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Hemodynamic evaluation of varicocele: the role of scrotal scintigraphy and Doppler ultrasonography in the prediction of postoperative seminal improvement

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Aim: The aim of this study was to evaluate the hemodynamics of varicocele using Doppler ultrasonography and scrotal scintigraphy, and to compare the value of these two methods in the prediction of seminal improvement after varicocelectomy. ***Materials and Methods:*** A total of 40 men with left sided varicocele presented for surgery because of infertility of at least one year in duration. Preoperative and postoperative sperm counts and per cent motility were obtained. Dynamic scrotal scintigraphy and Doppler ultrasonography were performed in all patients. Three perfusion patterns according to the time-activity curves (TAC) generated from scrotal perfusion images were defined. Type 1: radioactivity shows faster accumulation and maintenance of a higher level on the left side than on the right side. Type 2: time-activity curve rises gradually to a higher level on the left than on the right. Type 3: time-activity curve increases symmetrically and slowly on both sides. The relationship between preoperative TAC patterns and postoperative seminal findings, and preoperative Doppler grades and postoperative seminal findings were investigated. ***Results:*** Improvement in total motile sperm counts was not statistically significant (37.8% ± 3.2% versus 45.2% ± 8.5%) ($p = 0.751$). Following varicocelectomy, sperm concentration (million sperm per m*l*) increased from 16.9 ± 3.3 to 26.6 ± 8.6 ($p = 0.015$). According to the Doppler examinations, postoperative improvement in sperm concentration was demonstrated in patients with grade 1 varicocele (66%). Scintigraphic evaluation showed improvement in patients showing TAC-2 and TAC-3 patterns (63%). ***Conclusion:*** Local hemodynamics of varicoceles demonstrated by scintigraphy and Doppler seemed to be different. Grade 1, TAC-2 and TAC-3 patients may be better candidates for varicocelectomy. Scintigraphy and Doppler ultrasonography showed similar success rates in the prediction of improvement following varicocelectomy in the present study.

Key words: varicocele, scrotal scintigraphy, Doppler ultrasonography, semen, infertility

INTRODUCTION

VARICOCELE is an abnormal dilatation and tortusity of the veins of the pampiniform plexus in the scrotum. It is the most frequently encountered, surgical correctable cause of male infertility. The incidence in general population is 10–23%, but 35% of all men evaluated for infertility have a varicocele.[1–3] Postoperative improvement in semen quality has been reported in 60–70% of the patients with varicocele by many investigators.[4,5] Although several studies indicate that larger varicoceles are associated with greater impairment of spermatogenesis, others suggest that the response to surgery is independent of varicocele size.[6–9] Testicular dysfunction in patients with varicocele is thought to results from impaired testicular perfusion. Such blood flow changes have been shown in experimental and clinical studies.[10,11] Scrotal perfusion scintigraphy can evaluate noninvasively local hemodynamics in the spermatic vessels. The relationship between scrotal hemodynamics demonstrated by radionuclide perfusion studies and the benefit from surgery have been focused on in a limited number of studies, but no definitive conclusion has been readed.[12,13] Considering the contraversy about

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prediction of improvement in semen quality after varicocelectomy regarding the grade of varicocele assessed by clinical or/and Doppler ultrasonography, we hypothesed that the radionuclide perfusion pattern of varicocele can provide a new insight into prediction of surgical success.

We aimed to determine scrotal hemodynamic patterns by radionuclide imaging in patients with varicocele and also to assess whether pattern types of scrotal perfusion can predict the surgical response. Also we compared the value of scintigraphy and Doppler ultrasonography in the prediction of postoperative seminal improvement.

MATERIALS AND METHODS

Patients: From October 2001 to June 2002, 40 men with a history of primary infertility for at least 1 year were included in the study. Patient age ranged from 19 to 37 years, with a mean age of 26.4 years. A detailed history and physical examination were performed in all patients. Varicocele was diagnosed by physical palpation with the patient standing with and without the valsalva maneuver and it was confirmed by color Doppler ultrasound. All patients had left sided varicocele. Patients with infection, history of genitourinary trauma, chromosomal disorders and bilateral varicocele were excluded from the study.

