

## ORIGINAL ARTICLE

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# The role of artery-preserving varicolectomy in subfertile men with severe oligozoospermia: a randomized controlled study

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**ABSTRACT**

**Background:** There is wide agreement nowadays that a clinical varicocele should be ligated to treat male factor infertility. However, the significance of testicular artery preservation in patients with severe oligozoospermia has not been addressed before.

**Objectives:** To assess the outcome of varicolectomy in infertile men with severe oligozoospermia and clinical varicoceles and to compare internal spermatic artery preservation vs. artery ligation.

**Materials and Methods:** This prospective randomized study included 302 infertile patients with severe oligozoospermia and clinical (grade II/III) varicoceles. Patients were randomized into two groups: group A (150 patients) underwent artery-preserving varicolectomy (APV) and group B (152 patients) underwent artery-ligating varicolectomy (ALV). The primary outcome was to assess the changes in sperm density and motility at 3 and 6 months postoperatively in both groups. The secondary outcome was to compare the natural pregnancy rate at 1-year of follow-up. Univariate and multivariate analyses were performed to determine factors affecting pregnancy rate.

**Results:** In both groups, there was a statistically significant improvement in sperm density and motility at 3 and 6 months postoperatively. In group A, there was a greater improvement in sperm density ( $p < 0.001$ ) and motility ( $p < 0.001$ ) compared to group B. At 1-year follow-up, overall 35.1% achieved a natural pregnancy. Group A achieved a significantly higher natural pregnancy rate (40% vs. 30%,  $p$  value = 0.03) compared to group B. Smaller testicular volume and ALV were the independent predictors of lower pregnancy rate (HR = 3.2, 95% CI 1.2–8.3,  $p = 0.01$ ) and (HR = 3.2, 95% CI 1.4–7.1,  $p = 0.003$ ), respectively.

**Conclusion:** In men with severe oligozoospermia and a clinical varicocele, APV results in improved outcomes as compared to ALV with respect to semen parameters and natural pregnancy rates. Therefore, all attempts should be made to preserve internal spermatic arteries (ISA) during varicolectomy in men with severe oligozoospermia.

**INTRODUCTION**

One in seven couples has difficulty conceiving with a male factor responsible in almost half of the cases. Varicocele is a recognized cause for impaired spermatogenesis and a potentially correctable cause for male factor infertility. They can affect up to 40% of men with primary and 80% of men with secondary infertility (Chiba & Fujisawa, 2016). Varicolectomy is now accepted as a cost-effective treatment in infertile men with clinically significant varicoceles and impaired semen parameters (EAU Guidelines 2017; Kroese *et al.*, 2012; Marmar *et al.*, 2007; French *et al.*, 2008).

More recently, varicolectomy has been reported to improve fertility potential in patients with severe oligozoospermia. A recent meta-analysis has demonstrated a strong trend toward improvements in natural pregnancy rate (PR) [OR = 1.69, 95%

CI (0.951, 3.020),  $p = 0.073$ ] and a statistically significant increase in live birth rates (LBR) [OR = 1.699, 95% CI (1.020, 2.831),  $p = 0.04$ ] following intervention. Varicolectomy has also been associated with a statistically significant increase in PR [OR = 2.3, 95% CI (1.022, 5.342),  $p = 0.044$ ] and LBR [OR = 2.2, 95% CI (0.994, 4.904),  $p = 0.05$ ] in men with non-obstructive azoospermia (Kirby *et al.*, 2016).

The impact of ligation of internal spermatic artery (ISA) during varicolectomy is controversial. The conventional view is that arterial ligation can negatively affect testicular function and decrease the likelihood of postoperative paternity (Chan *et al.*, 2005; Chiba & Fujisawa, 2016). However, a number of other investigators have reported that ligation of ISA is not associated with significant detrimental effects in postoperative semen parameters, testicular size, or PR in comparison to artery

preservation (Matsuda *et al.*, 1993; Yamamoto *et al.*, 1995; Salem & Mostafa, 2009). Moreover, laparoscopic artery-ligating varicocelectomy has been proven to be superior with respect to shorter operative time and lower recurrence rates with no difference in semen parameters or PR compared to laparoscopic artery-preserving varicocelectomy (Qi *et al.*, 2016).

