Objective: To evaluate whether dutasteride reduces the risk of incident biopsy-detected prostate cancer in men who are at increased risk for the disease.


Participants/Methods: Men, from 50 to 75 years of age, with a prostate-specific antigen (PSA) level between 2.5 ng/mL and 10 ng/mL were included in the study. All had undergone a single prostate biopsy within 6 months prior to enrollment. Eligible patients were randomized to 0.5 mg/day dutasteride versus placebo over 4 years. Ultrasound was used to measure prostate volume at randomization and 2 and 4 years later. Biopsies were performed at enrollment and at 2 and 4 years per protocol and at any other time they were clinically indicated. The primary end point was biopsy-detected prostate cancer after 2 or 4 years of treatment.

Results: Overall, a 22.8% reduction in biopsy-detected prostate cancer was seen over 4 years in the dutasteride group compared to the placebo group. However, the risk of tumors with Gleason scores of 8 to 10 increased greatly in the dutasteride group during the final 2 years of the study.

Conclusions: Dutasteride therapy reduced the risk of biopsy-detected prostate cancer over 4 years, but raised concerns over increasing the risk of higher grade cancer.

Reviewer's Comments: In the April 1, 2010, edition of the New England Journal of Medicine, Andriole and colleagues from the REDUCE study group report their findings. The study was over a 4-year period, included men aged 50 to 75 year, and allowed PSA from 2.5 to 10 ng/mL. The men had entry biopsies, year 2 and year 4 biopsies, and were allowed "protocol-independent" for cause biopsies as well. In the "efficacy analysis", or "per-protocol" for the 4 years of the study, 659 of the 3305 men in the dutasteride group who had a biopsy (19.9%) and 858 of the 3424 men in the placebo group who had a biopsy (25.1%) received a diagnosis of prostate cancer, for an absolute risk reduction of 5.1%. An absolute reduction of 5% means that 1 out of every 20 men treated will get the prevention benefit. Of all the cancers diagnosed on biopsy, the higher grade (7 to 10) tumors were not significantly different for the 2 study groups. However, tumors of grades 8 to 10 were found at an alarming rate during the final 2 years of the study in the dutasteride group (12 high-grade tumors) compared to the placebo group (1 high-grade tumor). Putting this into perspective, this difference corresponded to a number needed to harm of 224 men. In other words, out of every 224 men taking dutasteride, 1 of them had an extra high-grade tumor found. Comparing this risk to the prevention benefit seen suggests that for every 224 men treated, 11 men will avoid a cancer diagnosis while 1 man will be diagnosed with a higher grade tumor. (Reviewer-Stephen E. Canfield, MD).
Most Effective Strategy Is Also Most Expensive

Systematic Review of the Clinical Effectiveness and Cost-Effectiveness of Photodynamic Diagnosis and Urine Biomarkers (FISH, ImmunoCyt, NMP22) and Cytology for the Detection and Follow-Up of Bladder Cancer.

Mowatt G, Zhu S, et al:


Current bladder cancer practices using standard cystoscopy and cytology are not as effective as new alternatives; however, the societal cost of new technology in this field will likely become an issue in the future.

Objective: To determine the clinical utility and cost-effectiveness of standard cystoscopy (rigid white light cystoscopy [WLC]), photodynamic diagnostic (PDD) cystoscopy, common urinary markers, and cytology for diagnosing and following bladder cancer.

Methods: A comprehensive systematic review with meta-analysis when possible was performed for studies comparing WLC to PDD and studies assessing the performances of fluorescence in situ hybridization (FISH), ImmunoCyt, nuclear matrix protein (NMP-22), and cytology when compared to the reference standard of biopsied tissue.

Results: PDD had better sensitivity but worse specificity overall than WLC. Short-term recurrence-free survival was also better with PDD used at transurethral resection of bladder tumor (TURBT), but long-term benefit was unclear. For the biomarkers, ImmunoCyt had the highest pooled sensitivity, and cytology had the highest specificity. The most effective treatment strategy was initial diagnostic office cystoscopy (flexible cystoscopy using white light [CSC]) with ImmunoCyt followed by PDD with CSC and WLC surveillance. This was not cost-effective. The least effective strategy was cytology and WLC for diagnosis and surveillance, but this was most cost-effective.

Conclusions: Diagnostic and surveillance strategies for bladder cancer that utilize WLC and cytology are cheap but not as effective as new alternatives. It is unclear which strategy provides the best cost-to-benefit ratio.

Reviewer's Comments: The variety of diagnostic and surveillance options has continued to expand for bladder cancer, making it difficult for the busy practitioner to keep ahead of all the data. A comprehensive review and meta-analysis for this topic is therefore a welcome tool. For the comparison of WLC to PDD cystoscopy, 27 studies were included with a total of 2949 patients. Sensitivity of PDD versus WLC was 92% and 71%. Four of the 27 studies were randomized trials (RCTs) that looked at effectiveness data (ie, survival statistics). With PDD, there were 73% fewer residual tumors after transurethral resection (TUR), and there was a 37% longer short-term recurrence-free survival. For the comparison of biomarkers, 71 studies were included with data on ImmunoCyt, FISH, NMP-22, and cytology, with a total of 43,665 patients. Sensitivity was highest for ImmunoCyt (84%), followed by FISH (76%) and NMP-22 (68%), with cytology last (44%). Cytology had the highest specificity (96%). Finally, the authors undertook an economic analysis for cost-effectiveness. The most effective strategy was initial ImmunoCyt and CSC followed by PDD for treatment of any findings, with CSC followed by WLC during follow-up. Unfortunately, this was also the most expensive strategy. The cheapest approach (and least effective), was cytology combined with WLC for diagnosis, initial treatment, and follow-up. This analysis helps define the best data we have on the performance of these technologies, and strategies to utilize them in practice for patient care. (Reviewer-Stephen E. Canfield, MD).

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Keywords: Superficial Bladder Cancer, Cost-Effectiveness Analysis

Print Tag: Refer to original journal article
Robotic pyeloplasty has outcomes similar to open pyeloplasty.

**Objective:** To determine outcomes of robotic-assisted laparoscopic pyeloplasty for ureteropelvic junction obstruction.

**Design:** Prospective, chart review.

**Participants:** 85 patients undergoing 86 robotic pyeloplasties were included.

**Methods:** Consecutive patients undergoing robotic pyeloplasty were evaluated for perioperative morbidity, complications, and long-term functional outcomes. A transperitoneal approach was performed in all patients including a transmesocolic approach on most of the left-sided repairs.

**Results:** 86 pyeloplasties were performed, including 1 bilateral, 41 right-sided, and 43 left-sided cases. The mean operative time was 121 minutes, with the anastomosis time of 47 minutes. Two conversions to open were encountered, and 3 patients had urine leaks. The mean length of stay was 2.5 days. The overall success rate was 97%, with a mean follow-up of 13.6 months.

