology Summit organizes updated Andrology meetings every year in different countries to promote international communication from a wide geographical area on male and female sexual health and also male reproductive diseases.

The first meeting was organized in Azerbaijan in 2006 followed up by subsequent meetings in Uzbekistan, Kyrgyzstan, Russia, Ukraine, Albania, Romania and Hungary. The 9th meeting in St. Petersburg will be hosted by the Professional Association of Andrologists of Russia and Russian Society of Urology.

We look forward to meet you in St. Petersburg, a city of significant history and natural beauty.

Prof. Selahittin ÇAYAN
President of the
Turkish Society of Andrology

Prof. Ateş KADIOĞLU
Secretary General of the
Eurasian Andrology Summit

Prof. Peter SCHEPLEV
President of the
Eurasian Andrology Summit

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SCIENTIFIC PROGRAM 25 April 2014, Friday

08:30-09:00 OPENING CEREMONY
S. Çayan (Turkey) President of the Turkish Society of Andrology
A. Kadıoğlu (Turkey) Secretary General of the Eurasian Andrology Summit
P. Scheplev (Russia) President of the Eurasian Andrology Summit

09:00-09:30 PANEL: HISTORY OF ANDROLOGY
Moderators: P. Scheplev (Russia), I. Korneyev (Russia)

09:00-09:15 Past and today of the Eurasian Andrology Summit
S. Çayan (Turkey)

09:15-09:30 History of the Russian Andrology
P. Scheplev (Russia)

09:30-10:15 PANEL: PELVIC HEALTH OF MALE
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E. C. Şerefoğlu (Turkey)

09:45-10:00 What is new in medical treatment for BPH/LUTS associated with erectile dysfunction?
Ö. Yaman (Turkey)

10:00-10:15 Newer minimal invasive techniques for BPH/LUTS: Are there any impact on men's sexual health?
I. Korneyev (Russia)

10:15-10:30 COFFEE BREAK

10:30-11:30 PANEL: MALE REPRODUCTIVE HEALTH
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M. Başar (Turkey)

10:45-11:00 Advances in spermatogonial stem cells for the treatment of male infertility
D. Lamb (USA)

11:00-11:15 Increased cancer risk and azoospermia
D. Lamb (USA)

11:15-11:30 Varicocele: When and how should we treat?
S. Çayan (Turkey)

11:30-12:15 PANEL: MANAGEMENT OF DIFFICULT CASES IN ANDROLOGY
Moderator: A. Kadıoğlu (Turkey)
Panelists: M. Boiko (Ukraine), I. Ahmedov (Azerbaijan), S. Shavakhabov (Uzbekistan), E. Uçaner (Northern Cyprus), D. Lamb (USA)

12:15-13:30 LUNCH

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E. Kandıralı (Turkey)

13:45-14:00 Comprehensive management of erectile dysfunction in men with late onset hypogonadism
A. Atan (Turkey)

14:00-14:15 Update in the management of female sexual dysfunction
A. Armağan (Turkey)

14:15-14:30 COFFEE BREAK

14:30-15:45 CONTEMPORARY SURGERY OF ANDROLOGY (with video presentation)
Moderators: I. Korneyev (Russia), B. Gümüş (Turkey), A. İmamoğlu (Turkey)

14:30-14:45 Simultaneous implantation of artificial sphincter and penile prosthesis
M. Çulha (Turkey)

14:45-15:00 Penile implant surgery in priapism
M. Usta (Turkey)

15:00-15:15 Surgical correction in patients with congenital penile curvature
M. Çakan (Turkey)

15:15-15:30 Surgical treatment of penile fracture
İ. Özbey (Turkey)

15:30-15:45 Update on the surgical treatment of male infertility
(Micro-TESE, Vaso-vasal and vaso-epididymal anastomosis)
A. Kadıoğlu (Turkey)

15:45-16:00 COFFEE BREAK

16:00-17:00 DISCUSSED POSTER PRESENTATION-1
(Male and female sexual dysfunction)
Moderators: A. Kadıoğlu (Turkey), S. Resim (Turkey), Z. Murodov (Uzbekistan)

26 April 2014, Saturday

09:00-11:00 DISCUSSED POSTER PRESENTATION-2
(Male reproductive diseases)
Moderators: İ. Orhan (Turkey), M. Dinçer (Turkey)

EURASIAN ANDROLOGY SUMMIT
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Text of the Presentations

PAST AND PRESENT OF THE EURASIAN ANDROLOGY SUMMIT

Selahittin ÇAYAN, MD
President of the Turkish Society of Andrology
University of Mersin School of Medicine, Department of Urology, Mersin, Turkey

The Eurasian Andrology Summit was founded in 2005, during the National Andrology Meeting, in Istanbul, Turkey with participants from Turkey, Azerbaijan, Kyrgyzstan, Uzbekistan and Kazakhstan. The summit has been expanded to include Bulgaria, Russia, Ukraine, Albania, Iran and Northern Cyprus.

The Eurasian Andrology Summit aims to increase the standard of andrology in member countries by improving educational exchange programs, and encouraging the production and dissemination of information to the citizens of member countries about men and women's sexual health and male reproductive medicine. This summit also aims to create educational and research resources for member countries.

The Eurasian Andrology Summit's vision is to be the professional society for the advancement of treatment for patients with male and female sexual dysfunction or male infertility. The mission includes promoting the highest standards of sexual and reproductive medicine, and andrological surgery through education, research and in the formulation of health care policy.

The Eurasian Andrology Summit organizes updated andrology meetings every year in different countries to promote international communication from a wider geographical area on male and female sexual health, and male reproductive medicine.

The first symposium organized by the Eurasian Andrology Summit was held on 29 -30 April 2006 in Baku, Azerbaijan with 200 participants. The second meeting was 9 April 2007 in Tashkent, Uzbekistan with 250 participants. On 31 May 2008, the third meeting was held in Issık Lake, Kyrgyzstan with 180 participants. The fourth summit was on 30-31 May 2009 in Sochi, Russia during the national Russian Andrology meeting. Urologists of the several participating countries came together during an extensive scientific program. The fifth meeting was held on 5 May 2010 in Kiev, Ukraine. The 6th Eurasian Andrology Summit was held in Tirana, Albania on 15 April 2011 with 150 participants. The 7th summit was held on 21 April 2012 in Bucharest, Romania with 120 participants, hosted by the Romanian Association of Sexual Medicine. The 8th summit was held in Budapest, Hungary on 20-21 April 2013. Updated andrological topics were discussed among 150 participants coming from Turkey, Hungary, Kosovo, Bulgaria, Azarbaijan, Ukraine, Uzbekstan, Kyrgyzstan and Turkish Republic of Northern Cyprus.

The Eurasian Andrology Summit is celebrating its 9th anniversary, and we are now in St Petersburg, Russia for the 9th Eurasian Andrology Summit. This summit is hosted by the Professional Association of Andrologists of Russia.

CURRENT TREATMENT MODALITIES IN PREMATURE EJACULATION

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It has been more than a century since the initial report regarding PE was published (1) but the definition, classification, prevalence and effective treatment options of PE are still under debate (2). PE is classically accepted to be the most common sexual dysfunction (3-7), however the number of PE patients who seek treatment for this condition is rather low (7-8). Therefore, almost ¾ of urologists in the U.S. reported that they saw less than one PE patient per week (9), and 41.4% of European urology residents noted that they saw no PE patients at all (10).

Although the treatment alternatives for PE were once limited to psychological and behavioural therapies, today pharmacologic therapies are the most commonly applied first line treatment (9). Of note, no medications have yet been approved by the U.S. Food and Drug Administration (FDA) for PE; therefore, patients must be informed about the risks and benefits of all therapeutic options. At the end, treatment should be individualized according to the type of PE complaint, and both the patients' and their partners' preferences and expectations.

Psychological/Behavioural Strategies
Although effective pharmac¬ological therapies have reduced the popularity of tradit-ional psychological-behavioural treat¬ment of PE, these methods are still considered to be a mainstay treatment in patients with natural variable PE and premature-like ejaculatory dysfunction (8,11). In addition to patients with these PE syndromes, providing basic psychosexual education and therapy to all patients seeking treatment for PE may be beneficial, as PE results in reduced sexual satisfaction and function, along with increased levels of personal distress and interpersonal difficulty that results as a significant psychological burden (12). These therapies can be administered either alone or in combination with pharmacotherapy to patients with lifelong and acquired PE (13-15).

Pharmacotherapy
Topical Agents: Topical anesthetic compounds were the first medical treatment proposed for PE (16). These lidocaine-prilocaine creams decrease the sensation of the penis and significantly increase intravaginal ejaculatory latency time (IELT) when applied for 20 minutes prior to sexual activity (17-19). The current PE guidelines recommend topical treatments, thus they should be considered a viable option in the management of this condition (13,20). However, some patients may complain about application difficulties, significant hyposthesia, condom use, transvaginal absorbtion causing vaginal numbness (21). Other side effects include penile and/or vaginal dermal irritations which can turn into systemic reactions (19).

Oral Therapies: Ejaculation delaying effect of tricyclic antidepressant resulted in recommendation of these drugs for treating PE (22-27) and since then, serotonergic antidepressants are considered the mainstay of oral PE treatment modalities. Treatment with a selective serotonin reuptake inhibitor (SSRI) interacts with 5-HT2C receptor causing a delay in ejaculation (28-29). Ejaculation delay may start a few days after daily SSRI intake; however, maximal delay is usually not evident until completion of 1 to 2 weeks of treatment (30-33). Guidelines for lifelong PE often recommend oral serotonergic management as the first line medical therapy (13,20).

Dapoxetine is a SSRI that has been develoed most recently and is unique in that it is relatively quickly absorbed and rapidly cleared (34). Due to these properties side effects are limited and tolerable, and dapoxetine may be used as an on-demand treatment option for PE; in trials it has been found to increase IELT by a factor of 2.5 to 3 (35).

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WHAT IS NEW IN MEDICAL TREATMENT OF BPH/LUTS ASSOCIATED WITH ED

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Lower urinary tract symptoms (LUTS) are a common, age-related condition in men and epidemiologic studies using validated symptom scales, such as the International Prostate Symptom Score (IPSS), have shown an overall prevalence rate of >50% in men aged >50 years. benign prostatic hypertrophy (BPH) usually causes this condition and main symptoms are urinary frequency, urgency, decreased force of stream, and nocturia (1-4).

The Massachusetts Male Aging Study (MMAS) had pointed out the increasing prevelance of erectile dysfunction (ED) and showed that 34.8% of men aged 40–70 years had moderate to complete ED, which was strongly related to age, diabetes, depression, and cardiovascular disease (5). Therefore investigation of association of LUTS and ED has gained popularity and more recent studies, examining clinic as well as community samples, have shown a significant association between LUTS and male sexual dysfunction (6,7). Additionally not only erectile but also ejaculatory problems were reported more frequently in men with moderate-to-severe LUTS (8).

The Multinational Survey of the Aging Male (MSAM-7), investigate the relationship between LUTS and sexual problems in aging men by use of standardized and internationally validated scales of LUTS and sexual dysfunction. Overall, the study showed that sexual activity is common in older men and that men with sexual problems reported a high degree of bother in association with these problems. Additionally, the study confirmed the importance of LUTS as an independent risk factor for sexual dysfunction in aging men. The National Health and Social Life Survey suggested that LUTS are a significant risk factor for ED, with an odds ratio (OR) of 3.13 in 1410 men aged 18–59 years (9). In an other study, which included men aged 50–78 years, logistic regression showed that, regardless of age, severe LUTS were strongly associated with ED (OR 7.5; compared with no LUTS) (10). Taken together, this evidence implies that both LUTS/ BPH and ED are associated with aging, but that the association between severity of LUTS/BPH and ED is independent of age. Alterations in mechanisms associated with metabolic syndrome and cardiovascular disorders are crucial to understanding the pathways and underlying links between these symptoms

The pathophysiology of LUTS/BPH and ED is complex and likely to be multifactorial involving numerous mechanisms affecting the entire lower urinary tract. Reduced nitric oxide (NO)/cyclic guanosine monophosphate (cGMP) mainly in the prostate, urethra, and bladder but also in the pelvic neuronal and vascular bed; increased RhoA kinase pathway activity; increased autonomic nerve activity; and pelvic hypoxygen-ation and ischemia are the major underlying mechanisms. In humans, phosphodiesterase type 5 is expressed in the whole of the LUT, including the urethra, prostate, and bladder – all potential targets of PDE5-Is. In all these organs, PDE5 was prominently localized in the stroma and in the vas¬cular bed (endothelial and smooth muscle cells), suggesting a possible action of PDE5-I either on smooth muscle contraction and/or blood flow (11-13).

Medical management of LUTS is currently successfull in most of the men. However, altough the efficacy of all currently available treatments for LUTS/BPH is well defined, the negative impact of all therapies on erectile function (EF) is still under evaluation. The aim of the treatment must be alleviation of both symptoms. Lifestyle modifications and phytotherapies have no or minimal impact on sexual function but these are also less effective on lower urinary tract symptoms. In contrast, α-blockers, 5α-reductase inhibitors, and prostatic surgery, although associated with a strong improvement in LUTS, are usually associated with worsening sexual function, the more invasive the treatment, the greater the occurrence of adverse events . After the widespread use of PDE5-Is, this type of drug has been the standart treatment for ED and further studies have extensively reported efficacy and safety of chronic treatment with PDE5-Is – either alone or in combination

with conventional therapies – in ameliorating LUTS in men with or without ED.

In 2007, McVary et al. evaluated for the first time the efficacy and safety of tadalafil for the treatment of LUTS/BPH in men with or without ED. A total of 479 patients were screened and the authors found out that tadalafil significantly improved LUTS at week 6 (mean IPSS change from baseline for 5 mg tadalafil was −2.8 compared with −1.2 for placebo) but improvement of LUTS was even better at week 12 with dose escalated tadalafil (5/20 mg tadalafil −3.8 vs placebo −1.7) (14). In 2008, Roehrborn et al. published their report on a randomized, double-blind, placebo-controlled, 12-week study performed in ten countries and 92 centers in order to evalu¬ate the optimal dose of tadalafil for the treatment of LUTS/BPH. In this study the authors concluded that determined that tadalafil 5 mg once daily is the best dos¬age for the treatment of LUTS/BPH, providing an effective response to LUTS, with a minimal occurrence of AEs and rate of discontinuation (15).

In 2011, Porst et al. evaluated the efficacy and safety of once-daily tadalafil 5 mg for the treatment of LUTS/BPH in an international, randomized, double-blind, placebo-controlled, 12-week trial. There was a significant reduction in IPSS already at week 4 (tadalafil 5 mg −5.3 vs placebo −3.5, P = 0.003) and after week 12 and a remarkable improvement in IIEF in sexually active men with ED who were treated with tadalafil 5 mg versus placebo (+6.7 vs +2.0, P , 0.001) at week 12 was also observed in this study. This long-term study showed that tadalafil 5 mg once daily is well tolerated during a treatment period of 1 year and that the drug maintains or even improves stor¬age and voiding symptoms, but the cost-effectiveness of the long-term chronic use of tadalafil was not evaluated (16).

In 2012, Oelke et al54 evaluated for the first time tadalafil 5 mg and tamsulosin 0.4 mg once daily for the treatment of LUTS/BPH in an international, placebo-controlled, randomized, double-blind, 12-week trial comparing separately and indepen¬dently these two drugs with placebo. Compared with placebo, there was a significant decrease in IPSS of 1.5 points after only 1 week of treatment with tadalafil or tamsulosin (P , 0.01). After 12 weeks, decrease in IPSS with tadalafil (2.1 points, P = 0.001) was even more pronounced than with tamsulosin (1.5, P = 0.023) compared with placebo. Significant and clinically meaningful improvement in LUTS/BPH with tadalafil 5 mg once daily, was observed after only 1 week, a further improvement in LUTS/BPH after 12 weeks, and improve¬ment of QOL and treatment satisfaction parameters only with tadalafil, and an unexpected but remarkable improvement of urinary flow rates at week 12 were also observed (17).

Many preclinical and clinical studies emphasize the close link between LUTS/BPH and ED. The majority of active treatments for LUTS/BPH have a negative impact on EF. The remarkable improvement of both LUTS/BPH and ED with tadalafil 5 mg once daily suggests a leading role for this PDE5-I treatment for men with comorbid BPH and ED. PDE5-I treatment is associated with a low rate of AEs and any AEs that do occur tend to be of low severity.

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NEWER MINIMAL INVASIVE TECHNIQUES FOR BPH/LUTS: ARE THERE ANY IMPACT ON MEN'S SEXUAL HEALTH?

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Introduction

Low urinary tract symptoms (LUTS) related to benign prostatic hyperplasia (BPH) have been recognized to affect seriously the patient's normal physical and social activities and may have profound effect on quality of life. Strong correlation between LUTS severity and degree of sexual dysfunction shown by population-based studies irrespective of patients' age was explained by common pathogenetic mechanisms and comorbidities with chronic inflammation and steroid hormone unbalance at the background. Aimed to decrease the degree of obstruction and symptoms, different treatment modalities however may produce a variable response in terms of sexual activity and satisfaction. The lowest rates of sexual dysfunction with medical therapies and varying rates of erectile dysfunction (ED) and retrograde ejaculation following open surgery and TURP for BPH have been reported. In the past two decades a number of less invasive alternative BPH-LUTS treatment techniques using a range of energy sources have been developed including laser, radiofrequency, and microwave, and ultrasound. In general, the incidence of side-effects on sexual function is less but the data available are limited [1].

Reviews

A systematic review of randomized controlled and cohort studies to evaluate the effects of minimally invasive procedures for BPH-LUTS treatment on male sexual function was performed by Frieben et al. [2].There were 21 study with laser surgeries, 6 – with TUMT, 4 – with TUNA, and 2 – with transurethral ethanol ablation of the prostate (TEAP) for men with symptomatic BPH in comparison with traditional transurethral resection of the prostate (TURP) or sham operations. No study was available regarding the effect of HIFU for BPH on male sexual function. The analysis showed that minimally invasive surgeries for BPH have comparable effects to those of TURP on male erectile function. Laser procedures, TUMT and TUNA resulted in about 15% of patients with both either decrease or increase of erectile function. More than one third of patients after with holmium, potassium-titanyl-phosphate and thulium laser BPH treatment develop ejaculatory dysfunction, the rate similar to the one as observed with TURP. In contrast TUMT, TUNA and neodymium:yttrium aluminum garnet visual laser ablation or interstitial laser coagulation for BPH has less incidence of ejaculatory dysfunction. This benefit is somewhat overbalanced by less effectiveness for BPH treatment when compared with conventional TURP.

The most recent meta-analysis of effect of transurethral procedures for BPH-LUTS on male sexual function was published by Zonget al. in 2011 [3]. Twelve randomized controlled trials involving 1886 men were included, compared with conventional TURP for BPH, and referred to male erectile and ejaculatory function. Among them there were 2 trials comparing TURP and watchful waiting, 6 comparing TURP with transurethral electrovaporization of the prostate (TUEVP), and 4 comparing TURP with holmium laser treatment (HLT). TURP was associated with a higher occurrence of retrograde ejaculation compared with watchful waiting but not to TUEVP or HLT and associated with a lower incidence of male erectile dysfunction compared with TUEVP but not HLT. According to the analysis, TURP lead to a higher prevalence of retrograde ejaculation compared with watchful waiting but had less of an effect on erectile function than TUEVP. TURP did not have a significantly different effect on erectile or ejaculatory function compared with HLT.

Laser Resection/Vaporization

With regard to largely abandoned in the treatment of BPH interstitial laser coagulation, it has been found that ND:YAG laser surgery had the same effect as TURP on erectile function in men. In the cohort study 7.9% and 20.4% of patients reported increased erectile function after ND:YAG and TURP [4]. When compared with TURP ND:YAG laser appears to cause less ejaculatory dysfunction (15%-80% and 3%-35% respectively).

Significant changes in erectile function following prostate vaporization with 120 W lithium triborate laser were observed in a trial of Hossak and Woo [5]. At 3 months, the mean post-operative IIEF-5 score was unchanged compared to baseline. A major decline in erectile function was seen in 12.4% and 24% of men at 3 and 12 months, respectively, and a major improvement in erectile function was seen in 8.3% and 6% at 3 and 12 months, respectively. There was no correlation in change in erectile function with urinary function, quality of life and loss of emission on orgasm. Loss of emission on orgasm was reported in 65% of respondents.

The most recent study of impact on IIEF score of 120-W 2-µm continuous wave (cw) laser vapoenucleation of the prostate versus TURP in 122 consecutive BPH patients was done by Wang et al. (2014) [6]. Although an increase in IIEF-EF score by 2 points was reported by 16 (25.4 %) and 14 (23.7 %) patients, in two groups respectively, the mean EF score did show a marginal but not significant increase postoperatively in both groups. Intercourse satisfaction, sexual desire domain, and overall satisfaction scores in each group did not change significantly after surgery, but there was a significant decrease in the orgasmic function domain score one year after surgery in both groups and the prevalence of postoperative retrograde ejaculation was significantly higher than at baseline assessment in two groups.

Greenlight Laser

A potassium-titanyl-phosphate-(KTP-) crystal doubles the frequency of pulsed Neodymium: Yttrium-Aluminum-Garnet (Nd:YAG) laser energy to a 532 nm wavelength, which is in the green electromagnetic spectrum (Greenlight-laser) and is selectively absorbed by hemoglobin and not at all by water. Because of the instant and nearly complete absorption in blood, the depth in vascularized tissue such as prostate is only 0.8 mm. The superficial coagulation prevents the large tissue necrosis that is seen with the Nd:YAG laser, leading to long lasting irritative symptoms due to sloughing of necrotic tissue [7].

Guo and Jin performed a prospected 2-years follow-up analysis of sexual function and voiding in 128 consecutive BPH patients after photoselective green light laser vaporization of the prostate [8]. Patients were divided into two groups according to the volume of prostate (<70 ml, n = 58 and ≥ 70 ml, n = 70). While main objective and subjective voiding parameters significantly improved compared to baseline similarly in both groups, the larger volume of prostate following PVP treatment has negative influence on sexual function in the long term.

Another prospective study of overall sexual function in 102 men with BPH after GreenLight photovaporization of the prostate was done by Terrasa et al. [9]. Compared with baseline, postoperative erection symptom score was not significantly different, whereas ejaculation symptom score was significantly worse. Global sexual satisfaction also improved and was significantly associated with IPSS but not with erection and ejaculation score in a multivariable model.

Kumar et al. [10] performed a prospective study to assess the short-term effect of 80 W GreenLight laser photovaporization on erectile function in BPH patients with LUTS categorized in two groups: IIEF ≥19 and IIEF <19. In patients with normal IIEF erectile function decreased significantly postoperatively up to follow-up of 1 year. In patients with preoperative ED, however, the procedure did not significantly decrease IIEF score.

A multicenter randomized controlled comparative study was conducted by Luckacs et al. [11] to access the effects of GreenLight High Performance System 120-W photoselective vaporization of the prostate and monopolar TURP in 139 patients. Sexual outcomes were slightly better in the vaporization group without reaching statistical significance. Pereira-Correia et al. [12] in a similarly designed study found no significant change in IIEF-5 scores. The incidence of erectile dysfunction and retrograde ejaculation following thulium:yttrium-aluminium-garnet laser prostate vaporesection was 20% and 56%, respectively in a study of Yee et al. [13].

