Varicocele: Selected Treatments

Policy

Aetna considers percutaneous embolization (by means of balloon or metallic coil) or ligation medically necessary for the treatment of varicocele for any of the following conditions:

1. Adolescents with grade 2 or 3 varicoceles associated with ipsilateral testicular growth retardation; or
2. Males with infertility problems who have decreased sperm motility and lower sperm concentrations; or
3. Post-surgical (ligation) recurrence of varicoceles; or
4. Scrotal pain associated with varicoceles.

Aetna considers percutaneous embolization or ligation of varicoceles for persons who do not meet these criteria experimental and investigational.

Aetna considers microsurgical varicocelectomy an acceptable alternative method of treating a varicocele when any of the aforementioned criteria is met.

Aetna considers surgical treatment (ligation, embolization) for subclinical varicocele experimental and investigational because of insufficient evidence to support its effectiveness.
Aetna considers the following interventions experimental and investigational because their effectiveness has not been established:

- Addition of a sclerosant agent to coil embolization to improve outcomes
- Endoluminal occlusion devices (e.g., the ArtVentive endoluminal occlusion system)
- Endovenous laser ablation (EVLA) of the spermatic vein for the treatment of varicocele

**Background**

Varicoceles (dilations of the pampiniform venous plexus) are found in 10 to 15% of the male population and they occur predominantly on the left side. The etiology may be a longer left spermatic vein with its right-angle insertion into the left renal vein and/or absence of valves, which results in a higher hydrostatic pressure in the left spermatic vein causing dilatation. Also, the left renal vein may be compressed between the superior mesenteric artery and the aorta. This "nutcracker phenomenon" may result in elevated pressure in the left testicular venous system. Moreover, the incidence of varicocele in men with impaired fertility is about 30%; varicoceles are the most common surgically correctable cause of male infertility. A clinical grading system classifies varicoceles into 3 grades: (i) grade 1 (small) – palpable only during a Valsalva maneuver, (ii) grade 2 (moderate) – palpable without the need of the Valsalva maneuver, and (iii) grade 3 (large) – visible.

Although varicoceles can be diagnosed by a thorough physical examination, ultrasonography is the most practical and accurate non-invasive method in diagnosing this condition. Surgical ligation (varicocelectomy) is the conventional approach in managing varicoceles. However, percutaneous embolization by means of balloon or metallic coil has been shown to be a safe and effective alternative to ligation in treating varicoceles. Embolization (of spermatic veins) of varicoceles in males with semen abnormalities has been demonstrated to improve sperm count and motility in up to 75% of patients, and reported
pregnancy rates after ablation of varicoceles vary from 30 to 60 %. Furthermore, embolization therapy has been reported to increase testicular size in adolescents with testicular hypotrophy.

Polito and colleagues (2004) stated that the impact of varicocele on male infertility is still controversial since its role on the impairment of semen quality has never been fully demonstrated. These researchers studied a series of young adult males (n = 426) undergoing percutaneous treatment of varicocele and semen parameters were evaluated at baseline and 12 months of follow-up. They concluded that the correction of varicocele in young adults is not a major indication when semen alteration is the only clinical problem. This is in agreement with the findings of Nabi et al (2004) who compared the semen quality in men with or without pregnancy after percutaneous embolization of varicoceles in the management of infertility (n = 102). They concluded that varicocele embolization is a technically feasible, minimally invasive, outpatient procedure that improves semen quality significantly in patients with a pre-embolization semen density of 10 to 30 million/ml. However, no correlation was found between the improvements in semen quality and the pregnancy rate.

Bechara et al (2009) compared the treatment outcome of percutaneous embolization treatment versus laparoscopic varicocelectomy in patients with symptomatic varicoceles. Patients with varicoceles undergoing either laparoscopic varicocelectomy or percutaneous coil embolization of the testicular vein during a recent 5-year period were analyzed. Treatment outcome and hospital costs of these two minimally invasive treatment modalities were compared. A total of 41 patients underwent percutaneous coil embolization of the testicular vein, which were compared with a cohort of 43 patients who underwent laparoscopic varicocelectomy. Technical success in interventional and laparoscopic treatment was 95 % and 100 %, respectively. The mean operative time or procedural time was 63 +/- 13 mins and 52 +/- 25 mins for interventional and laparoscopic cohorts (not significant), respectively. Embolization treatment resulted in 2 recurrent varicoceles (4.8 %) compared to 1 patient following laparoscopic repair (2.3 %, not significant). Embolization treatment was associated with a lower complication rate than laparoscopic repair (9.7 % versus 16.3 %, p = 0.03). Regarding cost analysis, no significant difference in hospital cost
was noted between the interventional or laparoscopic treatment strategies. Both laparoscopic varicocelectomy and coil embolization are effective treatment modalities for varicoceles. With lower treatment complication rates in the interventional treatment group, coil embolization of the testicular vein offers treatment advantage compared with laparoscopic repair in patients with varicoceles.

