The influence of varicocele on parameters of fertility in a large group of men presenting to infertility clinics*

World Health Organization‡‡

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Objective: To assess the role of varicocele in male infertility.

Design: Data analysis of a large population of couples who were systematically investigated for infertility.

Settings: Couples were recruited in 34 World Health Organization coordinating centers in 24 countries.

Interventions: None.

Main Outcome Measures: Physical findings, semen characteristics, coincident pathology, and spontaneous pregnancies.

Results: Varicocele was found in 25.4% of men with abnormal semen, compared with 11.7% of men with normal semen. It was accompanied by decreased testicular volume, impaired sperm quality, and decline of Leydig cell secretion. Spontaneous pregnancies were as frequent in couples in whom the man ever did or did not have varicocele.

Conclusion: Varicocele is clearly associated with impairment of testicular function and infertility.


Since the original observations of Tulloch (1), numerous investigators have supported the concept that the presence of varicocele can have a detrimental effect on fertility (2-4). These claims have been based on the relative frequency of varicoceles in men requesting investigation of infertility...
ported between 20% and 40%, in comparison with the frequency of varicocele in an unselected male population (1.9% to 14.7%) (5, 6). The alleged improvement of semen parameters and pregnancy rates (PFRs) after varicocele ligation (+) has added support to this concept. However, the latter must be viewed with caution because several studies have questioned the beneficial effect of treatment (8, 9). The fact that varicocele treatment would not restore fertility in all or the great majority of cases does not exclude varicocele from being responsible for the impaired fertility.

Experimental induction of varicocele in animal models has been shown to cause damage to the testis similar to that seen in men with varicocele (10-12). This study reports the findings concerning varicocele in the largest systematic investigation of infertility couples at 34 centers distributed throughout the world.

MATERIALS AND METHODS

A general description of the study population and the methods of assessment have been published in earlier reports (13, 14). In brief, men presenting as partners consulting for infertility of at least 12 months' duration were evaluated in 34 centers by a standardized protocol that included a detailed historical taking and physical examination as well as two semen analyses. Additional investigations were performed to establish a diagnosis of infertility, depending on the outcome of the above assessment and using a well-defined diagnostic flowchart. All diagnoses were cross-checked by a computer program designed to ensure that the protocols and diagnostic criteria had been fulfilled.

Diagnosis of Varicocele

Investigators at the collaborating centers were issued a manual of instruction that included the following statement: "With the patient standing, check both testes for site, position, consistency, and tenderness. Check for the presence of varicocele on both sides: 'visible' if lesion can be seen, 'palpable' if lesion is felt only, and 'valsalva positive' if the varicocele is present only on coughing or straining, i.e., by an increase of intra-abdominal pressure by forcible exhalation against the closed glottis."

Additional Data

The volume of each testis was measured using the Prader orchiosimeter, and two semen analyses were performed according to the method described in the World Health Organization Laboratory Manual (15). Serum testosterone (T) concentration was measured using standard radioimmunoassay (World Health Organization [WHO] program for matched reagents) in 2,887 men.

Description of Groupings Used in This Study

The total population consisted of 9,038 men in the 34 centers, who were enrolled in the protocol for the investigation of the infertile couple. Although some men did not complete all aspects of the protocol, relevant data have been included in particular sections of this paper.

The partners of these men also underwent a protocol designed to detect causes of female infertility. Women with normal ovulatory and anatomical status were categorized as having no demonstrable cause for infertility. Women with detectable causes for infertility have not been subdivided further for the purpose of this report (16).

Statistical Analysis

Differences between values were calculated using the two sample t-test. One-way ANOVA contrast was used to assess differences between groups where needed.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Total Testicular Volume, Total Sperm Count, Sperm Motility, and Sperm Morphology Versus Varicocele Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade</td>
<td>Total testicular volume mL</td>
</tr>
<tr>
<td>--------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td>0</td>
<td>38.7 ± 5.0</td>
</tr>
<tr>
<td>1</td>
<td>40.5 ± 8.7</td>
</tr>
<tr>
<td>2</td>
<td>37.3 ± 8.0</td>
</tr>
<tr>
<td>3</td>
<td>35.7 ± 10.5</td>
</tr>
<tr>
<td>4</td>
<td>34.2 ± 8.2</td>
</tr>
<tr>
<td>5</td>
<td>36.5 ± 9.2</td>
</tr>
<tr>
<td>6</td>
<td>36.9 ± 9.5</td>
</tr>
<tr>
<td>7</td>
<td>37.6 ± 9.4</td>
</tr>
<tr>
<td>8</td>
<td>39.9 ± 9.1</td>
</tr>
<tr>
<td>9</td>
<td>37.5 ± 9.1</td>
</tr>
<tr>
<td>10</td>
<td>35.7 ± 9.5</td>
</tr>
</tbody>
</table>

* Values are means ± SD.