Doppler imaging: Doppler ultrasonography was performed in all patients using a 7.5 mHz. Doppler probe which was placed over the spermatic cord in the upper scrotum to localize the spermatic artery. Assessment was done in the upright and supine positions before and during the valsalva maneuver. The detection of increased venous flow in the pampiniform plexus with or without valsalva maneuver was considered an indication of incompetent valves in the spermatic veins. According to the diagnostic criteria of Doppler ultrasonographic assessment the diagnosis of varicocele was made and the varicoceles were classified as follows. Grade 1, Brief reflux lasts <2 seconds during the Valsalva maneuver; Grade 2, Intermediate reflux lasts <2 seconds during the Valsalva maneuver; Grade 3, Permanent reflux lasts >2 seconds after the Valsalva maneuver or during normal respiration.[14] All grading was performed by the same examiner.

Semen analysis: Semen analysis were made at least twice before the operation and at 3 months after surgery. Semen was obtained by masturbation after a minimum 3 days of abstinence. Specimens were examined within 1 hour of collection and assessed for sperm concentration, and per cent motility. The sperm density and per cent motility were determined with a Makler chamber. A sperm concentration exceeding 20 million per m*l*, and sperm motility 50% or greater were considered normal. Sperm morphology was not considered for this study. Analysis was done according to World Health Organization guidelines.[15]

Scrotal scintigraphy: The patients was positioned with legs far apart, as close to the collimator face as possible. The penis was taped on the anterior abdominal wall in the midline. They stood in front of the camera to improve scan quality, and to assist in clinical detection of varicoceles. A large field of view gamma camera with equipped by low energy, all purpose collimator was used (Elscint SPX-6, Haifa, Israel). After the injection as a bolus of 550 MBq Tc-99m pertechnetate via an antecubital vein acquisition was started and images were collected at 2 seconds per frame during 1 minute in a 64 × 64 matrix. After the acquisition, the scrotum was recognized on summed images and the time-activity curves (TAC) were generated from regions of interest drawn over bilaterally scrotal areas.

Surgical technique: All men underwent varicocelectomy with subinguinal ligation of the internal spermatic veins under local anesthesia.

Statistics: Average values of semen parameters in the study group are expressed as the mean plus or minus standard error. Differences in sperm density and motility before and after varicocelectomy were evaluated for significance using the nonparametric Wilcoxon signed rank test. Kruskall-Wallis analysis was done to assess the correlation between Doppler grade and changes in seminogram after surgery and between the scintigraphic pattern and postoperative changes in seminogram. Differences were considered statistically significant when the p value was <0.05.

RESULTS

The mean interval between varicocele repair and mean follow-up was 18 months (range 12 to 28). Complete follow-up data were available for all 40 subjects.

Sperm motility was abnormal in all 40 patients. postoperative improvement in per cent of motility was noted in

Table 1 Comparison of semen parameters before and after varicocelectomy

	Preoperative (mean ± sd)	Postoperative (mean ± sd)	P value
Sperm counts (× 10^6/m*l*)	16.98 ± 3.35	26.69 ± 8.62	0.015
Motility (%)	37.80 ± 3.21	45.12 ± 8.05	0.751

Table 2 Relationship between TAC pattern and Doppler grade of varicocele in all patients

Scintigraphy	Doppler USG			P value
	Grade 1	Grade 2	Grade 3	
TAC-1 n (%)	3 (30)	1 (10)	6 (60)	0.016
TAC-2 n (%)	8 (45)	7 (39)	3 (16)	0.431
TAC-3 n (%)	7 (59)	5 (41)	0 (0)	0.033
Total	18	13	9	

