

QUANTITATIVE DOPPLER ASSESSMENT OF FLOW CHARACTERISTICS IN PAMPINIFORM VENOUS PLEXUS, IN PATIENTS WITH VARICOCELE: IS THERE ANY RELATIONSHIP WITH SEMEN ANALYSIS?

Tahmasbi Morteza, Assare Ehsan

Department of Radiology , Jondishapur University of Medical Sciences, Golestan Hospital, Golestan Blvd. Ahvaz, Iran

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ABSTRACT

BACKGROUND: Ultrasound is used as the key-tool in diagnosis of varicocele, using vein diameter & venous reflux as diagnostic criteria .This study was aimed to assess the significance of presence of reflux & its quantification in relation to sperm analysis. **MATERIALS AND METHOD:** In this analytic study; 69 patients with clinical diagnosis of varicocele were examined with Doppler sonography at rest and during Valsalva maneuver in supine position assessing the presence of reflux & quantifying it to reveal any correlations with sperm analysis. X^2 test and T test were used where appropriate. **RESULTS:** Overall 29 patients (42%) showed evidences of venous reflux at Doppler ultrasound, with 16 (23%) showing continuous venous reflux during breath-holding. This continuity of reflux of either sides (right or left) was present in 15 (93.8%) with abnormal semen analysis & just 1(6.3%) with normal semen analysis ($p=0.001$). Right-sided reflux was seen in 9 (13%), left-sided in 29 (42%). Unilateral right-sided reflux was not seen. Left-sided reflux was present in 20 (69%) with abnormal semen analysis and 9 (31%) with normal analysis, representing significant statistical difference between left-sided venous reflux & abnormal semen analysis ($p=0.01$). Right-sided reflux was seen in 6 patient with abnormal semen analysis and 3 patients with normal semen analysis, with no statistical difference ($P=0.47$). Patients with normal semen analysis never showed bilateral venous reflux ($p=0.02$). **CONCLUSION:** Presence of bilateral venous reflux or continuous venous reflux of either side has significant predictive value for abnormality of semen analysis.

Keywords: Varicocele; Doppler ultrasound; Venous reflux; Flow volume.

Introduction

A strong correlation between presence of varicocele and infertility has been documented in multiple studies, evidenced by improving in semen quality after spermatic vein ligation.¹ Varicocele is significantly more prevalent in infertile men population (40%), compared to normal population (15%).¹ Decrease in countercurrent heat exchange, due to poor venous drainage, has been considered the main pathogenesis of impaired spermatogenesis in patients with varicocele.²

Introduction of Doppler ultrasound significantly improved our capabilities to diagnose varicocele and eliminates the need for more invasive & time-consuming techniques like thermography and venography.² Ultrasound has gained acceptance in diagnosing varicocele, because of its availability, non-invasiveness, low cost & specially, reproducibility of findings with no adverse effects. Few studies have showed the potential role for Doppler evaluation of flow parameters (presence of venous reflux, peak retrograde velocity) to predict the quality improvement in semen analysis after varicolectomy.^{3,4} However, a brief review in published articles and references will reveal the wide range of discordance , mostly in the significance of retrograde

Correspondence : Dr. Assare Ehsan
Department of Radiology,
Jondishapur University of Medical Sciences,
Ahvaz, Iran. Ph: 0098-611-3743034
E-mail: ehsat19@gmail.com

flow. Furthermore, quantitative Doppler analysis has not come into attention yet.

So, regarding the high prevalence of varicocele in infertile men, it appears beneficial performing additional surveys to evaluate the more detailed results of Doppler indices (e.g. presence of reflux, flow volume & duration of venous reflux) as additional markers for varicocele diagnosis and prognostic determinants. This study aimed at assessing the significance of venous reflux and flow volume in regarding to semen analysis in clinically and sonographically proven cases of varicocele.

Materials and Methods

Local ethics committee approval and patient's documented informed consent were obtained. During March to September 2010, a total number of 35 infertile men (mean age, 28.9 ± 5.2 years) were selected consecutively, from patients referring to fertility clinic. Also 34 patients as Control group (mean age, 28.1 ± 4.2 years) were selected consecutively, from patients referring to urology clinic with scrotal symptoms and clinically diagnosed varicocele without history of infertility, whom proved to have varicocele by ultrasound and normal semen analysis. Age factor was adjusted by selecting appropriate control group. Exclusion criteria were age under 18 and above 40, history of scrotal trauma, infection or surgery (scrotal or abdominal) and any concomitant systemic illness.

Referred patients were examined in supine position with linear multi frequency probe (5-10 MHZ) of Siemens G-40 ultrasound unit (with pulsed-wave color Doppler capability), all performed by a single operator. Venous diameters of pampiniform plexus were measured for each side. A minimum diameter of two millimeters at rest was considered cutoff point for diagnosis of Varicocele.^{5,10} Then the venous plexus of either side were scrutinized for any retrograde flow during rest and Valsalva maneuver. The Valsalva force was standardized by educating patients to blow into an anesthetic flow limiter set (AGA) up to a pressure of 25 cm of water.