Also, isolation of ISA may be difficult during subinguinal varicocelectomy due to compression of external oblique aponeurosis and its inherent anatomical variation. In fact in 29% to 57% of cases, the ISA is surrounded by an adjacent varicose 'network' of veins and adherent to nearby veins (Lee *et al.*, 2016). Thus, there is a substantial risk of accidental ligation of the ISA during subinguinal varicocelectomy.

It is therefore unclear in the literature if ligation of ISA has a deleterious effect on the fertility outcomes in patients with severe oligozoospermia. This prospective randomized study was conducted to assess the impact of ISA preservation/ligation during subinguinal varicocelectomy on fertility outcomes in patients with severe oligozoospermia.

## MATERIALS AND METHODS

### Patients

Patients with a clinical varicocele (grade II/III) and severe oligozoospermia (<5 million/mL) who attended an outpatient clinic seeking medical treatment for infertility were assessed for eligibility and inclusion in this study. The inclusion criteria were adult infertile patients (aged >18 years) with clinical varicocele (grade II and III), severe oligozoospermia, and the ability to provide written consent.

The exclusion criteria were men <18 years, recurrent varicocele, sperm concentration >5 million/mL, history of previous inguinal surgery, concomitant female factor infertility, and refusal to participate in the study.

### Study design

This prospective randomized blinded study was performed between January 2013 and November 2015. Patients who met the inclusion criteria were randomly assigned to undergo either artery-preserving varicocelectomy (APV) [group A] or artery-ligating varicocelectomy (ALV) [group B]. Independent randomization (in a 1:1 ratio) was conducted using a computer-generated random table with stratification according to APV or ALV. All patients provided written informed consent and were unaware of the randomization (Fig. 1).

### Ethics and IRB approval

Approval of our local ethical committee (R/17.06.13) was obtained, and the study was performed strictly according to the governance policies and regulations at our institution. Moreover, the trial was registered with ClinicalTrials.gov. (ID: NCT03344588).

### Intervention

In all patients, sub-inguinal varicocelectomy was performed under spinal anesthesia, by a single surgeon (KS), using a surgical microscope. A 2–3 cm pre-pubic incision was performed. The cord was grasped with a Babcock clamp and isolated over a vessel tape. Any external cremasteric veins were identified and ligated using vicryl 3/0. After opening the spermatic fascia, the

vasal compartment including the vasal and cremasteric arteries and the lymphatics were separated from the pampiniform plexus and preserved. In group A (APV), testicular arteries were spared with aid of intraoperative Doppler US (VTI intraoperative Doppler system 20 MHz). The arteries were carefully dissected with a micro-dissector, separated over a vessel loupe, and then the remaining veins were double-ligated using 3/0 vicryl. In group B (ALV), all vascular channels were double-ligated without identifying or sparing the internal spermatic arteries. At the end of the procedure, the spermatic fascia was closed.

