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ORIGINAL PAPER

Intraoperative hydrodissection and Doppler ultrasound during magnified varicocelectomy: A comparative study

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Summary

Methods: *We performed a non-randomized comparative trial that recruited infertile men with varicocele who were scheduled to undergo MSV. Eligible patients were allocated by the investigators in a 1:1 ratio to receive intraoperative Doppler (group I) or intraoperative Doppler plus hydrodissection (group II).*

Results: *Sixty men were included in each group. The two study groups showed a comparable number of ligated veins on the right (4.22 ±1.57 versus 4.42 ± 1.65; p = 0.49) and left side (6.77 ± 2.14 versus 6.98 ± 2.29; p = 0.59). On the contrary, group II showed a significantly higher number of preserved arteries on the right (2.42 ± 0.56 versus 1.47 ±0.5 in group I) and left side (2.6 ± 0.53 versus 1.63 ± 0.55 in group I), with p-value < 0.001. The sperm motility was significantly higher in group II than in group I (21.25 ± 13.73 versus 13.85 ± 12.25, respectively; p = 0.002). In both groups, the sperm motility increased significantly at the end of follow-up compared to the preoperative period. The postoperative sperm mortality remained significantly higher in group II than in group I (p = 0.008).*

Conclusions: *Intraoperative Doppler plus hydrodissection (D+IH-MSV) has advantages in preserving more arteries and enhancing the motility of sperms. Based on these findings, we strongly recommend D+IH-MSV when treating infertile men with varicocele.*

KEY WORDS: *Intraoperative Doppler; Hydrodissection; Magnified subinguinal varicocelectomy; Infertility; Varicocele.*

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INTRODUCTION

Varicoceles is one of the main risk factors of male infertility, which is present in both primary and secondary infertility, with an estimated prevalence of 50% and 81%, respectively (1). Varicocelectomy is the main procedure for treating varicoceles, resolving testicular pain, increasing spontaneous pregnancy rates, and improving semen parameters (2). Successful varicocelectomy should maintain the vas deferens, spermatic arteries and lymphatics and interrupts the retrograde backflow through the pampiniform plexus of veins, which increases the spontaneous pregnancy rate. Besides, varicocelectomy aims to preserve the perivasal veins for venous outflow (3). Regarding improving spontaneous pregnancy, many studies have demonstrated that magnified varicocelectomy is the most effective procedure with undetectable complication rates, whether it was *magnified inguinal* (MIV) or subinguinal varicocelectomy (MSV) (4, 5). The magnified subinguinal varicocelectomy might preserve more arteries and veins than the magnified inguinal varicocelectomy. However, it raises the operation's complexity and the risk of artery damage (6).

It was observed that antegrade flow during magnified subinguinal varicocelectomy and pulsatile movement could help visualize the main spermatic artery; however, it can be difficult for various reasons, including differences in anatomic architecture and blood pressure that can be low to be able to detect pulsatile movement (7). Although papaverine droplets are applied to enhance arterial pulsation, vigorous manipulation of the arteries during dissection might cause spasms, making it challenging to identify arterial pulsation (8). Furthermore, arteries are often found near to or buried beneath complex venous branching, requiring the development of a technology that can adequately detect these small arteries. To our knowledge, only a few studies have used intraoperative vascular Doppler ultrasound-assisted magnified subinguinal varicocelectomy (IVDU-MSV), which enhanced accurate visualization and preservation of arteries and veins (7, 9). In this trial, we compared the fertility and postoperative outcomes of combining intraoperative Doppler and hydrodissection, versus intraoperative Doppler alone in infertile men with varicocele undergoing magnified subinguinal varicocelectomy.

MATERIALS AND METHODS

The local ethics committee approved the protocol of the current trial of *Faculty of Medicine for girls, Al-Azhar University* (FMG-IRB) met at *Faculty of Medicine for Girls, Nasr City, Cairo, Egypt* (Study ID 894). Then, written informed consent was obtained from all participants. All procedures run in compliance with the standards of the Declaration of Helsinki (10).