Table 3 Relationship between semen parameters and Doppler grade

	Sperm count ($\times 10^6$/m*l*)			Sperm motility (%)		
	preop (mean ± sd)	postop (mean ± sd)	p value	preop (mean ± sd)	postop (mean ± sd)	p value
Grade 1	12.00 ± 4.95	21.36 ± 3.5	0.012	38.83 ± 3.55	56.94 ± 8.44	0.234
Grade 2	19.11 ± 2.35	27.15 ± 8.15	0.562	40.53 ± 2.12	51.92 ± 2.26	0.566
Grade 3	18.00 ± 3.13	26.40 ± 7.54	0.741	36.60 ± 5.73	51.00 ± 3.56	0.477

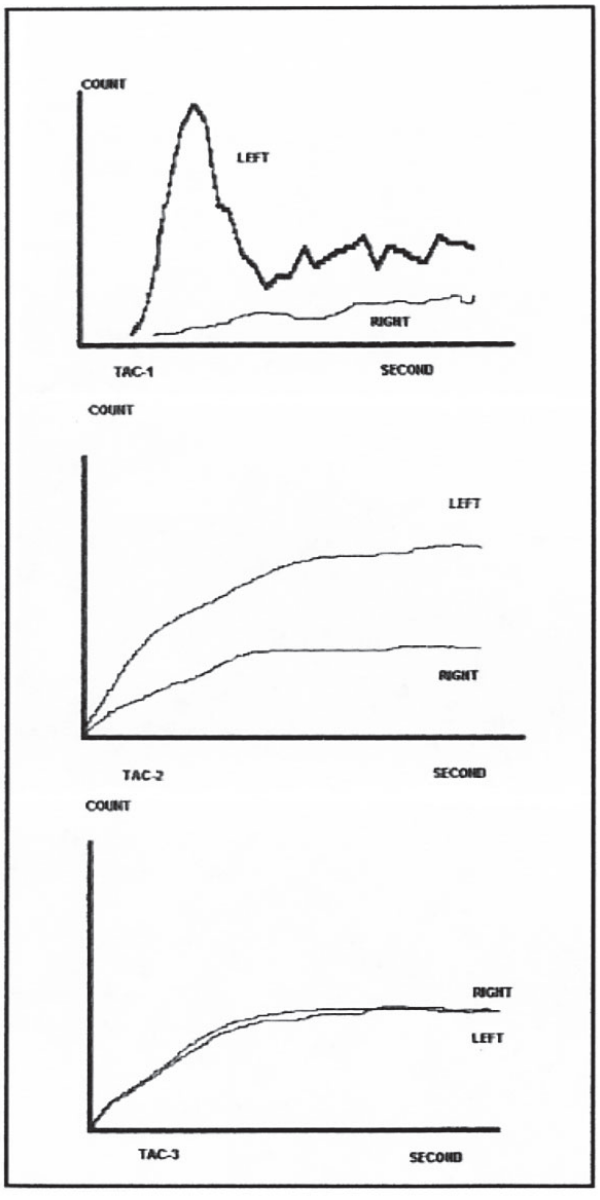

Fig. 1 Representative time-activity curves.

14 of these 40 patients (35%), whereas 26 showed no improvement in motility after varicocelectomy. Improvement in total motile sperm counts was not statistically significant (37.8% ± 3.2% versus 45.2% ± 8.5%) (p = 0.751).

A total of 40 patients had preoperative sperm concentrations of less than 20 million per m*l*. An increase in sperm count was observed in 27 of 40 patients (67.5%) and 10 of them (70%) showed postoperative sperm counts over 20 million per m*l*. Following varicocele repair sperm concentration (million sperm per m*l*) increased from 16.9 ± 3.3 to 26.6 ± 8.6 and the difference was significant (p = 0.015). The preoperative and postoperative semen values were shown in Table 1.

In Table 2, comparison of Doppler grades and scintigraphic patterns in all patients were shown. In preoperative Doppler imaging, grade 1 varicocele was observed in 18 patients, grade 2 in 13 and grade 3 in 9. Mean sperm concentrations increased significantly after repair of varicocele of grade 1, while grade 2 and 3 varicoceles did not shown any significant increases in sperm concentration. Improvement in motility did not show any significant difference between the grades. Results were shown in Table 3.

