

Ultrasonographically determined size of seminiferous tubules predicts sperm retrieval by microdissection testicular sperm extraction in men with nonobstructive azoospermia

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Objective: To investigate the value of the ultrasonographically determined size of seminiferous tubules and other conventional parameters for predicting sperm retrieval by microdissection testicular sperm extraction (micro-TESE).

Design: Clinical retrospective study.

Setting: Two urological clinics.

Patient(s): Eight hundred six men with nonobstructive azoospermia.

Intervention(s): Micro-TESE.

Main Outcome Measure(s): Sperm retrieval.

Result(s): Sperm retrieval was successful in 240 (29.8%) of the 806 men. In a receiver operating characteristic analysis of sperm retrieval, the area under the curve (AUC) for seminiferous tubules, assessed as 0, 100, 200, 250, or 300 μm , was no less than 0.82 (95% confidence interval [CI] 0.79–0.85). Sensitivity and specificity at a cutoff point of 250 μm were 76.7% and 80.7%, respectively. An AUC of 0.85 (95% CI, 0.81–0.88) was attained in a parsimonious multiple logistic regression model that included age (<30, 30–39, and 40–59 years), low follicle-stimulating hormone (<14 IU/L), history of cryptorchidism, and sex chromosome abnormality in addition to the diameter of seminiferous tubules.

Conclusion(s): The gray-scale image in testicular ultrasound was shown to be highly predictive of sperm retrieval in micro-TESE in a large series of men with nonobstructive azoospermia. (Fertil Steril® 2020;113:97–104. Copyright ©2019 The Authors. Published by Elsevier Inc. on behalf of the American Society for Reproductive Medicine. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).)

El resumen está disponible en Español al final del artículo.

Key Words: Nonobstructive azoospermia, microdissection testicular sperm extraction, receiver operating curve, seminiferous tubules, ultrasonography

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Azoospermia, the absence of spermatozoa in the ejaculate, is classified as either obstructive or nonobstructive. The latter con-

dition involves testicular failure due to hereditary or nonhereditary causes whereas spermatogenesis is normal in the former condition (1). In nonob-

structive azoospermia (NOA), spermatogenesis is not totally absent and may be present in small areas in the testis (1).

Microdissection testicular sperm extraction (micro-TESE) followed by intracytoplasmic sperm injection is currently the standard treatment for infertility due to NOA (1). Micro-TESE was first described by Schlegel (2) and achieves a higher sperm-recovery rate with a lower risk of damaging the testis than previous sperm retrieval methods

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(1). A meta-analysis showed that sperm retrieval in micro-TESE was 1.5-fold higher than that in conventional TESE (3). However, sperm retrieval rates vary among centers, ranging from 40% to 60% (3), and particularly depend on the clinical background of azoospermia (4).

The prediction of sperm retrieval in micro-TESE is essential information for patients with NOA as well as surgeons for performing micro-TESE with confidence (4–6). Klinefelter's syndrome, chromosomal Y microdeletion, cryptorchidism, and cytotoxic medication or radiation are known causes of male infertility and have been studied in relation to sperm retrieval in micro-TESE (4, 5). Testicular volume and sex hormones such as follicle-stimulating hormone (FSH), luteinizing hormone (LH), testosterone, and inhibin B have also been studied as potential predictors of sperm retrieval in micro-TESE (4–6). However, neither a single factor nor a combination of these factors satisfactorily predicts sperm retrieval (7–11).

We identified an easy way to visualize the seminiferous tubules on gray-scale ultrasound (US) images of the testis. The principle of micro-TESE is to target biopsies of seminiferous tubules in which spermatogenesis is active, which are larger and more opaque than other tubules (2), and we conjectured that such enlarged tubules could be visualized in US images. No previous study has investigated the usefulness of gray-scale US images for predicting sperm retrieval in micro-TESE. Our study investigated the value of the US-determined size of seminiferous tubules as well as of conventional parameters such as testicular volume, serum FSH, and chromosomal karyotype in the prediction of sperm retrieval by micro-TESE in men with NOA.