### Patient assessment

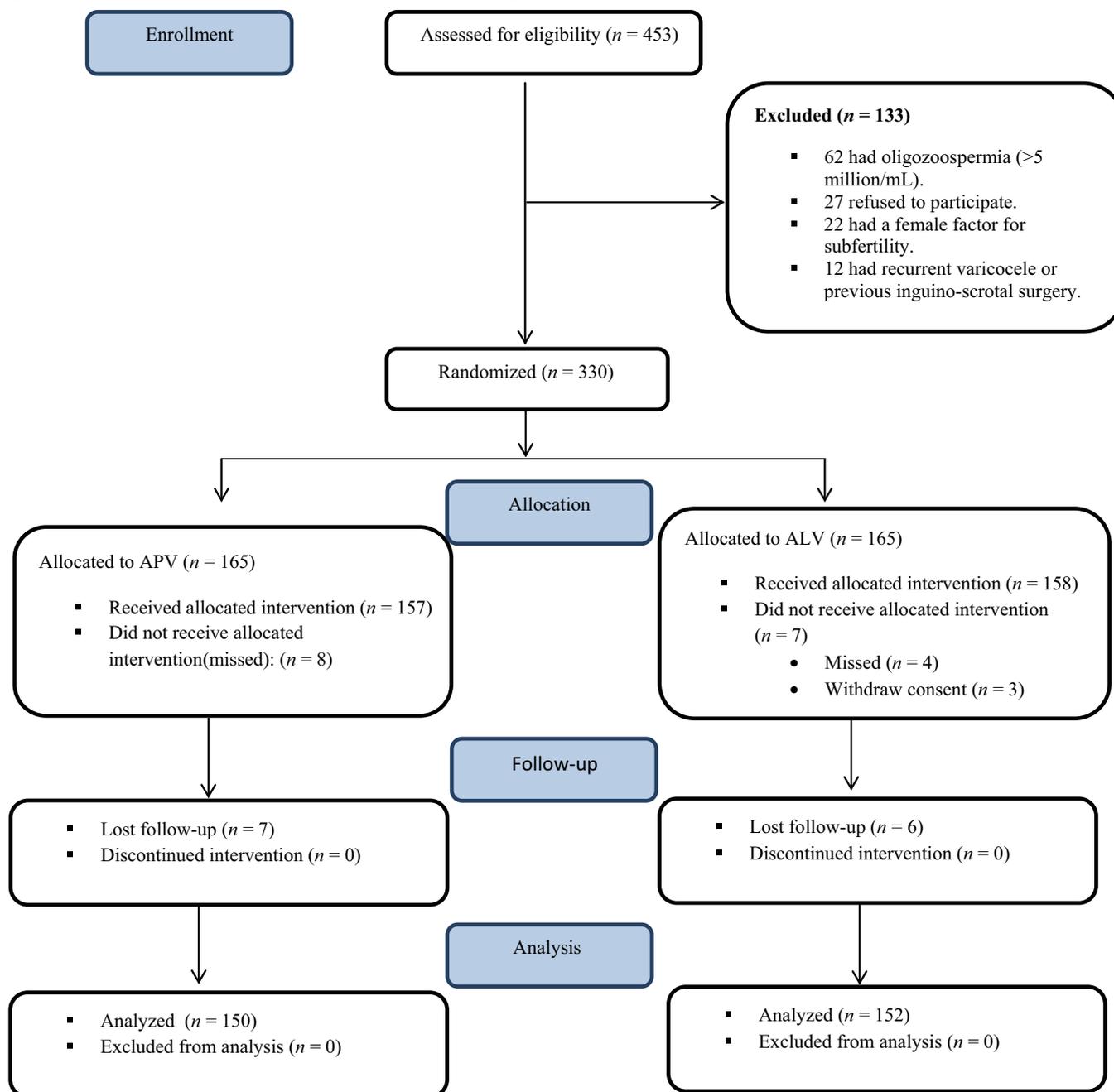
At baseline, all patients were evaluated with a full history including age, medical co-morbidities, and duration of infertility. A thorough physical examination documenting the side and grade of varicocele was performed. Varicoceles were graded according to Dubin and Amelar classification (Dubin & Amelar, 1988) Two baselines seminal analyses were performed according to 2010 WHO standard criteria with recommended abstinence period of 2–7 days (World Health Organization 2010) Sperm density and motility were recorded. In all patients, an inguino-scrotal duplex US was performed by a radiologist to confirm the clinical diagnosis of varicocele and to assess the testicular volume using the following formula:  $L \times W \times H \times 0.71$  (De Jonge, 2012). Operative time, hospital stay, and post-operative complications were also recorded. All patients were discharged on the same day of surgery. A semen analysis was performed at 3 and 6 months postoperatively. At 12 months, a follow-up visit was scheduled for evaluation of testicular volume by duplex US and face to face interview to assess natural pregnancy rates (PR).

