Effects of Varicocele on Serum Testosterone and Changes of Testosterone After Varicocelectomy: A Prospective Controlled Study

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OBJECTIVE To examine the hypotheses that clinical varicoceles affect baseline serum total testosterone levels (T) and varicocelectomy improves T.

MATERIALS AND METHODS This prospective, nonrandomized, controlled study involved 4 groups of adult men. Varicocele-infertile treatment group (VIT) included 66 men who underwent varicocelectomy. Thirty-three varicocele-infertile control men (VIC) and 33 varicocele-fertile control men (VFC) were only observed. Normal-control (NC) group included 33 fertile men without varicocele. Varicocele groups were stratified into baseline hypogonadal (T <300 ng/dL) or eugonadal (T ≥300 ng/dL) subgroups. Main outcome measurements were between-group baseline T differences; and within-group T changes at 6- and 12-month follow-ups of men with varicocele. $P < .05$ was considered significant.

RESULTS Means (standard deviations) of baseline T in VIT, VIC, VFC, and NC were 347.4 (132.1), 339.7 (125.8), 396.6 (164.9), and 504.8 (149.7) ng/dL, respectively. The baseline T levels of varicocele groups were comparable, whereas they were significantly low compared with NC group. At 6-month follow-up, VIT demonstrated significant T improvements (mean change = 44.7 ng/dL; 12.9%; $P < .0001$). T changes were more remarkable among baseline hypogonadals (mean change = 93.7 ng/dL; 40.1%; $P < .0001$) compared with eugonadals (mean change = 8.6 ng/dL; 2.01%; $P = .1223$). These improvements were persistent at 12-month follow-up. Contrariwise, VIC and VFC exhibited nonsignificant T changes. Postvaricocelectomy T changes correlated significantly and inversely with baseline T ($r = -0.689$; $P < .0001$). This correlation was stronger and more significant among hypogonadals ($r = -0.528$; $P = .004$) than eugonadals ($r = -0.400$; $P = .013$). T improvements also exhibited significant positive correlations with preoperative and postoperative sperm concentrations.

CONCLUSION Baseline T was significantly low in men with varicocele compared with normal men. Varicocelectomy yielded significant T improvements among hypogonadal men but insignificant changes in eugonadals. T changes correlated strongly and significantly with baseline T and sperm concentrations. UROLOGY 84: 1081–1087, 2014. © 2014 Elsevier Inc.

Clinical varicocele is a prevalent condition affecting 15% of general male population, 35% of patients with primary infertility, and 81% of men presenting for the management of secondary infertility.[1,2] The associations between clinical varicocele, impaired spermatogenesis, and male infertility have long been recognized,[2,3] and several studies have documented improvements in semen quality and pregnancy rates after varicocele repair.[4-8]

On the other hand, the association between clinical varicocele and impaired testosterone production is less clearly understood. Although the conceptions of the negative impact of clinical varicocele on Leydig cell functions and the beneficial effect of varicocele repair on testosterone production have been proposed for decades,[9-11] only scanty studies have examined such issues, with most of them being retrospective, having contradictory results, or addressing testosterone changes as secondary outcomes.[12,13]

The present study was designed to examine the following hypotheses: (1) Clinical varicoceles affect

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baseline serum total testosterone levels (T) and (2) Varicocele repair improves serum testosterone levels. Another objective of the study was to identify the variables correlating with testosterone changes after varicocele repair.

MATERIALS AND METHODS

Setting

The study was conducted from April 2009 to October 2013 at King Abdulaziz University, Jeddah, Saudi Arabia. Ethical committee approved the study and each patient provided an informed consent.

Study Design

This prospective, nonrandomized, controlled 4-group study incorporated adult men aged between 20 and 50 years. The study involved 1 treatment group: varicocele-infertile treatment group (VIT). Additional 3-control groups were recruited: varicocele-infertile control group (VIC), varicocele-fertile control group (VFC), and normal control group (NC).