MATERIALS AND METHODS

Patients

The patients in the present study were a consecutive series of men with NOA who underwent micro-TESE from July 2003 to December 2018 at two urological clinics in Japan (Ebisu Tsuji Clinic in Tokyo and Tenjin Tsuji Clinic in Fukuoka). Of the total 867 micro-TESE procedures, 43 were excluded due to patients aged 60 years or older ($n = 3$), XX male ($n = 5$), AZFa and/or AZFb deletion in Y chromosome ($n = 12$), unreadable testicular US mainly due to severe microlithiasis ($n = 11$), and a posteriori diagnosis of obstructive azoospermia ($n = 12$). Furthermore, 18 of the remaining 824 procedures were in men who received a second ($n = 17$) or third ($n = 1$) micro-TESE. Thus, 806 cases were used in the present analysis. All clinical, laboratory, and surgical procedures were performed after written informed consent was obtained. The present study was based on information collected in routine clinical practice and was approved by the institutional review board at the IVF Nagata Clinic, Fukuoka, Japan, protocol no. 181127.

Laboratory Measurements

The laboratory tests were performed before the surgical procedure. Sex hormones other than FSH were routinely measured, but only FSH was used in the present analysis. Serum concentrations of FSH were measured by a chemiluminescent immunoassay at an external laboratory. Analyses of

karyotype and chromosome Y microdeletion were performed at another external laboratory. We determined AZF deletion by reverse sequence-specific oligonucleotide with polymerase chain reaction (PCR-RSSO; Luminex) method (12) and DAZ deletion by the fluorescence in situ hybridization (FISH) method (13). In 2012, the analysis of AZF deletion replaced the analysis of DAZ deletion.

Ultrasonography

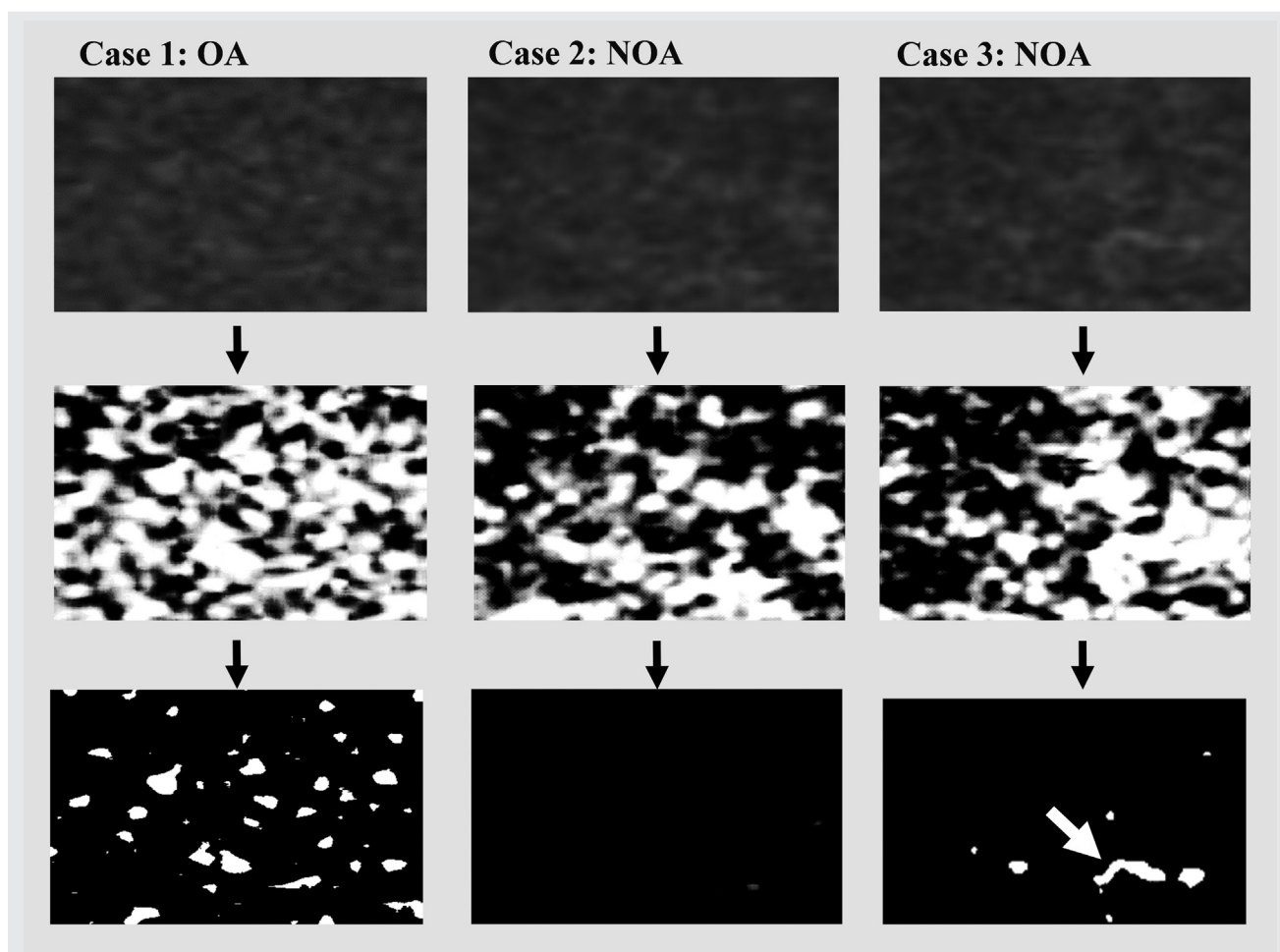
All patients underwent gray-scale and color Doppler US by a board-certified sonographer at each clinic using a high-frequency transducer (10–14 MHz; Aloka SSD3500, Aloka; Toshiba SSA-580A, Toshiba) before surgery. Multiple gray-scale images of the testes were obtained in the transverse and longitudinal planes, and the testicular length, width, and height were measured using electronic calipers (14). The largest measurement in each dimension was used to calculate the testicular volume according to the Lambert (15) formula: $(\text{Length}) \times (\text{Width}) \times (\text{Height}) \times 0.71$. The gray-scale images of the testicles in JPEG format were stored on the hard-drive of the US units and then were transferred to a personal computer (PC) for evaluation of the morphology of seminiferous tubules.