If reflux was detectable (using the minimum of PRF and wall filter turned off), quantification was performed by duration and flow volume, using spectral wave analysis after angle correction (50-60 degrees), (Formula 1). Retrograde flow of less than one second

at beginning of Valsalva maneuver, was considered physiologic.⁶ Also, Valsalva-induced flow reversal, which persisted over the entire breath-holding, was considered as continuous reflux. Formula 1: Flow Volume = Mean Velocity x Area

Then, two samples of semen were obtained from each patient, two weeks apart, after Abstinence period of 72 hours and by masturbation. Semen analyses were performed manually by the same technician and laboratory, according to the protocol described in the 1992 WHO Laboratory Manual;⁷ those complying with it were considered normal. Statistical analysis then performed using SPSS 17 software and ANOVA test, X² test, Pearson correlation coefficients and T test, where appropriate. P= 0.05 was considered the minimum level of statistical significance.

Results

Overall 29 patients (42%) showed evidences of venous reflux at Doppler ultrasound. none of them had reflux without straining.

Right-sided reflux was seen in nine patients (13%), left sided reflux in 29 patients (42%).

16 patients (23%) showed continuous venous reflux during breath-holding, this continuity of reflux was present in 15 patients (93.8%) with abnormal semen analysis & just one patient (6.3%) with normal semen analysis, which in turn, representing strong correlation between continuous venous reflux of either sides (right or left or bilateral), with semen analysis abnormality (P=0.001)

Left-sided reflux was present in 20 patients with abnormal semen analysis (69%) & nine patients with normal semen analysis (31%), (P=0.01)

Right-sided reflux was seen in 6 patient with abnormal semen analysis and 3 patients with normal semen analysis, with no statistical difference between the two groups (P=0.47).

None of the patients with normal semen analysis showed bilateral venous reflux (P=0.02). Also, right-sided unilateral reflux was never seen in patients.

The average volume of reflux on the left side in patients with abnormal test was 10.9 CC per minute (SD=5.95) and it was 8.1 CC per minute in patients with normal sperm tests (SD =2.31) (P= 0.18). The average volume of reflux in the right side in patients with abnormal test was 10.5 CC per minute (SD =9.87) and in patients

with normal test, it was six CC per minute (SD=1). (P= 0.46)

Discussion

Generally, the main positive finding was significant correlation between the presence of continuous reflux of either sides with abnormal semen analysis (p=0.001). Although this has not been evaluated separately in any study, but a number of them showed that basal (not valsalva-induced) reflux of continuous type becomes significantly more prevalent as the vein diameter increases.⁸

Annoni and colleagues showed that basal continuous reflux is an indication for ligation of spermatic vein in patients with abnormal semen analysis.¹ Liguori et al, proposed continuous venous reflux (more than 1sec) should be present, in addition to vessel diameter, for diagnosis of varicocele.⁹ However we found patients with abnormal semen analysis and vein diameters as large as four millimeters, without evidences of flow reversal, even on gray-scale exam. Ghafouri also found 20% of patients without detectable reflux.¹¹ Kocakoc et al showed that flow volume of reflux is more accurate than reflux or venous diameter for diagnosing degree of varicocele.¹⁰ Hoekstra and Witt suggested 3.5 mm as the cutoff point, above which reflux is always present.¹²

In a study by Hirsch in 1980, the incidence of clinical varicocele and Valsalva-induced reflux was similar in both fertile and infertile groups of patients.⁸ This could be explained by differences in methods, as they evaluated reflux by audible flow signal; instead of color Doppler exam. Also they compared patients based on fertility, not based on semen analysis. Concerning the theory of increased venous pressure as the leading cause of varicocele, and subsequently sperm abnormality, it seems logical to have more degrees of retrograde flow in patients with abnormal sperm analysis.

The other finding was the statistical difference between the presence of left-sided reflux in the two groups with abnormal and normal semen analysis. This was not confirmed in any studies.

Hirsch and colleagues didn't find any difference between groups of fertile and infertile patients in left-sided reflux.⁸ But Hussein F, recommended varicocelectomy in cases of testicular vein diameter greater than 2.5 mm and in cases of reflux of any

grade detected in the veins at the lower pole of the testis.¹³ Volume of Retrograde flow did not show meaningful difference in the two groups of patients. Although this has not been evaluated in studies separately, but Ghafouri and colleague didn't find any correlation between flow volume and vein diameters.¹¹ A significant difference in presence of continuous reflux in two groups of patients with different semen analysis results reveals its high value predicting abnormality in semen analysis.

However, a brief review of the published data about varicocele and the significance of reflux and its quantity, discloses a wide range of discordance even in diagnosis of varicocele as well as maximum diameter of normal veins and significance of reflux. For example, Cinna et al, defined 3.7 mm as upper normal limit (97th percentile) of peritesticular vein diameter.¹⁴

Regarding high prevalence of varicocele in infertile men, it appears beneficial to perform large, prospective studies to define reliable criteria, diagnosing varicocele and to determine prognostic factors.

In our experience we found that some unidentified and interfering factors could be present. For example, the effect of temperature and contraction of cremasteric muscle (which could lead to increased intra scrotal pressure), has not been taken into account yet. Similarly, looking at the body as a dynamic responder, changes in diameter and flow volume of vascular tree could be due to timing of the study (e.g. through daytime). In addition, variability in ultrasound equipment and operators in different centers, limit the validity of results to more degrees.

At last, it could be concluded that routine quantitative Doppler exam in adolescents and young adult males, referred for scrotal ultrasound, could have some diagnostic and prognostic values, and is recommended because of wide range of availability and reproducible results, as well as low cost. But more studies are needed to define more exact criteria.

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