Ayechu-Diaz et al (2009) stated that there are still doubts as to the most suitable criteria when considering surgery as the indication and optimal treatment for adolescent varicocele. These investigators reviewed the hospital and primary health care histories of patients diagnosed by ultrasound for varicocele over the last 7 years. Data were taken from computerized clinical histories and hard copy back-up material stored and processed in computer format. They studied 135 cases (mean age of 12.8 years). A total of 125 were referred for scrotal swelling or as a result of chance detection, except for 10 patients who reported pain or scrotal asymmetry; 73 underwent surgery and 62 continued as controls over the study period. The surgical indication was significant progressive asymmetry in testicular volume (n = 28), high grade varicocele (n = 41) as well as other reasons (n = 4). These researchers undertook percutaneous embolization in 44 patients (with a 66 % relapse rate) and laparoscopic section of the spermatic cord with no arterial preservation in 29 (no relapses but 7 post-surgery hydroceles). No testicles were lost. At the end of the study 10 children continued as controls, 34 were discharged after recovery, 56 were referred to urology due to their age group, and 35 were lost to the study. The authors concluded that in the controversy over the treatment of varicocele, their experience showed a high degree of relapses after embolization. Section of the spermatic vessels (including the artery) with no lymphatic preservation is highly effective but involves 27 % post-surgical hydroceles, usually self-limiting (only 1 patient had to undergo surgery later), with no testicular atrophy or other complications. These investigators prefer complete laparoscopic section of the spermatic pedicle to embolization; but it would be advisable to introduce modifications to avoid post-surgical hydrocele. Embolization must be reserved for patients with 1 testicle or with bilateral disease.

Storm and colleagues (2010) noted that post-operative hydrocele development is a frustrating complication of varicocele surgical repair. To avoid this complication, these investigators began to offer percutaneous
embolization as a treatment option. They presented their initial experience with this technique. There were 27 patients with a mean age of 16 years (range of 13 to 19 years). Indications included pain (48 %), varicocele size (30 %) and persistent testicular asymmetry (22 %). Four patients had experienced failure of a previous surgical repair. Follow-up data were available for 21 patients (mean of 9 months). The varicocele resolved in 19 patients (91 %) with no evidence of hydrocele formation in any of the boys. There was resolution of pain in all patients for whom this was the indication for the procedure. In the 2 failures, access to the lower spermatic vein was not possible owing to the number and tortuosity of the vessels. The authors concluded that percutaneous embolization and sclerotherapy represent a truly minimally invasive treatment with low morbidity, minimal pain and rapid recovery. In the authors' experience, since lymphatic channels are completely avoided, there appears to be no risk of hydrocele formation.

Microsurgical Varicocelectomy

Kondoh et al (2010) stated that surgical ligation for varicocele is primarily used in the management of male infertility patients. However, effectiveness of the ligation for painful varicocele is still controversial. These investigators reviewed records from 18 patients (average age of 17.8 years) who underwent varicocele ligation done for pain at the authors' institution from June 1999 to May 2010. The varicocele was on the left side and was grade III in 15 cases and grade II in 3 cases. The pain was classified into 3 types: (i) discomfort, (ii) dull pain, and (iii) sharp pain. Microsurgical varicocelectomy was done with inguinal or subinguinal approach. Evaluation of post-operative pain was available in 17 patients, and 15 patients (88 %) reported complete resolution of the pain with averaged follow-up duration of 11 months (3 to 53 months). The authors concluded that microsurgical varicocelectomy using the inguinal or subinguinal approach was an effective treatment modality for varicocele-associated pain.

Seo et al (2010) evaluated the improvement of seminal characteristics and pregnancy rates after microsurgical varicocelectomy in men with subclinical varicocele. A total of 143 patients with a subclinical left-sided varicocele were included in this study. Patients who agreed to microsurgical varicocelectomy (n = 25, surgery group), medical treatment
with L-carnitine (n = 93 drug group), and those who did not agree to any
treatment (n = 25, observation group) were enrolled. Semen
characteristics were re-evaluated twice 6 months after treatment. The
natural pregnancy rates were estimated by telephone interview between 1
and 2 years after treatment. In the surgery group, sperm counts
improved significantly after microsurgical varicocelectomy. In the drug
group, however, sperm parameters did not significantly improve after
treatment. Natural pregnancy rates were 60.0 % in the surgery group,
34.5 % in the drug group, and 18.7 % in the observation group. The
natural pregnancy rate of the surgery group was higher than the other
groups, and there were statistically significant differences among the 3
groups. The authors concluded that surgical treatment is the best option
for management of subclinical varicocele.