Inclusion Criteria

- VIT: Included clinical men with varicocele with ≥1 yr of infertility and impairment of at least 1 semen parameter, who underwent subinguinal microsurgical varicocele repair with arterial and lymphatic sparing.[6]
- VIC: Included men with criteria similar to VIT, who preferred conservative management or using an assisted reproductive technique.
- VFC: Involved fertile men with clinical varicoceles presenting with scrotal pain and/or swelling or incidental clinical varicoceles, who were managed conservatively.
- NC: Included men from the stone clinic and comprised otherwise healthy fertile men without varicoceles, whose baseline serum total testosterone levels were used for comparison with VIT, VIC, and VFC.

Exclusion Criteria

Exclusions were men with subclinical varicoceles, recurrent varicoceles, or azoospermia or men receiving exogenous androgens, clomiphene citrate, or aromatase inhibitors. Men lost to follow-up were as well excluded from analysis.

Baseline Assessment and Follow-up

Varicoceles were physically assessed and graded according Dubin and Amelar grading system.[14] As we do not routinely encourage patients with isolated grade-1 varicoceles to undergo repair, grade-1 varicoceles were corrected (VIT) only after thorough counseling and in context of patients' preference. Scrotal ultrasonography further documented the varicoceles and testicular volumes. Testosterone measurements were done at baseline for all groups and were repeated at 6- and 12-month after surgery (VIT) or after baseline assessment (VIC and VFC). A second test was requested after 2 weeks of each measurement. The second test was essential for men demonstrating T <300 ng/dL at any point of time. When ≥2 measurements were available, the average was considered for statistical analysis. All testosterone measurements were obtained in our laboratory between 8:00 AM and 10:30 AM. Semen analyses and serum levels of luteinizing hormone (LH) and follicle stimulating hormone (FSH) were tested at baseline and at follow-up visits of varicocele groups.

Outcome Measurements

The following differences were measured: (1) cross-sectional baseline T differences among all groups, (2) within-group testosterone changes at follow-up among varicocele groups, and (3) between-group T differences at follow-ups among varicocele groups.

Sample Size

Based on a preliminary retrospective review of medical records of 30 consecutive patients having inclusion criteria similar to the VIT group, a size effect of 14% increase in T after varicocelectomy was estimated. Assuming no expected change in VIC, 66 and 33 men were required for VIT and VIC groups, respectively, to accomplish a statistical power of 80% at 5% alpha level and 0.5 ratio. Additional 33 men were suggested for each of VFC and NC groups.

Statistical Analysis

GraphPad Prism, version 6.03, was used for analysis. A 2-tailed P <.05 was considered statistically significant. Descriptive statistics of means (standard deviations [SDs]), frequencies, and percentages were calculated. Repeated-measures analysis of variance, paired t test, and Wilcoxon matched-pairs signed-ranks test were performed to analyze within-group changes as appropriate. Analysis of variance, unpaired t test, and Mann-Whitney test were used for between-group comparisons. According to the cutoff value for biochemical hypogonadism (T <300 ng/dL), VIT, VIC, and VFC were further stratified into hypogonadal (<300 ng/dL) or eugonadal (≥300 ng/dL) men. The risk of experiencing biochemical hypogonadism in men with varicocele during the follow-up period was presented as frequency, percentage, absolute risk reduction (ARR), and the number needed to treat to benefit (NNT). Multivariate analyses of patients' age, testicular volume, varicocele grade, varicocele laterality, sperm characteristics (concentration, motility, and morphology), LH, FSH, and baseline T were used to identify the variables correlating with changes in T after varicocelectomy.

RESULTS

Patients' Characteristics

We recruited a total of 171 men to per-protocol analyze 66 (VIT), 33 (VIC), 33 (VFC), and 33 (NC) men after excluding 5 men who were lost to follow-up and 1 patient who violated the study protocol.

The means (SDs) of age were 31.7 (6.2), 29.3 (7.5), 32.1 (8.1) and 32.4 (7.3) years for VIT, VIC, VFC, and NC groups, respectively, with insignificant age differences. The demographics and clinical characteristics of the studied men are displayed in Table 1.

