Statin Use May Affect Aggressive Prostate Cancer

Is Statin Use Associated With Prostate Cancer Aggressiveness?

Loeb S, Kan D, et al:

BJU Int 2009; November 3 (): epub ahead of print

In men undergoing prostatectomy, prior statin use may be protective against aggressive pathological features.

Objective: To determine if statin use in patients undergoing radical prostatectomy (RP) affect perioperative and pathologic cancer features.
Design: Retrospective cohort study.
Participants: 1351 men who underwent RP from 2003 to 2009.
Methods: 504 patients taking statins at time of surgery were compared to 847 who were not.
Results: Significant differences were seen in older age and increased body mass index for statin users, but also in lower preoperative prostate-specific antigen, lower positive margin rate, and lower tumor volume.
Conclusions: Statin users in this series had a decreased risk of aggressive pathological features.
Reviewer's Comments: Use of cholesterol-lowering statins for chemoprevention has been a controversial topic for a long time. Reasons include plausibility, safety, and cost. Statins have been shown to induce cancer cell stasis and death in the lab, so it is plausible that they can act this way in real life. Furthermore, they are relatively safe and cheap -- the perfect combination for a preventive drug. Unfortunately, data on true prostate cancer prevention have been conflicted, with little hard evidence in support of this, and well-done studies suggesting no actual effect. The current study adds support to the notion that there is a protective effect of statins on prostate cancer, but this must be understood in its proper context. Loeb and colleagues present a retrospective series of patients from their large dataset of radical prostatectomies. The report focuses on immediate perioperative and pathological features between cohorts, and does not provide any outcome information. Therefore we are not provided real, patient-important information, such as survival, but merely surrogate markers which likely correlate with survival. The most interesting such finding was the incidence of positive surgical margins, which was 18.0% in the non-statin group and 13.7% in the statin group. Adjusting for stage and grade using multivariate analysis resulted in an odds ratio (OR) of 0.71 for reduced positive margins in statin users. What does all this mean? Should our RP patients be taking statins prior to surgery from now on? It would be wonderful news if this was the case, but these data are merely provocative. It currently only applies to this particular group of mostly Caucasian (98%) men, who all had a diagnosis of prostate cancer already, and chose RP as their treatment. It doesn't shed light on statins as chemopreventive agents. But it does suggest they might modulate the aggressiveness of prostate cancer, which is potentially remarkable. Hopefully future research will provide more conclusive data on the role of statins for prostate cancer. (Reviewer-Steven E. Canfield, MD).

Keywords: Prostate Cancer, Statins, Prostatectomy, Pathology, Aggressive

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Metastatic Prostate Cancer Tx Should Include Bisphosphonates

Adjuvant Therapy With Oral Sodium Clodronate in Locally Advanced and Metastatic Prostate Cancer: Long-Term Overall Survival Results From the MRC PR04 and PR05 Randomised Controlled Trials.

Dearnaley DP, Mason MD, et al:

Lancet Oncol 2009; 10 (September): 872-876

Men with metastatic prostate cancer should be offered treatment with a bisphosphonate.

Objective: To determine if bisphosphonates impact survival in men with prostate cancer.
Design/Methods: 2 randomized, placebo-controlled trials were done with sodium clodronate, a first generation oral bisphosphonate. The Medical Research Council (MRC) PR04 studied men with localized disease and MRC PR05 studied men with hormone sensitive metastatic disease.
Results: Men with localized disease received 4 pills a day of medication versus placebo for 5 years, while men with metastatic disease received the same for 3 years. In metastatic prostate cancer, intervention reduced the risk of death (HR 0.77; 95% CI, 0.60 to 0.98; *P* =0.032), while in localized disease it did not.
Conclusions: Oral bisphosphonate can improve survival in men with metastatic prostate cancer.
Reviewer's Comments: The Medical Research Council performed 2 important trials in tandem which looked at the role of the oral bisphosphonate sodium clodronate in patients with localized prostate cancer, mostly treated with radiotherapy, and with metastatic cancer treated with hormonal therapy. Sodium clodronate is a first generation bisphosphonate, which is a weaker antagonist to osteoclastic activity in the bones than alendronate, for example. Primary outcome measure was symptomatic bone metastasis and prostate cancer death. These results have been available for a few years, and showed a trend toward improved outcomes in the metastatic group which was not statistically significant, and no difference in the localized cancer group. The current study presents long-term follow-up for overall survival, a secondary endpoint of the studies. Again, there was no difference seen in survival for the localized cancer group. In the metastatic group, median follow-up was 11.5 years, and 93% of participants with available survival data had died. In this group, a significant difference was seen for overall survival. At 5 years, estimated survival was 21% versus 30% for placebo and clodronate, respectively, and at 10 years was 9% versus 17%, respectively. Results of this study are extremely useful for urologists for a number of reasons. One of the mainstays of current bisphosphonate therapy is intravenous zoledronic acid, which has been shown to reduce "skeletal related events" in metastatic, hormone refractory prostate cancer. Most urologists, however, treat patients with metastatic prostate cancer while they remain hormone sensitive. Additionally, most urology offices are not set up to administer IV medication. This study demonstrates the utility of oral bisphosphonate therapy in the hormone sensitive state, and is therefore easily implementable in our daily practice. The bottom line is that bisphosphonate therapy in some form should be part of the treatment plan for patients with metastatic prostate cancer. (Reviewer-Steven E. Canfield, MD).

Keywords: Prostate Cancer, Bisphosphonates, Survival

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Can We Lower CT Radiation Exposure While Maintaining Effectiveness?

Effect of Low Dose Radiation Computerized Tomography Protocols on Distal Ureteral Calculus Detection.

Jellison FC, Smith JC, et al:

J Urol 2009; 182 (December): 2762-2767

Low-dose radiation CT protocols may potentially limit radiation exposure with the same effectiveness in detecting distal ureteral stones.

Objective: To compare detection rates of ultra-low-dose and conventional CT protocols on distal ureteral calculi in cadaveric model.
Design: Prospective single-blinded study.
Participants: 85 calcium oxalate stones 3 to 7 mm long were placed in 14 human cadaveric distal ureters in 56 random configurations.
Methods: Intact kidneys, ureters, and bladders were placed in a human cadaveric vehicle and CT was performed at 140, 100, 60, 30, 15, and 7.5 mA seconds while keeping other imaging parameters constant. Images were independently reviewed in random order by 2 blinded radiologists to determine sensitivity and specificity of each mA second setting.
Results: Overall sensitivity and specificity were 98% and 83%, respectively. Imaging using 140, 100, 60, 30, 15, and 7.5 mA second settings results in 98%, 97%, 97%, 96%, 98%, and 97% sensitivity, and 83%, 83%, 83%, 86%, 80%, and 84% specificity, respectively. Interobserver agreement was excellent. There was no significant difference in sensitivity or specificity at any mA second settings. All false-negative results were noted for 3-mm calculi at a similar frequency at each mA second setting.
Conclusions: Ultra-low-dose CT protocols detected distal ureteral calculi in a fashion similar to that of conventional CT protocols in a cadaveric model. These protocols (7.5 mA) may decrease the radiation dose up to 95%, reducing risk of secondary malignancies.
Reviewer's Comments: This study had an excellent design protocol to determine if ultra-low-dose CT scans could detect distal ureteral stones in a cadaveric model. The importance of this study revolves around limiting radiation exposure during imaging studies. Traditional non-contrast renal colic CT exposes a patient to 20 mSv of radiation and many stone patients receive several CT scans yearly. The Food and Drug Administration (FDA) recommends a maximum of 50 mSv of radiation exposure yearly, and there is no known "safe limit" under which the risk of secondary malignancies does not increase. In this study, radiation exposure of a 7.5 mA CT scan protocol is only 0.95 mSv which is equivalent to radiation exposure of a plain x-ray of kidneys, ureters, and bladder. Specificity and sensitivity were equivalent to standard CT protocol. Images definitely do have more "noise" as the radiation exposure decreases. Ultra-low-dose protocol may also not be good at assessing other potential etiologies of flank pain and/or may not work in obese patients. However, as the authors emphasize, this type of protocol may work well in known stone patients, in patients undergoing imaging to check for residual stones, and/or in the pediatric population. More clinical work needs to be done before applying this technology to living individuals, but it is promising that we may be able to substantially reduce the radiation dose of CT scan looking for urolithiasis. (Reviewer-David A. Duchene, MD).

