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Importance of Diffusion-Weighted MRI of the Testes in Varicocele Patients

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ABSTRACT

An abnormal dilation of the pampiniform plexus is known as a varicocele.Around fifteen percent of male adolescents and ten to fifteen percent of adult males have varicocele. Clinical varicoceles are often associated with male infertility. Twenty to forty percent of infertile men have varicoceles, which are known to reduce the amount of semen and testicles. Researchers have looked at the histology of varicocele in testicles and found thicker tubular basement membranes, narrowed luminal spaces, increased fibrous tissue between the testicles, and thickened walls of interstitial blood vessels.

Surgical and percutaneous approaches are available for the treatment of varicocele, a condition that causes male infertility. Researchers at SRM Medical College Hospital included fifty consecutive patients with varicocele who visited the infertility clinic and urology outpatient department (OPD) between January 2015 and March 2016. When patients presented with infertility, testicular discomfort, or both, a physical examination was used to confirm the clinical diagnosis of varicocele.

Researchers compared testicular varicocele patients with the general population to determine the use of diffusion-weighted magnetic resonance imaging for the detection and management of this condition.

Keywords: Varicoceles, Valsalva maneuver, ADC

I. INTRODUCTION

Varicoceles refer to the tortuous & dilated veins of pampiniform plexus. They are of idiopathic in nature or occur secondary to inept spermatic veins valves & usually associated with infertility in men [1].

Varicoceles are found very common into younger adults teenagers. It affects almost 15% of adult males though higher occurrence has been reported amongst patients joining sterility hospitals, upto 80% amongst those by secondary infertility[2-4]. The left side is predominantly affected while bilateral varicoceles are seen in only 10% [5,6]. Varicocele is classified into primary and secondary, the latter due to an increased pressure on spermatic veins and generally manifests on right [7]. In older age group patients, isolated right-sided varicoceles should raise the suspicion of an intra-abdominal mass [1].

II. REVIEW OF LITERATURE

A mass of enlarged, tangled veins in pampiniform venous plexus is tell-tale sign of varicocele, (Fig.1).Primary, secondary infertility in males are most often caused by varicocele, which is a common but curable condition[26].

ETIOLOGY OF VARICOCELE:

When a man is standing, LTV travels vertically before making right angle entry in left renal vein[27].Right spermatic cord venous dilatation is less common because right testicular vein flows in oblique way to enter in inferior vena cava, reducing right testicular vein flow turbulence and back pressure(Fig.2).

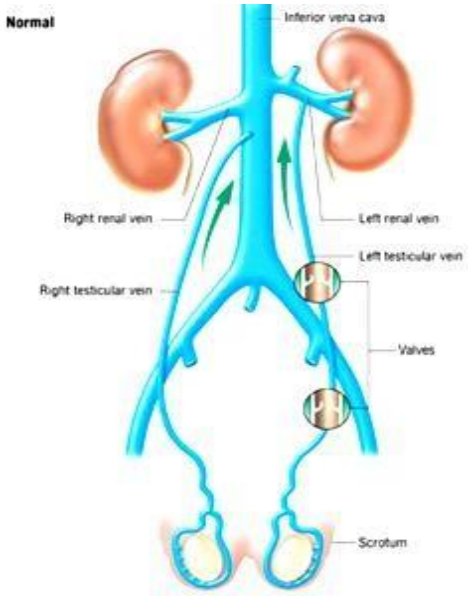


Fig 1: Blood from left testicular vein draining in left renal vein from right angle.Vein that drains right testis angles downward in inferior vena cava.

Because of potential for an increase in LTV pressure due to incompetent valves due to an upright human position, venous distension, dilatation may occur(Fig.3)

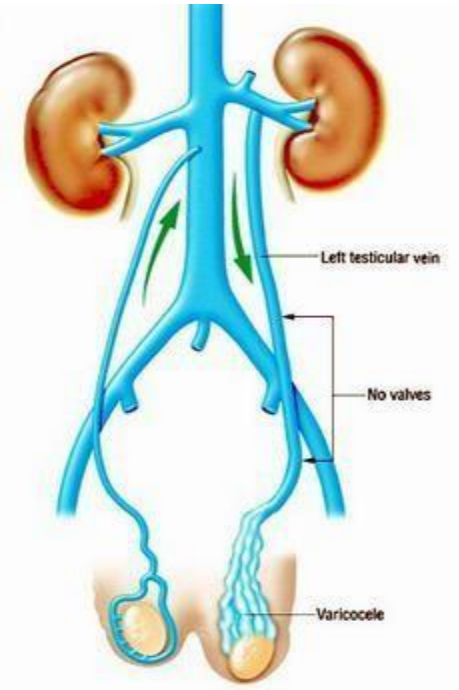


Fig 2: Absent or ineffectual venous valves in spermatic veins increase LTV pressure, Consequently, this causes veins to swell and expand, a condition known as varicocele.

It is speculated that there is a similar shift in dynamics of interstitial fluid found in testicles [44] Moreover, in varicocele, microvascular fluid exchange is disrupted (Fig.4)[51,52,55].

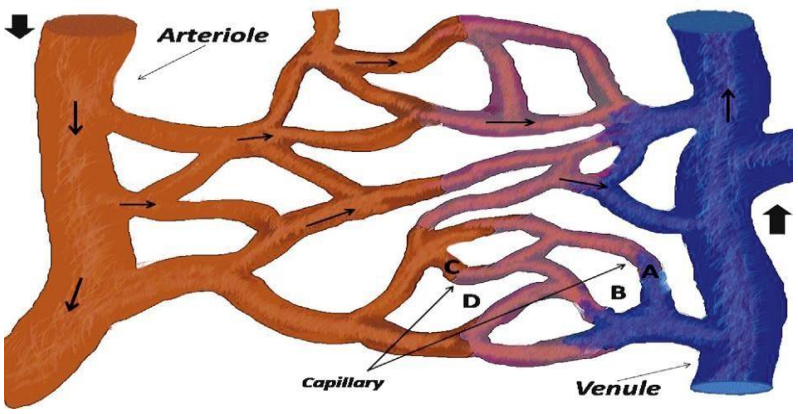


Fig 3: As a consequence of varicocele, hydrostatic pressure into testicular venules, ultimately, in vein ending of capillary rises (Point-A). Extratesticular space is indicated by B and D. General inability of venous ending of testicular capillaries for reabsorbing extracellular fluid causes a reduction in pressure differential (pressure at point-B (-) pressure in point A). Artery end of capillary is at pressure, shown by point C. As a consequence, nutrients are unable to leave artery end of capillaries due to a reduction in pressure differential (pressure at point C(-) pressure at point D).