Baseline Differences of Testosterone

The means (SDs) of baseline T in VIT, VIC, VFC, and NC groups were 347.4 (132.1), 339.7 (125.8), 396.6 (164.9) and 504.8 (149.7) ng/dL, respectively (Table 2). Baseline T levels of VIT and both VIC and VFC groups were

Table 1. Demographics and characteristics of the study groups at baseline

Characteristic	VIT (n = 66)	VIC (n = 33)	VFC (n = 33)	NC (n = 33)
Age, y, mean ± SD	31.7 ± 6.2	29.3 ± 7.5	32.1 ± 8.1	32.4 ± 7.3
Testicular volume, mL				
Left, mean ± SD	13.3 ± 1.3	14.2 ± 1.8	16.0 ± 1.5*	17.5 ± 2.2*
Right, mean ± SD	15.2 ± 1.7	16.1 ± 2.4	18.1 ± 1.8*	18.3 ± 2.1*
Varicocele side, n (%)				N/A
Left	48 (72.7)	23 (69.7)	25 (75.8)	
Right	0	0	0	
Bilateral	18 (27.3)	10 (30.3)	8 (24.2)	
Total varicoceles, n	84	43	41	
Varicocele grade,† n (%)				N/A
Grade 1	10 (15.2)	6 (18.2)	4 (12.1)	
Grade 2	24 (36.4)	11 (33.3)	15 (45.5)	
Grade 3	14 (21.2)	6 (18.2)	6 (18.2)	
Grades 1+1	9 (13.6)	5 (15.2)	4 (12.1)	
Grades 2+1	5 (7.6)	2 (6.1)	2 (6.1)	
Grades 3+1	3 (4.5)	3 (9.1)	2 (6.1)	
Grades 3+2	1 (1.5)	0	0	
LH, mIU/mL, mean ,± SD	3.92 ± 0.88	4.27 ± 1.12	4.06 ± 0.78	N/A
FSH, mIU/mL, mean ± SD	6.30 ± 2.11	5.61 ± 2.27	4.56 ± 1.26	N/A
Sperm, mean ± SD				N/A
Concentration, million/mL	17.84 ± 4.89	19.8 ± 5.5	43.92 ± 13.14	
Motility, %	26.77 ± 11.80	23.8 ± 5.1	45.18 ± 8.66	
Morphology, normal, %	31.55 ± 4.20	28.5 ± 8.2	41.82 ± 9.77	

FSH, follicle stimulating hormone; LH, luteinizing hormone; N/A, not applicable; NC, normal control group; SD, standard deviation; VFC, varicocele-fertile control group; VIC, varicocele-infertile control group; VIT, varicocele-infertile treatment group.
* Significant difference compared to VIT. Other differences were insignificant compared to VIT.
† Grades "*+*" imply left and right varicoceles, respectively.

comparable, with mean differences of 7.7 ($P = .6913$) and −49.1 ($P = .2166$) ng/dL, respectively (Table 3). On the other hand, baseline levels of the varicocele groups (VIT, VIC, and VFC) were significantly low compared with the NC group with mean differences of −157.4 ($P < .0001$), −165.1 ($P < .0001$), and −108.3 ($P = .0069$) ng/dL, respectively (Table 3).

Within-group Changes

At 6-month follow-up, T levels of VIT men demonstrated significant within-group improvements from baseline (mean change = 44.7 ng/dL; 12.9%; $P < .0001$). T changes were obvious among the baseline hypogonadal subset of men who demonstrated highly significant improvements (mean change = 93.7 ng/dL; 40.1%; $P < .0001$). However, baseline eugonadal subset of men demonstrated insignificant changes (mean change = 8.6 ng/dL; 2.01%; $P = .1223$). The improvements were persistent at the 12-month follow-up (Table 2). Contrariwise, VIC and VFC men exhibited nonsignificant within-group T changes during follow-up; whether they were hypogonadals or eugonadals at baseline (Table 2).