Keywords: X-Ray Computed Tomography, Nephrolithiasis, Ureteral Calculi, Diagnostic Imaging, Radiation Dosing

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Endoureterotomy Successful for Many Benign Ureteral Strictures

Holmium Laser Endoureterotomy for Benign Ureteral Stricture: A Single Center Experience.

Gnessin E, Yossepowitch O, et al:

J Urol 2009; 182 (December): 2775-2779

Holmium laser endoureterotomy is an acceptable surgical option for benign ureteral strictures in correctly selected patients.

Objective: To assess the long-term outcome of laser endoureterotomy for benign ureteral strictures.
Design: Retrospective chart review.
Participants: 35 patients selected from a database of 69 who underwent retrograde holmium laser endoureterotomy for benign ureteral strictures.
Methods: Patients with ureteropelvic junction obstruction, ureteroenteric anastomotic stricture, previous failed procedures, extrinsic compression, stricture >2 cm, or patients with open or laparoscopic preference were excluded. Clinical characteristics, operative results, and functional outcomes were investigated. Success was defined as symptomatic improvement and radiographic resolution of obstruction.
Results: Median follow-up was 27 months. All patients completed clinical follow-up, but only 33 completed imaging. Of patients, 29 (82%) were symptom-free during follow-up and 26 (78.7%) were free of radiographic evidence of obstruction. All except one failure occurred <9 months postoperatively. Success rate was higher for non-ischemic strictures (100% vs 64.7%, P =0.027) and tended to be higher for strictures ≤1 cm (89.4% vs 64.2%, P =0.109).
Conclusions: Holmium laser endoureterotomy is effective for benign ureteral stricture in well-selected patients. Most failures occur <9 months after surgery. Factors that may influence outcome are ischemia and stricture length.
Reviewer's Comments: This article is a nice series of patients undergoing retrograde, holmium laser endoureterotomy for benign ureteral strictures. It is the largest series currently published on the topic. Their objective success rates were very good for this type of procedure at 78.7%. I think that it demonstrates laser endoureterotomy is successful in carefully selected patients. It is very important to remember, however, that these 35 patients were selected from a starting database of 69 patients with several exclusion criteria as outlined above. It would be interesting to know what the success rate would be in their overall endoureterotomy series if the other patients were included; it would likely be much lower. A key issue in the success of endoureterotomy revolves around the blood supply to that segment of ureter and the stricture etiology. Success rates fell significantly to 64.7% when potentially ischemic strictures (status post radiation or surgery, impacted stones) were compared to non-ischemic strictures (non-impacted stones). Longer strictures (>1 cm) also had lower success rates. I think an attempt at endoureterotomy is reasonable in short, non-ischemic, benign strictures, but I would not quote success rates much more than 70%. This type of procedure also risks potentially increasing stricture length which may jeopardize other attempts (open ureteroureterostomy) at future repairs. Therefore, selected criteria are key to this procedure. If, when looking directly at the stricture, it appears long and ischemic, then an endoureterotomy may not be in the patient's best interest. (Reviewer-David A. Duchene, MD).

Keywords: Ureter, Ureteral Stricture, Solid-State Lasers, Ureteroscopy, Ischemia

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Tumor Size Does Matter: Predicting Collecting System Transection

Predicting Collecting System Transection at Laparoscopic Partial Nephrectomy: Analysis of Tumor Parameters.

Shikanov S, Lifshitz DA, et al:

J Endourol 2009; 23 (November): 1863-1866

Tumor size is the most powerful independent predictor of collecting system transection during laparoscopic partial nephrectomy.

Objective: To assess renal parenchymal tumor parameters that may predict collecting system (CS) transection and allow for improvement in preparing for laparoscopic partial nephrectomies (LPN).
Design/Participants: Prospective data collection for 165 LPN cases.
Methods: Particular attention was paid to tumor characteristics on preoperative axial imaging in relation to the visually assessed observation of CS violation during the procedure. These cases were performed by an experienced surgeon with a >50 case learning curve. CS violations were closed using continuous 2-0 Vicryl with LapraTyTM clips.
Results: CS transection occurred in 115 (61%) patients. Clinically detectable urinary leak was diagnosed in 3 (2.6%) patients with CS transection and repair. No patients demonstrated a urinary leak among those without an observed CS transection during the procedure. Among various patient and tumor characteristics compared based on CS transection status, only tumor appearance and size were statistically significant on multivariate analysis. Patients with CS transection had a higher proportion of solid tumors as opposed to cystic tumors. Also, patients with collecting system transection had larger tumors with a mean tumor diameter of 3.2 cm as opposed to 2.1 cm in patients without CS transection.
Conclusions: Classification and Regression Tree analysis demonstrated a 2.5-cm threshold as an optimal cutoff for tumor size as a predictor of collecting system transection. Each additional centimeter of tumor diameter triples the odds of CS transection and odds are 10-fold higher for tumors >2.5 cm.
Reviewer's Comments: This article is helpful for urologists early in their learning curve for LPN. Proper patient selection during the learning curve would include patients with tumors <2.5 cm and cystic tumors to minimize the risk of CS violation. CS transection complicates the repair and may extend warm ischemia time even for experienced urologists. Surprisingly, tumor depth was not a predictor of CS violation. Even with preoperative cross-sectional imaging and intraoperative ultrasound planning, I tend to more aggressively resect endophytic tumors because of less certainty of margin location. This aggressive resection would intuitively increase risk of CS transection, but this was not suggested in the current series. Despite lack of significance of tumor depth for collecting system transection, I would caution urologists on the learning curve to shy away from endophytic tumors also. (Reviewer-Kyle J. Weld, MD).

Keywords: Renal Parenchymal Tumor, Laparoscopy, Collecting System, Partial Nephrectomy

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LESS Is Not Better When Compared to Conventional Laparoscopic Pyeloplasty

Perioperative Outcomes in Patients Undergoing Conventional Laparoscopic Versus Laparoendoscopic Single-Site Pyeloplasty.

Tracy CR, Raman JD, et al:

Urology 2009; 74 (November): 1029-1034

All measured perioperative outcomes for laparoendoscopic single-site pyeloplasty are similar to those for conventional laparoscopic pyeloplasty.