### Outcomes

The primary outcome was to assess the changes in sperm density and motility at 3 and 6 months postoperatively in both groups. The secondary outcome was to compare the PR at 1-year follow-up.

### Statistical analysis

Assuming a type I statistical error of 5% and type II statistical error of 5%, we designed our study to have a power of 95%. Based on the results of previous studies, the expected difference between both groups with respect to sperm density improvement was 38% (Salem & Mostafa, 2009). The estimated dropout rate was calculated to be 10–20%. So, the sample size required to result in a significant difference was 165 patients in each arm. Primary analysis included all randomized patients and was conducted on the intention-to-treat basis. Comparison of the baseline value with end result was performed using a paired sample *t*-test. The difference between the two groups was assessed by repeated measure with ANOVA. A ROC curve was used to determine cut-off value of higher sensitivity and specificity for preoperative sperm density, motility, and testicular volume. Univariate and multivariate analyses were performed to identify preoperative and operative factors affecting PR. Univariate analysis was performed using the chi-square and Fischer exact test when indicated. Multivariate analysis was performed by logistic regression analysis. Statistical analysis was carried out using SPSS version 16 package (SPSS, Chicago, IL, USA), with a *p* value of <0.05 considered significant.

**Figure 1** CONSORT flow chart of enrollment and outcome. [Colour figure can be viewed at wileyonlinelibrary.com]

## RESULT

During the study period, 302 primary infertile male patients with mean  $\pm$  SD (95% CI) age of  $29.1 \pm 3.7$  (28.7–29.6) years were eligible for analysis. The mean  $\pm$  SD (95%CI) of female age was  $23 \pm 3.2$  (21.8–24.2) years. Figure 1 shows the CONSORT (Consolidated Standards of Reporting Trials) flow chart for enrollment and outcome. The study included 211 (70%) and 91 (30%) patients with left sided and bilateral varicoceles, respectively. Seventy percent had a grade III and 30% had a grade II varicocele. Median (IQ range) of FSH and LH was 7.5 (3.2–11) and 6.9 (3.2–8.5) IU/L, respectively. Median (IQ range) serum testosterone level was 11.3 (7.3–17) nmol/L. The median period of infertility was 3.5 (range 2–10) years. The mean  $\pm$  SD (95% CI) operative time was  $32.7 \pm 9.5$

(31.7–33.8) minutes with no intraoperative complications. The mean  $\pm$  SD (95% CI) hospital stay was  $6.6 \pm 1.1$  (6.48–6.71) hours. The two groups were comparable with regard to demographic data (Table 1).

The mean  $\pm$  SD (95% CI) sperm density increased from  $4.1 \pm 1.2 \times 10^6$  (4–4.21) to  $7.7 \pm 2.4 \times 10^6$  (7.5–8.02) ( $p < 0.001$ ) and  $10.9 \pm 3.5 \times 10^6$  (10.5–11.3) ( $p < 0.001$ ) after 3 and 6 months, respectively. Similarly, the mean  $\pm$  SD (95% CI) sperm motility increased from  $18 \pm 4.8\%$  (17.4–18.5) to  $25 \pm 4.2\%$  (24.6–25.57) ( $p < 0.001$ ) and  $39.2 \pm 8.1\%$  (38.4–40.2) ( $p < 0.001$ ) at 3 and 6 months, respectively. Overall, 69.4% and 54.4% of patients had more than a twofold increase in sperm density and motility after 6 months, respectively. The APV group had a statistically significantly greater

