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IS INGUINAL HERNIA A RISK FACTOR FOR VARICOCELE IN THE YOUNG MALE POPULATION?

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Summary.- *OBJECTIVES: The aim of this study is to investigate the role of the inguinal hernia over the development of varicocele, in cases with accompanying inguinal hernia.*

METHODS: The continuous variables were calculated from mean and standard deviation, and intermittent variables were calculated over percentage and frequency. Normality testing was performed on continuous variables using the Kolmogorov–Smirnov test. Univariate analyses were performed using the unpaired Mann–Whitney U test and Chi-squared test was used for proportions. Kendall's tau-b correlation coefficient was used for correlition coefficient. Logistic regression modeling were used to identify the impact of inguinal hernias on selected cases. The data were analyzed with SPSS™ for Windows 22 (SPSS,Chicago, IL).

RESULTS: Twelve cases (23.1%) in the inguinal hernia group also had varicocele, which was relatively high, whereas 12 cases with inguinal hernia in the varicocele group corresponded to only were 4.02% (12/52 (23.1%) vs 12/298 (4.02%)). On the other hand, as a result of the binary logistic regression, we found statistically significant difference in the probability of being diagnosed varicocele among the patients with inguinal hernia as 1.94 times.

CONCLUSIONS: We think that in addition to the direct compression of some of the inguinal hernias on testicular veins, the potential for a combination of common enzymatic and biochemical disorders in some of the cases involving these two disorders may be play role.

Keywords: *Varicocele. Inguinal hernia. Young male.*

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Resumen.- *OBJETIVOS: La finalidad de este estudio es investigar el rol de la hernia inguinal respecto al desarrollo de varicocele, en casos con acompañamiento de hernia inguinal.*

MÉTODOS: Las variables continuas fueron calculadas a partir de media y desviación standard, y las variables

discontinuas se calcularon con porcentaje y frecuencia. Se desarrollaron pruebas de normalidad para variables continuas utilizando el test de Kolmogorov-Smirnov. Se realizó análisis univariante usando el test U de Mann-Whitney sin emparejamiento y para proporciones y utilizó el test de Chi cuadrado. Se aplicó el coeficiente de correlación tau-b de Kendall para los coeficientes de correlación. Se usaron modelos de regresión logística para identificar el impacto de la hernia inguinal en casos seleccionados. La información fue analizada con SPSS™ 22 para Windows (SPSS, Chicago, IL).

RESULTADOS: Doce casos (23,1%) en el grupo de hernia inguinal tenían también varicocele, incidencia relativamente alta, mientras que solo había 12 casos con hernia inguinal en el grupo de varicocele, que correspondían a un 4,02 % [12/52 (23,1%) vs 12/298 (4,02%)]. Por otro lado, como resultado de la regresión logística binaria, descubrimos una diferencia estadísticamente significativa en la probabilidad de ser diagnosticado varicocele en los pacientes con hernia inguinal (1,94 veces).

CONCLUSIONES: Pensamos que además de la compresión directa de algunas de las hernias inguinales de las venas testiculares, el potencial para una combinación de alteraciones comunes enzimáticas y bioquímicas en algunos de los casos, implicando estas dos anomalías, podría desempeñar un papel importante/clave.