Objective: To compare outcomes of laparoendoscopic single-site (LESS) surgery with conventional laparoscopic pyeloplasty (CLP).
Methods: 14 patients undergoing LESS pyeloplasty were matched 2:1 with regard to age and side of surgery to a previous cohort of 28 patients who underwent CLP. All cases were performed for symptomatic ureteropelvic junction obstruction and delayed excretion on nuclear medicine renal scans. CLP was performed through a 12-mm umbilical trocar and two 5-mm trocars. LESS pyeloplasty was performed through a 25-mm umbilical incision which accommodated 3 trocars and another 5-mm trocar laterally. A drain was placed through the 5-mm lateral trocar site at the conclusion of the case. Articulating instruments were used in the LESS pyeloplasties, but a conventional needle driver and intracorporeal suturing was used after case #8.
Results/Conclusions: There were no significant differences in age, side of surgery, sex, body mass index, presence of crossing vessel, or history of previous endoscopic management of the ureteropelvic junction obstruction between groups. There were also no significant differences in length of hospital stay, inpatient administration of morphine equivalents, or complications between groups. LESS procedures had a significantly shorter mean operating room (OR) time (202 minutes compared to 257 minutes for conventional) and a significantly less mean estimated blood loss (35 mL compared to 85 mL for conventional). Shorter OR time for LESS procedures might be accounted for by the practice of cystoscopy and stent placement prior to 75% of the conventional cases necessitating patient repositioning as opposed to antegrade stent placement for all of the LESS cases. Long-term success rate for the conventional group is 95.8%, while short-term results for the LESS group show a 100% success rate.
Reviewer's Comments: I commend the authors for their efforts to develop and refine LESS. Comparison of CLP and LESS pyeloplasty showed no clinically significant advantage of one procedure over the other with the possible exception of better cosmesis for the LESS approach. However, this difference only amounts to the addition of one extra 5-mm trocar for the conventional technique using one umbilical trocar and two 5-mm non-umbilical trocars compared to LESS which uses an umbilical access and one 5-mm non-umbilical trocar. Further refinement of LESS techniques and advancements in technology are needed. (Reviewer-Kyle J. Weld, MD).

Keywords: Ureteropelvic Junction Obstruction, Pyeloplasty, Laparoscopy

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Several Factors Affect Incontinence Risk After Continence Surgery

Risk Factors Associated With Urge Incontinence After Continence Surgery.

Kenton K, Richter H, et al:

J Urol 2009; 182 (December): 2805-2809

Independent risk factors for postoperative urge urinary incontinence in women after incontinence surgery include detrusor overactivity, prior anticholinergic use, or preoperative urge symptoms.

Objective: To identify preoperative factors associated with postoperative, bothersome urge urinary incontinence (UUI) after continence surgery with either a sling or Burch procedure.
Design/Methods: Data from this paper came from the Stress Incontinence Surgical Treatment Efficacy Trial (SISTEr) with 655 enrolled participants. Eligibility criteria included 3 months of pure or predominant stress urinary incontinence (SUI) symptoms and a positive stress test. Of participants, 34 were excluded based on their re-treatment for SUI. Participants were randomized on the day of surgery to either a Burch colposuspension or sling procedure. Postoperative urinary incontinence was defined in 2 ways. One was a requirement for anticholinergic therapy to treat UUI ≥6 weeks after surgery and another was a symptoms-based definition of postoperative UUI.
Results: 132 women (20%) with a mean age of 51±10 years required treatment for postoperative UUI (50 Burch and 82 sling procedures). Odds of treatment for UUI after surgery was significantly higher for a sling procedure (OR 1.72, *P* =0.007).
Conclusions: A 10-point increase in the preoperative Medical, Epidemiologic, and Social Aspects of Aging urge score (MESA scale), prior anticholinergic use, or preoperative detrusor overactivity all independently increased the odds of urinary incontinence postoperatively.
Reviewer's Comments: This study demonstrated that patients with a 10-point unit increase in their baseline MESA urge score have a nearly 4-fold increase of UUI postoperatively. Women are also almost twice as likely to need treatment for UUI after a sling procedure as opposed to a Burch procedure. These facts should be taken into account when patients are counseled prior to surgery. (Reviewer-Karl J. Kreder, MD).

Keywords: Urinary Incontinence, Suburethral Slings, Overactive Bladder, Surgical Procedures

Print Tag: Refer to original journal article

Nerve Stimulation May Help Challenging Patients With Overactive Bladder

Long-Term Durability of Percutaneous Tibial Nerve Stimulation for the Treatment of Overactive Bladder.

MacDiarmid SA, Peters KM, et al:

J Urol 2010; 183 (January): 234-240

Percutaneous tibial nerve stimulation treatments demonstrate excellent durability at one year and may be a viable long-term treatment for overactive bladder.

Objective: To analyze the second phase of the Overactive Bladder Innovation Therapy Trial (OrBIT trial), designed to assess sustained therapeutic effect of percutaneous nerve stimulation (PTNS) over 1 year.
Design/Methods: Patients who participated in the initial OrBIT trial and finished 12 consecutive weeks of PTNS therapy were offered ongoing sessions of therapy for an additional 9 months. Of 35 patients in the initial OrBIT trial treated with PTNS, 33 elected to continue treatment. Follow-up was available on 32 patients at 6 months and on 25 patients at 12 months. Assessments used were voiding diary, overactive bladder questionnaire (OAB-Q) scales, and Indevus Urgency Severity Scale. In addition, both investigators and patients completed a global response assessment (GRA) at the 12-week, 6-month, and 12-month follow-up.
Results: At 12-month follow-up, average improvement in urinary frequency from baseline was 2.8 voids per day (P <0.001). Urge incontinent episodes at baseline were reduced by 1.6 (P <0.001), nocturia was reduced by 0.8 voids (P <0.05), and voided volume increased by 39 cc (P <0.05). GRA showed sustained improvement at weeks 12, 26, and 52, with 96% of patients as responders at 12 months. There were no serious adverse side effects.
Reviewer's Comments: Patients with overactive bladder symptoms can present a treatment challenge. This PTNS modality represents another option that may be used alone or in combination with pharmacologic therapy. It may be particularly useful in patients who are in poor health and not candidates for a permanent sacral nerve stimulator device or when there are concerns about cognitive impairment with anticholinergic therapy. (Reviewer-Karl J. Kreder, MD).

Keywords: Electric Stimulation Therapy, Nocturia, Tibial Nerve, Overactive Bladder, Urge Urinary Incontinence

Print Tag: Refer to original journal article

Fertility Preservation Attempts in Prepubertal Boys Are Feasible

An Experimental Protocol for Fertility Preservation in Prepubertal Boys Recently Diagnosed With Cancer: A Report of Acceptability and Safety.

Ginsberg JP, Carlson CA, et al:

Hum Reprod 2010; 25 (January): 37-41

Parents, if well informed about both the potential effects of treatment and the protocol, are willing to pursue fertility preservation for their son.