**Conclusions:** Robotic pyeloplasty is effective for managing ureteropelvic junction obstruction with low morbidity, quick recovery, and a durable success rate.

**Reviewer's Comments:** The authors add to a growing body of literature demonstrating that robotic pyeloplasty is becoming the standard of care for ureteropelvic junction repair. I congratulate the authors on that data with 97% success. However, this manuscript also highlights everything that is wrong with the current pyeloplasty literature. To begin with, we have no standardized outcomes for pyeloplasties. All authors agree that we need both radiographic and symptomatic/clinical success to be a "complete" success. The authors in this manuscript claim 97% success both radiographically and symptomatically, but do not define how they measure success radiographically or clinically. We do not know what the renal scan T1 half life for which the authors strive, and no quality of life questionnaire was administered. Next, the 2 conversions to open are considered successes since the outcomes were favorable. These cases should not be included in the "robotic" success category. In the conclusions, we are told that the patients have "durable" success rates. Again, I would argue that <1 year follow-up for most of the patients in the study still show good "short-term" success; the agreed length of time to follow patients or consider "long-term" is not standardized in the pyeloplasty literature. Throwing out a 97% success rate sounds impressive, but if we dig deeper, we discover that this is not likely a true reflection of the outcomes. I believe that robotic pyeloplasty is just as good from an outcomes perspective as open pyeloplasty, but we need more realistic numbers to compare techniques and to counsel our patients. (Reviewer-David A. Duchene, MD).

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**Keywords:** Robotic Pyeloplasty, Outcomes, Ureteropelvic Junction Obstruction

**Print Tag:** Refer to original journal article
Patients should be informed that PNL has superior treatment outcomes over SWL for lower pole stones.

**Objective:** To compare shock wave lithotripsy (SWL), percutaneous nephrolithotomy (PNL), and observation for asymptomatic lower caliceal stones.

**Design:** Prospective, randomized study.

**Participants:** 94 patients with asymptomatic lower caliceal calculi <20 mm in greatest diameter.

**Methods:** CT scans were done 3 and 12 months after intervention to determine stone status. Dimercaptosuccinic acid (DMSA) renal scintigraphy was performed at baseline and 6 and 12 months after intervention to assess renal scarring.

**Results:** Patients underwent PNL (n=31), SWL (n=31), or observation (n=32) in equal numbers. Mean follow-up was 19.3 months. All patients in the PNL group were stone free at 12 months and 1 (3.2%) had renal scarring. The SWL stone-free rate was 54.8%. Scarring occurred in 5 (16.1%). The observation group required intervention in 7 (18.7%) without any scars noted during observation. One (3.1%) had spontaneous stone passage. The median time to intervention was 22.5 months.

**Conclusions:** Stone events occurred in 20% of patients undergoing observation. PNL had a significantly higher stone-free rate with less renal scarring than SWL. Patients must be informed about all management options for lower pole calculi, especially focusing on PNL and its better outcome.

**Reviewer's Comments:** This manuscript is an additional verification of the initial Lower Pole Study 1, which showed that PNL is superior to SWL for lower pole calculi. The added arm in this prospective study was an observation arm, which showed that 1 in 5 patients needed intervention in a 19-month time frame. This prospective, randomized study also examined potential renal damage with the different modalities. A concerning 16% of patients undergoing SWL had renal scarring at follow-up compared to 3% of PNL patients. The SWL patients with scarring noted did have a total of 3 shock sessions in a relatively short time frame. Another concern was the poor stone-free success rate of 54.8% in the SWL group versus 100% success in the PNL group. The authors conclude, and I would agree, that PNL is a better modality to treat lower pole stones than SWL. The only missing arm in this study is a ureteroscopy group with which to compare outcomes and to compare potential renal scarring. So, what is the best modality to treat lower pole stones? Observation is least invasive, but tends to eventually lead to intervention; ESWL is an inferior modality to PNL and may cause more damage; PNL is the most successful but requires a hospital stay; and ureteroscopy was not examined in this study. Patients need to be aware of these different modalities and may be best served by PNL for lower pole stones. (Reviewer-David A. Duchene, MD).

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Keywords: Shock Wave Lithotripsy, Percutaneous Nephrolithotomy, Nephrolithiasis, Renal Function

Print Tag: Refer to original journal article
Increased Risk of Death Associated With Nephrectomy

Nephrectomy Induced Chronic Renal Insufficiency Is Associated With Increased Risk of Cardiovascular Death and Death From Any Cause in Patients With Localized cT1b Renal Masses.

Weight CJ, Larson BT, et al:
J Urol 2010; 183 (April): 1317-1323

Partial nephrectomy preserves renal function, and postoperative renal insufficiency is a significant independent predictor of overall and cardiovascular-specific survival.

Design/Participants: Retrospective study of 1,004 patients with a cT1b renal mass according to the 2003 TMN guidelines.
Participants/Methods: 524 patients underwent partial nephrectomy (PN), and 480 underwent radical nephrectomy (RN). The type of surgery was nonrandomized and left to the preference of the patient and surgeon. Cancer-specific mortality was based upon evidence of cancer progression before death or specific death certificate codes. Cardiovascular-related deaths included deaths due to ischemic heart disease, congestive heart disease, ischemic stroke, and peripheral vascular disease.
Results: The average decrease in estimated glomerular filtration rate (eGFR) was 16.6 mL/min per 1.73 m² for patients treated with PN and 23.5 mL/min per 1.73 m² for RN patients. Tumors removed by RN were more likely to be malignant. Because there were more tumors of higher grade and stage in the RN group, the PN and RN groups were stratified and compared grade-for-grade and stage-for-stage. In every analysis, PN was at least equivalent to RN in cancer control. In a multivariate analysis, pathological T stage and grade were independent predictors of cancer-specific survival, but surgical approach was not. The 5-year overall survival rate for patients treated with PN was 85% and statistically better than the 78% overall survival for patients treated with RN. Although kidney cancer was the leading cause of death at 38%, the second leading cause of death in this study was cardiovascular-related disease at 24%. Multivariate analysis demonstrated that final eGFR and preoperative history of coronary artery disease were independent predictors of cardiac-specific death. The excess renal loss associated with RN equated to a 25% increased risk of cardiovascular death and a 17% increased risk of death from any cause.
Reviewer's Comments: Although the performance of PN did not independently improve survival, preservation of renal function as a result of PN did improve survival. Naturally, the techniques of PN that preserve renal function, such as limiting ischemic time or inducing hypothermia, should be adhered to in order to realize this benefit. Since most renal tumors found currently are amenable to PN, these data and supporting data from other recent articles suggest that nephron-sparing surgery should be performed whenever technically feasible. (Reviewer-Kyle J. Weld, MD).