The question if the GreenLight High-Performance System (HPS™) laser photoselective vaporization

prostatectomy affects sexual function after treatment of lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH) has been answered in prospective study of Spaliviero et al. [14] in 72 patients: no detrimental effect on erectile function was found, and the incidence of new-onset retrograde ejaculation was 30%.

Laser Enucleation (HoLEP)

The effect of Ho:YAG laser enucleation of the prostate (HOLEP) to the sexual function of patients with BPH in 108 patients was studied by Meng et al. [15]. HOLEP did not affect the sexual function of patients with BPH but does did improve the ability of early morning erection, while causing retrograde ejaculation.

In 2012 Elshal et al. [16] presented a longitudinal study of 216 sexually active men who underwent laser prostatectomy (99 holmium laser enucleation of the prostate, 34 holmium laser ablation, and 58 greenLight-532-mm laser photoselective vaporization of the prostate) between 2005 and 2010. The author's conclusion was laser prostate surgery using more size-related laser energy might have possible negative influence on sexual function and patients with normal preoperative sexuality have higher risk of postoperative sexual dysfunction development.

In 2012 Jeong et al. [17] performed a study in 38 men to evaluate the serial changes in sexual function in the short-term period after holmium laser enucleation of the prostate for BPH and to investigate whether a change in each domain of the IIEF is associated with improvement of voiding function during 12-month follow-up. Most IIEF domain scores showed a slight decrease at 1, 3, and 6 months postoperatively but recovered to the baseline or even showed a marginal but nonsignificant increase at 12 months after surgery compared with baseline. Orgasmic function and the overall sexual satisfaction domain score remained slightly reduced up to 12 months postoperatively. No correlation was found between improvement of voiding and change in sexual function throughout the follow-up period after surgery.

Frieben et al. [18] analyzed all the study data available at 2010 and found holmium laser surgery had the same effect as TURP on erectile function in men. There were high incidences of ejaculatory dysfunction (mainly retrograde ejaculation or decreased ejaculates) after both holmium laser (range from 50% to 96%) and TURP (range from 50% to 86%) procedures for BPH.

Comparative analysis of impacts of TURP, transurethral electrovaporization of the prostate and holmium laser enucleation of the prostate in the treatment of benign prostatic hyperplasia (BPH) on male sexual function based on 9 randomized controlled trials involving 1050 BPH patients was performed by Zong et al. [19].TURP affected erectile function less than vaporization ($P = 0.04$), but the two had no significant difference in their influence on ejaculatory function. Nor was any significant difference found between laser enucleation and TURP in their influence on either erectile or ejaculatory function at 12 and 24 months after surgery.

TUMT

Limited data are available on TUMT versus TURP regarding to erectile function. Francisca et al in a study of 50 patients treated with TUMT or by sham operation found 20% of patients treated with either modality had a worsened sexual function at 26 weeks post-treatment [20]. The overall incidence of retrograde ejaculation was 11% and for lack of orgasms, 14%. There was no statistically significant difference between TUMT and sham treatment with regard to quality of life related to sexual function at baseline and at 12 and 26 weeks post-treatment. Collectively compared with TURP TUMT had less adverse effects on sexual function [21].

TUNA

Randomized control trials using validated questionnaires to evaluate erectile function [22] have shown TUNA is associated with fewer adverse events compared with TURP including erectile dysfunction, and ejaculation disorders, 7.9% and 20.4% of patients reporting increased erectile function after TUNA and TURP, respectively. Several studies reported no ED or retrograde ejaculation [23].

Ethanol Injections

No randomized trial is available to compare the ethanol injections and TURP on sexual function in BPH patients. In small patient number and short follow-up studies painful ejaculations (1 of 10 patients), and retrograde ejaculation (1 of 94 patients) were reported [24, 25].

Botulinum Toxin

Intraprostatic injection of bothulinum toxin in patients with BPH seem to have no impact on sexual function. The IIEF-5 score, the score for ejaculatory/orgasmic function and the sexual desire score remained little changed from baseline to month 6 postoperatively in a study of Silva et al. [26]

Conclusion

The analysis suggests that minimally invasive surgeries for the treatment of BPH-LUTS patients have comparable to TURP effects on male sexual function and can experience either a decrease or an increase in their erectile function and develop retrograde ejaculation. Sexual assessment is indicated preoperatively in every patient with symptomatic BPH as well as the discussion of potential risks and benefits of the scheduled treatment regimen.

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CURRENT MEDICAL TREATMENT OF IDIOPATHIC MALE INFERTILITY

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Many couples choose to have children by a natural way, and so, they are searching various medications for this purpose. However, some couples that will be obtained from the ART can be applied to various medical treatments for increasing the success rate. The main approach in the treatment of infertility should be treated the underlying problems.

There are two basic approaches in the treatment of male infertility: 1 - Corrective treatments for the underlying diseases (Specific treatments); and 2 – Using various medications in order to improve sperm development, especially in idiopathic cases (non-specific treatments). Although indications and protocols determined more precisely, and the results demonstrated more clearly for the specific treatment, there is not still a consensus for non-specific treatments, and their results are controversial (1, 2).

Medical treatment of male infertility should be considered as versatile because there are a lot of complex factors that play role in spermatogenesis and spermyogenesis. Nowadays, hypogonadotropic hypogonadism is accepted as the most realistic therapy group in infertile male. However, that group constitutes only 3-5 % of all patients. Therefore, indications for empiric therapy have been widely used in male although there is not a consensus in the indication.

Hormonal mechanisms and various molecular factors affect spermatogenesis and fertility. Oxidative stress is one of these factors. Physiological levels of reactive oxygen substances (ROS) produced by sperm mitochondria is required for normal sperm function. However, a high concentration of ROS shows a negative effect on spermatogenic activity (3, 4). Leukocytes and immature spermatozoa are the main sources of ROS production in the seminal plasma. Spermatids and mature spermatozoa are quite sensitive to ROS because of their membrane structure including the high concentration of polyunsaturated lipids. High concentrations of ROS can affect sperm motility and morphology, and can cause the sperm cells' death (3). On the other hand, there are several antioxidant substance including superoxide dismutase (SOD), catalase, glutathione perooxydase (GPx), α-tocopherol, β-carotene, ascorbate etc. in seminal plasma, and they retain gamete from the harmful effects of ROS. Decrease in the level of antioxidants substances in the seminal plasma shows negative effect on spermatogenesis and spermyogenesis (5).

Hormonal Agents

Antiestrogens: Estrogen agonists have been used in the treatments of idiopathic male infertility for many years (6). These agents eliminate the blocking effect of estrogen in the hypothalamus, and, thus, stimulate the release of GnTH from the pituitary gland. As a result, testicular testosterone production and spermatogenesis is stimulated. Clomiphene citrate and tamoxifen are very popular for being easy to use and their low cost. Despite widespread usage of these agents in the treatment of male infertility, their effects remain controversial. In placebo-controlled trials of tamoxifen 10 mg/day for 6 months, Willis et al. reported that there were significant changes in hormonal parameters in patients, but similar effects have not been observed for seminal parameters (7). On the other hand, spontaneous pregnancy rate is reported as 12.5% in the control group and 15.4% in the patients using tamoxifen (8). Similar results were obtained with clomiphene citrate. There are several controversial studies about the effect on seminal parameters in the literature (9-11).

As a result, it is shown in the Cochrane meta-analysis that anti-estrogens are expressed as insufficient in the increasing of pregnancy rates (12).

GnRH Analogs: There has not been observed a significant increase in sperm parameters and pregnancy rates in controlled trials in iOAT cases. Matsumiya et al. reported a slight increase in hormone levels in iOAT patients (13). However, they did not evaluate the effect on pregnancy rates. As a results, GnRH analogs has not been recommended for use in the empirical treatment because their results have a controversial, and has not been found effective on the pregnancy rates.

GnTH Analogs: These agents are the first choice for the treatment of hypogonadotropic hypogonadism. There have been a lot of studies about empiric treatment with GnTH, but the majority of these studies are not controlled and randomized. There are only four randomized controlled studies comprising 278 patients in Cochrane meta-analysis. In these studies, they reported that the pregnancy rate was found as 13.4% in the patients treated with GnTH for 3 months and as 4.4% in the placebo group (14). Additionally, the spontaneous pregnancy rates were reported as 9.3% inn GnTH using groups and, as 1.7% in control cases (15, 16).

Empirical GnTH treatment should be started with hCG stimulation for 4-6 weeks. After serum FSH, LH and testosterone levels are evaluated; HMG treatment should be added for the next 4-6 weeks. The recommended doses are 1500-5000 IU / week for hCG, and 150-450 IU/week for hMG.

Androgens: Exogenous testosterone administration is suppressed testosterone production with the inhibitory effects on hypothalamo-pituitary axis, and inhibits sperm production. After cessation of the drug, testosterone level increases with the rebound effect, and thus, it is considered that spermatogenesis is stimulated. Although androgens have been used for the utilizing of this effect in the past, there have not demonstrated any benefit in patients with iOAT (20,21). Nowadays, exogenous androgen treatment is not a recommended approach to infertile patients.

Anti-Oxidant Agents

After detecting of ROS at high concentrations in seminal plasma of infertile males, and showing the effects of increased ROS on sperm function and DNA damage, the use of antioxidants has been raised in male infertility as a medical treatment method (3, 22). However, the real effects of these agents are still unclear. In experimental studies, while it has been reported that antioxidant agents have preventive effects on spermatozoa from the impact of exogenous oxidizing agent, the effects on endogenous ROS are controversial. There are no randomized, placebo-controlled clinical trials. In clinical studies, the increase rates of spontaneous pregnancy have not been established. Despite all this data, it was reported that antioxidants in sub fertile men resulted in ART 4-5 fold increase in the pregnancy rate with ART in Cochrane meta-analysis (23).

As a result, there has not been defined treatment protocol in the treatment of iOAT. Although the role of hormonal therapy known very-well for men with azoospermia having specific abnormalities the role, the results of empirical medical therapy in patients with idiopathic cases shown differences. On the other hand, large randomized studies on this issue are inadequate. Despite this limited data, empirical medical treatment is widely used among urologists. However, this treatment should be considered for a normal spermatogenic cycle limited to 3-6 months. On the other hand, empirical therapy is recommended in patients with recurrent application failed ART or the couples wait for starting to ART cycle.

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ADVANCES IN SPERMATOGONIAL STEM CELLS FOR THE TREATMENT OF MALE INFERTILITY

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Spermatogonial stem cells allow replenishment of the pool of spermatogonia throughout a man's adult lifetime. These cells undergo proliferation, self-renewal and have the ability to produce differentiated progency. The first adult stem cells to be identified in 1971 by Huckins, spermatogonial stem cells are of crucial importance given their regenerative potential for restoration of fertility following exposure to gonadotoxic agents. In 1994, Brinster and colleagues1 used experimental principles well established in the embryonic stem cell field based upon the presence of molecular markers of cell fate that demonstrated that these putative spermatogonial stem cells could indeed restore spermatogenesis in a testis devoid of germ cells after exposure to a chemotherapeutic agent (busulfan) that had destroyed normal spermatogenesis rendering the mouse infertile.

Obviously, these cells have the potential to restore spermatogenesis in patients exposed to gonadotoxins. It is likely that autologous transplantations will be the first application of spermatogonial stem cell technologies in humans. Spermatogonial stem cells can be isolated and enriched from testicular biopsy specimens. They can be cryopreserved indefinitely. Indeed, some pediatric hospitals are now isolating and storing testicular stem cells from young prepubertal patients (too young to collect a semen sample for banking) on a research basis with the hopes that the technology for stem cell enrichment will be developed by the time the child matures and wishes to attempt fatherhood. Importantly, the technology is not used in humans today because of technical challenges with ensuring the cells to be transplanted are not contaminated with residual cancer cells (the testis can serve as a reservoir for malignant cells) and there are difficulties to efficiently transplant the cells back into the seminiferous tubule given the dimensions of the seminiferous tubules in the human (very long and narrow). In the future, it is hoped that heterologous transplantations can be performed in patients with spermatogenic deficiencies to cure their infertility. Currently, studies are predominantly in rodents.

However the real significance of spermatogonial stem cells may be more justifiably realized by their pluripotency. Although spermatogonial stem cells were first thought to be "uni-potent" with the ability only to proliferate, undergo mitosis and differentiate ultimately to mature sperm, after isolation and culture under specific conditions, they acquire embryonic stem cell properties. They can spontaneously differentiate into mesoderm ectoderm and endodermal cells. In vitro spermatogonial stem cells can differentiate into cardiac, skeletal muscle and vascular cells (mesodermal lineages), dopaminergic neurons (neuroectoderm) or cells of ectodermal origin (keratinizing stratified epithelium, bile duct and hepatocytes) using mouse models[2]. Upon injection of these cells into a blastocyst, they can differentiate into various organs and there is germ line transmission. Shortly thereafter, investigators showed that human spermatogonial stem cells have similar regenerative capacity for a wide range of tissue types[3,4]. Importantly, these studies show that spermatogonial stem cells have the potential to be used instead of embryonic stem cells to regenerate cells and tissues for most of the body.

Spermatogonial stem cells may also facilitate effective gene therapy for a variety of genetic syndromes in the future. In mouse models, investigators have used adeno-virus vector gene transfer to demonstrate the ability of germ line gene therapy to (in this case) demonstrate the transmission of the gene construct to offspring and to be expressed in the offspring. While a number of risks remain, as well as ethical challenges with gene therapy that would be not justify its use in humans today, the technology offers great promise for the future.

Finally, investigators have worked to achieve complete spermatogenesis in vitro with varying success. While investigators, after nearly 60 years of attempting to produce sperm in vitro are finally successful, the quest continues because the efficiency is low and for translation to the human safety concerns remain, although the attainment of this goal is significant.

Spermatogonial stem cells offer the promise of regeneration of spermatogenesis after toxic insult, the possibility of use as surrogates for embryonic stem cells without the ethical concerns of destroying embryos, and as such the potential to be used in regenerative medicine to create virtually any tissue in the body, as well as a vector for gene therapy. The future applications using spermatogonial stem cells hold great promise for advancing the fields of andrology and male infertility, regenerative medicine and gene therapy for treatment of otherwise intractable genetic syndromes.

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INCREASED CANCER RISK AND AZOOSPERMIA

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Although non-obstructive azoospermia (NOA) affects about 1% of men, the causes remain largely unknown. Defects in DNA repair mechanisms and cell cycle abnormalities frequently occur in NOA men. Scientists are beginning to dissect the molecular pathways that underlie these defects and find that many of the genes involved in cancer syndromes also regulate key pathways required for gamete production and are required for homologous recombination during meiosis. These defects include mutations in DNA repair genes identified in mouse models as well as human patients, such as MLH1 or MSH2 (Lynch syndrome genes) and in the excision repair cross-complementing gene (ERCC1). When defective, these proteins cause azoospermia with severe testicular germ cell loss. Of note, these gene mutations are also associated with tumor development at early ages.

There is accumulating evidence that infertile men in general, and men with NOA in particular, may be at increased risk of cancer development. In a landmark paper by Honig, et al., significant medical pathologies were uncovered in 1.1% of 1236 patients presenting to a male infertility clinic[4]. 10 patients (0.8%) had tumors (6 testis cancers, 3 brain tumors and 1 spinal cord tumor) and their findings point to the need for urologic consultation when an infertile couple seeks treatment at an ART clinic.

Our studies show a 2.9-fold increased risk of cancer development for our NOA patients. Walsh and colleagues [1] evaluated data on 22,562 partners of infertile couples and showed the risk of testis cancer was nearly 3-fold higher in infertile men compared with normal men. Jacobsen, et al., similarly evaluated more than 32,000 men who had a semen analysis over a 30-year period and found a 1.6 increased risk of testis cancer in men with lower sperm count[2]. There was also an increased incidence of cancers of the peritoneum and other digestive organs in these men with low sperm count. Walsh and colleagues performed analysis of their patient cohort and showed that men with male factor infertility were 2.6 times more likely to be diagnosed with high grade prostate cancer[1,3]. Indeed, in addition to DNA repair and cell cycle deficiencies, diminished recombination frequencies during homologous recombination are present in azoospermic men and this characteristic is indicative of a tendency for aneuploidy to occur, impacting genomic health. **It is believed that there are common etiologic factors for infertility and cancer development, such as deficient DNA repair mechanisms [1,2,5].**

In our study, we analyzed the data collected by my clinical lab with more then 25 years of semen analysis data for 22,089 men tested. Although many patients were not American or did not reside in Texas, we identified 2238 NOA men who remained in Texas and compared their risk of developing cancer using the Texas Cancer Registry compared with other men seen during this time period for infertility, but not NOA. Using an unadjusted model, there were 29 cancer diagnoses in the NOA group compared with 16.7 expected with a 2.74 fold (1.31, 5.77, 95% CI; $p<0.01$) increased risk of cancer diagnosis in NOA men. The fully adjusted model (for age and income level) still shows that NOA men have about a 2.9 fold (SIR 2.9, 95% CI 1.4-5.4, $p=0.02$) increased risk of developing cancer. In contrast, infertile men without azoospermia had a similar rate of cancer to the general Texas population (SIR 1.4, 95% CI 0.9-2.2). **For younger men the risk was 8-fold higher. The risk may be even higher if we can follow these men for time longer periods**[6].

We also asked in a man's semen quality was associated with mortality. We determined if impaired semen parameters are associated with mortality in the years after an infertility evaluation. A total of 2,748 men were evaluated for infertility at our clinic in Texas with complete records. Men were stratified based on abnormal semen parameters as determined by the WHO 5th edition criteria. A fertile comparison group was comprised of men evaluated for vasectomy or vasectomy reversal (n=1,428). Mortality was determined by

data linkage to the National Death Index. The mortality rate was compared to an age-matched sample from men in the general Texas population. We also analyzed the risk of death in infertile men based on semen parameters using a Cox regression model. When stratified by semen parameters, men with reduced sperm counts and motility had significantly higher mortality rates compared with men with normal parameters ($p<0.05$). Moreover, while men with normal sperm concentration had a similar mortality rate compared to vasectomized men (hazard ratio, HR 0.4, 95% CI 0.1-1.8), men with oligospermia (HR 2.9, 95% CI 1.2-7.0) and azoospermia (HR 3.4, 95% CI 1.2-10.2) had significantly higher mortality rates. Despite a short follow up and the youthful age of the cohort, we noticed significant divergence in risk of death based on sperm parameters. Indeed, the increased risk of death among reproductive-aged men with low compared to normal sperm counts is comparable to that from smoking or having diabetes.[7,8] While reassuring that absolute risk of death remains low for men evaluated for infertility in the decade after an infertility evaluation, the current report suggests additional follow up of these men is warranted after reproductive efforts have ceased.

It is estimated that the majority of infertile men do not receive a male health evaluation in the United States prior to attempting to achieve a pregnancy using an assisted reproductive technology. With improved diagnosis and advances in our understanding of the molecular basis of male infertility, patients can be advised of any potential health risks and hopefully, earlier intervention can improve their outcomes.

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VARICOCELE: WHEN AND HOW SHOULD WE TREAT?

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Infertility is detected in 15% of couples who desire children, however, the ethiology is pure male factor in 20%, and male and female factors in 30-40% of the couples. Therefore, the assessment of male infertility plays important role in approximately 50% of the couples (1).

Varicocele is the most commonly seen and correctable cause of male factor infertility (2,3). Varicocele is among a cost effective treatment of infertility. The aim of the evaluation of infertile men with varicocele is to point out to diagnose correctable pathologies, to also determine use of assisted reproductive technologies (ART), if surgical treatment of varicocele is not indicated.

Physical examination is the reference standard to diagnose varicoceles in subfertile men. Additional radiologic imaging is not necessary to diagnose subcinical varicocele, because only a varicocele detected by physical examination should be considered potentially significant (8). When clinical palpable varicocele coexists with impaired semen quality, surgical repair may potentially restore spermatogenesis and fertility. Recent meta-analyses suggested that varicocele repair have beneficial effect on fertility status in infertile men with palpable varicocele (9,10). Ficarra et al reviewed randomized clinical trials for varicocele repair and found a significant increase in pregnancy rate in patients who underwent varicocele treatment (36.4%) compared with patients having no treatment (20%) (9). Marmar et al reported a 33% pregnancy rate in patients who underwent surgical varicocelectomy and a 15.5% pregnancy in the controls receiving no varicocelectomy (10).

Indications for treatment of varicocele are presence of clinical palpable varicocele with infertility history and abnormal semen parameters, and pain, if medical conservative treatment such as analgesics/anti-inflammatory drugs fails (11).

Treatment options for varicocele in infertile men include open surgical, radiologic and laparoscopic approaches (12,13). Postoperative pregnancies occur with a mean duration of 7 months (3-11 months) after surgery (4).

The best treatment modality for varicocele in infertile men should include higher seminal improvement and spontaneous pregnancy rates with lower complication rates such as recurrence or persistence, hydrocele formation and testicular atrophy. Therefore, the ideal technique should aim ligation of all internal and external spermatic veins with preservation of spermatic arteries and lymphatics (13).

Microsurgical varicocele repair can be performed via inguinal or subinguinal approach. Although the subinguinal approach to microsurgical varicocelectomy obviates the need to open the aponeurosis of the external oblique, it is associated with a greater number of internal spermatic veins and arteries compared with the inguinal approach. Subinguinal microscopic varicocelectomy has disadvantages, needing more skills because of higher number of internal spermatic vein channels, higher risk for arterial injury due to smaller artery in diameter at the level of the external inguinal ring (13).

Open microsurgical inguinal or subinguinal varicocelectomy techniques have been shown to result in higher spontaneous pregnancy rates and fewer recurrences and postoperative complications than conventional varicocelectomy techniques in infertile men. Use of higher magnification allows surgeons to preserve the internal spermatic artery and lymphatics and also to visualize and ligate all spermatic veins (14).

We published a review/meta-analysis to compare all techniques (13). Overall spontaneous pregnancy rates were 37.69% in the Palomo technique series, 41.97% in the microsurgical varicocelectomy techniques, 30.07% in the

laparoscopic varicocelectomy techniques, 33.2% in the radiologic embolization and 36% in the macroscopic inguinal (Ivanissevich) varicocelectomy series, revealing significant difference among the techniques. Overall recurrence rates were 14.97% in the Palomo technique series, 1.05% in the microsurgical varicocelectomy techniques, 4.3% in the laparoscopic varicocelectomy techniques, 12.7% in the radiologic embolization and 2.63% in the macroscopic inguinal (Ivanissevich) or subinguinal varicocelectomy series, revealing significant difference among the techniques. Overall hydrocele formation rates were 8.24% in the Palomo technique series, 0.44% in the microsurgical varicocelectomy techniques, 2.84% in the laparoscopic varicocelectomy and 7.3% in the macroscopic inguinal (Ivanissevich) or subinguinal varicocelectomy series, revealing significant difference among the techniques. We conclude that the microsurgical varicocelectomy technique has higher spontaneous pregnancy rates and lower postoperative recurrence and hydrocele formation than conventional varicocelectomy techniques in infertile men.

