Race Associated With Outcome in Early Stage Bladder Cancer

Racial Differences in Treatment and Outcomes Among Patients With Early Stage Bladder Cancer.

Hollenbeck BK, Dunn RL, et al:

Cancer 2009; October 28 (): Epub ahead of print

Black patients are at increased risk of death due to bladder cancer that does not appear to be influenced by differences in intensity of treatment or quality of care.

**Objective:** To analyze the outcomes by race of patients treated for early stage bladder cancer to determine if quality of care influences survival.

**Methods:** This study evaluated Surveillance, Epidemiology, and End Results (SEER)-Medicare linked dataset of patients with early stage bladder cancer between 1992 and 2002. Multivariate models analyzed the association between race and survival. Additional analysis examined whether the findings could be accounted for by differences in intensity of care or provider characteristics.

**Results:** There were small differences by race in how patients were managed. Black patients were more likely to undergo re-staging evaluations and cytology, whereas they had fewer endoscopic evaluations. Rates of aggressive therapy, such as cystectomy, did not vary by race. Black patients were at a 23% increased risk of death from any cause and 79% increased risk of death due to bladder cancer compared to white patients. This changed only marginally after accounting for differences in intensity of care and differences in providers.

**Conclusions:** Black patients with early stage bladder cancer are at an increased risk of death that does not appear to be influenced by differences in quality of care.

**Reviewer's Comments:** For some time now it has been appreciated that, for muscle invasive bladder cancer, there is a racial disparity in outcomes with black patients generally doing worse than white patients. To a significant degree, this difference appeared to be partially due to differences in quality of care and access to care. Whether such differences exist by race for patients with earlier stage disease and whether similar forces are at work was not known. This study is important in that it begins to address that very issue. Intriguingly, it appears that black patients have worse overall and cancer-specific survival than white patients with early stage bladder cancer even after accounting for differences in stage, grade, and quality of care. This raises the possibility that perhaps the differences may be related to unmeasured differences at a more biologic level. Perhaps this could be due to polymorphic differences in genes important in bladder cancer. The results from this trial support this hypothesis, but it is important to remember that any administrative database study, such as this one, has built in limitations that are well accepted. These include the inability to measure or account for some confounders and the fact that the results may not be generalizable to the whole population. The specific example here would be that this study could only include patients aged ≥65 years since it was linked to Medicare. Despite these limitations, this study raises an intriguing hypothesis that biology may be driving some of the differences seen here and more work is now needed to validate and test this hypothesis in future studies. (Reviewer-Peter E. Clark, MD).

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Keywords: Racial Disparity, Bladder Cancer, Treatment, Survival

Print Tag: Refer to original journal article
Patients with tumors >4 cm must be selected very carefully due to an increased risk of progression or death due to RCC.

Objective: To assess the outcomes among patients with a renal mass managed by observation due to advanced age or significant comorbidities.

Design/Participants: Retrospective cohort study of 63 patients between 2002 and 2007 with a renal mass concerning for malignancy who were managed by observation.

Methods: Mean patient age was 76.6 years. Mean tumor size was 4.3 cm. One third had poor performance status, >75% were ASA class 3 or higher, and patients had an average of 3 other medical conditions in addition to the mass.

Results: 5-year overall survival was 43%, but cancer-specific survival was high at 93%. Size was associated with cancer-specific survival, which was 100% at 5 years in those with tumors <4 cm compared to 83% in those with tumors >4 cm in size. In the subset of patients who ultimately had a histopathologic diagnosis, 83% had renal cell carcinoma (RCC). Only 1 tumor (3.7%) <4 cm grew faster than 1 cm per year, while this was true in 36% of tumors >4 cm.

Conclusions: Observation may be an option in patients with a renal mass <4 cm in size who are elderly or have multiple comorbidities. Those with tumors >4 cm must be selected very carefully due to an increased risk of progression or death due to RCC.

Reviewer's Comments: The management of patients with renal masses concerning for carcinoma has grown increasingly complex. Twenty years ago most were managed with nephrectomy, but now the options have expanded to include partial nephrectomy and ablative technologies delivered either laparoscopically or percutaneously. With all these variations, there is a growing appreciation that perhaps not all renal masses require immediate intervention. This concept has been explored quite extensively in the group of patients with tumors <4 cm in size who can do well with observation for up to 2 to 3 years. The tumor growth rates have generally been slow and the rates of progression to metastases or death due to carcinoma have been very low. This study adds to that literature by including in their analysis a significant number of tumors >4 cm in size. The key finding is that, even in an elderly population with significant comorbidities, there is an increased risk of death due to carcinoma in those with the larger tumors. This is a very important caveat to bear in mind when considering the options for management in the frail or elderly patient. Those with tumors >4 cm may be considered more heavily for an active intervention rather than observation. Failing that, they must be observed with increased scrutiny since the tumor growth rates are much higher as is their risk of death due to cancer. (Reviewer-Peter E. Clark, MD).

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Keywords: Observation, Renal Mass, Elderly, Comorbidity

Print Tag: Refer to original journal article
α-Blocker Impacts Stone-Free Rates After SWL

Is There an Adjunctive Role of Tamsulosin to Extracorporeal Shockwave Lithotripsy for Upper Ureteric Stones: Results of an Open Label Randomized Nonplacebo Controlled Study.

Agarwal MM, Naja V, et al:

Urology 2009; 74 (November): 989-992

In this study, stone-free rates were 2 times higher a week after shockwave lithotripsy if patients were given α-blockers.

Background: α-blockers have been demonstrated to be effective for medical expulsive therapy.

Objective: To evaluate the role of tamsulosin as an adjunct to shockwave lithotripsy (SWL) for upper ureteric stones.

Design: Prospective randomized open-label non-placebo controlled trial.

Participants: 40 patients with upper ureteric stones <15 mm in size.

Methods: Patients were randomized to take tamsulosin 0.4 mg daily or no medication for up to 3 months after SWL. SWL was performed with the Lithostar Multiline (Siemens, AG Medical Engineering) electromagnetic lithotripter at a rate of 120 shocks/minute, for a maximum of 3500 shocks. SWL was repeated at weeks 1, 3, and 5 if residual stones were demonstrated on KUB.

Results: Success rate was higher after 1 SWL in those treated with tamsulosin (55%) compared to those not treated (25%). No significant difference was seen in number of days to stone passage, pain scores, need for auxiliary procedures, development of steinstrasse, or number of SWL sessions required (average, 2).