Background: Future fertility is a potential issue for pediatric cancer patients, especially prepubertal males, as chemotherapeutic agents are known to adversely affect gonadal function.
Objective: To determine acceptability and safety of testicular tissue cryopreservation in prepubertal males diagnosed with cancer.
Methods: Prepubertal males with newly diagnosed advanced stage sarcomas or malignancies requiring "sarcoma-like" chemotherapy were offered testicular tissue acquisition and cryopreservation. During general anesthesia for necessary cancer care, a testicular biopsy was performed by a urologist and an adult testicular tissue freezing protocol was used for cryopreservation. Half of the sample was frozen for potential patient use and the other half was frozen for research. Procedure-related adverse events were recorded. Families were surveyed on factors influencing their decision.
Results: Of 21 eligible patients, 16 families consented to the testicular biopsy protocol. No biopsy-related adverse events occurred. The initial opinions of consenting families were "this is right for my child" in 68%, while 32% were either unsure or unwilling to proceed. All consenting families after biopsy indicated that "this was the right decision even if their son's fertility is not restored." In all 21 families, religious beliefs, finances, or ethics were not major factors in decision-making.
Conclusions: Families are interested in preserving their prepubertal sons' fertility and will proceed with testicular biopsy even without a guarantee of future fertility. Oncologists do not routinely offer fertility preservation in pediatric patients and should be educated about this possible option.
Reviewer's Comments: In 2006, the American Society of Clinical Oncologists released fertility preservation recommendations that include discussing fertility preservation options with patients shortly after cancer diagnosis, preferably before initiation of treatment, and referring them to a fertility specialist with expertise in fertility preservation methods. If eligible, men should seek sperm cryopreservation, and in cases of azoospermia or anejaculation, consider sperm extraction procedures. Previous studies have demonstrated a gross disparity between available fertility preservation techniques and their utilization. Most of these studies have examined adults. Any barriers to fertility preservation in adults are magnified in prepubertal children, as sperm banking is not possible, and no reliable means to utilize prepubertal testicular tissue yet exists. The authors are to be congratulated not only on their publication, but for being pioneers in actively advancing prepubertal fertility preservation feasibility, acceptance, and research. In the era before intracytoplasmic sperm injection when sperm banking yielded very low take-home baby rates, a few people insisted on storing sperm in anticipation of improved assisted reproductive techniques and were ultimately able to father children. As research on human prepubertal spermatogonial stem cells progresses, I am hopeful that children who freeze testicular tissue today will similarly be able to have their own genetic offspring in the future. (Reviewer-Tobias S. Kohler, MD).

Keywords: Fertility Preservation, Cancer, Prepubertal Males

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Stem Cell Advances Offer Fertility Hope to Pediatric Cancer Patients

Propagation of Human Spermatogonial Stem Cells In Vitro.

Sadri-Ardekani H, Mizrak SC, et al:

JAMA 2009; 302 (November 18): 2127-2134

Advances in human spermatogonial stem cells techniques potentiate new fertility preservation options.

Background: Infertility is an important long-term issue for prepubertal male patients undergoing cancer treatment since these patients do not yet have mature sperm to preserve for future use. Animal spermatogonial stem cell (SSC) culture and transplantation methods have been successful, but are not yet demonstrated in human SSC.
Objective: To establish in vitro propagation of spermatogonial stem cells in humans from small testicular biopsies and obtaining sufficient cell numbers for transplantation success.
Methods: Testicular tissue from 6 adult males undergoing orchiectomy for prostate cancer treatment was cryopreserved. Following tissue thaw, germ cells were isolated and cultured. SSCs were identified both by immunohistochemistry/immunofluorescence with promyelocytic leukemia zinc finger protein (PLZF) and gene expression analysis via polymerase chain reaction. Identified SSCs were then transplanted into mouse testes devoid of endogenous spermatogenesis and recovered periodically to determine functionality.
Results: Cultured SSCs required a mean 22.5 days to appear and could be propagated for up to 15 weeks. Cultured cells demonstrated a 53-fold increase in human SSCs within 19 days of transplantation into mice. Extended culture cells demonstrated an 18,450-fold increase in human SSCs within 64 days of transplantation.
Conclusions: This is the first report of successful long-term culture and propagation of human SSCs. These results represent a significant, promising development in fertility preservation but require further study with prepubertal testicular cells.
Reviewer's Comments: Improved patient survival with the newest pediatric cancer treatment protocols belies the increased rates of gonadotoxicity from chemotherapy, radiation, and debulking surgery. Risks of such treatments in males include impairment of penile erectile function, sympathetic nervous system damage that subsequently prevents normal seminal emission and ejaculation, injury to the genital duct system, disruption of the hypothalamic-pituitary-gonadal axis, and cytotoxic effects on the testicular germinal epithelium. The testis is particularly radiosensitive, with radiation therapy causing germ cell loss in a dose-dependent fashion with even very low doses affecting spermatogonia. In men able to bank sperm before cancer treatment, about 10% ultimately use it for assisted reproductive techniques. Because of the high efficacy of today's cancer treatments, the 5-year survival rate for patients aged <15 years with cancer at any site is approaching 75%. Family building becomes a central issue for a majority of patient's surviving cancer. The researchers are to be congratulated on this landmark article which describes an exciting technique offering hope to prepubertal cancer patients. Theoretical concerns for re-implanting nonsolid tumors into cured patients also exist, but no abnormal testicular growth was found in the transplanted mice in this study. (Reviewer-Tobias S. Kohler, MD).

Keywords: Fertility preservation, Spermatogonial Stem Cells, In Vitro, Prepubertal Males

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Macho Men -- Most Require No Treatment for ADT Hot Flashes

Efficacy of Venlafaxine, Medroxyprogesterone Acetate, and Cyproterone Acetate for the Treatment of Vasomotor Hot Flushes in Men Taking Gonadotropin-Releasing Hormone Analogues for Prostate Cancer: A Double-Blind, Randomized Trial.

Irani J, Salomon L, et al:

Lancet Oncol 2009; December 4 (): epub ahead of print

Hot flashes may be over treated, but effective medications exist for men on androgen deprivation therapy who need treatment.

Objective: To determine the impact of common pharmacologic treatments for women with hot flashes on men that experience hot flashes on androgen deprivation therapy (ADT).
Participants/Methods: 311 men that had already received 6 months of ADT were randomly assigned to 1 of 3 regimens daily for 12 weeks: 75 mg of venlafaxine, 100 mg cyproterone acetate (not available in the United States, but common in Canada and Europe), or 20 mg of medroxyprogesterone acetate. Patients also completed a 1-week hot flash diary before each clinical visit.
Results: Participants reported that 80% of their hot flashes on average were moderate to severe before the randomization period. Change in median hot flash score was -47% for venlafaxine, -94% for cyproterone, and -84% for medroxyprogesterone; this decrease was significant (P <0.0001) for each medication from baseline, but there was a significant improvement for the other 2 medications over venlafaxine. Approximately one quarter to one third of hot flashes in these 2 groups were completely eliminated.
Conclusions: Medroxyprogesterone or cyproterone work better against hot flashes compared to venlafaxine. Cyproterone is used as a treatment in some countries, but it also has a history of cardiovascular toxicity. Thus, medroxyprogesterone should be considered the standard treatment for hot flashes in men on ADT.
Reviewer's Comments: Holy hot flash, Batman! Do you realize what finding was not heavily advertised in the abstract?! Only 22% of men that had received ADT for 6 months actually requested hot flash treatment. In other words, only about 1 out of every 5 need hot flash pharmacologic treatment or perhaps they are just too macho to request it; however, that is probably not the case because they do not have testosterone. So, there is little doubt now from this and past studies that progesterone treatments (megesterol acetate pills or medroxyprogesterone depot injections or pills) are the most effective and safest pharmacologic treatments available for men with moderate to severe hot flashes. Still, they do have risks such as weight gain, HDL reduction, appetite stimulation, and may enhance sarcopenia, fatigue, and sexual dysfunction. So, again, (I cannot say this enough) I believe most men just need lifestyle changes on ADT. The few who do need pharmacologic treatment should be reassured that they work very well. Oh, and by the way, when are we going to learn that, in general, what works for hot flashes in women also works for men?! Finally, I wonder why they did not have a placebo group (sarcasm intended)!? (Reviewer-Mark Moyad, MD, MPH).

