

VARICOCELE IN MALE INFERTILITY COMPARISON OF DOPPLER AND CLINICAL PARAMETERS

S. Senthil Raj Kumar¹, D.Naveen², D. Vignesh³

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Corresponding Author:

Dr. S. Senthil Raj Kumar,

Email:

senthilraj कुमार1975@gmail.com

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¹Assistant Professor, Department of Radiodiagnosis, Dhanalakshmi Srinivasan Medical College and Hospital, Perambalur, Tamilnadu, India.

²Associate Professor, Department of Radiodiagnosis, Dhanalakshmi Srinivasan Medical College and Hospital, Perambalur, Tamilnadu, India.

³Assistant Professor, Department of Radiodiagnosis, Dhanalakshmi Srinivasan Medical College and Hospital, Perambalur, Tamilnadu, India.

Abstract

Background: Varicocele is a common condition that affects 15-20% of men, leading to pain, discomfort, and infertility. The study aims to assess the relationship between Doppler and clinical parameters of varicocele, establish the reliability of Doppler sonography in diagnosing varicocele, and to compare Doppler grading with pre-and postoperative semen parameters. **Materials and Methods:** This prospective study was conducted at Dhanalakshmi Srinivasan Medical College and Hospital, Preambalur, from February 2022 to February 2023. Fifty male patients with primary infertility were enrolled in our study, and informed consent was obtained from all patients. Patients underwent clinical examination and sonography for varicocele, and semen analysis was performed to assess sperm count, motility, and morphology. Doppler reflux grading was used to compare pre-and postoperative semen parameters. **Results:** Most out of 50 patients had bilateral varicocele. Doppler Grading showed that most cases belonged to Grade II on the left side and Grade I on the right side. Doppler demonstrated reflux in all 10 cases (100%), clinically diagnosed as not having varicocele. The mean venous diameter was (0.21) on the left and (0.25) on the right and showed statistically significant relationship with clinical and Doppler grading. Statistically significant relationship exists between Doppler grading and sperm concentration in pre-operative semen analysis. There was improvement of 7.04 million in mean sperm concentration and 4.93% in mean sperm motility after the surgery. **Conclusion:** Doppler ultrasonography is reliable for diagnosing varicocele. Doppler grading shows statistically significant relationship with venous diameter and preoperative sperm concentration.

INTRODUCTION

Varicocele is a common condition that affects approximately 15-20% of men in the general population.^[1,2] It is characterized by the enlargement of veins within the scrotum, which can cause pain, discomfort, and infertility. While varicocele is not always associated with infertility, it has been shown to harm male fertility in some cases.^[3] The exact cause of varicocele is not fully understood, but it is believed to be related to the abnormal flow of blood through the veins in the scrotum. This can increase the temperature within the testicles, damaging sperm production and motility.

Varicocele is often diagnosed during a physical examination by a healthcare provider. The condition may also be detected during an evaluation for infertility. In some cases, varicocele may be

asymptomatic and go undetected for years. The prevalence of varicocele varies depending on the population being studied. Studies have shown that the prevalence of varicocele among men attending infertility clinics ranges from 30-40%, while population-based studies estimate a prevalence of 15-20%.^[4] This suggests varicocele may be more common among men with fertility issues.

While not all men with varicoceles experience infertility, there is evidence to suggest that varicoceles can harm male fertility. Studies have shown that men with varicoceles are more likely to have reduced sperm count, poor sperm motility, and abnormal sperm morphology compared to men without varicoceles.^[5] The association between varicocele and male infertility has been studied extensively.^[6,7] Researchers have investigated various aspects of this relationship, including how

varicoceles affect fertility, diagnostic methods for identifying varicoceles, and treatment options for improving fertility outcomes in men with this condition.

