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Impact of ligating gonadal or adrenal collateral veins with the left renal vein on renal function and histology in right-nephrectomized rats

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ABSTRACT

Background: In cases of trauma to the left renal vein (LRV), its ligation near the inferior vena cava (IVC) is considered, but the consequences are not always good. We investigated the role of collateral venous drainage after ligation of the LRV by studying the renal function and histology after ligation of the LRV near the IVC alone or with ligation of the gonadal or adrenal collaterals, in right-nephrectomized (RN) rats. *Material and methods:* Ligation of the LRV near the IVC alone (group 1) or with ligation of the adrenal

(group 2) or gonadal (group 3) collaterals was studied in RN Wistar rats (n = 18 per group). The renal histopathology (ischemic cortical necrosis) and functional status (urea, creatinine, sodium, and potassium) were compared.

Results: In RN rats, the results were better when ligating the LRV near the IVC alone or with the adrenal collaterals [mortality 4/18 (22.2%) and 3/18 (16.7%), respectively] than when ligating the LRV near the IVC plus the gonadal collaterals [mortality 15/18 (83.3%)] (p < 0.0001). All early deaths occurred within three days and resulted from serious histopathological (ischemic cortical necrosis) and functional (increased urea, creatinine, and potassium; decreased sodium) renal damage.

Conclusion: In right-nephrectomized rats, the LRV near the IVC and the adrenal collateral can be ligated, while the gonadal collateral should be preserved.

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1. Introduction

Clinical studies have shown that the left renal vein (LRV) may be ligated as part of aortic surgery,^{1,2} *en bloc* resection of malignant tumors,³ iatrogenic artifacts,⁴ and in some cases of trauma.⁵ The LRV may be ligated safely in close proximity to the inferior vena cava (IVC), but not near the hilum of the kidney.

In general, trauma to veins merits their repair,⁶ but this cannot always be performed because of the type and severity of trauma, vital signs and status of the patient, or resources available to the surgical team. In trauma patients who undergo right nephrectomy,

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the sites of ligation of the LRV and its collaterals are very important and can cause morbidity and mortality,³ especially when the LRV and one of its collaterals must be ligated.

This study investigated the importance of ligation of the LRV and its collaterals in right-nephrectomized rats, based on the similarity of the renovascular anatomy in humans and rats. We demonstrated that the LRV could be ligated close to the IVC together with ligation of the adrenal collateral, while the gonadal collateral should be preserved.

2. Material and methods

This study was authorized by the Ethics Review Board of our institute and was performed according to the Helsinki Declaration.⁷

Fifty-four 12-week-old Wistar rats of both sexes (250–300 g) were used. They were allowed to acclimatize to their new environment for 1 month before the start of the study. The rats were housed in steel-

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wire cages in rooms at 21 °C and had free access to dry pellet food and water.

The rats were divided randomly into three groups of 18: group 1 (G1), right nephrectomy and ligation of the LRV close to the IVC; group 2 (G2), right nephrectomy and ligation of the LRV close to the IVC plus ligation of the left adrenal vein (Fig. 1); and group 3 (G3), right nephrectomy and ligation of the LRV close to the IVC plus ligation of the left gonadal vein.

The rats were anesthetized by inhalation of diethyl ether. The abdominal skin was shaved and cleaned with povidone-iodide solution. A median laparotomy (length, 3 cm) was performed, followed by a right nephrectomy. The largest collaterals and the left adrenal and gonadal veins were dissected, and the LRV near the IVC was ligated with 5/0 silk. In G1, this constituted the entire procedure. In G2 and G3, the left adrenal and left gonadal veins, respectively, were also ligated with 5/0 silk. Physiological saline (0.9%; 1 cm³) was injected into the peritoneum after closing the abdomen with a continuous suture of 3/0 silk. Water and food were started on the first postoperative day.

The three groups were further subdivided into groups of six, and the rats were killed on day 7, 15, or 60. Rats were sacrificed after inducing anesthesia with high-dose ethyl ether and drawing intracardiac blood to measure potassium, urea, and creatinine. The left kidneys were removed for histopathological studies. Identical procedures were performed on any rats that died before sacrifice, and blood samples were taken from these rats shortly after death.

The blood was placed in test tubes containing normal gel and centrifuged in a Hettich centrifuge (Hettich, Tuttlingen, Germany) at 3000 rpm for 10 min: the serum obtained was frozen at -70 °C until studied. Serum urea levels were measured using the urease method in a Hitachi Modular P autoanalyzer (Roche Diagnostics, Mannheim, Germany) using a Roche kit (Roche, Basel, Switzerland). Serum creatinine was measured using the same system according to the Jaffe method; serum sodium and potassium were measured with the same system using the ion-selective electrode method.