Keywords: Vasomotor Hot Flushes, Male, Pharmacologic Treatment, Androgen Deprivation Therapy

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Moderate Soy Does Not Reduce Negative ADT Side Effects in Men

Lack of an Effect of High Dose Isoflavones in Men With Prostate Cancer Undergoing Androgen Deprivation Therapy.

Sharma P, Wisniewski A, et al:

J Urol 2009; 182 (November): 2265-2273

Moderate amounts of soy protein or isoflavones do not change quality of life in men on androgen deprivation therapy.

Background: Soy protein and plant estrogens ("isoflavones") found in soy have been extensively studied in peri- or post-menopausal women with mixed results. Men on androgen deprivation therapy (ADT) experience so-called "male menopause" and may find some quality-of-life improvement with greater soy intakes comparable to what has been found in some studies with women. However, despite discussions by clinicians to incorporate more soy in the diet of men on ADT, there have been very few studies that have addressed the impact of soy in men on ADT.
Objective: To test the impact of a moderate soy protein and isoflavone intake of men on ADT.
Design: Randomized, double-blind, placebo-controlled 12-week pilot trial.
Participants: 33 men undergoing ADT.
Methods: Participants were assigned to either 20 grams of soy protein (160 mg total isoflavones, n=17) daily, or a taste-matched placebo that consisted of 20 grams of whole milk protein (n=16). Cognition, sexual function, vasomotor symptoms, and quality of life were measured at baseline, 6, and 12 weeks.
Results: Men in the soy group had greater baseline prevalence of hot flashes and less intercourse satisfaction compared to the placebo group. At 12 weeks, there were no significant differences between any outcome measures between groups. Nothing became worse and nothing got better compared to placebo.
Conclusions: Soy, in moderation, does not impact quality of life for men on ADT compared to a placebo protein powder.
Reviewer's Comments: Soy does not bring joy?! Is that what we should tell patients? Not exactly, or maybe I am a poet and I do not even know it. This is a fabulous study, but we need to know other things about it to help construct a few more conclusions. For example, did the men on ADT lose weight or drop their cholesterol? Thus far, soy is considered a heart-healthy food so I like to recommend it for patients on ADT as a way to get good, quality protein and low calories to combat sarcopenia, lose weight or waist, and to lower cholesterol. Perhaps other options like whey or milk protein would also suffice and maybe we have given too much credit to soy. However, this study is critical because it suggests that in order to derive potential benefits, men are going to have to consume more soy protein a day (perhaps 20 to 40 grams) which can easily be done, but will increase the risk of gastrointestinal side effects and hurt compliance rates. Ultimately, recommending low-calorie protein powder intake for men on ADT may be wisest recommendation. (Reviewer-Mark Moyad, MD, MPH).

Keywords: Isoflavones, Prostate Cancer, Androgen Deprivation Therapy

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Predicting Non-Prostate Cancer Death After PSA Recurrence

Comorbidity, Body Mass Index, and Age and the Risk of Nonprostate-Cancer-Specific Mortality After a Postradiation Prostate-Specific Antigen Recurrence.

Nguyen PL, Chen M-H, et al:

Cancer 2009; December 2 (): epub ahead of print

Age, body mass index, and comorbidities can help predict risk of dying in men who fail radiotherapy for prostate cancer.

Objective: To determine, in men experiencing biochemical recurrence after radiotherapy (RT) for unfavorable risk prostate cancer, if the risk of non-prostate cancer-related death can be predicted from age, body-mass index (BMI), or comorbidity score.
Design/Methods: Retrospective analysis was done on 87 men from a randomized trial of RT with or without hormonal therapy (HT) who had biochemical failure. These men were assessed for age, comorbidity score, and BMI, which were correlated with cause of death.
Results: At a median follow-up of 4.4 years post prostate-specific antigen (PSA) recurrence, there were 15 non-prostate cancer related deaths and 16 prostate cancer deaths. Risks for non-prostate cancer deaths were moderate or severe comorbidity (hazard ratio [HR] 3.15), BMI ≥27.4 (HR 2.98), and increasing age at PSA recurrence (HR 1.17).
Conclusions: Age, BMI, and comorbidity may help predict non-prostate cancer deaths in patients experiencing biochemical recurrence after RT for prostate cancer. This information may guide the decision to initiate HT in these patients.
Reviewer's Comments: In the setting of biochemical failure after primary RT for prostate cancer, most men will be started on salvage HT at some point, although there is limited evidence to support the timing of this strategy. Side effects of HT are becoming clearer all the time and they are not subtle. Ways to predict who would benefit the most from HT and who can effectively be surveyed are therefore welcome. This study takes a different approach than most, by looking for predictors of non-prostate cancer death. The authors found that in this setting, age >76 years, BMI >27 kg/m2,and a comorbidity score of intermediate to severe were significant predictors for risk of non-prostate cancer death. To add clinical utility to this information they created risk groups associated with 5-year, non-prostate cancer mortality, demonstrating 0% for low risk, 19% for intermediate (no-to-mild comorbidity, higher age, and BMI) and 38% for high risk (moderate-to-severe comorbidity). These risk groups could potentially be used to guide HT decisions in these patients. For example, patients with low prostate cancer death risk (eg, long PSA doubling time), but higher non-prostate cancer death risk, HT might be strategically put on hold in a surveillance fashion. While the data presented here are retrospective and limited, the concept is thought provoking and the information may be very useful for some practitioners. (Reviewer-Steven E. Canfield, MD).

Keywords: Prostate Cancer, Biochemical Failure, Hormonal Therapy

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Satraplatin in End-Stage Prostate Cancer -- Survival Not Improved

Multinational, Double-Blind, Phase III Study of Prednisone and Either Satraplatin or Placebo in Patients With Castrate-Refractory Prostate Cancer Progressing After Prior Chemotherapy: The SPARC Trial.

Sternberg CN, Petrylak DP, et al:

J Clin Oncol 2009; 27 (November 10): 5431-5438

A small delay in progression was achieved with satraplatin in end-stage prostate cancer, with no overall survival benefit. The added toxicity may not be worth this benefit.

Objective: To determine if, in men with metastatic, castrate-refractory prostate cancer (CRPC), satraplatin plus prednisone compared to prednisone alone can improve progression free (PFS) and overall survival (OS).
Design/Methods: 951 patients were randomized in 2:1 fashion to receive satraplatin plus prednisone or placebo plus prednisone and continued until progression, toxicity withdrawal, or death. Study was blinded at all important points.
Results: Median PFS was 11.1 weeks (95% CI, 10.3 to 12.3 weeks) for satraplatin versus 9.7 weeks (95% CI, 9.3 to 10.0 weeks) for placebo arm (*P* =0.001). There was a 33% risk reduction for progression noted for satraplatin (hazard ratio 0.67), but there was no overall survival benefit. There was also a 36% reduction in "time to pain progression", a secondary endpoint.
Conclusions: Satraplatin provided a small progression delay for metastatic CRPC patients but no survival benefit.
Reviewer's Comments: There remains little hope for men with metastatic, castrate-resistant prostate cancer. Docetaxel based therapies are currently the only regimens with proven survival benefit, of only about 2-3 months. This disease state will continue to be a heavy focus of prostate cancer research as there is so much room for improvement and so little headway. The Satraplatin and Prednisone Against Refractory Cancer (SPARC) trial is a very well done study of satraplatin, an oral platinum drug which showed promise due to its ability to overcome resistance seen with similar compounds. While progression and pain were slowed in the satraplatin arm, survival was not improved. Additional toxicity from the drug included gastrointestinal and myelosuppressive effects and serious adverse events were significantly higher with satraplatin than placebo (8.7 vs 2.9%, respectively). Therefore, the question remains whether or not a patient would opt for these benefits over these risks. Given the absence of a survival benefit, the trade off may not seem worthwhile. (Reviewer-Steven E. Canfield, MD).

