

Doppler Resistive Index as a Predictors of Sperm Retrieval in Azoospermic Iraqi Patients

فحص الدوبلر باستخدام عامل الممانعة كمتنبئ استخلاص الحيوانات المنوية في المرضى العراقيين الذين يعانون من عدم وجود النطف

Dr.Hayder Kadhum Hussein Al-Fatlawi *

Dr.Saad Al -Deen Ghali Al -Essawi **

Dr.Ahmed Mohsin Jasim Al-Haidery ***

الخلاصة:

هدف البحث: تقييم دور الفحص بالموجات فوق الصوتية (الدوبلر) بالإعتماد على عامل ممانعة جريان الدم في توقع نجاح عملية إستخلاص النطف في المرضى العراقيين المصابين بفقدان النطف التام .
المنهجية: أجريت هذه الدراسة في مركز الدوبلر التابع لوحدة الأشعة و مركز الخصوبة في مدينة الصدر الطبية في محافظة النجف الاشراف للفترة من أبريل ٢٠١٣ الى كانون الثاني ٢٠١٤ وعمدت على تتبّع حالة ٧٢ مريض وبأعمار تتراوح بين ٢٠ سنة إلى ٥٠ سنة. أجريت لهم فحوصات السونار والدوبلر وثبتت نتائج الفحص وتم إجراء عمليات استخلاص النطف بواسطة الجراح المختص. تم إجراء التحليل الإحصائي باستخدام برنامج spss الإصدار ٢٠ الذي نستخدم فيه جدولين أثنتين لحساب جدول دقة مختلف.
النتائج: بينت النتائج نجاح العملية في إستخلاص النطف في ٣٣ مريض بينما كانت النتيجة سلبية في ٣٩ مريض . وأثبتت الدراسة أن هنالك دور مهم لعامل ممانعة جريان الدم في التنبؤ بنجاح عملية إستخلاص النطف حيث كانت الدقة ٧٦.٤% . بينت هذه الدراسة أن نسبة نجاح إستخلاص النطف أكبر في حال كان عامل ممانعة جريان الدم اقل من ٠.٧ وحجم الخصية طبيعي لتصل الدقة إلى ٨٢.٢% . أما إذا كان عامل ممانعة جريان الدم مساوي إلى أو أكثر من ٠.٧ وحجم الخصية صغير كانت الدقة ٦٦.٧% .
الاستنتاج: أستخلصت هذه الدراسة أن الفحص بالدوبلر باستخدام عامل ممانعة جريان الدم ذا قيمة عالية في توقع نجاح عملية إستخلاص النطف في المرضى المصابين بمرض فقدان النطف التام . وإن هذه القيمة تكون أعلى إذا اقترن عامل ممانعة جريان الدم مع عامل حجم الخصية.
التوصيات: أوصلت الدراسة باعتماد عاملي ممانعة جريان الدم لتقييم الاستفادة من عملية استخلاص النطف من عدمه في المرضى المصابين بفقدان النطف التام مع الأخذ بنظر الاعتبار عامل حجم الخصية .

Abstract:

Objective: To evaluate the Doppler ultrasound in prediction the success of sperm retrieval in Iraqi azoospermic patient using the resistive index (RI).

Methodology: This cross sectional study conducted in the Doppler unite and the Fertility centre in the AL-Sadder Medical City in a period between April 2013 and January 2014 .The study included 72 patients with azoospermia, their age ranging from 20 to 50 years , US and Doppler study were done for them prior to testicular sperm extraction (TESE) . Statistical analysis was done by using SPSS version 20 in which use two by two tables to compute different accuracy measures.

Results: There were 33 patients with positive post surgical results and 39 patients with negative results. The accuracy of RI in predicting post surgical result was (76.4%). The study shows that when the size of the testis was normal and the RI was < 0.7, the accuracy of the successful rate of sperm retrieval will be higher (82.2%) and when the size of the testis was small and the RI ≥ 0.7, the accuracy was lower (66.7%).

Conclusion: This study concludes that Doppler ultrasound using RI parameter can be use as a predictor of sperm retrieval in azoospermic patients and this will be increase if taken with testicular size parameter.

Recommendations: This study recommends the use of RI parameter of Doppler ultrasound and testicular size as a predictor of sperm retrieval in azoospermic patients .