Varicocele repair has significant potential not only to obviate the need for ART, but also to downstage the level of ART needed to bypass male factor infertility (4). After varicocelectomy, intrauterin insemination (IUI) may be tried again for men who had not achieved pregnancy by natural intercourse. Following varicocelectomy, the results with IUI seem improved or 11-21% pregnancy rates per cycle (15). The initial sperm concentration is predictive of unassisted pregnancy outcome in this population (16,17). Varicocelectomy may also enhance spermatogenesis within the testis, potentially increasing the chance of successful testicular sperm extraction surgery in patients with previously failed in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) (11).

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MANAGEMENT OF DIFFICULT CASES IN ANDROLOGY

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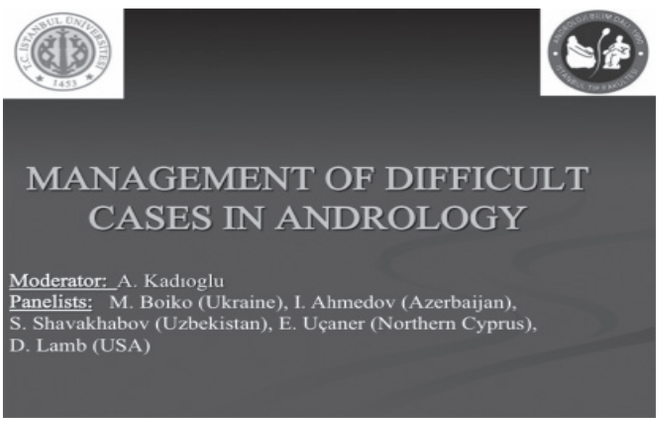
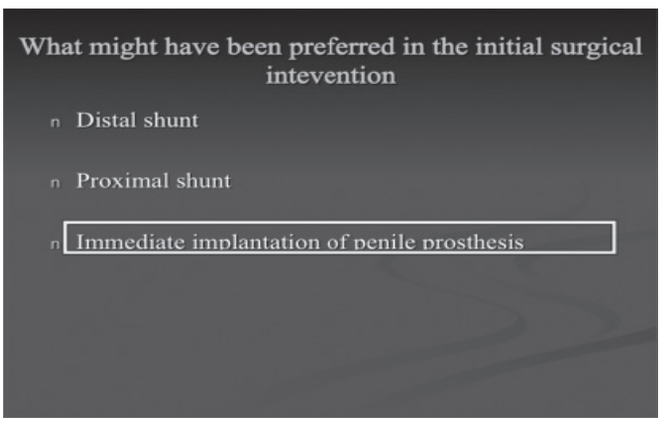
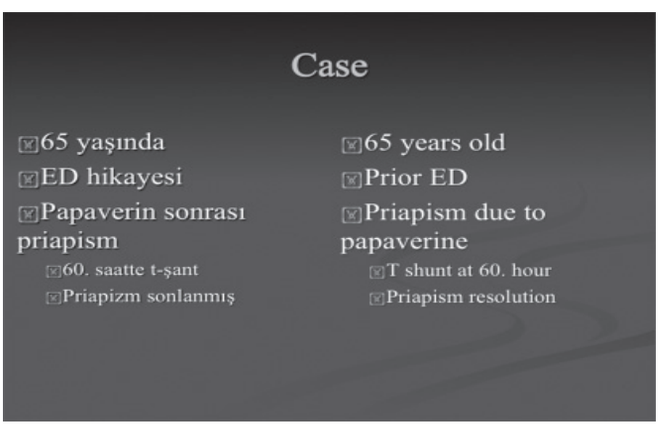
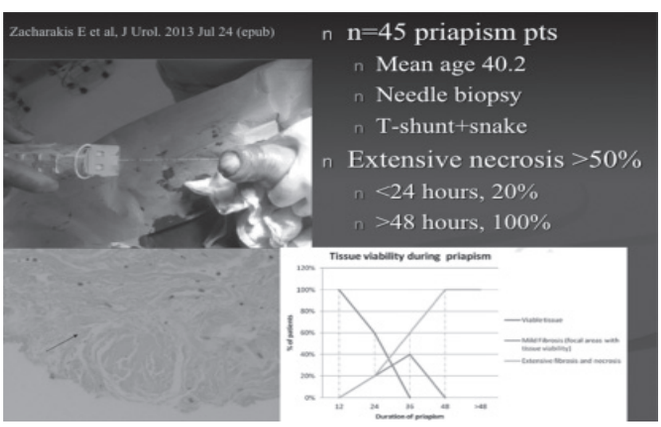
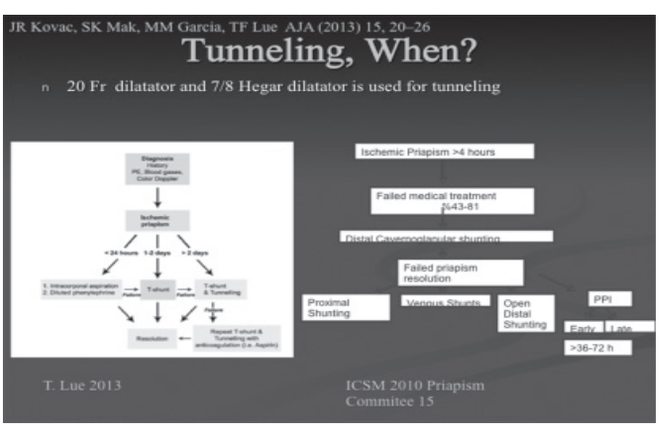
Panelists: M. Boiko (Ukraine), I. Ahmedov (Azerbaijan), S. Shavakhabov (Uzbekistan), E. Uçaner (Northern Cyprus), D. Lamb (USA)

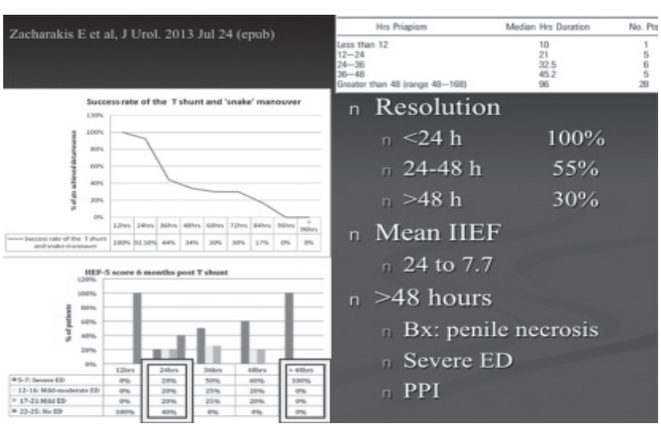












Shunt/PPI Time Threshold

- 24 hours (Pryor)
- 36 hours (Bennett)
- 48 hours (Ralph)
- 72 hours (Lue)

1. Pryor, J. P., Hehir, M.: The management of priapism. Br JUrol, 54: 751, 1982
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(n=13)	Priapism time	Resolution (%)	EF(%)
3	0-36	100	100
4	36-72	100	75
6	>72	84	50

Overall resolution rate: %92
Overall EF: %70

	Priapism time	Resolution	Postop ED
Segal	60	80	40
Brant	64	92	38
Ralph	96	64	93

Vakadan Öğrenilmesi Gerekenler/Educational aspects of the Case

- PPI'da ikinci insizyon oranı normalde de 6.6%
- Enfeksiyon/tekrar operasyon -
- IIEF 17
- Al-Ghorab sonrası da benzer sonuçlar
- Erozyon yada mekanik başarısızlık yok
- Normal rate of second incision in PPI 6.6%
- No infection/reoperation
- IIEF 17
- Similar results post Al-Ghorab
- No erosions or mechanical failure

A Bella, Abstract 1859, AUA 2012 Atlanta

2 month later

- ☒Ağrı veya ereksiyon yok
- ☒PDE 5 i dirençi ED
- ☒IIEF 10
- ☒No pain or tumescence
- ☒PDE 5i refractory ED
- ☒IIEF 10

Vaka Sonucu /Case Conclusion

- Priapism için penil protez uygulamasına ilgi artmakta
- PPI'nun hemen uygulanması uzamış priapismde daha iyi bir seçenek
- PPI'in zamanlaması ve priapizmin geri dönülmez olarak kabul edilme süresi hala tartışmalı
- Penile prosthesis for priapism is gaining traction
- Immediate PPI seems a better option for prolonged priapism
- Timing of PPI and definition of irrecoverable priapism is still debated

What should be done at this stage

- Delayed insertion of penile prosthesis

Vaka/Case

- 18 yaşında erkek hasta
- Skrotal ağrı şikayeti
- Bekar
- 18 years old male
- Scrotal pain
- Single

Vakadan Öğrenilmesi Gerekenler/Educational aspects of the Case

- n=5,
- Başarısız T-şant
- Doppler US ile doğrulama
- Postop 3. ayda, PPI
- Yoğun distal fibroz,
- İkinci küçük ventral bir kesi (<3 cm)
- Eksizyon ve dilatasyon
- n=5,
- Failed T-shunt
- Color Duplex ultrasound confirmation
- Postop 3 mo, PPI
- Dense distal fibrosis,
- Second small ventral incision (<3 cm)
- Excision and dilation

A Bella, Abstract 1859, AUA 2012 Atlanta

Vaka/Case

- PE
  - Right testis: 17 cc,
  - Left Testis: 14 cc
  - Palpable vas deferens

Vaka/Case

- Which diagnostic tests?
  - Semen analysis (2)
  - Scrotal Doppler US

EAU male infertility guideline 2013

Cerrahi Teknikler / Surgical Techniques

Treatment	Ref.	Recurrence/ persistence %	Complication rates
Antegrade sclerotherapy	18	9	Complication rate 0.3-2.2%: testicular atrophy, scrotal haematoma, epididymitis, left-flank erythema
Retrograde sclerotherapy	19	9.8	Adverse reaction to contrast medium, flank pain, persistent thrombophlebitis, vascular perforation
Retrograde embolisation	20,21	3.8-10	Pain due to thrombophlebitis, bleeding haematoma, infection, venous perforation, hydrocele, radiological complication (e.g., reaction to contrast media), misplacement or migration of coils, retroperitoneal haemorrhage, fibrosis, ureteric obstruction
Open operation			
Scrotal operation		-	Testicular atrophy, arterial damage with risk of devascularisation and testicular gangrene, scrotal haematoma, postoperative hydrocele
Inguinal approach	22	13.3	Possibility of missing out a branch of testicular vein
High ligation	23	29	5-10% incidence of hydrocele (< 1%)
Microsurgical inguinal or subinguinal	24,25	0.8-4	Postoperative hydrocele arterial injury, scrotal haematoma
Laparoscopy	26,27	3-7	Injury to testicular artery and lymph vessels; intestinal, vascular and nerve damage; pulmonary embolism; peritonitis; bleeding; postoperative pain in right shoulder (due to diaphragmatic stretching during pneumoperitoneum); pneumoscrotum; wound infection

EAU male infertility guideline 2013

Vaka/Case

- Semen Analysis
  - SA1: 1.6cc / 10 M / 28%
  - SA2: 2.2cc / 12 M/ 24%
  - Dilation of pampiniform pleksus of the left testis (5 mm), reflux +

Vaka/Case

- SA (3 mo later) → 2.5cc / 15 mil / %33
- SA (6 a mo later) → 2.3 cc / 19 mil / %45
- Right testis 18 cc, Left testis 17 cc

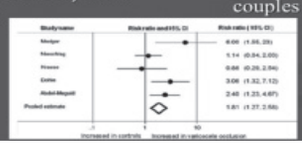
Vaka/Case

- Treatment
  - Left microscopic varicocelectomy

Cochrane Study

- 11 RCT, n=894
  - Gebelik oranı, OR 1.3
- Subgrup
  - 5 RCT, n=505
  - Clinic varikosel
  - Anormal SA
  - PR, RR 1.8
  - 7 tedavi edilen çiftte 1 gebelik

- 11 RCT, n=894
  - Pregnancy rate, OR 1.3
- Subgroup
  - 5 RCT, n=505
  - Clinic varicocele
  - Abnormal SA
  - PR, RR 1.8
  - 1 pregnancy for 7 treated couples



Kroese ACJ et al Cochrane Database Syst Rev 2012;10:CD000479

Varikosel Endikasyonlar/ Varicocele İndiciations

- Adolesanda
  - Bilateral VX
  - Anormal SA
  - Hipoplastik testis

veya

- Klinik varikoseli saptanan
- Oligospermia
- 2 yılı geçen açıklanamayan infertilite

§Adolescents:
§Bilateral Vx
§Abnormal SA
§Hypoplastic testis

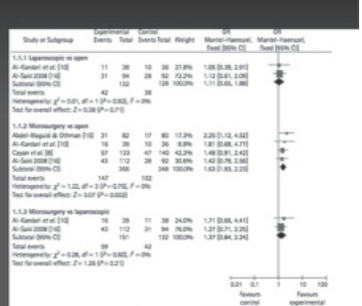
or

§Clinical varicocele
§Oligospermia
§2 years of unexplained infertility

•EAU male infertility guidelines-2013, EAU peadiatric guuidelines-2013

Best Technique-Pregnancy Rate

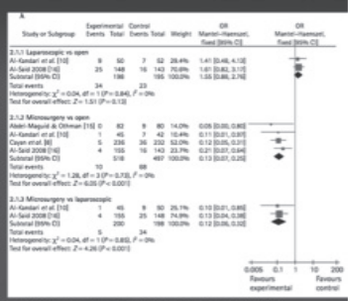
- The pregnancy rate was higher microsurgery than open varicocelectomy (OR = 1.63, 95% CI: 1.19–2.23).
- There was no significant difference between laparoscopic and open varicocelectomy (OR = 1.11, 95% CI: 0.65–1.88)
- The pregnancy rate was higher microsurgery than lap. varicocelectomy (39.1% vs 31.8%), although there was no statistical difference (OR = 1.37, 95% CI: 0.84–2.24)



Meta-analysis Of Varicocelectomy For Male Infertility-2012 BJU INTERNATIONAL | 110, 1536–1542

The Incidence of Recurrent Varicocele

- The incidence of recurrent varicocele was significantly lower after microsurgery than after laparoscopic or open varicocelectomy
- (OR = 0.12, 95% CI: 0.05–0.32)
- There was no significant difference between laparoscopic and open varicocelectomy
- (OR = 1.55, 95% CI: 0.88–2.75).



Meta-analysis Of Varicocelectomy For Male Infertility-2012 BJU INTERNATIONAL | 110, 1536–1542

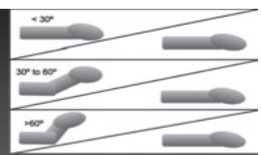
Tedavi/Treatment

- Nesbit + Plaque incision and grafting

Vakadan öğrenilmesi gerekenler/ Educational aspects of the case

- Varikosel hala erkek infertilitesinde gerekli bir cerrahi yöntemdir
- Varicoselectomy is still a valid surgical technique for male infertility

Curvature and Sex



- 114 PD pts with normal EF
- Sexual disability: Inability to penerate vagina
- 30% of the pts have sexual disability

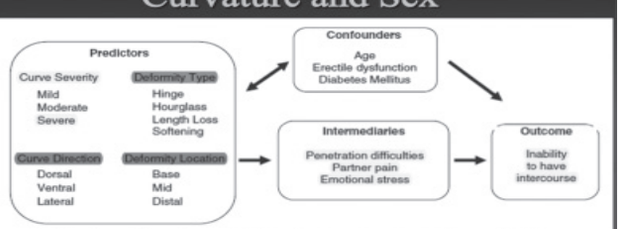
Walsh TJ, Hotaling JM, Lue TF, Smith JF: Int J Impot Res. 2013 Jan 24

Olgu/Case

- 62 yaşında erkek
- 5 yıldır Penil kurvatur
- IIEF: 22 (hafif ED)
- DM -, HT +

- 62 years old man
- Penile curvature for 5 years
- IIEF:22 (Mild ED)
- DM-, HT+

Curvature and Sex



- Only significant predictor is severe curvature (>60 deg.)
  - 38 vs 63% sexual disability
  - (p<0.001, OR:3.2)

Walsh TJ, Hotaling JM, Lue TF, Smith JF: Int J Impot Res. 2013 Jan 24

- CIS test(+)
- S deformitesi
  - Proksimalde ventral 30 derece
  - Distalde kum saati
- Kum saati

- CIS test (+)
- S deformity
  - Ventral curvature 30 degrees
  - Hourglass at distal part
- Hourglass deformity

One Thousand and One Patients (1001)

Kadioglu A et al J Androl 2011;32:502–508

Kelami classification	%	IIEF < 26 (ED) %
Notching, hourglass	12.3	67.3
<30 deg.	39.5	66.2
30-60 deg.	34.5	56.7
>60 deg.	13.5	40.4
Total	100	60.1

- 60.1 % ED (IIEF <26)

Erectile Dysfunction and PD

- ED rate >50-60% of PD pts.
- 16% of pts. present only with ED
- This rate is 30% in notching pts.
- ED rate 70% in notching pts. (12%)

EAU guidelines 2013
Kadioglu A et al Int J Imp 2004;16, 540–543
M Cakan et al J Sex Med 2007;4:1174–1178

Olgu/Case

- 29 yaşında erkek
- Eşi 25 yaşında
- İki yıldır primer infertil
- Kadın faktörü yok
- FM: Her iki testis 20 cc
- Vaz deferensler palpabl
- Bilateral kauda epididimde nodül
- Varikosel yok

- 29 years old male
- His wife is 25 years old
- Primary infertile for 2 years
- No female factor
- PE: Both testes were 20 cc
- Bilateral vasa deferentia are palpable
- Bilateral nodules in cauda epididymis

No varicocele

PDQ

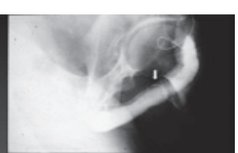
- n=832, PD, >12 mo
- Mean age 57, duration 4.1 yrs
- Mean degrees 50.5 (30-90)
- Vaginal intercourse difficulty 70.8%
- PDQ very/extremely bothered
  - Q.11 How bothered are you with the penis you looked
  - >60 deg. 71.5%
  - <60 deg. 58.1%*

Gelbard M et al J Sex Med. 2013 Nov;10(11):2822-31

Hangi testleri yaparsınız/Which tests do you do?

Semen analizi	Semen analysis
Hormon profili	Hormone profile
FSH, Testosteron	FSH, Testosterone

Penile Doppler in PD



- Mean PSV 14-15 cm/s
- Mean EDV 3.2-3.2 cm/s

- Penile vascular disease 57-82%
  - Mixed vascular disease 4-41.1%
  - Cavernosal disease 8-23.2%
  - Arterial disease 12.5-64*%

*LA Levine Vol. 1996: 155, 1270-1273
Chung E et al BJU J Sex Med. 2012 Dec;8(12):3446-51
Kadioglu A et al J Androl 2011;32:502–508
Erdogru T et al Asian J Androl. 2002 Sep;4(3):187-90.
^Deveci S1, Palese M, Parker M, Guhring P, Mulhall JP. J Urol. 2006 May;175(5):1807-11;

- SA:4 cc/azoospermia/pellet(-)
- SA:4.2 cc/azoospermia/pellet(-)
- FSH:2.8 mIU/ml(1.5-12.4 mIU/ml)
- T: 3.78 ng/ml (2.6-9 ng/ml)

Smith JF et al… Lue TF J Sex Med. 2009 Oct;6(10):2858-67.
Chung et al J Sex Med 2011;8:3446–3451

Table 3 Relationships between demographic and clinical characteristics and sonographic findings

	Calcification		Septal fibrosis		Intracavernosal fibrosis		Tunical thickening	
	OR	*P* value	OR	*P* value	OR	*P* value	OR	*P* value
Age								
<40	1.0	ref	1.0	ref	1.0	ref	1.0	ref
40–49	2.4	0.02	1.0	0.96	0.6	0.26	1.0	0.93
50–59	2.4	0.004	0.8	0.36	0.8	0.59	2.2	0.005
60–69	1.3	0.51	0.6	0.14	0.4	0.04	4.8	<0.001
70+	0.4	0.21	0.1	0.07	0.6	0.50	4.7	0.003
Married	1.1	0.80	0.7	0.12	0.8	0.29	1.8	0.02
Current tobacco use	0.9	0.83	0.9	0.80	0.9	0.70	0.9	0.67
Diabetes	1.8	0.06	0.3	0.04	1.2	0.73	1.1	0.80
Hypertension	1.0	0.89	0.5	0.03	0.9	0.73	1.2	0.38
Hypercholesterolemia	1.2	0.26	0.7	0.16	1.2	0.48	1.2	0.25
Coronary artery disease	0.9	0.79	0.2	0.05	0.7	0.59	1.1	0.76
Vascular disease	0.3	0.22	N/A		1.6	0.61	1.2	0.75

Doppler Findings	%	Associated Factors
Penile calcifications,	31-53*	40-59 age, DM, cur >60 (p=0.06)
Septal fibrosis	12*-25	(DM, HT, CAD) less common, onset <1 yrs, -length loss, unable to have sex- less common
Tunical thickening (>2 mm)	50-65*	50-70 age, Married Unable to have sex, no prior penile injury
Intracavernosal fibrosis	15-25*	Young age, no penile pain, penetration difficulty, seconder penile deformity, rapid onset

Tanı/Diagnosis

- Obstruktif azoospermi Obstructive azoospermia

Tedavi/Treatment

Tedavi alternatifleri?	Treatment alternatives?
Epididimovazostomi ± sperm dondurma	Epididymovasostomy ± cryopreservation
Epididimovazostomi+ sperm dondurma + ICSI	Epididymovasostomy + cryopreservation+ ICSI
MESA+ICSI ± sperm dondurma	MESA+ICSI ± cryopreservation
PESA+ICSI ± sperm dondurma	PESA+ICSI ± cryopreservation

Vakadan Öğrenilmesi Gerekenler Educational aspects of the case-2

Uç-yan teknik:
Epididimal kan akımı daha iyi korunur.

Intussussepsiyon yöntemi:
Anastomozun sızdırmazlığı artırılır.

3 sütürlü intusseption yöntemi (Triangulasyon):
İlk sütür yerleştirildikten sonra kollaps ve sızdırma problemi

Sütürler arası üçgen bölgeden tubulotominin zorluğu

End to side technique:
Better protection of epididimal blood flow

Intussusception technqiue:
Increase in the water-tightness of the anastomosis

Intussusception technique with 3 sutures (Triangulation):
Collaps and leakage problem after the placement of the initial suture

Toughness of tubulotomy in the region between the sutures.

Obstruktif azoospermi Obstructive azoospermia

- Azospermi vakalarının %15-20'si OA
- Epididimal obs. %30-67
- OA'de %25 epididimde sperm bulunmaz
- %15 vakada testiküler obstruksiyon
- Patens oranları %60-87, kümülatif gebelik oranları %10-43 arasındadır.

