Varicocele treatment for fertility
AUC September 2013

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INTRO

• 15% Normal population (11% in EAU)
• 40% men with infertility (25% in EAU)
• 80% of varicocele have no infertility

• Only palpable varicoceles have been documented to be associated with infertility
• Imaging should not be used for subclinical varicocele.  
Varicocele

- Varicocele is the abnormal tortuosity and dilation of the testicular veins within the spermatic cord.
The diagnosis

- Medical and reproductive history
- Physical examination in both recumbent and standing position
- Typically USS demonstrate 3.5mm veins with reversal venous flow after Valsalva
Varicoceles

• Associated with;
  – Impaired semen quality
  – Decreased Leydig cell function
    • Progressive in nature

• Repair – improves both spermatogenesis & Leydig cell function

• Recognised as;
  – ‘the most surgically correctable cause of male infertility’ &
  – ‘most commonly performed surgical procedure in the Rx of male infertility’
Impact of varicocele on semen parameter

• Although majority of men with varicocele are fertile
• The semen samples from men with varicocele have
  • Decreased motility (90%)
  • Concentration of less than 20 millions/ml in 65%.
Mechanism of infertility

• The mechanism of which varicocele affects testicular function is unclear.
• The intratesticular temperature has a difference of 0.5 to 0.78 degree Celsius compared with the men without varicocele.
Grading

– **Subclinical**

– **Grade I** = Small, palpable only with valsalva manoeuver

– **Grade II** = Moderate size, easily palpable without valsalva manoeuver

– **Grade III** = Large, visible through scrotal skin

• Hudson et al, Fertil Steril 1986
Indications for treatment

• Infertile adult male with a varicocele is considered a candidate for repair if:

  – All of the following 4 conditions are met:

    • Couple has known infertility
    • Female has normal fertility or potentially treatable cause
    • Varicocele is palpable or confirmed by USG
    • Male partner has abnormal semen parameters

Report on Varicocele and Infertility 2004
AUA, ASRM
Evidence for

• Baazeem A et al, Eur Urol 2011
  • recent meta-analysis of four RCTs
  • trend in favour of surgical correction
  • combined OR was 2.23 (95% CI, 0.86-5.78; \( P = 0.091 \))
  • effect was not statistically significant
Marmar JL, Agarwal A, Prabakaran S, et al. **Reassessing the value of varicocelectomy as a treatment for male subfertility with a new meta-analysis.**
Fertil Steril 2007; 88:639

### Table 1  Confidence intervals and odds ratio for pregnancy after varicocelectomy among men with palpable lesions and at least one abnormal semen parameter

<table>
<thead>
<tr>
<th>Study</th>
<th>Varicocelectomy n/N</th>
<th>Control n/N</th>
<th>OR (random) 95% CI</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Grasso et al., 2000</td>
<td>1 / 34</td>
<td>2 / 34</td>
<td>0.48 [0.04, 5.61]</td>
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<td>Madgar et al., 1995</td>
<td>16 / 25</td>
<td>2 / 20</td>
<td>13.50 [2.55, 71.40]</td>
<td></td>
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<tr>
<td>Marmar et al., 1994</td>
<td>66 / 186</td>
<td>3 / 19</td>
<td>2.93 [0.82, 10.44]</td>
<td></td>
</tr>
<tr>
<td>Okuyama et al., 1998</td>
<td>43 / 141</td>
<td>15 / 83</td>
<td>1.99 [1.02, 3.86]</td>
<td></td>
</tr>
<tr>
<td>Onozawa et al., 2002</td>
<td>6 / 10</td>
<td>5 / 18</td>
<td>3.90 [0.76, 19.95]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>396</td>
<td>174</td>
<td>2.87 [1.33, 6.20]</td>
<td></td>
</tr>
</tbody>
</table>

Total events: 131 (Varicocelectomy), 27 (Control)
Test for heterogeneity: Chi² = 8.47, df = 4 (P = 0.17), r = 38.1%  
Test for overall effect Z = 2.68 (P < 0.00001)

OR, odds ratio; n, number of couples achieving pregnancy with male partners diagnosed with clinical varicoceles; N, total number of cases. Published with permission from [11**].
1\textsuperscript{st} meta-analysis showed no benefit

2\textsuperscript{nd} analysis whittled down 101 articles to five studies (two randomized, three observational) after careful critical appraisal and methodologic evaluation

In addition, these five studies only included men with palpable varicocele and at least one abnormal semen parameter treated with surgical varicocele ligation.

