The clinical significance of left inferior phrenic vein in retroperitoneal laparoscopic adrenalectomy

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Research

Keywords: CAV, IPV, landmark, RLA, significance

Posted Date: May 5th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-25361/v1>

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Abstract

Background

The clinical significance of left inferior phrenic vein (IPV) during left retroperitoneal laparoscopic adrenalectomy (RLA) for adrenal tumors is unclear. We aimed to investigate the surgical feasibility and value of IPV as a landmark during RLA.

Methods

Between September 2016 and November 2018, 92 consecutive left RLAs were performed by the same surgeon. All the operations were performed through the approach of three relative avascular planes. Then we searched for IPV between superior margin of renal artery and anterior aspect of psoas major muscle. The left IPV was used as an anatomical landmark to identify and ligate the central adrenal vein (CAV).

Results

All 92 operations were performed successfully with one conversion to open surgery. We identified the CAV following left IPV in all cases. The left IPV drained into the CAV in 100% of cases, and variant venous anatomy (2 CAVs) was encountered in 2 pheochromocytoma cases (2.17%). Peritoneum perforation occurred in one case in operation (1.09%). Postoperative complications (fever) occurred in 3 patients (3.26%). The mean operative time was 75.82 ± 21.55 minutes. The average postoperative hospital stay was 3.57 ± 0.76 days. Pathological examination revealed: cortical adenoma in 72 cases (78.26%), adrenal cyst in 11 cases (11.96%), pheochromocytoma in 6 cases (6.52%), cortical hyperplasia in 1 case (1.09%), medullary hyperplasia in 1 case (1.09%), and hemangioma in 1 case (1.09%).

Conclusions

Using left IPV as a landmark to search for and handle CAV has important clinical significance in left RLA.

Introduction

Laparoscopic adrenalectomy (LA) has replaced open adrenalectomy and become the gold standard treatment for most adrenal tumors especially benign adrenal tumors. There are 4 different approaches of LA: transperitoneal laparoscopic adrenalectomy (TLA) in supine or lateral position, and retroperitoneal laparoscopic adrenalectomy (RLA) in lateral or prone position. TLA approach can give surgeons wide working space, identifiable anatomic landmarks, and early control of the adrenal vein^[1]. However, RLA is now regarded as a better approach for small benign adrenal tumours in terms of a shorter operative time

and hospital stay, earlier recovery of bowel function, less postoperative pain, and faster recovery than TLA [2, 3]. RLA in lateral position is the most widely used technique for LA in most centers in China.

An utmost important procedure of LA is the early identification and ligation of the central adrenal vein (CAV). Although variations of CAV may exist [4, 5, 6], venous drainage of most adrenal gland depends on only one CAV: the left CAV converging with the left inferior phrenic vein (IPV) before draining into the left renal vein, while the right vein draining directly into the inferior vena cava (IVC) [4]. Left IPV has recently received attention for its anatomical relationship with CAV [7] and the involvement in the drainage of esophageal varices in patients with liver cirrhosis [8]. However, studies taking left IPV as a landmark to identify CAV and variant CAV anatomy rate in RLA have not been reported. In our study, we collected and analyzed clinical data of left RLAs, and demonstrated anatomical characteristics of IPV and CAV under retroperitoneal laparoscopic view.

Methods

Patient information

The study was performed in accordance with the Declaration of Helsinki and was approved by the ethical committee of the Affiliated Hospital of Qingdao University. From September 2016 to November 2018, 92 left RLAs were performed using standard 3-port technique in lateral position by the same surgeon. Surgical Indications included functioning and non-functioning adrenal tumors or cyst (more than 2cm). Contraindications were locally invasive adrenal carcinoma or metastatic lesions. All cases underwent enhanced computed tomography or magnetic resonance imaging examination. Hormones were assessed routinely preoperatively in all patients, including plasma renin, angiotensin, aldosterone, ACTH, cortisol, and catecholamines. Perioperative and intraoperative information was obtained from medical records system. The baseline demographics and perioperative outcomes of all subjects are shown in **Table 1**.