† Trend analysis P < 0.01.

‡ Trend analysis P < 0.001.

RESULTS

Frequency of Varicocele and Comparison Between Left and Right Side

Three thousand four hundred sixty-eight men who completed the protocol were classified as having no demonstrable cause of infertility because their sexual and ejaculatory functions were adequate and semen analysis was categorized normal. Of these men, 11.7% had varicocele on physical examination. Among the 3,626 men with abnormal semen analysis, 25.4% had varicocele. The varicocele were detected at the left side in 11.4% of all investigated men, at the right side in 1.5%, and at both sides in 4.6%.

A wide variety of the relative proportion of varicocele diagnosis was observed in different centers ranging from 6% to 47%. This difference could not be explained by regional factors nor by the fact that the proportion of other pathology (e.g., sexually transmitted disease associated alterations or female pathology) varied substantially between centers. The frequency of varicocele diagnosis was highest in centers acting as primary (13.3%) as compared with secondary referral centers (16.2%, P < 0.01). The presence of a trained urologist or andrologist as part of the team of investigators resulted in a higher frequency of varicocele detection.

Influence of Varicocele on Testicular Volume and Sperm Semen Characteristics

The testicular volume (left + right testes added) in men with varicocele (37.4 mL) was similar to that in men without varicocele (37.5 mL), but among the former the mean volume of the left testis (18.5 mL) was significantly lower than that of the right testis (19.5 mL, P < 0.001). This was in contrast to the findings in men without varicocele in whom there was no significant difference between the left and the right testes (mean volume left testis: 18.5 mL, right testis: 19.0 mL).

Furthermore, there was a significant decrease in testicular volume with increasing varicocele grade, regardless of whether semen analysis was categorized as normal or abnormal. For each varicocele grade, the total testicular volume was lower in the men with abnormal semen quality than in those with normal semen quality (Table 1).

The total sperm count per ejaculate was significantly lower (P < 0.001) in men with varicocele than in those without, and it decreased with increasing grade of varicocele. These trends were evident regarding whether the entire population of men with varicocele was considered or that they were subdivided according to semen classification (Table 1). The values for sperm morphology and motility were not related to the varicocele grade. There was no significant difference in the occurrence of azoospermia among men without varicocele (7.1%) and patients with varicocele (6.7%).

Coincidence of Varicocele and Other Diagnoses

There was a higher overall frequency of additional diagnoses (excluding idiopathic sperm abnormalities) in cases without varicocele (31.5%) than with varicocele (19.5%, P < 0.001). Among cases with more than
ported between 20% and 40%, in comparison with the frequency of varicoceles in an unselected male population (1.9% to 14.7%) (5, 6). The alleged improvement of semen parameters and pregnancy rates (PFRs) after varicocelectomy (7) has added support to this concept. However, the latter must be viewed with caution because several studies have questioned the beneficial effect of treatment (8, 9). The fact that varicoceles treatment would not restore fertility in all or the great majority of cases does not exclude varicoceles from being responsible for the impaired fertility.

Experimental induction of varicoceles in animal models has been shown to cause damage to the testes similar to that seen in men with varicoceles (10-15). This study reports the findings concerning varicoceles in the largest systematic investigation of infertility couples at 34 centers distributed throughout the world.

MATERIALS AND METHODS

A general description of the study population and the methods of assessment have been published in earlier reports (13, 14). In brief, men presenting as partners consulting for infertility of at least 12 months' duration were evaluated in 34 centers by a standardized protocol that included a detailed historical taking and physical examination as well as two semen analyses. Additional investigations were performed to establish a diagnosis of infertility, depending on the outcome of the above assessment and using a well-defined diagnostic flowchart. All diagnoses were cross-checked by a computer program designed to ensure that the protocols and diagnostic criteria had been fulfilled.