The kidneys were placed in 10% formaldehyde solution before histopathological examination. The broadest surfaces were analyzed by sectioning through the pelvis in 4-µm-thick slices, which were stained with hematoxylin-eosin. A pathologist who was blind to the study protocol evaluated the renal ischemic cortical necrosis. The extent of (cortical) necrosis was graded from 0 to 3 as follows: 0 (none) = no necrosis; 1 (mild) = necrosis confined to the inner one-third of the cortex, primarily the S3 segment (pars recta) of the proximal tubules; 2 (moderate) = necrosis extending into the upper two-thirds of the cortex; and 3 (severe) = extensive necrosis of all areas of the cortex and necrotic tubules present near the surface of the kidney.⁸

Statistical analyses were carried out using SPSS for Windows ver. 10.0 (SPSS, Chicago, IL, USA). Multiple groups were compared using the Kruskal-Wallis test for non-parametric values and analysis of variance (ANOVA) for parametric values. Two-group comparisons of non-parametric and parametric values were made using the Mann-Whitney U test and Tukey test, respectively. Levels of statistical significance were accepted as p < 0.05 in two-group comparisons, p < 0.0167 in three-group comparisons, and p < 0.0125 in four-group comparisons (with the Bonferroni correction).

3. Results

The gonadal vein was larger in caliber than the adrenal vein in all animals at retroperitoneal exploration.

During the laparotomy, after ligating the vessels, some congestion, edema, and cyanosis of the left kidney were observed immediately in all groups. The congestion was most severe in G3, and small hemorrhagic foci were observed in some kidneys in G2 and G3.

After sacrifice with high-dose ethyl ether, the intraperitoneal cavity was observed in all groups, and no other visceral abnormalities were seen. The rats that died prematurely had very edematous, hemorrhagic kidneys on macroscopic examination. The dimensions of the left kidney in rats sacrificed on days 7 and 15 were increased, and the kidneys were swollen and purple in color. The dimensions of the left kidney in rats sacrificed on day 60 were normal or slightly reduced, but the kidneys were partly cyanotic. The unligated branches of the renal vein were dilated in all rats. although no macroscopic thrombi were seen in the LRV or its branches.

There were no abdominal wall problems during wound healing, and no infections were observed in the surviving rats.

There were four (22.2%), three (16.7%), and 15 (83.3%) deaths in G1–G3, respectively. There were significantly more deaths in group G3 (G1 vs. G3: p < 0.0001; G2 vs. G3: p < 0.001), whereas there was no significant difference between G1 and G2 (p = 0.67). The deaths in all groups are shown in Fig. 2. Deaths occurred in the first three postoperative days, and no further deaths were observed until day







Fig. 2. Mortality rates of groups in the first three days (days 7, 15 and 60).

The results of biochemical analyses of the groups.

	Group 1 (G1) (<i>n</i> = 18)	Group 2 (G2) (<i>n</i> = 18)	Group 3 (G3) (<i>n</i> = 18)	р
Urea (mg/dL) (mean \pm SD)	51.2 ± 6.6	49.5 ± 7.2	58.4 ± 7.0	G1–G3: <i>p</i> = 0.008; G2–G3: <i>p</i> = 0.001
Creatinine (mg/dL) (mean \pm SD)	$\textbf{0.55} \pm \textbf{0.25}$	0.53 ± 0.23	$\textbf{0.94} \pm \textbf{0.31}$	G1–G3: <i>p</i> < 0.0001; G2–G3: <i>p</i> < 0.0001
Sodium (mEq/L) (mean \pm SD)	120.6 ± 6.7	119.6 ± 4.8	113.4 ± 6.8	G1–G3: <i>p</i> = 0.003; G2–G3: <i>p</i> = 0.012
Potassium (mEq/L) (mean \pm SD)	5.0 ± 0.7	5.2 ± 0.6	5.8 ± 0.6	G1–G3: <i>p</i> = 0.001; G2–G3: <i>p</i> = 0.014

60. Consequently, the mortality in the first three days equaled the total mortality on day 60 (Fig. 2).

The urea, creatinine, and potassium levels were higher in G3 than in the other groups (Table 1), and the sodium levels were lower in G3. The biochemical analyses of the subgroups are shown in Table 2 and Fig. 3. In G1 and G2, there were differences in biochemistry among the different time points (subgroups). In G3, the biochemical levels in the rats that died prematurely were poorer than those in the other subgroups, but this was not analyzed statistically because only one animal remained in each of the subgroups (Table 2, Fig. 3).