Surgical procedures

The patient was placed in the full lateral decubitus position with overextension under general anesthesia. RLA was performed using standard 3-port technique by an experienced surgeon [9].

After retroperitoneal space was established, the retroperitoneal fat was removed firstly. Next, Gerota's fascia was vertically incised from the inferior margin of the diaphragm to the upper margin of the iliac fossa. And then, three relative avascular dissection planes were created to expose and separate the adrenal gland, as Xu Zhang described [9]. The first dissection plane was between perirenal fat (PF) and the anterior renal fascia, the second plane was between posterior renal fascia and PF, the third plane was located on the parenchymal surface of the upper renal pole and PF. The adrenal gland or the **contour** of tumor will appear under our direct vision after the three steps. Diverging from the traditional method used in RLA, we easily searched and identified left renal artery according to our previous study [10], and then searched for IPV between superior margin of renal artery and anterior aspect of psoas major muscle

(PMM). Under retroperitoneal vision, we could observe that IPV travelled following anterior margin of PMM and toward diaphragmatic crus. Subsequently, we traced IPV toward the proximal side and found the bifurcation between IPV and CAV. Then the CAV was exposed, clipped, and transected (**Figure 1**). Other smaller periadrenal vessels were divided using ultrasonic dissection. At last, we mobilized adrenal gland and tumor from neighboring tissues with blunt and sharp dissection alternatively. The specimen was placed into a retrieval bag and removed, then drainage tube was placed, and the incision was routinely sutured.

Statistical analyses

Statistical analysis was performed using SPSS program (version 19.0, SPSS, Chicago, IL, USA). Quantitative data were expressed as mean±standard deviation (SD) and were analyzed by the Student's *t*-tests or ANOVA analysis. Categorical variables were reported as percentages and were analyzed by chi-squared statistic tests. A *P* value of less than 0.05 was considered statistically significant.

Results

All 92 procedures were performed successfully. Of these procedures, only one case with pheochromocytoma converted to an open adrenalectomy due to evident tumor adhesions to adjacent [peritoneum](#). The estimated intraoperative blood loss was approximately 20–200 mL (average was 26.09 mL). The operation lasted from 40 to 145 minutes (average was 75.82 minutes). No patient required transfusion. The drainage tube was removed after 2–5 days (2.39 ± 0.63 days). The patients started to ambulate 1–2 days after the surgery, and the mean postoperative hospital stay was 2–7 days (3.57 ± 0.76 days).

One peritoneum perforation occurred during operation and we clipped it with one Hem-o-lock. Three postoperative fevers occurred. The 3 patients with fever recovered with active surveillance and treatment. Postoperative pathology confirmed that among the 92 cases, cortical adenoma cases were mostly of the conventional cell type ($n=72$; 78.26%), adrenal cyst in 11 cases (11.96%), pheochromocytoma in 6 cases (6.52%), cortical hyperplasia in 1 case (1.09%), medullary hyperplasia in 1 case (1.09%), and [hemangioma](#) in 1 case (1.09%). All cases were benign lesions. Detailed patients' intraoperative and postoperative outcomes are shown in **Table 1**.

During left RLA, after the three relative avascular dissection planes were dissected, the contours of adrenal tumor were observed. We successfully identified renal artery according to MAL on PMM and mobilized the upper margin of it (92 out of 92 cases, 100%). We found IPV in the zone between upper margin of renal artery and anterior aspect of PMM and then followed it and identified CAV successfully in all patients. The main venous drainage was made by a single CAV for 90 patients, while two patients with pheochromocytoma appeared to have duplicated CAVs. Based on the positioning of IPV, we successfully processed the CAV in a short time period and completed RLA. As both of 2 cases of variant adrenal venous drainage were pheochromocytoma, we especially compared characteristics of pheochromocytomas and the other adrenal tumors. As shown in **Table 2**, there were significant

differences between the two groups in terms of tumor size ($p=0.043$), operative time ($p=0.03$), blood loss ($p<0.001$), drainage day ($p=0.013$), conversion rate ($p=0.065$) and adrenal venous drainage type distribution($p=0.004$).