Study design and patients

We performed a non-randomized comparative trial that recruited consecutive infertile men with varicocele who were scheduled to undergo magnified subinguinal varicocelectomy at *Al-Azhar University Hospitals* through the period from December 2018 to August 2021. Men were considered eligible if aged more than 18 years old and had a confirmed history of primary infertility due to unilateral or bilateral primary varicocele. The diagnosis of

varicocele was based on the findings of a Duplex scan of the scrotal region and classified according to *Sarteschi* (1). We excluded patients with painful varicocele, recurrent cases, history of inguinal or scrotal surgery, the co-existence of hydrocele, and/or the presence of technical difficulties in performing selective ligation of veins or preservation of arteries due to excessive fat content in the cord or cord lipoma that prevent proper dissection or occurrence of injured vessels during dissecting and hematoma formation that cause indistinct visualization. Cases that we failed to separate the spermatic artery from adjacent veins due to anatomic architecture were excluded as well. Eligible patients were allocated according to the investigator's decision in a 1:1 ratio to receive magnified intraoperative Doppler alone (group I) or intraoperative Doppler, and hydrodissection (group II).

Study's procedures and follow-up

All patients were assessed preoperatively and underwent preoperative semen analysis, which was performed after ≥ three days of abstinence. The semen analysis was performed using the *World Health Organization* (WHO) guidelines (12). The samples were collected through masturbation in a sterile container; only non-spermicidal lubricants were allowed. Samples were kept at 20-37°C until liquefaction. Macroscopic examination was performed to assess the semen characteristics, followed by microscopic examination on a fixed cell counting chamber. In case of abnormal semen analysis, another sample was collected after one month for confirmation.

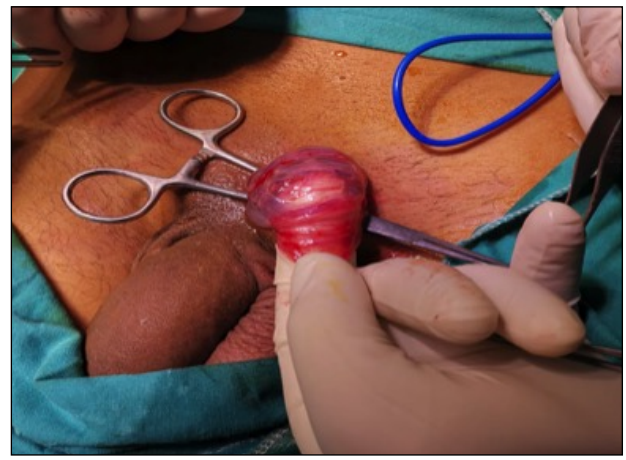
The same surgeon performed all procedures. Patients underwent spinal or general anesthesia according to the surgeon and anesthetist decision. Then, a three-cm skin incision was conducted over the external inguinal ring transversely. This incision dissected the *Camper*'s and *Scarpa*'s fascias to reach the spermatic cord, which was situated over a Penrose drain using a Babcock forceps. An 8-15x microscope was employed to identify all dilated veins. These veins were tied by 4-0 or 5-0 vicryl sutures according to size of ligated veins and sparing the artery with assistance of Doppler during the operation (Group I). In group II Doppler and hydrodissection were employed to identify the pulsating arteries using saline injection introduced directly in the cord by syringe without needle (Figures 1, 2). Following the incision of spermatic fascia, the vas deferens and its vessels were examined and suited in the posterior fascial compartment to create a window between vas and vessels using the Penrose drain or forceps. We made another window between the internal spermatic vessels and the external spermatic fascia and its structures. The saline injection was introduced again to this a window created to separate the vessels from each other (Figure 3). The internal spermatic arteries were then freed from the surrounding veins and irrigated with diluted warm papaverine; the surrounding veins were ligated by 3-0 vicryl, sparing the internal spermatic artery and lymphatic vessels.