Diagnosis of Varicocele

Investigators at the collaborating centers were issued a manual of instruction that included the following statement: "With the patient standing, check both testes for size, position, consistency, and tenderness. Check for the presence of varicoceles on both sides: 'visible' if lesion can be seen, 'palpable' if lesion is felt only, and 'valsalva-positive' if the varicocele is present only on coughing or straining, i.e., by an increase of intra-abdominal pressure by forcible exhalation against the closed glottis."

Additional Data

The volume of each testis was measured using the Prader orchioscope, and two semen analyses were performed according to the method described in the World Health Organization Laboratory Manual (15). Serum testosterone (T) concentration was measured by standard radioimmunoassay (World Health Organization [WHO] program for matched reagents) in 2,857 mm.

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The total population consisted of 9,038 men in the 34 centers, who were enrolled in the protocol for the investigation of the infertile couple. Although some men did not complete all aspects of the protocol, relevant data have been included in particular sections of this paper.

The partners of these men also underwent a protocol designed to detect causes of female infertility. Women with normal ovulatory and anatomical status were categorized as having no demonstrable cause for infertility. Women with detectable causes for infertility have not been subdivided further for the purpose of this report (16).

Statistical Analysis

Differences between varicoceles were calculated using the two-sample t-test. One-way ANOVA was used to test differences between groups where needed.

RESULTS

Frequency of Varicocele and Comparison Between Left and Right Side

Three thousand four hundred sixty-eight men who completed the protocol were classified as having no demonstrable cause of infertility because their sexual and ejaculatory functions were adequate and semen analysis was categorized normal. Of these men, 11.7% had varicoceles on physical examination. Among the 3,626 men with abnormal semen analysis, 25.4% had varicoceles. The testes were detected at the left side in 11.4% of all investigated men, at the right side in 1.5%, and at both sides in 4.6%.

A wide variability of the relative proportion of varicocele diagnosis was observed in different centers ranging from 6% to 47%. This difference could not be explained by regional factors nor by the fact that the proportions of other pathology (e.g., sexually transmitted disease associated alterations or female pathology) varied substantially between centers. The frequency of varicocele diagnosis was higher in centers acting as primary (19.3%) as compared with secondary referral centers (16.2%, P < 0.01). The presence of a trained urologist or andrologist as part of the team of investigators resulted in a higher frequency of varicocele detection.

Influence of Varicocele on Testicular Volume and Semen Characteristics

The total testicular volume (left + right testis added) in men with varicocele (37.4 mL) was similar to that in men without varicoceles (37.5 mL), but among the former the mean volume of the left testis (18.5 mL) was significantly lower than that of the right testis (19.5 mL, P < 0.001). This was in contrast to the findings in men without varicoceles in whom there was no significant difference between the left and the right testis (mean volume left testis: 18.8 mL, right testis: 18.9 mL, P = 0.90).

Furthermore, there was a significant decrease in testicular volume with increasing varicocele grade, regardless of whether semen analysis was categorized as normal or abnormal. For each varicocele grade, the total testicular volume was lower in the men with abnormal semen quality than in those with normal semen quality (Table 1).

The total sperm count per ejaculate was significantly lower (P < 0.01) in men with varicoceles than in those without, and it decreased with increasing grade of varicocele. These trends were evident regardless of whether the entire population of men with varicoceles was considered or that they were subdivided according to semen classification (Table 1). The values for sperm motility and morphology were not related to the varicocele grade. There was no significant difference in the occurrence of azoospermia among men without varicocele (7.1%) and patients with varicocele (6.7%).

Coincidence of Varicocele and Other Diagnoses

There was a higher overall frequency of additional diagnoses (excluding idiopathic sperm abnormalities) in cases without (31.5%) than with varicocele (19.5%, P < 0.001). Among cases with more than

Table 1 Total Testicular Volume, Total Sperm Count, Sperm Motility, and Sperm Morphology Versus Varicocele Grade