Palabras clave: *Varicocele. Hernia inguinal. Varón joven.*

INTRODUCTION

The surgery of inguinal region is frequently related to the testicular descent, thus, the inguinal hernia is the most common disease of the inguinoscrotal pathology, with a 1-2% incidence in men (1,2). Its incidence is 16-25% in premature and low-birth-weight infants and 2-7% for infants (1). The anatomical classification of inguinal hernias is as follows: Lateral hernias origin from the deep inguinal ring, resulting from a patent processus vaginalis (3); they proceed within the inguinal canal and can exit from the superficial ring (4). Medial hernias occur presumably due to weakened transversalis fascia in the Hesselbach's triangle (4). Furthermore, different clinical disorders may be related with this region and among these disorders, varicocele is the most common. The testicular veins originate in the testicle and form the pampiniform plexus. Venous blood then travels up through the inguinal canal as part of the spermatic cord, forms the internal spermatic or testicular vein and terminates in the abdomen. The right internal spermatic vein terminates directly into the low-pressure inferior vena cava while on the left side, it joins with the relatively high-pressure left renal vein. This anatomy explains why the majority of clinically detectable varicoceles are on the left side (5). The dilatation of the plexus panpinoformis venules in the spermatic cord and abnormal irregularation is specific for varicocele. Additionally, it is the most common correctable cause of male infertility (6,7). Varicoceles are far more common (80% to 90%) in the left testicle (8). Due to high venous pressure in the left renal vein, collateral venous anastomoses and valvular failures of internal spermatic venules develop (6,7). It has been pointed out in the literature that inguinal hernias may cause pain in varicocele patients by increasing the intra-abdominal pressure, especially after intense physical activities (9). Furthermore, impaired collagen organization do to abnormal degradation of the extracelluler matrix can lead to mechanical failure of the structure in which collagen represents the supportive matrix for structures such as vessels of abdominal transversalis fascia (10). Raffaele Serra and et al. reported the abnormal expression of metalloproteinase-9 activation as a least common denominator between varicocele, inguinal hernia and chronic venous disorders (11). Coincidental occuring of varicocele and inguinal hernia are expected to be more frequent, compared with the previous studies (12,13), considering the common pathogenesis of both diseases, stated by Shiou-Sheng Chen and et al. (7).

The aim of this study is to investigate the role of the inguinal hernia over the development of varicocele, in cases with accompanying inguinal hernia. We believe that this study will contribute to the limited number of literature for varicocele development from a source of inguinal hernia.

MATERIALS AND METHODS

Until the taken the ethical board permission; The study was planned to be carried out in a single center, and conducted with coordination by the three different specialists, common process (general surgeon, urology specialist and with radiology specialist). Especially, to investigate the effect of inguinal hernia on varicocele development as a hypothesis, two physicians with different knowledge levels and experience in their fields of general surgery and urology have worked in coordination. Each branch's physician investigated and diagnosed their patients with a diagnosis of inguinal hernia or varicocele, and exchanged the patients and confirmed if the patient had the other diagnosis additionally, and they both recorded the patient data. The data was screened ret-

rospectively after the approval of the ethics committee of Gülhane Medical Faculty on December 15, 2015. All patients who presented with inguinal or scrotal pain to both urology and general surgery outpatient clinics in Beytepe Military Hospital and diagnosed with varicocele and/or inguinal hernia were included in the study.

PATIENTS

The retrospective documentation scanning included the information written by the general surgeon after the physical examination and confirmed by ultrasonography in the inguinal hernia cases. On the other side, the varicocele cases had been recorded by the urologist, in terms of the physical examination, sperm analysis and doppler ultrasound. Patients with strangulated or undescended testis, atrophic testis and hypospadias were excluded. Ultrasonographic findings in both inguinal hernia and varicocele cases were collected from the data examined by the same radiologist who actively participated in the study.

The data were obtained from medical documentation and inconsistent or incomplete data were excluded. The age of the total population ranged between 20-30 years, which showed a young population, and the mean age was 24.12 ± 2.56.

Twelve infertile patients with impaired sperm parameters in Grade III Stage had varicocelectomy and four of these 12 patients also had severe testicular pain. Apart from this group, patients with Grade I and Grade II varicocele who had mild pain complaints were followed by spermiogram and analgesic medical treatment was applied. On the other hand, inguinal herniorrhaphy operation was performed in all cases with inguinal hernia. We used the Lichtenstein technique for herniorrhaphy and microsurgical varicocele ligation for varicocelectomy. All patients have signed consent, and the study was approved by Gulhane School of Medicine Institutional Review Board. Staging of the patients with inguinal hernia was performed according to Nyhus classification, which was established in 1991, focusing on the functional status of the inner ring of Nyhus and the posterior wall of the inguinal canal (4,14).

Type I: Indirect hernias in which the inner ring is in normal diameter, structure and configuration. The hernia sac can extend from just distal to the inner mouth to the middle of the channel, but the Hasselbach triangle is normal.

Type II: Indirect inguinal hernias that the inner ring is weakened but not covered by the whole channel. The Hasselbach triangle is pathophysiologically normal. The hernia sac does not reach the scrotum but can retain the entire inguinal channel.