- OA 15-20% of azospermia
- Epididymal obs. 30-67%
- 25% no sperm detected in epididiymis for OA
- 15% testicular obstruction
- Patency rates range between 60% and 87% and cumulative pregnancy rates between 10% and 43%

EAU male infertility guideline 2013

Vakadan Öğrenilmesi Gerekenler Educational aspects of the case

	End to end	End to side	Triangulation intussusception	Longitudinal intussusception	P
Patency (%)	73	74	84	80	0.95
Pregnancy (%)	20	40	46	44	0.07
Shut down (%)	30	50	7.6	0	0.04

- Postop 6. ay
- SA:2.2 cc/21 million/10%

- Postop 6 mo
- SA:2.2 cc/21 milyon/%10

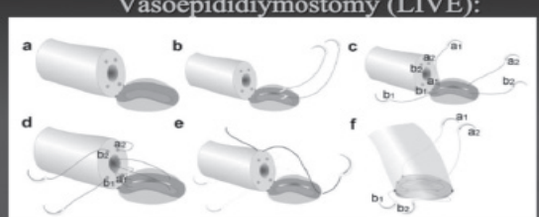
Which technique should be used?

- Microsurgical Longitudinal Intussusception Vasoepididiymostomy

Vakadan öğrenilmesi gerekenler/Educational aspects of the case-1

- Epididimal obstruksiyona bağlı azoospermi gelişen hastalarda, uç uca ya da uç-yan mikrocerrahi epididimovazostomi tercihen intussusesiyon tekniği önerilir.
- In patients with azoospermia due to acquired epididymal obstruction, end-to-end or end-to-side microsurgical epididymovasostomy is recommended with microsurgical intussusception being the

Microsurgical Longitudinal Intussusception Vasoepididiymostomy (LIVE):



a) Vas is sutured to the edge of epididymis with 9.0 sutures (2 or three)
b) Placement of two 10.0 double armed needles in longtidunal fashion to open incision
c-d) Sutures are placed into the vas with inside to out fashion
e-f) A tension reduction suture is placed to position both lumens face to face

Chan PT et al. AJA 2013 15:49-55

Which technique should be used?

- Open vs Robotic

Six Years Experience With Microsurgical Longitudinal Intussusception Vasoepididiymostomy (LIVE): A Prospective Analysis

- Patens (>10.000 sperm/ml) %92
- Sperm sayısı 12.9 (0.01-24) milyon/ml
- Motilite %23 (0-48)
- Anastomoz kapanması (1.yıl) %4
- Doğal gebelik (1. yıl) %31
- IVF/ICSI %39 (Taze ejakülat spermi ile)

- Patency (>10.000 sperm/ml) 92%
- Sperm count 12.9 (0.01-24) milyon/ml
- Motility 23% (0-48%)
- Shut-down rate (1.yr) 4%
- Natural pregnancy (1. yr) 31%
- IVF/ICSI %39 (Fresh ejaculated sperm)

Chan PT et al, AJA 2013 15:49-55
Chan PT, AUA 2008

Robotic vs Open VE

- Open vs Robotic
  - Time 150 vs 120 min
- REV earlier sperm return
- Similar TMSC
- RVE advantages
  - Easier surgical technique
  - Decreased fatigue
  - Improved stability and motion

Parekattil SJ et al J Reconstr Microsurg 2012; 28:435-44

Patency Associated Factors

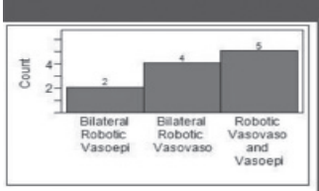
- n=73, OA, yaş 31
- LİVE cerrahisi
- Ortalama takip 15 ay
- Toplam patency 71.7%
  - Epididymal doluluk 87%
  - Bilateral cerrahi 81%
  - Corpus anastomosis 79%
  - Caudal anastomosis 100%
  - Hareketli sperm görünen akışkan sıvı 84%
- Doğal gebelik 33%

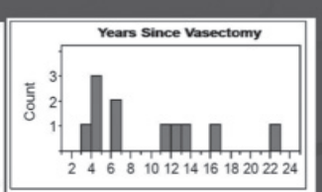
- n=73, OA, mean age 31
- LİVE surgery
- Mean follow up 15 mo
- Overall patency 71.7%
  - Epididymal fullness 87%
  - Bilateral surgery 81%
  - Corpus anastomosis 79%
  - Caudal anastomosis 100%
  - Flowing fluid with motile sperm 84%
- Natural pregnancy 33%

Peng J et al Urology. 2012 Jan;79(1):119-22.

Robotic EV

- n=11, post vasectomy surgery
- 6/11 patient 7. week SA
- 6/6 sperm





C Mechlin et al AUA 2013 Abstract V 1591

IVF/ICSI Success Predictors

- Fresh vs Frozen?
- Other factors?

Six Years Experience With Microsurgical Longitudinal Intussusception Vasoepididiymostomy (LIVE): A Prospective Analysis

- N=72 Azoospermi
- Epididimal obstrüksiyon
- Ortalama obstrüksiyon süresi: 18.7 yıl
- Longitüdinal intussussepsiyon epididimovazostomi

- N=72 Azoospermia
- Epididiymal obstruction
- Median duration of obstruction: 18.7 yrs
- Longitudinal intussusception epididiymovasostomy

Chan PT et al, AJA 2013 15:49-55
Chan PT, AUA 2008

Fresh vs Frozen for ICSI

- Meta-analiz
- n=11 çalışma
- NOA hastalar
- Donmuş sperm/
  - Gebelik oranı %26.4
- Taze sperm/
  - Gebelik oranı %28.7
- (p=0.91)

- Meta-analysis
- n=11 studies
- NOA patients
- Frozen sperm /
  - pregnancy rate %26.4
- Fresh sperm/
  - pregnancy rate %28.7
- (p=0.91)

THE PROSTATE AND SEX HORMONES

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The human prostate begins its morphogenesis at about 10–12 weeks of gestation and prostatic growth continues while fetal plasma androgen levels remain high. The fetal testis secretes testosterone into the circulation at sufficient levels to stimulate the differentiation and growth of the urogenital sinus tissues, leading to formation of the prostate gland. After birth, plasma testosterone decreases to a low baseline level and the prostate does not resume growth until puberty, when large amounts of androgens secreted from the testes stimulate prostatic cells to undergo morphofunctional maturation, giving rise to the various histological zones and functional tubuloalveolar glands. the human prostate reaches its full size of approximately 20 g and mature morphology at 18–20 years of age (1). Sex steroid hormones, including androgens and estrogens, are synthesized from a common sterol precursor, cholesterol, by the concerted actions of multiple enzymes . in the normal male, testes are the major source of circulating androgens and the principal testicular androgen is testosterone. Besides testosterone, the testes also secrete small amounts of other sex steroids including androstenedione, DHT, estradiol and estrone. Besides the testes, another important source of circulating androgens in man is the adrenal gland. Major adrenal androgens include dehydroepiandrosterone (DHEA), DHEA sulfate and androstenedione. Although these adrenal androgens are weak androgens compared with testosterone, they can be converted to more active steroid metabolites and thus indirectly alter prostate growth and function. the most potent androgen in men, DHT, is believed to be largely converted from testosterone in peripheral tissues such as prostate and skin by the action of 5α-reductase isozymes (2). During fetal development it is DHT that drives differentiation of the urogenital sinus into prostate and is responsible for virilization of the external genitalia and secondary sexual characteristics. As such, DHT may be the most important prostatic androgen in development and aging. Many lines of evidence support that androgens are permissive but insufficient for the induction and maintenance of BPH. For example, anti-androgen therapy with Flutamide or 5α-reductase inhibitors and surgical castration causes rapid reduction in prostate size emphasizing androgen necessity . Additionally, in castrated animals treatment with androgens induces prostatic regrowth, proliferation and increased prostate size. Contrasting this, androgens may not influence prostate growth because supplementation of men with androgens does not appear to increase the incident risk of BPH or LUTS. Furthermore, BPH prevalence increases with age, while levels of serum androgens decline. Thus while androgens are clearly important in BPH, other factors are likely involved (3-4). Type II 5α-reductase is the predominant isozyme in the human prostate and is targeted by Finasteride, which decreased prostate size by 25% on average in men with BPH, improved LUTS, and increased urinary flow rates. Another 5α-reductase inhibitor, Dutasteride, inhibits 5α-reductase types I and II; because type I 5α-reductase is the predominant isozyme in the hair follicle it has the added benefit of increasing hair growth in male pattern hair loss . Less is known about 5α-reductase type III but it may also participate in prostatic proliferation because it is expressed in prostate cancers . Therapy with 5α-reductase inhibitors also has the favorable effect of decreased risk prostate cancer in men who are regularly screened. The efficacy of 5α-reductase inhibitors may be due to the dependence of prostate luminal epithelial cells on DHT for maintenance of terminal differentiation and secretory function or alternatively the effects of DHT on stromal derived growth factors . Men and mice with reduced expression of 5α-reductase do not develop normal sized prostates . Furthermore, in men with congenital 5α-reductase deficiency, palpable prostates are not found and normal prostatic epithelium is rare, reaffirming DHT's role in differentiation of the urogenital sinus into prostate. Despite several earlier studies that reported higher levels of DHT in BPH specimens, when compared to fresh cadaveric control prostates, BPH specimens do not contain increased levels of DHT . Despite the important role of 5α-reductase inhibitors in treatment of BPH, anti-androgen based therapies are not effective in all men with BPH, and androgen supplementation does not appear to increase the risk of BPH, further suggesting that factors other than androgens are involved in BPH pathologies (5-6).

Estrogens In Men

Estradiol-17β (E2) is considered the most potent estrogen in men and is important for a variety of physiologic processes including bone maturation and mineralization, peak bone mass, and skin and lipid metabolism. In men, the majority of circulating E2 is formed from aromatization of T, mainly in fat and muscle, while up to 20% is secreted by Leydig cells of the testes. However, serum levels of E2 do not necessarily reflect tissue levels of E2 (7). In this regard, prostate in situ E2 production may influence local estrogen regulated processes. Such local production of E2 has been implicated in prostatic hyperplasia and loss of aromatase expression causes decreased estrogen-induced prostate proliferation. However, an important question remains: which estrogens or estrogen interactions affect prostate pathologies? The prostate is commonly thought of as an androgen target tissue, but it is also an important target of estrogens. Although E2 is the primary estrogen evaluated in prostate research, a number of other potential estrogenic sources may play significant positive or negative roles in the prostate, as outlined in. These estrogens can be divided into multiple categories including those that are found systemically (in serum) or those produced in situ in the prostate. Local steroids with estrogen receptor agonist activity include E2, 5α-androstane-3β, 17β-diol (3βAdiol), and 7α-hydroxy-DHEA (7HD). The effects of these sex steroids are not fully appreciated but are likely to influence prostate hyperplasia. Their mechanism of action, including promotion or suppression of proliferation and differentiation is dependent upon their specificity and activation of estrogen receptors (ERs). Estrogens exert their effects on target cells and tissues through interaction with estrogen receptors (ERs), notably ER-α and ER-β. ERs, like ARs, are ligand-modulated nuclear transcription factors. ER-β is highly homologous to ER-α in the DNA-binding and ligand-binding domains, but differs with respect to the N-terminal A/B transactivation domain. Binding of estrogen ligand to ER in the cytoplasm induces conformational changes in the ligand-binding domain, leading to interactions with coactivators, co-repressors and dimerization. The estrogen-ER complex can bind directly (classical signaling) to estrogen response elements (EREs) in the promoters of target genes or indirectly (non-classical signaling) by interacting with AP1 and SP1 sites in promoters of estrogen-regulated genes . Extra-nuclear signaling (i.e. non-genomic signaling) of ERs results in rapid biochemical effects, such as increased intracellular calcium or nitric oxide, or induction of enzymes, especially by phosphorylation(8).

Summary

The roles of sex steroid hormones in the multifactorial pathogenesis of BPH are well established yet their molecular mechanisms have yet to be elucidated. Androgens signaling through androgen receptors act permissively and are necessary for the development of BPH. Androgens may also serve as a potential “pool” for metabolism to estrogens that can promote or inhibit prostatic proliferation. Estrogens, whether systemic or local, are numerous and may have beneficial growth-inhibiting effects or negative growth promoting effects in the prostate depending upon the estrogen type, timing of exposure, stage of prostate disease, ER-signaling methods, and cell type. Determination of the molecular mechanisms involved in estrogen hormone action, especially on dimerization states, affected downstream pathways, and stromal epithelial-interactions will lead to a better understanding of these processes in prostate biology, BPH pathogenesis, and other diseases. Novel and genetically tractable models for BPH are sorely needed and will assist in the genetic dissection of pathways involved with specific pathologic subtypes of BPH, as well as, BPH overall. Ultimately, a better understanding of molecular mechanisms involved in the induction and maintenance of BPH will lead to the development of better therapies in prevention and treatment of this disease(9).

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COMPREHENSIVE MANAGEMENT OF ERECTILE DYSFUNCTION IN MEN WITH LATE ONSET HYPOGONADISM

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According to World Health Organization data, a worldwide people aged 65 and older in the year 2000 is 400 million and this number is projected to double by 2025 and to reach 2 billion by 2050 eventually. Testosterone (T) decreases progressively with advancing age and many of the men over the age of 60 years will suffer from hypogonadism. This is called Late Onset Hypogonadism (LOH). LOH is a syndrome characterized primarily by decreased libido and erectile dysfunction (ED) (1).

Causes for T decrease in older men: Although the exact mechanism for age-associated T decrease is not clear, the gradual decrease of T activity in older men are thought to be due to decreasing Leydig cell mass, attenuation or disorder in pulsatil luteinising hormone (LH) secretion, increase in the levels of sex hormone binding globuline (SHBG), decrease of concentration or down-regulation of androgen receptors (2).

Why is T important for erectile function? T plays a key role in erectile function to induce smooth muscle cell apoptosis, to reduce the expression of endothelial and neuronal nitric oxide (NO), to promote accumulation of adipocytes in corpus cavernosum, to accumulate adipocytes in the subtunical region of the corpus cavernosum, to change the corpus cavernosum architecture including the arrangement of elastic fibers and connective tissue, to reduce phosphodiesterase type 5 (PDE-5) enzym gene and protein expression, to produce ultrastructural changes in the dorsal nerve of the penis, and to make the tunica albuginea significantly thinner (3).

Ed Treatment In Men With Loh (4)
1. T monotherapy
2. Combination treatment (Testosterone replacement treatment [TRT] and PDE-5 enzym inhibitors [PDE-5is])

Critical points for TRT: The patient should also be informed about the advantages and disadvantages of TRT. The aim of TRT is to increase and maintain serum T levels within the physiological range. Supraphysiological levels should be avoided. In choosing the T formulation, several factors in the patients' profiles and preferences should be taken into account. Since the possible development of a contraindication during treatment (especially prostate carcinoma) requires rapid discontinuation of TRT, short-acting preparations should be preferred over long-acting depot preparation in patients with LOH.

How To Give TRT?
1. Intramuscular (IM) injections: IM injections have commonly been used in treating hypogonadism for many years. Injectable T preparations in oily depot include short and long acting formulations.

a. Short acting T Enanthate and Cypionate: They must be injected at intervals of 1 to 2 weeks (75 to 100 mg per injection in the former case, 150 to 200 mg in the latter). Such injections may induce supraphysiological serum peak levels of T for 2 to 5 days after injection, followed by a rapid decline to subphysiological levels in 10 to 14 days. The highs and lows of T may produce unpleasant fluctuations in patient's mood, sexual desire and activity, and energy level (roller coaster effect).

b. Long acting T Undecanoate: It shows a more favorable kinetics with serum T levels in the mid normal range for about 12 weeks. One ampul (4 ml) includes 250 mg/ml T. It requires only four to five injections in a year. The side effects due to the serum fluctuation levels of T are not observed with this formulation.
Complications Related To Trt On Prostate Is Problem For This Form.

2. Transdermal gel:
a. Patches: The patches can be scrotal and non scrotal (5-10 mg/d). Dose adjustment should be considered since the skin absorption can vary among men. Skin irritation is a common side effect with the patches. Adequate scrotal surface and the fre¬quent need for shaving for scrotal pathches are important. Patch is placed nightly on the clean, dry, and

unbroken skin on the back, abdomen, upper arms, or thighs only. The sites of application should be rotated weekly and should not be used more fre¬quently than every 7 days. This may reduce the risk for skin irritation.

b. Gel: Another very common and popular option is 1% T gel. It may be applied to the abdomen, shoulders, or upper arms. Daily applications of 5–10 g cause an increase of serum T levels back to normal levels after 1 day of use, with a steady state being reached within 5 days. It is a simple method and is well tolerated due to the lack of needles, and negligible localized skin reactions. Patient's compliance with T gel seems much better than with T patches. Bathing or swimming within the first hours after application may reduce absorption.

c. Recently, a 2% topical solution to be applied to the underarm once a day, using a metered dose applicator, has also been approved by the American Food and Drug Administration.

3. Oral formulations: The oral route is the easiest one to replace T. Absorption of oral formulations can be variable. Bioavailability is frequently poor due to the first-pass effect of the liver. Frequent administration is often required. It is difficult to achieve sustained blood levels with oral formulations and most of them are weakly active. The 17a-alkylated derivatives are more active, but may cause hepatotoxicity. The only active and safe oral formulation is T Undecanoate. However, its absorption is variable and highly dependent on the lipid content of fat of the meal and two or three doses must be taken daily (2-3 x 40 mg/d).

4. Tranbuccal formulations: Transbuccal administration provides the absorption of T through the oral mucosa, avoiding intestinal pass and liver inactivation. It is presented as a biopellet to be placed on the gum above the incisor tooth. The pharmacokinetic profile of transbuccal T is similar to that of T gel but it is used 30 mg twice a day. It delivers mean T levels equivalent to those achieved with a T gel.

5. Subdermal pellet implants: T pellets have a prolonged period of action (3 to 6 months). There is 200 mg T in each pellet. They need a specialist to be implanted. There are uncommon risks of infection and extrusion.

How long should be waited for having efficacy of TRT in men with LOH? Significant improvement in libido starts within 3 weeks of starting TRT, with maximum improvement occurring at 6 weeks. Up to 6 months of TRT may be required before significant improvement in erectile and ejaculatory function is observed (5).

Combination treatment with T and PDE-5is: TRT as a first line treatment in hypogonadal men with ED should be used before PDE5is (6). TRT alone in hypogonadal men can restore erectile function. In hypogonadal patients with ED who fail to respond to TRT alone, combination with T and PDE-5i should be considered for ED treatment. Hypogonadism is significantly associated with failure of sildenafil. Replacing T would be beneficial in augmenting the efficacy of sildenafil in elderly men (7).

In a recent study, 49 hypogonadal men with ED received T-gel for 6 months. Sildenafil was added at 3 months to those with no efficacy of T-gel alone. A total of 31 patients reported significant improvement in the sexual desire and erectile function with TRT alone. In spite of normalisation of total and bioavailable T values, and significant improvement of sexual desire, the erectile function of 17 men did not improve. These men received combined T-gel and sildenafil, after which all reported improvement in erectile function. In conclusion, combination therapy with T and PDE5 inhibitors improves erectile function in patients who failed to respond TRT alone (8).

Complications Of TRT

1. Prostatic health: According to present data, TRT neither increases the risk of BPH nor contributes to worsening of LUTS (9). In contrary, there is evidence that TRT improves lower urinary tract symptoms in hypogonadal men with mild benign prostatic hyperplasia (10). There is no evidence that TRT will convert sub-clinical prostatic lesions to clinically detectable prostate cancer (PCa) although we as urologists have a fear coming from history. Analysis of worldwide data from 18 prospective studies (more than 3000 cases and 6000 controls) found no association between serum testosterone concentrations and prostate cancer (PC) risk (11). Another meta-analysis showed no significant association between TRT and the incidence of PCa or the need for prostate biopsy when compared with the placebo/non-intervention group (12).

2. Hematocrit: Polycythemia is the most frequent adverse event associated with TRT. Hematocrit needs to be assessed during treatment due to the risk of thrombosis associated with polycythemia. Hematocrit starts to increase within one month of treatment initiation. Hematocrit level should be kept less than 52–54%. In higher level, TRT should be stopped until hematocrit normalization and in case of urgency, phlebotomy is considered.

Contraindications to testosterone therapy (13):

- History of breast or PCa
- Presence of palpable prostate nodule or induration
- Serum prostate-specific antigen >4 ng/mL or >3 ng/mL in men at high risk for prostate cancer such as African-Americans, or men with first degree relatives with pros¬tate cancer, without further urological evaluation
- Untreated severe obstructive sleep apnea
- Uncontrolled or poorly controlled heart failure
- Severe lower urinary tract symptoms with International Prostate Symptom Score above 19 (symptoms unchanged or even improved)
- Hematocrit >50%

Follow-up: There is no standart follow-up protocol. Bhasin et al suggested that after initiation of TRT, patients should be monitored for clinical response, serum testosterone level, serum PSA level, hematocrit level and digital rectal examination findings at 3. months, 6 months and annually thereafter (14).

Conclusion: In hypogonadal patients with ED, TRT is first-line therapy. If patients are unresponsive to TRT alone or sildenafil alone, combined use may improve erectile function and enhance the therapeutic effect of PDE-5is.

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UPDATE IN THE MANAGEMENT OF FEMALE SEXUAL DYSFUNCTION

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Female sexual dysfunction (FSD) is a common health matter, with approximetely 10-15% of women over 18 years old reporting sexual problems associted with distress and it has multifaceted etiologies. Affected patients have a lowered quality of life, a decreased level of well-being and relationship issues and it requires hormonal and nonhormonal consideration. FSD basically is classified as hypoactive sexual desire disorder (HSDD), sexual aversion disorder, female sexual arousal disorder (FSAD), female orgasmic disorder, dyspareunia and vaginismus. A number of researchers have studied that various therapeutic strategies including pysicological, hormonal and nonhormonal to manage FSD. Pysicological intervention may include basic counseling, sensate focus, cognitive behavioral therapy and couple therapy. While hormonanal treatments include estrogens, androgens, tibolone and DHEA, nonhormonal treatments contain flibanserin, phosphodiesterase type 5 inhibitor (PDE5I), melanocyte-stimulating hormones analogs, adrenoreseptor antagonists, prostaglandins, oxytocin, monoamine pharmacological agents, L- arginine, Levodopa and natural aphrodisiacs. This paper focuses to management of female sexual dysfunction particularly hormonal and nonhormonal medical treatment.

Clasification of Female Sexual Dysfunction

Acording to DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, sexual dysfunctions are defined as “disturbances in sexual desire and in the psycho-physiological changes that characterize the sexual response cycle and cause marked distress and interpersonal difficulty”(1). The categories defined by the DSM-IV are hypoactive sexual desire disorder (HSDD) (most common), sexual aversion disorder, female sexual arousal disorder (FSAD), female orgasmic disorder, dyspareunia and vaginismus. On the other hand, American Urological Association Foundation (AUAF) recommends a new diagnostic and classification system as follow; Sexual desire/interest disorder, subjective sexual arousal disorder, genital sexual arousal disorder, combined genital and subjective arousal disorder, persistent genital arousal disorder, women’s orgasmic disorder, dyspareunia, vaginismus and sexual aversion disorder.

Nonpharmacologic Management of Female Sexual Dysfunction

Psychological treatments may include basic counseling, sensate focus, cognitive behavioral therapy and couple therapy (Table). Basic counseling should include a thorough medical, medication and sexual history, history of current life context and past psychosexual development and contextual variables. Individual cognitive therapy, which focuses on individual’s thoughts, feelings and behavior, encourages the patient to become more aware of irrational beliefs and dysfunctional thoughts, and in doing so, may help to modify their thinking and approach (2). The aim of couple therapy is to improve communication skills between couple, reduce the stress and anxiety level, and make the patient become more aware of her thoughts and feelings that accompany sexual behaviors.

