https://doi.org/10.17816/uroved10133-38

BLOOD FLOW CONDITION IN THE LEFT RENAL VEIN IN OPERATIVE TREATMENT OF PATIENTS WITH VARICOCELE

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For citation: Krupin VN, Uezdnyj MN, Zubova SYu, Petrova PI. Blood flow condition in the left renal vein in operative treatment of patients with varicocele. *Urology reports (St. Petersburg)*. 2020;10(1):33-38. https://doi.org/10.17816/uroved10133-38

Received: 14.01.2020 Revised: 18.02.2020 Accepted: 19.03.2020

The purpose of the study was to evaluate the blood flow in the left renal vein after ligation of the internal spermatic vein with varicocele and to study the changing of the level of biological markers of acute kidney damage in these patients. **Materials and methods.** Under observation were 64 men in age 18–23 years with the first hemodynamic type of varicocele. In 3 patients clinically significant compression of the left renal vein was revealed and the remaining 61 patients underwent surgery by Ivanissevich approach. Before the operation, on the 2nd, 10th, 30th and 90th days after the operation patients underwent Doppler blood flow rate by ultrasound with color mapping of the left renal vein with measurement of venous blood flow velocity. During these periods all patients underwent laboratory tests, including the study of the content of cystatin C and interleukin 18 in the blood and urine. **Results.** On the first day after ligation of the internal spermatic vein an increase in the concentration of biological markers of acute kidney damage in the blood and urine was noted. After surgery all patients showed an increase in the diameter of the left renal vein by 1.5–2 mm and a decrease in the linear blood flow velocity in the region of the renal vien by 5–6 cm/s. On the 10th day after the operation the diameter of the left renal vein was increasesd by 3–4 mm more and the linear blood flow velocity slows down by 2–2.5 cm/s. The restoration of blood flow velocity and the diameter of the left renal vein occurred within three months and in most cases returned to baseline and in 22.9% of patients recovery did not occur by the 90th day of observation. **Conclusion.** Ligation of the internal spermatic vein with varicocele is accompanied by impaired blood flow in the left renal vein and an increase in the concentration of biological markers of acute kidney damage, which is a manifestation of venous hypertension and renal hypoxia. In most patients these indicators normalize to the 90th day of observation after surgery.

Keywords: varicocele; venous hypertension; renal hypoxia.

СОСТОЯНИЕ КРОВОТОКА В ЛЕВОЙ ПОЧЕЧНОЙ ВЕНЕ ПРИ ОПЕРАТИВНОМ ЛЕЧЕНИИ ВАРИКОЦЕЛЕ

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Для цитирования: Крупин В.Н., Уездный М.Н., Зубова С.Ю., Петрова П.И. Состояние кровотока в левой почечной вене при оперативном лечении варикоцеле // Урологические ведомости. – 2020. – Т. 10. – № 1. – С. 33–38. https://doi.org/10.17816/uroved10133-38

Поступила: 14.01.2020 Одобрена: 18.02.2020 Принята к печати: 19.03.2020

Цель исследования. Оценить характер кровотока в левой почечной вене после перевязки внутренней семенной вены при варикоцеле и изучить динамику уровня биологических маркеров острого повреждения почки у этих пациентов. **Материалы и методы.** Под наблюдением находились 64 мужчины в возрасте 18–23 лет с первым гемодинамическим типом варикоцеле. У 3 больных выявлена клинически значимая компрессия левой почечной вены, остальным (61 пациент) выполнена операция Иваниссевича. До операции, на 2, 10, 30 и 90-е сутки после операции пациентам проводили ультразвуковую доплерографию с цветным картированием левой почечной вены с измерением скорости венозного кровотока. В эти сроки всем больным проводили лабораторные исследования, в том числе изучали содержание цистатина С и интерлейкина-18 в крови и моче. **Результаты.** В первые сутки после лигирования внутренней

семенной вены отмечалось повышение концентрации биологических маркеров острого повреждения почек в крови и моче. У всех пациентов после операции выявляли увеличение диаметра левой почечной вены на 1,5–2 мм и уменьшение линейной скорости кровотока в области ворот почки на 5–6 см/с. На 10-е сутки после операции диаметр левой почечной вены в области ворот увеличивался еще на 3–4 мм, а линейная скорость кровотока замедлялась на 2–2,5 см/с. Восстановление скорости кровотока и диаметра левой почечной вены происходило в течение трех месяцев и, в большинстве случаев, возвращалось к исходным показателям, а у 22,9 % пациентов восстановление к 90-му дню наблюдения не произошло. **Выводы.** Лигирование внутренней семенной вены при варикоцеле сопровождается нарушением кровотока в левой почечной вене и повышением концентрации биологических маркеров острого повреждения почек, что проявляется венозной гипертензией и почечной гипоксией. У большинства пациентов эти показатели нормализуются к 90-му дню наблюдения после операции.