<table>
<thead>
<tr>
<th>Varicocele Grade</th>
<th>Total testicular volume mL</th>
<th>Total sperm count X 10⁶</th>
<th>Sperm motility</th>
<th>Sperm morphology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>37.5 ± 8.0†</td>
<td>22.0 ± 6.4</td>
<td>32.8 ± 9.3†</td>
<td>68.6 ± 13.8</td>
</tr>
<tr>
<td>Left abscence (n = 1077)</td>
<td>39.7 ± 8.0†</td>
<td>24.8 ± 6.4†</td>
<td>33.8 ± 9.3†</td>
<td>69.5 ± 13.6</td>
</tr>
<tr>
<td>Right abscence (n = 148)</td>
<td>40.5 ± 8.1†</td>
<td>23.8 ± 6.3†</td>
<td>32.8 ± 9.3†</td>
<td>68.6 ± 13.8</td>
</tr>
<tr>
<td>Both abscence (n = 60)</td>
<td>37.2 ± 8.0†</td>
<td>25.9 ± 6.3†</td>
<td>34.8 ± 9.3†</td>
<td>69.5 ± 13.6</td>
</tr>
<tr>
<td>Men with abnormal T</td>
<td>35.7 ± 10.5</td>
<td>22.3 ± 6.3</td>
<td>33.3 ± 10.0</td>
<td>65.9 ± 24.3</td>
</tr>
<tr>
<td>Valasalva-positive (n = 31)</td>
<td>36.2 ± 8.3†</td>
<td>20.4 ± 4.6</td>
<td>32.6 ± 10.3</td>
<td>66.6 ± 23.2</td>
</tr>
<tr>
<td>Valasalva-negative (n = 974)</td>
<td>36.5 ± 9.28†</td>
<td>21.7 ± 6.3</td>
<td>33.3 ± 10.0</td>
<td>66.6 ± 23.2</td>
</tr>
<tr>
<td>Varicocele (n = 191)</td>
<td>35.6 ± 9.55†</td>
<td>23.6 ± 6.3</td>
<td>33.3 ± 10.0</td>
<td>65.9 ± 24.3</td>
</tr>
<tr>
<td>Juncal group</td>
<td>37.6 ± 9.41</td>
<td>24.4 ± 6.3</td>
<td>33.3 ± 10.0</td>
<td>65.9 ± 24.3</td>
</tr>
<tr>
<td>Varicocele (n = 4)</td>
<td>38.9 ± 8.71</td>
<td>26.4 ± 6.3</td>
<td>33.3 ± 10.0</td>
<td>65.9 ± 24.3</td>
</tr>
<tr>
<td>Valasalva-positive (n = 4)</td>
<td>37.5 ± 9.13†</td>
<td>24.4 ± 6.3</td>
<td>33.3 ± 10.0</td>
<td>65.9 ± 24.3</td>
</tr>
<tr>
<td>Valasalva-negative (n = 4)</td>
<td>35.7 ± 9.58†</td>
<td>24.4 ± 6.3</td>
<td>33.3 ± 10.0</td>
<td>65.9 ± 24.3</td>
</tr>
</tbody>
</table>

* Values are mean ± SD.
† Trend analysis P < 0.01.
‡ Trend analysis P < 0.001.

See Table 1 for details.
ported between 20% and 40%, in comparison with the frequency of varicose in an unselected male population (1.9% to 14.7%) (5, 6). The alleged improvement of semen parameters and pregnancy rates (PFRs) after varicose ligation (7) has added support to this concept. However, the latter must be viewed with caution because several studies have questioned the beneficial effect of treatment (6, 9). The fact that varicose treatment would not restore fertility in all or the great majority of cases does not exclude varicose from being responsible for the impaired fertility.

Experimental induction of varicocoele in animal models has been shown to cause damage to the testes similar to that seen in men with varicocele (10-12). This study reports the findings concerning varicocoele in the largest systematic investigation of infertility couples at 34 centers distributed throughout the world.

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Diagnosis of Varicocoele

Investigators at the collaborating centers were issued a manual of instruction that included the following statement: "With the patient standing, check both testes for site, position, consistency, and tenderness. Check for the presence of varicocoele on both sides: 'visible' if lesion can be seen, 'palpable' if lesion is felt only, and 'valsalva positive' if the varicocoele is present only on coughing or straining, i.e., by an increase of intra-abdominal pressure by forcible exhalation against the closed glottis."

Additional Data

The volume of each testis was measured using the Prader orchometer, and two semen analyses were performed according to the method described in the World Health Organization Laboratory Manual (16). Serum testosterone (T) concentration was measured by standard radioimmunoassay (World Health Organization [WHO] program for matched reagents) in 2,657 men.

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The total population consisted of 9,088 men in the 34 centers, who were enrolled in the protocol for the investigation of the infertile couple. Although some men did not complete all aspects of the protocol, relevant data have been included in particular sections of this paper.