Between-group Differences

At 6-month follow-up, the mean T difference between VIT and VIC was significant ($P = .0216$), whereas the mean VIT vs VFC difference was nonsignificant ($P = .6321$). Yet, the mean difference between VIT at 6-month and baseline NC was significant ($P = .0004$). The T differences at 6- and 12-month are listed in Table 3.

Risk of Biochemical Hypogonadism

At baseline, 28 of 66 (42.42%) of VIT, 16 of 33 (48.48%) of VIC, 12 of 33 (36.36%) of VFC, and 5 of 33 (15.15%) of NC men were hypogonadals. At 6-month follow-up, among VIT men, 20 (30.3%) were converted to eugonadals, whereas 8 men (12.12%) persisted as hypogonadals. None of VIT eugonadals (38 men) were converted to hypogonadals after repair of varicocele. On the other hand, none of VIC men were converted from baseline hypogonadal to eugonadal status. The risks of maintaining or attaining biochemical hypogonadism at 6-month follow-up were significantly lower among VIT compared to VIC men (ARR = 36.36% and NNT = 2.8; 95% confidence interval [CI] = 2.0, 4.4 patients). The risk reduction was more pronounced in the subset of men with pre-existing baseline biochemical hypogonadism among VIT compared with VIC (ARR = 71.4% and NNT = 1.4; 95% CI = 1.03, 2.2 patients).

Correlations

The increase in T after varicocele repair among VIT men demonstrated significant strong inverse correlation with baseline T ($r = −0.689$; $P < .0001$). A stronger and more significant inverse correlation was observed among the subset of 28 baseline hypogonadal men ($r = −0.528$; $P = .004$) than the 38 eugonadal men ($r = −0.400$; $P = .013$). Besides, testosterone changes within VIT group exhibited a significant positive correlation with both preoperative ($r = 0.409$; $P < .001$) and postoperative ($r = 0.352$; $P = .004$) sperm concentrations. None of the variables of age, testicular volume, grade, laterality, LH, FSH, or other sperm characteristics showed significant correlations with testosterone changes after varicocelectomy.

Table 2. Baseline T (ng/dL) and their within-group changes at follow-up

	Baseline	6 mo	12 mo
	T, Mean ± SD (95% CI)	T, Mean ± SD (95% CI), Mean Change (95% CI) [% Change]	T, Mean ± SD (95% CI), Mean Change (95% CI) [% Change]
Group VIT			
Overall (n = 66)	347.4 ± 132.1 (315.0 to 380.0)	392.2 ± 100.7 (367.4 to 416.9), 44.7 (30.0 to 59.4) [12.9], $P < .0001$	399 ± 98.5 (374.8 to 423.2), 51.6 (35.3 to 67.8) [14.9], $P < .0001$
Eugonadal (n = 38)	431.1 ± 108.8 (395.4 to 466.9)	439.8 ± 101.3 (406.5 to 473.1), 8.6 (0.21 to 17.1) [2.01], $P = .1223$	445.3 ± 98.7 (412.9 to 477.8), 14.2 (2.5 to 26) [3.3], $P = .0191$
Hypogonadal (n = 28)	233.8 ± 50.7 (214.2 to 253.5)	327.5 ± 53.2 (306.9 to 348.1), 93.7 (71.1 to 116.2) [40.1], $P < .0001$	336.1 ± 53.8 (315.3 to 357), 102.3 (77.4 to 127.2) [43.7], $P < .0001$
VIC			
Overall (n = 33)	339.7 ± 125.8 (295.1 to 384.3)	344.8 ± 128.3 (299.3 to 390.3), 5.1 (−7.1 to 17.3) [1.5], $P = .4004$	350.7 ± 125.7 (306.1 to 395.2), 10.9 (−1.1 to 23) [3.2], $P = .0734$
Eugonadal (n = 17)	435.6 ± 101.9 (383.2 to 488)	439.7 ± 103.7 (386.3 to 493), 4.07 (−16.3 to 24.5) [0.93], $P = .6780$	444.5 ± 99 (393.5 to 495.4), 8.9 (−10.6 to 28.4) [2.04], $P = .3492$
Hypogonadal (n = 16)	238 ± 34.3 (219.6 to 256.2)	244 ± 51.4 (216.7 to 271.4), 6.1 (−9.3 to 21.5) [2.56], $P = .4083$	251 ± 51.4 (223.6 to 278.4), 13.08 (−2.9 to 29.1) [5.5], $P = .1023$
VFC			
Overall (n = 33)	396.6 ± 164.9 (338.1 to 455.0)	395.6 ± 154.7 (340.7 to 450.5), −0.96 (−15.84 to 13.95) [−0.24], $P = .8978$	392.3 ± 153.7 (337.8 to 446.9), −4.2 (−18.9 to 10.4) [−1.06], $P = .5590$
Eugonadal (n = 21)	483.3 ± 144.4 (417.6 to 549.1)	473.3 ± 138.6 (410.2 to 536.4), −10.0 (−30.4 to 10.4) [−2.07], $P = .3179$	469.6 ± 137.8 (406.9 to 532.3), −13.7 (−33.6 to 6.1) [2.83%], $P = .1650$
Hypogonadal (n = 12)	244.7 ± 41.0 (218.7 to 270.8)	259.6 ± 54.7 (224.9 to 294.3), 14.9 (−5.7 to 35.5) [5.74], $P = .1401$	257.0 ± 53.5 (223.0 to 291.0), 12.3 (−8.8 to 32.8) [5.03%], $P = .2125$
NC			
(n = 33)	504.8 ± 149.7 (451.8 to 558.0)	N/A	N/A

