A Comparison of Scintigraphy, Thermography, Ultrasound and Phlebography in Grading of Clinical Varicocele

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Varicocele, a varicosity of the pampiniform plexus, usually on the left side, is a common urologic problem. It may be associated with symptoms of local discomfort or abnormal spermatogenesis. Internal spermatic vein phlebography is the "gold standard" investigative technique, but it is invasive. Noninvasive studies include: labeled blood-pool scintigraphy, thermography and ultrasound. Two hundred sixty-three patients were investigated with various combinations of these modalities. The degree of abnormality for each modality was graded semiquantitatively and the results compared. In addition, the results of semen analysis were correlated to imaging results. Ninety-six patients were investigated with all four tests (scintigraphy, thermography, ultrasound and phlebography). The correlation of positive phlebography to positive scintigraphy was 98%, to thermography 100% and to ultrasound 98%. The concordance (grade for grade) was 71% for scintigraphy, 68% for thermography and 62% for ultrasound. There was no obvious correlation between abnormalities of semen analysis and grading of varicocele. We conclude that the diagnostic accuracy and grading of severity by noninvasive techniques (including scintigraphy) compare very favorably with that of phlebography. Moreover, scintigraphy allows the noninvasive evaluation of reflux through the internal spermatic vein, which may be useful in planning therapy.

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Varicocele is a varicosity of the veins of the pampiniform plexus, probably due, as suggested by Ivanissevich in 1981, to a reflux of blood via the internal spermatic vein (ISV) (*1*). This can result from an absence or incompetence of the venous valves, collateral by pass vessels and/or an increased pressure gradient between the inferior vena cava and the left renal vein (*2,3*).

In 80%–97% of cases, the varicocele involves only the left side; it may be bilateral in up to 20%, although the right sided varicosity is usually smaller (*4–7*). A unilateral right sided varicocele is very uncommon (*8*).

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Phlebography, first introduced in 1966 by Ahleberg (*9*), is generally accepted as the "gold standard" for the depiction of varicocele (*10–12*). It is nevertheless invasive, uncomfortable, carries some risks and is not physiologic (*13*). For these reasons, other diagnostic approaches, such as thermography (*14*), scintigraphy (*15,16*), ultrasound (*17,18*) and echo-Doppler (*19*), have been proposed, with the aim of finding an imaging modality as sensitive as phlebography, but without its drawbacks.

By means of various imaging techniques, it has been possible to distinguish between a palpable enlargement of the pampiniform plexus, defined as clinical varicocele, which may be staged as Grades 1, 2, and 3 by the classification of Dublin and Amelar (*20*), and sub-clinical varicocele defined as reflux through the internal spermatic vein, without any palpable distension of the pampiniform plexus (*21*). Many of the papers published on the topic deal with the associated alterations of spermatogenesis and consequently highlight the ability to detect subclinical varicocele, since this is considered by some to be as important as clinical varicocele in decreasing fertility (*13,22–25*).

The purpose of this study was not to evaluate the ability of the various imaging techniques to distinguish clinical from subclinical varicocele as defined above, because we did not study patients presenting with infertility. Rather we examined the ability of radionuclide studies, thermography and ultrasound, to objectively confirm the presence of varicocele which was clinically diagnosed or suspected on the basis of patient discomfort or physical examination. We also compared the grading of these techniques with that of phlebography. In the majority of our patients, the results of semen analysis (sperm counts, motility and morphology) were available and were correlated with the three phlebographic grades of varicocele.

MATERIALS AND METHODS

From 1987 to 1989 we studied 263 patients in whom a varicocele had been diagnosed (185 cases) or suspected (78 cases) on the basis of patient complaints of swelling, discomfort or physical examination.

We did not study patients presenting with infertility and ab-

normalities of semen analysis unless they also had a clinically suspected or verified varicocele. The mean age was 22.8 yr (s.d. 7.2 yr). A large fraction of our patients (over 80%) came from the army and this may explain the narrow age s.d. Military service starting at 19 yr is mandatory in Italy. Regulations may exempt inductees from service if they suffer from significant varicocele. Thus, those seeking to avoid service may complain in the absence of varicocele and those seeking a military career may find varicocele a barrier, unless the condition is effectively treated. Under these circumstances, there is a need for accurate, noninvasive and objective techniques for the documentation and grading of varicocele.