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Keywords: Nephrectomy, Carcinoma, Renal Cell, Survival, Renal Insufficiency

Print Tag: Refer to original journal article

**Objective:** To review the natural course of positive surgical margin (PSMs) and negative surgical margin (NSMs) tumors and to identify factors predictive of recurrence and of death from cancer in patients with PSMs.

**Methods:** Retrospective data from 26 medical centers were collected on patients who underwent either open or laparoscopic partial nephrectomy (PN) for a renal tumor. Of these patients, 111 had PSMs defined as the presence of tumor cells on the inked surface of the tumor on the final pathology report. None of these patients had nodal or distant metastasis. Multiple patient and tumor parameters were analyzed including elective versus imperative indication, stage, grade, local or distant recurrence, and cancer-specific survival.

**Results:** The mean patient age was 61 years, and mean tumor size 3.5 cm. The indication was imperative in 39%, and 84% had T1 tumors. Patients with positive margins were managed with observation in 84%, radical nephrectomy in 13%, and repeat PN in 3%. Among the patients who underwent a second surgery, residual tumor was found in 39%. With a mean follow-up of 37 months, 10% of patients had recurrences and 11% of patients died, including 5% whose deaths were related to cancer progression. The PSM patients were compared with a group of unmatched NSM patients and, to avoid selection bias, with a NSM group matched for indication, tumor size, and grade. In both comparisons, the PSM patients had significantly more tumors that were centrally located in the kidney and significantly more likely to recur; however, rates of cancer-specific survival and overall survival were statistically similar regardless of margin status.

**Conclusions:** A multivariate analysis showed that indication and tumor location were the only factors that could predict recurrence; PSM status had no effect on recurrence.

**Reviewer’s Comments:** After tumor resection, the typical procedure of a partial nephrectomy involves application of an energy device such as TissueLink or argon beam to the resection bed to achieve hemostasis. Then, parenchymal stitches are placed which exert some degree of ischemia to the surgical margin. Either of these maneuvers may destroy residual tumor cells and account for the current study's findings of residual tumor in only 39% of those patients who underwent a secondary surgery. This article supports other recent articles that suggest that a PSM does not invariably predict cancer recurrence. In light of the new data on the survival benefit of nephron-sparing surgery and the increased risk of cardiovascular death with radical nephrectomy, urologists should embrace the results of this article and perform more PNs. (Reviewer-Kyle J. Weld, MD).

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**Keywords:** Renal Cell Carcinoma, Nephron-Sparing Surgery, Survival

**Print Tag:** Refer to original journal article
Objective: To determine whether urodynamic measures of urethral function (valsalva leak point pressure [VLPP], maximum urethral closure pressure [MUCP], functional urethral length, and supine empty bladder stress test [SEBST]) correlate with each other and whether they correlate with subjective and objective measures of urinary incontinence (UI).

Methods: The data from this trial comes from the Trial of Mid-Urethral Slings (TOMUS), a multicenter study conducted within the United States under the direction of the Urinary Incontinence Treatment Network (UITN). A total of 597 women were enrolled in this trial based on a positive response to the stress incontinence question on the Medical Epidemiologic and Social Aspects of Aging (MESA) questionnaire. Patients were randomly assigned to undergo either a retropubic or transobturator midurethral sling procedure. All patients demonstrated preoperative stress UI on a bladder stress test. Patients were excluded for low capacity bladder, elevated residuals, previous history of sling surgery, or the requirement of concomitant surgery necessitating a graft. All subjects underwent urodynamic studies and the surgeons were blinded to the urodynamic results.

Results: The subjective measures of severity (MESA, Urogenital Distress Inventory, and the Incontinence Impact Questionnaire) had weak to moderate correlation with each other. The objective measures also had moderate correlation with each other, and the urodynamic measures, VLPP and MUCP, had moderate correlation with each other. Subjective measures of incontinence severity had moderate correlation with the objective measures of severity; however, urodynamic measures of urethral function had little or no correlation with any subjective or objective measurement of severity.

Reviewer's Comments: The strength of this particular study includes the large number of women with stress incontinence that had standardized and urodynamic technique and interpretation of the studies. A question that is left unanswered is whether urodynamic measures can predict surgical success rather than simply predicting incontinence severity. This trial does not answer this question and will require a subsequent investigation to determine. (Reviewer-Karl J. Kreder, MD).

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Keywords: Correlation, Empty Bladder Stress Test, Maximum Urethral Closure Pressure Severity, Stress Urinary Incontinence, Urodynamics, Valsalva Leak Point Pressure

Print Tag: Refer to original journal article
Consider Macroplastique® as a First Choice Agent for Urethral Bulking

Durability of Urethral Bulking Agent Injection for Female Stress Urinary Incontinence: 2-Year Multicenter Study Results.
Ghoniem G, Corcos J, et al:
J Urol 2010; 183 (April): 1444-1449

This study demonstrates that Macroplastique appears to be safe and effective as a long-term treatment for female stress incontinence.

**Objective:** To evaluate the durability of the urethral bulking agent Macroplastique® in the treatment of female stress urinary incontinence at 24 months after injection.

**Methods:** Over a 3-year period, patients were enrolled in a multicenter trial with Macroplastique and were followed for 1 year. This represents an additional year of follow-up to the original trial. Patients completed baseline and end-of-study assessments with medical history, 3-day voiding diary, physical examination, cystoscopy, urodynamics, the Incontinence Quality of Life questionnaire, 1-hour pad weight test, and Stamey grade as well as the Patient Global Impression of Improvement. The primary outcome of this report is the maintenance of continence status as measured by Stamey grade from 12 to 24 months after Macroplastique injection.

**Results:** The patients included in this trial were those who reported a positive response as measured by improvement in Stamey grade at 12 months after Macroplastique injection. Overall, there were 75 such patients; several withdrew, and 67 were evaluable. Of the 67 evaluable patients, 56 (84%) had sustained success from 12 to 24 months. Of 38 patients who were completely dry at 12 months, 33 (87%) were dry at 24 months. In 16% of patients, Stamey grade actually improved between 12 and 24 months after injection.

**Conclusions:** “The durability of Macroplastique shows its effectiveness as a viable long-term therapy for female stress urinary incontinence primarily due to intrinsic sphincter deficiency.”

**Reviewer’s Comments:** Macroplastique has been available outside the United States for almost 20 years, and there are several intermediate and long-term reports of cure rates similar to those reported in this North American trial. Based upon the reports to date, it is reasonable to consider Macroplastique as a first choice agent for urethral bulking. (Reviewer-Karl J. Kreder, MD).

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Keywords: Urethra, Silicone Elastomers, Urinary Incontinence, Stress, Injections

Print Tag: Refer to original journal article
New Etiology, Tx for Premature Ejaculation Is Proposed

The Role of Short Frenulum and the Effects of Frenulectomy on Premature Ejaculation.
Gallo L, Perdonà S:
J Sex Med 2010; 7 (March): 1269-1276

Frenulectomy is a safe and effective surgical treatment for lifelong premature ejaculation in patients with short frenulum.