We closed the fascia, subcutaneous tissue and the skin using 2-0 Vicryl sutures and subcuticular 4-0 Proline or 3-0 Vicryl, respectively. The incision was infiltrated with 0.5% Marcaine solution with epinephrine, and a dry sterile dressing was applied.

Figure 1.
Technique of hydrodissection (direct injection of saline in the cord).

Figure 2.
The spermatic cord after saline injection.

Figure 3.
The cord after hydrodissection.



Study's outcomes

The primary outcome of the present study was the impact of employing intraoperative Doppler and Hydrodissection on the number of ligated veins and preserved arteries among men undergoing MSV. The secondary outcomes of this study included the incidence of postoperative complications and semen analysis findings. The patients were followed up every three months for one year after the operation. The postoperative semen analysis was performed six months after surgery.

Statistical analysis

Retrieved data were summarized and processed with IBM SPSS statistical software (version 25). Frequencies were used to describe varicocele grade and postoperative complications. On the other hand, age, semen analysis findings, number of ligated veins, number of preserved arteries, duration of surgery, and hospital stay were summarized, according to normality, into mean (± *standard deviation* [SD]) or median (range) values. The hypothesis of significant differences between the type of procedures and primary or secondary outcomes was challenged using the independent t-test or Chi-square test for continuous and categorical data. Within group comparison was done using paired t-test. P-value < 0.05 was regarded as statistically significant.

Results

Sixty men were included in each group. The mean age of the patients was comparable between the intraoperative Doppler group (group I) and Doppler plus intraoperative hydrodissection group (group II) (29.52 ± 5.48 versus 29.42 ± 4.64, respectively; p = 0.91). On the right side, the most commonly encountered varicocele grade was II (58.3% and 53.3% in group I and II, respectively; p = 0.88). However, on the left side, grade III was the most common subtype in group I (50% compared to 41.7% in group II) (p = 0.081) (Table 1).

The operative time was significantly longer in group II (65.62 ±15.1 minutes) than in group I (35.18 ± 11.6; p < 0.001). Concerning the number of ligated veins, the two study groups showed a comparable number of ligated veins on the right (4.22 ± 1.57 *versus* 4.42 ± 1.65; p = 0.49) and left sides (6.77 ± 2.14 *versus* 6.98 ± 2.29; p = 0.59). On the contrary, group II showed a significantly higher number of preserved arteries on the right (2.42 ± 0.56 versus 1.47 ± 0.5 in group I) and left sides (2.6 ± 0.53 versus 1.63 ± 0.55 in group I), with p-value < 0.001. Two patients (3.3%) in group I showed recurrent varicocele and hydrocele respectively, compared to no patients in group II (p = 0.24 for both). There were no cases of testicular atrophy in both groups (Table 2).

In addition, group I and II showed statistically significant increases in the sperm count at the end of follow-up, compared to the preoperative period (from 9.88 ± 4.77 to 35.22 ± 36.22 and from 11.07 ± 5.04 to 29.73 ± 27.62, respectively; p = 0.014 and 0.009, respectively).

However, there were no significant differences between the two groups concerning both pre and postoperative sperm count (p = 0.189 and 0.35). Group I and II showed statistically significant increases in the sperm normal morphology at the end of follow-up, compared to the preoperative period (p = 0.001), with no significant differences between both groups. Preoperatively, the sperm motility was significantly higher in group II than group I (21.25 ± 13.73 versus 13.85 ± 12.25, respectively; p = 0.002). This trend was consistent during the postoperative period (p = 0.008). In both groups, the sperm motility increased significantly at the end of follow-up compared to the preoperative period (Table 3).

Table 1.
Comparison of preoperative characteristics of the study groups.