Keywords: Doppler US, azoospermia, testicular sperm retrieval.

* (M.B.Ch.B.FIBMS) . Assistant prof. Radiology .College of medicine/University of Kufa . Najaf - Iraq . [E-mail: dr.hayderk@yahoo.com](mailto:dr.hayderk@yahoo.com)

** (M.B.Ch.B.FIBMS). Assistant prof. Urology .College of Medicine .University of Kufa . Najaf -Iraq . [E-mail:saadaldeen@yahoo.com](mailto:saadaldeen@yahoo.com)

*** (M.B.Ch.B.DMRD). Radiology . Al-Refae Hospital –Nasseria - Iraq . [E-mail:ahmedalhaidary34@yahoo.com](mailto:ahmedalhaidary34@yahoo.com)

introduction:

The testes are a pair, slightly flattened bodies of whitish color. Each testis placed within the cavity of the scrotum in such a manner that its long axis directed upwards, slightly forwards, and laterally. Usually the left testis is a little lower than the right one (1). Blood supply of the testes and scrotum are distinct, the paired testicular arteries arise directly from the abdominal aorta(2). Each crosses obliquely over the ureter and the lower part of the external iliac artery to reach the abdominal inguinal ring, through which it passes, and accompanies the other constituents of the spermatic cord along the inguinal canal to the scrotum, where it becomes tortuous, and divides into several branches (3).

Azoospermis is the medical condition of a man not having any measurable level of sperm in his semen. Clinically azoospermia defined as the absence of spermatozoa in the ejaculate after assessment of centrifuged semen on at least two occasion(4).

Azoospermia, the most severe form of male infertility, caused generally by obstructions in the genital tract or by testicular failure(5).

Pretesticular azoospermia is characterized by inadequate stimulation of otherwise normal testicles and genital tract. Typically, follicle-stimulating hormone (FSH) levels are low (hypogonadotropic) commensurate with inadequate stimulation of the testes to produce sperm. Examples include hypopituitarism (for various causes), hyperprolactinemia, and exogenous FSH suppression by testosterone. Pretesticular azoospermia are in about 2% of azoospermia. In testicular azoospermia the testes are abnormal, atrophic, or absent, and sperm production severely disturbed to absent. FSH levels tend to be elevated (hypergonadotropic) as the feedback loop is interrupted (lack of feedback inhibition on FSH). The condition is to be occurring in 49-93% of men with azoospermia. Testicular failure includes absence of failure production as well as low production and maturation arrest during the process of spermatogenesis. Causes for testicular failure include congenital issues such as in certain genetic conditions (e.g. Klinefelter syndrome), some cases of cryptorchidism or Sertoli cell-only syndrome as well as acquired conditions by infection (orchitis), surgery (trauma, cancer), radiation, or other causes. Generally, men with unexplained hypergonadotropic azoospermia need to undergo a chromosomal evaluation. In post testicular azoospermia, sperms are produced but not ejaculated, a condition that affects 7-51% of azoospermic men. The main cause is a physical obstruction (obstructive azoospermia) of the post testicular genital tracts. The most common reason is a vasectomy done to induce contraceptive sterility. Other obstructions can be congenital (example agenesis of the vas deferens as seen in certain cases of cystic fibrosis) or acquired, such as ejaculatory duct obstruction for instance by infection(6,7).

Testicular sperm retrieval done by scrotal incision, the testis is exposed, the tunica is incised, and a piece of protruding testicular tissue is excised. The tunica is sutured and the incision is closed. An easy method is that can be performed by any surgeon, and yields a good amount of tissue. In men with obstructive azoospermia, sperm may be retrieved from the epididymis and/or the testis, while in men with non-obstructive azoospermia only testicular sperm retrieval procedures are useful (8).

Testicular sperm extraction (TESE) is a technique can be used to not only to diagnose the cause of a man's azoospermia, but also to obtain sufficient tissue for sperm extraction to be used either fresh or as a cryopreserved (frozen) specimen for IVF with ICSI. It involves one or multiple small incisions in the testes and can performed in the office with a nerve block or under anesthesia in an ambulatory surgery center (2).