Ключевые слова: варикоцеле; венозная гипертензия; гипоксия почки.

INTRODUCTION

Compression of the left renal vein in the zone of origin of the superior mesenteric artery leads to impairment of the venous blood flow and increased venous pressure in the kidney. In consequence, confluence of the varicose veins develops into the left renal vein, which compensates for the resultant increased pressure [1–3]. The varicose veins of the spermatic cord are a common and easily diagnosed symptom of regional renal venous hypertension [4]. The development of varicocele is secondary to hemodynamic impairment in the left renal veins [5, 6]. Past studies have shown that surgical treatment of varicocele, while eliminating the compensatory mechanism of renal venous hypertension, can increase the hemodynamic disorders and result in the development of arterial hypertension [7].

It is generally accepted that the diagnostic criteria for hemodynamically significant compression of the left renal vein include the anteroposterior size of the renal vein in the constricted area of ≤1.5–2.5 mm, which is determined by ultrasound examination, along with a local increase in the blood flow velocity of >110 cm/s [8]. However, these data are presented for situations with functioning collaterals (such as internal spermatic vein and adrenal vein). The manner in which the hemodynamics changes occur in the left renal vein during collateral elimination remains unclear. According to intraoperative tonometry, before and after ligation of the internal spermatic vein, the hemodynamic disorders in the system of the left renal vein are not registered, provided that the branch of the lumbar vein is preserved [9, 10]. From another perspective, any methods of occlusion of the internal spermatic vein are accompanied by impaired renal venous hemodynamics and a change in the reaction of the kidneys [11].

After embolization of the superior spermatic vein in 145 patients, the left renal vein pressure was found to increase by 1 mm Hg in 22.7%, by 2 mm Hg in 4.8%, by 3 mm Hg in 2.0%, and by 4 mm Hg in 1.4% of the patients; in other words, almost one-third of the patients showed an increase in the venous pressure intraoperatively [12]. During the postoperative period in patients with varicocele after ligation of the internal spermatic vein, impairment of venous hemodynamics in the left renal vein system may increase in association with an increase in renal ischemia, which may cause acute damage to its parenchyma. The main damaging factor of renal tissues is renal tissue hypoxia that occurs in hypertension of the renal vein, which can lead to fibrous degeneration of a portion of the renal glomeruli [13–15].

It is highly probable (up to 73%) that the development of acute renal damage within the next 24 h can be determined by the level of biological markers [16–18]. The study of the early kidney reaction to acute damage, including ischemic damage, provides prominence to biomarkers such as cystatin C, KIM-1, L-FABP, and interleukin-18 (IL-18) [19].

The present study aimed to assess the nature of blood flow in the left renal vein after ligation of the internal spermatic vein in varicocele as well as to examine the dynamics of the level of biological markers in acute kidney damage patients.

MATERIALS AND METHODS

Ultrasonic dopplerography combined with color imaging on the Philips Epiq 5 apparatus was used to examine 64 patients aged 18–23 years with hemodynamic type 1 of varicocele. The diameter of the left renal vein at the hilum of the kidney and in the area between the superior mesenteric artery and the aorta was measured, and the linear velocity of the blood flow in these zones was also estimated. Ivanissevich surgery was performed in all patients,

with the exception of 3 patients with clinically significant compression of the left renal vein. Subsequently, on days 2, 10, 30, and 90 after the surgery, the state of the left renal vein and the velocity of venous blood flow along it at the level of the renal hilum were monitored by ultrasonic dopplerography. In addition, in order to identify the onset of acute renal lesion and to assess the dynamics of its development in patients with varicocele, the blood and urine levels of cystatin C and IL-18 for all operated men were assessed before their surgical treatment as well as on days 2, 10, 30, and 90 of the surgery. The results obtained were statistically processed using the Microsoft Excel 7.0 and Statistica for Windows 6.0 programs. The significance of the differences in the mean values was assessed using the parametric Student's test for dependent and independent samples.