Keywords: Prostate Cancer, Castrate-Resistant, Satraplatin

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Medical Expulsive Therapy for Urolithiasis Underutilized

Trends in Medical Expulsive Therapy Use for Urinary Stone Disease in U.S. Emergency Departments.

Hollingsworth JM, Davis MM, et al:

Urology 2009; 74 (December): 1206-1209

Medical expulsive therapy for urolithiasis has had sluggish dissemination into the broader medical community.

Objective: To determine the uptake of medical expulsive therapy (MET) to promote stone passage in the broader medical community.
Design: Retrospective, national health care survey review.
Methods: Data were analyzed from the National Hospital Ambulatory Medical Care Survey (2000-2006). Sampled emergency department (ED) visits for stones were identified. Use of MET was determined by prescription of a calcium channel blocker or α-blocker at the ED visit. National estimates of the prevalence of MET use were then computed. Logistic regression was used to examine linear and nonlinear time trends in MET prescription.
Results: MET usage increased throughout the study period. The odds of being treated with a medical expulsion approach more than doubled each successive year. However, overall prevalence of use was only 1.1% during this time frame. Based on previous randomized controlled trials and the number needed to treat of 4, this implies a missed opportunity to spare approximately 260,000 individuals annually from stone surgery and its risks.
Conclusions: Despite the growing body of evidence to support its safety and efficacy, this analysis reveals sluggish dissemination of MET into the broader medical community. This likely represents a block in the translation of clinical science into practice and raises quality of care concerns.
Reviewer's Comments: Over 11 randomized, controlled trials (along with several meta-analyses) have been published demonstrating the benefit of medical expulsive therapy for ureteral calculi. The 2007 American Urological Association practice guidelines for ureteral calculi management also have MET as a recommended part of the treatment algorithm. Even with this information, routine use of medical expulsive therapy by urologists has been slow, so I am not surprised that it has not disseminated into the broader medical community. Some roadblocks to this information dissemination include: the fact that nearly all medical expulsive therapy articles have been published in subspecialty urology journals; the use of calcium channel blockers and alpha blockers for medical expulsive therapy is off-label use of these medications; and limited indications (ureteral stones <10 mm) even in our urology guidelines. However, I believe we (as urologists) need to do a better job in using MET ourselves, and also do a better job of educating our colleagues in emergency medicine, family practice, and internal medicine on the benefits of MET for ureteral calculi. (Reviewer-David A. Duchene, MD).

Keywords: Renal Colic, Urolithiasis, Medical Expulsive Therapy, Practice Trends

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Preexisting Ureteral Stent May Increase Ureteroscopic Success

Impact of Preoperative Ureteral Stenting on Outcome of Ureteroscopic Treatment for Urinary Lithiasis.

Shields JM, Bird VG, et al:

J Urol 2009; 182 (December): 2768-2774

Preplaced ureteral stents have a trend towards better success during ureteroscopy, but are not necessary in most patients.

Objective: To determine impact of preexisting ureteral stents on outcomes of ureteroscopic management for urinary lithiasis.
Design: Retrospective chart review.
Participants: 259 ureteroscopic procedures for both ureteral and renal calculi over 5 years.
Methods: Data were abstracted on stone side, size, number and site, patient demographics, total stone burden, use of ureteral access sheath, preoperative ureteral stent, ureteroscopy type, and outcome. Statistical analysis was performed.
Results: Success rate of 1 and 2 ureteroscopic procedures was 86.9% and 97.3%, respectively. Primary analysis concentrated on the 221 initial procedures. Success by location included 91.9% for the distal ureter, 89.7% for the proximal ureter, 83.3% for renal pelvis, 80.5% for lower pole, and 82.4% for the interpolar/upper pole. Success was negatively associated with primary stone size (P =0.02), total stone number (P =0.001), and cumulative stone burden (P <0.001). Stone site was not a statistically significant predictor of success (P =0.394). A preexisting stent was positively associated with success, but it was not statistically significant (P =0.254).
Conclusions: Ureteroscopic lithotripsy and stone extraction for ureteral and renal calculi may be performed with a high success rate. Success is significantly inversely related to stone size, cumulative stone burden, and number of stones. Success is positively related to a preexisting ureteral stent, but not to a statistically significant degree.
Reviewer's Comments: This article is a nice review of a modern series of ureteroscopic treatment of ureteral and renal calculi. Primary endpoint of whether preexisting stents affected success rates did not reach statistical significance, but did show a trend in favor of preexisting ureteral stents. Interestingly, twice the number of patients treated successfully had a preexisting ureteral stent which demonstrates the practice/referral pattern at their institution. Stents passively dilate the ureter and allow easier access of the ureteroscope, better ability to place a ureteral access sheath, and better navigation capabilities once in the collecting system. It is rare not to be able to gain access to the ureter if a stent has been preplaced, and I am not surprised that the success rates trended towards better success with a preexisting stent. However, as shown in the study, many individuals without a stent had successful outcomes. Therefore, it is not necessary to subject all patients to the morbidities of an indwelling ureteral stent prior to ureteroscopy. If one is unable to be successful during initial ureteroscopy without a preexisting stent, then a stent can be placed at that time and another attempt can be made after passive ureteral dilation. (Reviewer-David A. Duchene, MD).

Keywords: Ureter, Ureteroscopy, Stents, Urolithiasis, Lithotripsy

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Renal Artery Pseudoaneurysm Delays After Partial Nephrectomy

Renal Artery Pseudoaneurysm Following Laparoscopic Partial Nephrectomy.

Shapiro EY, Hakimi AA, et al:

Urology 2009; 74 (October): 819-823

Renal artery pseudoaneurysms typically present as a delayed hemorrhage with gross hematuria, flank pain, and a decreased hematocrit.