Scrotal ultrasound is an imaging technique used for the diagnosis of suspected abnormalities of the scrotum. Doppler ultrasound uses harmless, high-frequency sound waves to form an image. The sound waves reflected by scrotal tissue to form a picture of internal structures. It is not invasive and involves no radiation. Color Doppler ultrasound (which can reveal scrotal blood flow) is used in the assessment of acute scrotal symptoms (pain or swelling) (9,10).

Blood flow is the total amount of blood moving past a certain point, affected by two factors when flowing through a vessel, i.e. pressure and resistance, expressed as: flow pressure/resistance (11). CDUS is one of the most reliable and rapid methods of measuring blood flow. Doppler indexes used to obtain information about blood flow and vascular impedance that cannot be obtained from velocity information alone. Two widely used indexes are the pulsatility index (PI) and RI. For the measurement of intratesticular blood flow, the RI used in this study. CDUS with resistive index (RI) or Pourcelot index is a popular parameter for characterizing the arterial waveform at Doppler ultrasonography (2,12).

Objective:

To evaluate the Doppler ultrasound in predicting the success of sperm retrieval in Iraqi azoospermic patients using the resistive index (RI).

Methodology:

This study was conducted at the AL-Sadder Medical City in Al-Najaf Health Directorate in a period between April 2013 and January 2014. This cross-sectional study was done with 72 azoospermic patients, their ages ranged between 20-50 years with a mean of 29.7 ± 6.4 years. Patients with history of testicular trauma, surgery or varicocele, excluded from the study because it is considered difficult to ascertain whether spectral trace data related to testicular trauma, disease and surgery, or to altered spermatogenesis. Furthermore, men suspected of having obstructive infertility due to a vas deferens obstruction excluded from the study. The U/S, CDUS were done in the Doppler unit, by (2010 /516 SSA-660 Toshiba, Japan) ultrasound machine with a 7-12 MHz linear array probe. Scrotal US with CDUS undertaken in a warm room with the azoospermic patients examined in a supine position, the penis resting on the lower abdomen. The testis examined in orthogonal transverse and longitudinal planes. The size of the testis was assessed by volume measurements.

Volume of each testis calculated as (length x height x width x 0.51) (3). A total volume (both testes) of greater than 30 ml and a single testicular volume of 12-15 ml is generally considered as normal (13). Doppler flow was measured in each testis using a trans-scrotal approach, the RI were calculated by the machine, recorded bilaterally for each patient, the RI is calculated as: $(PSV - EDV)/PSV \times 100$, where PSV is peak systolic velocity and EDV is the end diastolic velocity. After that the patient underwent surgery for sperm retrieval by TESE method in the theatre of fertility centre by the urologist, nearly about one week after the ultrasound examination. A small longitudinal scrotal incision performed to expose the tunica albuginea and to allow visualization of the vessels underneath it. Two or three incisions made in the tunica albuginea at different positions in each testis, avoiding injury to the vessels and extracting testicular tissue, the sample extracted in a random fashion and divided into quartiles, the first quartile sent to histological analysis, the remaining specimens placed in a Petri dish and immediately sent to the adjacent reproduction biology laboratory. The results recorded a negative or positive accordingly, if the patient was positive the sperm count is recorded and the percentage of the active motile sperm is also recorded.

Statistical analysis was done by using SPSS (statistical package for social sciences) version 20 in which we use two by two table to compute different accuracy measures.

Results:

The result of this study which was consist of 72 azoospermic patients

Table (1): Comparison between successful and failed post surgery in correlation with the age of the patient.

	Post surgical result	Mean of age	Std. Deviation	P value
Age	+ve	29.8182	7.25627	0.962
	-ve	29.7436	5.81612	

In table (1) There was no significant difference in predicting post surgical results regarding the age of the patients.

Table (2) : The accuracy of RI in predicting post surgical results.

RI	Post surgical result		Total
	Positive	Negative	
<0.7	30	14	44
≥0.7	3	25	28
Total	33	39	72

In table (2) of 72 male patients with azoospermia, there were 33 (45.8%) had positive post surgical result and 39(54.2%) had negative post surgical results in correlation with RI accuracy

Sensitivity=90.9%, specificity= 64.1%, PPV=68.2%, NPV=89.3% and accuracy=76.4% .