**Table 1** Demographic, biochemical, and operative characteristics of group A (APV) and group B (ALV) patients

	Group A (APV)	Group B (ALV)	<i>p</i> values
Age: Mean ± SD	29.3 ± 4.5	29 ± 2.7	0.4
Symptoms: No. (%)			
Subfertility	99 (66)	87 (57.3%)	0.1
Subfertility and pain	51 (34)	65 (42.7%)	
Grades of varicocele: No. (%)			
Grade II	45 (30%)	46 (30%)	0.9
Grade III	105 (70%)	106 (70%)	
Laterality: No. (%)			
Left	105 (70%)	106 (70%)	0.9
Bilateral	45 (30%)	46 (30%)	
FSH level: IU/L <sup>a</sup> : Median (IQ range)	7.7 (3.2–11)	7.2 (4.3–10.6)	0.9
LH level: IU/L <sup>b</sup> : Median (IQ range)	7.2 (4–8)	7.3 (3.2–8.5)	0.6
Testerone level: nmol/L <sup>c</sup> : Median (IQ range)	10.6 (7.3–17)	11 (8.2–16.7)	0.3
Duration of subfertility: Median (IQ range) in years	3.5 (2–10)	3.7 (2–9)	0.8
Operative time: Mean ± SD in minutes	35.7 ± 9.4	29.7 ± 8.6	<0.001
Hospital stay Mean ± SD in hours	6.7 ± 1.2	6.6 ± 1.1	0.9

ALV, artery ligation varicocelectomy; APV, artery-preserving varicocelectomy.

<sup>a</sup>Reference values was (1.5–12.4)IU/L. <sup>b</sup>Reference value was (1.7–8.6) IU/L.

<sup>c</sup>Reference value was (7.6–31.4) nmol/L.

**Table 2** Difference in semen parameters and testicular volume comparing groups A and B

	Group A (APV)	Group B (ALV)	<i>p</i> value <sup>c</sup>
Semen density: ( $\times 10^6$ /mL)			
Preoperative	4.1 ± 1.2	4.2 ± 1.1	0.4
3 months postoperative	8.4 ± 2.5	7.1 ± 2	<0.001
6 months postoperative	12.3 ± 3.7	9.5 ± 2.8	<0.001
<i>p</i> value <sup>a,b</sup>	<0.001, <0.001	<0.001, <0.001	
Sperm motility			
Preoperative	17.5 ± 4.6	18.5 ± 5	0.06
3 months postoperative	25.5 ± 3.5	24.6 ± 4.7	<0.001
6 months postoperative	43 ± 8.4	35.6 ± 5.9	<0.001
<i>p</i> value <sup>a,b</sup>	<0.001, <0.001	<0.001, <0.001	
Testicular size: (cm <sup>3</sup> )			
Preoperative	13.5 ± 0.44	13.6 ± 0.47	0.5
12 months postoperative	13.8 ± 0.3	13.7 ± 0.4	0.07
<i>p</i> value	0.001	0.08	

ALV, artery ligation varicocelectomy; APV, artery-preserving varicocelectomy.

<sup>a</sup>Comparison between preoperative and 3 months postoperative. <sup>b</sup>Comparison between preoperative and 6 months postoperative. <sup>c</sup>Comparison in changes in both groups.

improvement in sperm density and motility after 3 and 6 months postoperatively (Table 2). Ninety percent of the APV patients had a twofold increase in sperm density, compared to 48.8% of ALV group ( $p < 0.001$ ). Similarly, 70% and 38.8% had a twofold increase in sperm motility in APV and ALV groups, respectively ( $p < 0.001$ ).

Theoretically, the outcome of unilateral cases could be affected by contralateral testicular function. To eliminate this variable and consolidate our conclusions we performed a sub-analysis of the changes in semen parameters in bilateral cases in both groups (Table 3). Interestingly, sperm parameters improved to the same degree, compared to the overall analysis of both groups (Tables 2 and 3).