Background: Premature ejaculation (PE) is a very common male sexual dysfunction, but the etiology remains unclear despite significant study. Within urology, anatomic abnormalities, such as short frenulum, have long been thought to contribute to PE.

Objective: To present the first investigation of short frenulum in relation to PE.

Methods: Men with lifelong PE (defined by the International Society of Sexual Medicine criteria) and short frenulum (defined as prepuce movement restriction by gentle pressure on frenulum and 20° ventral curvature of the glans major on prepuce retraction) were treated with frenulectomy under local anesthesia. Intravaginal ejaculatory latency time (IELT) and PE diagnostic tool (PEDT) score (range, 0 to 20; score of 20 indicates severe PE) were measured at baseline and every 3 months following frenulectomy.

Results: Out of 137 men with lifelong PE, 59 (43%) demonstrated short frenulum. Forty men, with a mean age 38.2 years, underwent frenulectomy without complications and with a mean follow up of 7.3 months. At baseline, mean IELT was 1.65 minutes and mean PEDT score was 15.8. After frenulectomy, mean IELT was 4.11 minutes demonstrating a 2.46 minute increase (P <0.0001), and mean PEDT score was 9.85 demonstrating a 5.95 point decrease (P <0.0001).

Conclusions: Short frenulum is a common anatomic abnormality among men with lifelong PE, and therefore, physical examination should be considered an integral part of evaluation. Considering these results and the procedure’s simplicity, frenulectomy may be offered as first-line treatment to men with lifelong PE and short frenula.

Reviewer’s Comments: Frenulum breve, or short frenulum, is described by the authors as a suspected mechanism of PE dating back to 1917. The definition of frenulum breve set by the authors is somewhat arbitrary at a 20° deflection of the penis with prepuce retraction, but this conveys the sense of a frenulum that essentially causes ventral chordee. An amazingly high prevalence of this condition (43%) was found in the men with PE. This begs the question, what is the prevalence of frenulum breve in the general population? Interestingly, the innervation of the frenulum is through the perineal nerve not the pudendal, despite it being an extremely dense epicenter of nerve endings. Of the men who underwent frenulectomy, impressive improvements in both IELT and PEDT scores were obtained. These were on par with previous "successful" dapoxetine and TEMPE trials (both of which have not been yet released in the U.S.). Several techniques for frenular release have been described, many of them using only EMLA cream as anesthesia, and most have minimal to no complications. The few times I have used these techniques in clinical practice have been for recurrent frenular tearing and dyspareunia. The authors are to be commended on an innovative approach to a difficult problem that gives us a new tool for a relatively empty tool box. (Reviewer-Tobias S. Kohler, MD, MPH).

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Keywords: Premature Ejaculation, Short Frenulum, Frenulectomy

Print Tag: Refer to original journal article
Isolated subclinical varicocele repair remains controversial and should be avoided.

**Background:** The incidence of varicocele in men with abnormal semen parameters is 25% versus 11.7% of normal men, and is present in up to 40% of men seen in infertility clinics. Subclinical varicocele is defined as nonpalpable on valsalva maneuver, but present on radiographic procedures such as ultrasound. Repair of this type of varicocele is very controversial.

**Objective:** To evaluate fertility after treatment of subclinical varicoceles.

**Participants/Methods:** 143 patients who met the inclusion criteria of a subclinical left varicocele only, normal hormone parameters, normal testicular size, normal partners, and no prior fertility treatments were included. Every patient was given the option of microsurgical repair, drug therapy with L-carnitine, and no treatment. The groups were then divided into surgical repair (n=25), medical therapy (n=93), and observation (n=25). Two semen samples were obtained prior to treatment and 2 were obtained 6 months after therapy. Natural birth rates were then determined by phone interview at 1 to 2 years after therapy.

**Results:** There were no significant differences in the groups regarding age of patient or partner, testicular size, and semen parameters. The sperm count of the surgery group did show significant improvements from a mean of 39.3 million/mL to 57.5 million/mL. The sperm count of the drug group was 54.6 million/mL before therapy and 55.8 million/mL after therapy. Natural pregnancy rates for the 3 groups were 60% for the surgery group, 34.5% for the drug group, and 18.7% for the observation group. Follow-up rate for the groups was 91 of 143 (64%).

**Conclusions:** Microsurgical repair for subclinical varicocele may improve sperm counts and pregnancy compared to medical therapy and observation.

**Reviewer's Comments:** According to a meta-analysis of 2,466 varicocelectomies by Pryor & Howards, repair improves semen parameters in 55% to 78% of men and allows natural pregnancy in 24% to 53% of couples. Nagler et al in a recent meta-analyses report comparable results and show a correlation between improvement in sperm concentration and sperm motility. Repair of subclinical varicocele has previously been discouraged as it has been implicated for failure of improvement of randomized trials on varicocele repair. Although acknowledged by the authors, this study is flawed due to lack of randomization with uneven distribution of low sperm counts in the surgical groups versus nonsurgical groups (39 vs 52 million/mL, attrition bias; 64% overall follow-up, surgery group highest), and lack of improvement in sperm motility. Although the author's report a statistical difference with ANOVA of those with follow-up between the 3 groups (P=0.031), careful analysis shows no statistical difference in pregnancy rate between the medication and surgical groups (P=0.06). A lack of understanding of the pathophysiologic mechanism of varicoceles continues to confound definitive conclusions regarding varicocele treatment. Repair of isolated subclinical varicoceles should be approached with great trepidation. (Reviewer-Tobias S. Kohler, MD, MPH).

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Keywords: Varicocele, Pregnancy Rate

Print Tag: Refer to original journal article
The Mediterranean diet is not only heart healthy, but it may improve a variety of aspects of overall health, including sexual health.

**Objective:** To determine the relationship between a greater adherence to the Mediterranean diet and sexual function in a population of women with type 2 diabetes.

**Participants/Methods:** Women with type 2 diabetes for at least 6 months completed a food frequency questionnaire and the Female Sexual Function Index (FSFI). Mediterranean diet adherence was based on a 9-point scale with a higher number associated with greater adherence.

**Results:** The mean age of participants was 57 years. A total of 595 women (90% response rate) completed the FSFI. Diabetic women with the highest adherence to the diet had lower body mass index (BMI), waist circumference, metabolic syndrome, and depression as well as increased physical activity. Women with a higher Mediterranean diet adherence score had a significantly lower risk of female sexual dysfunction, were more sexually active, and were more likely to have increased libido and overall sexual satisfaction. These associations were still significant after adjusting for multiple confounding variables.

**Conclusions:** Women with type 2 diabetes who have a greater adherence to the Mediterranean diet were significantly less likely to experience female sexual dysfunction.