Of the 263 patients studied with various combinations of techniques (Table 1), 96 were studied with phlebography, scintigraphy, thermography and ultrasound. Semen analysis was obtained in 146 patients.

Scintigraphy

Scintigraphic evaluation was performed with the patient in the upright position, the legs somewhat apart, the penis taped to the midline of the anterior abdominal wall and the scrotum located in the lower third of the field of view. The patient's red blood cells were in-vivo labeled by injecting 0.15 μg/kg of stannous ions in the form of pyrophosphate 20 min before the intravenous administration of 370 MBq [^{99m}Tc]pertechentate. Imaging was performed using a small field of view gamma camera (S.E.L.O., Italy) equipped with a parallel-hole, low-energy collimator and a zoom factor of 1.4. Sixty 2-sec images were acquired in a 64 × 64 byte matrix on an online minicomputer (Maps 2000, Link System, UK) starting with the rapid bolus injection (less than 1 cc) of 370 MBq (10 mCi) [^{99m}Tc]pertechnetate via a forearm vein. The 2-sec frames thus acquired were summed as sequential 8-sec and 30-sec frames for interpretation and hardcopy records.

Subsequently a 300-sec image, usually with more than 500K counts, was obtained and this was considered to depict the blood-pool. To improve contrast and facilitate interpretation, a threshold of up to 40%-50% was used when needed.

TABLE 1
Patients Studied by Various Modalities

Left internal spermatic vein phlebography, thermography, ultrasound	82
Left internal spermatic vein phlebography, right internal spermatic vein phlebography, scintigraphy, thermography, ultrasound	14
Left internal spermatic vein phlebography, scintigraphy, thermography	54
Left internal spermatic vein phlebography, scintigraphy, ultrasound	8
Left internal spermatic vein phlebography, thermography, ultrasound	13
Left internal spermatic vein phlebography, scintigraphy	4
Left internal spermatic vein phlebography, thermography	11
Left internal spermatic vein phlebography, ultrasound	3
Left internal spermatic vein phlebography (only)	7
Scintigraphy, thermography	66
Scintigraphy, ultrasound	1
Total	263

Occasionally vasovagal symptoms occurred, but these rarely interrupted the study. When they did, it was during blood-pool imaging and a sufficient number of counts was always acquired so that a final interpretation was possible (*15*).

Thermography

This was performed with the patient in the upright position after an adaptation period (15–20 min) to room temperature, which was kept constant at 20–22°C. The scrotum was thermally isolated from the body and the penis taped to the midline of the anterior abdominal wall. Anterior and oblique views were obtained using an AGA Thermovision unit, number 680, with a temperature discrimination of 0.5°C. Quality control was maintained using a thermal marker kept at a constant 31°C for standardization and control of instrument stability (*14,21*).

Ultrasound

Ultrasound was performed with the patient in the supine position at rest and during a Valsalva maneuver. The scrotum was scanned in the longitudinal and transverse planes (Fig. 1) using a Hitach 7.5 MHz linear probe with a spatial discrimination ability below 1 mm (*17,18,21*).

Selective Spermatic Vein Phlebography

This was performed by means of a selective catheter usually inserted through the right femoral vein and injection of 10–20 ml contrast medium (2–3 ml/sec) with the patient semiupright (30°–50°) using a Zeitler type catheter for the left (Fig. 2) and a side-winder catheter for the right internal spermatic vein (*9–12*).

Semen Analyses

These were obtained according to standard techniques (*26*): sperm number was quantified as million/ml, while morphology and motility (after 2 hr) were expressed as percentage of structurally normal cells and spermatozoa having "active forward motility," respectively.