The gray-scale images in routine US showed no difference in intratesticular echogenicity between patients with obstructive azoospermia and those with NOA, except for the size of the testis. However, we confirmed that normal seminiferous tubules were visualized as hyperechogenic by the water-immersion method. We found that seminiferous tubules could be visualized by a simple two-step procedure of adjusting the contrast and brightness of JPEG images (Fig. 1).

A total of six images in the transverse plane at the upper, middle, and lower part of each testis per patient was used for assessment. The JPEG images were processed by PowerPoint 2013 or later versions (Microsoft). Portions of the image other than the testis were trimmed away, and the image of testis was enlarged to fill the PC screen. The contrast and brightness were set at 96% and 50%, respectively, and then the brightness was gradually reduced to 30%. This gradual decrease in brightness revealed heterogeneity in the diameter of seminiferous tubules. The contrast and brightness settings were based on our experience.

Thick and cell-rich tubules remained as hyperechoic bands, whereas narrow tubules and stromal tissue disappeared. Once a seminiferous tubule was identified, the tubular diameter was measured on the first-visualized image and classified as 0 μm (invisible tubules), 100 μm (very thin), 200 μm (thin), 250 μm (thick), or 300 μm (evidently thick). The maximum tubule size was used as the value for each patient. The tubule size as determined on US images obtained by the immersion method roughly approximated the width of the surgically removed tubules (Supplemental Fig. 2, available online).

Two sonographers (S.N. and K.N.) analyzed the images obtained by testicular US. They classified the tubule sizes independently and finalized discordant classifications by discussion. The image analysis required roughly 10 to 20 minutes per patient.

FIGURE 1

Unprocessed and processed gray-scale US images in patients with obstructive azoospermia (OA) or nonobstructive azoospermia (NOA). Top row: Unprocessed images. Middle row: First-step processed images with the highest contrast (96% in PowerPoint) and moderate brightness (50% in PowerPoint). Bottom row: Second-step processed images with decreased brightness (30% in PowerPoint). Bands of seminiferous tubules emerged in case 1 with OA and case 3 with NOA (right and left in bottom row). No bands of tubules appeared in case 2 with NOA (middle in bottom row).

Nariyoshi. Prediction of sperm retrieval in NOA by US. Fertil Steril 2019.

Micro-TESE Procedure

Micro-TESE was performed as described elsewhere (2). While Schlegel used general anesthesia, we performed surgery under local anesthesia. All patients underwent an initial micro-TESE on the larger testis, and the contralateral testis was explored if a sufficient number of sperm was not retrieved. The testicular parenchyma was examined systematically and carefully with an operating microscope at 16- to 25-fold magnification to locate opaque and dilated seminiferous tubules. Small samples (10–15 mg) were excised from the larger and more opaque tubules. Dilated tubules were excised and then checked for spermatozoa under an inverted microscope ($\times 300$).