At 1-year follow-up, there were 106 (35.1%) natural pregnancies without the use of assisted reproductive technologies. Among those with improved ( $\geq 2$ -fold increase) sperm density and motility, 80/222 (36%) and 64/174 (36.8%) achieved natural

**Table 3** Difference in semen parameters and testicular volume changes among patients with bilateral varicocele in both treatment groups

	Group A (APV)	Group B (ALV)	<i>p</i> value <sup>c</sup>
Semen density: ( $\times 10^6$ /mL)			
Preoperative	4 ± 0.8	3.3 ± 1.7	0.01
3 months postoperative	7.1 ± 0.23	5 ± 2.1	<0.001
6 months postoperative	12 ± 2.1	6.7 ± 2.1	<0.001
<i>p</i> value <sup>a,b</sup>	<0.001, <0.001	<0.001, <0.001	
Sperm motility:			
Preoperative	16.6 ± 2.3	13.3 ± 2.3	0.01
3 months postoperative	23.3 ± 2.3	22.2 ± 5.2	<0.001
6 months postoperative	36.6 ± 6.3	31.8 ± 7.1	<0.001
<i>p</i> value <sup>a,b</sup>	<0.001, <0.001	0.01, 0.03	
Testicular size: (cm <sup>3</sup> )			
Preoperative	13.5 ± 0.41	13.3 ± 0.23	0.1
12 months postoperative	13.9 ± 0.3	13.6 ± 0.21	0.06
<i>p</i> value	0.01	0.04	

ALV, artery ligation varicocelectomy; APV, artery-preserving varicocelectomy.

<sup>a</sup>Comparison between preoperative and 3 months postoperative. <sup>b</sup>Comparison between preoperative and 6 months postoperative. <sup>c</sup>Comparison in changes in both groups.

pregnancy, respectively. Group A had a statistically significantly higher PR compared to group B (40% vs. 30%,  $p$  value = 0.03). There was no statistically significant difference in PR between APV and ALV subgroups who had improved sperm density (41% vs. 33.3%,  $p = 0.2$ ). However, there was a statistically significant difference in PR between APV and ALV subgroups with improved sperm motility (51% vs. 32%,  $p = 0.003$ ).

On univariate analysis, increased patient age ( $>29.1$  years), bilateral varicocele, lower preoperative sperm concentration ( $\leq 4.1 \times 10^6$ ), sperm motility  $\leq 18\%$ , testicular volume  $\leq 13.5$  cm<sup>3</sup>, and ALV were associated with lower PR (Table 4). On multivariate analysis, smaller testicular volume ( $\leq 13.5$  cm<sup>3</sup>) and ALV were associated with 3.2-fold risk of reduced natural pregnancy at 1-

**Table 4** Univariate analysis of factors affecting natural pregnancy rate in patients with severe oligozoospermia

	Spontaneous Pregnancy	No spontaneous pregnancy	<i>p</i> value
Age			
$\leq 29.1$ years	76 (48.7%)	80 (51.3%)	<0.001
$>29.1$ years	30 (18.9%)	128 (81.1%)	
Grade			
Grade II	30 (33.3%)	60 (66.7%)	0.3
Grade III	76 (35.8%)	136 (64.2%)	
Laterality			
Left	106 (50.2%)	105 (49.8%)	<0.001
Bilateral	0	91 (100%)	
Preoperative sperm count			
$4.1 \times 10^6$	46 (30.4%)	105 (69.6%)	0.03
$>4.1 \times 10^6$	60 (39.7%)	91 (60.3%)	
Preoperative sperm motility			
$\leq 18\%$	15 (11%)	121 (89%)	<0.001
$>18\%$	91 (54.8%)	75 (45.2%)	
Preoperative testicular size			
$\leq 13.5$ cm <sup>3</sup>	45 (24.8%)	136 (75.2%)	<0.001
$>13.5$ cm <sup>3</sup>	61 (50.4%)	60 (49.6%)	
Technique			
APV	60 (40%)	90 (60%)	0.03
ALV	46 (30%)	106 (70%)	
Partner age			
$<23$ years	63 (37.5%)	105 (62.5%)	0.3
$\geq 23$ years	49 (32.2%)	103 (67.8%)	

ALV, artery ligation varicocelectomy; APV, artery-preserving varicocelectomy.

year follow-up ( $p$  value (HR, 95% CI) of 0.01(3.2, 1.2–8.3) and 0.003 (3.2, 1.4–7.1), respectively).