Outcome measure was limited to spontaneous pregnancy rate.

They found the odds of spontaneous pregnancy after varicocelectomy compared with no or medical treatment for clinical varicocele to be \textit{2.87}\;[95\% confidence interval (CI), 1.33–6.20, \textit{P} < 0.01] using the inverse variance random-effects model [odds ratio (OR)\textit{1}/42.63 (95\% CI 1.60–4.33, \textit{P} < 0.0001) with the fixed-effects model].

Of the 396 patients who underwent surgery, 131 (33.0\%) had pregnancies compared with 27 (15.5\%) of 174 control patients. The number needed to treat was \textit{5.7}\;[95\% CI 4.1–9.5].
J Androl 2009; 30:33-40

- Meta-analysis of 4473 patients with palpable varicoceles and abnormal semen parameters. A spontaneous pregnancy rate was reported in 39.07% after varicocele repair

- reviewed the clinical outcomes of 118 consecutive infertile couples with clinical varicocele and isolated asthenospermia.
- After varicocele repair, the total motile sperm count was significantly increased (29.610^6 preoperatively vs. 39.010^6 postoperatively).
- The spontaneous pregnancy rate was significantly higher (65 vs. 32%) and the combined spontaneous and intrauterine insemination pregnancy rate was also significantly higher in the surgery group compared to the control group (74 vs. 36%, respectively).


- natural pregnancy rates were 60.0% in the varicocelectomy group and 18.7% in the observation group.
- Moreover, the pregnancy rates after varicocelectomy correlate negatively with the infertility period [43.9 vs. 31.7% (P<0.05) for 0–3 years and >9 years, respectively]
Mean sperm count, sperm concentration and sperm progressive motility improved significantly after varicocelectomy from 18.3 x 106 to 44.4 x 106, 4.8 x 106/ml to 14.3 x 106/ml and 16.7% to 26.6%, respectively (p <0.001). The DNA fragmentation index decreased significantly after surgery from 35.2% to 30.2% (p = 0.019).

After varicocelectomy 37% of the couples conceived spontaneously and 24% achieved pregnancy with assisted reproductive technique.

The mean postoperative DNA fragmentation index was significantly higher in couples who did not conceive spontaneously or with assisted reproductive technique (p = 0.033).

11 publications from the previous 20 years regarding to the interest of varicocele repair in patients with nonobstructive azoospermia.

A total of 233 patients were analyzed. After varicocele repair 91 (39.1%) patients had motile sperm in the ejaculate and 14 spontaneous pregnancies were reported

A higher spontaneous pregnancy rate or improvement in semen analysis was reported in patients with maturation arrest (42.1%) or hypospermatogenesis (54.5%) than in those with Sertoli-cell-only (11.3%) after varicocele repair (P<0.001).

Patients with late maturation arrest had a higher significant probability of success (45.8%) than those with early maturation arrest (0%).
242 infertile men with a history of clinical varicocele who underwent intracytoplasmic sperm injection. Of the men

- 80 underwent prior subinguinal microsurgical varicocelectomy (treated group 1) and 162 had any grade of clinical varicocele (untreated group 2) at sperm injection.

- an improved total number of motile sperm (6.7 x 10^6 vs 15.4 x 10^6, p <0.01) and a decreased sperm defect score (2.2 vs 1.9, p = 0.01) after vs before varicocele repair.

- The clinical pregnancy (60.0% vs 45.0%, p = 0.04) and live birth (46.2% vs 31.4%, p = 0.03) rates after the sperm injection procedure were higher in the treated than in the untreated group.