The surgeon's subjective impression of the tubular diameter was classified as either thick or thin. Tissue specimens were excised and fixed in Bouin's solution for pathological examination. When no large seminiferous tubules were found, testicular tissue was systematically biopsied from at

least six sites for each testis. The pathological findings were classified as hypospermatogenesis, maturation arrest, Sertoli cell-only syndrome, and no-cell histology based on the predominant histologic pattern (16). No-cell histology was defined if no seminiferous epithelial cells were found (i.e., tubular sclerosis).

Statistical Analysis

The background characteristics of the study participants are presented as the mean and standard deviation (SD) for continuous variables and as proportions for categorical variables. The associations of clinical and laboratory factors with the TESE outcome were assessed in terms of odds ratio (OR) and 95% confidence interval (CI) estimated by a logistic regression analysis. In the univariate logistic regression analysis with respect to FSH and testicular volume, the patients were

categorized into four groups by using the quartiles of each variable for a potential lack of a linear relationship. A receiver operating characteristic (ROC) analysis was used to assess the ability to predict sperm retrieval in micro-TESE, and the area under the curve (AUC) was calculated as an overall measure of prediction. A two-sided $P < .05$ was considered statistically significant. All statistical analyses were performed using Stata version 13 (Stata Corporation).

RESULTS

The clinical and laboratory characteristics of the study patients and sperm retrieval according to these factors are summarized in Table 1. Most of the patients were aged in their 30s. There were very few patients aged 50–59 years ($n = 14$), and they were combined with those aged 40–49 years. Some of the patients (7%) reported a prior medical history that was possibly associated with azoospermia. Klinefelter's syndrome, the most common chromosomal abnormality, accounted for more than 10% of the patients.

The mean age at TESE was 35.5 years (SD 5.8), the mean concentration of plasma FSH was 21.8 IU/L (± 11.6 IU/L SD) and the mean testicular volume was 7.1 mL (± 3.7 mL SD). Most of the patients had visible seminiferous tubules, with a diverse variation in tubule size. The number of patients with each histopathology was as follows: hypospermatogenesis 66 (8.2%), maturation arrest 185 (23.0%), Sertoli cell-only syndrome 497 (61.7%), and no-cell histology 58 (7.2%). Overall, sperm retrieval was successful in 240 (29.8%) of the 806 men undergoing micro-TESE.

The results of the univariate logistic analysis are also shown in Table 1. We found that TESE was successful less frequently in men aged 20–29 years and more frequently in those aged 40–59 years. The sperm retrieval rate was lower at the Fukuoka clinic. A history of cryptorchidism was associated with a marked increase in the odds of successful TESE. Compared with the patients who had a normal chromosomal pattern, those with Klinefelter's syndrome showed a statistically significant decrease in the odds of successful TESE, and those with structural abnormality of the Y chromosome had a lower rate of success in TESE, albeit the association was not statistically significant.

The three highest categories of FSH levels showed decreases in the OR of sperm retrieval to almost the same extent, and the OR was increased in patients with the highest quartile of testicular volume. The OR of successful TESE progressively and markedly increased with an increase in the size of the seminiferous tubules.

In the ROC analysis (Supplemental Fig. 2, available online), FSH (AUC 0.61) and testicular volume (AUC 0.59) were poor predictors of successful TESE. In contrast, the AUC for seminiferous tubules was no less than 0.82 (95% CI, 0.79–0.85). The sensitivity and specificity at a Youden's cutoff of 250 μm were 76.7% and 80.7%, respectively. Thirty percent of the men had seminiferous tubules ≥ 250 μm .

In the multiple logistic regression analysis, to avoid unstable estimation due to small numbers, two indicator variables for chemotherapy/radiotherapy and cryptorchidism were used with respect to past medical history; Klinefelter's

TABLE 1

Univariate analysis of sperm retrieval in micro-TESE in relation to demographic, clinical, and laboratory variables.