Hormonal Treatment of Female Sexual Dysfunction

Hormone therapy includes treatment with estrogens, testosterone, dehydroepiandrosterone (DHEA) and tibolone (Table)

Estrogens

Estrogen (E) therapy are highly effective in reversing vulvo-vaginal atrophy (VVA) and sexual function as well. Estrogens may be prescribed for patients whose history and physical findings are consistent with depletion of estrogen. Transdermal is preferred therapy for depleted estrogen and its symptoms (3,4). It is the most effective therapy available for reducing vasomotor symptoms and associated menopausal symptoms with minimal adverse effects. In recent years, concerns have arisen about adverse reactions associated with oral estrogen. Most of these events have been linked to ‘‘first-pass effect,’’ the administration of a large oral steroid

load through the liver. The most notable event related to oral estrogens and progestins was publication of a large multicenter trial conducted in the U.S., the Women's Health Initiative (WHI) (5), which demonstrated that a conjugated estrogen plus medroxyprogesterone acetate combination was associated with a small increase in risk of breast cancer and cardiovascular (thrombotic) events in older women. The results of the recent Phase III and IV studies showed that application of the 0.06% transdermal estradiol gel the lowest practical dose of estrogen therapy in the treatment of VVA result in significant improvements from baseline in the vaginal maturation index by 12 weeks with good tolerability (6). In adition, newer selective estrogen receptor modulators (7). are other promising options for treatment of VVA. Finally, intravaginal estrogens or DHEA, combined with mechanical dilatations, may be administered with little systemic absorption. Both are also highly effective for treatment of vaginal atrophy.

Testosterone

Androgens play an important role in female physiopathology. The age-related reduction in the production of ovarian and adrenal androgens may significantly affect women's health. Both in the central nervous system and peripheral tissues, there are multiple ways whereby androgens target their specific actions through a particular tropism of the brain areas that are involved in sexual function, behavior and cognition. Treatment with transdermal testosterone also has been shown to significantly improve sexual function in women with natural, surgical menopausal and hypopituitism (8,9). Improvement in sexual desire and interest with oral methyltestosterone (methylT) therapy were reported in several clinical trials (10,11). However, oral methylT lowers HDL-cholesterol and may increase weight and visceral fat accumulation has resulted in diminished interest in its use and the development of nonoral testosterone therapies for women. With respect to the local vaginal effects of testosterone, there is a preliminary evidence that the vaginal application of 300 µg testosterone per day over a course of 4 weeks improves objective and subjective measures of signs and symptoms of vaginal atrophy related to aromatase inhibitors without increasing estradiol or testosterone levels (12). However, longer-term trials are warranted. Safety outcomes have been included in all of the randomized placebo-controlled trials of the testosterone patch for women. Transdermal therapy with the testosterone patch releasing 300 µg/day has been associated with an increased rate of hair growth, but over 1 year of blinded treatment the rate of acne, alopecia and voice change did not differ between testosterone and placebo-treated groups. Application site reactions have been seen with TTP therapy, but it results in discontinuation rate of 10%. This is not an issue with transdermal testosterone cream and gel therapy. Transdermal testosterone therapy with the 300 µg/day patch has not been associated with any adverse hematological or metabolic effects (13). Although off-label use of testosterone injections and transdermal testosterone formulated for men is in widespread use, these products result in inappropriately high testosterone levels for women and should not be prescribed to treat FSD.

DHEA

The pre-androgens, androstendione and DHEA, are produced by both ovaries and adrenals, with the adrenals also being the main site of production of DHEAS. In the USA, DHEA is readily available as an over-the- counter nutritional supplement for the purposes of maintaining sexual function, youthfulness, well-being and memory; however, the efficacy of systemic DHEA as a treatment for FSD in postmenopausal women have consistently shown no benefit (14).

Tibolone

Tibolone is a synthetic steroid that exhibits combined estrogen, progestin and androgen effects. It is in widespread use in Europe and Asia-Pacific countries as an alternative to conventional estrogen or estrogen/ progestin therapy to alleviate menopausal symptoms. It has good tolerability and is associated with a low incidence of vaginal bleeding and breast pain. Tibolone has been shown to be associated with improved sexual function, particularly sexual desire and arousal, to a greater extent than traditional HRT in healthy postmeno- pausal women as evidenced by the Female Sexual Function Index score over 24 weeks (15). It has also been shown to reverse vaginal atrophy and improve cervical mucus resulting in less vaginal dryness, dyspareunia and urinary symptoms.

Nonhormonal Treatment Of Female Sexual Dysfunction (Table)

Flibanserin

Flibanserin is a nonhormonal, centrally acting molecule that acts as an agonist at postsynaptic serotonin (5-HT1A) receptors and as an antagonist at 5-HT2A receptors. In two well-designed clinical trials in premenopausal women with HSDD, flibanserin 50 and 100 mg once daily at bedtime for a 24-week treatment period were found to be well tolerated and associated with significant improvements in satisfying sexual events (SSE), sexual desire and overall sexual function, and reduction of sexual distress, versus placebo (14).

Phosphodiesterase Type 5 Inhibitor (PDE5I)

Genital engorgement is one of the physiological responses to sexual stimulation in women. Consistent with the result of a literature review (16), sildenafil may be beneficial in select groups of pre- or postmenopausal women diagnosed with FSD, regardless of the dose used. It appears to be effective in enhancing genital vasocon- gestion in a subgroup of individuals with neurodegenerative diseases leading to FSD. However, given the numerous limitations of the trials, especially the inconsistent use of validated assessment tools, the evidence does not conclusively support sildenafil to be considered as a standard treatment option for all women affected with FSD, especially FSAD, which is believed not to be predominantly a disorder of genital engorgement.

Melanocyte-Stimulating Hormone Analogs

Melanocortins affect multiple physiological responses, including sexual behaviors. To date, two Phase II randomized controltrials studied the effect of bremelanotide on female sexual arousal and desire disorder (14).

Adrenoceptor antagonists (phentolamine)

Phentolamine is a combined alpha-1 and alpha-2 adrenergic antagonist, which has been shown to inhibit sympathetic tone and facilitate penile smooth-muscle relaxation. Its potential effect on FSAD has been assessed in a pilot study among postmenopausal women experiencing lubrication difficulties and lack of subjective arousal (14).

Prostaglandins (alprostadil)

Triggered by favorable vasodilatory responses of intracavernosal of alprostadil USP (prostaglandin E1 or PGE1) in male erectile dysfunction, its effect has been examined in the treatment of FSAD. Preliminary studies supported its effectiveness in enhancing subjective and physiological arousal during visual sexual stimulation and intercourse (14).

Oxytocin

Oxytocin is a nonapeptide hormone best known for its role in lactation and parturition. Oxytocin implicated in social behavior and sexual relationships. Plasma oxytocin levels increase during sexual arousal, and orgasm in men. RCTs of intranasal oxytocin in men showed equivocal results (17). Future studies are needed to examine the facilitating effects of oxytocin on sexual function in men and women.

Monoamine pharmacological agents

Pharmacological agents that modulate monoamines may help alleviate sexual dysfunction. Bupropion is a second-generation. Controlled trials have shown bupropion to reduce the incidence of sexual dysfunction in depressed patients either as adjunctive treatment or as single therapy. Data in nondepressed patients demonstrated some improvement in sexual function, but it was not associated with an increase in frequency of sexual activity. Given its attractive side effect profile, and lack of other medical treatments for decreased sexual function, bupropion remains an option until other, more specific agents, become available on the market (18).

L-Arginine: Arginmax

L-arginine has been well established as a NO precursor. Arginmax for women is a proprietary nutritional supplement that combines L-arginine, panax ginseng, ginkgo biloba and damiana leaf (turnera aphrodisiaca) with several vitamins and minerals. One RCT has shown some benefit in sexual dysfunction in pre and perimenopausal women. Postmenopausal women primarily showed an increased in level of sexual desire (19).

Levodopa

The effect of levodopa (100 mg) on sexual response in men and women has been investigated in a double-blind, placebo-controlled crossover design. Genital and subjective sexual arousal was not affected by levodopa. However, the drug resulted in an increase in Achilles tendon reflex magnitude (a measure of somatic motor preparation) in response to sexual stimulation in men, but not in women (20).

Natural Aphrodisiacs

The current body of objective evidence does not support the use of any natural aphrodisiac as an effective treatment for male or female sexual dysfunction (21).

Table: Nonpharmacologic, hormonal and nonhormonal therapies for FSD.

Nonpharnacologic	Hormonal	Nonhormonal
Basic counseling	Estrogens	Fibanserin
Sensate focus	Testosterone	PDE5I
Cognitive Behavioral	Tibolone	MSHA
Couple treatment	DHEA	Phentolamine
		Alprostadil
		MAPA
		L-Arinine:Arginmax
		Levodopa

DHEA; dehydroepiandrosterone, PDE5I; phosphodiesterase type 5 inhibitor, MSHA; melanocyte-stimulating hormone analogs, MAPA; monoamine pharmacological agents

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SIMULTANEOUS IMPLANTATION OF ARTIFICIAL SPHINCTER AND PENILE PROSTHESIS

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Simultaneous implantation of artificial sphincter and penile prosthesis is indicated for patients who have total incontinence due to sphincter insufficiency and erectile dysfunction(ED) in whom other terapies have failed or not possible or even or not desired(1) The inflatable penile prosthesis (IPP) is the standart of care for men with medically refractory ED. It has consistently performed well with high patient satisfaciton and prosthesis survival rates(2) All dual cases require meticulous attention to detail to minimize the risk of infection. The operating room is kept at minimum traffic. Intravenous antibiotics consisting of vancomycin and gentamicin is administered 1 hour before incision time. Patients are shaved in the operating room. A timed 10-min scrub to the genitourinary region with chlorexidine and alcohol based disinfectant is performed to decrease intraoperative-colonization. Copious antibiotic infused irrigation fluid with gentamicin,amikacin and poliymyxin is used throughout the entire case. A 14 French foley catheter is inserted to drain bladder and facilitate dissection of the urethra.In general artificial urinary sphincter (AUS) is placed first followed by IPP. This is to ensure that in the event of accidental urethrotomy, surgery can be aborted without discarding the penile prosthesis components(3).

Surgical Procedure

A 4cm single trans-scrotal incision is utilized. This incision readily exposes underlying urethra and both corpora.This incision tends to heal rapidly and produces a very fine, almost invisible scar. The scar is also hidden by the penis when it hangs in the dependent position(4). Dissection is carried to the bulbospongiosus muscle where it is split and the corpus spongiosum is identified and dissected as proximal as possible. This enhancements to the one-scrotal incision technique allow more proximal cuff placement as evidenced by the bulbucavernous muscle dissection and use of larger cuffs with comparable continence rate to perineal placed cuffs(5). Dissection is carried posteriorly to the junction between spongiosum and cavernosa and a window is created. The window is enlarged to at least 1,5 to 2cm width with right angle clamp to allow American medical systems (AMS) cuff measurement and the placement of the cuff. At this juncture, it is approtiate to assess for occult urethral injury by injecting saline in a retrograde fashion. Any leakage at the site of dissection confirms urethral injury and the operation is subsequently terminated.

The pressure regulating balon is placed retropubically through the designated external external inguinal ring after puncturing transversalis fascia. The subdartos pocket is formed and AUS pump is inserted in dependent position on the ipsilateral hemiscrotum. Tubings are connected using quick-connect system. At this point The AUS is cycled and locked in the deactivated mode(3). Exposure is then maintained with Scott's ring retractor for corporotomy and stay sutures are placed through the tunica albuginea. After the corporotomy, dilatation is completed with Hegar dilators through the proksimal and distal parts of the corpora cavernosa. Based on the measurement of both corpora cavernosa with Furlow an appropriately sized CX cylinders is selected. Cylinders, pump and reservoir filled with normal saline to displace the air. The saline is then evacuated because all parts will be implanted empty. The suture at the tip of the cylinder is threaded into a 2-inch straight needle and this needle is threaded into the distal tip of a Furlow cylinder inserter. The Furlow inserter is then inserted into the distal corpus cavernosum. The trochar on the cylinder is pushed inward., causing the straight needle to emerge through the glans penis. The needle is then grasped with a clamp and removed from the glans. This results in both sides of the guide suture being drawn through the glans. The guide suture is then used to draw the cylinde into the distal corpus cavernosum. If necessary the proper size rear tip extender is applied to the proximal end of the cylinder. The cylinder is then inserted proximally to the corpus cavernosum. The corporotomy is then closed with running 2-0 polydioxanone suture. The other cylinder is implanted to the opposite corpus cavernosum using the technique already described. After implantation of both cylinders another subdartos pocket is formed on the other side of the scrotum opposite to the AUS pump to make a compartment for penile prosthesis pump. A clamp is used to spread tissue

within this pouch in order to make it large enough to receive the pump. After that, the transversalis fascia is perforated with guide of the finger with scissor. The scissor is spread so that the surgeon can introduce the finger through the fascial defect. The surgeon should be able to feel the back wall of the symphisis pubis and the Foley catheter in the bladder. The empty reservoir is inserted through the fascial defect as the surgeon withdraws the finger. The reservoir is then filled with 60 ml normal saline. The surgeon checks by palpating with the finger that the reservoir is beneath the fascia and that the tubing exits directly through the fascial defect. The two tubes of the prosthesis are then connected. Rings from the quick connect system are then applied and a straight connector is inserted. Normal saline is used to irrigate any air or blood from the tubing prior to making connection.

After the connection is made, the closure tool is used to force the rings into each end of the connector in order to secure the connection(4). We do not place suction drains on a routine basis but this is generally optional and is surgeon-dependent. Penile prosthesis is partially inflated. It is important to have tubings for each device compartmentalized separataley to avoid cross over. The penoscrotal fascia is closed with running 3-0 Dexon suture A tight circumferential wrap with Kerlix gauze is used for additional hemostasis and prevention of hematoma formation. All patients are discharged the next operative day following removal of Foley catheter on stool softeners, oral antibiotics, and analgesia.Patients return to the clinic in 6 weeks for activation of both prostheses(3).

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PENILE IMPLANT SURGERY IN PRIAPISM

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Priapism has been reported as a persistent penile erection in the absence of sexual desire; it is not a commonly encountered clinical antity, being idiopathic in up to 60% of cases. Basically the clinical condition is classified into three groups including ischemic, non-ischemic and stuttering priapism. According to the literature there is not a widely accepted therapy for patients presenting at the late stage, or in whom first step medical approach has failed (1). It has been shown that in untreated low-flow priapism, progressive ischemia of the cavernosal smooth muscle occurs, which ultimately leads to corporal necrosis, fibrosis and finally erectile dysfunction. Although the critical time when irreversible damage to the smooth muscle occurs is unknown it has been reported that ischemia of the smooth muscle with related pain is already a feature in priapism of nearly 6 hours duration (1,2,3). Unsuccessful treatment of low-flow priapism by conservative approach results in cavernosal fibrosis, with supsequent induration and penile shorthening. In this kind of cases a penile prosthesis implantation can be difficult due to fibrosis. Therefore surgery for ischemic priapism has a well-known purpose for acute clinical presentations of the condition and is usually performed when conservative therapy options fail. On the other hand, early penile prosthesis implantation in cases with ischemic priapism has been performed for the management of acute ischemic priapism, with particular utility in situations when penile shunting would be predictably unseccessful (4). Recently it has been reported that, penile shunting has limited success for priapism cases lasting ≥72 hours, especially in circumstances of substantial cavernous thrombosis which causes to blood aspiration from the corpora cavernosa unfeasible (4). There are sevral reports in the lietrature suggesting the application, indications and advantages of immediate penile prosthesis surgery for ischemic priapism. This intervention was first popularized by Rees et al in an initial series of eight patients with ischemic priapism. Further the same group of investigators expanded subsequent series in totally 50 of cases. In the study group the authors described successful malleable penile prosthesis insertion in 43 patients and successful inflatable prosthesis implantation in seven cases. In this series, all patients had failed conservative treatment options including penile shunt surgery in 13 patients, and all had shown evidence of cavernosal smooth muscle necrosis. The results of this study clearly revealed the simplicity of prosthesis surgery in acute setting for refractory ischemic priapism and the advantage of this approach in preserving penile length which migth otherwise be reduced by corporal fibrosis following a significant delay. Furthermore, a variation of early applying penile prosthesis surgery in the case of refractory ischemic priapism, that includes corporectomy with delayed prosthesis implantation, has also been reported (1,5)

Penile prosthesis surgery in the late stage namely after resolved ischemic priapism is indicated for the men who is unable to perform satisfactory sexual intercourse because of insufficient erectile capasity (4). In this situation, the purpose of the approach resembles that for any man who has severe erectile dysfunction electing penile prosthesis surgery due to other modalities for treating the pathology are undesirable, contraindicated or unefficient. The approach of penile prosthesis insertion for this indication is generally consistent with widely used standart procedures. Several investigators have reported on their penile prosthesis surgery experiences and suggested special considerations for this approach of relevance for sickle cell disease patients. In one of this reports the authors suggested the insertion of semi-rigid prosthetic devices while others recommended corporal dissection and dilation maneuvers to implant the prosthetic devices with high success rate (6,7). More recently, authors have accknowledged the challenges of corporal fibrosis and suggested to perform an early implantation for sickle cell disease patients within 6-18 months after priapism. It has been widely accepted that earlier surgery has several advantages including easy dilation without need of corporal tissue excision (8). Additionally, it has been postulated that the easier execution of prosthesis implantation, when major penile scarring is limited, may reduce the risk of procedure related complications such as urethral injury, tunical erosions and infection (9). Wilson suggested some maneuvers to facilitate penile prosthesis implantation into fibrotic corporal bodies. According to his experience he suggested to use specially designed

cavernotomes to create cavernosal cavities for penile prosthesis effectively when routine corporal dilation is challengig. Furthermore, the initial insertion of downsized prosthesis cylinders, that prevent the corporal fibrotic contraction and serve as tissue expanders, and then reimplantation of larger cylinders about a year later may considered as a technical option. More importantly, the use of specially designed type of prostheses should be preferred in the case of a fibrotic corpus cavernosum. Titan Narrow (Coloplast) which has narrow rear tip extenders (9 mm, compared with 12.8 mm for the Titan) and AMS700-CXR are accepted as the most appropriate devices for fibrotic cavernosal tissue (10). Montague and Angermeier described an operative technique including complete exposure of the entire corpora cavernosa with wide corporal incision and excision off all fibrotic tissue, before a successful prosthesis cylinder placement (11). Additionally Shaeer reported a corporoscopic excavation technique by using an optical urethrotome for cavernosal tissue resection after which the prosthesis was implanted easily (12).

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SURGICAL CORRECTION IN PATIENTS WITH CONGENITAL PENILE CURVATURE

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Congenital penile curvature (CPC) is rare. There is no evident cause. A single study analysing the ultrastructure of the tunica albuginea (TA) demonstrated widening and fragmentation of collagen fibres, with complete disappearance of striation and transformation into electron-dense, fibrous granulated material and elastin accumulation (1). It is caused by length disproportion of the corpora cavernosa and corpora spongiosa. The most frequent type of angulation is ventral (50%). Pure lateral angulations are rare. The reported prevalence of this condition is 0.04-0.6%(2). It became manifest nearly at 25 years(3). It usually causes a few, if any, symptoms. The aim of surgery is to straighten the penis but allowing a normal erection, enabling satisfactory penetration and sensation during sexual intercourse. Congenital penile curvature can be corrected by corporoplasty with high curvature correction rates (67–97%)(4). The first CPC was treated by Nesbit in 1954(5). The most commonly used methods for corporoplasty include: (1)excisional corporoplasty (Nesbit operation): the excision of ellipses of the TA either transversally or longitudinally (2) incisional corporoplasty: a) making longitudinal incisions on the healthy convex aspect of the penis and closing them horizontally using the Heineke-Mikulicz method; b) dorsal plication of the tunica albuginea after a 4–6 mm parallel incision, made through the tunica; (3) plicational corporoplasty: dorsal plication of the TA with no incision (sutures only). The majority of CPC can be corrected with simple degloving or plication techniques. Residual curvature can be addressed with additional plication or more extensive surgical correction, such as dermal graft placement and, in rare cases, complete penile disassembly.

1- Excisional Corporoplasty (Nesbit Operation): This procedure described in 1965 by Nesbit (1). This is the most widely used surgical technique for correcting CPC. A 5–10 mm transverse ellipse on the TA is excised (approximately 1 mm for every 10^{o} of curvature). The reported success rates of 96.2% for the procedure for treating CPC(6). However, the procedure is time-consuming and has a high incidence of complications, such as hematoma, glans numbness, de novo erectile dysfunction, and over-correction(7). Therefore, various modifications have been made in the original technique to decrease the complications. In Kelami modification, diamond shaped segments are removed with its cutting edge upward in order to prevent erectile tissue injury. Then, two stay sutures are applied to the distal corners of the opening, and the edges of the opening are closed(8). Giammuso et al. were excisied a diamond of tissue from the intracavernous septum and reported that this technique provide better quality straightening and less shortening of the shaft than Nesbit operation(9). Rolle et al. introduced a ‘‘U’’ stitch which is positioned under the Allis forceps and an area of the albuginea is excised(10). Popken et al. described a modified corporoplasty that the edges of the tunica albugenia being brought together with a continous, blood-tight, intratunical suture, and the knots buried(7). Belgrano et al. describe a technique for treatment of complex penile curvature by the excision of asymmetric ellipses of TA(11). Rehman et al. modified this technique by using a partial thickness shaving of the tunica to avoid possible bleeding and cavernosal injury and improves adhesion of plicated tunical layers (12). Egydio et al modified the conventional Nesbit technique by applying multiple superficial TA excisions, according to the geometric principles of the Egydio technique(13). Schwarzer et al. described the tunica underlap technique that combines elements of the orginal Nesbit procedure with features of tunical plication techniques(14).

2- Incisional Corporoplasty: a) In 1990, based on an inverted Heineke–Mikulicz principle, Yachia proposed single or multiple 1-1,5 cm longitudinal incisions to the convex side of TA which are subsequently closed horizontally(14). The knots are buried by inverting sutures using the same suture material. Recent studies show patient satisfaction rates for this procedure of 78–83% and rate of complete straightening of 93%(14,15). There are some advantages of this procedure. Once, the repair heals by primary intention. Moreover, there is no excision needed with a higher chance of erectile tissue damage and there is less need for mobilization of the neurovascular bundle with less likelihood of injury compared to the Nesbit procedure. Lastly, girth of the

erectile bodies is enlarged in the most dysplastic part of the penis. However, a common slight deformity of the surface of the erect penis, on which a type of small paired ballooning emerges at each side of any suture after this procedure. In addition, the repair does require an incision in the tunica, thus theoretically putting erectile tissue at risk. Based on incisional corporoplasty principles, Colpi et al. described a modification that, instead of the couple of dorsal incisions made paralel to the neurovascular bundle, a midline longitudinal incision is made in the bed of the deep dorsal vein (DDV) and the incision is closed horizontally(17). The disadvantage of this technique is need to resect the DDV and the circumflex branches at the area of the convexity to perform the incision.

b) In 1994, Baskin and Duckett modified the Nesbit procedure and avoided elliptical excisions in favor of plicating the transversally incised TA, fixing the outer edges with permanent sutures, and dunking the intervening tissue(18). They recommended that dorsal plications of the TA on each side of the penis at the 2-o'clock and 10- o'clock positions be taken at the point of maximal bend and Buck's fascia with the neurovascular bundles be elevated on each side. Since then, this plication technique has been prevalent for the correction of penile curvature. In 2000, however, after histologic observations showed that only the 12-o'clock position was nerve free which also appears to be the area of greatest TA thickness and strength, they recommended that penile plication be conducted at the 12-o'clock position without incision of the TA. Baskin et al. made no attempt to mobilize the dorsal veins or incise the TA, but put the stitches in and tied them. In spite of that, Hayashi et al. cut Buck's fascia longitudinally at the 12-o'clock position, made paralel incisions transversally on the TA after dividing the dorsal veins bilaterally, and approximated the outer edges of the incisions to achieve a firm tuck on the TA(19).