Varicocele's physiological effects on sperm:

When a varicocele forms on one side, it might disrupt secretory activity of both of body's Leydig cells[75] influences secretory function of Sertoli cells and, by extension, testosterone content of testicles on both sides[76]. Defects in spermatogenesis are not the only possible outcome of low intratesticular testosterone level, androgen-binder protein movement.When a left varicocele forms, it affects both testicles, leading to problems with spermatogenesis and spermatozoa maturation in epididymis (Fig.5).

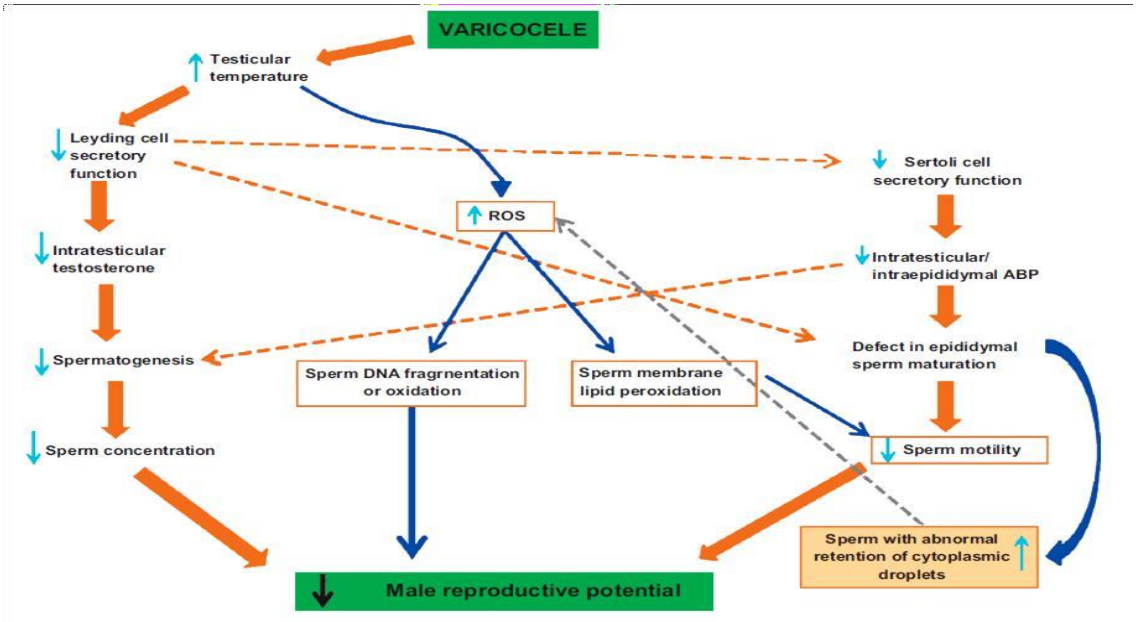


Fig 4: Biological and cellular processes leading to negative impact of varicocele on a man's fertility.

A left varicocele causes a chain reaction of adverse biochemical effects upon sperm & testes physiology, but these effects may be reversed by lowering testicular temperature, which is accomplished during healing (Fig.6).

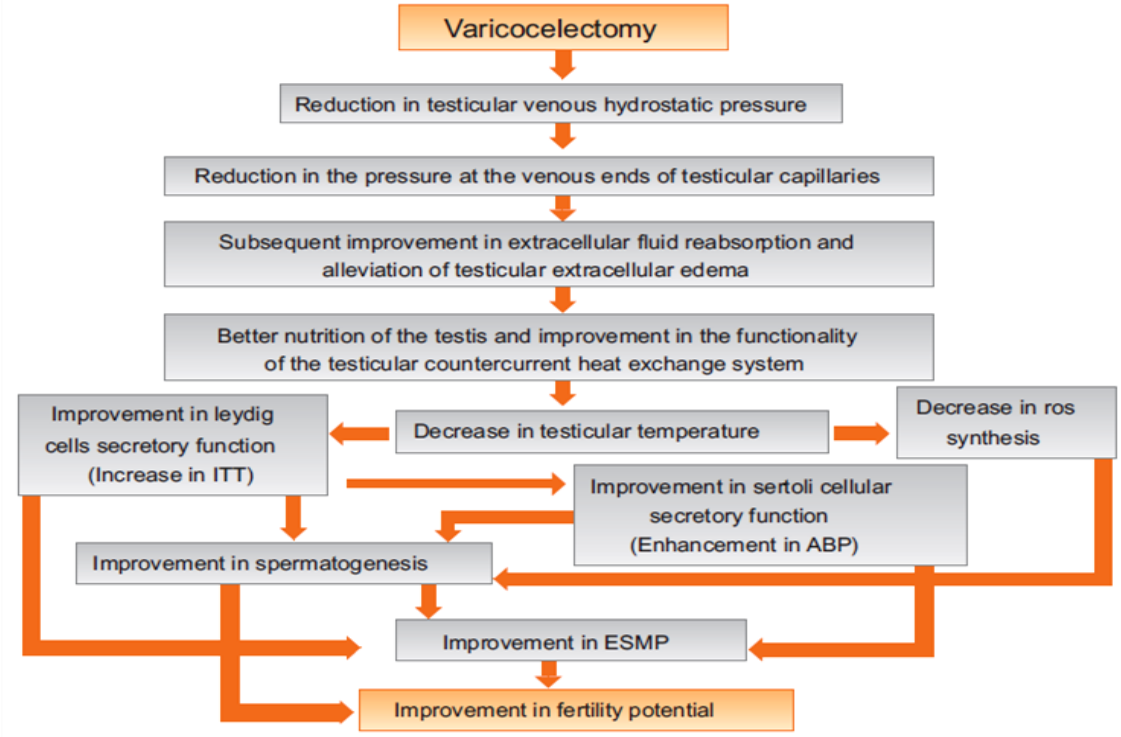


Fig 5: Mechanisms accountable for progress in male fertility potential after varicocelectomy.