Discussion

LA has gained wide acceptance as a standard treatment for most adrenal tumors. Identification and processing of the CAV are crucial steps in LA^[11]. During TLA, as renal vein is located at the ventral side and easier to get exposed, surgeons can identify and separate left renal and gonadal vein firstly, and then can search for left CAV at the opposite side of gonadal vein. By contrast, retroperitoneal approach lacks identifiable anatomic landmarks and does not have advantage of quickly exposing CAV. Few clinical studies reported landmarks to search for CAV during left RLA. Besides, there lack clinical studies with regard to variability of adrenal vein distribution under retroperitoneal vision. In the present study, we successfully used left IPV as a landmark to identify CAV and found that left IPV converged with left CAV before draining into left renal vein in 98% cases under retroperitoneal laparoscopic view. Moreover, we recorded variants in the left adrenal venous drainage in different tumors during RLA. To our knowledge, our study firstly demonstrated anatomical characteristics of IPV and CAV and the clinical significance of IPV as an important landmark to identify CAV in left RLA.

Anatomic RLA, first reported by Zhang et al. in 2007, greatly shortened the operation time and decreased the complication rate^[9, 12], and we adopted the anatomical three-plane technique, in which we can quickly and directly separate and expose the adrenal tumor. However, we found that one can expose CAV only after separating small periadrenal vessels and neighbor tissues thoroughly and uplifting the tumor cranially with this surgical method. In our present study, we thoroughly separated PPM plane and exposed the area between superior margin of renal artery and PMM, in this way we could found left IPV successfully and traced it toward renal hilum from lateral to medial to identify CAV trunk as the kidney is rotated inferiorly and medially in retroperitoneal approach, and then found and processed CAV trunk successfully in all cases. Compared with Zhang's approach, our method provides more space and more ideal angel to observe IPV and CAV from dorsal side, especially for overweight and obese patient whose CAV was too deep to expose. Besides the benefits of IPV as a landmark in RLA, early locating IPV and dissecting CAV can reduce the surgeon's mental stress. In patients with pheochromocytoma, although early ligation of CAV may cause venous congestion and more bleeding, reducing the risk of excessive catecholamine excretion and blood pressure fluctuation were more important^[13]. In our study, the more blood loss and longer drainage time for pheochromocytomas were mainly caused by significantly larger tumor size and larger resection area with more ooze rather than early ligation of CAV.

In regard with excision scope, we performed total rather than partial adrenalectomy in case of recurrence in all procedures no matter whether boundaries between lesions and adrenal glands were clear or not.

Familiarity with the types and variability of adrenal venous drainage is helpful for surgeons to identify and process the adrenal vein during RLA, especially for patients with large adrenal tumors or

pheochromocytomas. The frequency of variation in adrenal venous drainage is less on the left side than the right side ^[11]. Main variant of the left adrenal vein reported in previous studies was duplication, with CAV and IPV draining into the renal vein separately ^[4] or with 2 adrenal veins draining into the renal vein and left lumbar vein respectively ^[14]. However, as shown in **Table 3**, cadaver studies focused on venous drainage of normal adrenal glands rather than pathologic ones with tumors.