3- Plicational Corporoplasty: In 1973, Horton and Devine introduced the corporeal plication technique to treat penile curvature(20). In 1985 Ebbehoj and Metz introduced the technique of simple albuginea plication(21). According to this technique, the convex part of the TA is shortened either by simple plicating sutures(22) or by double cross-over stitching(21), applying non-absorbable stitches grasping deep into the tunica. Plication surgery has been reported to have high success rates, generally between 80% and 95%, compared with the Nesbit technique(23). After recognizing that the middorsal part of TA is the thickest and most resistant portion, Gholami and Lue further simplified the procedure by incising the Buck's fascia at the 12 o'clock position and placing multipl parallel plication sutures on each side of dorsal vein after identifying the dorsal arteries with a high patient satisfaction rate (16-dot plication method)(24). By doing this, all of these sutures are tied with minimal tension, thus preventing subsequent problems of suture breakage or cut. Ju-Ton Hsieh et al described a modified corporeal plication technique, two, interrupted, U-shaped sutures with 2-zero polyglactin were applied to create bumps on the TA(25). Mantovani et al modified Ebbehoj-Metz technique by a "straightening-reinforcing" double stitch: the first performs the plication, the second tightens it, thus preventing tension during erection(26).

Plication of the TA is the least invasive technique for correction of CPC, and it is often performed using only local anesthetic. Bleeding, hematoma, penile numbness, erectile dysfunction, and over or under correction occurs less frequently than excisional corporoplasty. Disadvantages of this approach are that the sutures can cut through the TA during firm erections before complete healing occurs, and that palpable knots are left permanently beneath the penile skin. However, the knots can be buried between the folds of the plication by using an inverted suture technique. Leonardo et al. introduce the superficial scalpel incisions of the albuginea surface and positioning of a double ''X'' introflecting stitch with the knot hidden in the plication and, for this reason, less perceivable to touch(27). Traditionally, nonabsorbable sutures have been used for corporeal plication, and are thought to cause certain complications. Van der Horst et al. reported that polytetrafluoroethylene sutures result in significantly less patient complaints of discomfort than polypropylene sutures (13% vs 52%) when a similar plication technique is used(28). Basiri et al. compared for the first time the results of corporeal plication using absorbable versus nonabsorbable suture for treating CPC and reported that corporeal plication technique using absorbable suture provides reasonable success rate with less frequent palpable suture knots(29).

All these techniques above mentioned have been criticized for their shortening of the penis. Penile shorthening is caused by segmental resection or plication of the tunica albugenies and a decrease of 1-2mm per 10^0 angulation is to be expected. Therefore, neither Nesbit's corporoplasty nor its modifications causes significant penile shortening. Indeed, penile reconstructive surgery for CPC is associated with significant improvements in overall relationship, sexual relationship, confidence, libido, and satisfaction and improvements in two of the four domains of the IIEF(30). The long-term results of this technique in childhood were poorly reported previously(15). Some urologists raised concerns that dorsal plication in childhood may result in penile shortening and subsequent erectile dysfunction in adulthood. Chertin et al claimed that the technique has no negative implications later in adulthood (31).There are no data are available to suggest which technique is preferable for patients with congenital or acquired curvature. Only Poulsen and Kirkeby reported a larger study assessing the plication and excision techniques in patients with congenital and acquired curvature(30). In the former they reported a success rate of 80% for the Nesbit and 22% for the plication technique.

In conclusion, correcting penile curvature using plication of the TA is the treatment of choice in patients with CPC. The technique has low morbidity and offers excellent functional and cosmetic results.

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SURGICAL TREATMENT OF PENILE FRACTURE

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Introduction

Penile fracture is a rare, but underreported, crucial urological emergency. Fractures of the penis generally occur during an erection as an outcome of direct blunt trauma that bends the erect organ in an unphysiological manner. The first report of penile fracture is credited to Abul Kasem more than 1,000 years ago (1). The largest single series to date was reported by Zargooshy who described 172 cases in a single province of Iran (2). Penile fracture occurs mainly in the young adults, and it is a true urological emergency that may have physical, functional, and psychological consequences. So, penile fracture can be immediately diagnosed and appropriately managed (3).

Etiology and Pathophysiology

Under physiological states, intracorporeal pressure increases up to 180 mmHg during intercourse. Rupture of the tunica albuginea, and subsequently of the corpus cavernosum at erection occurs when the intracavernosal pressure exceeds 1,500 mmHg. Rupture of the tunica albuginea occurs due to the marked thinning from a resting thickness of 2 mm down to 0.25-0.5 mm. on erection together with the associated marked short-term pressure increases, which approach or exceed the tunical tensile strength during acute abrupt loading or bending of the penis (4).

Causes of penile fracture were reported in different articles at varying ratios as traumatic coitus, violent penile manipulation, masturbation, or rolling over in bed onto an erect penis. In our series, the most common causes of fracture were straightening or bending penis by hand and sexual intercourse (5). Nevertheless, other rare and strange causes such as turning in or falling from the bed, slamming in a door, impaling penis into a mattress, placing an erect penis into tight pants, striking a toilet seat, hitting a bedpost, falling from a tree, masturbating into cocktail shaker and the horse kick were also reported in the literature. However, patients generally fail to provide the true reason for its occurrence (1-5). We think that causes of penile fracture can vary among various cultures.

Rupture of the tunica albuginea is usually unilateral, occurring proximally near the base of the penis and located ventrally in coital injuries. The right side is more often affected than the left with an incidence as high as 75%. An explanation to this predilection cannot be made; however, most of patients who were right-handed manipulated the penis to the left side. Bilateral corporal ruptures were reported in 4-10% of cases. Concomitant injury of corpus spongiosum and urethra ranges from 0% to 40% (3) In our series, there were not seen any urethral and/or spongiosal injury. The presence of ventral tunical tear and bilateral corporal rupture poses increased risk of urethral injury.

Diagnosis

At the time of injury, the patient and his partner typically notice a cracking sound and penile pain, associated with a sudden loss of erection. Even though an optimal diagnostic method has not yet been established, penile fracture is diagnosed on the basis of clinical criteria. The pain may vary from mild to severe. Purple ecchymosis, acute swelling, and penile deformity follow giving rise to so-called “eggplant” or “aubergine” sign. Penile deviation is generally seen opposite the tear (Fig 1a,b). When Buck’s fascia is violated, the hematoma extravasates around Colles’ fascia producing the “butterfly” pattern of ecchymosis in the perineum, scrotum and lower abdominal wall. The presence of blood-stained urethral meatus or gross hematuria or inability to urinate should alert for the possibility of concomitant urethral injury. Although hematuria, blood in the meatus, and voiding symptoms often signal a urethral injury, the absence of these features does not exclude the possibility of a urethral injury (3). The only recommended imaging modality, retrograde urethrography, should be used selectively to diagnose concomitant urethral tears that may occur in association with penile

fracture. The false-negative ratios for urethrography are 15%. Careful urethroscopy prior to exploration can be made to assessement of possible urethral injury (3,5).

Cavernosography has long been preferred method, showing mainly an indirect defect due to the hematoma. Its use, however, remains controversial because it has risks of false-negative results, priapism and infection. In my opinion, cavernosography is not indicated in the diagnosis of penile fracture, and it can only be used intraoperatively to detect exact location of tunical tear.

Penile ultrasonography (US) or magnetic resonance imaging (MRI) can be obtained but often adds little to the diagnosis and causes delay in surgical exploration. Some authors suggested that US advantages are that it is easily performed, noninvasive, and useful in determining localized sub-Buck's fascia hematoma and presence of hematoma or due to its disruption with presence of tear or due to causes other than tunical tear as ruptured superficial or deep dorsal vein. Penile MRI, unfortunately, is limited by its high cost, time consuming and limited availability (Fig 2). However, our series demonstrated that diagnosis based on history and physical examination can be sufficient, and no additional diagnostic tests were required. Bar-Yosef et al. reported that in 9 of 17 procedures, the tunica albuginea was intact and the only pathological finding was a ruptured dorsal vein, and they suggested that dorsal vein tears may mimic penile fracture (6). In our series, dorsal vein tears were seen in only 4/42 cases and tunical rupture accompanied in all of them (5). Therefore, we suggest that all patients with suspected penile fracture should undergo surgical repair. Only the patients suffered necrosis of penile skin caused by penile violation without rupture of tunica albuginea can not be explored, they can be managed conservatively (Fig 3a,b).

Treatment

Treatment of penile fracture comprises 3 different methods:
-Traditional conservative measures
-Immediate surgical repair
-Delayed surgical repair

Conservative Measures

Although conservative treatment has long been used in the past, in the present time, this method is not preferred by most of surgeon. Currently,however, some patients are declined the surgical repair caused by their fear of surgery. Therefore, conservative treatment can be a choice for these patients. The literature about conservative treatment for penile fracture is poor. In our series, only 5 of 42 patients (11.9%) were denied surgical treatment, and they received conservative measures. Conservative measures consist of Foley catheterization, pressure dressing, cold compress, anti-inflammatory drugs, antibiotics, anti-androgens and sedative drugs. Because this method has many drawbacks such as long hospital stay (average: 14 days), increased complication ratios (i.e. expanded hematoma, infected hematoma, abscess formation, arterial-venous fistulas severe penile deviation, painful erection, penile nodule, and erectile dysfunction), this approach has fallen into disfavor. In long follow-up period, almost all patients (80 %) received conservative treatment are suffered at least one complication mentioned above (3,5,6).

Immediate Surgical Repair

Currently, immediate surgical repair is the standard of care with fewer complications, shorter hospital stays, better outcome, and increased patients satisfaction.

The principles of immediate surgical repair are as follows:
-Prophylatic antibiotics
-Urethral catheterization
-Exposure
-Evacuation of hematoma
-Identification of fracture locations and concomitant urethral, spongiosal or venous injury (Fig 4)

-Ligation of bleeding vessels
-Minimal debridement of the wound
-Suturing of tears in the tunica albuginea
-Urethral repair, if required
-Artificial erection to exclude penile curvature and possibly other rupture sites
-Correction of penile curvature, if present
-Minimally pressure dressing of the penis

The Foley catheter aids orientation of the penis during surgery. The type and location of the incision is operator dependent. The proposed incision types are circumcising degloving incision, midline, penoscrotal, inguinoscrotal, and lateral incision. Most surgeons prefers the circumcising degloving incision, because it has some advantages; it allows an evaluation of all three corporal bodies and ability to repair injuries anywhere, as well as repair of urethra and correction of penile curvature if present, it also has good cosmetic results. Penoscrotal incision might be preferred if tissue edema and hematoma do not allow a degloving incision or if the main hematoma is in the penoscrotal area and the suspected site of injury is deeper. In my personal experience degloving incision is the best one.

There are some controversies about suture material to closure of the tunica. In a recent published article, El Housseiny at al reported that long-term outcome of immediate surgical intervention was excellent; the authors had used absorbable suture material (polydioxanone or or polyglycolic acid) in 142 cases and nonabsorbable suture material in 13 cases, and followed-up the patients for a mean 107 months, and they suggested that interrupted absorbable sutures were favored for repair of tunica as nonabsorbable sutures show high icidence of increased scarring (5,7,8). In my opinion, closure of the tunica laseration is best performed with running or interrupted ***absorbable*** sutures.

After tunical repair is completed, then, an artificial erection should be made to exclude penile curvature and possibly other rupture sites (Figure 5a,b). If penile curvature was present, it can be corrected in the same operation.

Repair of the urethral rupture can be performed using 3/0 or 4/0 absorbable interrupted sutures. A siliconized urethral catheter can be left for 1-2 weeks in cases of urethral rupture. In patients without concomitant urethral rupture, urethral catheter can be removed the day after operation, and the patients can be discharged from hospital in 1-2 days. All patients should be instructed to abstain from sexual activity during the first 6 weeks (8).

Delayed Surgical Repair

Some patients may delay seeking immediate medical care because of social and personal scenarios surrounding the occurrence of these events. In such patients, diffuse penile edema and friable tissues may make more difficult degloving technique and increases risk of operative complication. Therefore in such patients, surgical repair should be delayed (7-14 days) and conservative measures should be done until inflamed and edematous tissues subsided. After conservative treatment, direct incision on the rupture site can be choised and delayed repair of the tunica can be made with principles of immediate repair. Nasser and Mostafa described 24 patients with delayed presentation of penile fracture who were managed with conservative treatment for 7-12 days, and then underwent a direct surgical repair under local anesthesia. No intra-operative or pos-toperative complications were encountered and all patients regained their sexual activity 4-6 weeks after the repair (96).

Conclusions

We suggest that diagnosis of penile fracture can be based on history and physical examination; diagnostic tests such as US and MRI are generally not required. Fractures must be repaired either immediately or delayed. Because management with emergency surgical repair is the most effective approach, with the

lowest complication rate, surgical treatment should be preferred to a conservative approach.

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Figure 1 a,b. Gross appearence of two different penile fracture

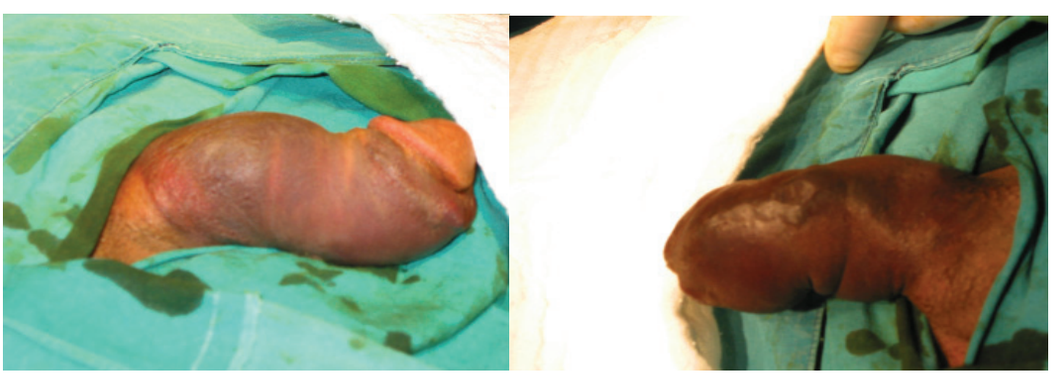


Figure 2. MRI showing left ventral tunical tear and haematoma

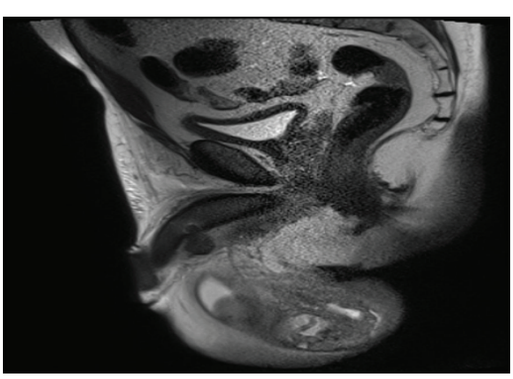


Figure 3 a,b. Penile skin necrosis caused by penile violation mimicking penile fracture

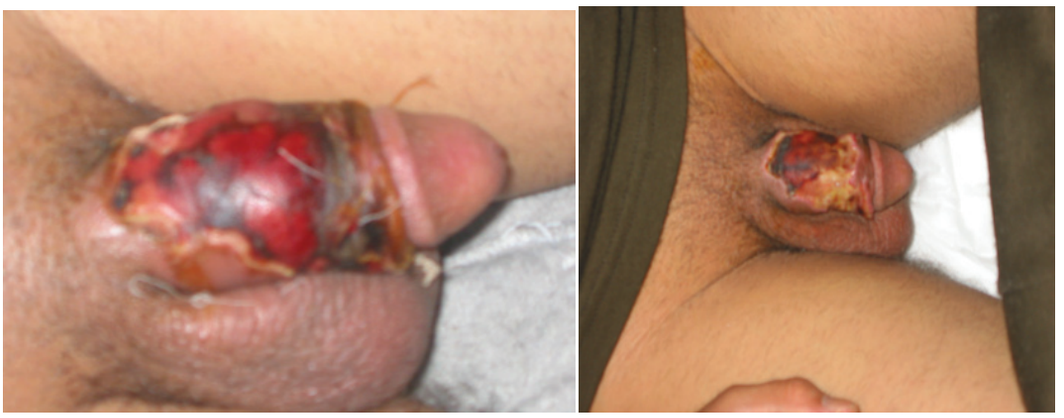


Figure 4. Intraoperative view of tunical tear.

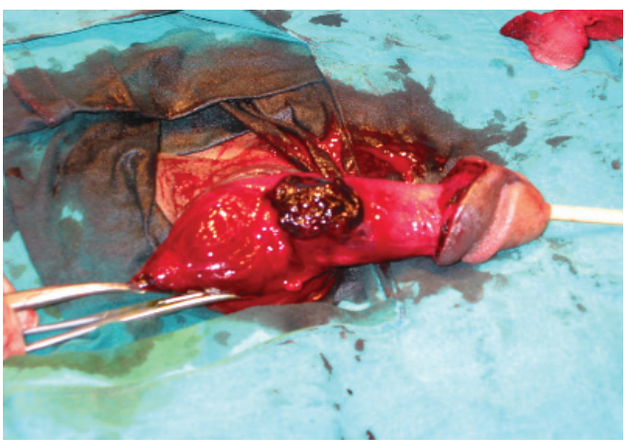
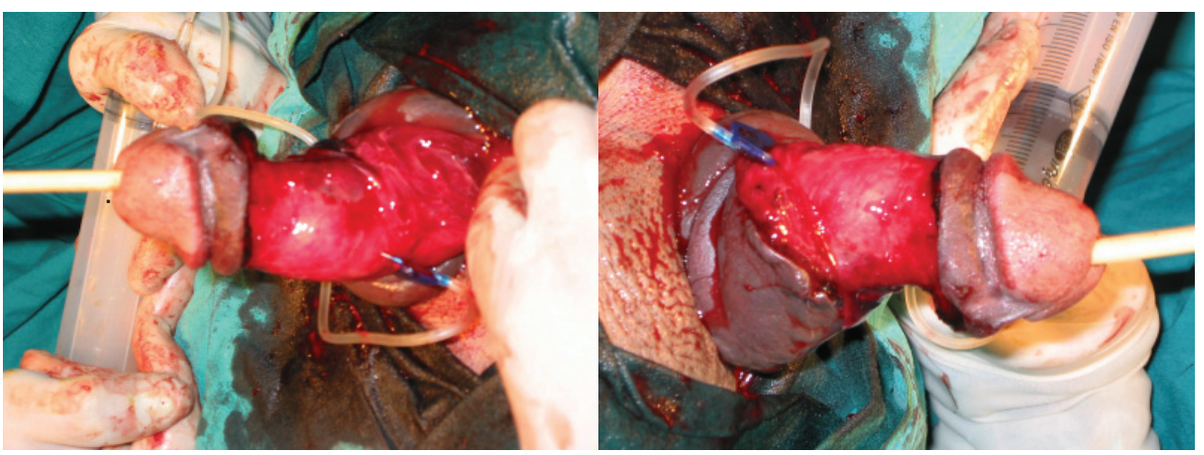


Figure 5 a,b. Artificial erection after tunical repair. Slight ventral deviation of the penis is seen.



UPDATE ON THE SURGICAL TREATMENT OF MALE INFERTILITY (MICRO-TESE, VASO-VASAL AND VASO-EPIDIDYMAL ANASTOMOSIS)

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Male factor is the sole reason or a component for infertility in 20% and 30% of cases respectively. The management of the disease may be via medical or surgical treatment. The surgical approach is classified as techniques which improves sperm production and delivery in order to achieve spontaneous pregnancy or sperm retrieval techniques prior to ART (Assisted Reproductive Techniques).

Varicocelectomy is the most common surgery performed for the sperm production improvement. After the surgery the prominent improvements are observed in motility and morphology with a higher chance of success in men with >10 million sperm/ml. Testosterone increase, approximately 100 ng/dl, is also reported for patients with a baseline testosterone below 400 ng/dl. The spontaneous pregnancy odds ratio after varicoselectomy was reported as 2.63 in patients with palpable varicocele and abnormal semen parameters(1-3).

Surgery to allow sperm delivery are applied to patients with proximal and distal seminal duct pathologies. The obstructed passageway may be caused by a congenital or acquired anomaly or iatrogenic but the existence of sperm in ejaculate to allow spontaneous pregnancy is the main objective of this surgery. Microscopic vasavasostomy and epididymovasostomy are the elementary surgeries of this subject but technological developments such as robotics may be applied as developed. Microscopic vasovasostomy was reported to have patency and pregnancy rates of 92% and 53% with an interval of 3 years. For vasoepididymostomy patency and pregnancy rates of 48-63% and 21-45% had been reported with a mean interval of 16 months. Usage of robotic assisted VE has been suggested for increased precision and decreased operation times. TUR-ED is the endoscopic technique which is performed in distal duct pathologies. Sperm parameter improvement had been reported up to 94% in men with distal duct obstructions(4).

Sperm retrieval techniques are treatment modalities used to gather sperm from the testis and epididymis of azospermic infertile males prior to ART. These techniques are applied to obstructive azoospermic (OA) and non-obstructive azoospermic (NOA) males.

General Sperm Retrieval Techniques Are Listed As:

1. Percutanoues Epididymal Sperm Aspiration (PESA)
2. Microscopic Epididymal Sperm Aspiration (MESA)
3. Testicular Sperm Aspiration (TESA)
4. Conventional Testicular Sperm Extraction (TESE)
5. Micro-surgical Testicular Sperm Extraction(m-TESE)

PESA: Despite its minimal invasive, easy and prompt nature, inadequate material aspirates and greater risk of hematoma complication had made this technique obsolete.
MESA: This technique is used for obstructive azospermia not suited for reconstructive surgery. Number of gathered sperm is which is sufficient for both ART and cryopreservation. The SRR and pregnancy rates are 90% and 14-66% respectively. The ART success rates of epididymal sperms are similar to testicular ones.
TESA: It become reserved for obstructive azoospermia subsequent to the introduction of TESE. The general SRR for OA and NOA patients are 100% and 27% respectively. Although adequate number of sperms are gathered for ART, cryopreservation may not be possible all the time. This technique is not preferred anymore because of possible vascular injury and insufficient sperm numbers.
TESE: The SRR of this technique is 36% via multiple biopsies and drops to 23% for single biopsy. Conventional TESE is replaced by mTESE in routine practice because of low SR rates.

mTESE: Requirement of micro surgical skills, greater learning curve and longer operation time is balanced by much higher SRR for this technique. In addition preservation of testicular tissue and vascular structure are further advantages. The SRR is correlated with seminefer tubule diameters with a threshold value of 110 microns. This rate was demonstrated to be 84% and 36% for >300 micron and <300 micron diameters of seminifer tubule respectively. Up to 60% sperm retrieval rate was reported for mTESE which is superior to its conventional counterpart. The predictive factors for SRR are accepted as experience of the surgeon, duration of the operation and histopathology of testis(5-7).