Type III: There are 3 subgroups in these hernias and the integrity of the posterior wall is always impaired.

Type IIIA: Direct inguinal hernia is in which with weakened transversalis fascia. The transversalis fascia may protrude out in front of the hernia sac.

Type III B: Indirect inguinal hernias (massive scrotal, sliding, pants hernias) that have enlarged in the inner mouth and progressing medially to the Hassalbach triangle.

Type III C: Femoral hernias.

Type IV: Recurrent hernias.

Type IV A: Recurrent direct hernias.

Type IV B: Recurrent indirect hernias.

Type IVC: Recurrent femoral hernias.

Type IVD: Recurrent combined hernias (4,14).

The gold standard method for diagnosis is physical examination. Three grades are determined according to Dubin grading system for varicocele (15). Varicose veins that can be palpable with valsalva maneuver are defined as first grade. Second grade is defined as varicose veins palpated without any maneuver. Third grade is defined as varicose veins are observed easily in the scrotum without any maneuver (15).

STATISTICAL ANALYSIS

In descriptive analysis; continuous variables were calculated from mean and standard deviation, and intermittent variables were calculated over percentage and frequency. Normality testing was performed on continuous variables using the Kolmogorov-Smirnov test.

In univariate analyses, as the continuous variables such as age were calculated as nonparametric statistics according to the Kolmogrov-Smirnov test, this type of nonparametric continuous variables were calculated using unpaired Mann-Whitney U test. Intermittant variables were calculated by Chi-squared test. $p < 0.05$ was considered statistically significant. Univariate analyses were performed using the unpaired Mann-Whitney U test for nonparametric continuous

Table I. The comparison of the subgroups and total population in terms of age.

Age	Mean ± Std. Deviation	p
Varicocele group vs Hernia group	24.08 ± 2.55 vs 23.84 ± 1.60	.826
Total patients' vs Varicocele group	24.12 ± 2.56 vs 24.08 ± 2.55	.328
Total patients' vs Hernia group	24.12 ± 2.56 vs 23.84 ± 1.60	.487

variables and Chi-squared test was used for proportions. Kendall's tau-b correlation coefficient was used for non-parametric distribution. Logistic and binary regression modeling were used to identify the impact of inguinal hernias on selected cases. All odds ratios were reported with a 95% confidence interval. The data were analyzed with SPSS™ for Windows 22 (SPSS, Chicago, IL).

RESULTS

A total of 2185 patients were detected to have admitted to the general surgery or urology clinic with the complaints of inguinal or scrotal pain. Inguinal hernia was detected in 52 patients and varicocele was detected in 298 patients. In addition, it was seen that 12 pateints who belonged to these groups had both varicocele and inguinal hernia.

The mean age in the group of inguinal hernia (Group 1) was 23.84 ± 1.60 years, with a range between 20-26 years. The mean age in the varicocele group (Group 2) was 24.08 ± 2.55 years, with a range between 20-28 years. The mean age for the total population was 24.12 ± 2.56 years, with a range of 20-30 years. There was no statistically significant difference between groups in terms of age ($p>0.05$) (Table I).

Comparison of independent nonparametric groups: Kendall's tau-b test correlation coefficient between hernias and varicocele was statistically significant, with which we also used to compare the dichotomous variables [(Correlation Coefficient: 0.043 ($p<0.049$)] (Table II).

Twelve cases (23.1%) in the inguinal hernia group also had varicocele, which was relatively high, whereas 12 cases with inguinal hernia in the varicocele group corresponded to only were 4.02% [12/52 (23.1%) vs 12/298 (4.02%)]. On the other hand, as a result of the binary logistic regression, we found statistically significant difference in the probability of being diagnosed varicocele among the patients with inguinal hernia as 1.94 times higher in the confidence intervals, compared with vice versa (AOR 1.937 (1.004, 3.737) $p<0.049$) (Table III).

According to the Nyhus classification of the cases diagnosed as inguinal hernia, 19 cases were Grade I, 20 cases were Grade II, 12 cases were Grade III, and 1 case was Grade IV. According to the obtained data by examining both operation notes, preoperative physical examination and ultrasound results, in concomitant varicocele and hernia cases, the distribution of the cases were as; 5 varicocele cases were Grade II, 6 cases were Grade III B, and 1 case was Grade IV B. According to the results of spermiogram performed in the preoperative period, 3 cases

Table II. The correlation coefficient between varicocele and inguinal hernias.