- The chance of achieving clinical pregnancy (OR 1.82; 95% CI 1.06-3.15) and live birth (OR 1.87, 95% CI 1.08-3.25) by the sperm injection procedure were significantly increased while the chance of miscarriage was decreased (OR 0.433, 95% CI 0.22-0.84) after varicocele was treated.
• Observation (N = 185), patients who had varicocele correction (N = 137).
• Pregnancy rate (PR) in corrected and uncorrected varicocele groups did not differ significantly, but when subjects with infertility beyond 2 years were considered, varicocele-corrected subjects had a significantly greater PR than uncorrected varicocele patients (p = 0.025).
• Together with infertility duration, spermatozoa progressive motility appears the most important predictor of fertility, whereas neither grade of varicocele nor age of the couple (within the age limits of this study) influenced the outcome.
• Similarly, CAG repeat length did not affect the outcome of varicocele correction.
• These data suggest that varicocele correction at 1 year of infertility does not result in a significantly higher PR than that achieved by men with uncorrected varicocele.
• In view of the high spontaneous PR in subjects with an infertility of less than 2 years, varicocele correction aimed at restoring fertility appears to be most appropriate for men whose infertility extends beyond 2 years.
Evidence against


- The meta-analysis of the Cochrane Database that suggested a lack of benefit in terms of natural conception after treatment of varicoceles but the methodology of this study allowed inclusion of patients with subclinical varicoceles and without abnormal semen parameters
Evidence ‘against’ for subclinical varicoceles

• Subclinical varicocele
  – Varicocele diagnosed by imaging studies
  – No impact on fertility
  – Repair does not improve fertility rates

Jarow et al 1996
### Evidence summary

<table>
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<tr>
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<td>Points</td>
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<td>Improvement in semen results</td>
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<td>Improvement in sperm density</td>
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<td>60% vs 10% for no repair</td>
<td>Improved pregnancy rates</td>
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<td>Nagler and Martinis, 1997</td>
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<td>50-60% experienced improvement in semen variables</td>
<td>30 – 40 % pregnancy</td>
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### 6.6 Conclusions and recommendations for varicocele

#### Conclusions

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<tr>
<td>Current information supports the hypothesis that the presence of varicocele in some men is associated with progressive testicular damage from adolescence onwards and a consequent reduction in fertility.</td>
<td>2a</td>
</tr>
<tr>
<td>Although the treatment of varicocele in adolescents may be effective, there is a significant risk of overtreatment.</td>
<td>3</td>
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<tr>
<td>Varicocele repair may be effective in men with subnormal semen analysis, a clinical varicocele and otherwise unexplained infertility.</td>
<td>1a</td>
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#### Recommendations

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<th>GR</th>
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<td>Varicocele treatment is recommended for adolescents with progressive failure of testicular development documented by serial clinical examination.</td>
<td>B</td>
</tr>
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<td>No evidence indicates benefit from varicocele treatment in infertile men who have normal semen analysis or in men with subclinical varicocele. In this situation, varicocele treatment cannot be recommended (15-17).</td>
<td>A</td>
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<td>Varicocele repair should be considered in case of a clinical varicocele, oligospermia, infertility duration of ≥ 2 years and otherwise unexplained infertility in the couple.</td>
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Types of intervention

Surgical

• Open
  • Retroperitoneal (Palomo)
  • Inguinal (Modified Ivanissevich)
  • Sub-inguinal
  • Scrotal
  • Laparoscopic

Radiological intervention

• Antegrade

Retrograde sclerotherapy
### Table 9: Recurrence and complication rates associated with treatments for varicoceles

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<th>Ref.</th>
<th>Recurrence/ persistence %</th>
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<td>20,21</td>
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<td>Pain due to thrombophlebitis, bleeding haematoma, infection, venous perforation, hydrocele, radiological complication (e.g., reaction to contrast media), misplacement or migration of coils, retroperitoneal haemorrhage, fibrosis, ureteric obstruction</td>
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<td>Inguinal approach</td>
<td>22</td>
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<td>26,27</td>
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<td>Injury to testicular artery and lymph vessels; intestinal, vascular and nerve damage; pulmonary embolism; peritonitis; bleeding; postoperative pain in right shoulder (due to diaphragmatic stretching during pneumoperitoneum); pneumoscrotum: wound infection</td>
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Outcomes