On comparing the histopathological scores it was found that ischemic cortical necrosis (Fig. 4) was greater in G3 (Table 3). The histopathological scores of the subgroups are shown in Table 4 and Fig. 5. In G1, the ischemic cortical necrosis scores differed between the early death rats and the rats killed on days 7 (p = 0.016), 15 (p = 0.029), and 60 (p = 0.016). There was no difference between the other subgroups (Table 4, Fig. 5). In G2, the ischemic cortical necrosis scores differed between the early death rats and the rats killed on days 7 (p = 0.036), and 60 (p = 0.057; nearly significant), 15 (p = 0.036), and 60 (p = 0.024). There was no difference between the other subgroups (Table 4, Fig. 5). In G3, the ischemic cortical necrosis scores in the early death rats were poor. Statistical analyses were not performed because only one animal survived in each of the subgroups (Table 4, Fig. 5).

4. Discussion

Ligation of the right renal vein, which does not have collaterals, is inappropriate with serious renal lesions.^{9,10} Ligation of the LRV,

which has many collaterals, may be undertaken as a temporary measure or as a permanent solution to facilitate some surgical procedures.^{11–15} The LRV is single and longer than the right renal vein; it flows into the IVC after crossing the aorta anteriorly. The LRV has gonadal, adrenal, inferior phrenic, and ureteral collaterals, and a pericapsular network connected with lumbar, retroaortic, and prevertebral venous plexi.^{10,16,17}

Ligation of the LRV can create many complications that increase morbidity (e.g., loss of renal function leading to hemodialysis, retroperitoneal hemorrhage, increased creatinine levels, renal vein congestion, renal necrosis, and rupture of the left kidney). To avoid these complications, reanastomosis of the LRV at the end of the surgery is recommended in various surgical procedures that may require ligation of the LRV.^{3,18–21} Saving the right kidney to compensate for the temporary loss of renal function is encouraging. A solitary left kidney, or the inability of the other kidney to compensate, is a serious problem. The surgeon must be more careful in children, owing to their insufficient collateral development.^{18,22,23}

In one series of LRV ligation during surgery for aortic aneurysm, no serious problem was observed. It was concluded that the LRV can be ligated safely^{11,21} and that reconstruction of the vein at the end of surgery is helpful.^{19,23,24}

In most patients undergoing right nephrectomy because of a kidney tumor, a deterioration in renal function was detected after ligation of the LRV, and hemodialysis was indicated for some.^{3,12,18,25} In a study by James et al.²¹ renal failure occurred in only one of 10 patients who underwent right nephrectomy and LRV ligation; in the one case of renal failure, the LRV had been ligated at the hilus.

Patients subject to trauma tend to be younger than those in whom elective surgery is performed. Erlik et al.¹³ reported that an

Table	2
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The results of biochemical analyses of the subgroups.

Group	Subgroup	Urea (mg/dL) (mean \pm SD)	Creatinine (mg/dL) (mean \pm SD)	Sodium (mEq/L) (mean \pm SD)	Potassium (mEq/L) (mean \pm SD)
Group 1 $(n = 18)$	Dead $(n = 4)$	59.3 ± 2.8	0.94 ± 0.18	118.8 ± 6.7	5.9 ± 0.4
	Day 7 $(n = 5)$	54.2 ± 3.2	0.50 ± 0.16	123.4 ± 5.9	4.7 ± 0.6
	Day 15 $(n = 4)$	48.0 ± 4.8	0.39 ± 0.05	126.0 ± 1.6	4.9 ± 0.5
	Day 60 (<i>n</i> = 5)	44.2 ± 1.8	0.40 ± 0.03	120.4 ± 2.3	4.6 ± 0.5
Group 2 ($n = 18$)	Dead $(n = 4)$	60.0 ± 2.0	0.95 ± 0.15	112.0 ± 5.3	6.0 ± 0.2
Group 1 (<i>n</i> = 18) Group 2 (<i>n</i> = 18) Group 3 (<i>n</i> = 18) Group 1	Day 7 $(n = 5)$	53.5 ± 3.3	0.54 ± 0.16	122.3 ± 2.9	5.1 ± 0.6
	Day 15 $(n = 4)$	46.8 ± 5.6	0.40 ± 0.18	121.4 ± 4.0	5.1 ± 0.6
	Day 60 $(n = 5)$	43.8 ± 4.5	0.44 ± 0.07	120.0 ± 2.3	4.9 ± 0.5
Group 3 ($n = 18$)	Dead $(n = 4)$	60.4 ± 5.2	1.02 ± 0.26	111.8 ± 6.3	6.0 ± 0.5
Group 3 $(n = 18)$	Day 7 $(n = 5)$	54	0.57	122	5.1
	Day 15 $(n = 4)$	52	0.49	118	4.8
	Day 60 $(n = 5)$	40	0.51	124	5.0
Group 1	Dead-day 7 Dead-day 15	n = 0.001	p = 0.001	p = 0.011	p = 0.012
	Dead-day 15	p = 0.001	p < 0.0001	p = 0.005	n - 0.005
	Day 7-day 60	p < 0.0001 p = 0.001	<i>p</i> < 0.0001		p = 0.005
Group 2	Dead-day 7		n = 0.008	p = 0.009	
	Dead-day 15	p = 0.005	p = 0.001	p = 0.012	
	Dead-day 60	p = 0.001	p = 0.001	r	p = 0.001
	Day 7-day 60	p = 0.019	F		r