Conclusions: Tamsulosin improves the clearance of upper ureteric stones after SWL.

Reviewer's Comments: The study is limited by a lack of placebo control and this would be a bigger issue had the authors noted an improvement in pain scores with tamsulosin. The study is also limited by the reliance on KUB for stone-free results. The authors note that stone size correlated with the number of sessions required, days needed for stone passage, and level of pain intensity. In view of this, it would be useful to perform a multivariate logistic regression to confirm that the use of α-blockers remains a significant variable to explain stone-free rates. Alternatively, it may be useful to evaluate the results stratified by stone size to determine if the impact of α-blockers is seen primarily with larger stones as compared to smaller stones. Indeed, it was noted that steinstrasse developed in two thirds of patients with stones >10 mm. The authors’ approach to repeat shockwave at 1 week diverges from common practice in the United States. It would be helpful to evaluate the stone-free rate and ancillary procedure rate at 2 to 4 weeks following single-session SWL. The authors have not adapted the techniques of ramp-up in energy settings or slow-treatment rates that have been demonstrated to improve stone fragmentation and decrease fragment size. With smaller fragment size, it is possible that the advantage of α-blockers may diminish. (Reviewer-Manoj Monga, MD).

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Keywords: Shockwave Lithotripsy, Ureteral Calculus

Print Tag: Refer to original journal article
Either α-blockers or anticholinergics help alleviate ureteral stent-related urinary symptoms and pain.

**Objective:** To evaluate the effects of tolterodine and alfuzosin on ureteral stent-related symptoms.

**Design:** Prospective randomized placebo-controlled study.

**Participants:** 52 patients undergoing ureteral stent placement following ureteroscopy, percutaneous nephrolithotomy, and ureteroplasty.

**Methods:** The Ureteral Stent Symptom Questionnaire was administered 6 weeks after stent placement.

**Interventions:** Patients received 4 mg tolterodine extended release (ER) daily, alfuzosin 10 mg daily, or placebo for 6 weeks.

**Results:** Significant improvements in urinary symptoms, pain scores, and analgesic use were noted with each medication compared to placebo. No significant difference was noted between the 2 medications. Urinary frequency was decreased with each medication, though urinary urgency and nocturia was decreased with tolterodine only. No significant difference was noted in general health, sexual health, or work performance scores.

**Conclusions:** Tolterodine ER and alfuzosin each improve ureteral stent-related pain and urinary symptoms.

**Reviewer's Comments:** The authors present a heterogeneous group of patients undergoing ureteroscopy, percutaneous nephrolithotomy, or ureteroplasty. Indeed, the associated pain, morbidity, incisional discomfort, and risk of urinary or irrigant extravasation vary greatly between these 3 surgical groups. Unfortunately, evaluating the primary end point at 6 weeks introduces another limitation of the study. Typically, ureteral stents are left indwelling for only 5 to 10 days after an endoscopic urologic procedure; therefore, the impact of adjunct medical therapy on pain and urinary symptoms must be evaluated earlier in the postoperative course than was conducted in this study. The authors do not report their method of randomization or allocation -- indeed there is imbalance in numbers between the treatment and placebo groups. It is not reported as to whether patients and physicians were blinded to the treatment allocation. The authors do not present a power analysis to justify their sample size, yet they do note that the study was terminated early due to difficulty with recruitment. A study evaluating combination therapy would be a natural extension of this clinical trial. (Reviewer-Manoj Monga, MD).

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**Keywords:** Ureteral Stent, Pain, α-Blocker, Anticholinergic

**Print Tag:** Refer to original journal article
Management of post-varicocelectomy hydroceles should be conservative for 18 to 24 months, with a minimum of 3 aspirations where indicated.

**Objective:** To assess aspiration alone as a modality in the treatment of post-varicocelectomy hydrocele.

**Design/Methods:** A retrospective review was performed to identify patients having undergone varicocelectomy with the subsequent development of hydrocele. Over an 18-year period (1990 to 2008), 256 varicocelectomies were considered. Patients with postoperative hydroceles were reexamined every 3 months. After 2 consecutive visits with an enlarged hydrocele (>20 mL), aspiration was performed ≥3 times before offering surgical repair. This was performed in the office setting, and the volume of aspirate recorded.

**Results:** 31 patients (11%) developed postoperative hydroceles after laparoscopic varicocelectomy. All were noted to develop within the first 6 months of follow-up. Age of patients ranged from 14 to 18 years. Nine (29%) underwent surgical hydrocelectomy after 3 aspirations. Seven (22%) had spontaneous resolution of the hydrocele. Fifteen patients (49%) were treated with aspiration only. Volume aspirated correlated with success, with <50 mL aspirated yielding resolution in 60% of patients. Complications included scrotal hematomas, which developed in 2 patients.

**Conclusions:** Aspiration is effective in treating post-varicocelectomy hydroceles. Management of post-varicocelectomy hydroceles should be conservative for 18 to 24 months, with a minimum of 3 aspirations where indicated.

**Reviewer's Comments:** The authors present their algorithm for treating post-varicocelectomy hydroceles. Aspirating the hydrocele in the office setting seems well tolerated and I have used it in my practice. It is certainly appealing when compared to re-operation with its associated cost, post-surgical pain, edema, and convalescence. This information is also helpful in preoperative counseling to reassure patients that if a postoperative hydrocele develops, it will most likely respond to observation or aspiration. (Reviewer-John Gatti, MD).

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Keywords: Varicocele Hydrocele Aspiration

Print Tag: Refer to original journal article
Progressive perineal dilation is effective in creating a functional neovagina in women with vaginal agenesis with high success and minimal morbidity.

**Objective:** To report the authors’ experience over a 12-year period with progressive perineal dilation as a minimally invasive technique to create a functional vagina in the setting of vaginal agenesis.

**Design/Methods:** A retrospective review was performed over a 12-year period identifying women with vaginal agenesis who elected progressive perineal dilation with vaginal dilators 2 to 3 times daily for 20 minutes. Success was defined as the ability to achieve sexual intercourse, vaginal acceptance of the largest dilator without discomfort, or a vaginal length of 7 cm.