Parnaby et al ^[4] reported left adrenal vein anatomy in 83 cases of patients with adrenal tumors who underwent LA. They found that 3 patients (3.6%) had adrenal vein variants. These variants were duplicated adrenal veins and present in patients with pheochromocytoma. Anouk Scholten et al ^[11] reported left venous variants occurred in 26 of 296 patients (8.8%) and all these cases were in TLA, and found no venous variants in 19 retroperitoneal adrenalectomies. The above two studies were based TLA, and few studies reported the frequency of venous variants in retroperitoneal approach. Our study showed that left venous variants occurred in 2 cases of 92 patients (2.17%), and the frequency was lower than that of previous studies ^[4, 11] mainly preferring TLA approach. It is possible that the adrenal venous anatomy is not easier to be observed through retroperitoneal approach compared with transperitoneal approach. Both of the two cases were diagnosed as pheochromocytoma and have duplicated CAVs, one CAV converged with IPV before draining into renal vein, the other drained into the renal vein separately. In our study, patients with pheochromocytoma are more frequent to have variant adrenal vein anatomy compared with those with non-pheochromocytoma, and our results were in consistent with previous study ^[11]. A possible explanation could be an increase in angiogenesis and vasculogenesis, compression of the original CAV by the large tumor which caused preferential venous return to the second adrenal vein in pheochromocytoma ^[18].

In terms of relationship between left IPV and CAV, Matthieu Siebert et al ^[19] reported left IPV drained into an adrenal vein in 100% of 44 adult cadavers cases, and are not consistent with the findings of Loukas ^[8], who found a connection between CAV and IPV in only 25% of cases. The difference could be explained by the two different protocols of anatomy. And our study is in consistent with the former conclusion, and has helped confirm the constant nature of left IPV and CAV drainage.

Our study clarified the anatomical relationship between left IPV and CAV under retroperitoneal view, and we believed that following IPV as a guidance to identify CAV under retroperitoneal laparoscope is reasonable and applicable. The clinical significance of left IPV as an important landmark in left RLA should get enough attention during left RLA and other upper urinary tract laparoscopic surgeries that require handling CAV. Besides, more attention should be paid to adrenal vein variants during RLA in patients with pheochromocytoma.

There were some limitations in our study. First, the main limit of the study was the lack of the control group using a retroperitoneal technique without searching for IPV as a landmark. Second it was conducted at a single center, the limited sample size may reduce the strength of the study.

Conclusions

The data from our study for the first time demonstrated anatomical characteristics of IPV and CAV including CAV variant rate under retroperitoneal laparoscopic view. Besides we provided a novel method to accelerate the process of identifying IPV and CAV. Using left IPV as a landmark to search for and handle CAV has important clinical significance in left RLA.

Declarations

Funding

No funding was obtained for this study.

Availability of data and materials

The raw data that was used in this study is available upon request from the corresponding author.

Authors' contributions

Conceived and designed: Fang-Ming Wang; Wrote the paper: Fang-Ming Wang; Explained the results: Gui-Ming Zhang, Yong Liu. All authors have read and approved the final manuscript.

Competing interests

None.

Ethics approval and consent to participate

The study was performed in accordance with the Declaration of Helsinki and was approved by the ethical committee of the Affiliated Hospital of Qingdao University. For this type of retrospective study, formal patient consent is not required.

