

Results after laparoscopic left anterior transperitoneal submesocolic adrenalectomy for the treatment of pheochromocytoma



Ann. Ital. Chir., 2019 90, 3: 220-224
pii: S0003469X19030161

Andrea Balla*, Silvia Quaresima*, Monica Ortenzi**, Livia Palmieri*, Francesca Meoli*, Diletta Corallino*, Mario Guerrieri**, Pietro Ursi*, Alessandro M. Paganini*

*Department of General Surgery and Surgical Specialties "Paride Stefanini", Sapienza, University of Rome, Rome, Italy

**Department of General Surgery, Università Politecnica delle Marche, Ancona, Italy

Results after laparoscopic left anterior transperitoneal submesocolic adrenalectomy for the treatment of pheochromocytoma

AIM: Minimally invasive adrenalectomy is the treatment of choice for benign adrenal lesions including pheochromocytoma (PHE) and in selected patients with malignant lesions. The aim of the present study is to evaluate the authors' results after laparoscopic left anterior transperitoneal submesocolic adrenalectomy (LLATSA) for unilateral PHE.

MATERIAL OF STUDY: This study is a retrospective analysis of prospectively collected data. From 1994 to 2018, 552 patients underwent laparoscopic adrenalectomy (LA). Of these, 34 patients (14 men, 20 women, mean age 52.8 years) underwent LLATSA for PHE.

RESULTS: Mean operative time was 93.1 ± 44.9 minutes. Conversion to open surgery occurred in two patients due to difficult identification of the anatomy. Intraoperative blood pressure and heart rate instability were observed in four cases, but with no need for conversion. Postoperative morbidity was nil. One American Society of Anesthesiologists (ASA) III patient died on postoperative day 4 from acute myocardial infarction. Mean postoperative hospital stay was 3.8 ± 1.8 days (range 2 - 8).

DISCUSSION: The main advantage of this approach is the early ligation of the main adrenal vein prior to any gland manipulation. This reduces the risk of catecholamines' spread and consequently the risk of hemodynamic instability. Intraperitoneal dissection is limited and there is no need to mobilize the colon or pancreas, with a lower risk of complications from organ manipulation.

CONCLUSIONS: LLATSA is feasible and safe for the treatment of PHE. A randomized trial design and a larger cohort of patients would be required to confirm these conclusions.

KEY WORDS: Adrenal tumors, Adrenal lesions, Laparoscopic adrenalectomy, Pheochromocytoma, Transperitoneal anterior approach, Laparoscopic left anterior transperitoneal submesocolic adrenalectomy (LLATSA)

Introduction

In 1992, Michel Gagner proposed the first laparoscopic transperitoneal adrenalectomy with patients in lateral decubitus position¹. Since then, laparoscopic adrenalectomy (LA) has rapidly become the surgical treatment of choice for benign adrenal gland lesions including pheochromocytoma (PHE)^{2,3}, as well as in selected

patients with malignant lesions, due to lower postoperative morbidity and pain and shorter hospital stay in comparison to open surgery. Later, other minimally invasive approaches for adrenal gland removal have been reported, including the retroperitoneal with patient in lateral or prone decubitus position and the anterior transperitoneal with patient supine. To date, consensus has yet to be reached concerning the ideal surgical approach for minimally invasive adrenalectomy^{2,4-9}. Laparoscopic left anterior transperitoneal submesocolic adrenalectomy (LLATSA) is another option that was reported in the last two decades, mostly by the authors of the present paper who have used it almost routinely. Our aim was to evaluate the perioperative results in patients undergoing LLATSA for the management of PHE.

Pervenuto in Redazione Dicembre 2018, Accettato per la pubblicazione Gennaio 2019

Correspondence to: Andrea Balla, MD, Department of General Surgery and Surgical Specialties "Paride Stefanini", Sapienza, University of Rome, Azienda Policlinico Umberto I, Viale del Policlinico 155, 00161 Rome, Italy (e-mail: andrea.balla@gmail.com)