The study aims to assess the relationship between Doppler and clinical parameters of varicocele, establish the reliability of Doppler sonography in diagnosing varicocele, and set a Doppler diagnostic criterion. Additionally, the study aims to compare the Doppler grading with pre- and post-varicocelectomy semen parameters to evaluate the effectiveness of the surgery.

MATERIALS AND METHODS

This prospective study was conducted at Dhanalakshmi Srinivasan Medical College and Hospital, Preambalur, from February 2022 to February 2023. Fifty male patients with primary infertility and abnormal semen analytic parameters were enrolled in our study. Ethical clearance was obtained from the institutional review board before conducting the study and informed consent was obtained from all patients.

Inclusion Criteria

Married male patients, more than one year, couples living together (no separation), actively practising unprotected sexual intercourse, complaining of primary infertility, no sexual dysfunction, wife fertile, fructose positive semen, with abnormal concentration and motility, normal hormonal assay, unilateral/ bilateral venous reflux on Doppler ultrasound, and presence of varicocele confirmed by clinical examination and sonography were included.

Exclusion Criteria

Married males less than one year, couples living separately, secondary infertility, sexual dysfunction present, wives are known to have infertility problems, fructose-negative Azoospermia, abnormal hormonal assay, and no reflux in Doppler ultrasound were excluded.

The data collected from each patient included age, duration of infertility, semen analysis results, clinical examination findings, and colour Doppler ultrasound findings.

All patients underwent clinical examination and sonography for the presence of varicocele.

Clinical grading was done by Dubin criteria and on Gray scale ultrasound, diameter (> 0.2 cm) was considered as dilated pampiniform venous plexus.

In our institution, through Doppler sonography we graded the reflux based on duration of reversal flow in time (seconds) during Valsalva maneuver by spectral analysis, with patient

in supine position. Venous reflux graded by doppler as Grade 0 - No reflux or reflux (< 1 sec), Grade I - Reflux for (1- 3) secs, Grade II – Reflux for (3- 5) secs, Grade III – Reflux for (> 5) secs. Continuous reflux lasting for (>5 seconds), reflux during normal respiration and intratesticular reflux were considered as Grade III.

Semen analysis was performed to assess sperm count, motility, and morphology. Only two parameters were included in semen analysis and normal standard value was set according to 1999 WHO criteria: Sperm Concentration (≥ 20 million/ml) and motility ($\geq 50\%$) with progressive motility.

The patients were followed up and semen analysis was done again after three months, and any change in semen analytical parameters [Concentration and Motility] compared to pre-operative parameters were studied. A comparison between Doppler reflux grading and pre & postoperative semen parameters was made.

The collected data were entered into a Master chart and fed into the computer. Frequencies, Percentages, Mean, Standard deviation, Chi-square and 'p' values were calculated using the "Epidemiological Information Package (EPI 2002)" software developed for the World Health Organization. Kruskal Wallis' Chi-square test for the significance of the relationship was used. A "p" value less than 0.05 were taken to denote a significant difference.

RESULTS

Among 50 patients, the majority (50%) belong to the 30-39 age group. The average age of the patients was 32.3 years. Bilateral varicocele was present in 42 (82%) cases and unilateral varicocele in 8 (16%) cases. All unilateral cases were on the left side, with no unilateral right-side varicocele.

Table 1: Patient characteristics of the study

		Frequency	Percentage
Age group	20-29	17	34
	30-39	25	50
	40-49	8	16
Reflux in Doppler Sonography	Bilateral Reflux	42	84
	Unilateral Reflux	8	16
Clinical Grading		Right	Left
	No varicocele	21 (42%)	10 (20%)
	I	18 (36%)	13 (26%)
	II	11 (22%)	20 (40%)
	III	0	0
Doppler Grading	Grade 0	8 (16%)	0
	Grade I	20 (40%)	10 (20%)
	Grade II	16 (32%)	21 (42%)
	Grade III	6 (12%)	19 (38%)

As per Clinical Grading, there were no cases belonging to Grade III on the right side. On the left side, 40% of the cases were graded as Grade II. Clinically there was no varicocele in 21 (42%) of the cases on the right side and 10 (20%) on the left side. By Clinical diagnosis, there was no varicocele in 31 (31%) sides on both the right and left sides. As per Doppler grading, most cases belonged to Grade I - (40%) on the right side. On the left side, most cases belonged to Grade II - (42%) [Table 1].