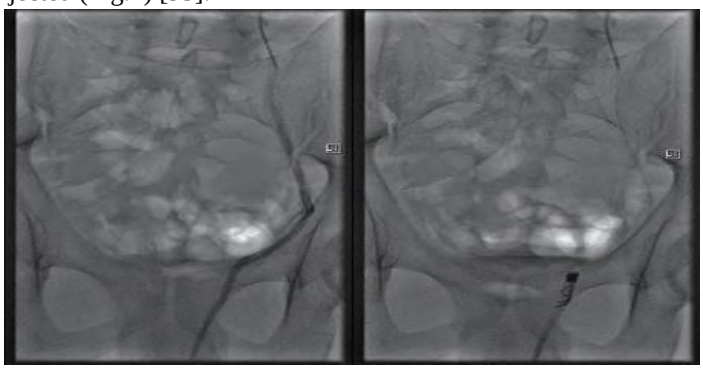
CLINICAL EXAMINATION:Patients are clinically examined by palpation and scrutiny while upright, both before and after Valsalva maneuver. Clinical varicoceles are categorized according to WHO standards (Table 1).

Table1:WHO grouping of clinical varicocele

Grade 1	Palpable during Valsalva maneuver
Grade 2	Palpable without the Valsalva maneuver
Grade 3	Visible through the scrotal skin

VENOGRAPHY

In most cases, a catheter is advanced to the spermatic vein via right femoral or interior jugular vein, and then retrograde contrast is injected (Fig.7) [95].



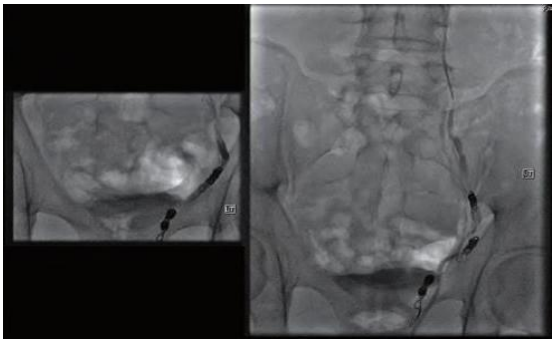


Fig6: Embolic occlusion of a grade 3 left-sided varicocele created with venography [99].

ULTRASOUND

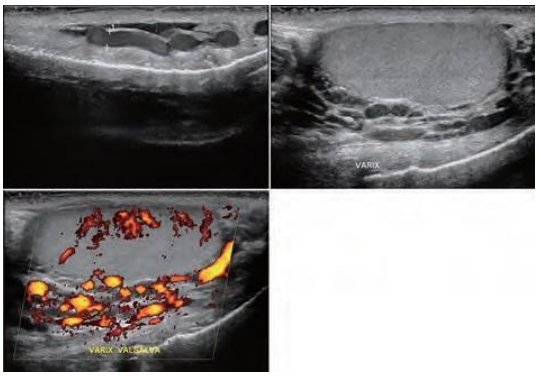


Fig 7: Grade 3 left-sided varicocele ultrasound image. [99].

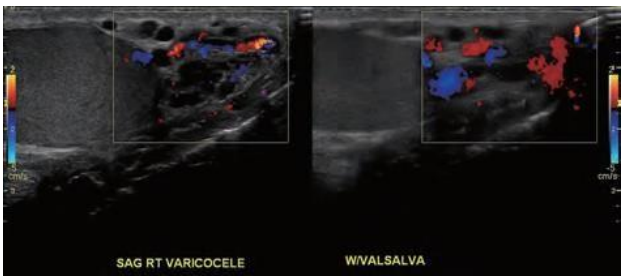


Fig 8: Grade 3 right-sided varicocele ultrasound image. [99].

Table 2: Sarteschi grading for varicocele

Grade 1	During Valsalva maneuver, blood does not back up from scrotum into spermatic cord veins in groin.
Grade 2	Valsalva's technique causes reflux in prominent veins near testicular pole.
Grade 3	When doing Valsalva technique, even supine, dilated veins will reflux.
Grade 4	In absence of Valsalva maneuver, reflux from veins that have widened occurs.

Table 3: Dubin grouping

0	Weak, momentary reflux of venous blood during Valsalva maneuver
1	Reflux of veins that does not stop when Valsalva maneuver is performed
2	There was a continuous venous response throughout whole Valsalva procedure.
3	Preexisting venous reflux that does not improve after Valsalva technique

Table 4: Chiou et al Scoring system

	SCORE
Maximum vein diameter (mm)	
<2.5	0
2.5-2.9	1
3.0-3.9	2
≥4.0	3
Plexus / sum of diameter of veins	
No plexus identified	0
Plexus (+) with sum diameter <3 mm	1
Plexus (+) with sum diameter 3-5.9 mm	2
Plexus (+) with sum diameter ≥ 6 mm	3
Change of velocity on Valsalva maneuver	
< 2 cm s^{-1} or duration <1 s	0

Table 5: Image modalities utilised for diagnosing varicoceles. [114]

Methods	Diagnostic criteria
Sonography	When performing Valsalva manoeuvre, anechoic edifices close with testis correlate with diluted veins of pampiniform plexus, which have calibres of 2-3 mm.
Colour Doppler Sonography	Valsalva-induced spermatic vein reflux may be either static (grade-I) or intermittent (grade II) or continuous (grade-III)
Magnetic Resonance Imaging	Injection of contrast medium causes pampiniform plexus vessel dilation, with signal intensity varying with flow rate.

Philip et al. conducted a histological analysis of testicular biopsies & spermatogenesis disruption into infertile males having varicocele, and they observed hypo spermatogenesis (80.88%) with sloughing(Fig.10).

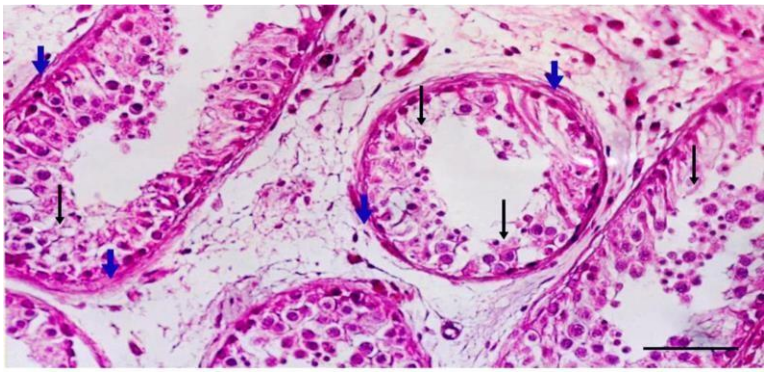


Fig 9: Photomicrograph showing hypo spermatogenesis with thickening of basement membrane..

III. AIMS AND OBJECTIVES

1. For evaluating part of ADC values into patients by testicular varicocele and to compare it with normal population.
2. To correlate ADC values to testicular varicocele grading.