Parameters		Group		P-value *
		D (= 60)	D + IH (n = 60)	
Age	Mean ± SD	29.52 ± 5.48	29.42 ± 4.64	0.91
Grade (right) **	0	4 (6.7%)	3 (5%)	0.88
	I	18 (30%)	21 (35%)	
	II	35 (58.3%)	32 (5.3%)	
	III	3 (5%)	4 (6.7%)	
Grade (left)	0	0	0	0.081
	I	4 (6.7%)	4 (6.7%)	
	II	25 (41.7%)	31 (51.7%)	
	III	30 (50%)	25 (41.7%)	

*D: Doppler; IH: intraoperative hydrodissection; SD: Standard deviation. * Chi-square test. ** Based on Sarteschi (11).*

Table 2.
Comparison of intra and postoperative characteristics of the study groups.

Parameters		Group		P-value *
		D (= 60)	D + IH (n = 60)	
Operative time in minutes	Mean ± SD	35.18 ± 11.6	65.62 ± 15.1	< 0.001
Ligated veins (right)	Mean ± SD	4.22 ± 1.57	4.42 ± 1.65	0.49
Ligated veins (left)	Mean ± SD	6.77 ± 2.14	6.98 ± 2.29	0.59
Preserved arteries (right)	Mean ± SD	1.47 ± 0.5	2.42 ± 0.56	< 0.001
Preserved arteries (left)	Mean ± SD	1.63 ± 0.55	2.6 ± 0.53	< 0.001
Hospital stay in days	Mean ± SD	1	1	N/A
Recurrent varicocele	No. (%)	2 (3.3%)	0	0.24
Atrophy	No. (%)	0	0	N/A
Hydrocele	No. (%)	2 (3.3%)	0	0.24

*D: Doppler; IH: intraoperative hydrodissection; SD: Standard deviation. * Chi-square test.*

Table 3.
Changes in the semen analysis parameters in the study groups.

Parameters		Group		P-value *
		D (= 60)	D + IH (n = 60)	
Count (million per milliliter)	Pre-operative	9.88 ± 4.77	11.07 ± 5.04	0.189
	Post-operative	35.22 ± 36.22	29.73 ± 27.62	0.35
P-value **		0.014	0.009	
Morphology (%)	Pre-operative	17.25 ± 17.7	12.27 ± 9.93	0.06
	Post-operative	31.65 ± 24.27	26.55 ± 18.92	0.22
P-value		0.001	0.001	
Motility (%)	Pre-operative	13.85 ± 12.25	21.25 ± 13.73	0.002
	Post-operative	29.98 ± 9.57	35.18 ± 11.57	0.008
P-value		< 0.001	0.004	

*D: Doppler; IH: intraoperative hydrodissection; SD: Standard deviation. * Mann-Whitney U test. ** Wilcoxon signed-rank.*

Discussion

Varicocele repair appears to improve seminal parameters and to aid infertile couples in achieving spontaneous conception, according to current evidence. This disease has been treated with various open surgical methods, including retroperitoneal, MIV, and MSV (13). Based on the previous literature, there was no significant difference

between these methods in terms of improving fertility; however, they have different recurrence rates and potential complications (14). In addition, hypoxia produced by artery damage during the surgery disrupts energy metabolism, leading to spermatogenesis injury (15).

Consequently, several attempts have been made to reduce complication and recurrence rates following the surgery, allowing for better preservation of the testicular artery and lymphatic arteries and reduced incidence of hydrocele (16, 17). Furthermore, even without testicular atrophy, ligation of the testicular artery can compromise the seminiferous tubules; thus, a dissection approach that preserves the spermatic artery and all branches is preferable (9).

