Clinical varicocele is the most commonly identifiable pathology in infertile men (1). The Male Infertility Best Practice Policy Committee of the American Urological Association and The Practice Committee of the American Society for Reproductive Medicine Report on varicocele and male infertility recommend a minimum of two semen analysis (SA) for routine evaluation of infertile man with varicocele (2). Treatment of varicocele is considered in the infertile male with palpable varicocele and abnormal semen parameters regardless of their absolute values (2).

The recommendation of performing more than one SA stems from a significant technical and biologic within-subject variability in semen parameters. Numerous studies indicate the need of several samples to establish a homeostatic setting point for sperm concentration, motility, and morphology in an attempt to obtain an accurate characterization of a man’s fertility status (3–7). Although multiple SA are hardly practical in most of the infertile men with clinically diagnosed varicocele, two consecutive abnormal SA are widely accepted as sufficient indication for varicocele treatment. However, if both SA are consistently abnormal, the significance of a second SA as a necessary component of treatment decision making could be minimal at best. We speculate that only one initial abnormal SA is sufficient to consider treatment of varicocele. The goal of our pilot study was to test this hypothesis by determining the correlation between the first and second SA in the infertile male with varicocele.

MATERIALS AND METHODS

A retrospective chart review of 160 infertile males with varicocele and initial abnormal SA was performed. The varicocele was diagnosed on physical exam by one physician (Y.S.). Men with azoospermia, low semen volume, and leukocytospermia were excluded from the study because these findings require additional testing (azoospermia and low semen volume) or initial medical treatment (leukocytospermia). Additional exclusion criteria were febrile illness within the last 3 months, habitual or occupational heat exposure, recreational drug intake, and anabolic steroid abuse. A total of two semen analyses were performed in the same university-based andrology laboratory about 3 to 8 weeks apart under strict guidelines for routine SA (8). Samples were collected by masturbation after 3 to 4 days of sexual abstinence. The SA was considered normal or abnormal according to World Health Organization criteria (8). Statistical analysis was performed using the Student t test. A value of $P<.05$ was considered significant.

RESULTS

We identified 112 patients with available data and appropriate criteria for evaluation: 96 men with bilateral varicocele (85.7%), 14 men with left varicocele (12.5%), and 2 men
TABLE 1

First and second SA in 112 men with varicocele.

<table>
<thead>
<tr>
<th>Sperm parameters</th>
<th>First SA</th>
<th>Increase</th>
<th>Decrease</th>
<th>P value&lt;sup&gt;b&lt;/sup&gt;</th>
<th>P value&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concentration (10&lt;sup&gt;6&lt;/sup&gt;/mL)</td>
<td>60.2 ± 68.2</td>
<td>68 (61%)</td>
<td>77.6 ± 86.9</td>
<td>0.14 44 (39%)</td>
<td>59.1 ± 79.8 0.93</td>
</tr>
<tr>
<td>Motility (%)</td>
<td>44.9 ± 17.3</td>
<td>66 (59%)</td>
<td>47.8 ± 15.7</td>
<td>0.15 46 (41%)</td>
<td>43.0 ± 16.2 0.10</td>
</tr>
<tr>
<td>Morphology (%)</td>
<td>12.6 ± 11.5</td>
<td>62 (55%)</td>
<td>12.7 ± 8.9</td>
<td>0.97 50 (45%)</td>
<td>10.0 ± 7.1 0.13</td>
</tr>
</tbody>
</table>

*Note: Values are means ± SD.*

<sup>a</sup> Number of patients (%) with increased and decreased absolute value of individual sperm parameter.

<sup>b</sup> Increased values of sperm parameters in the second SA versus first SA.

<sup>c</sup> Decreased values of sperm parameters in the second SA versus first SA.

Clinical varicocele is detected in 35% to 40% of men who present for infertility evaluation (14, 15). The National Survey for Ambulatory Surgery estimates that 67% of patients undergoing surgery for male infertility have the diagnosis of varicocele (16). Palpable varicocele in the infertile man with abnormal SA is a sufficient indication for varicocele treatment (2). Current guidelines recommend a minimum of two SA for routine evaluation of an infertile male with varicocele, and more than two SA are rarely performed in clinical practice. Because the guidelines do not include specific cutoff values for abnormal sperm parameters, multiple SA to determine a true homeostatic setting point or baseline for sperm concentration, motility, and morphology seem to be impractical and largely redundant.