Table (3): Comparison between testicular size and post surgical results.

size of testis		post surgical results		Total
		Positive	Negative	
Normal	Normal	28	17	45
	Small	5	22	27
Total		33	39	72

In table (3) there is clear different post surgical results between normal and small size testis, which is higher in normal size testis.

Sensitivity=84.8%, specificity=56.4%, PPV=62.2%, NPV=81.5% & accuracy=69.4

Table (4): The accuracy of RI in predicting post surgical results when the size of testis was normal.

RI	Post surgical results		Total
	Positive	Negative	
<0.7	25	5	30
≥0.7	3	12	15
Total	28	17	45

In table (4) the accuracy of RI was higher when the testicular size was normal, in predicting the post surgical results(positive in 28 of the cases) than when the testicular size was small, and its higher when the RI <0.7 .

Sensitivity=86.3%, specificity=70.6%, PPV=83.3%, NPV=80% & accuracy=82.2%.

Table (5): The accuracy of RI in predicting post surgical results when the size of testis was small.

RI	Post surgical results		Total
	Positive	Negative	
<0.7	5	9	14
≥0.7	0	13	13
Total	5	22	27

In table (5) the accuracy of RI was lower when the testicular size was small, in predicting the post surgical results (positive in 5 cases only) in comparison when the testicular size was normal and its higher when the RI<0.7.

Sensitivity=100%, specificity=59.1%, PPV=35.7%, NPV=100% & accuracy=66.7%.

This study found that most of the patients with negative sperm retrieval had RI values lie between 0.7 to 1, while most of those with positive results had RI values between 4.6 and 6.9. In this study, the peak systolic velocities in the intratesticular arteries founded to lie between 9-14cm/sec.

Discussion:

The study reveals that the age is not correlates with post surgical results .There were 33 (45.8%) had positive post surgical results and 39(54.2%) had negative results. This study uses 0.69 as upper normal limit of RI, the result was 44 patients less than 0.7 from them 30 had positive post surgical results and 14 are negative.

Twenty-eight patients were their RI ≥ 0.7, from them only three had positive post-surgical result the other were negative. Sensitivity 90.9%, specificity 64.1%, PPV 68.2%, NPV 89.3% and the accuracy=76.4%.

This study agrees also with Sorin M. Dudea, which shows that in the adult, low resistance flow, with broad systolic component is recorded in the intratesticular artery. The peak systolic velocity in the centripetal, intratesticular arteries is less that 15 cm/sec. Normal mean resistance index (RI) is 0.6, ranging from 0.5 to 0.7⁽⁵⁾. Like Sorin M. Dudea, this study use RI of 0.69 as upper limit of normal⁽⁵⁾.

This study agree with AL-Naffakh H. study that found individuals with normal sperm counts had the mean (SD) RI = 0.566(0.0342), those with abnormal pathological sperm counts had mean (SD) the RI=0.673(0.093) .Statistical analysis show significant difference between the two groups P=0.002⁽¹¹⁾.

This study disagree with Pinggera GM. et al which reveals 0.6 might be suggestive of a pathological sperm count in andrological patients⁽²⁾.

This study demonstrates that the intratesticular RI as measured by CDUS is a reliable indicator for routine clinical use to identify sub fertile men in agreement with Souza C.A.B. et al, who suggest that in the evaluation of systems with low blood flow as the testis , the microvascularity evaluation can usually only be done with the association of CDUS⁽¹³⁾.

This study agrees with Hosam Ghazy et al study who reveals that Doppler ultrasound can differentiate obstructive azoospermia from non-obstructive azoospermia ⁽³⁾.

The accuracy of RI in predicting post surgical results when the size of testis is normal found to be higher in this study with sensitivity 86.3%, specificity 70.6%, PPV 83.3%, NPV 80% & accuracy 82.2%. When compare the results with other studies, this

study disagrees with Bonarriba CR. et al that did a subjective categorization according to the physical examination in three groups: normal, small, and atrophic. The sperm retrieval rate was 55.5% for normal-sized testes, 39.1% for small ones, and 16.6% for atrophic ones, but the differences found were not statistically significant ($P = 0.133$)⁽¹⁴⁾.