This study introduced a new technique by making another window between the internal spermatic vessels and the external spermatic fascia and its structures, which allowed us to separate the vessels from each other after injecting the saline. The internal spermatic arteries were then freed from the surrounding veins and irrigated with diluted warm papaverine; the surrounding veins were ligated by 4-0 & 5-0 vicryl, sparing the internal spermatic artery and lymphatic vessels. By comparing the outcomes of the procedure in both groups, *Doppler* (D) and *Doppler+hydrodissection* (D+IH), our findings showed that the mean age of the patients was comparable between both groups. Varicocele grade II was the most common in the right side, while grade III was the most common in the left side. The operative time was significantly longer in the D+IH group than in the D group ($p < 0.001$). There were no significant differences between both groups in terms of ligated veins, sperm count, sperm morphology; however, the D+IH group was associated with higher preserved arteries and sperm motility than the D alone ($p < 0.001$ and $p = 0.008$), respectively.

Guo et al. (7), conducted a randomized trial to compare between magnified subinguinal varicocelectomy and *intraoperative vascular Doppler ultrasound* assissted (IVDU) magnified subinguinal varicocelectomy in infertile males with varicoceles. Their findings showed that intraoperative vascular Doppler ultrasound reduced the operative time by about 10 minutes compared with the classic magnified subinguinal varicocelectomy ($p < 0.05$), which differs from our findings. In addition, they observed that the number of preserved arteries and spermatic veins ligated was significantly higher in the intraoperative vascular Doppler ultrasound group than in the classic microsurgical subinguinal varicocelectomy group ($p < 0.05$). These findings can be explained by the precise identification of small veins using IVDU. Some reports showed that IVDU helps remove more veins that were adherent as a dense complex to arteries. *Shindel et al.* (18), demonstrated that the total number of veins ligated was significantly and positively correlated with improvements in total sperm motility, indicating that ligating a larger number of veins should result in a more significant reduction in the reflux of warm blood and/or toxic substances, resulting in less insult to spermatogenesis. In terms of sperm motility and concentration, *Guo et al.* demonstrated that IVDU-microsurgical subinguinal varicocelectomy was more efficient than the classic microsurgical subinguinal varicocelectomy ($p < 0.05$). A recent systematic review showed that microsurgical varicocelectomy significantly improves spermatogenesis as reflected by biomarkers of infertile men including semen parameters and sperm DNA fragmentation (19). On the other hand, there was no significant difference between both groups in terms of preserved lymphatics and sperm morphology. These findings align with the findings of many meta-analyses, which indicated that varicocelectomy could considerably enhance seminal parameters.

In the study conducted by *Cocuzza et al.*, they found that there was no significant difference between IVDU-MSV and MSV ($p = 0.37$). Besides, the number of injured arteries and preserved lymphatics was comparable in both groups ($p = 0.06$ and $p = 0.21$), respectively. On the other hand, the number of arteries preserved, and veins ligated was significantly higher in the IVDU-MSV group than in MSV group ($p < 0.01$ and $p = 0.02$), respectively (9).

Hydrocele formation after varicocelectomy in adolescents has not been thoroughly studied. The frequency of post-varicocelectomy hydrocele varies significantly, with rates as high as 39% in individuals who had ligation at internal inguinal ring (20). A range of 3.1% to 13% has been observed in previous investigations, with more significant ligation causing more hydroceles (21). IH of the spermatic cord lymphatics during varicocelectomy, according to *Atteya et al.* (22), is a simple method that permits precise separation of the spermatic cord veins from its lymphatics, lowering the risk of post-varicocelectomy hydrocele development.

We acknowledge that this study has some limitations, including the relatively small size, single center-based, and short follow-up period; however, this is the first study that combined D with MSV and compared its outcomes with the IVDU+IH-MSV. The fact that preoperative motility in group II was significantly higher than in group I is another limitation.

Conclusions

In conclusion, our findings suggested that both D-MSV and D+IH- MSV are effective methods for improving spermatic parameters in patients with varicocele, with a natural conception rate of 41.7% 46.7%, respectively. In addition, D+IH-MSV has advantages in preserving more arteries and enhancing the motility of sperms. Based on these findings, we strongly recommend D+IH- MSV when treating infertile men with varicocele.

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Conflict of interest: The authors declare no potential conflict of interest.