**Results:** 69 females met inclusion criteria. Mayer-Rokitansky-Küster-Hauser syndrome was the predominant diagnosis (n=64). Age ranged from 14 to 35 years and mean follow-up was 19 months. Four patients were lost to follow-up, 7 patients (12%) failed due to noncompliance, 50 (88%) achieved functional success at median of 18 months, and 8 were currently enrolled in the program at the time of report. Success correlated with frequent dilation and the initiation of sexual activity. Complications were minor. Eighteen sexually active patients reported satisfactory intercourse without dyspareunia.

**Conclusions:** Progressive perineal dilation is effective in creating a functional neovagina in women with vaginal agenesis with high success and minimal morbidity. Given its lower complication rate compared to published surgical series, it should be offered as first-line therapy.

**Reviewer's Comments:** The authors report their extensive experience with perineal dilation for vaginal agenesis. They argue that this technique has a high success rate and minimal morbidity. Proponents of bowel vaginoplasty argue that bowel substitution may not require long-term dilation and is not as prolonged a process. The debate will not end here. The take-home message is that perineal dilation is a safe and successful technique in those who are motivated to dilate. In the setting of failure, these patients may actually be better candidates for more aggressive surgical repair, given their self-dilating experience. (Reviewer-John Gatti, MD).

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Keywords: Vaginal Agenesis, Dilation, Mayer-Rokitansky-Küster-Hauser Syndrome

Print Tag: Refer to original journal article
Obturator approaches appear to have similar long-term results irrespective of surgical approach.

**Objective:** To compare overall surgical outcomes as well as subjective quality-of-life perceptions of 2 different procedures, tension-free "inside-out" (TVT-O) and Monarc (outside-in) transobturator tapes after a minimum 2-year follow-up.

**Design/Methods:** This is a prospective comparison of 2 groups, one undergoing ‘outside-in’ and the other undergoing ‘inside-out’ transobturator approaches. In total, 191 patients were included, with 93 receiving TVT-O and 98 receiving outside-in (Monarc) for treatment of genuine stress urinary incontinence (SUI). All patients underwent preoperative evaluation as well as short form version of Incontinence Impact Questionnaire-7 and Urogenital Distress Inventory-6 for follow-up of quality of life. In addition, all patients were assessed for a cure of SUI as voiced by any loss of urine with physical activity. Additionally, complications—immediate and chronic—were also assessed.

**Results:** Between 2 and 4 years (span of follow-up), 72% of TVT-O inside-out patients were cured of their incontinence whereas 65% of the outside-in (Monarc) were cured. Another 12% and 21%, respectively, were improved over their baseline status. Interestingly, quality-of-life variables were improved in both arms but were not different between arms in terms of patient perception of outcomes. Five vaginal erosions were encountered in the study arms (no different between groups), and 5 women in the TVT-O group and 4 women in the outside-in group required a secondary procedure for urinary incontinence.

**Conclusions:** At a minimum 2- to 4-year follow-up, these 2 approaches were equally safe and effective in managing SUI. No essential difference was noted between the 2 groups.

**Reviewer’s Comments:** Comparison between outside-in and inside-out approaches for transobturator tape placement showed essential quality both in efficacy and subjective quality-of-life outcomes. (Reviewer-Roger R. Dmochowski, MD).

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Keywords: Monarc, Stress Urinary Incontinence, Transobturator Tape, TVT-O

Print Tag: Refer to original journal article
Urodynamics Can Be Very Useful for Predicting Outcomes

Incontinence and Detrusor Dysfunction Associated With Pelvic Organ Prolapse: Clinical Value of Preoperative Urodynamic Evaluation.

Araki I, Haneda Y, et al:

Int Urogynecol J Pelvic Floor Dysfunct 2009; 20 (November): 1301-1306

Preoperative evaluation of filling and emptying characteristics of bladder detrusor overactivity and demonstration can be useful for predicting postoperative condition such as pelvic organ prolapse.

Objective: To assess the use of preoperative urodynamic findings as a tool for predicting urinary problems after surgical repair of pelvic organ prolapse.

Design/Participants: 87 women who underwent preoperative urodynamics were reviewed retrospectively after undergoing pelvic organ prolapse procedures. Preoperatively, cough stress test and urodynamic testing including both filling and emptying phases were performed with and without reduction. Postoperative evaluation included assessment of symptoms, uroflowmetry, and post-void residuals. Symptom assessment was performed using standardized questionnaire evaluation. All patients underwent surgical correction of prolapse, with 85 patients undergoing cystocele repair, 25 undergoing rectocele repair, 18 had rectocele and uterine and vault prolapse, and 7 had uterine and vault prolapse concomitantly. All patients were at least grade 2 in degree of magnitude, with the majority being stage 3 (46) and the remainder being stage 4 (34).

Results: A cough stress test during filling was sufficient for the diagnosis of occult stress urinary incontinence in all patients. Detrusor overactivity, when noted, was a good predictor of the outcome of postoperative urge symptomatology or urge urinary incontinence. Interestingly, low post-void residual volumes increased immediately after surgery, but usually recovered by 1 month. Pressure flow studies were used to predict large post-void residual when considering contractility evaluation on pressure flow analysis preoperatively.

Conclusions: Preoperative evaluation of filling and emptying characteristics of bladder detrusor overactivity and demonstration will be useful for predicting postoperative condition such as pelvic organ prolapse; however, the authors remained uncertain as to its cost effectiveness.

Reviewer’s Comments: Urodynamic evaluation, including both outlet as well as storage functions, is able to predict postoperative functional outcomes when undergoing mixed prolapse correction procedures. (Reviewer-Roger R. Dmochowski, MD).

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Keywords: Bladder Dysfunction, Detrusor Overactivity, Incontinence, Pelvic Organ Prolapse, Urodynamics

Print Tag: Refer to original journal article
ED May Serve as Sentinel Marker for CVD

Erectile Dysfunction and Mortality.
Araujo AB, Travison TG, et al:

J Sex Med 2009; 6 (September): 2445-2454

ED is as strongly associated with CVD mortality as some prominent risk factors for CVD.

**Background:** The relationship between erectile dysfunction (ED) and coronary vascular disease (CVD) has received substantial attention. The prevailing notion supported by relatively scant data is that ED may serve as a sentinel marker for CVD.

**Objective:** To examine the association of ED with all-cause and cause-specific mortality in a well-characterized cohort of men who were followed for a mean of 15 years. The authors tested the hypothesis that ED predicts all-cause mortality primarily through its association with CVD mortality.