In a prospective, non-masked, parallel-group randomized, controlled trial,
Abdel-Meguid and colleagues (2011) examined if varicocele treatment is
superior or inferior to no treatment in male infertility from an evidence-
based perspective. Married men 20 to 39 years of age who had
experienced infertility greater than or equal to 1 year, had palpable
varicoceles, and with at least 1 impaired semen parameter (e.g., sperm
counting less than 20 million/ml, progressive motility less than 50 %,
or normal morphology less than 30 %) were eligible. Exclusions included
subclinical or recurrent varicoceles, normal semen parameters, and
azoospermia. Sample size analysis suggested 68 participants per arm.
Participants were randomly allocated to observation (the control arm
[CA]) or subinguinal microsurgical varicocelectomy (the treatment arm
[TA]). Semen analyses were obtained at baseline (3 analyses) and at
follow-up months 3, 6, 9, and 12. The mean of each sperm parameter at
baseline and follow-ups was determined. These researchers measured
the spontaneous pregnancy rate (the primary outcome), changes from
baseline in mean semen parameters, and the occurrence of adverse
events (AE-the secondary outcomes) during 12-month follow-up; p < 0.05
was considered significant. Analysis included 145 participants (CA: n =
72; TA: n = 73), with a mean age plus or minus standard deviation of 29.3
+/- 5.7 in the CA and 28.4 +/- 5.7 in the TA (p = 0.34). Baseline
characteristics in both arms were comparable. Spontaneous pregnancy
was achieved in 13.9 % (CA) versus 32.9 % (TA), with an odds ratio of
3.04 (95 % confidence interval [CI]: 1.33 to 6.95) and a number needed to
treat of 5.27 patients (95 % CI: 1.55 to 8.99). In CA within-arm analysis,
none of semen parameters revealed significant changes from baseline (sperm concentration [p = 0.18], progressive motility [p = 0.29], and normal morphology [p = 0.05]). Conversely, in TA within-arm analysis, the mean of all semen parameters improved significantly in follow-up versus baseline (p < 0.0001). In between-arm analysis, all semen parameters improved significantly in the TA versus CA (p < 0.0001). No AEs were reported. The authors concluded that these findings provided level 1b evidence of the superiority of varicocelectomy over observation in infertile men with palpable varicoceles and impaired semen quality, with increased odds of spontaneous pregnancy and improvements in semen characteristics within 1-year of follow-up.

Diegidio and colleagues (2010) reviewed all the various techniques and their results and efficiencies to provide practicing urologists with some guidance for choice of technique. These investigators discussed improvements of varicocelectomy techniques in the last 15 years and their impact on results of surgery. Pregnancy rates were highest with microsurgical subinguinal technique. Varicocele recurrence rates were lowest with microsurgical subinguinal technique. Hydrocele formation rates were lowest with microsurgical inguinal technique. Surgical complications were highest in the laparoscopic technique. Varicocelectomy by itself or in conjunction with in-vitro fertilization is cost-effective. The authors concluded that microsurgical subinguinal or microsurgical inguinal techniques offer best outcomes; and varicocelectomy is a cost-effective treatment modality for infertility.

The European Association of Urology (EAU)'s guidelines on pediatric urology (Tekgul et al, 2009) stated that for the treatment of varicocele in children and adolescents, surgical intervention is based on ligation or occlusion of the internal spermatic veins. Ligation is performed at different levels: (i) inguinal (or subinguinal) microsurgical ligation, and (ii) suprainguinal ligation, using open or laparoscopic techniques. The advantage of the former is the lower invasiveness of the procedure, while the advantage of the latter is a considerably lower number of veins to be ligated and safety of the incidental division of the internal spermatic artery at the suprainguinal level. Moreover, lymphatic-sparing varicocelectomy is preferred to prevent hydrocele formation and testicular hypertrophy development and to achieve a better testicular function according to the
luteinizing hormone-releasing hormone stimulation test. The methods of choice are subinguinal or inguinal microsurgical (microscopic) repairs, or suprainguinal open or laparoscopic lymphatic-sparing repairs.

Furthermore, the EAU's guidelines on male infertility (Dohle et al, 2010) stated that several treatments are available for varicocele, and that the type of intervention chosen depends mainly on the therapist's experience. Moreover, an accompanying table in the EAU guideline reported a lower recurrence rate (0.8 % to 4.0 %) with microsurgical varicocelectomy than with alternative approaches (3.0 % to 29.0 %).