Variable	Total, n	Positive, n (%)	OR (95% CI)
Age (y)			
20–29	108	24 (22.2)	0.71 (0.43–1.16)
30–39	516	148 (28.7)	1.00 (reference)
40–59	182	68 (37.4)	1.48 (1.04–2.12)
Clinic			
Ebisu, Tokyo	452	152 (33.6)	1.00 (reference)
Tenjin, Fukuoka	354	88 (24.9)	0.65 (0.48–0.89)
Past medical history			
None	751	217 (28.9)	1.00 (reference)
Chemo-/radiotherapy	29	5 (17.2)	0.51 (0.19–1.36)
Cryptorchidism	16	13 (81.3)	10.7 (3.01–37.8)
Mumps orchitis	3	3 (100)	—
Spinal cord injury	7	2 (28.6)	0.98 (0.19–5.11)
Chromosomal test			
46, XY (normal)	590	181 (30.7)	1.00 (reference)
47, XXY	100	20 (20.0)	0.56 (0.34–0.95)
47, XYY	2	2 (100)	—
Y structural abnormality	17	2 (11.8)	0.30 (0.07–1.33)
Autosomal abnormality	7	3 (42.9)	1.69 (0.38–7.65)
47,XY+ marker	1	0 (0.0)	—
Not tested	89	32 (36.0)	1.27 (0.80–2.02)
DAZ deletion			
None	207	40 (19.3)	1.00 (reference)
Present	23	6 (26.1)	1.47 (0.55–3.98)
Not tested	104	30 (28.8)	1.69 (0.98–2.92)
AZF deletion			
None	285	94 (33.0)	1.00
AZFc(gr/gr) deletion	111	30 (27.0)	0.75 (0.46–1.22)
AZFc partial deletion	7	1 (14.3)	0.34 (0.04–2.85)
AZFc total deletion	25	17 (68.0)	4.32 (1.80–10.4)
Not tested	44	22 (50.0)	2.03 (1.07–3.86)
FSH (IU/L)			
Q1 (<14)	208	101 (48.6)	1.00 (reference)
Q2 (14–19.9)	187	90 (20.3)	0.27 (0.17–0.42)
Q3 (20–27.7)	207	52 (25.1)	0.36 (0.23–0.54)
Q4 (≥ 28)	204	49 (24.0)	0.33 (0.22–0.51)
Testicular volume (mL)			
Q1 (<5)	205	53 (25.9)	1.00 (reference)
Q2 (5–6.9)	163	38 (23.3)	0.87 (0.54–1.41)
Q3 (7–9.9)	244	70 (28.7)	1.15 (0.76–1.75)
Q4 (≥ 10)	194	79 (40.7)	1.97 (1.29–3.01)
Seminiferous tubules (μm)			
0	29	2 (6.9)	0.56 (0.13–2.42)
100	92	8 (8.7)	0.72 (0.33–1.57)
200	392	46 (11.7)	1.00 (reference)
250	194	98 (50.5)	7.68 (5.06–11.7)
300	99	86 (86.9)	49.8 (25.7–96.2)

Note: CI = confidence interval; FSH = follicle-stimulating hormone; OR = multivariate adjusted odds ratio.

Nariyoshi. Prediction of sperm retrieval in NOA by US. *Fertil Steril* 2019.

syndrome or structural abnormality of Y chromosome were combined regarding karyotype. Furthermore, the ROC-based cutoff points were used for low FSH (<14 IU/L) and high testicular volume (≥ 11 mL) because the univariate analysis suggested thresholds in the associations with these factors.

The results of the multiple logistic regression models are summarized in Table 2. The associations with clinic location and high testicular volume disappeared. The size of seminiferous tubules was strongly associated with TESE positivity, and the OR progressively increased with thick (250 μm) and evidently thick (300 μm) tubules. Positive associations with

TABLE 2

Multiple logistic regression of sperm retrieval in micro-TESE in two different models.

Variable	Model 1		Model 2	
	OR (95% CI)	P value	OR (95% CI)	P value
Age class (y)				
20–29	0.52 (0.28–0.97)	.04	0.51 (0.27–0.94)	.03
30–39	1.00 (reference)	—	1.00 (reference)	—
40–59	1.20 (0.75–1.90)	.45	1.24 (0.78–1.95)	.37
Clinic (Fukuoka vs. Tokyo)	0.81 (0.55–1.21)	.31	—	—
Chemotherapy/radiotherapy	0.80 (0.26–2.46)	.70	—	—
Cryptorchidism	4.20 (0.93–19.0)	.06	4.24 (0.97–18.5)	.05
Sex chromosome abnormality	0.58 (0.30–1.11)	.10	0.57 (0.30–1.09)	.09
Low FSH (<14 IU/L)	1.71 (1.08–2.71)	.02	1.60 (1.04–2.47)	.03
High testicular volume (≥ 11 mL)	0.78 (0.47–1.32)	.36	—	—
Seminiferous tubules (μm)				
0	0.96 (0.20–4.54)	.96	0.93 (0.20–4.37)	.92
100	0.93 (0.41–2.11)	.86	0.91 (0.40–2.07)	.83
200	1.00 (reference)	—	1.00 (reference)	—
250	7.52 (4.83–11.7)	$<10^{-18}$	7.26 (4.69–11.2)	$<10^{-18}$
300	45.3 (22.6–90.9)	$<10^{-26}$	43.7 (22.1–86.5)	$<10^{-26}$