After 12 months of follow-up, the mean (95% CI) testicular volume increased from 13.5 (13.4–13.6) to 13.8 (13.7–13.9)  $\text{cm}^3$  for ALV and from 13.6 (13.4–13.5) to 13.7 (13.67–13.77)  $\text{cm}^3$  for APV group with no statistically significant difference between both groups ( $p = 0.07$ ). With regard to complications, there were no cases of recurrence or testicular atrophy in the study groups. In the ALV group, one patient developed a moderate hydrocele and two patients developed azoospermia at last follow-up.

## DISCUSSION

Varicoceles are the most common surgically correctable cause of male infertility. They may have cumulative detrimental effects on testicular function via a number of different pathophysiological mechanisms, including increased intra-testicular temperature, hypoxia, accumulation of intra-testicular gonadotoxins, reflux of renal and adrenal toxic metabolites and anti-sperm antibodies. It has also been suggested that there is an association between varicocele and increased levels of intra-testicular reactive oxygen species, which results in oxidative damage, apoptosis, and reduced sperm quality due to cell membrane and DNA damage. This may lead to recurrent pregnancy loss from both natural conception and assisted reproductive technologies (ART) (Wang *et al.*, 2012; Pathak *et al.*, 2016).

Subinguinal varicocelectomy has been shown to improve semen parameters in 60–80% of men with a PR of 35.5–44.8% (Diegidio *et al.*, 2011). Moreover, ART outcomes have been shown to be higher with respect to PR (OR: 1.82, 95% CI: 1.06–3.15) and LBR (OR: 1.87, 95% CI: 1.08–3.25), as well as lower miscarriage rates (OR: 0.43, 95% CI: 0.22–0.84) (Esteves *et al.*, 2010).

It has been suggested that the efficacy of varicocelectomy is limited in patients with severe oligozoospermia and ART should be considered as the treatment of choice in this group of patients. However, in a prospective study evaluating 102 patients with severe oligozoospermia, 41.1% of men had an improvement in sperm density and motility. Moreover, natural pregnancy was achieved in 17.6% (Enatsu *et al.*, 2014). Furthermore, Ishikawa *et al.* reported improvement of sperm density in 31 of 54 patients with severe oligozoospermia after varicocelectomy (Ishikawa *et al.*, 2008). In addition, it was also reported that varicocelectomy in these patients improved the outcomes from ART. In this present study, repair of varicocele significantly improved the sperm density and motility in 69.4% and 54.5% of patients with severe oligozoospermia and 106 (35.1%) achieved natural pregnancy within one year; thus supporting the role of varicocelectomy in men with severe oligozoospermia.

Postoperative evaluation of sperm density and motility was undertaken at 3 and 6 months according to the recommendations of American Society of Reproductive Medicine (ASRM) in terms of the expected time frame to detect improvement in semen parameters (Practice Committee of the American Society for Reproductive Medicine, 2014). It should be noted that PR in the present study is much higher in comparison to those previously reported. This difference could be attributed to the younger female partner's age and higher preoperative sperm density in the current study. Enatsu *et al.* similarly studied the effect of microsurgical varicocelectomy in infertile men with severe oligozoospermia with a 16.7% PR. Only preoperative sperm

concentration appeared to be independently related to varicocelectomy outcome on multivariate analysis (Enatsu *et al.*, 2014).

The effect of testicular ischemia was previously reported by Silber *et al.* who found a significant detrimental effect on the germinal epithelium, whilst Sertoli and Leydig cells seemed to be resistant to ischemia (Silber, 1979). However, testing this in a particular cohort of patients with severe oligozoospermia, who may be more sensitive to ischemic changes, is lacking and was the rationale behind this study.