**Reviewer's Comments:** Okay, I hate to say it, because I know I say this all the time, and that is "heart healthy equals all healthy," and "heart health equals sexual health." Is this really such a shock! We have seen these same results in men from several studies, including a landmark previous randomized trial by this same group. A Mediterranean diet involves the following points: moderate alcohol intake; healthy fat consumption; a high intake of fish, fruit, vegetable, legumes, nuts/seeds, whole grains; and a low intake of meat. How many of these points do you have or do the patients in your clinic have? The good news is that the Mediterranean diet is really an "everything in moderation" diet, and that is why I love it so much. It does not say you cannot have dairy, meat, or alcohol. Although, there is a problem with this study and other studies like it, they are never going to be advertised or promoted on the radio or television. So, please mention these studies to patients and practice what you preach. (Reviewer-Mark A. Moyad, MD, MPH).

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Keywords: Type 2 Diabetes, Mediterranean Diet, Sexual Function

Print Tag: Refer to original journal article
It may be time to question which, or if any, multivitamins should be recommended to patients.

**Objective:** To determine the impact of multivitamins and other dietary supplements on the risk of breast cancer in women.

**Participants/Methods:** A prospective study was done of 35,329 cancer-free women who completed a self-administrated 350-items questionnaire in 1997; the women were followed for 9.5 years. A total of 974 women were diagnosed with breast cancer during this time period.

**Results:** Multivitamin use was correlated with a statistically significant increased risk of breast cancer. The multivariate relative risk (RR) was 1.19, and this association did not differ significantly by hormone receptor status. The only other supplement that demonstrated a notable increased risk was zinc (RR=1.55), but this was not significant. In addition, multivitamin users were significantly more likely to take more individual supplements compared to those not taking multivitamins.

**Conclusions:** Multivitamin use may be associated with an increased risk of breast cancer.

**Reviewer's Comments:** What is going on here? The multivitamin is the best selling dietary supplement for men and women in the U.S., and has been for as long as I have been on this earth, but where is the evidence? We are waiting on a randomized major trial in the next year or 2 for Centrum®, but in the meantime, there is a suggestion of harm as much as a neutral or potential benefit with multivitamins. Some believe it is the zinc, others believe it is the folic acid because it is so easily utilized by cells, and others believe that there is no risk. However, I believe that when that oath said "first do no harm" that we were supposed to really follow it. Right? So, looks like I will only be recommending children's multivitamins for adults or nothing at all until someone can give me some idea or clue that these massive pills do something more than cost patients a bunch of money. (Reviewer-Mark A. Moyad, MD, MPH).

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Keywords: Multivitamins, Breast Cancer Risk

Print Tag: Refer to original journal article
Patients in need of NU for UTUC should be assessed for renal function and offered neoadjuvant chemotherapy when appropriate.

Objective: To determine the prevalence of chronic kidney disease (CKD) before and after nephroureterectomy (NU) for upper tract urothelial carcinoma (UTUC) and how this impacts the ability to provide chemotherapy when needed.

Methods: A retrospective review of the NU database at Cleveland Clinic from 1992 to 2008 was conducted. The estimated renal function (estimated glomerular filtration rate [eGFR]) was calculated from existing data when possible for before and after NU. Eligibility for chemotherapy was based on National Kidney Foundation guidelines for CKD (eGFR <60 mL/min per 1.73 m2).

Results: Of 396 patients who underwent NU, 336 had enough data for analysis. The overall median preoperative eGFR was 59, corresponding to 52% of patients ineligible for chemotherapy. Overall postoperative eGFR was 48, corresponding to 78% of ineligible patients. The pre- and postoperative percentages of CKD in high-risk disease patients, who would clearly have benefited from chemotherapy, were 60% and 76%, respectively. This represented a 49% loss of opportunity for high-risk patients.

Conclusions: There appears to be a high prevalence of CKD in patients with UTUC requiring NU. The prevalence increases dramatically after NU, and many opportunities for beneficial adjuvant chemotherapy are lost.

Reviewer's Comments: The impact on renal function after nephrectomy for renal cell carcinoma is well known. This information is lacking for patients undergoing NU for UTUC, a disease which may require intact renal function even more due to beneficial effects of cisplatin-containing chemotherapy regimens. The current study by Lane et al is an eye opening investigation into this lack of knowledge. The authors retrospectively assessed renal function data on 363 patients who underwent NU at the Cleveland Clinic. There was an extremely high prevalence of CKD (which would preclude chemotherapy [52%] in this population), which got dramatically worse after NU (78%). For the subset of patients who had documented high-risk disease and would clearly have benefited from chemotherapy, there was a 49% loss of adequate renal function after NU. Limitations of the retrospective information may be reflected by a 15% missing data rate (60 of 396 NU patients), a nonstandardized surgical approach, (lymph node dissection), and a tertiary referral center selection bias. However, the numbers are striking and should not be ignored. It appears critical to assess these patients preoperatively for CKD and offer neoadjuvant chemotherapy when appropriate. (Reviewer-Steven E. Canfield, MD).

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Keywords: Upper Tract Urothelial Cancer, Chronic Kidney Disease

Print Tag: Refer to original journal article
PROSTVAC-VF shows early promise as a treatment for metastatic castration-resistant prostate cancer.

**Objective:** To determine if PROSTVAC-VF (a poxviral prostate-specific antigen [PSA] targeted recombinant viral vaccine) improves progression-free survival (PFS) and overall survival (OS) in men with metastatic castration-resistant prostate cancer (mCRPC).

**Methods:** A multicenter blinded trial randomized 2:1 for vaccine therapy versus placebo was conducted. Vaccine therapy was administered according to a previously proven schedule of induction and booster pox vaccines along with immune stimulatory molecules and factors. Primary outcomes were PFS and OS.

**Results:** 125 men underwent randomization at 43 centers in the United States. PFS was assessed at 6 months, at which time there was no difference between the groups. Median OS was 25.1 versus 16.6 months for vaccine and placebo, respectively, an 8.5-month difference. The hazard ratio (HR) for the vaccine was 0.56, corresponding to a 44% reduction in death rate.

**Conclusions:** In this phase II randomized, controlled trial, the prostate cancer vaccine PROSTVAC-VF was associated with significantly increased median OS in men with mCRPC.