In a randomized study, Pourmand et al (2014) examined if addition of L-carnitine therapy to standard varicocelectomy adds any extra benefit in terms of improvement in semen parameters or deoxyribonucleic acid (DNA) damage. A total of 100 patients enrolled in this study and were randomly divided into 2 groups (50 patients in each group). In group 1, standard inguinal varicocelectomy and, in group 2, standard inguinal varicocelectomy plus oral anti-oxidant therapy (oral L-carnitine, 250 mg 3 times a day) were performed for 6 months. For all patients, routine semen analysis and DNA damage test of spermatozoa (by 2 methods of terminal deoxynucleotidyl transferase dUTP nick end labeling and protamine damage assay) were performed at baseline and at 3 and 6 months post-operatively. In both groups, the improvement in semen analysis parameters and DNA damage was observed, but there was not any statistically significant difference between the 2 groups in these parameters, although the slope of improvement in DNA damage was slightly better in group 2 (that was not statistically significant). The authors concluded that addition of 750 mg of L-carnitine orally daily to standard inguinal varicocelectomy does not add any extra benefit in terms of improvement in semen analysis parameters or DNA damage.

In a Cochrane review, Showell and colleagues (2014) evaluated the safety and effectiveness of oral supplementation with anti-oxidants for subfertile male partners in couples seeking fertility assistance. These investigators searched the Cochrane Menstrual Disorders and Subfertility Group Specialised Register, CENTRAL, MEDLINE, EMBASE, CINAHL, PsycINFO and AMED databases (from inception until January 2014); trial registers; sources of unpublished literature and reference lists. An updated search was run in August 2014 when potentially eligible studies
were placed in 'studies awaiting assessment'. These researchers included randomized controlled trials (RCTs) comparing any type or dose of anti-oxidant supplement (single or combined) taken by the subfertile male partner of a couple seeking fertility assistance with a placebo, no treatment or another antioxidant. Two review-authors independently selected eligible studies, extracted the data and assessed the risk of bias of the included studies. The primary review outcome was live birth; secondary outcomes included clinical pregnancy rates, adverse events, sperm DNA fragmentation, sperm motility and concentration. Data were combined, where appropriate, to calculate pooled odds ratios (ORs) or mean differences (MD) and 95% CIs. Statistical heterogeneity was assessed using the I(2) statistic. The authors assessed the overall quality of the evidence for the main outcomes using GRADE methods. This updated review included 48 RCTs that compared single and combined antioxidants with placebo, no treatment or another anti-oxidant in a population of 4,179 subfertile men. The duration of the trials ranged from 3 to 26 weeks with follow-up ranging from 3 weeks to 2 years. The men were aged from 20 to 52 years. Most of the men enrolled in these trials had low total sperm motility and sperm concentration. One study enrolled men after varicocelectomy, 1 enrolled men with a varicocele, and 1 recruited men with chronic prostatitis. Three trials enrolled men who, as a couple, were undergoing in-vitro fertilization (IVF) or intra-cytoplasmic sperm injection (ICSI) and 1 trial enrolled men who were part of a couple undergoing intra-uterine insemination (IUI). Funding sources were stated by 15 trials; 4 of these trials stated that funding was from a commercial source and the remaining 11 obtained funding through non-commercial avenues or university grants; 33 trials did not report any funding sources. A limitation of this review was that in a sense these researchers had included 2 different groups of trials, those that reported on the use of anti-oxidants and the effect on live birth and clinical pregnancy, and a second group that reported on sperm parameters as their primary outcome and had no intention of reporting the primary outcomes of this review. These investigators included 25 trials reporting on sperm parameters and only 3 of these reported on live birth or clinical pregnancy. Other limitations included poor reporting of study methods, imprecision, the small number of trials providing usable data, the small sample size of many of the included studies and the lack of adverse events reporting. The evidence was graded as 'very low' to 'low'. The data were current to January 31, 2014. Live birth: anti-oxidants may have increased live birth rates (OR
4.21, 95% CI: 2.08 to 8.51, p < 0.0001, 4 RCTs, 277 men, I(2) = 0 %, low quality evidence). This suggested that if the chance of a live birth following placebo or no treatment is assumed to be 5 %, the chance following the use of anti-oxidants is estimated to be between 10 % and 31 %. However, this result was based on only 44 live births from a total of 277 couples in 4 small studies. Clinical pregnancy rate: anti-oxidants may have increased clinical pregnancy rates (OR 3.43, 95% CI: 1.92 to 6.11, p < 0.0001, 7 RCTs, 522 men, I(2) = 0 %, low quality evidence). This suggested that if the chance of clinical pregnancy following placebo or no treatment is assumed to be 6 %, the chance following the use of anti-oxidants is estimated at between 11 % and 28 %. However, there were only 7 small studies in this analysis and the quality of the evidence was rated as low. Miscarriage: only 3 trials reported on this outcome and the event rate was very low. There was insufficient evidence to show whether there was a difference in miscarriage rates between the anti-oxidant and placebo or no treatment groups (OR 1.74, 95% CI: 0.40 to 7.60, p = 0.46, 3 RCTs, 247 men, I(2) = 0 %, very low quality evidence). The findings suggested that in a population of subfertile men with an expected miscarriage rate of 2 %, use of an anti-oxidant would result in the risk of a miscarriage lying between 1 % and 13 %. Gastro-intestinal upsets: there was insufficient evidence to show whether there was a difference in gastro-intestinal upsets when anti-oxidants were compared to placebo or no treatment as the event rate was very low (OR 1.60, 95% CI: 0.47 to 5.50, p = 0.46, 6 RCTs, 429 men, I(2) = 0 %). These researchers were unable to draw any conclusions from the anti-oxidant versus anti-oxidant comparison as not enough trials compared the same interventions. The authors concluded that there is low quality evidence from only 4 small RCTs suggesting that anti-oxidant supplementation in subfertile males may improve live birth rates for couples attending fertility clinics. Low quality evidence suggested that clinical pregnancy rates may increase. There is no evidence of increased risk of miscarriage but this is uncertain as the evidence is of very low quality. Data were lacking on other adverse effects. They stated that further large well-designed RCTs are needed to clarify these results.

