Comparison of Antisperm Antibody levels following totally extraperitoneal inguinal hernia repair and Lichtenstein hernia repair.

A randomized controlled trial

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Ömer Özduman*, Tolga Dinç**, Ilgaz Kayilioğlu***, Esin Çalci****, Faruk Coşkun**

**Department of Gastrointestinal Surgery, Kartal Kosuyolu Yüksek Ihtisas Training and Research Hospital, Istanbul, Turkey*
***Department of General Surgery, Health Sciences University, Ankara City Hospital, Ankara, Turkey*
****Department of General Surgery, Sitki Koçman University, Muğla, Turkey*
*****Uşak Public Health Laboratory, Uşak, Turkey*

Comparison of Antisperm Antibody levels following totally extraperitoneal inguinal hernia repair and Lichtenstein hernia repair. A randomized controlled trial.

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PURPOSE: *We compared laparoscopic totally extraperitoneal (TEP) hernia repair and open Lichtenstein hernia repair (LHR) in terms of Antisperm Antibody Levels (ASA), pain, operative times, return to work times, hernia recurrence, and postsurgery complications.*
METHODS: *The patients were randomly divided into two groups as LHR and TEP. Blood samples were obtained for analysis of levels of ASA. Postoperative pain scores were assessed on the first day after repair using the Visual Analog Scale (VAS), and hernia recurrence, operation times, return to work times, and early and late postoperative complications were recorded.*
RESULTS: *Sixty male patients enrolled in the study. All patients were negative for ASA presurgery. ASA were detected in two patients in the LHR group postsurgery. The VAS score of the patients in the TEP repair group was significantly lower than that in the LHR group (median: 4.0 vs. 6.0) (p <0.001). The mean operation time in the TEP hernia repair group (50 min) was significantly longer than that in the LHR group (40 min) (40.0) (p <0.011). The median return to work time in the TEP hernia repair group (7 d) was significantly shorter than that in the LHR group (15 d)(p <0.001). There was no statistically significant difference between the two methods in terms of ASA,recurrence, or postoperative complications (p> 0.05).*
DISCUSSION: *Many studies have compared the superiority of different inguinal hernia repair methods. Which*
CONCLUSION: *It is not possible to determine the superiority of concerning technics in reducing infertility after surgery. TEP inguinal hernia repair is superior to LHR in in terms of postoperative pain and return to work times.*

KEY WORDS: Lichtenstein, Antisperm antibody, İnfertility, Inguinal hernia, Totally extra peritoneal repair

Introduction

Inguinal hernia repair is a common surgical operation worldwide. Despite the frequency of such surgery in general surgical practice, the long-term effect of the surgery on infertility remains unclear. Spermatic cord damage and deterioration of the blood–testicular barrier lead to the generation of antisperm antibodies (ASA) and are responsible for infertility in men after hernia operations. Antisperm antibodies (ASA) prevent basic conception-related events, such as the acrosome reaction, involvement of sperm to the cervical mucus, and binding to the ovum [1]. ASA also affect sperm hypomotility [1], and 10% of infertile men test positive for ASA [2]. In previ-

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Correspondence to: Tolga Dinc, MD, 1424 Cad, 25/24 Çukurambar, Çankaya, Ankara, Türkiye (e-mail: tolga_dr@hotmail.com)

ous research, sperm motility and sperm counts were lower in men with ASA than in men without ASA [3].
The aim of this study was to assess the superiority of laparoscopic totally extraperitoneal (TEP) hernia repair versus open Lichtenstein hernia repair (LHR), with superiority assessed in terms of autoimmunity (i.e., levels of ASA), postoperative pain, operative durations, return to work times, hernia recurrence, and early and later complications of surgery.