Correlations				
			VARICOCELE	HERNIA
Kendall's tau-b	VARICOCELE	Correlation Coefficient	1.000	.043*
		Sig. (2-tailed)	.	.045
		N	2185	2185
	HERNIA	Correlation Coefficient	.043*	1.000
		Sig. (2-tailed)	.045	.
		N	2185	2185

*. Correlation is significant at the 0.05 level (2-tailed).

Table III. The efffect of inguinal hernias over varicocele occurance.

The number of varicocele cases: 298 **The number of hernia cases: 52**	**Inguinal Hernia (+)**	**Inguinal hernia (-)**	**Totally**	**P**	***Adjusted Odds Ratio (95% CI)/Adjusted Mean Difference (95% CI)**	**p**
Varicocele (+) (n:298)	**12 (23.1%)*** [Varicocele (+) cases in hernia group]	**286 (95.8%)** [Varicocele (+) cases in hernia(-) group]	298: [**(12)4.02 %*** hernia and varicocele concomiant cases(+)] vs.[(286)95.98% pure varicocele cases)]			
Varicocele (-) (n:1887)	**40 (76.9%)**	1847 (86.6%)	1887: [(40) 2.4% pure hernia cases] vs[(1847) 97.6%nonvaricocele and non hernia group]	0.045	1.937 (1.004, 3.737)	**0.049**
Total	**52 (100%)**	2133 (100%)	2185 (100%)			

** Logistic and binary regression performed; adjusting for differences in dichotome variables for outcomes.*
**p value is significant at the 0.05 level (2-tailed).*

of oligoasthenospermia (Grade III varicocele) and 5 cases of asthenospermia (Grade II) were present and spermiogram results of the other 4 cases were normal. In both varicocele and hernia cases, the hernias were graded according to the Nyhus classification: 7 cases were Grade III B and 5 cases Grade II. Of varicoceles, 8 cases were on the left side and 4 on the right side. Of the concomitant hernia and varicocele cases, 7 cases were on the right side, 5 cases on the left side, and 1 case was bilateral. Seven of 12 patients with concomitant varicocele and inguinal hernia meet Grade IIIB Nyhus and the other 5 cases fit the Grade II Nyhus classification, and thus, we believe that the potential for compression in the cord of such hernias, has a role in the development of varicocele with chronic compression in the testicular blood flow. Eight patients with oligoasthenospermia and asthenospermia underwent both inguinal herniorrhaphy and varicocelectomy in the same session.

DISCUSSION

A patent processus vaginalis is a risk factor for developing lateral hernias. Both persistent smooth muscle cells (16-20) and insufficient release of calcitonin gene-related peptide from the genitofemoral nerve may play a role in failed obliteration (21-23).

Despite the successful surgical repair performed for defective patent processus vaginalis; high levels of intra-abdominal pressure, or daily activities such as lifting and standing/walking, seem to cause lateral recurrences (24). Since the formation of the inguinal hernia is closely related to the descent of the testicle, the hernia is 6 times more frequent in boys than in girls (25). Patients often suffer and complain from swelling in the in the inguinal region and/or scrotum, due to the increased intra-abdominal pressure (26).

In addition, in some studies, it has been shown that some inguinal hernia cases have alteration in their connective tissue compared with control cases, regarding the ratio of fascia architecture, collagen fibers, and level of enzymes involved in connective tissue homeostasis (27-33). Some connective tissue diseases also have been reported to be related with the occurance of inguinal hernia, such as Marfan syndrome, Ehlers-Danlos syndrome and osteogenesis imperfecta (34). The structure of collagen features are essential for the soundness of fascia transversalis (10). Serra et al. reported in another study that metalloproteinase-9 deficiency was a strong marker of varicocele and inguinal hernia in chronic venous diseases (11). Ribarski et al. suggested that mutation 1090C>T in ubiquitin-specific protease (USP) 26

Figure 1. Indirect inguinal hernia and varicocele.

Figure 2. Varicocele vein ligation.