Notes: CI = confidence interval; FSH = follicle-stimulating hormone; OR = multivariate adjusted odds ratio.

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a history of cryptorchidism and low FSH remained statistically significant. A parsimonious model was then developed with variables that showed a statistically significant or nearly statistically significant association in the first multivariate model. The magnitude of OR did not change in the parsimonious model.

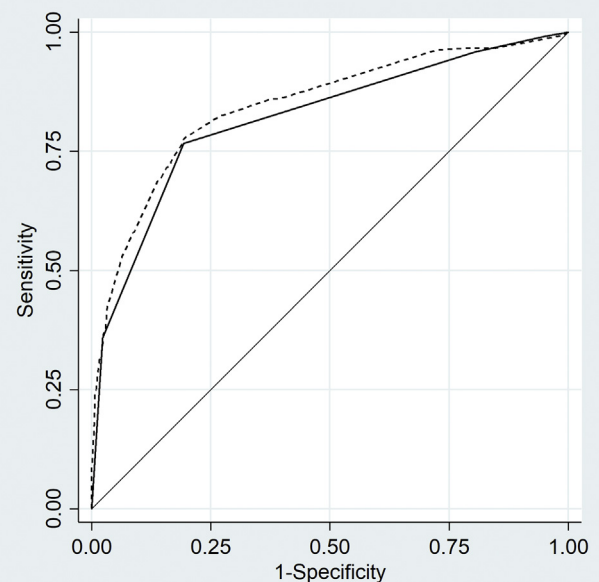
The ROC analysis following the multiple logistic regression demonstrated that both models were highly predictive of sperm retrieval. The AUC values were 0.85 (95% CI, 0.82–0.88) in the full model and 0.85 (95% CI, 0.81–0.88) in the parsimonious model. The ROC curves for the parsimonious multivariate model and the model including only seminiferous tubules were compared. The difference in the AUC between the two models was apparently small, but highly statistically significant ($P=.0002$) (Fig. 2).

DISCUSSION

The present results represent the most accurate prediction of sperm retrieval in micro-TESE that has ever been reported in the literature. The US-determined size of seminiferous tubules alone was found to be highly predictive to such an extent that the ROC analysis resulted in an AUC of 0.82. The addition of conventional factors such as FSH, cryptorchidism, and Klinefelter syndrome resulted in only a small increase in the AUC (from 0.82 to 0.85).

Single factors associated with sperm retrieval in micro-TESE have generally been poor at predicting sperm retrieval (6–8). Even combinations of these factors have not shown as high a predictive ability as that observed here. Testicular volume, FSH, and inhibin B were reported to be independently associated with sperm retrieval in micro-TESE, but an ROC analysis with these variables attained an AUC of no more than 0.66 (9). A more comprehensive model including FSH, testicular volume, Klinefelter syndrome, cryptorchidism, and varicocele resulted in an AUC of 0.64

FIGURE 2



Comparison of the receiver operating characteristic curves for the parsimonious multivariate model (dotted line) and seminiferous tubules only (solid line). The area under the curve values were 0.82 (95% CI, 0.79–0.85) for the latter and 0.85 (95% CI, 0.81–0.88) for the former.

Nariyoshi. Prediction of sperm retrieval in NOA by US. Fertil Steril 2019.

(10). A larger AUC of 0.76 was reported in a model including FSH, total testosterone, and inhibin B (11).