Materials and Methods

This study is a retrospective analysis of prospectively collected data. Informed consent from all individual participants included in the study and institutional review board approval were obtained. From January 1994 to August 2018, 552 patients underwent LA in the two authors' centers (Department of General Surgery and Surgical Specialties "Paride Stefanini", "Sapienza" University of Rome, and Department of General Surgery, Università Politecnica delle Marche, Ancona, Italy) which follow the same treatment protocol and identical surgical technique. Of these, 21 patients underwent bilateral adrenalectomy and 449 patients underwent unilateral adrenalectomy for adrenal disease other than PHE (Conn, Cushing, myelolipoma, cancer, metastases, cysts) and were excluded from this study. Of the remaining 82 patients with a diagnosis of PHE, 48 were excluded due to location of the lesion in the right adrenal gland in 43 patients and another 5 patients with left located PHE but who underwent transperitoneal anterior adrenalectomy (not submesocolic). Eventually 34 patients with PHE who underwent LLATSA were included in the present study (Fig. 1). For the purpose of the present study, data such as gender, age, body mass index (BMI), previous abdominal surgery, lesion size, associated surgical procedures, operative time, conversion to open surgery, postoperative complications (based on the Clavien-Dindo Classification ¹⁰), blood transfusions, postoperative hospital stay and definitive histology were collected in a Microsoft Excel program (Microsoft Corporation, Redmond, Washington, USA).

PREOPERATIVE PATIENTS' MANAGEMENT

At admission, all patients were evaluated by physical examination ^{2,6-8} and hormonal assessment. This included

catecholamines excretion and vanillylmandelic acid, aldosterone and urinary aldosterone, plasma cortisol and urinary free cortisol, adrenocorticotrophic hormone, dehydroepiandrosterone sulfate, testosterone, 17-OH progesterone, and supine and upright plasma renin activity ^{2,6-8}. Magnetic Resonance Imaging and Computerized Tomography scan were performed in each case ^{2,6-8}. Alpha-blockers (doxazosin 20 mg/day) were administered 15 days before surgery to all patients and beta-blockers (atenolol 100-200 mg/day) were administered in case of tachycardia episodes ^{2,6}. On the day before surgery, volume expansion was obtained by administering 2000 cc of normal saline solution and alpha-blockers were withdrawn ^{2,6}.

LAPAROSCOPIC LEFT ANTERIOR TRANSPERITONEAL SUBMESOCOLIC ADRENALECTOMY: SURGICAL TECHNIQUE

With the patient under general anesthesia in supine position on the operative table and with abducted legs, an oro-gastric tube, urinary catheter, intra-arterial catheter for blood pressure measurement and central venous catheter are positioned.

The surgeon stands in between the patient's legs and pneumoperitoneum is established at 12-13 mmHg by open technique and Hasson cannula or with a Veress needle and optical trocar above the umbilicus, based surgeon's preference in the individual patient. Three 12 mm trocars (one to the left of the midline above the umbilicus, one on the right midclavicular line below the right costal arch and one on the left midclavicular line along the transverse umbilical line) and one 5 mm trocar (on the left anterior axillary line) are employed. The operative table is placed in slight anti-Trendelenburg position and tilted with the patient's left side up in order to improve exposure of the left side of the patient.

Under vision with a 30°/45° optic, the assistant raises the greater omentum and transverse mesocolon with a grasper from the right trocar, and the surgeon displaces the first jejunal loops to the right side of the patient so as to expose the inferior mesenteric vein (IMV) and the superior duodenal recess. By means of a bipolar diathermy device (LigaSure™ tissue fusion, Covidien, Mansfield, Massachusetts, USA) or ultrasonic shears (Ultracision, Harmonic Scalpel, Ethicon Endo Surgery, Cincinnati, Ohio, USA) the posterior peritoneum is opened between the IMV and the duodenum-jejunal angle to reach and to open Toldt's fascia. After gentle upward retraction of the body of the pancreas, the superior margin of the left renal vein is identified and followed medially until the main left inferior adrenal vein is identified, prepared and divided between clips (AcuClip, Tyco/Healtcare, Norwalk, Connecticut, U.S.A. or Weck® Hem-o-lok®, Teleflex, North Carolina, USA). The gland is then completely mobilized and removed with a specimen extraction bag (Inzi® Retrieval Systems, Applied Medical,

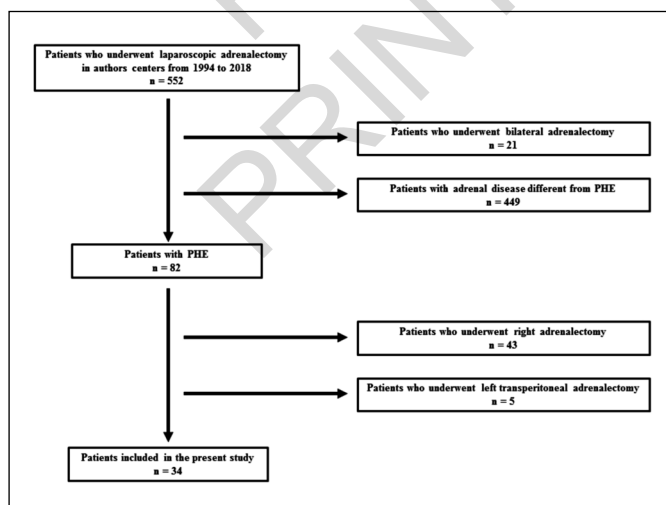


Fig. 1: Patients' flow chart.