The partners of these men also underwent a protocol designed to detect causes of female infertility. Women with normal ovarian and anatomical status were categorized as having no demonstrable cause for infertility. Women with detectable causes for infertility by diagnostic hysterosalpingography were subdivided further for the purpose of this report (16).

Statistical Analysis

Differences between values were calculated using the two sample t-test. One-way ANOVA with linear contrast was used to assess differences between groups where needed.

<table>
<thead>
<tr>
<th>Total testicular volume ml</th>
<th>Total sperm count x 10^9/ ejaculate</th>
<th>Sperm motility % progressive motility</th>
<th>Sperm morphology % normal forms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men with normal semen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varicocoele (n = 7073)</td>
<td>39.5 ± 6.0*</td>
<td>212.0</td>
<td>63.5 ± 12.9</td>
</tr>
<tr>
<td>Valsalva positive (n = 142)</td>
<td>40.6 ± 8.17</td>
<td>202.8</td>
<td>69.3 ± 15.3</td>
</tr>
<tr>
<td>Palpable varicocoele (n = 1742)</td>
<td>39.8 ± 7.87</td>
<td>198.8</td>
<td>62.9 ± 12.5</td>
</tr>
<tr>
<td>Visible varicocoele (n = 80)</td>
<td>37.5 ± 9.06</td>
<td>183.9</td>
<td>56.4 ± 18.7</td>
</tr>
<tr>
<td>Men with abnormal semen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varicocoele absent (n = 2769)</td>
<td>35.7 ± 10.5</td>
<td>252.5</td>
<td>33.0 ± 20.6</td>
</tr>
<tr>
<td>Valsalva positive (n = 220)</td>
<td>38.2 ± 9.05</td>
<td>255.9</td>
<td>32.6 ± 17.3</td>
</tr>
<tr>
<td>Palpable varicocoele (n = 274)</td>
<td>36.5 ± 9.27</td>
<td>233.6</td>
<td>31.0 ± 15.0</td>
</tr>
<tr>
<td>Visible varicocoele (n = 101)</td>
<td>35.0 ± 9.25</td>
<td>235.9</td>
<td>30.6 ± 18.4</td>
</tr>
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<td>Bilateral group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varicocoele absent (n = 5,841)</td>
<td>37.8 ± 9.4</td>
<td>115.7</td>
<td>64.9 ± 21.7</td>
</tr>
<tr>
<td>Valsalva positive (n = 424)</td>
<td>35.8 ± 9.72</td>
<td>106.8</td>
<td>62.1 ± 20.7</td>
</tr>
<tr>
<td>Palpable varicocoele (n = 549)</td>
<td>37.5 ± 9.13</td>
<td>87.1</td>
<td>41.6 ± 23.1</td>
</tr>
<tr>
<td>Visible varicocoele (n = 227)</td>
<td>35.7 ± 9.25</td>
<td>50.8</td>
<td>39.5 ± 21.5</td>
</tr>
</tbody>
</table>

* Values are means ± SD.
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Three thousand four hundred sixty-eight men who completed the protocol were classified as having no demonstrable cause of infertility because their sexual and ejaculatory functions were adequate and semen analysis was categorized normal. Of these, 11.7% had varicocoele on physical examination. Among the 3,026 men with abnormal semen analysis, 25.4% had varicocoele. The varicocoele were detected at the left side in 11.4% of all investigated men, at the right side in 1.5%, and at both sides in 4.8%.

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Furthermore, there was a significant decrease in testicular volume with increasing varicocoele grade, regardless of whether semen analysis was categorized as normal or abnormal. For each varicocoele grade, the total testicular volume was lower in the men with abnormal semen quality than in those with normal semen quality (Table 1).

The total sperm count per ejaculate was significantly lower (P < 0.001) in men with varicocoele than in those without, and it decreased with increasing grade of varicocoele. These trends were evident regardless of whether the entire population of men with varicocoele was considered or that they were subdivided according to semen classification (Table 1). The results for sperm morphology and motility were not related to the grade of varicocoele. There was no significant difference in the occurrence of azoospermia among men without varicocoele (7.1%) and patients with varicocoele (6.7%).

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Statistical Analysis

Differences between values were calculated using the two sample t-test. One-way ANOVA with linear contrast was used to assess differences between groups where needed.