Microscopic determination of tubular diameter during micro-TESE and postsurgical histopathology have been reported to be strong single predictive factors (5, 7), but these findings are available only intraoperatively or

postoperatively. In our present series, the sperm retrieval rates were 98.5% in hypospermatogenesis, 60.5% in maturation arrest, 10.7% in Sertoli cell-only syndrome, and 17.2% in no-cell histology. The AUC was estimated to be 0.82 (95% CI, 0.79–0.85) in the ROC analysis following a logistic regression analysis of sperm retrieval including indicator variables for hypospermatogenesis and maturation arrest with Sertoli cell-only and no-cell histology combined as a reference. The gray-scale US images analyzed before surgery in our method give as much information regarding sperm retrieval as histopathology obtained after micro-TESE.

Our present findings on cryptorchidism and AZFc deletion are compatible with the current knowledge (4, 5), but we found Klinefelter's syndrome was unexpectedly associated with decreased sperm retrieval. In fact, sperm retrieval in men with Klinefelter's syndrome (20%) was much lower than the previously reported values of 40–60% (17–20), but was fairly consistent with a recent report (21). Serum testosterone levels seem to be an important determinant of sperm retrieval in micro-TESE in Klinefelter's syndrome regardless of whether the overall sperm retrieval is high or low (18, 21). A testicular-stimulation treatment before micro-TESE was not a routine procedure in our clinics, and serum testosterone was not necessarily measured in the period of the present series.

An additional analysis indicated that the decrease in sperm retrieval among patients with Klinefelter's syndrome was attributed to distinct histopathologic features. The proportions of hypospermatogenesis, maturation arrest, Sertoli cell-only syndrome, and no-cell histology were 1%, 6%, 48%, and 45%, respectively, whereas the corresponding proportions for normal chromosome were 9%, 23%, 66%, and 2%, respectively. The OR for Klinefelter's syndrome versus normal chromosome was 1.59 (95% CI, 0.87–2.90) while adjusting for the histopathology. Young age (less than 30 years) was associated with a significantly lower odds of successful sperm retrieval in the multivariate models whereas the association was not statistically significant in the univariate model. In general, young age does not seem to adversely affect sperm retrieval in micro-TESE (22).

Again, histopathology differed according to the age group ($P=.01$ by the chi-square test); Sertoli cell-only syndrome was more frequent in younger patients (67.6% in 20–39 years, 63.4% in 30–39 years, and 53.3% in ≥ 40 years), and hypospermatogenesis was less frequent in men aged 20–29 years (7.4%) and 30–39 years (6.2%) than in those aged ≥ 40 years (14.3%). When histopathology was added to the second model in Table 2, the adjusted OR for the age group of 20–29 years was greatly attenuated to 0.65 (95% CI, 0.32–1.33; $P=.24$). The observed age-related pattern in histopathology is quite plausible. In some elderly patients, NOA was partly due to an age-related decline in spermatogenesis. Such patients have germ cells in the testicle and may have had sperm in the ejaculate when they were young.

Testosterone and inhibin B were not considered in the present study. The addition of serum levels of these hormones may increase the ability to predict sperm retrieval in micro-TESE to some extent, but not substantially. The usefulness of gray-scale US images is unlikely to vary with the serum

levels of testicular hormones. The measurement of tubule size was rather crude due to the low resolution of the image, which may be regarded as a weakness of the present method. In fact, tubules of less than 100 μm were not discernible, and visible tubules were broadly classified into at most four categories: 100, 200, 250, and 300 μm . However, it is unclear whether improved precision in measurement by a new type of probe could achieve a greater power of prediction (23). Doppler US imaging may offer higher resolution to identify spermatogenesis-rich areas (24). However, this would be disadvantageous with regard to cost and feasibility in clinical practice. Our method for assessing seminiferous tubules may also be useful for evaluating spermatogenesis in medical treatment for hypogonadotropic hypogonadism (secondary testicular failure).

Adjustment of contrast and brightness is an important element in the present image analysis. This method is not difficult and can be easily applied to gray-scale images of the testis in digital format. Practice using stored images of approximately 20 cases would suffice for sonographers to attain the necessary skill. Nevertheless, several points should be noted if the present method is to be more widely used in clinical practice. The heterogeneity of seminiferous tubules, which appeared under a gradual reduction in brightness, was not quantified in our study. Evaluation of this heterogeneity in addition to measurement of tubule size may enhance the prediction of sperm retrieval in micro-TESE. Topographic assessment in US image analysis would be useful for navigating micro-TESE and should be examined in future studies.