Rancho Santa Margarita, California, USA). The residual cavity is filled with hemostatic facilitators (FloSeal, Baxter Healthcare Corporation, Deerfield, Illinois, USA or Surgiflo Hemostatic Matrix Kit, Ethicon Endo-Surgery, Johnson & Johnson, Cincinnati, Ohio, USA) and a drainage is left in the residual adrenal lodge ^{2,6-8}.

Results

Fourteen male and 20 female patients (mean age 52.8 ± 16 years, range 22 – 82 years) were included in the present study. Mean BMI was 25.8 ± 3.9 Kg/m² (range 18 – 35 Kg/m²). Two patients (5.9%) had undergone previous abdominal surgery: appendectomy (1), hysterectomy and segmental liver resection (1) (Table I). Mean operative time was 93.1 ± 44.9 minutes (range 40 – 240 minutes). In one patient cholecystectomy was performed during the same intervention (2.9%). Mean lesion size was 4.3 ± 1.9 cm (1-10 cm). Conversion to open surgery occurred in two patients due to difficulties in anatomical identification. Blood pressure and heart rate were unstable in 4 cases (11.8%) but not to the point of having to convert to open surgery. Blood transfusions were not required and postoperative complications were not observed. On postoperative day 4, one HIV+, American Society of Anesthesiologists (ASA) III patients, who had undergone a previous coronary artery by-pass graft died from acute myocardial infarction (mortality 2.9%). Oral intake occurred on the first postoperative day in all patients. Mean postoperative hospital stay was 3.8 ± 1.8 days (range 2-8 days) (Table I).

Discussion

The authors analyzed the perioperative results of patients who underwent LLATSA for PHE and observed limited intraoperative hemodynamic derangements, low con-

version rate, no postoperative morbidity and short hospital stay.

In the literature, several approaches for laparoscopic adrenalectomy are reported. However, the best approach has yet to be defined ^{2,6-9,11,12}. Each one of the reported approaches has peculiar advantages and disadvantages ^{2,6-8}. The lateral transperitoneal displays a wide operative field but to reach the adrenal gland it requires extensive dissection to mobilize the spleno-pancreatic complex and the colonic flexure, which increases the risk of complications such as left pneumothorax and postoperative wandering spleen with gastric volvulus ^{2,6-8,18-20}. Furthermore, the patient's position on the operative table does not allow for rapid conversion to open surgery, should this be required, and it does not facilitate the execution of intraperitoneal associated procedures or a contralateral adrenalectomy in case of bilateral disease ^{2,6-8,13}. However, the lateral transperitoneal remains the most popular approach ^{2,6-8,14}.

The retroperitoneal approach with patient in prone position is preferred by some surgeons due to the absence of intraperitoneal dissection, avoiding bowel manipulation and reducing postoperative pain, and the possibility to perform contralateral adrenalectomy without the need to change the patient's position ^{2,6-8,15-17}. This approach provides more direct access to the gland which is located in the retroperitoneum ¹⁵⁻¹⁷. These advantages apply particularly in obese patients or patients who underwent previous abdominal surgery, but again, in case of conversion to open surgery the patient must be repositioned on the operative table and in some cases of PHE the prone position in itself may be the cause of hemodynamic instability ^{2,6,7,15-17}.

The transperitoneal anterior approach also requires a wide dissection and mobilization of the left colonic flexure to gain exposure to the left adrenal gland ^{2,6-8}. Although it allows to perform associated intraperitoneal procedures as well as contralateral adrenalectomy, and provides rapid conversion to open surgery without repositioning the patient on the table, it is more time consuming ^{2,6-8}.