Consent for publication

Not applicable

Acknowledgements

None

Conflict of Interest

The authors declare that they have no conflict of interest

References

- [1] Janetschek G, Neumann HP. Laparoscopic surgery for pheochromocytoma. *Urol Clin North Am*. 2001;28 (1):97-105.
- [2] Barczyński M, Konturek A, Nowak, W. Randomized clinical trial of posterior retroperitoneoscopic adrenalectomy versus lateral transperitoneal laparoscopic adrenalectomy with a 5-year follow-up. *Ann Surg*. 2014;260(5):740-7.
- [3] Constantinides VA, Christakis I, Touska P, et al. Retroperitoneoscopic or laparoscopic adrenalectomy? A single-centre UK experience. *Surg Endosc*. 2013;27(11):4147-52.
- [4] Parnaby CN, Galbraith N, O'Dwyer PJ. Experience in identifying the venous drainage of the adrenal gland during laparoscopic adrenalectomy. *Clin Anat*. 2008; 21(7):660-5.
- [5] MacGillivray DC, Khwaja K, Shickman SJ. Confluence of the right adrenal vein with the accessory right hepatic veins: a potential hazard in laparoscopic right adrenalectomy. *Surg Endosc*. 1996;10(11):1095-6.
- [6] Stack SP, Rösch J, Cook DM, et al. Anomalous left adrenal venous drainage directly into the inferior vena cava. *J Vasc Interv Radiol*. 2001; 12(3):385-7.
- [7] Cesmebasi A, Du Plessis M, Iannatuono M, et al. A review of the anatomy and clinical significance of adrenal veins. *Clin Anat*. 2014;27(8):1253-63.
- [8] Loukas M, Louis RG, Hullett J et al. An anatomical classification of the variations of the inferior phrenic vein. *Surg Radiol Anat*. 2005, 27(6): 566–74.
- [9] Zhang X, Fu B, Lang B, et al. Technique of anatomical retroperitoneoscopic adrenalectomy with report of 800 cases. *J Urol*. 2007;177(4):1254-7.
- [10] Luo L, Liu YN, Zhang Y, et al. An easy and effective method to locate renal vein during retroperitoneal laparoscopic radical nephrectomy: single-center experience. *Med Sci Monit*. 2018;24:5147-51.

[11] [Scholten A](#), [Cisco RM](#), [Vriens MR](#), et al. Variant adrenal venous anatomy in 546 laparoscopic adrenalectomies. [JAMA Surg](#). 2013 Apr;148(4):378-83.

[12] [Li S](#), [Wang J](#), [Zhang E](#), et al. Single-plane retroperitoneoscopic adrenalectomy: a new operative procedure for benign adrenal disease. [Sci Rep](#). 2018;8(1):4027.

[13] [Vassiliou MC](#), [Laycock WS](#). Laparoscopic adrenalectomy for pheochromocytoma: take the vein last? [Surg Endosc](#). 2009;23: 965-8.

[14] [Johnstone FR](#). The suprarenal veins. [Am J Surg](#). 1957;94(4):615-20.

[15] [Anson BJ](#), [Caudwell EW](#), et al. The anatomy of the para-renal system of veins, with comments on the renal arteries. [J Urol](#). 1948;60(5):714-37.

[16] [Clark K](#). The blood vessels of the adrenal gland. [J R Coll Surg Edinb](#). 1959;4(3):257-62.

[17] [Davidson JK](#), [Morley P](#), [Hurley GD](#), et al. Adrenal venography and ultrasound in the investigation of the adrenal gland: an analysis of 58 cases. [Br J Radiol](#).1975;48(570):435-50.

[18] [Zielke A](#), [Middeke M](#), [Hoffmann S](#), et al. VEGF-mediated angiogenesis of human pheochromocytomas is associated to malignancy and inhibited by anti-VEGF antibodies in experimental tumors. [Surgery](#). 2002;132(6):1056-63.

[19] [Matthieu Siebert](#), [Yohann Robert](#), [Romain Didier](#), et al. Anatomical Variations of the Venous Drainage from the Left Adrenal Gland: An Anatomical Study. [World J Surg](#).2017 41(4):991–6.

Tables

Table 1. Baseline characteristics of the study population

Variables	Subjects (n=92)
Gender (n (%))	
Male	41(44.57)
Female	51(55.43)
Age (years)	52.50±11.23
BMI (kg/m ²)	26.04±3.89
Diagnosis (n (%))	
Hyperaldosteronism	7(7.61)
Pheochromocytoma	6(6.52)
Hypercortisolism	3(3.26)
Adrenal cyst	11(11.96)
Nonfunctioning adenoma	62(67.39)
Adrenal medullary hyperplasia	1(1.09)
Adrenocortical hyperplasia	1(1.09)
Hemangioma	1(1.09)
Preoperative tumor size (cm)	2.96±1.64
Operative time (minutes)	75.82±21.55
Evaluated blood loss (ml)	26.09±21.17
Retroperitoneal drainage (days)	2.39±0.63
Drainage volume per day (ml)	41.67±34.24
Postoperative hospital stay (days)	3.57±0.76
Complications (n (%))	1(1.09)
Peritoneum perforation	3(3.26)
Postoperative fever	
Conversion (n (%))	1(1.09)
Transfusion (n (%))	0(0)

Data are expressed as n (%) or mean ± SD. BMI=body mass index.