In our study, the changes in individual sperm parameters between the first and second SA were not statistically significant. Reversal from abnormal to normal and vice versa have been documented for sperm concentration, motility, and morphology. Nevertheless, despite changes in one sperm parameter or their combinations, overall second SA remained ordered screening SA does not allow meaningful interpretation of this test. Correct management of male infertility primarily requires a clinical diagnosis, whereas SA helps to assess the severity of a condition and establish the indication for treatment (13).

Reported wide variation in results among laboratories because of lack of accuracy and standardization can complicate the interpretation of semen analyses performed in different laboratories (7). Only a few studies addressed the within-subject variability of semen parameters by the same lab (5, 6, 17). One study compared changes in semen parameters between two successive SA in men presented for infertility evaluation (17). The reversal rate from normal to abnormal and vice versa was higher for sperm motility followed by morphology and concentration. Maximal changes were observed for one sperm parameter and minimal for their combinations. However, the variation and reversal rate of total SA was not presented.

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with right varicocele (1.8%). Initial SA was abnormal in all patients. The second SA revealed fluctuations in sperm concentration, motility, and morphology, which were not statistically significant compared with the first SA (Table 1). Reversal of sperm concentration from normal to abnormal and vice versa was observed in 17 (15%), motility in 18 (16%), and morphology in 3 (3%) out of 112 patients. Despite variation in the individual sperm parameters, the second SA remained consistently abnormal in 111 out of 112 (99.1%) patients.

**DISCUSSION**

Approximately 15% of all couples who attempt to conceive fail to do so within the first year (9). It is speculated that about a third of infertility causes is because of the female alone, a third is because of the male alone, and the other third is because of the combination of male and female factors (10).

Semen analysis remains the most important clinical laboratory test available to evaluate male infertility. However, technical inter- and intralaboratory variations and significance between and within-subjects variation in semen parameters lead to difficulties in clinical interpretation of semen analysis result. Therefore, several studies suggested the need of multiple samples to establish the homeostatic setting point for sperm concentration, motility, and morphology in an attempt to obtain accurate characterization of man’s fertility status (3–7).

The number of necessary tests depends on the individual sperm parameter and acceptable dispersion of the results. Higher dispersion rate requires fewer samples but makes clinical interpretation of the results less meaningful. Lower dispersion of the results from the homeostatic setting point provides significantly better estimation but requires many more samples, for example, dispersion of <15% could be achieved with 14 samples for sperm concentration, 6 for motility, and 7 for morphology (4).

However, the limitations of SA in predicting fertility status are well known (11, 12). It has been widely accepted that thorough clinical evaluation must precede SA, and frequently
abnormal in 111 out of 112 (99.1%) patients with abnormal first SA. Therefore, a repeat SA had no additional impact on the treatment decision, and initial abnormal SA was sufficient indication for varicocele treatment.

Acceptance of WHO criteria as a gold standard for semen testing has been less than universal (7). In our opinion, SA has to be performed in the established andrology lab with identical objective methodologies under strict guidelines for semen collection, handling, and analysis. It will greatly improve reliability of the test and clinical confidence in its interpretation.

Our study suggests that only one initial abnormal SA is sufficient for the evaluation and treatment consideration in the infertile man with varicocele because consistently abnormal second SA has no impact on treatment decision. By reducing expensive testing, this approach will help to increase cost effectiveness of infertility evaluation and expedite treatment of infertile couples.

However, this approach must be individualized. Repeat SA is still necessary in men with varicocele and certain abnormal findings, for example, azoospermia, leukocytospermia, or low semen volume. Careful clarification of these abnormalities may assist in diagnosis and change treatment approach. It is also indicated when clinical evaluation identifies risk factors with known temporary negative impact on sperm parameters (e.g., drug intake, recent febrile illness, or habitual or occupational heat exposure). Elimination of these factors may improve SA and help to avoid unnecessary treatment.

Our study is limited by a relatively small size. A multiinstitutional study with pooled data is warranted to obtain a higher level of evidence and provide new recommendations for the routine evaluation of infertile men with varicocele.

REFERENCES