To resolve some of these drawbacks, for left adrenalectomy the authors have adopted the anterior transperitoneal submesocolic approach ^{2,6-8}. This approach in open surgery was first reported by Pierre Delbet, a French surgeon, in 1912 ²¹. The first two authors who reported this approach by laparoscopy were Sardi (1994) and Robertson (1995) who applied it in a few case reports ^{22,23}. In the authors' opinion, the main advantages of this approach are the early ligation of the main adrenal vein prior to any gland manipulation. This reduces the risk of catecholamines' spread in patients with PHE and consequently the risk of hemodynamic instability. Intraperitoneal dissection is limited and there is no need to mobilize the colon or pancreas, with a lower risk of complications from organ manipulation. Moreover, the possibility to explore the entire abdominal cavity and to perform associated surgical procedures, the ease of con-

TABLE I - Results. SD: standard deviation. BMI: body mass index.

Sex ratio (M:F)	14:20
Mean age $\pm$ SD, years (range)	52.8 ± 16 (22-82)
BMI $\pm$ SD, kg/m ² (range)	25.8 ± 3.9 (18-35)
Previous abdominal surgery, n (%)	2 (5.9)
Mean operative time $\pm$ SD, minutes (range)	93.1 ± 44.9 (40-240)
Associated procedures, n (%)	1 (2.9)
Mean lesion size $\pm$ SD, cm (range)	4.3 ± 1.9 (1-10)
Conversion rate, n (%)	2 (5.9)
Blood pressure and heart rate instability	4 (11.8)
Blood transfusions in patients, n (%)	0 (0)
Complications, n (%)	0 (0)
Mortality rate, n (%)	1 (2.9)
Mean hospital stay $\pm$ SD, days (range)	3.8 ± 1.8 (2-8)

version to open surgery, if required, and the ability to perform a contralateral adrenalectomy without changing the patient position, are perceived by the authors as additional benefits^{2,6-8}. The guidelines of the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) strongly recommend performing the approach the surgeon is most familiar with, was trained at and with which the best results are obtained⁹. In the authors' experience, this is the case with the submesocolic approach.^{2,6-8}

The results obtained in this series are comparable to those reported in the literature with the retroperitoneal or the lateral approach^{24,25}. In a recent comparative study, Vorselaars et al. reported a median operative time of 85 and 120 minutes for the retroperitoneal and the lateral approach, respectively, and a postoperative morbidity rate of 14% for both approaches²⁴. This data were confirmed in a recent meta-analysis by Costantinides et al., who report a conversion rate of 4% and 6% and morbidity rate of 6% and 8% with the lateral and retroperitoneal approach, respectively²⁵. Furthermore, the reported operative times with the lateral (77-423 minutes) and the retroperitoneal approach (75-300 minutes) are similar to that reported in the present series (mean 93.1 minutes, range 40-240 minutes)²⁵.

The main limitations of the present study are its retrospective nature, the lack of a control group, the small sample size and the fact that the authors' experience is mainly with the submesocolic approach represents a bias making the results difficult to reproduce if an adequate learning curve is not present.

Conclusions

Laparoscopic left anterior transperitoneal submesocolic adrenalectomy is feasible and safe for the treatment of PHE, with early ligation of the adrenal vein before any gland manipulation. However, the narrow operative field close to major vessels such as the left renal vein, the splenic vein and the aorta requires adequate surgical skill in advanced laparoscopic surgery. A randomized trial design and a larger cohort of patients would be required to confirm these conclusions.

Riassunto

OBIETTIVO: L'adrenalectomia mini-invasiva è il trattamento di scelta per le lesioni surrenaliche benigne incluso il feocromocitoma (PHE) e in pazienti selezionati con lesioni maligne. Lo scopo del presente studio è quello di valutare i risultati degli autori dopo la surrenalectomia sottomesocolica transperitoneale anteriore sinistra (SSTAS) per il PHE unilaterale.

MATERIALE DELLO STUDIO: Questo studio è un'analisi retrospettiva di dati raccolti in modo prospettico. Dal

1994 al 2018, 552 pazienti sono stati sottoposti a surrenalectomia laparoscopica (SL). Di questi, 34 pazienti (14 uomini, 20 donne, età media 52.8 anni) sono stati sottoposti a SSTAS per PHE.

RISULTATI: Il tempo operativo medio è stato di 93.1 ± 44.9 minuti. La conversione a chirurgia aperta si è verificata in due pazienti a causa della difficile identificazione dell'anatomia. La pressione sanguigna intraoperatoria e l'instabilità della frequenza cardiaca sono state osservate in quattro pazienti, ma senza necessità di conversione. Non sono state osservate complicanze postoperatorie. Un paziente American Society of Anesthesiologists (ASA) III è deceduto in quarta giornata postoperatoria per infarto acuto del miocardico. La degenza postoperatoria media è stata di 3.8 ± 1.8 giorni (range 2 - 8).