CI, confidence interval; T, serum total testosterone level; other abbreviations as in Table 1.

Eugonadal and hypogonadal subgroups imply ≥300 ng/dL and <300 ng/dL (the cutoff value for biochemical hypogonadism), respectively.

Table 3. Between-group differences of T (ng/dL) at baseline and at follow-up

	Mean Difference (95% CI) of T	*P* Value
Baseline		
VIT vs VIC	7.70 (−47.3 to 62.7)	.6913
VIT vs VFC	−49.1 (−110 to 11.7)	.2166
VIT vs NC	−157.4 (−215.9 to −99)	.0001
VIC vs VFC	−56.82 (−129 to 15.3)	.1403
VIC vs NC	−165.1 (−233.1 to −97.2)	.0001
VFC vs NC	−108.3 (−185.8 to −30.7)	.0069
6 mo		
VIT vs VIC	47.3 (0.54 to 94.1)	.0216
VIT vs VFC	−3.45 (−54.7 to 47.8)	.6321
VIC vs VFC	−50.8 (−120.7 to 19.1)	.2043
VIT vs NC*	−112.7 (−163.1 to −62.3)	.0004
12 mo		
VIT vs VIC	48.3 (2.6 to 94.1)	.0387
VIT vs VFC	6.7 (−43.9 to 57.3)	.3672
VIC vs VFC	−41.67 (−110.7 to 27.4)	.2381
VIT vs NC*	−105.9 (−155.7 to −56)	.0007

Abbreviations as in Tables 1 and 2.
* The baseline levels of NC were used for these comparisons.

COMMENT

There is an increasing body of evidence that varicoceles may impair Leydig cell functions, with subsequent low testosterone biosynthesis.[9-13,15-24] In an experimentally induced varicocele rat model, varicocele was hypothesized to impair Leydig cell functions and testosterone production by increasing apoptosis and suppressing StAR protein expression.[15] In men with idiopathic varicocele, testicular biopsies demonstrated decreased tubular diameters, hyperplasia and atrophy of Leydig cells with cytoplasmic vacuolization, and decreased number of testosterone-positive Leydig cells.[16]