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PS-01

ASSOCIATION BETWEEN THE ANDROGEN LEVELS AND ERECTILE FUNCTION, COGNITIVE FUNCTIONS AND HYPOGONADISM SYMPTOMS IN AGING MALES.

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PURPOSE: Aging in men is characterized by a moderate decrease in plasma testosterone (T) levels. However, the association between partial androgen deficiency of the aging male and clinical symptoms and the ideal screening test are controversial. In this study, we investigated the association between the androgen levels and erectile function, cognitive functions and hypogonadism symptoms in aging males.

MATERIALS-METHODS: We investigated the association between total (TT), calculated free (FT) and bioavailable (BT) testosterone, and various clinical and laboratory parameters in 103 healthy males, 50-80 years old. Biochemical assessment was done after overnight fasting. Questionnaires were used to test for hypogonadism symptoms, erectile and cognitive functions.

RESULTS: TT levels were not correlated with aging in this study. However, FT and BT were found to decrease with age due to rising sex hormone binding globulin. TT levels were strongly correlated with FT and BT levels (respectively $p = 0.0001$, $p = 0.0001$). TT, FT and BT were only correlated with cognitive functions ($p = 0.012$, $p = 0.004$, $p = 0.02$ respectively). There was no correlation between TT, FT and BT levels and erectile function and hypogonadism symptoms.

CONCLUSION: T values in our study sample did not correlate with clinical signs and symptoms of hypogonadism. Thus, according to our data, symptoms in the aging male should not be indiscriminately assigned to a decrease in TT, FT or BT levels.

Keywords: erectile function, cognitive functions, hypogonadism symptoms, aging males, testesteron

PS-02

COMPARISON OF SATISFACTION RATES IN PATIENTS TREATED WITH MALLEABLE AND 2-PIECE INFLATABLE PENILE PROSTHESIS IMPLANTATION

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INTRODUCTION: Penile prosthesis implantation is the treatment option for erectile dysfunction in patients who have failed to other conservative treatment options. The available type of penile prosthesis includes malleable and two piece or three piece inflatable. High satisfaction rates are reported with different types of penile prosthesis. In this study we aimed to compare the satisfaction rates among the patient including their spouses' satisfaction rates who undergone malleable or two piece inflatable penile prosthesis.

METHODS: Patients who underwent AMS (600/650) malleable or AMS ambicore two piece inflatable penile prosthesis placement between 1/1/2008 and 1/1/2013 were invited to complete modified Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS) questionnaire at six months. Patients were excluded if they were not Turkish speaking or deceased or their prosthesis were explanted within 6 month following the surgery. Demographic data and complications were recorded.

RESULTS: A total of 63 patients had penile prosthesis implantation during the study period. 17 patients who do not fit the inclusion criteria were excluded from the study. Out of patients a total of 46 patients responded to the EDITS questionnaire. The mean age of the patients was 56,7±12,9 and 58,6±9,5 in group 1 and 2 respectively (p: 0.52). In group 1 indications for penile prosthesis implantation were due to arterial insufficiency in 17, radical prostatectomy in 3 and priapsim in 3. In group 2 the indications were due to arterial insufficiency in 18 previous pelvic surgery in 4, and chronic renal failure (the patient with renal transplant) in 1 patient. While mean operation time for the first group was 74,2±25,6 min., it was 80,0±25,6 min. for the second group.(p:0,001). Table 1 represents the answers to modified EDITS questionnaires across the groups.

CONCLUSION: Two piece inflatable penile prosthesis was found to be more successful for overall satisfaction and it was found to be more appropriate for continue use when compared to malleable penile prosthesis.

Keywords: Penile Prosthesis; Patient Satisfaction; Erectile Dysfunction

PS-02

The answers to modified EDITS questionnaires across the groups.

Questions	Answers	Group 1 (%)	Group 2 (%)	p
Overall, how satisfied are you with your penile prosthesis?	Very satisfied	34,78	73,91	0,013
	Neither satisfied nor dissatisfied	30,43	13,04	
	Very dissatisfied	34,78	13,04	
During the past four weeks, to what degree has the treatment you received for you erectile dysfunction met your expectations?	Completely	30,43	52,17	0,061
	Half way	34,78	34,78	
	Not at al	34,78	13,04	
How likely are you to continue using your penile prosthesis?	Very likely	30,43	65,21	0,018
	Neither likely nor unlikely	34,78	21,73	
	Very unlikely	34,78	13,04	
During the past four weeks how easy was it for you to use this treatment?	Very easy	39,13	69,56	0,056
	Neither easy nor diffucult	26,08	13,04	
	Very diffucult	34,78	17,39	
How confident has your penile prosthesis made you feel about your ability to engage in sexual activity?	Very confident	47,82	78,26	0,106
	It has had no impact	26,08	4,34	
	Very much less confident	26,08	17,39	
Overall, how satisfied do you believe your partner is with the effects of this treatment for your erectile dysfunction?	Very satisfied	39,13	47,82	0,182
	Neither satisfied nor dissatisfied	26,08	39,13	
	Very dissatisfied	34,78	13,04	

PS-03

ASSESSMENT OF ANTIMICROBIAL ACTIVITY AND THE PRESENCE OF BIOFILM ON SILICON SURFACES COATED WITH MINOCYCLINE-RIFAMPIN, SILVER NITRATE AND NITROFURANTOIN FOR SHORT TERM URINARY CATHETERIZATIONS OF AN IN VITRO URINARY SYSTEM MODEL

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INTRODUCTION AND OBJECTIVES: Catheter associated urinary infections, which are a common problem, still await a solution. Antimicrobial activities and biofilm formation of different microorganisms was assessed in an in vitro urinary setting.

METHODS: Silicon surfaces were exposed to infected urine for 72 hours in an in vitro urinary setting designed by us and discharged without leaving any residue, for Escherichia coli, Enterococcus spp, Pseudomonas aeruginosa, Klebsiella spp, Enterobacter spp, Proteus mirabilis. The antimicrobial activities of the silicones covered with pure silicone (PS) in the control group and minocycline-rifampin (MR), silver nitrate (SN) and nitrofurantoin (NF) were investigated in blood agar and eosin-methylene blue media. Biofilm formations were analyzed via confocal microscopy.

RESULTS: Biofilm formation occurred in the whole PS control group and reproduction was observed in the cultures. An inhibition zone of >=15mm was observed in a total of 34 cultures in silicones coated with silver nitrate (SN), nitrofurantoin (NF), minocycline-rifampin (MR). The antimicrobial activity was not regarded as significant in catheters coated with MR for Escherichia coli and Proteus mirabilis ($p>0.05$). The antimicrobial activity in all three antibiotic coated silicones was observed to be high and close to each other for Proteus mirabilis and Enterococcus faecalis. The antimicrobial activity in silver coated silicones was observed to be more significant compared to the others ($p<0.001$). Although silicone discs were exposed to infected urines for a short period in our study, it was observed that the slime layer still constituted a problem.

CONCLUSION: Although the antimicrobial activity was observed to be better in SN coated silicones for short-term catheterization in an in vitro urinary system, it was also observed that the activity was as good as in SN with MR and was even better than NF. Due to the cost of silver nitrate, MR coated silicones may be preferred in short-term urinary catheterization.

Keywords: minocycline-rifampin, silver nitrate,nitrofurantoin,urinary catheterizations, sılıcon surface

PS-04

ASSESSMENT OF SEXUAL FUNCTIONS IN MEN DIAGNOSED WITH OVERACTIVE BLADDER

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OBJECTIVE: Overactive bladder (OAB) may lead to severe deterioration in quality of life and psychology in both genders. A psychological assessment was planned on the sexual functions of male patients with OAB.

METHOD: Anamnesis, physical examination, OAB examination, urination log, urinalysis, urine culture, urea, creatinine, abdominal ultrasonography, post void residual (PVR) testing, uroflowmetry, cystometry, International Index of Erectile Function (IIEF), SCL-90R psychological examinations were conducted on 31 male patients diagnosed with clinical and urodynamic overactive bladder between 2009-2014.

FINDINGS: Complaints of urgency, urgency incontinence and nocturia were more prominent in patients with a mean age of 38±7 years. No pathology was observed in the physical examination and biochemical and microbiological assessments. OAB scores were 27±5, nocturia was 4±3, fluid intake level was 1.437±312 ml/day, while urinary incontinence was 2±1/day for 11 patients. Premature ejaculation occurred in 14 patients. In the IIEF assessment, 13 patients (42%) had 14±4, 12 patients had (39%) 18±3 and 6 patients (19) had 20±4. Reduction in satisfaction and libido stood out in the assessment. They stated that feeling of guilt and worthlessness, nervousness and reduction in sexual interest and desire were prominent at SCL-90R, especially upon the detection of OAB. Pursuant to the administration of an anti-muscarinic therapy to all patients for 3 months, the OAB score was calculated as 13±3, while the mean IIEF was calculated as 23±4. Increase in energy and shyness and discomfort towards the opposite sex were observed to be prominent compared to the period prior to the recovery in SCL-90i.

CONCLUSION: Sexual dysfunctions and psychological findings of various degrees may be seen in the assessment of male patients diagnosed with overactive bladder. An improvement may be observed in the OAB score, IIEF and SCL-90R after the anti-muscarinic treatment.

Keywords: overactive bladder, IIEF

PS-05

IS RETROGRADE EJACULATION ASSOCIATED WITH OVERACTIVE BLADDER?

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OBJECTIVE: Investigation of the presence of overactive bladder (OAB) in patients complaining of retrograde ejaculation

METHOD: Anamnesis, International Index of Erectile Function (IIEF), overactive bladder questionnaire (OAB-q), urination log, physical examination, urinalysis, urine culture, urea, creatinine, fasting blood glucose (FBG), PSA, uroflowmetry, cystometry and abdominal ultrasound were performed between 2011-2013 in 21 patients complaining of retrograde ejaculation.

FINDINGS: Twenty-one male patients at a mean age of 39±6 years who expressed that they had no ejaculation since 4±2 years were enrolled in the study. They had 5±2 children on average. Sperm was detected in the urine after the ejaculation of patients. IIEF was calculated as 16±3. OAB-q result was as 21±3 in 9 patients. Nocturia (3±2) and urgency stood out in the urination log of these 9 patients. DM Type II was detected in the oral glucose intolerance test performed for threshold fasting blood glucose level in 3 patients. The blood and urine microbiology and biochemical values were normal. No pathologies were detected in the ultrasound. Qmax was 21±4 ml/sec in uroflow, Q average was 12±4 ml/sec. and post-urination and post-voiding residue was measured as 48±14 ml/sec. In the cystometric assessment it was observed that in 7 out of 9 patients with a high OAB-q result the bladder volumes were 320±47 ml, while hypersensitivity (first urge sensations 78±21 ml) and marked uninhibited contractions were observed in 5 of them. Pursuant to the administration of oral trospium chloride 30 mg 2x1/day to 9 patients with a high OAB-q, the OAB complaints of 4 patients improved, the ejaculation volume was 3.2±0.9 ml and sperm was observed in the ejaculation in the 3rd month.

CONCLUSION: Overactive bladder may be observed in the screening of patients complaining of retrograde ejaculation. Pursuant to the administration of an anticholinergic to these patients for OAB, improvement in OAB-q result and in retrograde ejaculation was observed in a limited number of patients.

Keywords: retrograde ejaculation, overactive bladder

PS-06

EVALUATION OF ERECTILE FUNCTION AFTER BUCCAL MUCOSA GRAFT URETHROPLASTY

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INTRODUCTION: The purpose of the study is to evaluate the effects of the buccal mucosa graft urethroplasty surgery on erectile funtion in patients who went through buccal mucosa graft urethroplasty because of urethral catheter or benign prostat hyperplasia and developed urethra stricture following the operation

MATERIALS-METHODS: The study included 15 patients who developed urethra stricture following iatrogenik transurethral resection (TUR) or urethral catheter insertion between 2011 and 2013. The questioning for erection was evaluated using international erectile function index (IIEF-5). All of the patients went through buccal mucosa graft urethroplasty surgery with Barbagli method. Changes were compared by questioning the erectile function with IIEF-5 before the surgery and 3 months after the surgery. The results were analyzed using student t-test.

FINDINGS: The mean age of the patients was 55.4 (33-75). Of the patients, 8 had urethral catheter, 7 had darlık development after the surgery. Urethrotomy interna was in the history of 12 patients. One patient had diabetes mellitus and hypertension, and 3 patient had hypertension. In the preoperative period, while erection was normal in 7 patients, it was mild in 4 patients, and there was mild-moderate erectil dysfunction (ED) in 4 patients. In the postoperative period, mild ED in 6 patients, and mild-moderate ED in 6 patients were determined. Erectil function was normal in 3 patients (Table 1). In the preoperative and postoperative IIEF-5 scores of the patients, there was difference in the mild, mild-moderate and total symptom scores, but no statistically significant difference was observed probably because of the small number of subjects.

CONCLUSION: Buccal mucosa graft urethroplasty may cause erectile dysfunction of the patients. Our study needs to be supported by wider case series.

Keywords: Urethral stricture, erectile function

Comparison of pre- and post-operative IIEF-5.

Erectile Disfunction	Preoperative (n	IIEF-5	Postoperative (n	IIEF-5	p
No Erectile Disfunction	7	23,3	3	22	p>0,5
Mild	4	19,5	6	19	p>0,5
Mild-Moderate	4	16	6	14,3	p>0,5*
Total	15	20,1	15	17,4	p>0,5*

**: In the preoperative and postoperative IIEF-5 scores of the patients, there was difference in the slight, mild and total symptom scores, but no statistically significant difference was observed probably because of the small number of subjects.*

PS-07

THE IMPACT OF SEXUAL ACTIVITY ON SERUM HORMONE LEVELS AFTER PENILE PROSTHESIS IMPLANTATION

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OBJECTIVES: Penile prosthesis implantation is the final treatment option for patients who have erectile dysfunction. Most of the patients use their penile prosthesis successfully and frequently for penile-vaginal intercourse. Previous literature showed that decrease in sexual activity resulted in decreased serum testosterone levels and vice versa. The aim of this study was to examine the impact of sexual activity on serum sex hormone levels after penile prosthesis usage.

MATERIALS-METHODS: In this study, we examined sixty-seven patients for their sex hormone changes who had penile prosthesis surgery 2.7±1.5 years ago.

RESULTS: Patients were using their penile prosthesis for sexual activity with a mean of 9.9±5.7 times per month. Dehydroepiandrosterone sulfate was significantly higher compared to pre-surgery results (5.3±2.6 vs 4.5±2.9; p=0.031). Mean serum total testosterone levels of patients before and after penile prosthesis usage were 15.78±4.8 nmol/L and 16.5±6.1 nmol/L, respectively. Mean serum luteinizing hormone levels of patients before and after penile prosthesis usage were 3.98±2.16 IU/L and 5.47±4.76 IU/L, respectively. No statistical significance difference was observed in the mean total and free testosterone, estradiol and luteinizing hormone levels between pre- and post-surgery.

CONCLUSIONS: It was demonstrated that sexual activity changed sex hormone levels positively among those men who were implanted penile prosthesis because of erectile dysfunction.

Keywords: androgens, erectile dysfunction, hypogonadism, luteinizing hormone, testosterone

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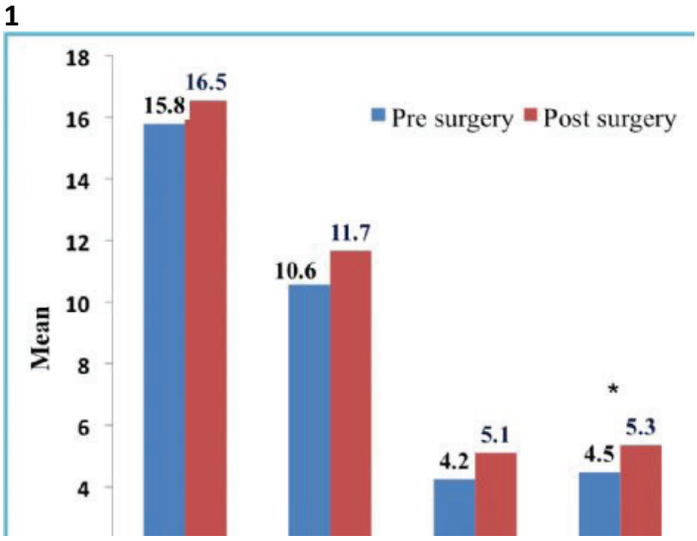

*Serum values of total testosterone, Luteinizing Hormone (LH), Estradiol and Dehydroepiandrosterone sulphate (DHEAS) levels. Values are expressed as means of 67 patients before and after usage of penile prosthesis. *p<0.05.*

Acknowledgement: The Medical Research Center of Hamad Medical Corporation financially supported this project.

PS-08

FEMALE SEXUAL FUNCTION INDEX LEVELS OF THE WIVES OF MEN WHO RECEIVED DAPOXETINE TREATMENT FOR PREMATURE EJACULATION

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PURPOSE: The aim of this preliminary study was to evaluate female sexual function index (fsfi) levels of the wives of men who were received dapoxetine for the treatment of premature ejaculation.

METHODS: Forty men suffering premature ejaculaton treated with dapoxetine 30 mg/day and their wives taken into study for three months. Men those were received dapoxetine before and after treatment compared with regard to intravaginal ejaculatory latency time (IELT), premature ejaculation profile item(PEP) and clinical global impression change(CGC). The wives of men also compared with regard to fsfi levels before and after treatment by using Wilcoxon Signed Rank Test. P-value of < 0,05 was taken as significant.

RESULTS: A total of 40 men and their wives included in this study. The median age of the patients 46,3(range25-67) years for men and 41,85(range 22-66) years for women. Median body mass index was 28,11(range 23,9-33,7)kg/m2 for men and 28,17(range 20,6-34,9) kg/m2 for women. Forty men received dapoxetine treatment. The mean IELT before and after the treatment was 1,3±0,4 min and 5,9±1,4 min respectively. The mean FSFI score before and after the treatment was 18,1±1,7 and 24,2±1,6 respectively and pain score was 4,6±0,9 and 4,6±0,5 respectively. A significant prolongation in the IELT and improvement in the FSFI score was observed (p<0,001). Pain score was not different before and after the treatment. No side effect was reported regarding dapoxetine treatment.

CONCLUSION: Dapoxetine treatment in men suffering premature ejaculation not only improve IELT scores but also improve FSFI scores of their wives. Large prospective randomized studies essential to promote these results.

Keywords: Dapoxetine, premature ejaculation, intravaginal ejaculatory latency time, female sexual function index.

Table 1: Demographic characteristics of the patients.

	Male(40)	Female(40)
Age(years)	(25-67)(46,3±12,3)	(22-66)(41,85±12,59)
BMI(kg/m2)	(23,9-33,7)(28,11±2,3)	(20,6-34,9)(28,17±3,57)

Table 2: Outcomes of the men and their wives before and after dapoxetine treatment.

	Pretreatment	Posttreatment	P value
IELT(min.)(men)	(1-2)(1,3±0,4)	(3-10)(5,9±1,4)	P < 0,001
FSFI(women)	(15-20,4)(18,18±1,72)	(19-28)(24,25±1,68)	P < 0,001
Pain Score(women)	(3,6-6)(4,66±0,9)	(4-5,6)(4,64±0,54)	P=0,2

PS-09

PATHOPHYSIOLOGY OF VARICOCELES IN THE ASYMMETRIC DIMETHYL-ARGININE (ADMA) EFFECTS ON NITRIC OXIDE METABOLISM

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PURPOSE: NO has a very important role in maintaining endothelial function.ADMA, nitric oxide synthase (NOS) activity by inhibiting the formation of NO, is a major inhibitor.In this study, experimental varicocele on testicular tissue in rats asymmetric dimethyl arginine (ADMA) and nitric oxide (NO) breakdown products, nitrite-nitrate levels were measured and statistically analyzed their relations with each other.

MATERIALS AND METHODS: Research was performed with 21 Spraque-Dawley male rats.Rats were divided into 3 groups including the control group (6 rats), sham group (6 rats) and experimental group (9 rats) In the experimental group after ether anesthesia, with partial ligation of the proximal left renal vein, left varicocele was created.After 8 weeks, the rats were sacrificed.Testes dissected and stored at -80 °C after being excised. For detecting biochemical changes in the testis, levels of SOD (superoxide dismutase) enzyme activity, and the end product of NO metabolism nitrite and nitrate salts were determined.To examine plasma nitrite-nitrate levels, 5cc blood samples were taken through the For analysing ADMA, ADMA kit was used which is a competitive-type ELISA kit.

FINDINGS: Due to increased oxidative stress, which is the primary antioxidant enzymes in the (SOD) values and all three groups had been viewed pairwise comparison and the groups revealed a statistically significant difference (p = 0 0002).This has emerged in response to increased oxidative stress.ADMA levels in the varicocele experimental group compared to the sham and control groups were found to be significantly higher (p = 0.004)In the sham group compared with control group. ADMA levels have been found in high amounts Plasma and tissue salts which are the end product of NO in the experimental group and the sham group was significantly lower than the control group (p = 0.0003).Responsible for the decrease in value is thought to be NOS inhibition located in the environment.

RESULT: The increase in ADMA levels are directly associated with endothelial dysfunction has been shown in earlier studies.In our study in rats with experimental varicocele model was created and increased NO synthesis of ADMA levels might lead to infertility are corrupting. Further studies on this topic are needed

Keywords: varicocele, asymmetric dimethyl-arginine (ADMA), Nitric Oxıde

PS-10

PHOSPHODIESTERASE 5 (PDE5) INHIBITOR PREFERENCE OF TURKISH UROLOGISTS FOR THEIR OWN USE AND RECOMMENDS FOR THEIR PATIENTS

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PURPOSE: We evaluated the phosphodiesterase 5 (pde5) inhibitors in the treatment of men with erectile dysfunction (ED) or performance enhancing agent preference of urologists for own use and recommended for their patients.

MATERIALS-METHODS: An electronic questionnaire form prepared including 7 questions. We quastioned their age, institution, geographic region of Turkey, marital status and average daily number of examined patients. Other question was “If you have any reason to use the pde5 inhibitors which one you think is more effective”. And the last one was “What do you propose as the first choice pde5 inhibitors for patients”. This form’s link was posted by email to male urology specialist. Personal informations were not recorded. Statistical tests and McNemar-Bowker consistency analysis was evaluated with SPSS 15.