DISCUSSIONE: Il principale vantaggio di questo approccio è la legatura precoce della vena surrenalica principale prima di qualsiasi manipolazione della ghiandola. Ciò riduce il rischio di diffusione delle catecolamine e di conseguenza il rischio di instabilità emodinamica. La dissezione intraperitoneale è limitata e non è necessario mobilizzare il colon o il pancreas, con un minor rischio di complicazioni dovute alla manipolazione di organi.

CONCLUSIONI: SSTAS è fattibile e sicuro per il trattamento del PHE. Per confermare queste conclusioni è necessario uno studio randomizzato controllato e una coorte di pazienti più ampia.

References

1. Gagner M, Lacroix A, Bolté E: *Laparoscopic adrenalectomy in Cushing's syndrome and pheochromocytoma*. N Engl J Med, 1992; 327(14):1033.
2. Paganini AM, Balla A, Guerrieri M, Lezoche G, Campagnacci R, D'Ambrosio G, Quaresima S, Antonica MV, Lezoche E: *Laparoscopic transperitoneal anterior adrenalectomy in pheochromocytoma: Experience in 62 patients*. Surg Endosc, 2014; 28(9):2683-689. doi: 10.1007/s00464-014-3528-4.
3. Janetschek G, Finksteden G, Gasser R, Waibel UG, Peschel R, Bartsch G, Neumann HP: *Laparoscopic surgery for pheochromocytoma: adrenalectomy, partial resection, excision of paragangliomas*. J Urol, 1998; 160(2):330-34.
4. Hazzan D, Shiloni E, Golijanin D, Jurim O, Gross D, Reissman P: *Laparoscopic vs open adrenalectomy for benign adrenal neoplasm*. 2001; 15(11):1356-358.
5. Salomon L, Rabii R, Soulie M, Mouly P, Hoznek A, Cicco A, Saint F, Alame W, Antiphon P, Chopin D, Plante P, Abbou CC: *Experience with retroperitoneal laparoscopic adrenalectomy for pheochromocytoma*. J Urol, 2001; 165(6 Pt 1):1871-874.
6. Scoglio D, Balla A, Paci M, Guerrieri M, Lezoche G, D'Ambrosio G, Fabiani B, Ursi P, Paganini AM: *Laparoscopic transperitoneal anterior adrenalectomy*. Ann Ital Chir, 2013; 84(4):411-16.
7. Paganini AM, Guerrieri M, Balla A, Quaresima S, Isidori AM, Iafrate F, D'Ambrosio G, Lezoche G, Lezoche E: *Management of*