MATERIALS AND METHODS 50 consecutive patients having Testicular varicocele, 50 patients for control group were recruited in research after acquiring conversant permission in writing before USG & DW-MR Imaging. Study was done at department of Radio-diagnosis, SRM MEDICAL COLLEGE HOSPITAL & RESEARCH CENTRE, KATTANKULATHUR, TAMILNADU.

KIND OF STUDY: Cross sectional study.

Ethical attention:

Research is performed under consent of institution's ethical review board.

INCLUSION CRITERIA

Patients clinically diagnosed with varicocele and confirmed with colour Doppler ultrasonography (USG).

EXCLUSION CRITERIA

Patients with h/o previous varicocele repair

2. Persons who have had scrotal surgery in past
3. Patients who have had hernia repair
4. Patients having h/o urogenital infection
5. Patients having singular testis
6. Patients having testicular torsion
7. Patients having testicular trauma
8. Patients having testicular tumours
9. Patients using medicines reported to alter ADC values
10. Patients contra-indicated for MRI.

IV. METHODOLOGY

A total of 50 consecutive patients with varicocele presenting to the Infertility clinic & Urology OPD of SRM Medical College Hospital through study period, January 2015 to March 2016,were taken into the study. Those individuals who presented with infertility, testicular discomfort, or both were given a medical analysis of varicocele following an physical test revealed condition. Color Doppler ultrasonography was also used to inspect them for further confirmation of diagnosis. Any patients meeting exclusion criteria were not included in analysis. Patient was examined medically under palpation examination whereas standing before to & while Valsalva maneuver.

V. RESULTS

CLINICAL PRESENTATION

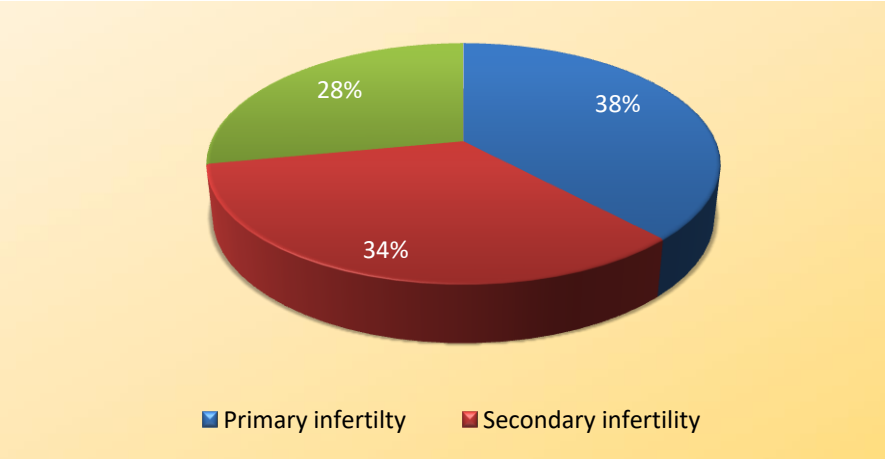


Fig 10: Clinical presentation

OBSERVATION:
Of the 50 patients in this study, 19 (38%) patients accessible with primary infertility, 17 (34%) presented by secondary infertility and remaining 14 (28%) patients presented with scrotal pain.

COMPARISON GROUPS

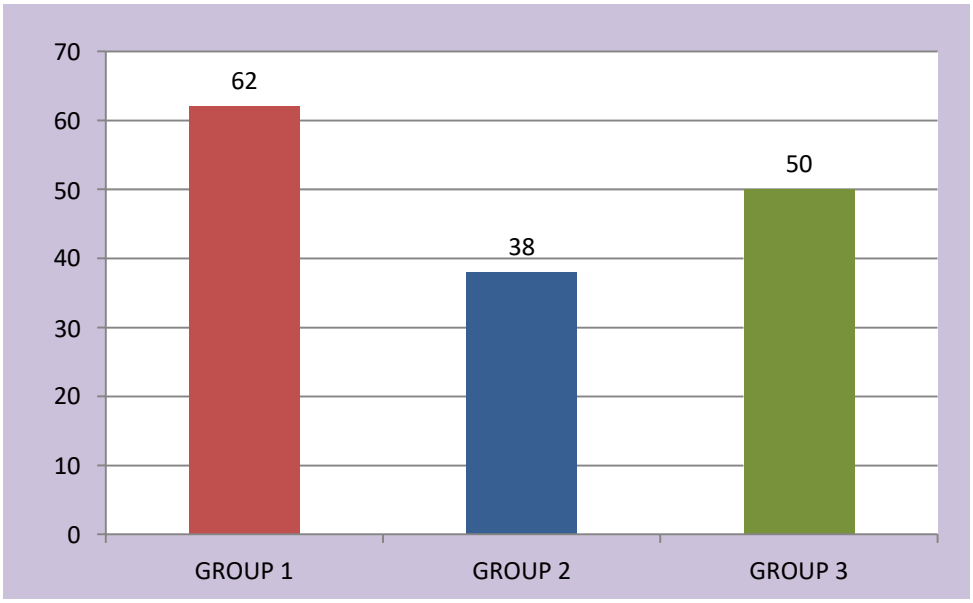


Fig 11: Study group distribution

OBSERVATION:
Out of 50 cases, 12 patients presented by bilateral varicocele (24 testes), 38 patients by unilateral varicocele (38 testes). This meant that 62 ipsilateral testes were placed in group 1, and 38 contralateral testes were placed in group 2. In third group, made up of 50 healthy volunteers.