In conclusion, the gray-scale image by testicular US was shown to be highly useful for predicting sperm retrieval in micro-TESE in a large series of men with NOA. The reported AUC was no less than 0.82, with a sensitivity of 77% and specificity of 81% at a cutoff of 250 μm . The addition of conventional predictive factors only slightly increased the diagnostic capability.

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La determinación del tamaño de los túbulos seminíferos mediante ecografía predice la obtención de espermatozoides mediante microdissección testicular en hombres con azoospermia no obstructiva

Objetivo: Investigar el valor de la evaluación del tamaño de los túbulos seminíferos medidos mediante ecografía, y de otros parámetros convencionales, para predecir la recuperación de espermatozoides mediante la extracción de espermatozoides por microdissección testicular (micro-TESE).

Diseño: Estudio retrospectivo clínico.

Entorno: Dos clínicas urológicas.

Paciente(s): Ochocientos seis hombres con azoospermia no obstructiva.

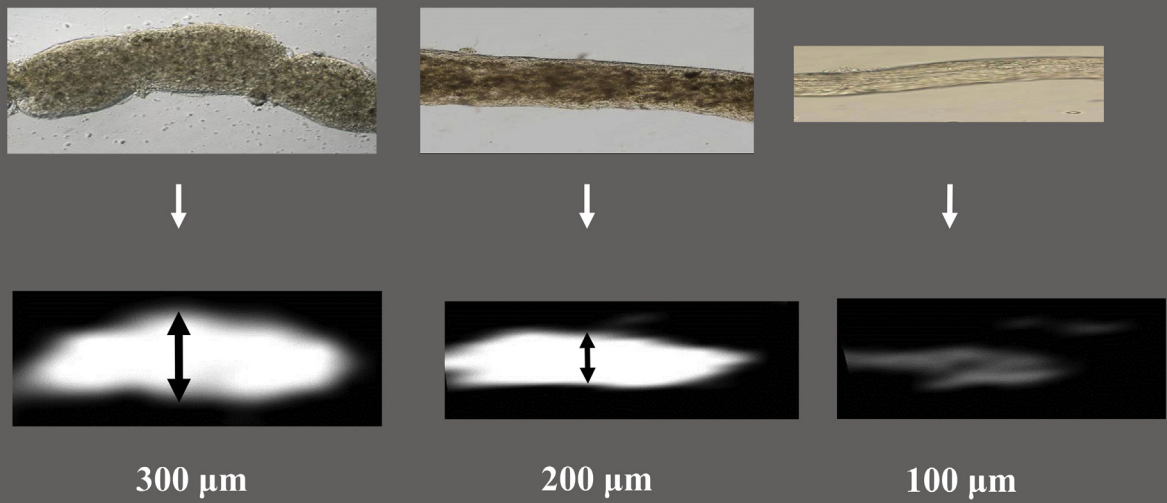
Intervención(es): Micro-TESE.

Medida(s) principal(es) de resultado: Recuperación espermática.

Resultado(s): La recuperación de espermatozoides tuvo éxito en 240 (29.8%) de los 806 hombres. En el análisis de la curva ROC (Característica Operativa del Receptor) para la recuperación espermática, el área bajo la curva (AUC) para la medición de los túbulos seminíferos, evaluada en 0, 100, 200, 250 o 300 mm, no fue inferior a 0.82 (intervalo de confianza [CI] del 95%: 0.79 a 0.85). La sensibilidad y la especificidad en un punto de corte de 250 mm fueron de 76.7% y 80.7%, respectivamente. Se logró un AUC de 0.85 (CI 95%, 0.81-0.88) en un modelo de regresión logística múltiple parsimonioso que incluía la edad (<30, 30-39, y 40-59 años), la hormona foliculoestimulante baja (<14 UI/L), los antecedentes de criptorquidia y la anormalidad de los cromosomas sexuales además de las medidas del diámetro de los túbulos seminíferos.

Conclusión(es): La imagen en escala de grises en el ultrasonido testicular mostró ser altamente predictiva de la recuperación de espermatozoides en el micro-TESE en una serie grande de hombres con azoospermia no obstructiva.

SUPPLEMENTAL FIGURE 1



Photographs and ultrasound (US) images of seminiferous tubules of different sizes. The upper panel shows magnified photographs of surgically removed seminiferous tubules, and the lower panel shows the corresponding US images taken by the water-immersion method.

Nariyoshi. Prediction of sperm retrieval in NOA by US. *Fertil Steril* 2019.

SUPPLEMENTAL FIGURE 2