Several clinical studies have added to the literature on the impact of varicocelectomy on serum testosterone levels.[13,17-24] In a retrospective study, Su et al[18] previously reported a significant increase in mean (SD) serum testosterone levels from a preoperative level of 319 (12) to 409 (23) ng/dL after repair; nevertheless, better improvements were seen in men having lower preoperative levels. Similar significant increase in mean serum testosterone was observed by Cayan et al[19] in their retrospective study of 78 infertile men who underwent varicocelectomy. More recently, Tanrikut et al[20] measured preoperative testosterone levels in 325 men with palpable varicoceles and in 510 men with vasectomy reversal without varicoceles who served as a comparison group. They found that men with varicoceles had significantly lower testosterone levels than the comparison group, with means (SDs) of 416 (156) and 469 (192) ng/dL, respectively. Additionally, testosterone levels significantly increased in two-thirds of their patients after correction of varicocele; from 358 (126) to 454 (168) ng/dL.[20] Likewise, Hurtado et al[21] reported significantly decreased testosterone production in men with varicocele compared with age-matched fertile men. Two independent studies by Zohdy et al,[22] and Srini and Veerachari[23] noted significantly improved serum testosterone levels in infertile men, especially those with hypogonadism after varicocelectomy. Men aged ≥40 years, also demonstrated significant improvements of serum testosterone after varicocelectomy according to the retrospective report of Hsiao et al[24] A recent meta-analysis of the effect of varicocele repair on testosterone production among infertile men exhibited significant changes of mean serum testosterone, which increased by 97.48 ng/dL (95% CI, 43.73-151.22) after repair.[13] Other reports showed that varicoceles might impair Leydig cell functions and decrease serum testosterone levels in men without infertility as well.[10,25] Although the vast majority of these studies were retrospective, varicocele repair has been advocated as an option to prevent and treat low serum testosterone, even in men with normal semen quality.[26]

Our findings resonate with previous studies hypothesizing that varicoceles negatively impact testosterone production.[18-24] The current study prospectively examined the trends in serum testosterone in populations of infertile men with varicocele, fertile men with varicocele, and fertile men without varicocele. Nonrandomly, the infertile men either underwent repair of their clinical varicoceles or were managed conservatively. Cross-sectional, the means of baseline T were nonsignificantly different among the infertile (VIT and VIC) and fertile (VFC) varicocele groups. However, the varicocele groups had significantly lower baseline T compared with fertile men without varicoceles (NC), with means differences of −157.4 (P <.0001), −165.1 (P <.0001), and −108.3 (P = .0069) ng/dL, respectively. Although a considerable difference between serum testosterone levels among infertile and fertile varicocele men might be anticipated, our findings, as well as other studies,[10,25] showed that varicoceles might impair Leydig cell functions and decrease serum testosterone levels among fertile men with varicocele as well. Longitudinally, repair of varicoceles of infertile men (VIT) resulted in a significant improvement of total testosterone (P <.0001), with an overall 12.9% change from the baseline mean. Yet, the mean change was more pronounced and more significant in men with baseline biochemical hypogonadism (40.1%; P <.0001) compared with baseline eugonadal men who demonstrated insignificant changes after varicocelectomy (2.01%; P = .1223). In contrast, neither the infertile (VIC) nor fertile (VFC) varicocele control men, with or without baseline hypogonadism, demonstrated significant changes of serum testosterone during follow-ups. The latter finding eliminates the regression toward the mean phenomenon [27] as an explanation for the more pronounced improvements after varicoceles repair in men with baseline hypogonadism. The mechanism driving these significant improvements in hypogonadal men still elusive and further studies addressing this issue are appropriate.

At the 6-month follow-up, testosterone levels were improved significantly (P = .0216) after varicocele repair (VIT) compared with no repair (VIC). Additionally, VIT

men demonstrated comparable T levels ($P = .6321$) with the fertile varicocele men (VFC). The latter finding raises a question whether the improved serum testosterone has a role in improving the fertility potential previously reported after varicocele repair.[4-8] Nevertheless, the improved testosterone after varicocele repair (VIT) did not achieve levels comparable with those of normal fertile men without varicoceles (NC; $P = .0004$). The observed improvements of testosterone in VIT at 6-month follow-up were further continued at 12-month follow-up.