**Design/Methods:** The sample size was the Massachusetts Male Aging Study (MMAS), which was a prospective observational cohort study of aging health and sexual function in men between the ages of 40 and 70 years.

**Results:** There were 403 deaths and 1306 surviving members of the MMAS. The largest number of deaths was 140 (37.7%) due to CVD. The ED men had higher body mass index (BMI) and waist circumference, higher caloric intake, lower HDL cholesterol, and higher blood pressure. Cancer mortality exhibited no association with ED. However, the risk of mortality due to CVD increased as ED severity increased ($P<0.001$). The age-matched hazard ratio for CVD death in men with moderate or complete ED compared to men with no or minimal ED was 1.87. Death due to CVD and all causes was significantly associated with ED. The hazard ratio for CVD mortality associated with ED was comparable with a number of conventional risk factors, such as BMI, diabetes, and hypertension.

**Discussion:** The hypothesis that any observed association between all-cause mortality and ED would be explained by the presence of an association of ED with CVD death and a lack or an inconsistent association with other causes. The models examined here (men with ED) have a 26% higher risk of all-cause mortality and a 43% higher risk of death due to CVD compared to men without ED. In this study, ED is as strongly associated with CVD mortality as some prominent risk factors for CVD.

**Reviewer's Comments:** The most important limitation concerns the measurement of ED. This self-assessment was not included at baseline, but added subsequently. Additionally, this study did not include assessments of other CVD risk factors, such as family history of diabetes, CVD, and self-reports of chronic disease; however, it emphasizes the need for primary care physicians and others to pay attention to the cardiovascular risk profiles of their patients with ED. (Reviewer-Kevin T. McVary, MD).

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Keywords: ED, Sexual Dysfunction, Cardiovascular Risk Factors

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In women with vestibulodynia, botulinum toxin type A injection does not reduce pain, does not improve sexual functioning, and there is no impact on quality of life compared to placebo at both 3 and 6 months' follow-up.

**Background:** Vulvar pain occurring in the absence of visible clinical findings is increasingly recognized as a problem among women, leading to chronic dyspareunia, chronic pelvic pain, and other sexual problems. It is reported to have a prevalence rate of 15% among women in the general population. The localized, provoked form of vulvodynia at the present time is named vestibulodynia, based on pain while attempting to insert an object into the vagina, pain on pressure to the vestibule, and vestibular erythema. In vivo animal research suggests that botulinum toxin has an antinociceptive effect that is independent of its neuromuscular activity.

**Objective:** To evaluate the effect of botulinum toxin A (Botox) as a treatment for vestibulodynia.

**Design:** Randomized double-blinded placebo-controlled study.

**Participants/Methods:** 64 patients were randomized to receive a placebo or botulinum toxin injection. After an extensive evaluation, the primary outcome was pain ratings using a visual analog scale, the Female Sexual Function Index, and the Female Sexual Distress Scale. An additional Manifest Female Sexual Dysfunction score was also used.

**Results:** 164 patients were assessed for eligibility, of which 65 were included and randomized. The results suggest that both interventions (botulinum toxin and placebo) resulted in a statistically significant reduction in pain at 6 months' follow-up compared to baseline. There were no significant differences in the mean pain between the botulinum toxin A group and the control group. Predefined relevant primary outcome, a 2-point reduction in the visual analog scale, did not differ significantly between the 2 groups. With regard to the Female Sexual Function Index, both groups resulted in significant improvements in scores. The Female Sexual Distress Scale similarly showed no difference between the groups. In the Manifest Female Sexual Dysfunction scale, there were significant improvements in both groups, with no differences between the 2 groups.

**Reviewer's Comments:** This is the first randomized placebo-controlled study to report botulinum toxin effect on vestibulodynia, concluding that injection of 20 units of Botox does not reduce pain experience in this type of patient. The authors surmise that the injection does not reduce pain, does not improve sexual functioning, and there is no impact on quality of life compared to placebo at both 3 and 6 months’ follow-up. (Reviewer-Kevin T. McVary, MD).

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Keywords: Botulinum Toxin Type A, Dyspareunia, Vestibulodynia

Print Tag: Refer to original journal article
Eggs Good for Eye Health and That Is No Yolk

Consumption of 2 and 4 Egg Yolks/D for 5 Wk Increases Macular Pigment Concentrations in Older Adults With Low Macular Pigment and Also Taking Cholesterol-Lowering Statins. 

Vishwanathan R, Goodrow-Kotyla EF, et al:

Am J Clin Nutr 2009; 90 (November): 1272-1279

Eating eggs should be recommended for eye and urologic health, especially for patients trying to find an alternative to high-dose zinc supplementation.

**Background:** Eye health supplements are very popular, but have been questioned lately due to recent research that suggests they may increase the risk of prostate cancer, stones, and urinary tract infections. In Canada, zinc is now limited to a maximum of 40 mg per eye health supplement pill. Patients are inquiring about healthy substitutes that can be utilized for eye health and it is known that egg yolks contain high concentrations of lutein and zeaxanthin, which are 2 carotenoids that have been linked to a lower risk of macular degeneration and cataracts.

**Objective:** To determine the bioavailability and ocular impact of consuming 2 and 4 egg yolks per day.

**Design/Methods:** Participants consumed 2 followed by 4 egg yolks/day for 5 weeks each with a 4-week egg-free or wash-out period at baseline and between the 2 interventions. A total of 52 individuals, 40% males, mean age 69 years, and most of who were on statins, were included in this clinical trial. An increase in macular pigment optical density (MPOD) was used as an indicator of potential lutein and zeaxanthin benefits.

**Results:** Individuals with lower MPOD experienced significant increases in this parameter with the consumption of egg yolks. Serum lutein and especially zeaxanthin increased significantly after consuming 2 and 4 egg yolks. Serum HDL (good cholesterol) also increased significantly ($P<0.05$) with egg yolks, but LDL did not increase significantly.

**Conclusions:** Consumption of several egg yolks per day can improve macular health, increase HDL, and not change LDL when taking a statin drug.