Table 2: Relationship between Clinical grading and Doppler Reflux grading of varicocele

Clinical Grade		Doppler Reflux Grade			
		I	II	III	0
Right side	I	14 (77.8%)	2 (11.1%)	2 (11.1%)	-
	II	-	9 (81.8%)	2 (18.2%)	-
	III	-	-	-	-
	No varicocele	6 (28.6%)	5 (23.8%)	2 (9.5%)	8 (38.1%)
Left side	I	5 (38.5%)	4 (30.8%)	4 (30.8%)	-
	II	-	13 (65%)	7 (35%)	-
	III	-	-	7 (100%)	-
	No varicocele	5 (50%)	4 (40%)	1 (10%)	-

On the right side, 31 (62 %) of the 50 cases had identical grading in both methods. In 21 cases clinically diagnosed as No varicocele, Doppler demonstrated reflux of various grades in 13 cases (61.9 %).

On the left side, 25 (50%) of the 50 cases had identical grading in both methods. In 10 cases clinically diagnosed as No varicocele on the left side, Doppler demonstrated reflux in all 10 cases (100%).

Combining both right and left sides (n = 100), 56 sides (56%) had identical grading in both clinical and Doppler methods. In 31 sides clinically diagnosed as No varicocele, Doppler demonstrated reflux of varying grades in 23 sides (74.2%) [Table 2].

Table 3: Venous diameter on both sides

		Venous Diameter	
		Right	Left
Sonography		0.21 ± 0.04	0.25 ± 0.05
Clinical Grading	Nil	0.18 ± 0.03	0.21 ± 0.03
	I	0.23 ± 0.03	0.23 ± 0.03
	II	0.24 ± 0.03	0.27 ± 0.04
	III	-	0.31 ± 0.01
	P-value	0.0001	0.0001
Doppler Grading	Nil	0.15 ± 0.01	-
	I	0.21 ± 0.02	0.21 ± 0.03
	II	0.24 ± 0.03	0.24 ± 0.04
	III	0.26 ± 0.03	0.29 ± 0.04
	P-value	0.0001	0.0001

The mean venous diameter in sonography was (0.21) on the right and (0.25) on the left. As the Clinical grading and Doppler grading increase, the mean values of venous diameter also increase. Statistically significant relationship in venous diameter between clinical grading and Doppler grading [Table 3].

Table 4: Pre-operative and Postoperative semen analysis

	Semen analysis parameters		
	Pre-operative Value	Postoperative value	Improvement
Concentration	11.75 ± 10.52	13.38 ± 14.65	7.04 ± 10.77
Motility	31.52 ± 19.11	38.62 ± 26.4	4.93 ± 8.98
Azoospermia	16 (32%)		

In the pre-operative semen analysis, the mean concentration was 11.75 + 10.52 million, and motility was 31.52% + 19.11%. The postoperative mean concentration was 13.38+ 14.65 million, and motility was 38.62% + 26.4 %. Azoospermia was present in 16 (32%) of the cases.

There was an improvement of 7.04 million in mean semen concentration and 4.93% in mean semen motility after the surgery. In Azoospermic cases, there was no significant improvement [Table 4].