In a systematic review and meta-analysis, Wang and Ji (2020) examined the overall safety and effectiveness of microsurgery versus laparoscopic surgery in the treatment of varicocele according to qualified RCTs. The following electronic databases were searched including PubMed,
Cochrane, Embase to identify the qualified studies and publications that were associated with this meta-analysis updated to February 2018 based on index words. The qualified studies only included RCTs. These researchers analyzed the main outcomes through MD and relative risk (RR) along with 95 % CI. This meta-analysis included a total of 23 studies with 1,178 patients in the group with microsurgery and 1,069 patients in the group with laparoscopic surgery. The results indicated that compared with the laparoscopic surgery group, the microsurgery group could significantly decrease the complication rate (RR: 0.40, 95 % CI: 0.21 to 0.75), as well as the hospital stay (weighed MD [WMD]: -0.53, 95 % CI: -0.85 to -0.21), increase the sperm concentration following the surgery (WMD: 3.00, 95 % CI: 1.23 to 4.76), and decrease the recurrence rate (RR: 0.35, 95 % CI: 0.22 to 0.55). In addition, there was no significant difference of operation time (standardized MD [SMD]: 1.61, 95 % CI: 0.71 to 2.51) and sperm motility (WMD: 2.38, 95 % CI: 0.39 to 4.37) between the 2 groups. The authors concluded that the findings of this study demonstrated that microsurgery would significantly decrease the complication, hospital stay, and recurrence rate and increase the sperm concentration when compared with laparoscopic surgery; microsurgery is a better alternative therapy for the treatment of varicocele than laparoscopic surgery.

Endoluminal Occlusion Device

Venbrux et al (2014) determined the safety and effectiveness of a new endoluminal occlusion device, ArtVentive endoluminal occlusion system (EOS), to occlude the spermatic vein in symptomatic males with varicoceles. The ArtVentive EOS device has been developed for percutaneous, peripheral occlusion of the peripheral arterial and venous vasculature. The system is comprised of an implantable occlusion device and a delivery catheter. At present, there are 2 device sizes: (i) size 1 for target vessels ranging between 3.5 and 5.5 mm in diameter, and (ii) size 2 for target vessels 5.5 to 8.5 mm in diameter. The treatment group included 6 adult males, aged 22 to 34 years; 9 target vessels were occluded and a total of 20 devices were implanted in 6 subjects. The acute occlusion rate at the end of the procedure was 100 % occurring in 9 of 9 vessels. The spermatic veins of all patients remained occluded on venography at 30 days follow-up. Pain scores related to varicoceles decreased in 5 of 6 patients. The authors concluded that although they
recognized this study was limited, initial experience indicated that the ArtVentive EOS is a safe and effective new device for occlusion of vessels (varicoceles). They stated that the device has potential applications in other clinical conditions requiring occlusion of veins or arteries.