Group 1= Testicle ipsilateral to varicocele

Group 2 = Testicle contralateral to varicocele

Group 3 = Healthy volunteer control subjects

AGE DISTRIBUTION

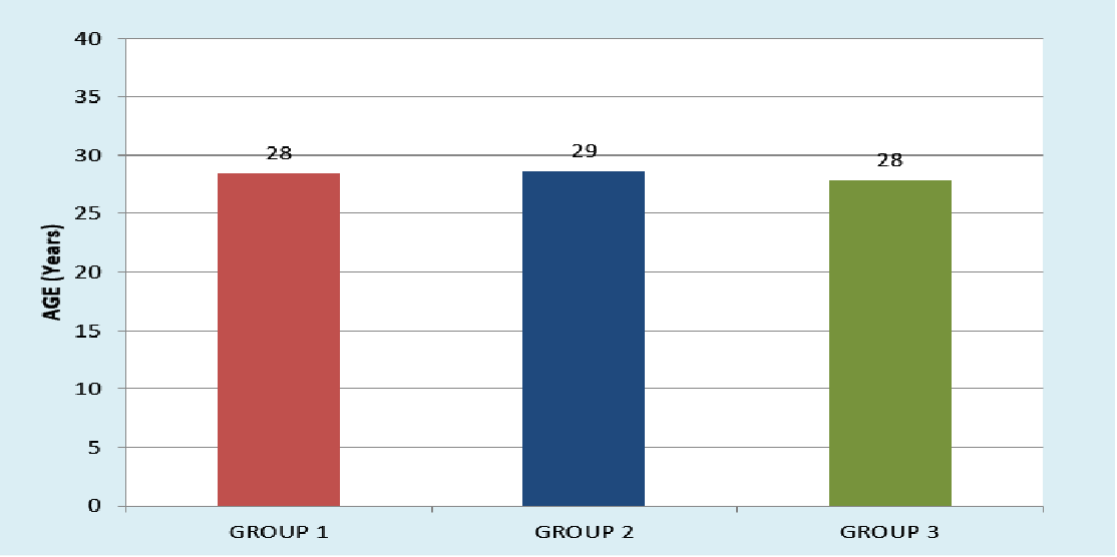


Fig 12: Age distribution of Groups 1, 2 & 3

	Group 1	Group 2	Group 3
Age (Years)	**28.42±4.11**	**28.68±4.37**	**27.84±4.2**

Group1= Testicle ipsilateral with varicocele or varicoceles
Group2 = Testicle contralateral with varicocele or varicoceles
Group3 = Healthy volunteer controlling subjects
OBSERVATION:
None of age differences between groups were significant.
TESTICULAR ADC VALUES OF GROUP 1, 2 AND 3

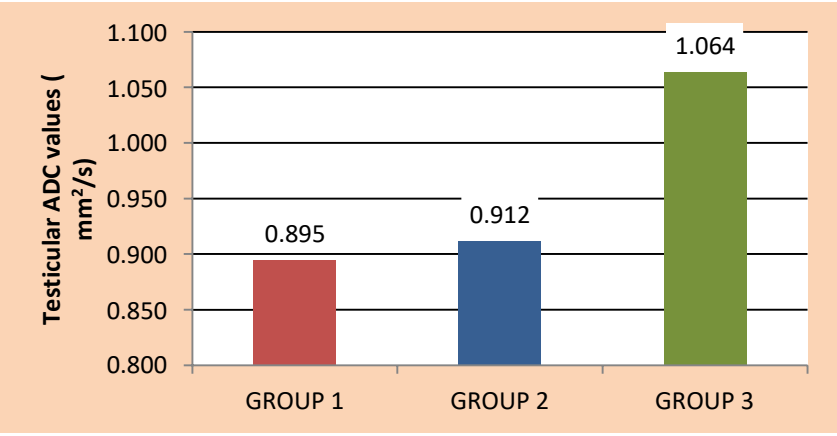


Fig13: Testicular ADC values of group 1, 2 and 3

	Group 1	Group 2	Group 3
Testicular ADC values(mm^2/s)	0.895 ± 0.049	0.912 ± 0.024	1.064 ± 0.037

Group 1= Testicle ipsilateral to varicocele

Group 2 = Testicle contralateral to varicocele

Group 3 = Healthy volunteer control subjects

OBSERVATION:
Mean ADC group 1, 2 and 3 value was 0.895, 0.912 and 1.064 respectively.

COMPARISON OF ADC VALUES BETWEEN GROUPS

Table 6: Comparison of ADC values between groups

	Group 1	Group 2	Group 3	p
Testicular ADC values(mm^2/s)				
Mean ± SD	0.895 ± 0.049	0.912 ± 0.024	1.064 ± 0.037	< 0.001[a]
Comparison				
Group 1 vs 2				0.103[b]
Group 1 vs 3				< 0.001[b]
Group 2 vs 3				< 0.001[b]

Group 1= Testicle ipsilateral to varicocele

Group 2 = Testicle contralateral to varicocele

Group 3 = Healthy volunteer control subjects

[a]$p < 0.05$ was regarded as important statistically.
[b]$p < 0.05$ was regarded as important statistically.

OBSERVATION:
Groups 1 and 3 were statistically different, as were groups 2 & 3. Group 2 was not substantially diverse from Group 1 statistically.

VENOUS DIAMETER AT REST FOR GROUP 1, 2 & 3

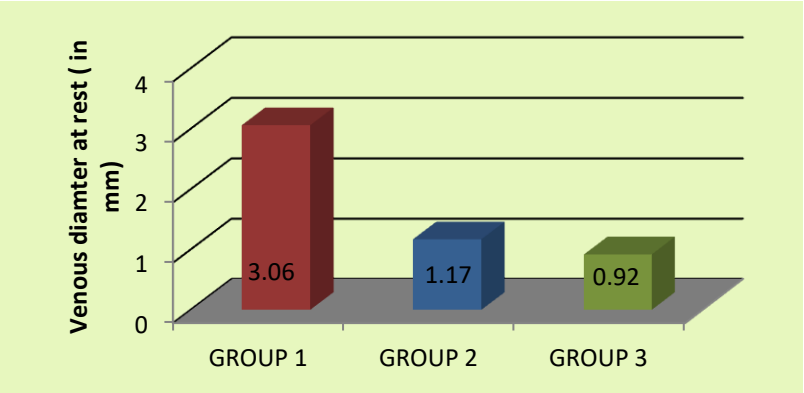


Fig 14: Venous diameter at rest for group 1, 2 & 3

Group 1= Testicle ipsilateral to varicocele

Group 2 = Testicle contralateral to varicocele

Group 3 = Healthy volunteer control subjects

OBSERVATION:
Venous diameter (Mean±SD) at relaxation for group 1,2 & 3 were 3.06±0.73mm, 1.17± 0.17 mm & 0.92±0.12mm correspondingly.