Scintigraphic evaluation revealed three distinct types of TAC as follows: TAC-1: faster accumulation of radioactivity and maintenance of a higher level on the left side than on the right side. TAC-2: time-activity curve rises gradually to a higher level on the left than on the right. TAC-3: bilaterally symmetrical and slow increase of TAC. Ten patients were classified as TAC-1, 18 as TAC-2 and 12 as TAC-3. Representative TAC's of each types were shown in Figure 1. Observed TAC patterns in our patients were similar to the patterns reported by Minayoshi et al.

Improvement in sperm concentrations and motility among the three TAC patterns were compared. While postoperative sperm concentrations changed significantly in TAC-2 and TAC-3 patients, no changes were observed in TAC-1 patients. P values of the results were shown in Table 4. No significant improvement in motility was achieved in these three groups.

When we evaluated the patients demonstrating postoperative increase in sperm counts >20 million and/or motility >50% according to the Doppler grades and scintigraphic patterns, the increase in sperm counts was more marked in patients with grade 1 than the other grades (Tables 5, 6). Patients with TAC-2 and TAC-3 patterns showed more improvement in sperm counts than TAC-1. The improvement in motility did not demonstrate any according to the grade or pattern.

Table 4 Preoperative and postoperative sperm parameters and TAC pattern in all patients

Scintigraphy	Sperm concentration (× 10^6/m*l*)			Sperm motility (%)		
	preop (mean ± sd)	postop (mean ± sd)	p value	preop (mean ± sd)	postop (mean ± sd)	p value
TAC-1	17.85 ± 1.41	26.27 ± 7.66	0.251	39.27 ± 2.24	54.18 ± 3.44	0.387
TAC-2	12.48 ± 3.35	21.25 ± 3.17	0.018	37.61 ± 5.62	41.33 ± 2.81	0.844
TAC-3	14.42 ± 2.4	25.43 ± 8.43	0.021	36.75 ± 2.15	47.00 ± 3.64	0.682

Table 5 Comparison of grades according to the postoperative semen parameters over threshold levels (1 = improvement only sperm counts >20 × 10^6/m*l*, 2 = improvement in motility >50%, 3 = improvement both sperm motility and counts, 4 = no improvement in any parameters)

Grade	Patient (n)	Postoperative sperm parameter			
		1 Sperm counts >20 × 10^6/m*l*	2 Motility >50%	3 Sperm counts >20 × 10^6/m*l* + motility >50%	4 No improvement
Grade 1	18	6	1	5	6
Grade 2	13	2	2	3	6
Grade 3	9	1	1	2	5

Table 6 Comparison of TAC patterns according to the postoperative semen parameters over threshold levels (sperm counts >20 × 10^6/m*l*, motility >50%)

TAC	Patient (n)	Postoperative sperm parameter			
		Sperm counts >20 × 10^6/m*l*	Motility >50%	Sperm counts >20 × 10^6/m*l* + motility >50%	No improvement
TAC-1	10	1	1	2	6
TAC-2	18	5	2	4	7
TAC-3	12	3	1	4	4

DISCUSSION

Varicocele often causes disturbance in the spermatogenic process. The effect of varicocele on sperm production in infertile men manifests with abnormal semen quality, including a low sperm count, decreased sperm motility and a high percent of abnormal sperm forms.[5,16] After varicocelectomy, there is no agreement on the nature of the improvement in sperm quality. Most reports showed that approximately two-thirds of the patients with varicocele show improvement in sperm quality after spermatic vein ligation.[16–19] Some reports showed improvement in all sperm parameters and some showed improvement only in sperm density or the motility, whereas others claimed that the sperm does not show any quantitative or qualitative improvement.[6,20–22] Pryor et al. noted improved semen parameters in 66% after varicocele ligation in a review of 15 published reports.[16] In present study, postoperative improvement in sperm concentration was noted in 27 of our 40 patients who had preoperative sperm concentrations less than 20 million per m*l*. Improvement in mean sperm count (67.5%) was significant and agreed with the findings of many other studies.