Objective: To present experience in managing renal artery pseudoaneurysms following laparoscopic partial nephrectomy (LPN).
Methods: From 259 LPNs, charts of patients diagnosed with a delayed hemorrhage were further investigated finding 6 patients (2.3%) with renal artery pseudoaneurysms. Patients were characterized based upon preoperative cross-sectional imaging and operative data. Of the 6 patients, 4 had primarily exophytic tumors and 2 had endophytic tumors. Renal hilar control was gained with clamping of vessels. All tumors were resected with entry into the collecting system. Collecting systems were repaired with renorrhaphy in all cases. At the surgeon's discretion, the argon beam coagulator, FloSeal and Tissel was used.
Results/Conclusions: Mean estimated blood loss was 408 mL. No patients required intraoperative transfusions, and there were no intraoperative complications. After surgery, 5 patients were discharged on mean postoperative day 4.2 with a stable hematocrit and no clinical signs of bleeding. The remaining patient presented while still in the hospital. Initial presentation of the delayed hemorrhage occurred on mean postoperative day 12. Of patients, 5 presented with complaints of gross hematuria, and 2 of these patients complained of flank pain. The sixth patient was diagnosed incidentally with pseudoaneurysm on renal ultrasound. All patients presented with a decreased hematocrit relative to their discharge hematocrit (38.8% vs 25.7%). Of patients, 3 required blood transfusions. Angiography with superselective embolization with platinum microcoils was performed in all cases. One patient developed recurrent gross hematuria and was found to have 2 newly diagnosed pseudoaneurysms which were also embolized. Otherwise, at follow-up with CT or MRA, all six patients were free from recurrence.
Reviewer's Comments: The most disturbing aspects of renal artery pseudoaneurysms after laparoscopic partial nephrectomy are that no predisposing factor for their development can be identified, they typically become symptomatic after discharge from the hospital, and they can result in life-threatening hemorrhage. Fortunately, they consistently present with gross hematuria and flank pain, are reliably diagnosed with CT or MRA, and are easily treated by minimally invasive angioembolization. The article underscores the importance of patient education for the possibility of renal artery pseudoaneurysm and maintaining a high index of suspicion in symptomatic patients that present with a drop in hematocrit. (Reviewer-Kyle J. Weld, MD).

Keywords: Renal Parenchymal Tumors, Laparoscopy, Complications, Pseudoaneurysm

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NOTES Is Feasible Option for Partial Cystectomy

Pure Natural Orifice Translumenal Endoscopic Surgery Partial Cystectomy: Intravesical Transurethral and Extravesical Transgastric Techniques in a Porcine Model.

Sawyer MD, Cherullo EE, et al:

Urology 2009; 74 (November): 1049-1053

Partial cystectomy via natural orifice translumenal endoscopic surgery is feasible.

Objective: To describe 2 pure natural orifice translumenal endoscopic surgeries (NOTES) for partial cystectomy in a porcine specimen.
Methods: For transurethral procedures, a 22 French rigid cystoscope was placed into the bladder, urine was evacuated, and the bladder was distended with carbon dioxide gas through the irrigation port. The bladder was marked with electrocautery at intended area of excision. An endoscopic loop device was placed through one port of the cystoscope and deployed around planned resection site. Using a flexible toothed grasper through the other port of the cystoscope and through the loop, center of the pseudotumor was grasped and invaginated through the loop and into the lumen of the bladder. With the loop surrounding the intended area of excision, the loop was cinched. A second loop was positioned and cinched around the tumor. The full-thickness bladder segment was excised using the cutting current. The bladder defect was then reapproximated with endoscopic clips. The transgastric partial cystectomy involved use of a standard dual channel gastric endoscope which was advanced into the stomach transorally. A small anterior gastrotomy was made through which the scope was passed, and a pneumoperitoneum was established. Using a similar technique as described above with endoscopic loops and graspers, a full-thickness bladder segment was excised. Because of the extravesical approach, the specimen was enclosed with the mucosal surface of the bladder on the inside. Endoscopic clips were then applied to reinforce the bladder defect. The gastrotomy site was not closed in the transgastric case which was a porcine non-survival case.
Results/Conclusions: For the 4 transurethral cases, 2 were survival cases for which no complications or leaks were observed.
Reviewer's Comments: The authors present another step forward in the development of NOTES. I think the transvesical approach is most appealing to urologists because of our familiarity with cystoscopic procedures. The use of the various endoscopic loops to facilitate these partial cystectomies provides the advantage of preventing potential urine spillage with tumor seeding. However, invaginating the portion of the bladder to be resected could pull adjacent extravesical structures with it that might be injured. Also, because of the thickness of the human bladder relative to the porcine bladder, the loop maneuver may become more technically challenging in human trials. As technology improves, multiple instruments and techniques will need to be evaluated to determine the safest and most efficient method. I congratulate the authors on their presentation of the first partial cystectomies via NOTES. (Reviewer-Kyle J. Weld, MD).

Keywords: Bladder Tumor, Partial Cystectomy, Natural Orifice Translumenal Endoscopic Surgery

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Targeting Afferent Nerves for OAB Treatment

Cizolirtine Citrate Is Safe and Effective for Treating Urinary Incontinence Secondary to Overactive Bladder: A Phase 2 Proof-of-Concept Study.

Zát'ura F, Všetica J, et al:

Eur Urol 2010; 57 (January): 145-153

Cizolirtine citrate maybe useful for treatment of overactive bladder, as an alternative or adjunct to standard muscarinic therapy, once its safety and efficacy profile are confirmed in phase 3 clinical trials.

Objective: To demonstrate the efficacy and safety of oral cizolirtine citrate for the treatment of overactive bladder (OAB).
Design: Randomized, double-blind, placebo, active-controlled multicenter trial.
Methods: Trial was carried out in 12 centers. Randomization was to cizolirtine, placebo, or oxybutynin. Eligibility criteria included age 18 to 80 years, a diagnosis of urinary incontinence with both urgency idiopathic detrusor overactivity confirmed on urodynamics, and >8 micturitions per day with 1 urge incontinence episode on a 24-hour diary. Patients were excluded if they were pregnant, breast-feeding, undergoing pharmacologic therapy for incontinence with diuretics, benzodiazepines, α-agonists or antagonists, or on medications with significant anticholinergic side effects.
Results/Conclusions: The majority of patients in this trial were female (92.6%) with a mean age of approximately 52 years. A significantly larger proportion of patients in the cizolirtine group left the study prematurely: 28.0% versus 5.6% in the placebo group and 11.1% in the oxybutynin group. The proportion of patients achieving <8 voids per 24 hours, complete dryness, or both at the end of treatment period was similar for cizolirtine (33.4%) and oxybutynin (34.3%) and greater than placebo (17.0%). It should be noted that cizolirtine caused fewer antimuscarinic but more gastrointestinal (nausea) and neurologic (headache, vertigo) side effects than oxybutynin.
Reviewer's Comments: Cizolirtine citrate is an inhibitor of calcitonin and gene related peptide (CGRP) and substance P release. Its mechanism of action reinforces the hypothesis that afferent abnormalities are important in the etiology of OAB. It is noteworthy because it is one of several medications in development that target afferent nerves to treat OAB. (Reviewer-Karl J. Kreder, MD).

Keywords: Cizolirtine, Efficacy, Overactive Urinary Bladder, Urinary Incontinence

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Cure Rate Drops With Repeat Versus Primary Sling Procedures

Repeat Synthetic Mid Urethral Sling Procedure for Women With Recurrent Stress Urinary Incontinence.

Stav K, Dwyer PL, et al:

J Urol 2010; 183 (January): 241-246

A repeat synthetic mid-urethral sling has a significantly lower cure rate and a higher incidence of de novo urgency and urge incontinence than a primary procedure.