Table 5: Pre-operative and Postoperative semen analysis on both sides

		Semen analysis parameters					
		Pre-operative Value		Postoperative value		Improvement	
		Conc in millions	Motility in %	Conc in millions	Motility in %	Conc in millions	Motility in %
Right side	Nil	15±4.69	47.17±11.11	19.2±24.32	47.4±26.79	19.2±24.32	10±12.63
	I	9.69±6.05	32.33±18.47	4.39±5.45	28.39±23.83	4.39±5.45	3.67±8.74
	II	6.67±1.63	48.18±17.17	4.69±6.85	26.08±30.58	4.69±6.85	3.23±7.14

	III	6.75±4.31	34.67±25.03	9.92±8.21	39.5±22.88	9.92±8.21	4.83±8.52
P-value		0.049	0.181	0.284	0.233	0.284	0.594
Left side	Nil	-	-	-	-	-	-
	I	11	36±20.59	5.2±7.12	16.6±24.14	0.8±1.1	0.6±1.34
	II	12.06±6.29	36.57±16.64	17.84±19.07	31.78±26.09	9.12±14.42	5.56±9.95
	III	6.25±2.94	41.79±21.65	11.26±9.5	35.21±27.18	6.66±7.23	4.42±8.53
P-value		0.005	0.779	0.240	0.328	0.216	0.601

On both the right and left sides, as Doppler grading increases, pre-operative concentration decreases, and this inverse relationship is statistically significant. There was no statistically significant relationship between Doppler grading and pre-operative sperm motility.

Regarding the postoperative semen parameters, there was no statistically significant relationship in the mean values of both sperm concentration and motility, with Doppler grading on the right and left side [Table 5].

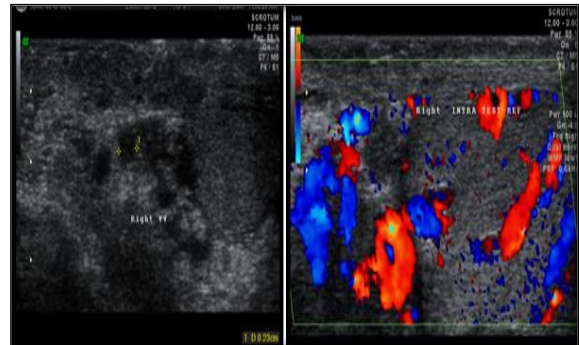


Figure 4: Infertile male patient of age 32 years with bilateral varicocele, showing dilated venous plexus (0.23) cm with intratesticular doppler reflux - Grade III on right side

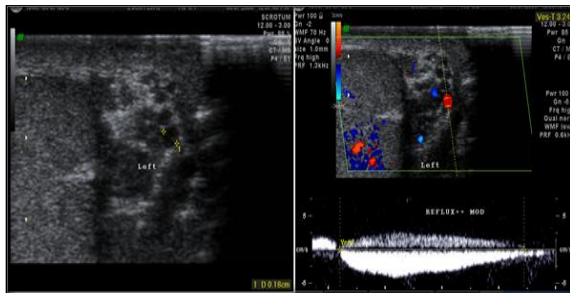


Figure 1: Infertile male patient of age 26 years; Gray scale image showing undilated venous plexus (0.18) cm, having moderate reflux in doppler, lasting for (>3secs) Grade II on left side during valsalva.

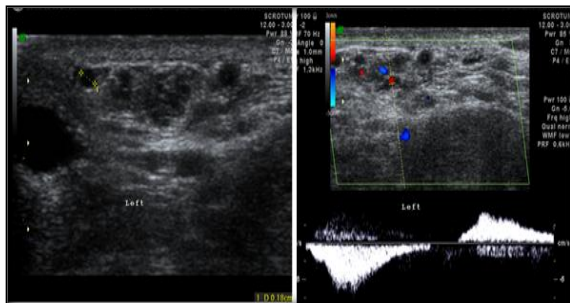


Figure 2: Infertile male patient of 30 years with unilateral varicocele; Gray scale image showing undilated venous plexus (0.18) cm, with mild reflux lasting for 2 secs on left side on doppler study.