RESULTS

Diagnostically significant compression of the left renal vein was detected in 3 patients (4.7%). In these cases, the renal vein diameter at the level of the renal hilum was 15, 15.5, and 16 mm, while that in the area between the aorta and the mesenteric artery was 2.5, 2.7, and 3.3 mm, respectively. At the same time, the linear blood flow velocity in the aortic-mesenteric section of the left renal vein exceeded 100–125 cm/s at a blood flow velocity in the renal vein at the hilum level of 19.5–31 cm/s. In the remaining 61 patients, the diameter of the left renal vein at the renal hilum was within the range of 8.8–11.2 (9.8 ± 1.2) mm, which was correlated with the renal vein diameter in the interval between the aorta and the superior mesenteric artery as 3:1, where it was determined within the range of 2.5–3.9 (3.4 ± 0.4) mm. The linear blood flow velocity in the renal vein at the hilum level was within 17.8–26 (20.3 ± 1.3) cm/s, while it was 36–63 (49.8 ± 1.8) cm/s in the constricted area; the velocity increased by no more than 2.5 times.

The Ivanissevich surgery was performed in all patients, except for 3 patients with clinically significant compression of the left renal vein. On the next day of the surgery, all 61 operated patients showed an increase in the diameter of the left renal vein by 1.5–2 mm (average: 11.1 ± 0.1 mm) (Fig. 1). The linear blood flow velocity in the renal hilum area decreased by 5–6 cm/s in all cases and became equal to 17.1 ± 0.7 cm/s (Fig. 2). On the day 10 of the surgery, the left renal vein diameter in the hilum area increased by another 3–4 mm, while the linear blood flow velocity decreased by 2–2.5 cm/s (Figs. 1, 2).

The linear blood flow velocity in the left renal vein at the renal hilum level decreased by 9–11 cm/s, while it increased to 101–115 cm/s in the constricted area. A similar trend was noted in 49 of the 61 patients. In the other cases (for the remaining 12 patients), the linear blood flow velocity in the constricted area increased to 80–97 cm/s.

Thus, by the day 10 of performing superior spermatic vein ligation, the diameter of the left renal vein as a whole increased by 4.5–6 mm (15.3 ± 0.3 mm) and remained that way for the next month after the surgery. By the day 30 of the surgery, the left spermatic vein diameter averaged 14.9 ± 1.4 mm. From the day 10 to day 30, the linear blood flow velocity remained low and amounted to 16.3 ± 1.6 and 16.2 ± 1.2 cm/s, respectively.

In 18 patients, after 3 weeks of the surgery, fresh erythrocytes (up to 10 in the field of view) and albuminuria were noted in the urine samples. After 3 months of the surgery, 47 operated patients showed a decrease in the diameter of their left renal vein in the area of the hilum, almost equal to the original size

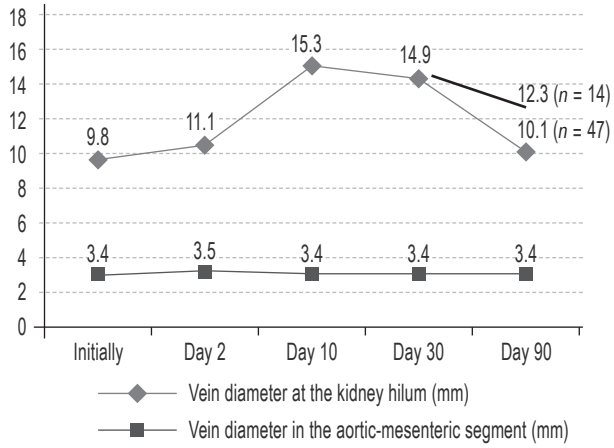

Fig. 1. Diameter of the left renal vein after varicocele surgery (Ivanissevich operation), mm (n = 61)
Рис. 1. Диаметр левой почечной вены после операции по поводу варикоцеле (операции Иваниссевича) (n = 61)

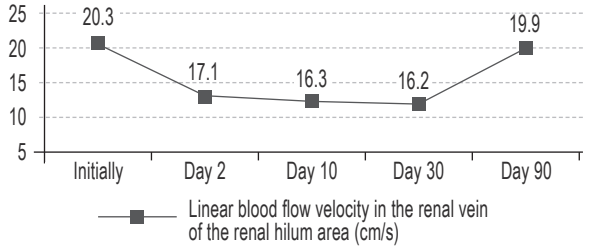

Fig. 2. Venous hemodynamics in the left renal vein after varicocele surgery (Ivanissevich operation), cm/s (n = 61)
Рис. 2. Венозная гемодинамика в левой почечной вене после операции по поводу варикоцеле (операции Иваниссевича) (n = 61)

Dynamics of biomarkers of acute kidney damage in blood and urine of patients before and after surgery (*n* = 61)
Динамика биомаркеров острого повреждения почек в крови и моче у пациентов с варикоцеле (*n* = 61)