Objective: To compare outcomes of repeat mid-urethral sling with primary mid-urethral sling in women with stress urinary incontinence (SUI).
Design: Retrospective review.
Methods: 1225 consecutive women with a mean age of 60±12.9 years underwent a mid-urethral sling between May 1999 and August 2007. Intrinsic sphincter deficiency (ISD) was defined as either maximum urethral closure pressure (MUCP) ≤20 cm H_2O or a Valsalva or cough leak point pressure of ≤60 cm H_2O. Of slings, 78% were retropubic and 22% were transobturator. Postoperatively, patients were scheduled for evaluation at 6 weeks, 6 and 12 months, and annually thereafter; however, most patients did not return after their second or third follow-up visit. The authors therefore interviewed these patients by telephone call with a structured questionnaire examining for urinary symptoms.
Results/Conclusions: Of patients, 77 had a repeat mid-urethral sling. Patients who underwent a repeat sling had significantly more ISD and a significantly lower preoperative MUCP compared to women who had a primary sling. Overall subjective cure rate was 85% in the primary sling group and 62% in the repeat sling group (*P* <0.001). Incidence of de novo urge urinary incontinence was significantly higher in patients undergoing a repeat sling (22% vs. 5%; *P* <0.001).
Reviewer's Comments: I believe this is the largest study to date of repeat mid-urethral slings in the literature. It is limited by its retrospective nature; however it may be helpful in counseling patients as to expected side effects and efficacy rates when undergoing a repeat sling procedure. Ideally, a prospective study to further investigate repeat sling procedures will be done in the future. (Reviewer-Karl J. Kreder, MD).

Keywords: Recurrence, Stress Urinary Incontinence, Suburethral Slings, Reoperation

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Female Sexual Dysfunction Underestimated, Undertreated

The Place of Female Sexual Dysfunction in the Urological Practice: Results of a Dutch Survey.

Bekker M, Beck J, et al:

J Sex Med 2009; August 17 (): epub ahead of print

Urologists underestimate prevalence of female sexual dysfunction and do not provide routine screening, assessment, or treatment.

Background: Data on the sexual function of females are lacking.
Objective: To assess perceived prevalence of female sexual dysfunction (FSD) and FSD screening and assessment practices among Dutch urologists.
Design/Participants: Anonymous mailed survey completed by 186 Dutch urologists.
Methods: Bivariate analysis of survey responses and demographic information of respondents.
Results: Of 405 urologists contacted, 190 responded and 186 eligible surveys were included in the analysis. Of urologists, 5.4% reported asking every female patient for sexual function; 81.8% reported asking for sexual function when a patient had a specific urologic complaint. The most commonly reported reason for not asking was that the urologist did not find it meaningful in urological practice (40.3%), followed by insufficient knowledge about how to ask (22.7%), lack of time (18.2%), lack of knowledge in therapeutic options (13.6%), and difficulty bringing up the topic (10.8%). The majority of surveyed urologists estimated FSD prevalence to be less than the documented prevalence of 48% to 64% in female urology patients. Of respondents, 37.8% estimated <10% of patients have FSD; 22.8% estimated 11% to 20%; 20.6% estimated 21% to 30%; 10% estimated 31% to 40%; 6.7% estimated 41% to 50%; and 2.2% estimated 51% to 60%. No respondents considered a prevalence >60%. A majority of respondents do address FSD prior to radical cystectomy, simple cystectomy, and incontinence surgery; however, only 47.3% ask about changes in FSD after these surgeries. Of respondents, 91.4% agree FSD topics should be included in urology residency programs.
Conclusions: Urologic assessment of female sexual dysfunction is suboptimal, as urologists underestimate prevalence of these problems and do not address FSDs routinely with patients. Undergraduate and postgraduate urology programs should include FSD training and education.
Reviewer's Comments: Awareness of prevalence of and treatment for FSD is decades behind male sexual dysfunction. In contradistinction, data on FSD prevalence in the general population is available and estimated around 43%. Of women with FSD, 12% to 24% state it causes personal distress. When looking at females in a urologic practice, these numbers clearly increase. Based on previous studies from the American Urogynecologic Society (AUGS) and the British Society of Urogynecology (BSUG), estimates from Dutch physicians responding to this survey seem comparable to American physicians. Cystectomy, prolapse, and incontinence surgery all have previously been shown to adversely affect FSD. Just as erectile dysfunction must be discussed and addressed prior to and after radical prostatectomy, FSD should be discussed and addressed prior to and after cystectomy, prolapse, and incontinence surgery. With the appropriate commitment and allocation of resources to female sexual dysfunction, both urologists and urogynecologists have the opportunity to become leaders in a field currently in its infancy. (Reviewer-Tobias S. Kohler, MD).

Keywords: Female Sexual Dysfunction, Urological Practice

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Testosterone Replacement Therapy Continuously Evolving

Subcutaneous Testosterone Pellet Implant (Testopel®) Therapy for Men With Testosterone Deficiency Syndrome: A Single-Site Retrospective Safety Analysis.

Cavender RK, Fairall M:

J Sex Med 2009; September 29 (): epub ahead of print

Testopel®appears to be a safe and effective alternative to other testosterone replacement strategies. True comparative cost-benefit information is yet to be determined.

Backgound: Testopel® is the only testosterone pellet implantation product available in the United States. Previously reported adverse event rates, such as pellet extrusion (8.5 % to 12%) or local infection (1.4% to 6.8%), are specific to Organon (Cambridge, United Kingdom) implants, which are larger than Testopel and have an irregular surface. However, limited studies exist on the adverse effects Testopel implantation.
Objective: To report the safety and efficacy of Testopel subcutaneous testosterone pellet implantation for the treatment of testosterone deficiency syndrome.
Design: Single-site, retrospective chart review.
Methods: Charts of Testopel patients from December 2003 to April 2008 were reviewed. Implantation technique is modified such that pellets were implanted side-by-side rather than end-to-end in the conventional technique. Primary outcome measure was local infection prevalence, pellet extrusion, and other adverse events. Patient satisfaction and relevant biochemical response to testosterone replacement was also assessed.
Results: 80 men met inclusion/exclusion criteria in whom 292 Testopel pellet implantation procedures were performed. Only 4 adverse events occurred: self-limited contact dermatitis from sterile adhesive strips, self-limiting local reaction, local infection of the pellet insertion tract, and immunologic foreign body reaction. The immunologic reaction occurred in a patient with previous similar reactions to testosterone injection or topical application. This patient required pellet excision six months later due to pain and lack of pellet dissolution. No other adverse event required treatment. Of patients, 69 reported satisfaction (86%) and testosterone level was significantly higher than baseline.
Conclusions: Testopel appears to have a lower prevalence of infection or pellet extrusion (0.3%) than historically reported for the Organon testosterone pellet. Along with effective testosterone replacement, Testopel may be safer than previously considered.
Reviewer's Comments: Testosterone replacement methodologies continue to evolve. Beyond bimonthly or monthly injections, which tend to be the most cost-effective strategies for those with suboptimal insurance, testosterone gels are readily available. Although not a new approach, long acting treatments including both Testopel and soon-to-be-released long-acting depot testosterone injections will likely have the highest patient convenience and most stable testosterone levels. My personal experience with pellet extrusion and medication seepage with Testopel has led me to close the incision with an interrupted suture. I have also had better luck with using 2 parallel rows for pellet placement. Metabolism of the testosterone pellets seems to be highly variable; a rough guideline is an increase of 25 ng/dL per pellet. However, in the study, the number of pellets used ranged from 6 to 20, with a mean of 13 pellets. This resulted in a mean testosterone change from 318 ng/dL to 619 ng/dL at a mean of 2 months follow-up. Thus, at least initial close follow-up of patient testosterone levels and symptomatology is required to establish the ideal individualized dosing regimen for number of pellets (I currently start with 10 to 12 pellets) and length of efficacy (2 to 6 months in my experience). This information is crucial for comparative cost-benefit analysis. (Reviewer-Tobias S. Kohler, MD).

Keywords: Testosterone, Subcutaneous Testosterone Pellet Implantation, Hypogonadism, Testosterone Deficiency Syndrome

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