• Correction of varicoceles also improves serum FSH and testosterone
  
  – Cayan and associates 1999
    • Increase in serum free testosterone
    • Improvement in sperm concentration and motility

• Decrease in mean FSH from 15.2mIU/mL (before) to 10.8mIU/mL (after)
Outcomes

• Serum testosterone
  – Mean increase from 319ng/dL – 409ng/dL

Stu et al 1995
Predictors of successful repairs

• Higher spontaneous post-repair pregnancy rates if:
  – Sperm concentration > 5 million/ml
  – 61% vs 8%

  Kamal, 2001 & Matkov, 2001

• Marks, McMahon and Lipshultz
  – Identified 4 preop factors a/w increased likelihood of postop pregnancy
    • Lack of testicular atrophy
    • Semen density > 50mil per ejaculate
    • Motility > 60%
    • FSH <300 ng/ml (normal 50-300ng/ml)
Retroperitoneal approach

• Palomo (1948)
  – 1\textsuperscript{st} to describe the high ligation of the entire spermatic cord above the internal ring

• Retroperitoneal approach
  – Involves ligation of the internal spermatic vein as it exits the inguinal canal
  – Preservation of the internal spermatic artery
Retroperitoneal approach

• Complications
  – Recurrence or persistence 11-15%
    Niedzielski and Paduch, 2001
  – Due to non-ligation of the cremasteric vessels
  – Recurrence rate Children > adults 15 - 45%
    Lemack, Minevich 1998
Laparoscopic approach

• Testicular artery and veins – dissected
  – Veins isolated and clipped/ligated

• Separate dissection of the spermatic vein and artery
  – challenging

• Some advocate – ligation of all the vessels including the testicular artery
  – Collateral supply thru the cremasteric and vasal arteries
    • Prevent testicular atrophy
Laparoscopic approach

• Complications
  – General
  – Recurrence rate < 2%
  – Hydrocele formation 5-8%

Nyirady 2002; Koyle, McManus 2004

• Chrouser et al, 2004
  – 62 lap varicocelectomy
  – 4.8% transient numbness of ipsilateral anterior thigh
  – Resolved/improved ~ 8/12
  – Cautery of peritoneum overlying spermatic cord & excessive traction of tissues
Inguinal approach

• Modified Ivanissevich
  – 3-4cm oblique incision
  – 2fb above the S. pubis (just above ext ring)
  – Spermatic cord mobilised near the P.tubercle

• Microsurgical technique
  – Int and ext spermatic fascia incised
  – Dilated veins identified
  – Testicular artery identified (doppler,papavarine)
  – Veins ligated or clipped
  – Lymphatic channels visualised and preserved
    • Prevent postop hydrocele formation
Subinguinal approach

- 2-3cm transverse incision @ external ring
- Spermatic cord identified as it exits external ring
- Cord mobilised and brought out
- Microsurgical approach
  - As described
Microvascular vs Non-Microvascular approaches

• Main advantage
  – Significant reduction in postop complications
    • Testicular artery injury
    • Hydrocele formation (3-39% vs rare)
    • Varicocele recurrence (1-2 % vs 9-16 %)

• Recurrence rate
  – Microscopic inguinal varicocelectomy 1-2%
  – Non-microscopic inguinal repair 9-16%

Cayan et al,2000
Percutaneous Embolisation

• Lima 1978 – 1st reported transvenous sclerotherapy for ablation of varicoceles
  – Coils
  – Balloons
  – Sclerotherapy

• Complications
  – Balloon deflation & migration
  – Recurrence
  – Failure of initial attempted procedures
Percutaneous Embolisation

• Success rates
  – 68%  

• Recurrence rates
  – 4-11%  

• Percutaneous embolisation
  – Especially useful in recurrent or persistent varicocele
    • when the anatomy needs to be radiographically clarified
Thank You