**Reviewer's Comments:** Here we go again! Remember being told over the past 20 years that eggs, especially egg yolks, were not good for you because they have too much cholesterol? This is what I like to call typical "food or beverage bias," where you judge something based on a single negative compound and ignore the sum of what else the product has to offer. Yes, eggs have cholesterol, but they are also a source of vitamin D; omega-3, one of the highest quality protein sources in the world; high in healthy fats; low calorie; and may be the best bioavailable food source of lutein and zeaxanthin on the planet. Come on people, the next time someone tells you that an egg is bad, ask them to answer you this "What came first, the high cholesterol or the egg," and the answer is that high-cholesterol is not caused by moderate egg consumption and especially when on a statin drug, so please leave my eggs alone! (Reviewer-Mark A. Moyad, MD, MPH).

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Keywords: Egg Yolk Consumption, Eye Health, Macular Pigment Concentration, Statins

Print Tag: Refer to original journal article
Resveratrol is a polyphenolic compound that may provide numerous health benefits, but the only way to significantly increase the blood level of this compound is to drink red wine in moderation.

**Background:** Resveratrol is a compound found in a variety of healthy foods, including grapes and red wine. It has been theorized that one of the principal reasons the Mediterranean diet is so healthy is that it includes higher intakes of red wine. In support of this thought, numerous laboratory or animal studies have now found a variety of potential health benefits with resveratrol supplementation, which has led to a surge in sales of this dietary supplement for individuals that believe it provides an anti-aging effect. However, few researchers have provided an objective overview of the clinical research with resveratrol.

**Objective:** To review the clinical data associated with resveratrol dietary sources and dietary supplements.

**Design/Methods:** This manuscript was a comprehensive review of laboratory and clinical data on resveratrol.

**Results:** Alcohol follows a J-shape curve when reviewing over 26 past clinical studies, which means in moderation, any type of alcohol (beer, red and white wine, and hard liquor) has been shown to lower cardiovascular risk, but any type of alcohol in excess can increase the risk of cardiovascular disease. No clinical trials have yet to support the numerous health benefits touted for resveratrol in the diet or from dietary supplements. Resveratrol has been found in grape skins (not grape seeds), peanuts, and healthy juices, but interestingly, red wine provides the largest source of bioavailable or free resveratrol.

**Conclusions:** Resveratrol is a polyphenolic compound that may provide numerous health benefits, but the only way to significantly increase the blood level of this compound is to drink red wine in moderation.

**Reviewer's Comments:** Wine contains over 500 natural compounds including resveratrol. Red wine is made in close contact with grape skins so it contains a higher resveratrol content. Alcohol enhances the absorption of numerous compounds, not only topically, but also within the gastrointestinal tract. Thus, the plasma level of free resveratrol is increased substantially when drinking red wine as opposed to drinking grape juice or taking the expensive dietary supplement. Tell patients that resveratrol is currently similar to past situations in urology where the supplement was thought to be so effective but the beverage or food source ended up making more sense. For example, the case with 8-carotene (vegetables are a good source), fiber (flaxseed), selenium (fish), vitamin E (almonds), and even zinc (seeds) demonstrated that the healthy food source was better and safer than the dietary supplement in these specific cases. Believe me, it is a matter of time before white wine makers will identify a compound in their beverage that is as healthy as resveratrol. (Reviewer-Mark A. Moyad, MD, MPH).

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Keywords: Resveratrol, Dietary Supplements, Red Wine, Cardiovascular Health

Print Tag: Refer to original journal article
Selective arterial embolization can be an effective long-term treatment for renal angiomyolipoma.

**Objective:** To evaluate the complication rates and long-term outcomes in patients who underwent selective arterial embolization (SAE) for renal angiomyolipoma (AML).

**Design/Methods:** Retrospective cohort study of the records of 41 patients and 48 kidneys in which SAE was performed for renal AML. Patients all had a planned, repeat angiography at 1 to 2 years to assess for re-canalization or neovascularity with possible repeat embolization. Mean follow-up was 4.8 years. Outcome measures included complication rates, recurrence rates, need for surgery, and disease-specific survival.

**Results:** Mean tumor size was 10.3 cm, and successful SAE was achieved in 91%, with a 16% minor complication rate and no major complications. No patients had a significant change in renal function. All kidneys except one were able to be spared long term, and the 5-year freedom-from-surgery rate was 94%. Thirty-seven percent of patients required repeat embolization, all at the time of routine repeat angiography due to evidence of neovascularity/recanalization and not due to symptoms or bleeding. No patient died of their disease.

**Conclusions:** SAE for renal AML can have long-term efficacy and preservation of the affected kidney and renal function.

**Reviewer's Comments:** For large or symptomatic renal angiomyolipomas, the options for management essentially revolve around partial nephrectomy or selective arterial embolization. While the short-term success with embolization has been documented in a number of series, the long-term efficacy has been less clear. This study was able to demonstrate that embolization can successfully treat renal AMLs while preserving the affected kidney and avoiding the need for surgery in the majority of patients. This was possible even with large tumors (since the mean tumor size in this cohort was >10 cm) and in patients with tuberous sclerosis. It is important to bear in mind that the authors would routinely repeat angiography 1 to 2 years after the initial procedure. This is important because it may account for the long-term success reported here. Routine repeat angiography is not necessarily practiced uniformly across institutions, so those who do not perform this technique may not have as much success in avoiding surgery or bleeding complications. This may also account for the relatively high rate of re-embolization (37%), since none of these cases were due to symptoms or bleeding but instead were pre-emptive due to evidence for neovascularity or recanalization of the lesion. Even with this caveat in mind, data such as those presented in this report justify embolization as a viable alternative to partial nephrectomy in the management of AML. (Reviewer-Peter E. Clark, MD).
In patients with bladder cancer, BCG with maintenance therapy has a lower recurrence rate than mitomycin C, but there is no difference in survival or progression.

**Objective:** To compare the efficacy of bacillus Calmette-Guérin (BCG) versus mitomycin C (MMC) in patients with non–muscle-invasive bladder cancer (NMIBC).

**Design/Methods:** Meta-analysis of 9 prospective, randomized trials comparing MMC and BCG for NMIBC using the individual patient data from these trials. Analyses included risk of recurrence, progression, and survival and whether BCG was given with maintenance.