The increase in motility was observed in 35% of patients but it was not found to be significant. There are controversial reports about motility after varicocelectomy, some reviews of the effect of varicocele repair on routine semen parameters corroborate improvement in motility.[23–25] Twelve studies reviewed by Schlesinger et al. showed improvement in motility after varicocele repair.[6] We think improvement in sperm motility may not be a consistent result of varicocelectomy as reported by Madgar et al.[17]

Testicular venography, Doppler ultrasonography, or scrotal scintigraphy can be used to evaluate scrotal hemodynamics. Beyond the demonstration of hemodynamics in the diagnosis of varicocele, demonstration of scrotal hemodynamics has recently become a current issue to predict surgical success of varicocele. Although the relationship between varicocele size and seminal improvement was investigated in many studies, in most of them ultrasonography and clinical grading were used, and only

a limited number of scintigraphic studies were reported.[12,13,26,27]

Some published data on infertile men undergoing surgery for varicoceles demonstrated similar postoperative improvement among the different Doppler grades of varicoceles.[28–30] In contrast, some reports noted that the varicocele size affects outcome after varicocelectomy. Some studies supported that large varicocele showed significant improvement whereas others showed grade 1 and 2 varicoceles showed marked improvement.[7,8] Our Doppler results supported that small varicoceles benefit from surgery.

We identified three different TAC patterns and compared the effects of surgery on seminogram among these three groups. TAC-2 and TAC-3 patients showed an improvement on postoperative seminogram but TAC-1 patients did not show significant changes in semen parameters. Our TAC-1 patients showed rapid retrograde perfusion and accumulation of radioactivity in varicocele and most of them clinically had a large varicocele. These results were concordant with the findings of some previous observations in which the velocity of the retrograde blood flow in the testicular vein and the size of the varicocele were positively correlated.[26] This also supported the previous observation that the large varicoceles show no improvement following varicocelectomy.

In the present study, large varicoceles had a tendency to show TAC-1 pattern more frequently, and small varicoceles tended to have TAC-3 pattern, but besides these tendencies we observed different TAC patterns in same size varicoceles suggesting that local hemodynamics may differ in the same grade of varicocele. Our findings can support that the scrotal scintigraphy partly reflects the grade of the varicocele as previously reported by Fuse et al.[13]

From our results we might predict the effect of varicocelectomy by Doppler grade and/or scintigraphic pattern. Grade 1, TAC-2 and TAC-3 patients seemed to be better candidates for surgery. For evaluating postoperative improvement, Fuse et al. concluded that the TAC can be more useful than the grade decision of varicocele by revealing local hemodynamics more accurately.[13] They showed improvement in type 1 pattern (large) while seminal findings were not improved after surgery in those who had type 2 (moderate), or type 3 (small) pattern. In another study reported by Minayoshi et al., a TAC classification was made using different reference regions over the femoral muscle, varicocele and artery. Although different ROIs were used in that study, TAC-1 represented usually large and TAC-3 small varicoceles. They found that TAC-1 and TAC-2 patients were better candidates for surgery. In contrast to these studies, we could not show improvement in TAC-1 patients. The lack of improvement in large varicoceles in the present study can be attributed to the differences in the number of patients and the severity of seminal abnormalities in previous studies. But, concordance between scintigraphy and Doppler studies in our patients with a large varicocele may support the accuracy of our results. Grade 1 and TAC-3 patients representing small varicoceles showed an agreement in the results of scintigraphy and Doppler such as large size. Because of the limited number of scintigraphic studies, it is difficult to reach a definite conclusion and the results of all these studies are under debate. Therefore, future studies assessing the role of scrotal scintigraphy in the prediction of seminal improvement should be designed.

As a results, we could not show any advantages of either of the two methods over the other. More randomized, and comparative studies with Doppler ultrasonography in larger populations and also postoperative scintigraphic control studies are needed for documenting the value of determination of hemodynamics in varicocele in the prediction of postoperative improvement.

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