Methods

This was a prospective randomized comparison study. The study was approved by the local ethics committee (E-16-1019/10.08.2016). Consecutive male patients with inguinal hernias who were admitted to the Ankara Numune Training and Research Hospital for surgery between September 2015 and January 2017 were enrolled in the study. Written informed consent was obtained from all the patients.
Patients who agreed to participate in the study were divided into two groups using a randomization table generated by randomization software: a laparoscopic totally extraperitoneal (TEP) hernia repair group and an open Lichtenstein hernia repair (LHR) group. Randomization was performed using a computerized program of numbers according to the stratified randomization method. The proportion of patients aged 20–30, 40–50, and 50–60 y was the same in the two surgery groups. All the surgeries were performed by general surgery specialists.
Serum levels of ASA were measured in both groups preoperatively and 6 mo after surgery. Presurgery, a detailed anamnesis was taken from all the patients, and all the patients underwent a detailed physical examination. The patients underwent physical examinations again 10 d, 6 mo, and 2 y postsurgery. At the follow-ups, the return-to-work times of the patients were recorded, as well as data on early complications, such as seromas, infections, and pain, and late complications (e.g., relapse, chronic pain, and numbness) after surgery.
Approximately 4 cc of venous blood was taken from the forearm of each patient on the day before surgery and 6 mo postsurgery to determine the levels of ASA. The venous samples were collected in a serum separator tube, centrifuged, and then placed in Eppendorf tubes and stored at -80° C until analyzed. Prior to the analysis, the samples were brought to room temperature, approximately -21° C. The levels of ASA were determined using a qualitative method (an immune fluorescence assay [IFA]). The results were evaluated as negative or positive. The Visual Analogue Scale (VAS) was used to assess postoperative pain at least 12 h after the last analgesic use on the first postoperative day. The patients were asked to mark their pain level on a scale of 1–10, and the values were recorded.

Inclusion and Exclusion Criteria

Male patients aged between 20 and 60 y with inguinal hernias were included in the study. Patients outside this age range, patients unwilling to accept the treatment allocation after randomization, patients with scrotal or incarcerated hernias, and patients with medical conditions that precluded either of the treatment methods to randomization were excluded from the study. Patients with a history of any hernia surgery or surgery involving the inguinal region, pelvic trauma, prostatitis, and sexually transmitted or autoimmune diseases were also excluded. In addition, patients unable to take part in the postoperative follow-ups and those in whom general anesthesia was contradicted were excluded.

Statistical Analysis

The SPSS 15.0 program (SPSS Inc. in Chicago) was used in the analysis of the data. To determine whether the data had a normal distribution, histogram graphics and the Kolmogorov–Smirnov test were used. Descriptive data are presented, along with the mean, standard deviation, and median values. Data without a normal distribution were evaluated using Mann-Whitney U and Kruskal-Wallis tests. Pearson's, chi-square, and Fisher's exact tests were used when making comparisons in categorical eyes. In all tests, a p value of <0.05 was considered statistically significant.

Results

Sixty patients were included in the study, with 32 patients were in the TEP hernia repair groups and 28 in the LHR group. The mean age of the patients was 42.0 ± 11.4 y, the mean operation time was 52.7 ± 25.6 min, the average postoperative first day VAS score was 5.0 ± 1.7, and the average return to work time was 10.7 ± 5.3 d. The rate of hernia recurrence was 3.3% (n = 2).
ASA were not detected in any of the patients prior to the surgery. After the surgery, ASA were detected in two (3.3%) patients in the LHR group and no patients in the TEP hernia repair group. In the TEP hernia repair group, a seroma was detected in two (6.25%) patients as an early complication of surgery. In this group, a cystic lesion on the spermatic cord occurred in one (3.13%) patient, and continuing numbness in the inguinal region occurred in one (3.13%) case. In the TEP hernia repair group, 12.5% of patients experienced complications (early and late). In the LHR group, only 1 (3.5%) patient developed a seroma. No other complications were observed in the LHR group.
The postoperative first day VAS score (median: 4.0) was significantly lower in the TEP group as compared to that in the LHR group (median: 6.0) (p < 0.001) (Fig. 1).

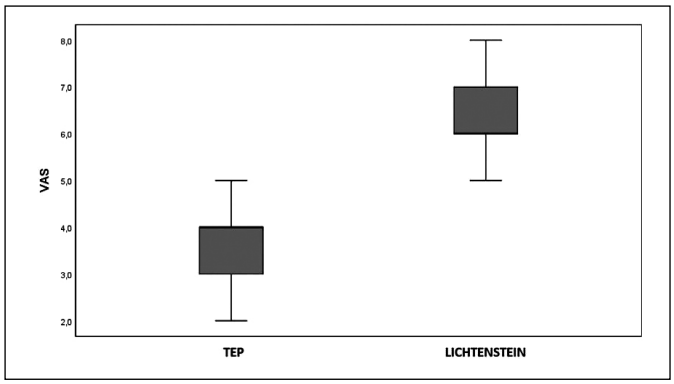

Fig. 1: Distribution of Po1 VAS values in TEP and Lichtenstein groups.