VENOUS DIAMETER DURING VALSALVA MANEUVER FOR GROUP 1, 2 & 3

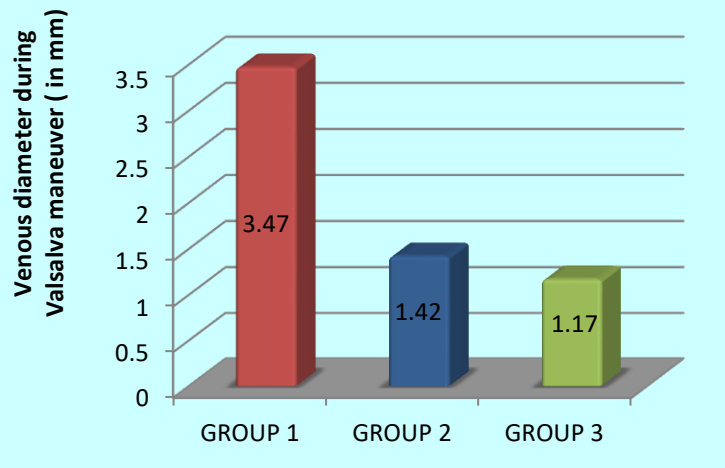


Fig 15: Venous diameter during Valsalva maneuver for group 1, 2 & 3

Group 1= Testicle ipsilateral to varicocele

Group 2 = Testicle contralateral to varicocele

Group 3 = Healthy volunteer control subjects

OBSERVATION:

Venous diameter at rest for group 1,2&3 were 3.47±0.76mm, 1.42±0.19mm & 1.17±0.13mm correspondingly.

VENOUS DIAMETER DURING REST AND VALSALVA MANEUVER

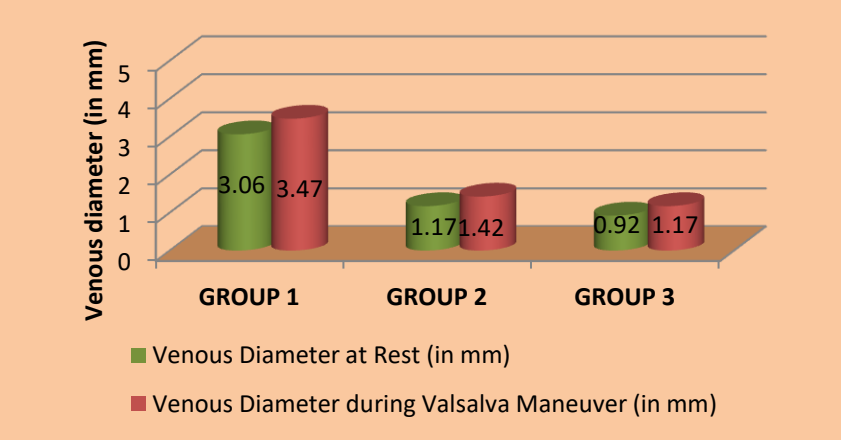


Fig16:Venous diameter during rest & Valsalva maneuver

Group 1= Testicle ipsilateral to varicocele

Group 2 = Testicle contralateral to varicocele

Group 3 = Healthy volunteer control subjects

OBSERVATION:

When compared to Groups 2 and 3, Group 1 had a larger venous diameter both at during & at rest Valsalva maneuver. Although group 2 had larger venous diameters than group 3, there had been no statistically substantial variance amongst 2 groups Valsalva maneuver.

RELATIONSHIP BETWEEN CHANGES IN TESTICULAR ADC VALUES AND VENOUS DIAMETERS AT REST IN PATIENTS WITH VARICOCELE

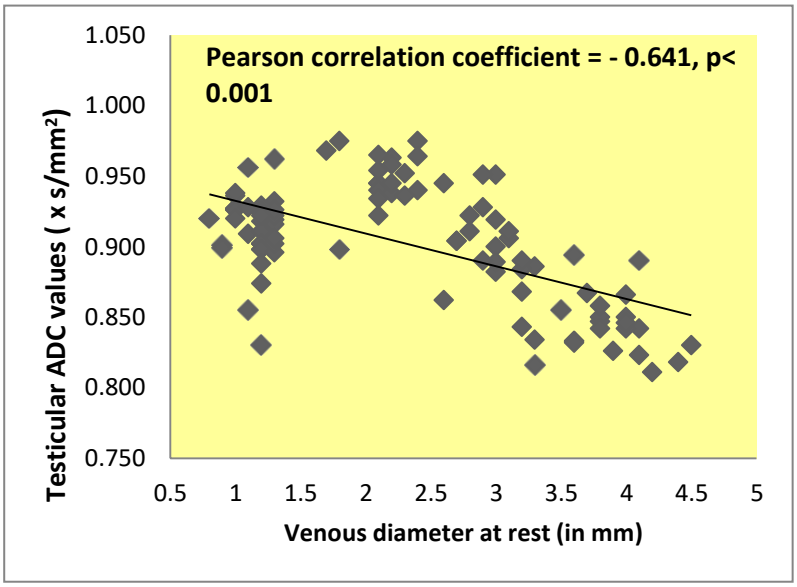


Fig17: Varicocele patients' resting venous diameters and their alterations in testicular ADC values

OBSERVATION:

In patients with varicocele, increased venous width at rest was connected with lower ADC values.

RELATIONSHIP BETWEEN CHANGES IN TESTICULAR ADC VALUES AND VENOUS DIAMETERS DURING VALSALVA MANEUVER IN PATIENTS WITH VARICOCELE

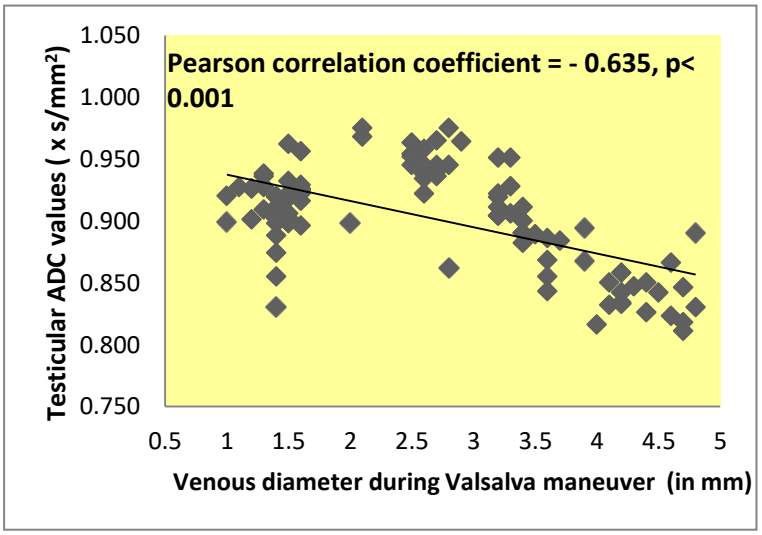


Fig 18: Relationship between variations in testicular ADC values & venous diameters at rest in patients by varicoclele

OBSERVATION:

In patients with varicocele, increased venous width during Valsalva maneuver was strongly linked with higher mean ADC values.