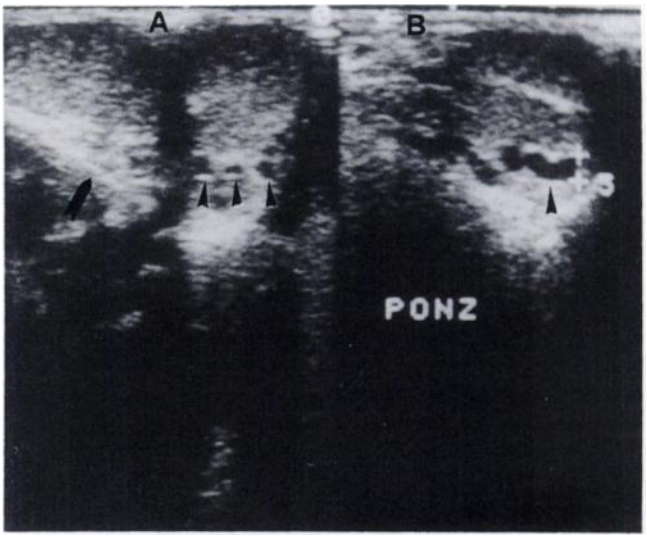

FIGURE 1. Scrotal ultrasound (axial views). (A) During quiet respiration. Normal right testis (large arrow). Left testis with slightly dilated veins in the pampiniform plexus demonstrated as small anechoic foci with some reinforcement of the posterior walls (small arrows). (B) During Valsalva maneuver. Striking increase in diameter of dilated vein to 5 mm (Grade 3) (small arrow).

CRITERIA FOR INTERPRETATION OF RESULTS

Results obtained from the different imaging modalities were classified on a scale from zero to three, according to the following criteria:

Blood-Pool Scintigraphy

0 = normal study (Fig. 3A).
1 = mild uptake (just above background) (Fig. 3B).
2 = moderate uptake (less than major normal vascular structures) (Fig. 3C).
3 = intense uptake (compared to major normal vascular structures) in a half or entire scrotum and along the internal spermatic vein (Fig. 3D).

The images taken during the flow phase were considered to be an expression of the degree of venous reflux, and the blood-pool scan was felt to reflect the varicocele volume (*27*). Varicocele grading was performed primarily on the blood pool images which are more comparable with ultrasound and thermography, as these depict only the varicocele volume and not the blood flow. In addition, we examined the flow phase, to verify whether significant reflux of blood occurred through the internal spermatic vein and whether the degree of reflux was related to the volume of the varicocele. To do this, we found it necessary to add four frames together to get a series of 8-sec images (Fig. 4). For better visual presentation of the studies, we also presented nuclear angiograms as four 30-sec added images starting from the time of injection (Fig. 5).

Blood Flow Scintigraphy

0 = no reflux.
1 = minimal reflux (just above background).
2 = moderate reflux (less than intensity of simultaneously visualized vascular structures).
3 = marked reflux (equal to intensity of simultaneously visualized vascular structures).

Thermography

0 = normal study (31°C)
1 = 32°C
2 = 33°C
3 = 34°C or greater

Ultrasound

0 = no change in pampiniform plexus diameter, considered normal up to 2 mm.
1 = very slight dilatation, up to 3 mm.
2 = moderate dilatation, up to between 3 and 5 mm.
3 = major dilatation, more than 5 mm.

Phlebography

0 = no reflux, continent valves.
1 = reflux in the ISV with a diameter less than 5 mm and opacification of a slightly enlarged pampiniform plexus.
2 = reflux in the ISV of a diameter between 0.5 and 1 cm and an evident varicocele.
3 = reflux in the ISV with a diameter greater than 1 cm and a wide varicocele.

FIGURE 2. Left ISV phlebography demonstrating a moderate (Grade 2) varicocele.

Semen Analysis

0 = more than 60 million sperm/ml, motility and normal cell morphology greater than 80%.
1 = between 25 and 60 million sperm/ml and/or motility and normal cell morphology between 50% and 80%.

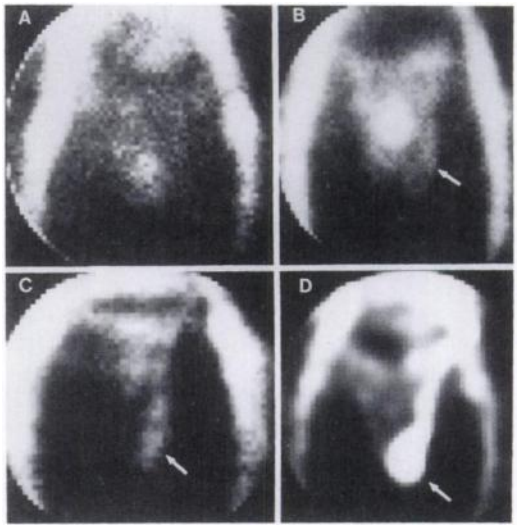

FIGURE 3. Examples of blood-pool scintigraphy demonstrating: (A) Grade 0 (normal study), (B) Grade 1 (minimal uptake), (C) Grade 2 (moderate uptake), and (D) Grade 3 (intense uptake).