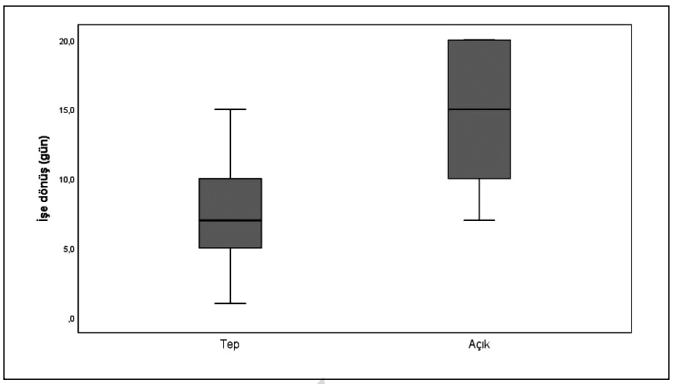

Fig. 2: Distribution of patients' back to work times in TEP and Lichtenstein groups.

TABLE I - *Patients' characteristics among TEP and Lichtenstein groups.*

		TEP		Lichtenstein		
		n	%	n	%	P value
Age*		42.8 ±12.3	45.0	41.1 ±10.5	45.5	0.4192
Po1 VAS*		3.7 ±1.0	4.0	6.4 ±1.1	6.0	<0.0012
Operation Duration (min)*		58.8 ±26.1	50.0	45.7 ±23.7	40.0	0.0112
Back to work (days) *		7.1 ±2.7	7.0	15.0 ±4.4	15.0	<0.0012
Recurrence	No	31	(96.9)	27	(96.4)	>0.9991
	Yes	1	(3.1)	1	(3.6)	
Hernia	Indirect	27	(84.4)	23	(82.1)	0.9301
	Direct	2	(6.3)	2	(7.1)	
	Combined	1	(3.1)	0	(.0)	
	Bilateral	2	(6.3)	3	(10.7)	
Hernia**	Indirect	27	(84.4)	23	(82.1)	>0.9991
	Others grouped	5	(15.6)	5	(17.9)	
Postoperative ASA	Negative	32	(100.0)	26	(92.9)	0.2141
	Positive	0	(0.0)	2	(7.1)	

[1]fisher test, [2]mann whitney u test; *Mean±Standard deviation values are given instead of numbers, Medians are given instead of percentages; **Variables are combined because of insufficient data.

The median operation time (50 min) in the TEP hernia repair group was significantly longer than that in the LHR group (40 min) (p = 0.011). The median return to work time was significantly shorter in the TEP hernia group (7 d) than in the LHR group (15 d) (p < 0.001) (Fig. 2). There was no statistically significant between two group difference in terms of the patient's age, hernia recurrence, type of hernia (direct vs. indirect), levels of ASA, and early and late complications of surgery (p > 0.05) (Table I).

Discussion

Inguinal hernia repair using the Lichtenstein open repair method is widely performed worldwide today. Many studies have compared the superiority of different inguinal hernia repair methods. The majority of studies on laparoscopic versus open repair of inguinal hernias have assessed superiority by evaluating recurrence, operative time, pain and such factors. In an early study published in 1993 on a series of 51 patients with inguinal hernias, McKernan reported similar operation times and postoperative work return times in patients treated with TEP hernia repair and open repair [4]. Since then, a number of studies have compared different outcomes of TEP hernia repair and LHR, and to date, there is no consensus on the superiority of the two methods [5]. To shed light on this issue, studies have attempted to evaluate the effect of TEP hernia repair and LHR on testicular function chronic groin pain, return to normal activities, and numbness [6]. In this study, we evaluated patients'

TABLE II - *Correlation between PO1 VAS operation duration and back to work time of patient.*

	Po1 VAS		Operation duration		Back to Work	
	R	P	R	P	R	P
Age	-0.068	0.606	0.128	0.328	0.034	0.797
Po1 VAS			-0.103	0.432	0.699	0.000
Operation duration	-0.103	0.432			-0.047	0.722
Back to work (days)	0.699	<0.001	-0.047	0.722		

Spearman correlation analysis; PO 1: Postoperative first day; VAS: Visial Analog Scale.

levels of ASA before and after TEP hernia repair and LHR to determine their potential impact on infertility. We also evaluated other parameters, including operation times, hernia recurrence, pain, and numbness, in a long-term follow-up. A previous study on the effect of inguinal repair on infertility focused on 14 patients with azoospermia who underwent TEP hernia repair [7]. The study reported that the mesh used in the surgery induced an allergic reaction, which led to fibroblast proliferation and an obstruction in the vas deferens. The study concluded that although fibroblast proliferation and granulation tissue may have caused the mechanical obstruction in the vas deferens, there was no definite correlation between the use of mesh and infertility. In another study, Lee et al. found that spermatic cord manipulation during inguinal hernia surgery caused a statistically significant change in testicle sizes, without affecting fertility [8]. Akbulut et al. evaluated FSH (follicle-stimulating hormone), LH (luteinizing hormone), testosterone levels, and testicular volumes in 26 patients who underwent LHR or TEP hernia repair [9]. In their study, in which the patient group was similar to ours, they found a significant postoperative decrease in testosterone and testicular volumes in the TEP hernia repair group as compared to those in the LHR group. In our study, we assessed serum levels of ASA as a marker of autoimmunity and infertility. In contrast to the findings of the aforementioned studies we detected no statistically significant difference in the presence of ASA in the two groups postsurgery.