AREA UNDER CURVE(AUC), CUT-OFF VALUE, SENSITIVITY & SPECIFICITY OF THE TESTICULAR ADC VALUES

Table 7: Testicular ADC values' area under curve (AUC), threshold, sensitivity, and specificity

Performance value	Group 1 (n = 62 testes)	Group 2 (n=38 testes)
AUC	1.000	1.000
Cut-off ADC value (x s/mm$^{2)}$	≤1.031	≤1.032
Sensitivity (%)	92	90
Specificity (%)	82	78

Group 1= Testicle ipsilateral to varicocele
Group 2 = Testicle contralateral to varicocele

AGE DISTRIBUTION (WHO GRADING)

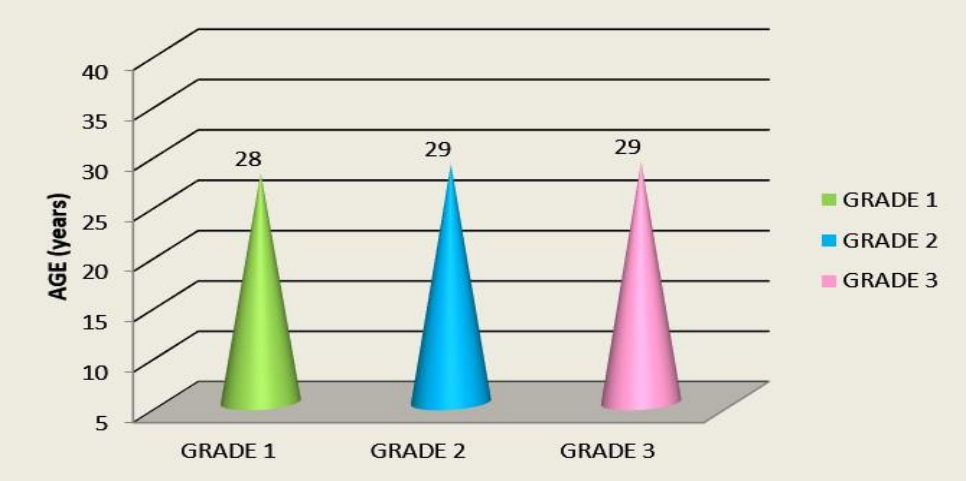


Fig19: Age distribution of WHO grade1, 2& 3

OBSERVATION:

The mean age for grade 1, 2 and 3 were 27.78±4.25 (n=23 testes), 28.68±3.90(n=19 testes) and 28.90±4.24 (n=20 testes)respectively. None of age differences between groups were significant.

TESTICULAR ADC VALUES OF WHO GRADING OF VARICOCELE

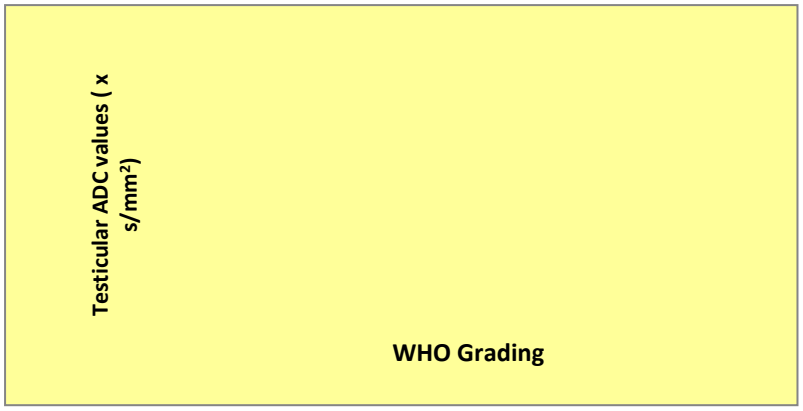


Fig20: TesticularADC values of WHO grading of varicocele

Grade 1	Palpable during Valsalva maneuver
Grade 2	Palpable without the Valsalva maneuver
Grade 3	Visible through the scrotal skin

OBSERVATION:

Mean testicular ADC values for grade 1, 2 and 3 were 0.945±0.024, 0.885±0.033 and0.846±0.021 respectively. The ADC values in testicles varied significantly across the groups.

AGE DISTRIBUTION OF SARTESCHI GRADING FOR VARICOCELE

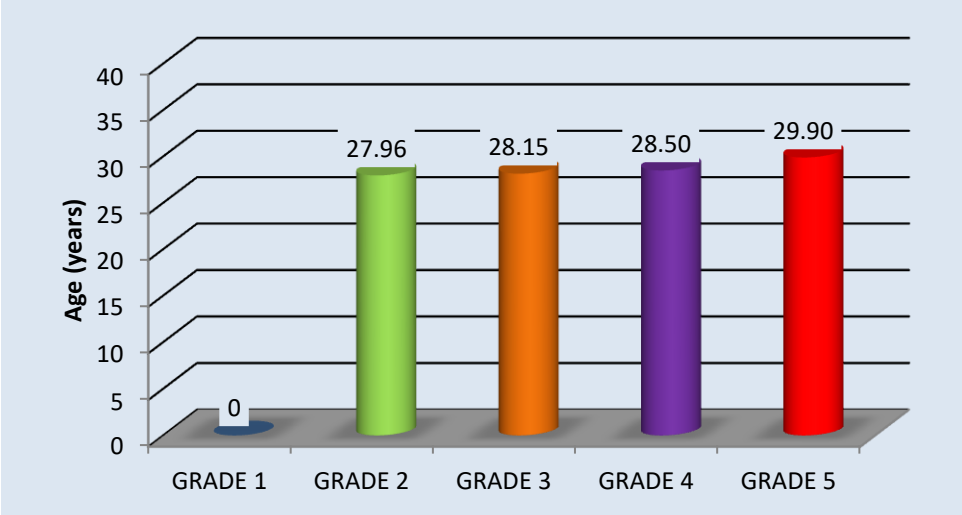


Fig 21:Age distribution of Sarteschi grading for varicocele

Grade 1	No dilated intra-scrotal veins, reflux in spermatic cord veins of the inguinal region during Valsalva's maneuver
Grade 2	Prominent veins at upper pole of testis, reflux at upper pole veins during Valsalva's maneuver
Grade 3	No major dilatation in supine position, dilated veins upto lower pole of testis seen only in standing position, reflux at lower pole veins during Valsalva maneuver
Grade 4	Dilated veins even in supine position, reflux during Valsalva's maneuver
Grade 5	Dilated veins reflux without Valsalva maneuver

OBSERVATION:
The mean age for grade 1, 2, 3, 4 and 5 were 0, 27.96 ± 3.94, 28.15 ± 4.49, 28.50 ± 3.29 and 29.90±5.13 respectively. None of age differences between groups were significant.No cases belonged to grade 1 in our study.