A number of technical refinements have been described to improve the efficacy and safety of varicocelectomy. Whilst they have been extensively used in clinical practice and proven to be efficacious, none of these modifications is without complications (Marmar, 2016). Although preservation of ISA during varicocelectomy is a controversial issue, it has become an integral part of microsurgical subinguinal varicocelectomy (Lee *et al.*, 2016). Yet, attempt of ISA preservation is usually challenging especially in subinguinal approach for many reasons. Firstly, the artery usually branches at the level of inguinal canal and multiple arteries are found to be present in 39–58% of patients during subinguinal varicocelectomy (Lee *et al.*, 2016). Secondly, arterial pulsations may be masked at this level due to compression on the artery by the edge of the external ring. Thirdly, there is a dense adherent network of veins to the artery at the subinguinal level. In this study, identification and dissection of the ISAs was facilitated with the use of intraoperative Doppler.

Herein, ISA preservation was associated with significantly longer operating time ( $p < 0.001$ ). Similarly, Yamamoto *et al.* (1995) reported that the mean operative time was  $17.2 \pm 3.2$  min for ALV and  $42 \pm 2.5$  min for APV ( $p < 0.02$ ).

Although both groups showed a statistically significant improvement in sperm density and motility at 3 and 6 months postoperatively, the improvement was significantly higher in APV group. In a prospective randomized study, Matsuda *et al.* (1993) reported no significant difference in density or motility between both groups. Similarly, in a previous retrospective study, ALV outcome was comparable to APV (Salem & Mostafa, 2009). In contrast, Yamamoto *et al.* (1995) reported improved sperm density in APV, although there was no statistically significant difference in sperm motility. It should be noted that these previous studies were underpowered and there was considerable heterogeneity in preoperative semen parameters.

In the present study, ALV was associated with statistically lower PR. However, in a recent meta-analysis, there was no difference in PR (RR = 0.95; 95% CI 0.65–1.40;  $p = 0.809$ ) between both groups. However, most of the studies included in the analysis were retrospective with a small number of patients and heterogeneity in preoperative sperm density (Qi *et al.*, 2016).

Interestingly, ALV was not associated with a reduction in testicular volume after 12 months of follow-up. In fact, there was marginal increase in testicular volume. Similarly, a number of authors have reported that intentional or accidental ligation of ISA was not associated with significant changes in testicular volume compared to artery preservation. This could be explained by the presence of collateral arterial flow to the testes via the vasal and cremasteric arteries (Matsuda *et al.*, 1993; Yamamoto *et al.*, 1995; Salem & Mostafa, 2009).

In this series, testicular volume and the technique of varicocelectomy were independent predictors of pregnancy

outcome. Larger testicular volume and APV were associated with higher PR. Enatsu *et al.*, (2014) demonstrated that preoperative sperm density and laterality of varicocele were independent predictors of outcome following varicocelectomy. Additionally, Kiuchi *et al.*, (2005) reported that the grade of varicocele, sperm motility, and FSH levels were independent predictors of outcome. However, the sample size in that study was relatively small compared to the present study, whilst study design was retrospective and azoospermic patients were also included.

To the best of our knowledge, this is the largest randomized prospective study that assesses the outcome of varicocelectomy in infertile men with severe oligozoospermia and compares APV to ALV in this specific cohort of patients. It provides an evidenced-based rationale for attempting ISA preservation during microsurgical varicocelectomy.

This study has a number of limitations. Firstly, we did not report on sperm morphology or progressive-only motility although it has been suggested that total motile count may be a better comparative indicator of fertility potential (Wang *et al.*, 2012). Also, the postoperative hormonal profile was not assessed because the preoperative values were within normal ranges. However, postoperative measurements may have provided a more objective indicator of postoperative testicular ischemia. Moreover, the impact of varicocelectomy techniques on the outcome of ART in patients not achieving spontaneous pregnancy was not evaluated.

## CONCLUSION

In patients with severe oligozoospermia, APV is associated with better postoperative sperm parameters and natural pregnancy outcomes compared to ALV. Therefore, all attempts should be made to preserve ISA during varicocelectomy in this particular group of patients.

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## CONFLICT OF INTEREST

Authors have no conflict of interest to disclose.

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