**Reviewer's Comments:** CRPC is one of the most challenging clinical stages of the disease. The only Food and Drug Administration-approved therapy, docetaxel, may increase median survival by about 3 months. Prostate cancer vaccines, utilizing various viral vectors and targets such as PSA, have gained much attention. Recent studies on these agents are now coming to light, such as the vaccine sipuleucel-T, which was associated with a 4.5-month increase in survival. The current study presents results on PROSTVAC-VF, a pox virus vector, PSA targeting vaccine. Investigators combined it with immune boosters and stimulating factors and found an increase in median survival of 8.5 months, which was a 44% reduction in the death rate over 3 years. This is somewhat remarkable and likely an overestimation of the true effect. Looking at the demographics between the groups, it appears that men in the placebo group were substantially older and had higher median PSAs. Also, 10% of the men in the vaccine group (vs 0% in the placebo group) had lymph node only disease, which affords a better prognosis compared to additional sites of metastases. All of these factors may have influenced survival results, and while they may all have occurred by chance, it is curious that they all tend to favor the treatment arm. However, reasonable skepticism in the form of "effect modifier analysis" was applied by the authors, and they did not find obvious confounders. Ultimately the follow-up phase III trial will be most informative for this potentially promising therapy. (Reviewer-Steven E. Canfield, MD).

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Keywords: Metastatic Prostate Cancer, Cancer Vaccine

Print Tag: Refer to original journal article
New Technique for Bladder Cuff Closure During Laparoscopic Nephroureterectomy

A Sealed Bladder Cuff Technique During Laparoscopic Nephroureterectomy Utilizing the LigaSure™ Electrosurgical Device: Laboratory and Clinical Experience.

Lambert EH, Schachter LR, et al:

J Endourol 2010; 24 (March): 327-332

The LigaSure™ electrosurgical device may be beneficial for bladder cuff closure during laparoscopic nephroureterectomy.

Objective: To evaluate the LigaSure™ bipolar electrosurgical device in laboratory investigations and during clinical laparoscopic nephroureterectomy to manage the distal ureteral bladder cuff.

Design: Controlled laboratory animal studies and clinical human studies.

Methods: Initial investigations were undertaken in a porcine model and in ex vivo human ureters from radical nephrectomy specimens. The tissue specimens were sealed with the LigaSure and stained with nicotinamide adenine dinucleotide and hematoxylin and eosin to examine the length of treatment effect and the viability of the ablated tissue. Clinically, 22 laparoscopic nephroureterectomies for proximal urothelial tumors were performed with the use of the LigaSure on the distal bladder cuff. Intraoperative cystoscopy evaluated for adequate cuff resection and bladder leakage.

Results: In the porcine model, the technique sealed the bladder effectively with a mean burst pressure of 14 mm Hg. Cellular staining revealed no viable urothelial tissue in the sealed area and an additional 2 mm outside this area. Eighteen of the 22 patients had successful seal/ablation intraoperatively. Cystoscopy demonstrated cautery artifact and blanching over the former position of the ureteral orifice.

Conclusions: The LigaSure device ablates and seals urothelial tissue with no viable cells in the clamped as well as the adjacent blanched tissue. The technique is technically feasible, typically maintains a closed urinary system, removes an adequate bladder cuff, and adheres to sound oncological principles in patients undergoing laparoscopic or open nephroureterectomy.

Reviewer's Comments: The ideal way to excise the distal ureter and bladder cuff during a laparoscopic nephroureterectomy has not yet been established. Several techniques have been described, but an open excision remains the oncologic standard of care. The technique described in this publication with the use of the LigaSure device does hold promise of being useful in both laparoscopic and open nephroureterectomy. It is very similar to the "staple technique," but no visible urothelial cells are left at the ablation line. The most difficult aspect of this technique is ensuring that the entire ureter has been excised since it is very easy to ligate the distal ureter and leave a stump. Therefore, I think the concurrent cystoscopy to ensure complete dissection is essential in this technique. Otherwise, it follows oncologic principles and may lessen operating room time.

(Reviewer-David A. Duchene, MD).

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Keywords: Urothelial Carcinoma, Laparoscopic Nephroureterectomy, New Technology

Print Tag: Refer to original journal article
Male-to-Female Ratio in Stone Disease Is Decreasing

Changes in Gender Distribution of Urinary Stone Disease.
Strope SA, Wolf JS Jr, Hollenbeck BK:

Urology 2010; 75 (March): 543-546

Stone disease is increasing in women and decreasing the male-to-female stone ratio.

**Objective:** To determine the extent to which gender-specific rates of stone disease are changing using population-based data.

**Design:** Retrospective database query.

**Methods:** The Florida State Ambulatory Surgical Database and the State Inpatient Database were queried for procedures related to renal colic or urolithiasis. Population-based rates of utilization were calculated for the years 1998 to 2004 by gender.

**Results:** 107,411 discharges occurred for stone disease in which 38% were female. Service utilization increased in both men and women, but the growth rate in women outpaced men ($P < 0.01$). Rates of outpatient and ambulatory surgery center utilization increased significantly in both men and women, but inpatient utilization only increased in women. The ratio of men to women discharged after urinary stone surgery decreased from 2 in 1998 to 1.6 in 2004. The ratio of men to women treated in the inpatient setting decreased from 1.8 in 1998 to 1.3 in 2004.

**Conclusions:** Resource utilization for stone disease continues to increase, and most of this increase appears to be due to an increase in disease among women. Increasing obesity, dietary changes, or decreased fluid intake may be contributing to the rapid increase in stone disease treatments in women.

**Reviewer’s Comments:** The current study provides more evidence that the incidence rate of stone disease is becoming less gender specific. Traditional teaching shows the incidence rate of stone disease in males was 2.2 to 3.4 times greater than in females. More recent studies have shown that this ratio has decreased to only 1.3 to 1.8 times greater in males in the United States. This manuscript explores Florida databases to determine the changing ratio from the years 1998 to 2004. The findings confirm a decreasing male-to-female ratio of 1.6 for overall stone discharges and a ratio of 1.3 for treatment in the inpatient setting. The reasons for the increase stone disease in women are not entirely known but thought to be related to increasing obesity, Western dietary habits, and decreased fluid intake. It is important to remember, however, that the etiology cannot be evaluated by this study design. We must also be cautious in generalizing the findings since these findings were done in the state of Florida, a state in the "stone belt" that may not represent the rest of the United States. The ratios were also calculated from billing data without patient identifiers, which has inherent errors in data collection. However, I think the data are real and that the genders are becoming equal in regard to stone formation. (Reviewer-David A. Duchene, MD).

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Keywords: Nephrolithiasis, Epidemiology, Resource Utilization

Print Tag: Refer to original journal article
Cryoablation of multiple renal lesions at one setting may be successfully performed with few complications.

**Objective:** To report the perioperative and short-term outcomes in a group of patients who underwent cryoablation of multiple renal lesions.

**Design/Participants:** This is a retrospective review of 7 patients who underwent synchronous laparoscopic cryoablation of multiple renal cortical neoplasms in a single kidney.

**Methods:** All tumors were demonstrated as enhancing masses on CT or MRI. The renal vessels were not clamped. Laparoscopic ultrasonography and intraoperative biopsy of each mass was performed in all cases. The number of 1.47-mm cryoablation probes was determined by the size of the lesion. Two freezing cycles each, followed by an active thaw, was performed. The ice ball was extended 1 cm beyond the tumor border. CT or MRI with contrast was performed at 3 months and annually.