A prospective randomized study of 120 patients by Singh et al. compared testicular function after LHR, Laparoscopic (transabdominal preperitoneal repair (TAPP)) hernia repair procedures [10]. Based on testicular resistive indexes and FSH and LH levels, they found that testicular volumes decreased only slightly in both groups (laparoscopic and LHR) in the postoperative period, with no statistically between-group difference. They detected a decrease in the testosterone level in both groups, but the decrease was statistically significant only in the LHR group. After surgery, the resitive index decreased in both groups, but the decrease was minimal in the LHR group. They detected no significant change in FSH and LH levels. Unlike our study, the TAPP procedure was applied in order to TEP, and prosthetic material was not fixed (in our study as mentioned before prosthetic material was fixed with tacker in TEP group). They reported that testicular function was maintained after laparoscopic surgery but not LHR and concluded therefore that laparoscopic surgery was superior to LHR [10].

Stula et al. compared changes in ASA levels and testicular blood flow in 43 patients with inguinal hernias treated with LHR or TAPP [11]. They used the ELISA (enzyme-linked immunosorbent assay) method to detect ASA. They found that the levels of ASA remained within the normal range in the postoperative period, although the levels increased significantly in the LHR group. However, neither the LHR method nor laparoscopic TAPP repair affected autoimmunity or testicular blood flow clinically. In the study by Stula et al., the median age of the patients was 61 y, which may have affected their results and be a limiting factor as spermatogenesis declines with age [11]. In our study, two patients in the LHR group were positive for ASA, but the finding was not statistically significant. This finding highlights the need for studies on large patient groups to determine the superiority of laparoscopic versus open repair methods. This finding highlights the need for studies on large patient groups to determine the superiority of laparoscopic versus open repair methods. We used an IFA, a qualitative method, to detect ASA. Although the use of a qualitative method can be considered a limiting factor, there is no consensus on the optimum laboratory technique for ASA detection. According to some expert opinion, the ELISA is an unreliable method for detection of ASA, with different results obtained [12].

In a review of randomized controlled studies published in 2016, the relationship between surgery and infertility was investigated in 35740 male patients who underwent inguinal hernia repair [13]. In 7223 patients whose inguinal hernia was repaired using the open technique without a mesh, no significant changes in testicular function (sperm count and motility, testicular volume and position, testosterone, and FSH and LH levels) were detected. The authors emphasized that open surgery without using a mesh would not have an effect on infertility. The review did not provide information on common problems, such as hernia recurrence and chronic groin pain, that occur after open hernia surgery without a mesh. Infertility was detected in 233 (8%) of 28537 patients who underwent hernia repair using a mesh. Azoospermia due to obstruction was detected in 10 patients. Although no subgroup analysis according to the operation technique was conducted, the authors reported infertility due to mesh use in 8% of patients. In 108 patients who underwent TEP hernia repair, sperm motility was affected in the early postoperative period (post-

operative 1-2 d), but no permanent sequelae occurred. In 4 of 52 patients who underwent TAPP hernia repair, azoospermia was detected [13]. According to a previous study, technical issues relating to spermatic cord manipulation and testicular vascular damage are the main causes of infertility after inguinal hernia surgery [14]. Therefore, regardless of whether open or laparoscopic hernia repair is performed, extreme care should be exercised during tissue dissection and mesh placement to prevent testicular vascular damage and to maintain fertility.

Regarding hernia recurrence, a comprehensive prospective randomized multicenter study on 1,983 patients reported a higher recurrence rate after laparoscopic repair as compared to open repair in a 2-y follow-up (10.1% vs. 4.9%) [15]. In our study, hernia recurrence occurred in one patient in both groups, with no significant between-group difference according to the technique used. The higher rate of recurrence in the multicenter study may be attributed to the large number of patients and the average age of the operated patients (58.6 ± 12.8 y). The multicenter study also reported a lower recurrence rate in laparoscopic repairs performed by more experienced surgeons.