Figure 3. High ligation of indirect hernial sac.

gene of the X-chromosome is a genetic risk factor for developing inguinal hernia, which might be associated with male infertility (35). Some authors believe that an inguinal hernia might be caused due to increased intra-abdominal pressure, and some varicocele patients may complain from scrotal pain after strenuous activity (7). We think that the fact that the existence of hernia is more significant in varicocele formation. At the same time, we believe that varicocele occurance is not effective for the development of inguinal hernia. In terms of the effect of inguinal hernias over varicoceles; both in the light of literature and due to the our results, we believe that the inguinal hernias in particular might be effective over the varicocele occurance. In their study, Tanyel FC. et al. have shown that unilateral incarceration in the prepubertal period causes inguinal hernia which results with impaired ipsilateral and contralateral testicular histology and decreased testicular exocrine function in rats (36). The testis is more vulnerable to trauma in non-scrotum locations than it is in the scrotum. Trauma may occur from the outside, or may be caused by compression in the inguinal canal (37). Purip et al. reported that drowning of hernia in the groin and the testis in boys, and the deterioration of ovarian blood in girls play an important role in infertility in the later stages of life (38). In addition, Eutermoser et al. specified that the inguinal hernia may lead to testicular ischemia (39). In our study, inguinal hernia was found as 1.94 times more effective for varicocele occurance than those without inguinal hernia. In a 2017 study by Michael L. et al., it was stated that there is still no incidence study showing the association of varicocele and hernia (40). However, in the same study, they referred to the study of Crawford P. et al. (41), in which a prevalence as high as 20% and 10% for varicocele and hernia, respectively, have been found; and they pointed out the coincidence of varicocele and hernia (40). The main focus here is that the percentage of having varicocele among patients with inguinal hernias (23.1%), is significantly higher with a risk ratio of 1.94, than the percentage of having hernia among patients with varicocele (4.02%). This suggests that the hernia is a more important risk factor for developing varicocele, and as a result of this preliminary study, we believe it is encouraging for broad-based and multi-center studies. In the mini-review published by J.Gandhi et al. In 2016 in the classification of the aetiology for the physiopathology of increased venous resistance, leading to testicular compartment syndrome; they mentioned the venous structures due to hernia compression and increased venous resistance (42). This is explained by a cascade mechanism; and they found that of testicular compartment syndromes, especially ischemia-reperfusion injury was effective in the aetiopathogenesis (42). Also in the same study (42); They stated that varicoceles that are not subclinical may be effective in testicular compartment syndrome, and that oxidative radicals may be effective in infertility due to the formation of severe varicocele (42). On the other hand, in the same mini-review, in reference to the study published by Gat Y. et al. (43) in 2006 about varicocele formation, it was stated that varicocele formation was associated with high hydrostatic pressure and insufficient valves, leading to stagnation of capillary blood flow, and resulting in ischemia. In

addition, that there would be an increase in liquid filtration into the interstitium (42). In another study (44), Girn HR et al. found especially venules to be at the risk of adherence of the blood cells and under the risk of edema due to increased P-selectin and NFκB transcription, which stimulates selectins and other proteins involved in the inflammatory response. When we look at all of this cascade mechanism, we also get the opinion that, especially in advanced inguinal hernias, there may be an increase in pressure in the testicular veins, and in time this may play a role in varicocele formation with high hydrostatic pressure and insufficient valve mechanism. Although the low number of cases is a limitation, we think that our preliminary results will be a light for further clinicopathologically advanced studies by drawing attention to this subject, which is epidemiologically limited in literature.

CONCLUSION

In addition to the direct compression of some of the inguinal hernias on testicular veins, the potential for a combination of common enzymatic and biochemical disorders in some of the cases involving these two disorders cannot be ruled out. As a next step; We are purposing to conduct multi center studies in a larger series about for this preliminary results.

THE CONTRIBUTORS

• Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; Sezgin Okçelik, MD, Urology & Selçuk Sarıkaya, MD, Urology, Selami İnce, MD, Radiology.

• Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; Özgür Albuz, MD, General Surgery & Mustafa Oğulluk, Family Medicine Specialist, MD.

• Drafting the work or revising it critically for important intellectual content and final approval of the version to be published; Hasan Ozan, MD, Professor, Anatomy.

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