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Results

Frequency of Varicocele and Comparison Between Left and Right Side

Three thousand four hundred sixty-eight men who completed the protocol were classified as having no demonstrable cause of infertility because their sexual and ejaculatory functions were adequate and semen analysis was categorized normal. Of these, 11.7% had varicoceles on physical examination. Among the 3,626 men with abnormal semen analysis, 25.4% had varicoceles. The varicoceles were detected at the left side in 11.4% of all investigated men, at the right side in 1.5%, and at both sides in 4.8%.

A wide variability of the relative proportion of varicocele diagnosis was observed in different centers ranging from 6% to 47%. This difference could not be explained by regional factors nor by the fact that the proportion of other pathology (e.g., sexually transmitted disease associated alterations or female pathology) varied substantially between centers. The frequency of varicocele diagnosis was higher in centers acting as primary care (19.3%) as compared with secondary referral centers (16.2%, P < 0.01). The presence of a trained urologist or andrologist as part of the team of investigators resulted in a higher frequency of varicocele detection.

Influence of Varicocele on Testicular Volume and Semen Characteristics

The total testicular volume (left + right testes added in men with varicocele (34.7 mL) was similar to that in men without varicoceles (37.5 mL), but among the former the mean volume of the left testis (18.5 mL) was significantly lower than that of the right testis (19.0 mL, P < 0.001). This was in contrast to the findings in men without varicocele in whom there was no significant difference between the left and the right testis (mean volume left testis: 18.8 mL, right testis: 19.0 mL). Furthermore, there was a significant decrease in testicular volume with increasing varicocele grade, regardless of whether semen analysis was categorized as normal or abnormal. For each varicocele grade, the total testicular volume was lower in the men with abnormal semen quality than in those with normal semen quality (Table 1).

The total sperm count per ejaculate was significantly lower (P < 0.01) in men with varicoceles than in those without, and it decreased with increasing grade of varicocele. These trends were evident regardless of whether the entire population of men with varicoceles was considered or that they were subdivided according to semen classification (Table 1). The values for sperm morphology and motility were not related to the grade of varicocele. There was no significant difference in the occurrence of azoospermia among men without varicocele (7.1%) and patients with varicocele (6.7%).

Influence of Varicocele and Other Diagnoses

There was a higher overall frequency of diagnostic exclusion (excluding idiopathic sperm abnormalities) in cases with varicocele (19.5%, P < 0.001). Among cases with more than

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Table 1: Total Testicular Volume, Total Sperm Count, Sperm Motility, and Sperm Morphology Versus Varicocele Grade

<table>
<thead>
<tr>
<th>Varicocele Grade</th>
<th>Total testicular volume mL</th>
<th>Total sperm count × 10⁹</th>
<th>Sperm motility</th>
<th>Sperm morphology</th>
</tr>
</thead>
<tbody>
<tr>
<td>No varicocele</td>
<td>39.7 ± 6.0*</td>
<td>212.0</td>
<td>65.3 ± 12.9</td>
<td>93.4 ± 13.8</td>
</tr>
<tr>
<td>Valvula positive (n = 142)</td>
<td>39.5 ± 6.1</td>
<td>202.8</td>
<td>63.2 ± 8.3</td>
<td>92.4 ± 13.8</td>
</tr>
<tr>
<td>Palpable varicocele (n = 172)</td>
<td>39.5 ± 6.07</td>
<td>198.8</td>
<td>62.9 ± 12.5</td>
<td>91.4 ± 13.8</td>
</tr>
<tr>
<td>Visible varicocele (n = 50)</td>
<td>37.3 ± 6.9*</td>
<td>183.9</td>
<td>56.4 ± 15.7</td>
<td>26.0 ± 25.2</td>
</tr>
<tr>
<td>Varicocele absent (n = 186)</td>
<td>35.7 ± 10.5</td>
<td>285.2</td>
<td>33.5 ± 20.6</td>
<td>45.9 ± 24.3</td>
</tr>
<tr>
<td>Valvula positive (n = 280)</td>
<td>36.2 ± 6.9*</td>
<td>356.1</td>
<td>32.6 ± 17.3</td>
<td>44.2 ± 23.2</td>
</tr>
<tr>
<td>Palpable varicocele (n = 274)</td>
<td>34.5 ± 6.71</td>
<td>316.6</td>
<td>31.0 ± 15.0</td>
<td>11.6 ± 23.0</td>
</tr>
<tr>
<td>Visible varicocele (n = 101)</td>
<td>35.0 ± 6.55</td>
<td>359.1</td>
<td>30.6 ± 14.1</td>
<td>44.0 ± 22.7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Scrotal group</th>
<th>Total testicular volume mL</th>
<th>Total sperm count × 10⁹</th>
<th>Sperm motility</th>
<th>Sperm morphology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varicocele absent (n = 581)</td>
<td>37.8 ± 6.4</td>
<td>244.1</td>
<td>69.4 ± 21.7</td>
<td>80.0 ± 22.3</td>
</tr>
<tr>
<td>Valvula positive (n = 451)</td>
<td>38.0 ± 6.75</td>
<td>266.1</td>
<td>62.1 ± 25.7</td>
<td>53.8 ± 24.1</td>
</tr>
<tr>
<td>Palpable varicocele (n = 548)</td>
<td>37.5 ± 6.9*</td>
<td>267.1</td>
<td>61.6 ± 22.1</td>
<td>51.3 ± 24.8</td>
</tr>
<tr>
<td>Visible varicocele (n = 255)</td>
<td>35.7 ± 6.25</td>
<td>285.1</td>
<td>59.8 ± 21.5</td>
<td>52.0 ± 23.6</td>
</tr>
</tbody>
</table>