**Results:** Individual data on 2820 patients were obtained for analysis. Of these patients, 71% had primary lesions, 43% had T1 disease, and 58% had grade 2 tumors. Median follow-up was 4.4 years. When analyzed as overall cohorts, there were no differences between MMC and BCG. When BCG was subdivided into those with or without maintenance, there was a 32% reduction in the risk of recurrence in those with BCG plus maintenance versus MMC compared to a 28% increased risk in those with BCG without maintenance. No differences were found in the risk of progression or overall survival between any of the groups.

**Conclusions:** BCG is superior to MMC for decreasing the risk of recurrence in NMIBC only among patients put on a maintenance regimen. There was no difference with regard to the risk of progression or overall survival.

**Reviewer's Comments:** Patients with NMIBC, especially those with higher-risk disease, can be particularly challenging. High-risk features such as lamina propria invasion or carcinoma in situ are an indication for intravesical therapy. Numerous trials have compared MMC and BCG. However, the importance of this study is that it synthesizes the results of several high-quality trials using a technique called a meta-analysis and does so in the most powerful way, by obtaining the individual patient data from each trial’s dataset, not just the published report. Using this powerful technique, the authors show that maintenance BCG is superior to MMC with regard to recurrence, but not progression or survival. There are a couple of key points to bear in mind. This study emphasizes the importance of maintenance therapy in those receiving BCG. Although toxicity can be an issue (something not addressed in this report), maintenance therapy has been shown repeatedly to improve the results of intravesical therapy with BCG. Another key point is that progression and survival were not significantly different. This is not to say that they might have been different if more patient data were available, but that can be determined only with more trials. It also does not imply that progression or survival might not be better compared to those in a placebo arm, which was not analyzed here. The main message is this: if patients are high risk and are to undergo BCG therapy, they should be strongly considered to undergo maintenance therapy. (Reviewer-Peter E. Clark, MD).

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Keywords: Bacillus Calmette-Guérin, Mitomycin C, Non–Muscle-Invasive Bladder Cancer, Maintenance Therapy

Print Tag: Refer to original journal article
The use of celecoxib in patients with ureteral calculi fails to decrease narcotic utilization and fails to facilitate stone passage.

**Background:** Celecoxib is a selective cyclooxygenase subtype-2 (COX-2) inhibitor. It has been demonstrated to reduce ureteral contractility in vitro and to decrease ureteral spasm by inhibiting the local release of prostaglandins.

**Objective:** To evaluate the efficacy of celecoxib as an analgesic and medical expulsive agent for ureteral colic.

**Design:** Prospective, randomized, double-blind, placebo-controlled trial.

**Participants:** 57 patients with ureteral calculi <10 mm in size.

**Methods:** Patients and investigators were blinded to the randomization schedule. Patients strained their urine and recorded the date and time of stone passage. Patients were imaged weekly with KUB or CT scan in the event of a radiolucent calculus. After 4 weeks, patients were counseled to proceed with surgical intervention if the stone had failed to pass spontaneously. The primary end point was narcotic utilization during the first 48 hours after presentation to the emergency department.

**Interventions:** Celecoxib 400 mg once a day followed by 200 mg twice a day for 10 days versus matched placebo.

**Results:** No significant difference was found in the time from onset of symptoms to presentation to the emergency department (average, 15 hours). Average stone size was 5 mm. Proximal ureteral stones accounted for 60% of cases in the patients enrolled. No significant difference was noted in the rate of spontaneous stone passage, days to stone passage, size of stone passed, pain scores, or analgesic use.

**Conclusions:** Celecoxib does not facilitate stone passage or decrease narcotic utilization in patients with an obstructing ureteral stone.

**Reviewer’s Comments:** The authors conducted a well-designed clinical trial and terminated it early at a planned interim analysis. A post hoc power analysis demonstrated that 1200 patients would be required to identify a difference in narcotic use between celecoxib and placebo. Recently, the literature supporting the use of celecoxib for pain relief after orthopedic surgeries has been retracted due to the quality and integrity of the studies. (Reviewer-Manoj Monga, MD).

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Keywords: Ureter, Calculi, Medical Expulsive Therapy

Print Tag: Refer to original journal article
The use of a modified 10-cc syringe barrel can extend the functional length of a percutaneous renal access sheath to facilitate PCNL in the morbidly obese.

**Background:** Percutaneous nephrolithotripsy (PCNL) can be challenging in the morbidly obese due to limitations in the length of the accessory instrumentation.

**Objective:** To report the use of a modified 10-cc syringe barrel to facilitate PCNL in the morbidly obese.

**Discussion:** The authors utilize this technique in morbidly obese patients who are undergoing PCNL. It is utilized to either retrieve an Amplatz sheath that has migrated deep into the retroperitoneal fat, or it can be used pre-emptively if migration of the sheath is anticipated. **Description of Technique:** The authors cut the nozzle end of the barrel of a sterile 10-cc syringe at a 15° bevel. This is loaded on an Amplatz introducer that has been placed over the working wire to the level of the Amplatz sheath. The barrel is then advanced under fluoroscopic guidance until it overlaps with the Amplatz sheath in a telescoping configuration. The rigid nephroscope can then be advanced through the barrel and into the sheath, with resumption of the endoscopic procedure. The tube-in-tube configuration prevents extravasation of irrigation and migration of stone fragments into the retroperitoneum. At the completion of the procedure, the migrated sheath can be retrieved using grasping forceps under direct vision through the syringe barrel.

**Reviewer’s Comments:** Alternatives for access in the morbidly obese include the use of operating laparoscopes, 25-cm long nephroscopes, and extra-long, special-order Amplatz sheaths. The authors report a novel approach to retrieval of a migrated Amplatz sheath during PCNL in the morbidly obese. It leaves one wondering where these innovative ideas come from. (Reviewer-Manoj Monga, MD).

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Keywords: Instrumentation, Percutaneous Nephrolithotomy, Obesity

Print Tag: Refer to original journal article
Stones in Children--Doxazosin vs Ibuprofen

Effectiveness of Doxazosin in Treatment of Distal Ureteral Stones in Children.
Aydogdu O, Burgu B, et al:

J Urol 2009; 182 (December): 2880-2884

Doxazosin is similar to ibuprofen with regard to stone expulsion rate and expulsion time in children with distal ureteral stones

Background: Alpha-antagonists have been shown to improve spontaneous stone expulsion rates and time to expulsion in ureteral stones in the adult population.

Objective: To assess the effect of doxazosin on stone expulsion rate and time to passage of ureteral stones in children.