TESTICULAR ADC VALUES OF SARTESCHI GRADING FOR VARICOCELE

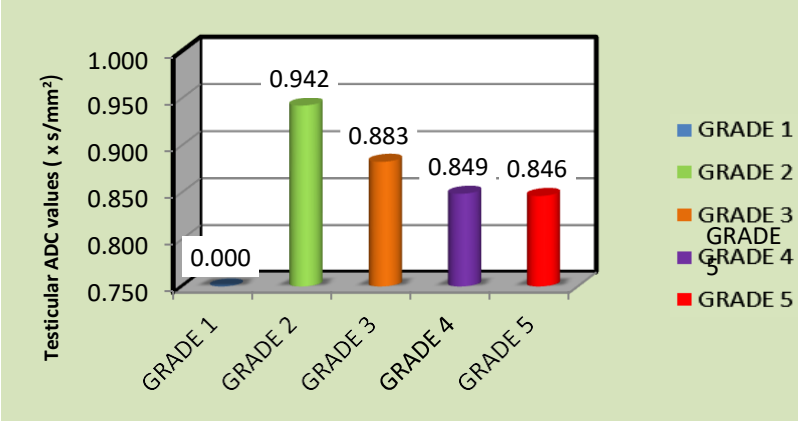


Fig 22: Testicular ADC values of Sarteschi grading for varicocele

VI. DISCUSSION

Diffusion weighted magnetic resonance imaging, also termed as diffusion tensor imaging, is subset of MRI that uses water molecule diffusion as an imaging contrast agent. Quantifying diffusion with the use of ADC maps is also possible. Moreover, there is a one-to-one correlation between the signal strength on ADC maps and the underlying diffusion changes inside tissue.

So far, there have been a plethora of international research on DWI of scrotal anomalies. However, there have been only limited studies on DWI of testes in patients with varicocele. As far as we are able to determine, not so many studies has been carried out in india till now. Primary and secondary male infertility caused by varicoceles are very frequent but easily cured[26].

Mean age (years) for group 1, 2 and 3 were 28.42+/- 4.11 , 28.68+/- 4.37 and 27.84+/- 4.2 respectively. There was no significant age disparity between groups.

Mean testicular ADC values for group 1, 2 and 3 were 0.895+/-0.049 x 10^{-3} , 0.912+/- 0.024 and 1.064 +/- 0.037 respectively. Group 1 was significantly different from Group 3, as was Group 2 from Group 3. Group 1 and Group 2 showed no statistically significant differences. As a result, the ipsilateral testicular parenchyma ADC values of patients of varicocele were lower than those of healthy volunteers. Patients with varicocele had lower ADC values in their contralateral testicular parenchyma compared to healthy controls.

In our study , the venous diameter (Mean +/- SD) at rest for group 1 , 2 and 3 were 3.06 +/- 0.73 mm , 1.17 +/-0.17 mm and 0.92 +/- 0.12 mm. correspondingly. Venous diameter (Mean +/- SD) at valsalva for group 1 , 2 and 3 were 3.47 +/- 0.76 mm , 1.42 +/-0.19 mm and 1.17 +/- 0.13 mm correspondingly. All three groups' resting and valsalva venous diameters were smaller than group 1's (all $p<0.001$). While group 2 had larger venous diameters than group 3, there was no statistically significant difference between groups at rest or during the valsalva maneuver ($p = 0.061$ and $p = 0.065$, respectively).

The classification of clinical varicocele will be based on the guidelines of WHO classification as Grade I is only detectable via Valsalva maneuver, Grade 2 is detectable even when not performing Valsalva, and Grade 3 may be seen through scrotal skin. In present study , the mean age (years) for grade 1 , 2 and 3 were 27.78 +/-4.25 (n = 23 testes) , 28.68 +/-3.90 (n = 19 testes) and 28.90 +/- 4.24 (n = 20 testes) years correspondingly. There was no significant age disparity between groups. Mean ADC values for grade 1, 2 and 3 were 0.945 +/-0.024 (n = 23 testes) , 0.885 +/- 0.033 (n = 19 testes) and 0.846 +/- 0.021 (n = 20 testes) x10^{-3} respectively. Mean ADC values in testes varied significantly across groups(p value <0.001). Thus , the ADC values decreases as grading increases.

In the current study, USG grading was done based on Sarteschi grading. The mean age (years) for grade I , 2 , 3 ,4 and 5 were 0 , 27.76 +/- 5.13 , 28.15 +/- 4.49, 28.50 +/- 3.29 and 29.90 +/- 5.13 respectively. No age disparity was seen that could be attributed to chance. No cases belonged to group 1 in our study. The mean testicular ADC values for grade 1 , 2 , 3 , 4 and 5 were 0 , 0.942 +/- 0.023 (n = 27 testes) , 0.883 +/- 0.036, 0.849 +/- 0.026 (n = 12 testes) and 0.846 +/- 0.019 (n = 10 testes) respectively.

Out of a total of 50 controls, 14 were aged 20–24, 18 were aged 25–29, 14 were aged 30-34, and 4 were aged 35–40 in the current research. Average ADC for those aged 20-24 was 1.062, for those aged 25-29 1.055, for those aged 30-34 1.073, and for those aged 35-40 1.075.

VII. CONCLUSION

The mean ADC values significantly differed between patients with varicocele and controls ($p<0.001$).

The mean ADC values of the contralateral testicular parenchyma of patients with varicocele were significantly lower than those of controls ($p<0.001$).

There was no statistically significant difference between mean ADC values of the testicular parenchyma ipsilateral to varicocele and contralateral to varicocele ($p=0.103$).

In patients with varicocele , the mean ADC values were significantly negatively correlated with larger venous diameters during rest and during the Valsalva maneuver (Rest : $R2 = 0.358$, Beta coefficient = -0.641 , $p <0.001$; Valsalva maneuver : $R2 = 0.345$, Beta coefficient = - 0.635 , $p < 0.001$).

The venous diameter of group 1 (Ipsilateral to varicocele) during rest and the valsalva maneuver were higher than those of Groups 2 (Contralateral to Varicocele) and 3 (controls).

The mean testicular ADC values were calculated for clinical grading as per WHO. There was statistically group difference in terms of testicular ADC values ($p<0.001$). Thus , the ADC values decreases as grading increases.

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