**Results:** Median follow-up was 23 months. One patient had von Hippel Lindau. Seventeen lesions were ablated. Five patients had 2 lesions ablated, 1 patient had 3 lesions ablated, and 1 patient had 4 lesions ablated. The mean tumor size was 2 cm. The tumors were exophytic (29%), endophytic (18%), mesophytic (29%), or hilar (12%). The mean blood loss was 138 mL. One patient required a blood transfusion, and another patient required a stent postoperatively due to a ureteral stone causing colic. To date, all lesions were undetectable on follow-up imaging. Intraoperative biopsies revealed malignancy in 65% of the lesions. Renal function, as measured by serum creatinine, increased from a mean preoperative value of 1.5 to 1.7 mg/dL postoperatively.

**Reviewer's Comments:** Several other larger series have reported on longer term follow-up results of renal cryoablation. In this literature, the occasional mention of synchronous treatment with cryoablation of a kidney with multiple tumors is made. This is the first article to specifically report on cryoablation for multiple tumors of the same kidney. One of the criticisms of cryoablation is the lack of margin status. Interestingly, another article reviewed in this cycle by Bensalah et al suggests that positive surgical margins after partial nephrectomy appear to have no impact on cancer-specific survival. Plus, intraoperative ultrasound allows for real-time monitoring of the ice ball as it approaches and extends beyond the margin. The benefit of cryoablation is maximal preservation of normal renal parenchyma. Extirpative nephron-sparing surgery requires an ischemic period that can be extended if >1 lesion requires excision. Cryoablation is a safe and effective option for patients with multiple tumors in 1 kidney, especially for those with syndromes that may require additional treatments for tumors that develop in the future. (Reviewer-Kyle J. Weld, MD).

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Keywords: Cryoablation, Renal Tumor, Laparoscopy

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Robot-Assisted Ureteroureterostomy -- An Important Alternative

Robot-Assisted Ureteroureterostomy in the Adult: Initial Clinical Series.
Lee DI, Schwab CW, Harris A:

Urology 2010; 75 (March): 570-573

Robotic-assisted ureteroureterostomy is a treatment option for ureteral strictures.

Objective: This report presents the first series of robotic-assisted ureteroureterostomies for benign stricture disease.
Methods: In all cases, the stricture was located in the mid-ureter above the iliac vessels with relatively short disease. Two of the strictures resulted from prior ureteral stone treatments, and 1 patient had a stapled ureter from a prior colectomy. The surgical technique was similar in all cases. The patient was positioned laterally. A 12-mm camera port was placed periumbilically, with 2 robotic working ports laterally in a triangle configuration. An assistant 5-mm port was placed in the mid-subxiphoid region. The robot was brought in over the patient's hip. The colon was reflected, and a significant amount of fibrosis was encountered at the level of the stricture. A 2- to 3-cm length of ureter was excised, and the ureteral ends were spatulated. A double-armed 4-0 Monocryl suture on RB1 needles was used for the anastomosis starting laterally and running continuously until tied medially. The stent was placed robotically. The authors point out that stents with a continuous coil of thin-gauge metallic wire should not be used when placing stents robotically since they may become kinked. The authors recommend using only silicone stents when placing them robotically. The stents were left in place for 5 to 6 weeks.
Results/Conclusions: With a minimum of 18 months of follow-up, all patients are pain free with radiographic ureteral patency demonstrated.
Reviewer's Comments: Although this series is small in number, it describes an important alternative for ureteral stricture disease. With proficiency in robotic-assisted pyeloplasty and the advantages offered by the robot, ureteroureterostomy is another procedure that can now be offered to these patients. If the strictures are near or overlying the iliac vessels, enthusiasm for endopyelotomy wanes. If the success rates of robotic-assisted ureteroureterostomy approach those seen with pyeloplasties, this procedure may overtake endopyelotomy as the minimally-invasive choice for ureteral stricture disease. (Reviewer-Kyle J. Weld, MD).

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Keywords: Ureteral Stricture, Ureteroureterostomy, Laparoscopy

Print Tag: Refer to original journal article
Does Combined Therapy Improve Urgency in Urinary Incontinence?

The Effects of Drug and Behavior Therapy on Urgency and Voiding Frequency.

Burgio KL, Kraus SR, et al:

Int Urogynecol J Pelvic Floor Dysfunct 2010; February 9 (): epub ahead of print

Drug therapy alone and combined therapy (drug and behavioral) each improved urgency in women with predominant urge incontinence; however, there was no added benefit for combined therapy on the magnitude of change over time.

Objective: To examine the effects of drug therapy alone compared with combined therapy (behavioral therapy plus drug therapy) on urgency and 24-hour urinary voiding frequency.

Participants/Methods: All patients enrolled in this trial (the Behavior Enhances Drug Reduction of Incontinence) were female. The trial was conducted at 9 clinical centers in the United States. Participants were required to have urge-predominant urinary incontinence and were randomly assigned to receive drug therapy alone using tolterodine 4 mg a day or to receive drug therapy combined with behavioral training. In the first portion of the trial, both groups received 10 weeks of active treatment. In the second portion immediately following active treatment, both drug and behavioral therapy were withdrawn. The primary outcome of the trial was the successful discontinuation of drug therapy. Treatment visits were conducted every 2 to 3 weeks over a period of 10 weeks. If patients did not tolerate full-dose tolterodine, the dose was decreased to 2 mg or another anticholinergic was substituted.

Results: 307 women who were randomized had sufficient data to be evaluable and ranged in age from 21 to 87 years (mean, 56.9 years). At baseline, the mean urgency ratings in both groups were in the mild-to-moderate range. Mean scores on the urgency/severity scale decreased significantly from baseline to 10 weeks within both the drug alone and combined groups. However, the magnitude of change between groups over this time was not statistically significant. The mean 24-hour voiding frequency at baseline was similar in both groups. Voiding frequency increased from baseline to 10 weeks in the drug alone group and decreased slightly for drug plus behavior therapy, and the amount of change was statistically significant.

Reviewer's Comments: One limitation of this study is that the urgency scores reported, on average, only mild degrees of urgency in the patients at baseline. This mild degree of urgency in patients at baseline may have minimized the differences in treatment effects between the 2 groups. (Reviewer-Karl J. Kreder, MD).

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Keywords: Urgency, Frequency, Medical Therapy, Women

Print Tag: Refer to original journal article
Specific Factors Affect the Effectiveness of Sling Procedures

Body Mass Index Does Not Influence the Outcome of Anti-Incontinence Surgery Among Women Whereas Menopausal Status and Ageing Do: A Randomised Trial.