RESULTS: Total 308 urologists answered the form. The mean age was 41,3 years (24-64years). The average daily number of patients who were examined was 31,3 patients (2-150 patients). Distribution of physicians according to Turkish geographic regions are in this way: west 48,1%, middle 17,0%, south 13,4%, east 12,7% and north 8,8%. 19 urologists were single and 279 of them were married. The hospital urologists works: 42,5% of university hospital. 22,7% of private hospital, 19,2% of state hospital, 14% teaching-research hospital and 1,6% of others. Urologists that they use for themselves and proposed pde5 inhibitors for their patients are summarized in the table. According to the analysis of McNemar-Bowker consistency analysis (kappa value), urologists who use for themselves sildenafil or tadalafil they suggest this pde5 inhibitors to their patients (statistically significant). There is no statistically significant relationship between other parameters.

CONCLUSION: Tadalafil is the first choice of the Turkish Urologist as PDE5 inhibitor that they suggest to their patients and for their own use.

Keywords: Turkish Urologists, PDE5 Inhibitors, Preference, Tadalafil, Sildenafil

Table: Number of urologists according to preferred PDE5 inhibitors

	Recommended for patients		Urologists for own use	
	n	Percent (%)	n	Percent (%)
Sildenafil	82	26,9	84	29,5
Vardenafil	47	15,4	39	13,7
Tadalafil	155	50,8	149	52,3
Udenafil	21	6,9	13	4,5
TOTAL	305	100,0	285	100,0

PS-11

CORRELATIONS BETWEEN PREIMPLANTATION GENETIC TESTING (PGT) AND EMBRYOSCOPIC FOLLOW-UP OF EMBRYOS FORMED IN PATIENTS WITH HIGH DNA FRAGMENTATION RATE (SDFI) AT CRYOSPERMIA AFTER MICRODISSECTION TESTICULAR SPERM EXTRACTION (MICRO-TESE)

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INTRODUCTION AND OBJECTIVES: A comparison was made between the PGT and embryoscopic results of patients with an sDFI of >30 in sperms frozen and melted after micro-TESE.

METHODS: Anamnesis, physical examination, scrotal color Doppler, karyotype analysis, AzF deletion and TUNEL test were performed between April 2011-2014 in 112 embryoscopically monitored patients who were diagnosed with azoospermia and underwent micro-TESE. FSH, total testosterone and prolactin were measured. Microdissection testicular sperm extraction (micro-TESE) was performed in all patients under local anesthesia. PGT was performed in all embryos prior to the transfer and the same embryos were followed up with an embryoscope (Embryoscope Unisense Fertilitech©).

RESULTS: The mean age of 112 patients was 43± 6 years. All patients were pellet (-) azoospermic. The duration of their marriages was 13±7 years. Thirty-nine of these patients had undergone single-site/bilateral varicoselectomy and 31 patients had undergone micro-TESE previously. Their genetic and microbiological findings were normal. FSH was 19±6 IU/ml and total testosterone was 343±21 ng/ml. Besides for 3 patients who had an sDFI between 15-30, the other patients had an sDFI of <15 prior to cryospermia. The sDFI resulted to be above 30 in 24 patients in the TUNEL test performed on melted sperms after cryo. Pathological genetic findings such as trisomy, monosomy, nullisomy 13, 16, 18, 21, haploidy, lack of nucleus and complex aneuploidy were detected in the PGT of 139 out of 196 embryos obtained from 24 patients with an sDFI of >30. A marked delay in reaching the cell in the time-lapse 3, 4, 5 of patients with an sDFI of >30 (53 hours) and evident morphokinetic dysfunctions in the embryo were observed (Fig. II).

CONCLUSION: A correlation was observed between the pathological PGT findings in the embryos of patients with high sperm DNA fragmentation after cryospermia and morphokinetic delay in embryoscope.

Keywords: embryoscop,cryospermia, tese,SDFI

PS-12

OUR MICRO TESTICULAR SPERM EXTRACTION (M-TESE) APPLICATIONS IN FAILED EJACULATE SPERM IVF-ICSI SUBJECTS

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METHOD: Anamnesis, physical examination, FSH, LH, total testosterone levels, TUNEL test for DNA fragmentation and spermiograms were evaluated in 137 couples who underwent at least 2 spontaneous ejaculate sperm IVF-ICSI but had no pregnancy between 2009-2014.

RESULTS: The mean age of men was 41±5 while the mean age of women was 32±4. The duration of their marriages was 9±5 years. Thirty-six men had previously undergone varicocele surgery. Thirteen women were diagnosed with polycystic ovary. IVF-ICSI was applied 4±2 times on average, intrauterine insemination (IUI) was applied 3 times, pregnancy occurred 2±1 times on average in 47 patients, not resulting in live birth, however. Diagnostic hysteroscopy was previously applied on 61 women, while 33 women had undergone myomectomy. Micro surgery was performed on 31 patients after diagnosing varicolece in the physical examination. The FSH level of men was 14±4.3 IU/ml, LH was 11.5 ± IU/ml and testosterone was 322±26 ng/ml, while the FSH level in women was 6.9±3.7 IU/ml, their LH was 5.9±2.1 IU/ml. No pelvic pathology was observed under ultrasonography in women. The volume in spermiogram was 4.2± 2.2 ml, the sperm count was sperm 7.5±5.9 x 106/ml, motility was 23±10% and abnormal morphology was 76±13%. The TUNEL test was measured between 15-30 in 8 patients, while it was >30 in 5 patients. The karyotype analysis of the patients was normal. Partial AZF b and c deletions were observed in 9 patients. Women. Micro-TESE was applied on all patients upon being provided information. No sperm as found in 16 patients. The DNA fragmentation rate of testicular sperms in the TUNEL tests was below <15. Pregnancy occurred after IVF-ICSI in 51 (42%) out of 121 patients in whom testicular sperm was found and 29 (23.9%) live births occurred. The pregnancy rate per IVF-ICSI with ejaculate sperm was 33 (24%) for all patients.

CONCLUSION: No DNA fragmentation was observed in the sperms obtained from the testicles of couples in whom IVF-ICSI failed with ejaculate sperm. It was also observed that the pregnancy rate increased and live birth occurred pursuant to the use of testicular sperm.

Keywords: sperm, TUNEL test, TESE

PS-13

COMPARISON OF SPERM DNA FRAGMENTATION RATES IN INFERTILITY ASSOCIATED WITH IDIOPATHIC OLIGOASTHENOTERATOSPERMIA, MORPHOKINETIC FOLLOW-UP OF EMBRYOS AND PREIMPLANTATION GENETIC DIAGNOSIS RESULTS: A PRELIMINARY REPORT

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INTRODUCTION AND OBJECTIVES: In this study, idiopathic oligoasthenoteratospermic males were selected within the patient group of a total 1.862 patients followed up embryoscopically.

METHODS: Anamnesis, physical examination, karyotype analysis, AzF deletion and TUNEL testing were performed between April 2011-2014 in 234 oligoasthenoteratospermic males whose spouses had a healthy menstrual cycle. Their FSH, total testosterone and prolactin were measured. Preimplantation genetic diagnosis (PGD) was performed on all embryos prior to the transfer and the same embryos were followed up with an embryoscope (Embryoscope Unisense Fertilitech©) (Fig. I)

RESULTS: The mean age was 41± 6 years. The mean age of the spouses was 29±4 years. The duration of their marriages was 12±5 years. Previously, 4±2 IVF-ICSI was performed on 143 patients. Single-site/bilateral varicoselectomy was performed on 102 patients and 36 patients underwent micro-TESE for testicular sperm due to failed IVF-ICSI. Their genetic and microbiological findings were normal. FSH was 12±6 IU/ml and total testosterone was 409±13 ng/ml. The sDFI in 12 patients was between 15-30, sDFI was >30 in 11 patients, while sDFI was <15 in other patients. A total of 1.634 embryos were obtained after ICSI. Pathologies such as trisomy, monosomy, nullisomy13,16, 18, 21, 22, haploidy, lack of nucleus and complex anoploidy were observed in the PGT in 78 out of 91 embryos of 11 patients with an sDFI of >30. A marked delay in reaching the cell in the time-lapse3, 4, 5 of patients with an sDFI of >30 (53 hours) (Fig. II). Chromosomal structural and numeric dysfunctions were detected in 39 PGT of 101 embryos obtained from 12 patients with an sDFI between 15-30 while numeric and structural dysfunctions were detected in 416 out of 1.670 embryos in the group with an sDFI of <15. The division time of the embryos with chromosomal structural and numeric dysfunctions extended by 59 hours or total fertilization failures were observed.

CONCLUSION: Morphokinetic dysfunction seen under embryoscope, relating to all patients including the group with a high sperm DNA fragmentation of infertile couples associated with idiopathic oligoasthenoteratospermia, were observed to be compatible with the chromosal structural and numeric dysfunctions at PGT.

Keywords: oligoasthenoteratospermia, embryoscope, preimplantation genetic diagnosis

PS-14

COMPARISON OF EMBRYOLOGICAL MORPHOKINETICS AFTER IN VITRO FERTILIZATION IN SMOKING AND NON-SMOKING SPOUSES, PRE-TRANSFER EMBRYO BIOPSIES, RATES OF PREGNANCY AND BRINGING HOME A BABY: PRELIMINARY REPORT

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INTRODUCTION AND OBJECTIVES: It is known that smoking has a negative impact on blastocyst and leads to implantation failure. Embryo development after IVF-ICSI in smoking and non-smoking spouses, pre-implantation genetics (PGT), pregnancy rates and the rate of bringing home a child will be assessed with embryoscope.

METHODS: The patients selected randomly among 1.668 embryoscopic follow-ups that underwent IVF-ICSI between 2011-2013 composed Group I of smokers (n=60) and Group II of non-smokers (n=60). Their physical examinations were made. Spermiogram, TUNEL test, karyotype analysis,Y deletions,FSH, LH and total testosterone (tt) were measured. FSH, LH, Estradiol (E2) was measured in women. Early embryological developments were assessed under the Embryoscope (Embryoscope and Unisense Fertilitech®).

RESULTS: Physical examinations were normal. Tunel tests were <15. The average FSH 12.4 IU/ml, LH 9.1IU/ml and tt 306 ng/ml releaved in men, while the average FSH was 13.4 IU/ml, LH was 7.4 IU/ml and E2 was normal with 46 pcg/ml in women. In Group I, 191 oocytes were collected, while 240 oocytes were collected in Group II. The conception rate was 84/191 in Group I and 147/240 in Group II. While it took 46 hours and 51 hours, respectively, to reach from 3 cells to 4 cells and 5 cells in Group I, this was calculated as 24 and 31 hours in Group II. Prior to the transfer, monosomy 13, trisomy 18, trisomy 19, monosomy 22, 45 XX, 46 XX (26), 45 XX-17 (3)/47 XY and different metaphase chromosome formations and chromosome abnormalities were observed in Group I. Different chromosome formations were observed in 34 out of 147 embryo biopsies, while no pathological findings were detected in the other embryos in Group II. Pregnancy occurred in 19 members of Group II (32%) and 31 members (51.6%) of Group II. Twelve live births occurred in Group I (20%) while 28 occurred in Group II (46.6%). Statistical differences were observed in pregnancy and live birth rates ($p<0.05$).

CONCLUSIONS: In addition to severe impairment, delay in fragmentation and structural and numerical chromosome abnormalities in PGT, also low pregnancy and live birth rates were detected in the spouses of smokers.

Keywords: embryoscope, smoking, embryo, morphokinetics

PS-15

COGNITIVE, AFFECTIVE PROBLEMS AND RENAL CROSS-ECTOPY IN A PATIENT WITH 48,XXYY/47,XYY SYNDROME

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Klinefelter syndrome is the most common sex chromosome abnormality in infertile patients and 47,XXY genomic configuration constitutes most of the cases. However, additional X's and/or Y such as 48,XXYY; 48,XXXY; and 47,XYY can occur less frequently than 47,XXY. Those configurations were considered as variants of Klinefelter syndrome. In this report, we present an infertile man with tall stature and decreased testicular volume. Semen analysis and hormonal evaluation supported the diagnosis of non-obstructive azoospermia. Genetic investigation demonstrated an abnormal male karyotype with two X chromosomes and two Y chromosomes consistent with 48, XXYY(17)/ 47, XYY (13). Additionally, the patient expressed cognitive and affective problems which were documented by psychomotor retardation and borderline intelligence measured by an IQ value between 70-80. Systemic evaluation also revealed cross-ectopy and malrotation of right kidney in the patient. The couple was referred to microTESE/ ICSI cycles and preimplantation genetic diagnosis. To the best of our knowledge, this is the first report of combination of XYY and XXYY syndromes associated with cognitive, affective dysfunction and renal malformation.

Keywords: 48 xxyy/47 xyy syndrome, renal malformation, balanced chromosomal translocation, klinefelter syndrome, spontaneous abortions, PGD

PS-16

ASSESSMENT OF TESTICULAR PATHOLOGIES, EMBRYOSCOPIC MORPHOKINETICS AND PRE-IMPLANTATION GENETIC TESTING (PGT) RESULTS FOLLOWING MICRO TESTICULAR SPERM EXTRACTION (TESE) IN PATIENTS WITH Y CHROMOSOME MICRO DELETION: A PRELIMINARY REPORT

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OBJECTIVE: The pathological findings, embryoscopic follow-ups and PGT results of azoospermic infertile patients with AzF deletion were assessed.

METHOD: Anamnesis, physical examination, spermiogram, karyotype, AzF deletions, FSH, total testosterone (tt) and scrotal color doppler was conducted in 66 with genetic pathologies out of 786 azoospermic patients who were admitted with the diagnosis of azoospermia as of April 2011.

FINDINGS: Mean age was 32±5 years while the duration of infertility was 12±4 years. Unilateral/bilateral microsurgery associated with varicocele was performed in the physical examination in 29 patients. Varicocelectomy had previously been performed in 19 patients. The mean testicular volume was 21.3 ml. The mean FSH was 19.4 IU/ml and tt was 291 ng/ml. Klinefelter syndrome was detected in 9 patients, 46 XY inv (10) (p11; q13) was found in 2 patients while 46 XXY /46 XY/ 46XXXY mosaic was detected in 1 patient. AzFc complete/partial deletions were detected in 38 patients, AzFb complete/partial deletions were found in 15 patients and partial deletions were detected in AzF (b+c) in 13 patients. Micro-TESE was performed on all patients. Twenty-five (37.8%) germ cell aplasia, 21 (31.8%) maturation arrest, 14 (%21) Johnson scores between 6-8, 1 (1.5%) tubular sclerosis and 5 (7.5%) hypospermatogenesis were detected. Sperm was found in 21% (n=14) of all patients. Pregnancy occurred in 9 patients in total and 7 live births occurred. It was observed that 23 morphokinetics (17.5%) of 131 embryos obtained from 14 patients in whom sperm was detected in embryoscopic follow-up and with AzF (b,c b+c) deletions were normal and that the duration of 3, 4, 5 cell fragmentation was 7.3 hours on average. No pathologies were observed in the chromosome number and structure of 51 embryos in the PGT performed on all patients.

CONCLUSION: Various testicular pathological findings were observed in Y chromosome micro deletions. Normal morphokinetics and fragmentation times were seen under embryoscope in these patients. Structural and numerical chromosome abnormalities in PGT were found to be correlated with the fragmentation and morphokinetic abnormalities in early embryoscopic follow-up. Pregnancy was not observed embryos with AzF deletions correlated both with embryoscopic and PGT abnormalities.

Keywords: embryoscope, pre-implantation genetic, AzF deletion

PS-17

THE EFFECTS OF REACTIVE OXYGEN RADICALS AND ANTIOXIDANTS ON SPERM PARAMETERS IN INFERTILE AND FERTILE MEN

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AIM: The male factors like oligospermia, asthenospermia, teratospermia are the anomalies of the spermiogram. Increased reactive oxygen species (ROS) in the semen plasma causes infertility via oligospermia, asthenospermia or defective sperm morphology. For this purpose, we studied the effects of ROS and antioxidants that prevents parameters. Patients and Methods The study included 30 fertile and 65 infertile men. The metil malonil dialdehit (MDA)as an oxidant, and katalas (CAT), superoxide dismutase (SOD), glutation peroxidase (Gpx) as antioxidants in the semen were measured biochemically. We evaluated the corelation between the sperm parameters (morphology, motility, concentration) and the levels of oxidant and antioxidants. Results Leukospermia, varicoceles, and both were found in 40%, 41.5%, and 18.4% of the patients, respectively. The patients with asthenospermia, oligospermia, or teratospermia (36.9%) had higher MDA levels than the control group, but this difference was not statistically significant and CAT, SOD, Gpx levels were similar to the control group. However, oligospermic (21.5%), teratospermic (30.7%). Asthenospermic (69.2%), oligoasthenospermic (21.5%), oligoteratospermic (13.8%), asthenospermic (27.8%) patients had significantly higher MDA levels than the control group ($p<0.005$). CAT levels were significantly higher in the patients with abnormal sperm parameters than the control group except the asthenospermic patients ($p<0.005$). It was observed the significant elevation in MDA and decrease in CAT levels in patients with abnormal sperm parameters. Neither MDA elevation nor CAT decrease was observed patients with varicocele and leukospermia. Conclusions We conclude that the the significantly high MDA levels is responsible for the concentration, motility, and morphology disturbances via the oxidative stress that negative effects the spermatozoa. In addition to the decrease of CAT in semen as a result of MDA elevation contributed to those negative effects.

Keywords: infertility, oxidative stress, antioxidants, reactive oxygen species (ROS)

PS-17

Table 1

Variables		MDA	CAT	SOD	Gpx
Control group (n=30) median (min.-max.)		157,69 (20,71-15724,76)	105856,19 (2331,50-185454,64)	12624,35 (6519,00-65821,90)	1,54 (0,29-6,97)
Oligoastenospermia (n=14) median (min.-max.)		251,62 (91,05-6057,26)	6461,43 (1272,15-33777,49)	12736,12 (6776,02-17618,61)	1,14 (0,77-2,79)
Oligoteratospermia (n= 9) median (min.-max.)		251,76 (186,38-6057,26)	6021,68 (1272,15-11527,81)	9555,40 (6776,02-17618,61)	1,10 (0,77-2,79)
Astenoteratospermia (n=18) median (min.-max.)		311,54 (28,70-6057,26)	6794,94 (1272,15-99193,81)	10872,08 (6776,02-25112,83)	1,28 (0,24-3,17)
P values	A B C	P<0,05 P<0,05 P<0,05	P<0,05 P<0,05 P<0,05	P>0,05 P>0,05 P>0,05	P>0,05 P>0,05 P>0,05

Comparison of the MDA, CAT, SOD and Gpx values in infertile group that have oligoastenospermia, oligoteratospermia and astenoteratospermia with the control group

PS-18

THE EFFECT OF SEMEN PH ON THE SPERM PARAMETERS

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OBJECTIVE: The World Health Organization(WHO) laboratory manual, last revised in 2010, states that the normal pH of semen ranges >= 7.2 (1). Our experience has been that values in our patient population are consistently higher than this range. To confirm this we reviewed >3021 semen records.

PATIENTS AND METHODS: All patient records from January 2001 to December 2012 that had semen pH measurements and sperm concentration and motility measurements recorded were included in this study. Semen samples were obtained from 2204 consecutive nonazoospermic men undergoing infertility assessment at the our infertility clinic, Kahramanmaras University Hospital. Among those men, average infertility period was 4.87 years (12 month - 40 years). All semen tests were performed according to the World Health Organization 2010 recommendations (1).

All pH measurements were made with pH paper on raw semen ejaculates at the time of semen analyses.

RESULTS: The mean (±SD) age of patients in our population was 31.6 ± 6.3 years. The mean (±SD) duration of abstinence before production of the specimen was 4.9 ± 1.4 days and the mean (±SD) time from specimen production to analysis was 31.4 ± 15 minutes.
For all semen analysis (n = 2204), mean (±SD) semen pH was 7.8 ± 0.4. The range was 6.5 to 8.5, with pH <7.2 in 6.6% of the samples.

The semen pH among the patients with normal sperm concentration, morphology, and motility values was statistically significant different from that among those with abnormal parameters ($p<0.001$). Also, we observed that the statistically significant differ between normal or abnormal semen pH with normal semen parameters ($p<0.001$).

DISCUSSION: The normal pH of semen has been defined as ranging from 7.2 to 8.0 according to WHO 1992. Some authors reported that the semen pH in their population was consistently higher than WHO reference values. Therefore, WHO laboratory manual, revised in 2010, states as the normal pH of semen ranges >= 7.2.

CONCLUSION: The present results demonstrate that semen pH can be has predictive value between normal and abnormal semen parameters such as concentration, motility, and morphology.

Keywords: pH, semen, sperm, World Health Organization (WHO)

PS-18

Table 1

Parameters (n:2204)	Concentration (cc)			Motility (a+b)		Morphology (Kruger Strict)	
	<=1 million (n=460)	1-15 million (n=460)	>= 15 million (n=1756)	< 40% (n: 1409)	>= 40% (n:795)	<4 (n:1968)	>= 4 (n:236)
pH < 7.2 (6.6%)	--	4.15%	2.45%	3.09%	3.72%	3.72%	1.43%
pH >= 7.2 (93.4%)	1,22%	37.40%	54.78%	42.39%	50.80%	62.46%	32.39%

Comparison of semen pH in patients with normal and abnormal sperm parameters

PS-19

THE OUTCOMES AND PREDICTIVE FACTORS OF MICRODISSECTION TESTICULAR SPERM EXTRACTION PERFORMED FOR NON-OBSTRUCTIVE AZOOSPERMIC MEN

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INTRODUCTION: The objective of this study was to demonstrate the outcomes of azoospermic patients who underwent mTESE and assess the predictive factors of mTESE.

METHODS: A total of 353 azoospermic men underwent mTESE between 2004-2013. Karyotype analysis and Y chromosome microdeletion have been routinely examined to exclude incurable cases. The clinical and biochemical features of the patients and their correlation with success rate were examined. Harvested testicular sperm were used for ICSI in fresh form or frozen form. Sperm Retrieval (SR), clinical pregnancy rates were retrospectively assessed.

RESULTS: While sperm retrieval rates were 32.4%, clinical pregnancy had been achieved in 60.1% of sperm positive couples. The mean age of the male and females were 35,1+16,7 years and 30,1+5,3 years respectively. The mean testicular volume of the males were 12+6,5 cc. The preoperative testosterone and FSH levels were analyzed as 4,8+5,2 ng/dl and 21,9+16 IU/L. Sertoli cell only syndrome (SCO) presented in 47.7% of cases and SRR was 15%. Hypospermatogenesis consisted 34.8% of cases and SRR was 33%. In cases with maturation arrest (6%) and normal spermatogenesis (11.6%) SRR rates were 13% and 89% respectively. While there was a significant correlation between FSH levels, testiscular volumes and sperm retrieval, no such correlation could be detected for testosterone levels and patients age. The mean FSH values for two groups (Sperm + and sperm -) were 17,4+13,9 and 24,1+16,8 IU/L(p=0.001). The mean testicular volumes for two groups (Sperm + and sperm -) were 13,6+5,9 and 11,4+6,2 cc (p=0.002).

CONCLUSIONS: In non-obstructive azoospermic males, SCO was the predominant etiology with lowest SR rates, which may explain the lower SRR by microdissection TESE. Low FSH levels and greater testicular volumes are significantly correlated with sperm retrieval rates. There is no relationship between preoperative testosterone levels, patient age and sperm retrieval.

Keywords: TESE,infertility,predictive factors

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