The risk of experiencing biochemical hypogonadism in varicocele men at 6-month follow-up was significantly less in VIT than VIC men with ARR of 36.36%. This risk reduction was more pronounced in the subset of men with pre-existing hypogonadism at baseline (ARR = 71.4%). The NNT adapted in our study represents the number of infertile men needed to undergo varicocele repair to avert 1 man from having biochemical hypogonadism at 6-month follow-up. The overall NNT of 2.8 men, and as low NNT as 1.4 infertile men with pre-existing baseline hypogonadism, clearly elaborate the efficacy of varicocele repair in biochemical hypogonadism risk reduction.

The changes in serum testosterone of infertile men after varicocele repair demonstrated significant strong inverse correlation with baseline T ($r = -0.689$; $P < .0001$). This inverse correlation was stronger and more significant among the subset of baseline hypogonadal men ($r = -0.528$; $P = .004$) than eugonadal men ($r = -0.400$; $P = .013$). Therefore, men with low baseline T are more likely to attain more noticeable changes after varicocele repair. Our findings corroborate those of Su et al,[18] who retrospectively observed an inverse correlation between baseline testosterone and changes in testosterone after varicocele repair, and further elaborate the positive impact of varicocele correction on Leydig cell functions and testosterone production. Testosterone changes in VIT men as well displayed significant positive correlations with both preoperative ($r = 409$; $P < .001$) and postoperative ($r = 0.352$; $P = .004$) sperm concentrations, further suggesting a role for testosterone changes in predicting improvements of sperm concentrations after varicocele repair. Cayan et al[19] also retrospectively noted that patients demonstrating no improvement in testosterone after varicocele repair had lower sperm counts after surgery, whereas patients achieving higher testosterone levels had higher sperm counts and motility. Similarly, Ishikawa and Fujisawa,[28] in their retrospective study, reported that sperm concentration before treatment was the only significant factor predicting free testosterone increase. None of our other examined variables correlated significantly with testosterone changes after varicocelectomy. Although repair of larger grade varicoceles may yield better improvements in sperm counts,[29] of note, the grade of clinical varicocele in our study did not correlate significantly with improvement of testosterone levels. This finding supports the evidence provided by Hsiao et al,[30] who retrospectively observed significant increases in serum testosterone levels after varicocelectomy, independent of varicocele clinical grade. Su et al[18] similarly reported no significant correlation between clinical grade and improvement in serum testosterone after varicocelectomy. The same investigators[18] also noted greater increase in serum testosterone after bilateral varicocelectomy as compared with unilateral cases, although Srini and Veerachari[23] and the present study failed to demonstrate such a significant difference.

A notable limitation of our study is the nonrandom design with its inherent drawbacks. Additionally, the study lacks head-to-head comparison after varicocele repair vs no repair among fertile men. Thus, the observed improvements of serum testosterone of infertile men after varicocelectomy may not apply to fertile varicocele men, warranting further studies. As biochemical hypogonadism is not necessarily associated with symptoms (clinical hypogonadism), whether the statistical improvement in serum testosterone has any clinical impact needs also to be examined in future investigations. Although the study was adequately powered to detect changes in serum T after varicocele repair, this power diminished with subgrouping. Nevertheless, our prospective controlled findings supplement the body of evidence that varicoceles impair testosterone production and varicocele repair improves serum testosterone levels. Furthermore, this study provides a foundation for future long-term, randomized, controlled studies assessing whether low serum testosterone levels should be viewed as a standalone indication for repair of clinical varicocele.

CONCLUSION

Baseline serum Ts were significantly lower in men with clinical varicoceles compared with normal men. Varicocelectomy yielded statistically significant improvements of testosterone levels among infertile men, which were driven only by the patients who were hypogonadal at baseline. Men who were eugonadal at baseline had insignificant differences in testosterone levels at follow-up. Testosterone level changes after varicocelectomy significantly correlated inversely with baseline serum testosterone, and positively with sperm concentrations. Improved serum testosterone may have a role in predicting improvement of sperm concentration after varicocele repair. Should low serum testosterone in men with clinical varicoceles be considered as a standalone indication for repair remains to be ascertained.

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