Participants/Methods: 39 children with distal ureteral stones <10 mm were randomly divided into 2 groups: group 1 (n=20) received ibuprofen for pain, and group 2 (n=19) received doxazosin (0.03 mg/kg per day). Children ranged from 2 to 14 years of age. Stone expulsion rates and time to expulsion were compared. Subgroups based on stone size <5 mm and 5 to 10 mm were considered.

Results: Expulsion occurred in 14 (70%) group 1 patients and 16 (84%) group 2 patients. Expulsion time was 6.1 and 5.9 days for group 1 and 2, respectively. Neither parameter reached statistical significance. No adverse effects were noted. Gender, stone size, and age did not appear to affect outcome.

Conclusions: Doxazosin was similar to ibuprofen with regard to stone expulsion rate and time in children with distal ureteral stones.

Reviewer's Comments: Other studies have shown a benefit in stone expulsion with alpha-blockers in adults. This study did not show any benefit of doxazosin over ibuprofen in children. However, this study was small in number and should not be considered the final word. With the growing off-label use of tamsulosin in children with regard to voiding dysfunction and its low side-effect profile given its affinity for the urinary tract, this may be a better alpha-antagonist drug for investigation, at least from a study design and institutional review board standpoint. (Reviewer-John Gatti, MD).

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Keywords: Children, Expulsive Therapy

Print Tag: Refer to original journal article
Consider MRU for Identifying Ureteral Ectopia

Role of Magnetic Resonance Urography in the Diagnosis of Single-System Ureteral Ectopia With Congenital Renal Dysplasia: A Tertiary Care Center Experience in India.

Joshi M, Parelkar S, et al:


MRU appears to be a better single imaging modality than other techniques for identifying ureteral ectopia in the setting of urinary incontinence and a normal voiding pattern.

Objective: To evaluate the role of magnetic resonance urography (MRU) in the diagnosis of single-system ureteral ectopia with renal dysplasia in children.

Methods: Girls with urinary incontinence and normal voiding patterns were evaluated with MRU and conventional radiographic imaging. All patients underwent laparoscopic nephroureterectomy after MRU diagnosis.

Results: MRU identified the dysplastic renal moiety, provided a functional assessment, and illuminated the course of the ectopic ureter in all 7 girls. All patients underwent initial screening ultrasound, revealing small, dysplastic kidneys in 2 patients. Ages ranged from 3 months to 5 years. Intravenous urography was ineffective in opacifying the dysplasia, as was the renal scan.

Conclusions: MRU appears to be a better single imaging modality than other conventional radiographic techniques for identifying ureteral ectopia in the setting of urinary incontinence and a normal voiding pattern.

Reviewer’s Comments: MRU is gaining popularity in the evaluation of many urologic anomalies in children. If one study is to be chosen to identify an ectopic ureter as a source of incontinence in a girl, this is probably the one. Unfortunately, these children usually undergo several studies to sort out the diagnosis. Before the availability of MRU, our institution used contrast CT scans with excellent results. The MRU provides equivalent or better images and spares the patient radiation, but it is generally quite expensive. The selling point is that, if all the other studies are avoided, the MRU may become cost effective. The authors report that their cost for the MRU is $60. In this regard, we may consider paying to fly our patients to Mumbai for their MRU as a cost-cutting measure. (Reviewer-John Gatti, MD).

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Keywords: Ectopic Ureter

Print Tag: Refer to original journal article
Anterior pelvic prolapse repair can yield both subjective and objective functionally good results. Minimal complications were encountered in the specific group in this trial.

**Objective:** To assess the 1-year outcomes after transvaginal prolapse surgery using a Prolift transvaginal mesh.

**Methods:** Patients underwent preoperative and postoperative assessment using the Pelvic Organ Prolapse Quantification (POP-Q) as well as subjective symptom and impact assessments using the Pelvic Floor Distress Inventory-20 and the Pelvic Floor Impact Questionnaire-7. Postoperative specific outcomes included vaginal tenderness, stricture, and patient satisfaction. Specific assessment for dyspareunia, other than questioning for its presence, was not evaluated.

**Results:** 48 patients underwent pelvic organ prolapse repair using the Prolift device at a mean age of 61 years. Mean follow-up was 425 days. All patients had significant POP-Q measurements. All subscale measurements in both the pelvic floor distress inventory and pelvic floor impact scales were significantly improved. Of the patients asked about satisfaction, 35 of 48 (73%) were completely satisfied, and 2 (4%) were not satisfied. Complications included graft erosion in 1 patient, dyspareunia in 2, and granulation of tissue in 3. No specific complications related to mesh erosion of the urinary tract were noted. Additionally, no significant intraoperative or postoperative blood transfusions were required. No patient experienced blood loss >1000 cc. Apparently, no impact on sexual function was noted after surgery; however, only 23 of 38 patients were sexually active.

**Conclusions:** Transvaginal repair of pelvic organ prolapse with mesh specifically with the Prolift kit showed significant improvement in 1-year anatomic and subjective responses.

**Reviewer's Comments:** Anatomic outcomes are produced functionally with poor results using graft repair, but in this particular study, few were noted. (Reviewer-Roger R. Dmochowski, MD).

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**Keywords:** Pelvic Organ Prolapse, Surgery, Prolift Mesh Graft, Outcomes

**Print Tag:** Refer to original journal article
Does Bladder Wall Thickness Indicate OAB Symptomatology?

Measurement of Detrusor Wall Thickness in Women With Overactive Bladder by Transvaginal and Transabdominal Sonography.

Kuo H-C:

Int Urogynecol J 2009; 20 (): 1293-1299

Detrusor wall thickness may be a useful biomarker for the evaluation of OAB and for detrusor overactivity. Detrusor wall thickness also may be an indicator of both bladder symptoms and bladder overactivity.

Objective: To assess bladder wall thickness as noted by ultrasound in women with detrusor overactivity to determine if bladder wall thickness is an indicator of overactive bladder (OAB) symptomatology.

Methods: Transabdominal ultrasonography and transvaginal ultrasonography were used to measure detrusor wall thickness in a group of normal women with either OAB-dry or OAB-wet syndrome. The basis of the classification was solely diary based from the standpoint of segregation between dry and wet. The urodynamic assessment was then further used to segregate patients into normal groups, hypersensitive groups (increased sensation-early volumetric perceived sensation), or detrusor overactivity by urodynamics. Detrusor wall thickness was measured by transvaginal ultrasound with the bladder empty and by transabdominal ultrasound when the bladder was approximately 250 cc full and also at bladder capacity. These measurements were assessed both among symptomatic and urodynamic groups.