Surgical Treatment for Subclinical Varicocele

In a systematic review and meta-analysis, Kim and colleagues (2015) noted that recent meta-analysis by the Cochrane collaboration concluded that treatment of varicocele may improve an infertile couple’s chance of pregnancy. However, there has been no consensus on the management of subclinical varicocele. These researchers determined the impact of varicocele treatment on semen parameters and pregnancy rate in men with subclinical varicocele. The RCTs that evaluated the presence and/or treatment of subclinical varicocele were included for systematic review and meta-analysis. Random effect model was used to calculate the weighted MD of semen parameters and ORs of pregnancy rates. A total of 7 trials with 548 participants, 276 in subclinical varicocelectomy and 272 in no-treatment or clomiphene citrate subjects, were included. Although there was also no statistically significant difference in pregnancy rate (OR 1.29, 95 % CI: 0.99 to 1.67), surgical treatment resulted in statistically significant improvements on forward progressive sperm motility (MD 3.94, 95 % CI: 1.24 to 6.65). The authors concluded that there is insufficient evidence to allow final conclusions because the quality of included studies was very low and further research is needed.

Furthermore, an UpToDate review on "Evaluation of nonacute scrotal pathology in adult men' (Eyre, 2016) states that "Subclinical varicoceles are often discovered as part of an infertility evaluation by demonstrating retrograde flow to the scrotum by Color Doppler ultrasonography. The role of surgical ligation for subclinical varicoceles associated with subfertility is not clear".

Addition of Sclerosants to Coil Embolization

In a retrospective study, Favard and associates (2015) evaluated pain, radiation and recurrence rates in patients undergoing varicocele embolization with 3 different embolic materials. This trial included a total
of 182 consecutive patients who underwent transcatheter retrograde varicocele embolization from July 2011 to May 2015 with glue (Glubran2) (group 1, n = 63), mechanical agents (coils and/or plugs) (group 2, n = 53) or a sclerosing agent (polidocanol) (group 3, n = 66). Patients were asked by telephone interview to evaluate pain during embolization and at 1, 7 and 30 days using a quantitative pain scale ranging from 0 to 10. Duration of scopy, kinetic energy released per unit mass (kerma) and dose area product (DAP) were assessed as radiation parameters during embolization procedures. Recurrence rates after treatment were also evaluated. Statistical analyses were performed using parametric and non-parametric tests. Patients in the 3 study groups were comparable for age, clinical indication and embolization side. No difference was noted for significant pain (pain score greater than or equal to 3) during embolization and at 1, 7 and 30 days after treatment. Discomfort (pain score less than 3) was more frequent in group 1 than in groups 2 and 3 at 7 days after the procedure (p = 0.049). No difference in discomfort was noted during embolization or at 1 and 30 days. Duration of scopy was shorter (p < 0.0001) and kerma was lower (p = 0.0087) in group 1 than in groups 2 and 3. DAP was lower in group 1 than in group 2 (p = 0.04) but no difference was noted between groups 1 and 3, and groups 2 and 3. The recurrence rate at a mean follow-up of 24.4 months (range of 2 to 53 months) was significantly lower in group 1 than in the 2 other groups (p = 0.032). The authors concluded that the use of Glubran2 acrylic glue as an embolic agent for percutaneous embolization of varicocele was a therapeutic alternative that is effective, safe, inexpensive, and easily feasible in an out-patient setting, and had a high technical success rate. Glubran2 triggered a local inflammatory reaction that promoted sclerosis and thrombosis, but without causing more significant pain than was the case with other embolic agents. The liquid nature of the embolization product allowed diffusion through the gonadal vein and its collaterals, which appeared to reduce recurrence rates and improve results. Lastly, the use of glue allowed fast procedures, leading to less radiation than treatment with mechanical or sclerosing agents.

The authors stated that this study had several limitations. First, this was a retrospective review of a cohort from a single center, with some patients lost to follow-up. Second, one goal of the study was to evaluate tolerance to embolization of the spermatic vein with different embolic materials during the procedure and at 1, 7 and 30 days. Almost 50 % ofthe
patients in each group had symptomatic varicocele. After embolization, it usually took a few weeks for the pain to disappear completely.

Consequently, it was difficult to know whether pain reported at 30 days in some patients was related to the procedure or just due to normal recovery in symptomatic patients treated with embolization. Third, the results of this study must be interpreted with caution. Indeed, although these researchers attempted to compare gluing, mechanical and sclerosing agents with each other for varicocele embolization, polidocanol was not used alone in the sclerotherapy group but in combination with coils. This could have led to longer procedure times and higher radiation during the procedure in comparison with sclerotherapy alone. Fourth, the fact that recurrence rate of varicocele, which required a new treatment, was significantly lower in group 1 than in the 2 other groups may have been due to 2 factors. The mean follow-up in this group was significantly shorter than in groups 2 and 3. Indeed, in the authors’ daily practice, glue has come into use more recently in this setting and is now the only embolic agent used for varicocele treatment. Furthermore, no systematic ultrasound imaging follow-up was performed beyond 2 months following the procedure, which could have led to potential lower detection rate of long-term varicocele recurrence. Lastly, infertility was the clinical indication for treatment in a large proportion of these patients. In this setting, varicocele was often asymptomatic and recurrence after embolization could not be determined without ultrasound imaging. The authors stated that the results of this study must be validated in future prospective RCTs with longer follow-up times to determine whether the embolic material can affect outcome.