Fig. 3. The graphical representation of biochemical analysis of subgroups: (a) urea; (b) creatinine; (c) sodium; (d) potassium.

underdeveloped collateral venous system is the most important factor determining renal function after LRV ligation. In trauma cases, patients are frequently in shock because of massive blood loss when they are admitted to the emergency department;



Fig. 4. Histopathological view (ischemic cortical necrosis $H+E \, \times \, 400)$ of the renal cortex of an early dead rat.

another problem is that single-vessel injuries are uncommon.³¹ Blaisdell reported that isolated LRV injuries are rare; the LRV is usually injured (along with the aorta or left renal artery) after penetrating trauma.³² The repair of injured veins increases the existing blood loss, and prolonged surgery would deepen acidosis, hypothermia, and coagulopathy, while increasing cardiac dysrhythmias. Ligation of veins instead of repair is recommended in these cases.^{26–30}

A few authors have ligated the LRV in right-nephrectomized animals. In Diniz et al.,³³ all mongrel dogs with right nephrectomy plus LRV ligation died within 10 days. Threefoot et al.³⁴ ligated the bilateral renal veins in rats and reported that most of the surviving rats were those in which the LRV was ligated close to the vena cava; most of the dead rats were those in which the LRV was ligated near the kidney.

In our study, all of the early deaths occurred in the first three days, as in Threefoot et al.³⁴ The urea, creatinine, and potassium levels in early death rats were higher than those in the sacrificed rats, whereas the sodium levels were lower. Early death was attributed to the insufficiency of the venous system, resulting in increased levels of urea, creatinine, and potassium and a decreased level of sodium level due to acute renal failure. Serious lesions that could potentially affect renal function and ischemic cortical necrosis were seen in the histopathological examinations of the dead rats. The functional and histopathological deterioration

Table 3

The results of histopathological (ischemic cortical necrosis) scores of the groups.

Parameters		Group 1 (G1) (<i>n</i> = 18)	Group 2 (G2) $(n = 18)$	Group 3 (G3) (<i>n</i> = 18)	р
Ischemic cortical necrosis	None	11	10	2	G1–G3: <i>p</i> = 0.001; G2–G3: <i>p</i> = 0.001
	Mild	3	4	1	
	Moderate	1	2	5	
	Severe	3	2	10	

 Table 4

 The results of histopathological (ischemic cortical necrosis) scores of the subgroups

Group	Subgroup	None	Mild	Moderate	Severe
Group 1 $(n = 18)$	Dead $(n=4)$			1	3
	Day 7 $(n = 5)$	3	2		
	Day 15 $(n = 4)$	3	1		
	Day 60 $(n = 5)$	5			
Group 2 ($n = 18$)	Dead $(n = 4)$			1	2
,	Day 7 $(n = 5)$	2	1	1	
	Day 15 $(n = 4)$	4	1		
	Day 60 $(n = 5)$	4	2		
Group 3 (<i>n</i> = 18)	Dead $(n = 4)$			5	10
	Day 7 ($n = 5$)		1		
	Day 15 $(n = 4)$	1			
	Day 60 $(n = 5)$	1			
Total ($n = 54$)		23	8	8	15

occurred in the group with ligation of the LRV close to the IVC plus ligation of the left gonadal vein, and most of the early deaths were in this group (83.3% vs. 16.7% and 22.2%).

In this experimental study, ligation of the LRV close to the IVC or ligation of both the LRV and adrenal vein resulted in acceptable changes in renal function and histology. The adrenal and gonadal veins together or the gonadal vein alone allowed ongoing venous drainage, whereas the adrenal vein alone is insufficient for venous drainage.

Among right-nephrectomized patients, in cases of LRV trauma, aortic surgery, or *en bloc* resection of malignant tumors, more care should be taken to protect the left gonadal vein. In the



Fig. 5. The graphical representation of histopathological (ischemic cortical necrosis) scores of subgroups.

postoperative follow-up, increased urea, creatinine, and potassium and decreased sodium levels can help diagnose acute renal failure after ligation of the left renal vein.

4.1. Study limitations

Dogs and rats have been used to assess ligation of the LRV because their vascular anatomy, hemodynamics, and immunology are similar to those in humans. Although there are some anatomic similarities, it was shown that better drainage is obtained with the collaterals in humans after LRV ligation.³⁵ Therefore, successful results may be more difficult to obtain in animals than in humans.

Conflict of interest

There are no conflicts of interest.

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Ethical approval

Ethical approval was given by the Ethical Committee of Taksim Training and Research Hospital, no: 033/2007.

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