Table 2. Clinical features of the study population stratified by diagnosis.

PHEO (n=6)	PHA (n=7)	HC (n=3)	Diagnosis				p ^a	p ^b
			NA (n=62)	Cyst (n=11)	Others (n=3)	Non- PHEO(n=86)		
3:3	3:4	1:2	26:36	5:6	3:0	38:48	0.529	1.0
48.17±	50.71±	33±	55.31±	47.82±	44±	52.80±	0.002	0.331
9.37	8.85	4.36	10.75	10.07	10.82	11.33		
							0.129	0.231
4(66.67)	1(14.29)	1(33.33)	26(41.94)	4(36.36)	3	35(40.70)		
2(33.33)	6(85.71)	2(66.67)	36(58.06)	7(63.64)	0	51(59.30)		
4.27±	2.16±	3.4±	2.58±	4.78±	2.9±	2.87±	<0.001	0.043
2.16	0.96	0.96	1.06	2.64	2.69	1.57		
94.17±	77.14±	108.33±	74.27±	64.55±	76.67±	74.53±	0.009	0.030
33.83	12.20	10.41	20.58	14.05	20.82	20.11		
65±	22.86±	30±	23.55±	20.91±	23.33±	23.37±	<0.001	<0.001
73.14	4.88	17.32	7.26	3.02	5.77	7.13		
3±	2.57±	3±0	2.31±	2.27±	2.33±	2.35±	0.055	0.013
1.10	0.79		0.56	0.47	0.58	0.57		
3.83±	3.71±	4.67±	3.5±	3.45±	3.33±	3.55±	0.138	0.375
1.17	0.76	0.58	0.74	0.52	0.58	0.73		
1(16.67)	0	0	0	0	0	0	0.013	0.065
							<0.001	
0.004								
4(66.67)	7(100)	3(100)	62(100)	11(100)	3(100)	86(100)		
2(33.33)	0	0	0	0	0	0		

Data are expressed as n (%) or mean ± SD. The bold value indicated statistical significance.

BMI=body mass index; PHEO=pheochromocytoma; PHA=primary hyperaldosteronism; HC= hypercortisolism; NA=nonfunctioning adenoma. p^a for comparison among different diagnosis groups; P^b for comparison between non-PHEO and PHEO groups.

Table 3 Variant Left Adrenal Venous Anatomy in Literature

Source	Left Adrenals (n)	Variant Venous Anatomy (n (%))
Anson and Caudwell, ¹⁵ 1948 ^a	450	1(0.2)
Johnstone, ¹⁴ 1957 ^a	10	1(10)
Clark, ¹⁶ 1959 ^a	16	5(31.3)
Davidson et al, ¹⁷ 1975 ^a	50	4(8)
Parnaby et al, ⁴ 2008	83	3(3.6)
Anouk Scholten et al, ¹¹ 2013	296	26(8.8)
Matthieu Siebert et al, ¹⁹ 2017 ^a	44	6(13.6)
Current study	92	2(2.17)

^a Cadaver study.

Figures

Figure 1

Key procedures of processing IPV and CAV during left retroperitoneal laparoscopic adrenalectomy and major intraoperative anatomical structures. (a) The IPV, CAV, surface of the upper kidney, and dorsal aspect of AT with perirenal fat was completely separated; (b) CAV trunk was ligated with one Hem-o-lok clip; (c) IPV was ligated with one Hem-o-lok clip; (d) CAV trunk was dissected. IPV: inferior phrenic vein; CAV: central adrenal vein; AT: adrenal tumor; K: kidney.