In a systematic review, Makris and colleagues (2018) evaluated the current evidence regarding the safety and effectiveness of the various embolic materials used in varicoceles embolization. A systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines. Databases were searched for clinical studies that investigated the clinical outcomes of embolization treatment for the management of testicular varicoceles. Study methodological quality was analyzed. A total of 23 retrospective and 7 prospective clinical studies were identified with a total of 3,505 patients. Technical success rates appeared to be above 90 % for all embolic materials without any significant differences. In terms of recurrence rates, glue (n = 251) appeared to have the lowest and sclerosants alone (n =
the highest recurrence rates, which were 4.2% (3.08 to 11%, SD: 5.9) and 11.03% (5.15 to 18.8%, SD: 6.06) within an average follow-up (f/u) of 16.13 and 25.48 months, respectively. Coils alone (n = 898) had an average recurrence rate of 9.1% (1.4 to 17.8%; SD: 5.79) and a mean f/u of 39.3 months. After an average of 12 months of f/u, the addition of sclerosants (n = 1,628) as an adjunct to coils did not improve recurrence rates (8.44%, 5.1 to 16.5%; SD: 3.4). No differences were reported regarding the safety profile of the various embolic materials. The authors concluded that despite the heterogeneity of the included studies, preliminary evidence supported the safe and effective use of the various embolic materials currently used for the management of varicoceles. At 1 year, glue appeared to be the most effective in preventing recurrence with coils being the second most effective. The addition of sclerosants to the coil embolization did not appear to have an impact on recurrence rates. They stated that further research is needed to elucidate the cost-effectiveness of these approaches.

Endovenous Laser Ablation of Spermatic Vein for the Treatment of Varicocele

Basile and colleagues (2017) examined the feasibility and the reliability of endovenous laser ablation (EVLA) of the spermatic vein for the treatment of varicocele. These researchers consecutively and prospectively treated 11 patients (age range of 24 to 45 years, mean of 31) with left varicocele, phlebographically classified as Bahren type I and with indication for percutaneous treatment. Clinical success was evaluated by color Doppler ultrasound (CDUS) 1 week, 1 months and 3 months after the procedures. These investigators also evaluated the pain feeling for 48 hours after the procedure on the basis of the visual analogue score (VAS) obtained through telephonic interview. Technical success was achieved in all cases. In all cases varicocele disappeared at CDUS at 1 and 3 months with reflux abolition; 2 cases of small vein laceration were noted without sequelae, no other complication has been described. All patients reported improvements either regarding symptoms and/or spermiographic parameters. The authors concluded that EVLA of spermatic vein was a feasible and safe treatment in patients with Bahren type I varicocele. The key advantage of this technique was the adoption of a standardized protocol, which remained one of the main problems in gaining scientific evidence in case of coil or sclerosant embolization (type and number of
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coils, amount of sclerosant agent, etc.). The main drawback of this study was the narrow population investigated, limited to Bahren type 1 for this first trial; these researchers awaited laser’s manufacturer to develop a dedicated radio-opaque marker for fiber’s tip.

Furthermore, an UpToDate review on “Treatments for male infertility” (Anawalt and Page, 2018) does not mention endovenous laser ablation as a therapeutic option.

**Microsurgical Varicocelectomy for Repair of Sperm DNA Fragmentation**

Yao and colleagues (2020) noted that sperm DNA integrity has been considered as one of the important determinants of normal fertilization and embryonic development in natural and assisted pregnancy. It is difficult for men with high levels of sperm DNA fragmentation (SDF) in semen to conceive their partners naturally and assist in conception.

Previous studies have found that the level of SDF in the semen of patients with varicocele (VC) was on the high side. In recent years, the effect of VC surgery on DNA fragmentation index has attracted the attention of researchers. In this study, these investigators will examine the effectiveness of VC repair as a means of alleviating SDF and improving male fertility.

Electronic databases including English databases (PubMed, Medline, Embase, Web of Science, Cochrane Library) and Chinese databases (China National Knowledge Infrastructure, China Biology Medicine Database, Wanfang Database, VIP Database) will be searched from their inception to December 2020 to recognize related studies. All the RCTs of microsurgical varicocelectomy for the management of VC patients will be included. The potential outcome will include improvement in SDF, oxidative stress markers (reactive oxygen species, nitric oxide, and lipid peroxidation products), sperm chromatin compaction, other advanced sperm function characteristics, follow-up of fertility results. These researches will carry out this study strictly according to the Cochrane Handbook for Systematic Reviews of Interventions. The study is a protocol for systematic review and meta-analysis without results, and data analysis will be performed after the protocol. These researchers will share their findings on April 5, 2021.