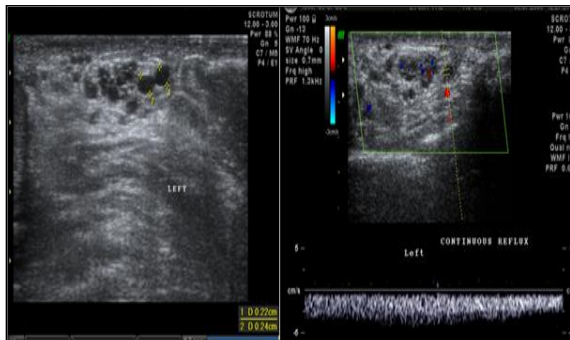


Figure 3: Infertile male patient of age 37 years, left sided dilated venous plexus (0.2) cm with continuous reflux on doppler study- Grade III

DISCUSSION

Varicoceles, or dilated veins in the scrotum, are a common abnormality in men with infertility. Evidence shows they can negatively impact the testis, but repairing them may reverse or prevent these effects. An Andrological exam is recommended for men with abnormal sperm analysis results. Varicoceles can be diagnosed through physical examination, but there is subjective variation, and some may be missed.

In our study group, the age distribution of patients was from (22-46) years. The majority of patients belonged to (30-39) group. The average age of the patient was (32.3 ± 5.7). One of the interesting outcomes of our study was the presence of bilateral Doppler reflux in 42 cases (84%) out of 50 cases. Unilateral reflux was seen only in 8 cases (16%), all on the left side, and there was no unilateral right-side reflux. The present study finds that varicocele, traditionally considered a predominantly unilateral abnormality, apparently has a strikingly high bilateral prevalence (84%). This finding coincides with the study conducted by Gat Y et al.8, in which they had a strikingly high bilateral prevalence (80.7%) of varicocele. This may suggest that we should consider varicocele bilateral disease. Our study may have important implications for treatment, indicating that patients with clinical evidence of unilateral left varicocele should be carefully evaluated for bilateral varicocele.

Doppler grading revealed reflux of various grades in 31 of 50 cases, while 25 of 50 cases had identical grading. In 10 cases, reflux was 100%. Combining sides, right and left (n = 100), in 56 sides (56%), there was identical grading in both clinical and Doppler methods. Even though not very significant, reasonable overlapping between Doppler and

clinical grading exists. Of 31 sides diagnosed as clinically No varicocele, Doppler demonstrated reflux of varying grades in 23 sides (74.2%). This implies the importance of using Doppler ultrasonography in the diagnosis of 'subclinical' varicoceles. Also, Doppler demonstrated reflux of varying grades on all 69 sides (100%), clinically diagnosed to have a varicocele on the right or left sides. We also measured the maximum venous diameter on both sides, and the mean venous diameter was (0.21 ± 0.04) on the right and (0.25 ± 0.05) on the left.

As the Doppler grading increases, the mean values of venous diameter also increase. A statistically significant relationship exists between venous diameter and Doppler grading ($P < 0.05$). This result shows larger the diameter of the pampiniform plexus, the higher the reflux grade. A similar relationship exists between Clinical grading and venous diameter, which was also statistically significant.

In two studies done by Lund L et al.^[9] and Liguori et al.^[10], they concluded with similar results that Color Doppler sonography is a new reliable and non-invasive diagnostic method in evaluating the evaluation of varicocele testes. Lund L et al.^[9] also suggested that all males evaluated in an infertility clinic undergo a colour Doppler scan with and without the Valsalva's manoeuvre and that a spectral analysis be performed to locate even small Varicoceles. We agree with their conclusion and suggest Doppler ultrasonography as a reliable and non-invasive diagnostic method for the evaluation of varicocele. This is demonstrated by the reversal of venous flow, which allows the detection of even subclinical varicocele. Doppler ultrasonography's capacity for measuring the pampiniform plexus's size and spermatic veins' blood flow parameters make it an effective diagnostic tool. Liguori et al.^[10] also suggested, at present, there is a lack of completely standardized diagnostic criteria. Still, when this problem is solved, clinical examination and CDU will certainly become the gold standard in the investigation of varicocele.