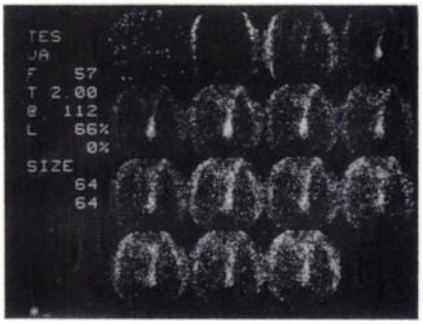

FIGURE 4. Example of flow phase scintigraphy demonstrating Grade 3 reflux via the left ISV. (Series of 8-sec frames, added from 2 sec per frame acquisition).

2 = between 5 and 25 million sperm/ml and/or motility and normal cell morphology between 30% and 50%.

3 = up to 5 million sperm/ml and/or motility and normal cell morphology up to 30% (*13*).

RESULTS

Among the 96 patients studied by scintigraphy, thermography and ultrasound who also had phlebography, each imaging modality was positive in the 85 patients with a clinically diagnosed varicocele (Grades 1–3 for phlebography). In the 11 patients with a clinically suspected varicocele, 9 had a positive phlebogram (Grades 1 or 2) and were also positive by scintigraphy, thermography and ultrasound in 8, 9 and 7 patients, respectively.

The three false-negative noninvasive studies (one for scintigraphy and two for ultrasound) had Grade 1 varicoceles by phlebography. In the two patients with a clinically suspected varicocele and normal phlebography, a false-positive study was obtained in one case by ultrasound and in another by both scintigraphy and thermography (all Grade 1).

Table 2 presents the correlations between grading by scintigraphy, thermography, ultrasound and phlebography with an overall agreement, grade for grade, from 62% for ultrasound to 71% for scintigraphy. The closest correlations were obtained in the highest grade of varicocele, with a positive correlation of 82% by scintigraphy and 80% by thermography, respectively. In looking at the discrepancies in grading, we observed that scintigraphy overestimated by one grade in 14% and two grades in only 2%; thermography and ultrasound overestimated by one grade in 20% and 6%, respectively. In no case did thermography or ultrasound overestimate by two grades.

TABLE 2
Concordance in Grading Between Scintigraphy, Thermography, Ultrasound and Phlebography*

Phlebography (grading)	3 (50 patients)	2 (35 patients)	1 (9 patients)
Scintigraphy	41 (82%)	23 (65%)	3 (30%)
Thermography	40 (80%)	19 (54%)	5 (56%)
Ultrasound	28 (56%)	25 (71%)	5 (56%)

* Concordance was grade for grade between modalities. Overall agreement for all patients was 71% for scintigraphy, 68% for thermography and 62% for ultrasound.

A one grade underestimation occurred in 11%, 12%, and 27% with scintigraphy, thermography, and ultrasound, respectively. An underestimation by two grades was obtained in 1% by scintigraphy and in 4% by ultrasound. In no case was there an underestimation of two grades by thermography (Table 3).

For a majority of the 94 patients with positive phlebography, the scintigraphic flow-phase demonstrated reflux of the same grade as varicocele volume (86 of 94, 91%). In the remaining eight cases there was an underestimation of two grades in one case and of one grade in another and an overestimation of one grade in six cases. There was no patient with a left-sided varicocele, without at least a mild increase in flow through the left ISV demonstrable by flow phase scintigraphy.

In 8 of the 14 patients who had right-sided ISV phlebography, this was normal, confirming the findings by scintigraphy, thermography and ultrasound. In the other six, phlebography was positive as were scintigraphy, thermography and ultrasound. The disease was graded phlebographically as Grade 2 in two cases and Grade 1 in four (Scintigraphy was positive for a right varicocele in a total of 23 patients and this was confirmed by phlebography in 6, by thermography in 5, and by ultrasound in 1.)

Sixty-seven patients with only mild clinical suspicion of varicocele (left) had at least two negative noninvasive studies and were not subjected to phlebography and were considered not to have varicocele.