Results: Consistently across all groups, transvaginal ultrasound found detrusor wall thickness to be significantly greater at the bladder neck than at any other site in the bladder wall. No significant difference in transvaginal ultrasound measuring detrusor wall thickness was noted among any of the subgroups. Using transabdominal sonography to measure detrusor wall thickness found no difference between any of the subgroups at 250 cc, but detrusor wall thickness and bladder capacity seemed significantly greater in the OAB-wet and in the urodynamic group, which is consistent with detrusor overactivity (not all the same patients). This information segregated these 2 groups and all other groups under study.

Conclusions: Detrusor wall thickness and capacity measured by transabdominal ultrasound would be a useful biomarker for patients either with detrusor overactivity or with OAB symptomatology. These results could be used for segregating the patient groups in larger-scale studies.

Reviewer’s Comments: Detrusor wall thickness is best measured during bladder filling and with the transabdominal technique. This information could be used for segregating groups in larger studies. (Reviewer-Roger R. Dmochowski, MD).

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Keywords: Bladder Wall, Overactive bladder, Ultrasound

Print Tag: Refer to original journal article
There has been no noted difference between open, laparoscopic, or robotic prostatectomy surgery in terms of erection recovery.

**Background:** Preservation of erectile function (EF) has become an important goal in prostate cancer surgery, given better understanding of the cavernous nerve anatomy and the use of nerve-sparing prostatectomy. The reported incidence of long-term erectile dysfunction (ED) after radical prostatectomy ranges from 14% to 90%. This wide range is not useful in clinical care and in treatment-selection decision making.

**Design/Objective:** The present study used a meta-analysis methodology to analyze highly selected quality publications and to address the question of the actual incidence of ED after radical prostate surgery.

**Methods:** The authors reviewed English language publications published between 1985 and 2008.

**Results:** Of the 2482 articles reviewed, only 22 studies (10%) met full inclusion criteria. The mean patient age was 61 years, and the average study size was 226. Sixteen studies involved open radical prostate surgery, 4 involved laparoscopic surgery, and 2 involved robotic surgery. The definition of a favorable EF outcome varied considerably, as the authors found 22 different definitions. The overall fixed-effect EF recovery rate was 58%, with significant heterogeneity among effect sizes. Factors that influenced erectile recovery rate included single-center studies, those with >18 months of follow-up, bilateral nerve-sparing versus unilateral nerve-sparing procedures, and younger patient age.

**Conclusions:** The variability in reported EF outcomes originates in the discrepancy in subject age, presurgery erectile level, comorbidities, surgical techniques, definition of EF recovery, collection methods, duration after surgery, utilization of other prostate cancer treatments, and the use of erectogenic therapies. Of note, the quality of the articles in large part was substandard, in that all selected publications meeting inclusion criteria were published after 2000. In the 13 publications included in this analysis, it was stated clearly that subjects used erectogenic therapy, but none of the publications presented a detailed report on the extent of erectogenic therapy and its effect on outcomes. No difference was noted between open, laparoscopic, or robotic surgery.

**Reviewer's Comments:** The ideal study to describe EF rate after radical prostatectomy should be designed prospectively with an age comorbidity profile baseline EF matched control group using accurate measurement tools (before and after therapy). It should also be adjusted for other factors such as surgical technique and the use of erectogenic therapy postoperatively. (Reviewer-Kevin T. McVary, MD).

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Keywords: Erectile Dysfunction, Prostate Cancer

Print Tag: Refer to original journal article
Absorption of Testosterone Gel 1% (Testim) From Three Different Application Sites.

Guay AT, Smith TM, Offutt LA:

J Sex Med 2009; 6 (): 2601-2610

In subjects with clinical hypogonadism, the application of Testim to the arms, chest, or legs resulted in a mean increase over pre-dosing levels.

**Background:** The Endocrine Society recommends against offering replacement therapy to all older men with low testosterone levels. Instead, the society advocates treatment for symptomatic men with androgen deficiency syndromes and low testosterone levels. The indication is to maintain secondary sexual characteristics, improve sexual functioning, well being, muscle mass, strength, and bone mineral density.

**Objective:** To determine if Testim (1% gel) can effectively be applied to sites other than the arms and shoulders as detailed in the product insert and still provide adequate blood testosterone levels.

**Design/Methods:** This was a prospective, open-label, parallel, cross-over design in which subjects were assigned to a rotating schedule of tests and applications: arms-chest-legs; chest-legs-arms; and legs-arms-chest. This study did not include a washout period between alterations.

**Results:** 21 men with hypogonadism ranging in age from 39 to 77 years participated. The level of testosterone increased significantly above pretreatment levels into the normal range following the application of Testim over all sites tested. A higher mean level of testosterone in the mid-normal range was achieved when applied to the arms compared to the chest, and compared with the low-normal levels when applied to the lower extremities. The differences in mean testosterone levels between the chest and lower extremity application sites were not significant. Testim applied to the arms, chest, and legs resulted in 85.7%, 90%, and 57.1% of subjects achieving testosterone levels >300 ng/mL, respectively. Changes in the calculated free testosterone level mimic those of total testosterone. PSA values were measured at the end of each month before switching application sites and at the end of the study. These levels were unchanged from pretreatment values and were unaffected by site or sequence of testosterone supplementation.

**Conclusions:** The prescribing information for Testim limits the application to the arms and shoulders and warns against applying it to the abdomen. In subjects with clinical hypogonadism, the application of Testim to the arms, chest, or legs resulted in a mean increase over pre-dosing levels. However, the authors did observe that the arms and shoulders had higher to mid-normal levels of testosterone than when the gel was applied to the chest, abdomen, or legs.

**Reviewer’s Comments:** The major limitations of this study were that it was not blinded or controlled with a placebo-containing gel and that very few subjects participated. The study also did not include a washout period between switching from one administration site to another, and the trial was not designed to correlate absorption with clinical response or to compare with AndroGel absorption and response. (Reviewer-Kevin T. McVary, MD).

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Keywords: Sexual Dysfunction, Androgen Supplementation, Testosterone

Print Tag: Refer to original journal article