* Values are means ± SD. † Trend analysis P < 0.01. ‡ Trend analysis P < 0.001.

Statistics for difference between varicocele grades P < 0.001. Statistics for difference between varicocele grades P < 0.01.

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one diagnosis, congenital factors, iatrogenic or systemic causes, acquired testicular damage or endocrine causes were relatively less common (Table 2). Testosterone concentration was not different in the serum of men with or without varicocele under age 30 (20.5 and 19.9 nmol/L, respectively) or over age 30 (19.1 and 19.5 nmol/L). However, the mean T concentration of men with varicocele older than 30 years of age (19.1 nmol/L) was significantly lower than that of younger varicocele patients (20.5 nmol/L, P = 0.03), whereas such difference was not found in men without varicoceles.

### Pregnancies in Partners of Men With or Without Varicocele

There was no difference in the proportion of couples in whom pregnancy occurred during or immediately after the infertility work-up, whether the man had varicoceles or not, irrespective of the duration of infertility (Fig. 1). Also, the spontaneous PR was similar if the female partner had no demonstrable abnormalities (6.4%) or presented some pathology (6.8%). The PR tended to be lower when semen was abnormal (4.9%) than when semen was normal (7.4%), irrespective of the presence or absence of varicocele (data not shown).

### DISCUSSION

This large study on couples consulting for infertility supports the concept that varicocele is associated with impairment of male fertility because there is a higher frequency of varicocele among men with abnormal semen than in those with normal semen quality and because normal quality is worse in men with varicocele than in those without it. Furthermore, the data indicate that increasing varicocele size is associated with progressive reduction of sperm production and testicular volume. Hence, the data confirm and amplify the detrimental effect of varicocele on testicular function.

The findings of this study are contrary to those of two other studies dealing with smaller groups of healthy men (17) or potential semen donors (18). Whether the fact that the men in our study were partners of infertile couples or the much larger size of the present study accounts for the differences cannot be determined. It is, however, noteworthy that Hadsell et al. (18) also noted a significant decrease of the volume of the left testis in men with varicocele. In 28.7% of cases with abnormal semen quality, more than one diagnosis was applicable. The frequency and pattern of coincidental pathology were different among men with or without clinical varicocele. There is no simple explanation for this finding. It has been speculated that male accessory gland infections, immunological factors, and sexual dysfunctions result from impairment of venous drainage, deterioration of the epididymis (19), or direct compression of the efferent ductules (30). The present data also support that varicocele impairs Leydig cell function, resulting in a decrease of T concentration in men over 30 years of age (21).

The highly variable relative frequency of varicocele detection among the male partners of infertile couples does not seem to relate with regional differences in the population but appears to be because of differences in the between-center expertise and interest in detecting this condition during investigation. The latter underscores the usefulness of simple methods for varicocele detection such as contact-thermography and Doppler ultrasonography (22).

The present data do not support the observations of Baker et al. (23) that varicocele is associated with a higher probability of treatment-independent conceptions. The conception rate seems to depend largely on the duration of infertility (Fig. 1) but not on the etiologic factors associated with poor semen quality.

Despite the limitations of this study, the results indicate the magnitude of the problem of varicocele-associated fertility impairment. This stresses the need for randomized trials on the possible effect of early detection and treatment of varicoceles at pubertal age (24, 25) as well as in infertile men.

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