In terms of early and late complications of surgery, the rate was 12.5% in the TEP hernia repair group. In the multicenter study, Neumayer et al. detected no between-group difference in long-term complications, but the complication rates in the intraoperative and early postoperative period were higher in the laparoscopic repair group [15]. Pain felt on the first day after inguinal hernia surgery is considered an important parameter affecting patient comfort and return to work times. In our study, on postoperative day 1 the VAS scores of those in the TEP hernia repair group were significantly lower than those in the LHR group on postoperative day 1 (3.7 vs. 6.6).

One of the limiting parameters in terms of the applicability of laparoscopy in hernia repair is the duration of the operation. A major advantage of LHR is that it is easy to learn and perform. In our study, the mean duration of surgery in the laparoscopic hernia repair group was significantly higher than that in LHR group. In a meta-analysis that included 5,588 patients, laparoscopic repair took approximately 15.2 min longer than LHR [16]. Another study that compared return to normal activity times in hernia patients treated with laproscopic or open repair methods reported that the return to normal activity time was 7 d earlier in those who underwent laparoscopic hernia repair [6]. However, the authors clarified that the number depended on what was defined as "normal activity" [6]. In our study, we compared the two techniques in terms of return-to-work times and found that those who underwent TEP hernia repair returned to work 8 d earlier than those who underwent LHR, similar to the findings in the literature. However, based on our experience, we believe that return to work times after both laparocopic and open hernia repair methods are usually longer in our country We attribute this to the more liberal use of resting reports in our country.

To the best of knowledge, our study is one of only a few randomized prospective studies on postsurgery complications, including infertility, after TEP hernia repair and LHR. In terms of standardization, all procedures were performed by the same surgeons. Likewise, all postoperative follows were performed by the authors. In terms of its limitations, the sample size was small, which may explain the relatively low incidence of antibody positivity. Large multicenter studies are needed to shed light on aspects of hernia repair on infertility whether laparoscopic or LHR method applied.

Conclusion

In conclusion, based on our findings, it is not possible to determine the superiority of TEP hernia repair versus LHR in reducing infertility postsurgery. TEP inguinal hernia repair is superior to LHR in in terms of postoperative pain and return to work times.

Riassunto

Abbiamo confrontato il tasso degli anticorpi antisperma (ASA), il dolore, la durata dell'intervento, l'intervallo del ritorno all'attività, la recidiva erniaria e le complicanze post chirurgiche tra la riparazione totalmente extraperitoneale (TEP) dell'ernia laparoscopica e quella con la tecnica aperta di Lichtenstein (LHR).

Metodi: I pazienti sono stati divisi casualmente in due gruppi come LHR e TEP. Sono stati ottenuti campioni di sangue per l'analisi dei livelli di ASA. I punteggi del dolore postoperatorio sono stati valutati il ™ primo giorno dopo la riparazione utilizzando la scala analogica visiva (VAS) e sono state registrate la recidiva dell'ernia, i tempi di intervento, i tempi di ritorno al lavoro e le complicanze postoperatorie precoci e tardive.

Risultati: Sono stati arruolati nello studio sessanta pazienti di sesso maschile. Tutti i pazienti erano negativi per ASA preoperatoriamente. ASA sono stati rilevati in due pazienti nel gruppo postchirurgico LHR. Il punteggio VAS dei pazienti nel gruppo di riparazione TEP era significativamente inferiore a quello del gruppo LHR (mediana: 4,0 vs 6,0) (p <0,001). Il tempo medio di intervento nel gruppo di riparazione dell'ernia TEP (50 min) era significativamente più lungo di quello del gruppo LHR (40 min) (40,0) (p <0,011). Il ritorno mediano al tempo di lavoro nel gruppo di riparazione dell'ernia TEP (7 giorni) è stato significativamente inferiore a quello del gruppo LHR (15 giorni) (p <0,001). Non c'era alcuna differenza statisticamente significativa tra i due metodi in termini di ASA, recidiva o complicanze postoperatorie (p> 0,05).

Discussione: molti studi hanno confrontato la superiorità di diversi metodi di riparazione dell'ernia inguinale.

Quale tecnica sia la migliore in termini di fertilità è ancora controversa.
CONCLUSIONE: non è possibile determinare la superiorità delle tecniche relative alla riduzione dell'infertilità dopo l'intervento chirurgico. La riparazione dell'ernia inguinale TEP è superiore alla LHR in termini di dolore postoperatorio e tempi di ritorno al lavoro.

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