Rechberger T, Futyma K, et al:

Int Urogynecol J Pelvic Floor Dysfunct 2010; February 24 (): epub ahead of print

While BMI does not influence the clinical effectiveness of retropubic or transobturator suburethral sling procedures in women with stress urinary incontinence, menopausal status and age do influence the results of anti-incontinence surgery.

**Objective:** To assess the clinical efficacy of 2 suburethral tape operations (retropubic or transobturator sling procedure) for the surgical treatment of female stress urinary incontinence stratified by the obesity and menopausal status as well as the age of the patient.

**Design:** A single-center study conducted from January 2003 to December 2005.

**Participants/Methods:** 398 women had data complete enough for evaluation at 18 months. Patients with significant degrees of prolapse were excluded. Menopause was defined as the absence of menstruation for at least 6 months. The patients were randomized to either a transobturator or retropubic sling procedure and were evaluated with urodynamic studies preoperatively. Follow-up visits were scheduled at 1, 4, 6, 12, and 18 months following surgery. The efficacy of the operation was determined by both symptoms and cough test in the supine and standing position as well as the patient's self-report of the use of hygienic pads.

**Results:** The groups investigated were not significantly different preoperatively in terms of their demographic or urodynamic parameters. The clinical effectiveness of both types of midurethral slings did not depend on the patient's body mass index or the type of sling, whereas menopausal status and age significantly influenced the outcome of either anti-incontinence procedure.

**Reviewer's Comments:** The data in the literature regarding body mass index and the influence on the subsequent outcome of sling procedures are somewhat mixed. Several studies have demonstrated that suburethral sling surgery may be used with a high degree of success even in morbidly obese patients. Conversely, a study by Helberg found an increased rate in patients with a body mass index >30 treated with the tension-free vaginal tape procedure. In this study, there was a significant decrease in the cure rate from 81% of normal weight women to 52% in the obese group. (Reviewer-Karl J. Kreder, MD).

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Keywords: Female Urinary Incontinence, Sling Procedure, Obesity, Menopause, Ageing

Print Tag: Refer to original journal article
Stress Is Bad for Sperm

Semen Quality in Fertile Men in Relation to Psychosocial Stress.

Gollenberg AL, Liu F, et al:

Fertil Steril 2010; 93 (March 1): 1104-1111

Psychological stress is a modifiable factor that may contribute to decreased semen quality.

**Background/Objective:** Among many factors affecting semen quality and subsequent infertility, stress has been studied but is difficult to quantify. This study attempts to measure psychological stress based on the number of stressful events in the male’s life and its relationship to semen parameters.

**Methods:** Male subjects analyzed were from a multicenter pregnancy cohort study. Semen samples were analyzed for sperm concentration, total count (TC), percent motility, and percent normal morphology and then compared to World Health Organization (WHO) semen analysis standards as primary outcomes. Participants also completed an adapted questionnaire to assess stressful life events experienced in the previous 3 months.

**Results:** 744 men completed questionnaires and donated semen. Stressors were analyzed as a dichotomous variable (≥2 vs <2) and as a discrete variable (total events reported). Two or more recent stressful events were reported by 22% of participants who were also more likely to demonstrate nonwhite race, lower educational attainment, younger age, smoking history, higher body mass index, and a history of sexually transmitted disease (P <0.05). After adjusting for these and other factors, these men's sperm concentration, TC, and percent motile sperm remained lower than both those reporting <2 stressful events and the WHO standard parameters.

**Conclusion:** Multiple recent stressful events appear to occur more often in certain populations. Males in these populations are more likely to demonstrate lower overall semen quality. These findings may be important in identifying correctable causes of male factor infertility among a large battery of etiologies. Further study is necessary to elucidate whether effective management of life stressors improves semen parameters.

**Reviewer's Comments:** This is a well done study that accounts for several confounders of stress including smoking, body mass index, and financial difficulties. Ultimately after adjustment for all recorded confounding variables, men who had ≥2 stressful life events were 2 times more likely to have sperm concentrations <20 million/mL, 1.5 times as likely to have poor motility (<50%), and 1.9 times as likely to have abnormal morphology (<4% normal forms) as compared to men with less stress. Stress is speculated to affect sperm through hormonal manipulation. Stress causes low testosterone and luteinizing hormone levels. Adrenocorticotropic hormone and cortisol can decrease testosterone production in leydig cells and result in deleterious increases in nitric oxide and decreases in arginase. In this study, no change in hormone levels was found, but it could be because the timing of the stress and blood draws did not overlap or perhaps only intratesticular testosterone levels may be affected. (Reviewer-Tobias S. Kohler, MD, MPH).

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Keywords: Fertile Men, Psychosocial Stress, Semen Quality

Print Tag: Refer to original journal article
Smoking ≥1 pack per day of cigarettes lowers the fertility index in males.

**Background:** Results of previous studies on the direct effects of cigarette smoking on sperm quality and semen parameters have been mixed despite a highly suspected causal relationship between smoking and impaired reproductive function.

**Objective:** To determine if smoking negatively influences semen quality in men with idiopathic infertility.

**Design/Participants:** Retrospective analysis of 271 smoking and nonsmoking men with idiopathic infertility.

**Methods:** Semen samples from all subjects were analyzed with conventional semen analysis and transmission electron microscopy (TEM), and fertility indices and percentages of sperm apoptosis, necrosis, and immaturity were determined.

**Results:** No statistically significant differences between smokers and nonsmokers were found in semen pH, volume, sperm concentration, motility, apoptosis, immaturity, or necrosis. Statistically significant ($P<0.05$) reductions in sperm concentration and fertility index were found in heavy smokers (≥20 cigarettes per day) as compared to mild smokers and nonsmokers.

**Conclusions:** Semen quality in idiopathic infertile males is not significantly affected by smoking; however, heavy smoking may reduce sperm concentration and fertility index.

**Reviewer's Comments:** The results of this study add to the arsenal of data indicating the potential negative impact of smoking on male fertility. This study incorporated a method of quantitative sperm analysis based on TEM as opposed to light microscopy, with the aim of elucidating if or how smoking may alter sperm morphology. Although only "heavy smokers" in this study showed reduced sperm concentration and fertility index, smoking ≥1 pack/day was deemed as heavy smoking. It is important to remember that since these patients already had idiopathic infertility, perhaps the negative effects of smoking were hidden or buffered. This information is clinically important due to the high prevalence of smoking in young, adult males and provides further data to promote smoking cessation. Urologists are afforded a great opportunity to help patients quit smoking as we now know it causes erectile dysfunction, can lower testosterone levels, and impairs fertility. Emphasis on these topics is much more likely to change behavior than nebulous warnings of lung cancer or hypertension. In my opinion, cigarette carton warnings should read "Cigarettes Cause Erectile Dysfunction and Infertility." Indeed, cigarette smoking lowers fertility in women by 50%. (Reviewer-Tobias S. Kohler, MD, MPH).

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Keywords: Smoking, Semen Quality

Print Tag: Refer to original journal article