In Table 4, correlations between semen analysis and

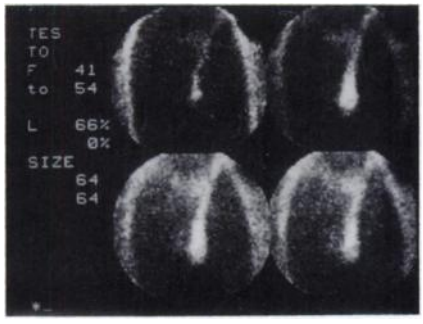

FIGURE 5. Example of flow phase scintigraphy demonstrating Grade 3 reflux via the left ISV (series of 30-sec frames, added from 2 sec per frame acquisition).

TABLE 3
Percentages of Overall Concordance for Each Imaging Modality Compared to Phlebography in the 94 Patients with a Positive Phlebogram

	Scintigraphy	Thermography	Ultrasound
Concordance	71	68	62
+1 overestimate	14	20	6
+2 overestimate	2	0	0
−1 underestimate	11	12	26
−2 underestimate	1	0	4
False-negative	1	0	2

TABLE 4
Semen Analysis Abnormalities (Grades 1–3) Related to Phlebography Patient Groups (Grades 1–3)

Semen analysis (3)	(55%) 5	(49%) 17	(62%) 31
Semen analysis (2)	(11%) 1	(26%) 9	(28%) 14
Semen analysis (1)	(33%) 3	(26%) 9	(10%) 5
Phlebographic grading	(Group 1) 9	(Group 2) 35	(Group 3) 50

phlebography grading are shown. There is a similar percentage (about 60%) of the most severe degree of sperm abnormality in all grades of phlebographic abnormality.

DISCUSSION

Our results with a large series of patients confirm the reliability of scintigraphy, thermography and ultrasound in detecting and objectively confirming clinically diagnosed or suspected varicocele and, as such, are in keeping with published data (*14–21*). Sensitivity as high as 92% and specificity of 97% have been reported for scintigraphy versus a venographic gold standard (*32*). We believe that by using these noninvasive techniques it may be possible to identify those patients who may benefit from a therapeutic intervention. Before proceeding to phlebography, when a varicocele is suspected on clinical grounds, the noninvasive imaging modalities may be performed as a screening device.

Scintigraphy is able to demonstrate the blood flow reflux through the ISV, allowing the evaluation of filling rate (in the "flow phase") and varicocele volume (in the blood-pool image) (*27*). These closely correspond to phlebographic sizing and thus be useful for comparison after therapeutic interventions to verify adequacy of cure or severity of recurrence. Moreover, the flow phase of scintigraphy may distinguish ISV reflux from obstruction of the hypogastric or iliac vessels. The latter is a rare cause of varicocele but, when present, carries serious prognostic implications.

Finally, the evaluation of reflux through the ISV may be useful in discriminating between recurrences due to spermatic vein collaterals and flow through perirenal or distal pelvic vessels.

Each of these noninvasive techniques yield comparable overall results in grading varicocele volume. We believe scintigraphy to be less operator-dependent than thermography and ultrasound for both performance and interpretation. We thus believe scintigraphy to be a valid noninvasive technique to objectively document and grade the severity of clinically diagnosed or suspected varicocele. In the specific patient population studied, the need for an accurate noninvasive study yielding objective documentation of varicocele is of special importance and may have a major impact on the lives and careers of the young men involved. The nature of the patient referral pattern has resulted in a patient population that is different from previously studied groups in which infertility, with or without clinical varicocele, was a major indication for study (*2,4,12–15,19,20,22*).

We confirmed a much lower incidence of a right-sided varicocele, which in our series never occurred without a simultaneous left side involvement (*4–8*).

Semen analysis revealed the absence of any obvious correlation between varicocele size and the severity of seminal abnormalities. The young mean age of our patients (22 yr) could have resulted in a shorter duration of the disease which might explain these results. We did not study patients with infertility who had no clinical evidence of varicocele. The relationship of varicocele to infertility remains somewhat controversial; nevertheless, in at least a subset of patients there does appear to be a cause and effect relationship that may be reversed by the treatment of the varicocele. The mechanism of this phenomenon is also somewhat controversial but may be related to the reflux of core temperature blood into the varicocele which raises testicular temperature above that for optimal spermatogenesis (*29–31*).

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