Eskew LA et al.^[11] suggested the best predictor of a varicocele was internal spermatic vein diameter. But in, a study conducted by Jung SM et al.^[12] reported that retrograde flow might provide a more reliable indicator than the spermatic vein diameter for diagnosing varicocele. Retrograde flow is the main criterion for diagnosing varicocele. The Duplex Doppler ultrasonographic values for retrograde flows are poorly defined.

Tasci et al.^[13], in their study, tried the standardization of diagnostic criteria for varicocele. Three types of venous flow patterns were found in the spectral analysis, and they classified them as Type I, II and III. They concluded Spectral analysis of Doppler waves should be combined with Color Doppler Ultrasound to diagnose varicocele. Similarly, Chiou RK et al.^[14] prospectively studied patients with Color Doppler, and they developed a

new scoring system. Using their proposed new scoring system, they suggested CDU be a reliable and accurate method of diagnosis for varicoceles compared to the current reference standard physical examination.

The grading method proposed by us, measuring the duration of reflux in time (seconds) by Doppler spectral analysis, also appears reliable as it has reasonable overlap with clinical grading and a statistically significant relationship with mean venous diameter. Only 42 cases underwent varicolectomy, unilateral and bilateral, as indicated. Surgery was not done in 8 cases due to various reasons. Different opinions and controversial results exist in the literature regarding improvement in semen parameters after varicolectomy and whether varicocele repair could be done or not for males with features of infertility.

Evers et al.^[15], in their study, suggested Varicocele repair does not seem to be an effective treatment for male or unexplained subfertility. But, Park JS et al.^[16], in their research, had concluded that, in infertile couples with no specific problem other than subclinical varicocele, performing a microsurgical varicolectomy is worthwhile. Krause W et al.^[17] reported no significant increase in pregnancy rate in the treated group compared to the controls. They suggested they would like to encourage further collaborative study groups to start another prospective, randomized study to avoid the costs and risks of varicocele treatment when its success remains unclear.

Our study found that pre-operative semen concentration was 11.75 ± 10.52 million, and motility was $31.52\% \pm 19.11\%$. Postoperative mean concentration was 13.38 ± 14.65 million, and motility was $38.62\% \pm 26.4\%$. Azoospermia was present in 16 (32%) of the cases, and there was an improvement of 7.04 million in mean semen concentration and 4.93% in mean semen motility after the surgery. However, there was no significant improvement in Azoospermic cases. Doppler grading and semen parameters on both the right and left sides showed that as Doppler grading increases, pre-operative concentration decreases. However, there was no statistically significant relationship between Doppler grading and pre-operative sperm motility.

Regarding the postoperative semen parameters, there was no statistically significant relationship in the mean values of both sperm concentration and motility, with Doppler grading on the right and left side. This may be due to a short postoperative follow-up (3 months). We suggest further studies can be conducted, regarding the semen parameters, with adequate and long periods of postoperative follow-up (6-12) months.

Limitations

One limitation of our study was its small sample size. Future studies with larger sample sizes are needed to confirm our findings. Further research is

needed to determine the optimal treatment approach for men with varicocele-associated infertility.

CONCLUSION

Varicocele is a bilateral disease that can cause infertility in men. The colour Doppler ultrasonography is a reliable modality for diagnosing varicocele by demonstrating the reversal of venous flow and measuring the diameter of the pampiniform venous plexus. Doppler spectral analysis correlates statistically significantly with a venous diameter and pre-operative sperm concentration, but there is no significant relationship between Doppler grading and pre-operative sperm motility. Regarding the postoperative semen parameters, there was no statistically significant relationship in the mean values of both sperm concentration and motility. Further studies should be conducted with adequate and long postoperative follow-ups.

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