Biomarker	Initially	Day 2	Day 3	Day 10	Day 30	Day 90
Blood cystatin C, ng/mL	986.9 ± 96.4	1295 ± 113.2	1187 ± 121.3	–	–	–
Urine cystatin C, ng/mL	1112 ± 101.2	2301.3 ± 173.2	2106 ± 213.4	1978 ± 121.1	1482 ± 98.8	1267±112.2
Blood IL-18, ng/mL	33.4 ± 3.4	41.5 ± 3.8	67.8 ± 7.8	–	–	–
Urine IL-18, ng/mL	19.2 ± 1.9	49.3 ± 4.8	30.4 ± 3.0	28.4 ± 2.4	24.2 ± 4.1	20.9 ± 2.1

(10.1 ± 1.1 mm). The linear blood flow velocity in the constricted area of the left renal vein (the area of its passage between the aorta and the superior mesenteric artery) in these patients also returned to the initial values of 19.9 ± 1.9 cm/s. In 14 (22.9%) patients, these indicators did not return to the initial values, although they altered, and the diameter of the vein at the level of the kidney hilum was 12.3 ± 0.3 mm, and the linear velocity was 17.4 ± 0.4 cm/s.

The study of blood and urine biomarkers of acute renal injury showed a change in their concentration both immediately at the postoperative period and that after 90 days of surgery.

The initial indices of biomarkers in both the blood and urine samples differed insignificantly from the normal indices (e.g., blood cystatin C871.7 ± 89.1 ng/mL, urine cystatin C1058.7 ± 83.5 ng/mL; blood IL-1832.7 ± 2.6 pg/mL, urine IL-1818.8 ± 2.1 pg/mL) [19]. Thus, the initial level of blood cystatin C averaged to 986.9 ± 96.4 ng/mL; 1 day after the surgery, this indicator increased to 1295 ± 113.2 ng/mL, and, after 3 days, it was 1187 ± 121.3 ng/mL. The level of cystatin C in the urine sample at the baseline was 1112 ± 101.2 ng/mL in patients with varicocele; the level at 1 day after the surgery was 2301.3 ± 173.2 ng/m:, while it was 2106 ± 213.4 ng/mL after 3 days. On days 10, 30, and 90 after the surgery, only the urinary cystatin C level was examined. The dynamics of changes in the level of IL-18 in the blood and urine was also a characteristic for the development of acute kidney lesion in the immediate postoperative period (Table 1).

DISCUSSION

The results of this study indicated an impairment of the venous blood flow in the left renal vein system that lasted for 90 days. Ligation of the superior spermatic vein in patients with the hemodynamic type 1 of varicocele is accompanied by the development of clinical signs of renal venous hypertension (such as hematuria and albuminuria) in several patients. After ligation of the internal spermatic vein, the ratio of the diameters of the left renal vein in the area of the hilum and in the aortic-mesenteric zone changes, along with the ratio of blood flow velocities in these areas during the postoperative period, which together indicates the development of renal venous hypertension. Despite the fact that, in most patients, hemodynamic disorders in the left renal vein after Ivanissevich surgery are reversible (probably due to the development of other collateral pathways of the venous blood outflow from the kidney instead of the ligated internal spermatic vein), prolonged ischemia of the renal tissues (up to 90 days) can adversely affect its functional abilities. In addition, in 14 patients (22.9%), hemodynamic disorders in the left renal vein system did not recover to their initial values by 90 days.

Increase in ischemia of the renal tissues due to impaired venous blood flow can lead to the emergence and development of acute renal injury. An increase in IL-18 level in the urine by almost 2-fold on the next day of ligation of the spermatic vein indicates the development of an injury of the renal glomerular system, which is caused by increasing ischemia. In the postoperative period, all patients also showed an increase in the urine and blood levels of cystatin C. The gradual decrease in the level of biomarkers of acute kidney lesion both in the blood and in urine may be attributed to the activation of compensatory mechanisms of both the renal hemodynamic system and the compensatory functioning of other collaterals of the renal blood flow. However, the biomarkers that remained elevated relative to the baseline values within 3 months enabled inferring about the current ischemia of the renal tissues.

CONCLUSIONS

The ligation of the internal spermatic vein in varicocele is accompanied with impaired venous blood flow in the left renal vein system, which lasts up to 3 months, and it is not restored during this duration in 22.9% of the cases.

Abnormality of venous hemodynamics in the left renal vein after ligation of the internal spermatic vein in 18 of the 61 patients was accompanied with microhematuria and albuminuria, which indicate renal venous hypertension.

On day 1 after ligation of the internal spermatic vein, an increase in the concentration of biological markers of acute kidney injury were noted in the blood and urine samples of the patients, with the preservation of these changes for ≥3 days.

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