- adrenal incidentaloma by laparoscopic transperitoneal anterior and submesocolic approach. *Langenbecks Arch Surg*, 2016; 401(1):71-9. doi: 10.1007/s00423-015-1367-y.
8. Balla A, Quaresima S, Palmieri L, Ortenzi M, Sbardella E, Puliani G, Isidori AM, Guerrieri M, Paganini AM: *Is laparoscopic left adrenalectomy with the anterior submesocolic approach for Conn's or Cushing's syndrome equally safe and effective as the lateral and anterior ones?* *Surg Endosc*, 2018; doi: 10.1007/s00464-018-6601-6.
9. Stefanidis D, Goldfarb M, Kercher KW, Hope WW, Richardson W, Fanelli RD: *Society of gastrointestinal and endoscopic surgeons: Sages guidelines for minimally invasive treatment of adrenal pathology.* *Surg Endosc*, 2013; 27(11):3960-980. doi: 10.1007/s00464-013-3169-z.
10. Clavien PA, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, de Santibañes E, Pekolj J, Slankamenac K, Bassi C, Graf R, Vonlanthen R, Padbury R, Cameron JL, Makuuchi M: *The Clavien-Dindo classification of surgical complications: five-year experience.* *Ann Surg*, 2009; 250(2):187-96. doi: 10.1097/SLA.0b013e3181b13ca2.
11. Tai CK, Li SK, Hou SM, Fan CW, Fung TC, Wah MK: *Laparoscopic adrenalectomy: Comparison of lateral transperitoneal and lateral retroperitoneal approaches.* *Surg Laparosc Endosc Percutan Tech*, 2006; 16(3):141-45.
12. Dickson PV, Alex GC, Grubbs EG, Ayala-Ramirez M, Jimenez C, Evans DB, Lee JE, Perrier ND: *Posterior retroperitoneoscopic adrenalectomy is a safe and effective alternative to transabdominal laparoscopic adrenalectomy for pheochromocytoma.* *Surgery*, 2011; 150(3):452-58. doi: 10.1016/j.surg.2011.07.004.
13. Assalia A, Gagner M: *Laparoscopic adrenalectomy.* *Br J Surg*, 2004; 91(10):1259-274.
14. Chen H, Sippel RS, O'Dorisio MS, Vinik AI, Lloyd RV, Pacak K: *North American Neuroendocrine Tumor Society (NANETS): The North American Neuroendocrine Tumor Society consensus guideline for the diagnosis and management of neuroendocrine tumors: pheochromocytoma, paraganglioma, and medullary thyroid cancer.* *Pancreas*. 2010 Aug; 39(6):775-83. doi: 10.1097/MPA.0b013e3181ebb4f0.
15. Mohammadi-Fallah MR, Mehdizadeh A, Badalzadeh A, Izadseresht B, Dadkhah N, Barbod A, Babaie M, Hamedanchi S: *Comparison of transperitoneal versus retroperitoneal laparoscopic adrenalectomy in a prospective randomized study.* *J Laparoendosc Adv Surg Tech A*, 2013; 23(4):362-66. doi: 10.1089/lap.2012.0301.
16. Nigri G, Rosman AS, Petrucciani N, Fancellu A, Pisano M, Zorcolo L, Ramacciato G, Melis M: *Meta-analysis of trials comparing laparoscopic transperitoneal and retroperitoneal adrenalectomy.* *Surgery*, 2013; 153(1):111-19. doi: 10.1016/j.surg.2012.05.042.
17. Cabalag MS, Mann GB, Gorelik A, Miller JA: *Comparison of outcomes after laparoscopic versus posterior retroperitoneoscopic adrenalectomy: a pilot study.* *Surg Laparosc Endosc Percutan Tech*, 2014; 24(1):62-6. doi: 10.1097/SLE.0b013e31828fa71f.
18. Corcione F, Tricarico F, Barbaros U, Marzano E, Montini F, Trombetti A: *Gastric volvulus after laparoscopic left adrenalectomy: Case report.* *Surg Laparosc Endosc Percutan Tech*, 2008;18(2):207-8. doi: 10.1097/SLE.0b013e318169ce4f.
19. Piccoli M, De Luca GM, Pasculli A, Angelini M, Guicciardi L, Mullineris B, Marchi D, Melotti G: *Laparoscopic transperitoneal left adrenalectomy and wandering spleen risk.* 2014; 18(3). pii: e2014.00278. doi: 10.4293/JLS.2014.00278.
20. Henry JF, Defechereux T, Raffaelli M, Lubrano D, Gramatica L: *Complications of laparoscopic adrenalectomy: Results of 169 consecutive procedures.* *World J Surg*, 2000; 24(11):1342-346.
21. Benedetti-Valentini S, Rossodivita I: *Delbet's submesocolic approach for surgery of the left adrenal gland.* *Osp Ital Chir*, 1968; 18(3):285-88.
22. Sardi A, McKinnon WM: *Laparoscopic adrenalectomy in patients with primary aldosteronism.* *Surg Laparosc Endosc*, 1994; 4(2):86-91.
23. Robertson CS, Chung SC, Bouchier-Hayes D, Cockram CS, Li AK: *Laparoscopic left adrenalectomy: A new approach.* *Aust N Z J Surg*, 1995; 65(8):619-20.
24. Vorselaars WMCM, Postma EL, Mirallie E, Thierry J, Lustgarten M, Pasternak JD, Bellantone R, Raffaelli M, Fahey T 3rd, Vriens MR, Bresler L, Brunaud L, Zarnegar R: *Hemodynamic instability during surgery for pheochromocytoma: Comparing the transperitoneal and retroperitoneal approach in a multicenter analysis of 341 patients.* *Surgery*, 2018; 163(1):176-82. doi: 10.1016/j.surg.2017.05.029.
25. Constantinides VA, Christakis I, Touska P, Palazzo FF: *Systematic review and meta-analysis of retroperitoneoscopic versus laparoscopic adrenalectomy.* *Br J Surg*, 2012; 99(12):1639-48. doi: 10.1002/bjs.8921.