The authors stated that this systematic review will provide more evidence
to examine if varicocelectomy is an effective intervention for patients with SDF. The results will be published in a public issue journal and offer the urologists help in clinical decision-making.

In a meta-analysis, Wang and associates (2020) examined the effect of primary varicocele and related surgery in male infertility. These researchers carried out a systematic search of the literature using the Medline, Embase, Cochrane, and CNKI databases; the search was up to September 2019. Article selection proceeded according to the search strategy based on Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) criteria. Data were analyzed using RevMan 5.2. A random-effects model was used to calculate the overall combined risk estimates. After screening 687 articles, 4 RCTs with 349 patients were included; 172 patients were addressed in embolization/ligation, with 177 patient's observation treatment. The number of spontaneous pregnancies in the 2 groups was 41 and 40, respectively. There was no significant difference in pregnancy rate between the operation group and the control group; RR = 1.05 (0.72, 1.54). The authors concluded that there was insufficient evidence to explain the surgical treatment of varicocele could improve the natural fertility of the infertile couples, and there is still a need for more of prospective RCTs to verify the efficacy of varicocele surgery for treating of male infertility. These researchers did not deny the importance of this operation, they just wanted to call on everyone to strictly grasp the indications of the operation, avoid ineffective medical expenses, and avoid unnecessary pain to patients.

Furthermore, UpToDate reviews on “Approach to the male with infertility” (Anawalt and Page, 2021a) and “Treatments for male infertility” (Anawalt and Page, 2021b) do not mention microsurgical varicocelectomy as a management / therapeutic option.

CPT Codes / HCPCS Codes / ICD-10 Codes

*Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by *+*.

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
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<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
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</thead>
<tbody>
<tr>
<td>37241</td>
<td>Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; venous, other than hemorrhage (eg, congenital or acquired venous malformations, venous and capillary hemangiomas, varices, varicoceles)</td>
</tr>
</tbody>
</table>

CPT codes not covered for indications listed in the CPB

Endovenous laser ablation (EVLA) of the spermatic vein no specific code

Other CPT codes related to the CPB

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
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<tbody>
<tr>
<td>37799</td>
<td>Unlisted procedure, vascular surgery</td>
</tr>
<tr>
<td>55530</td>
<td>Excision of varicocele or ligation of spermatic veins for varicocele [not covered for subclinical varicocele]</td>
</tr>
<tr>
<td>55540</td>
<td>Excision of varicocele or ligation of spermatic veins for varicocele [not covered for subclinical varicocele]</td>
</tr>
<tr>
<td>55550</td>
<td>Laparoscopy, surgical, with ligation of spermatic veins for varicocele [not covered for subclinical varicocele]</td>
</tr>
</tbody>
</table>

HCPCS codes not covered for indications listed in the CPB

ArtVentine endoluminal occlusion system, Sodium tetradecyl sulfate (Sotradecol, Trombovar), Polidocanol (Asclera, Aethoxysclerol, Varithena), Sodium morrhuate (Scleromate), Hypertonic sodium chloride solution, Sodium chloride solution with dextrose (Sclerodex), Chromed glycerin (Sclerno), Polyiodinated iodine - no specific code

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<tr>
<th>Code</th>
<th>Code Description</th>
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<tbody>
<tr>
<td>J1430</td>
<td>Injection, ethanolamine oleate, 100 mg</td>
</tr>
</tbody>
</table>

ICD-10 codes covered if selection criteria are met

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
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<tbody>
<tr>
<td>E29.1</td>
<td>Testicular hypofunction</td>
</tr>
<tr>
<td>I86.1</td>
<td>Scrotal varices</td>
</tr>
<tr>
<td>N46.01</td>
<td>Azoospermia</td>
</tr>
<tr>
<td>N46.029</td>
<td>Azoospermia</td>
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</table>
## Varicocele: Selected Treatments

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>N46.11</td>
<td>-</td>
</tr>
<tr>
<td>N46.129</td>
<td>Oligospermia</td>
</tr>
</tbody>
</table>

The above policy is based on the following references:

4. Anawalt BD, Page ST. Treatments for male infertility. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed February 2018; February 2012b.


17. Eyre RC. Evaluation of nonacute scrotal pathology in adult men. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed February 2016.


Varicocele: Selected Treatments

There are no amendments for Medicaid.

Updated 04/23/2021