According to the Rupin Shah, in men with obstructive azoospermia, epididymal sperm can usually be retrieved by percutaneous epididymal sperm aspiration. If this fails then testicular sperm are obtained by needle aspiration biopsy. In men with non-obstructive azoospermia, testicular sperm retrieval is required. Percutaneous retrieval by needle aspiration biopsy can be tried first. If that fails then testicular sperm extraction (TESE) is performed⁽⁸⁾, but Van Peperstraten A.M. et al shows that there is insufficient evidence to recommend any particular surgical techniques⁽¹⁵⁾.

CONCLUSION:

This study reveals that CDUS is able to predict the success of sperm retrieval surgery. These results suggest that CDUS using RI parameter can use as a simple, safe, rapid and non-invasive predictor test for spermatogenesis and infertility. Testicular size is another parameter that could correlate with spermatogenesis.

RECOMMENDATION:

This study recommends the use of Doppler study as predictor of successful sperm retrieval surgery by using RI and testicular size parameters.

REFERENCES:

1. Giuseppe S. and Carmelo R. Morphological and surgical overview of adolescent testis affected by varicocele. *The scientific world journal*: 2013: Vol.13:47-58.
2. Pinggera GM., Mitterberger M., Bartsch G., Strasser H., Gradl J., Aigner F. et al .2008.Assessment of the intratesticular resistive index by color Doppler ultrasonography measurements as a predictor of spermatogenesis. *BJUI international* : 2008 :Vol. 101 : 722-726
3. Hosam Ghazy, Dalia Monir, Hosam Zayton, Mohamed El. Rakhawy, Galal El Hawary et al. 2009. Doppler analysis of the testicular artery can be used in assessment of spermatogenesis, *Egyptian Journal of Surgery*: 2009 :Vol. 28: No. 2 :223
4. Donoso P., Tournaye H., Devroey P. 2007: Which is the best sperm retrieval technique for non-obstructive azoospermia?. A systematic review., *Clinica Alemana, Vitacura* . 2007:5951: Vol.13: No.6: 539–549.
5. Sorin M. Dudea, Anca Ciurea, Angelica Chiorean, Carolina Botar-Jid . 2010 . Doppler applications in testicular and scrotal disease. *Medical Ultrasonography*: 2010 :Vol. 12: No.1: 43-51.
6. Jarvi K., Lo K. , Fischer A, Grantmyre J., Zini A., Chow V. et al. 2010. "CUA Guideline": The workup of azoospermic males". *Canadian Urological Association Journal*.2010. 4 (3): 163–7.
7. Gert R.Dohle. 2010. "Male infertility in cancer patients: Review of the literature". *International Journal of Urology*.2010. 17 (4): 327–331.
8. Rupin Shah . 2011 . Surgical sperm retrieval: Techniques and their indications. *Indian J Urol*. 2011 Jan-Mar: 27(1): 102–109.
9. Appelbaum L., Gaitini D., Dogra V. 2013. Scrotal ultrasound in adults. *Semin Ultrasound CT MR*. 2013: 34(3): 257-273.
10. Mirochnik B, Bhargava P, Dighe MK, Kanth N. 2012. Ultrasound evaluation of scrotal pathology. *Radiol Clin North Am* . 2012 :50(2): 317–332.
11. Al-Naffakh H. 2012 . Testicular Doppler resistive index parameter as predictor test for male infertility. *Kufa Med. Journal* : 2012 :Vol.15:No.1: 295-296

12. Ammar T., Sidhu P., Willikins C. 2012: The role of imaging in diagnosis and management. *Male infertility*; 2012 :Nov.85:59-68.
13. Souza C.A.B., Cunha Filho J.S., Santos D., Gratao A., Freitas F.M , Passos E.P. et al. 2003. Predictive factors for motile sperm recovery using testicular biopsy in non obstructive azoospermic patients. *Int Urol and Nephrol*: March 2003: Vol.35 issue 1: 53–57.
14. Bonarriba C.R., Burgués J.P., Vidaña V., Ruiz X., Pizá P., Mallorca S. et al . 2013. Predictive factors of successful sperm retrieval in azoospermia. *Actas Urol Esp*. 2013: 37: 266-272.
15. Van Peperstraten A.M., Nelen W., Hermens R., Jansen L., Scheenjes E., Braat D. et al. 2008. Why don't we perform elective single embryo transfer? A qualitative study among IVF patients and professionals. *Hum Rep*. 2008 Sep:23(9) : 2036-2042.