Original Article

Open surgery for pheochromocytoma: Current indications and outcomes from a retrospective cohort

Pradeep Prakash, Rashmi Ramachandran[1], Nikhil Tandon[2], Rajeev Kumar*

Departments of Urology, [1]Anaesthesiology and [2]Endocrinology and Metabolism, All India Institute of Medical Sciences, New Delhi, India

*E-mail: rajeev.urology@aiims.edu

ABSTRACT

Introduction: Minimally invasive approaches are the current standard of care for pheochromocytoma/paraganglioma (PC/PG) surgery. However, a number of patients still undergo open surgery for these tumors. We evaluated the current indications and outcomes of open surgery for PC/PG to define the role of this approach.

Methods: Data of patients undergoing PC/PG surgery between July 2008 and July 2017 were retrieved from our prospectively maintained electronic database and hospital records. Tumor characteristics, operative and recovery parameters, and complications were evaluated for indications of open procedure and outcomes.

Results: During the study period, 106 patients underwent 124 procedures for PC/PG, including 18 simultaneous bilateral procedures. Surgeries included 102 adrenalectomies, 18 PG excisions, one partial adrenalectomy, and three partial cystectomies. Twenty-five (23.6%) patients (mean age 38.2 ± 16.1 years) underwent an open procedure, including four bilateral procedures. This included 16 adrenalectomies and 9 PG excisions. The indications for open surgery were unilateral large tumours (5; size 8–16, mean 11 cm), bilateral large tumours (2; size 6–10, mean 8.2 cm), retrocaval tumour extension (4), inter aortocaval PGs (8), Retro-mesenteric PG (1), concomitant procedures (3), and conversion from laparoscopy (2). Mean operative time was 217 ± 63.8 min, blood loss was 868 ± 734.2 ml, 11 patients required blood transfusion, and hospital stay was 6.44 ± 2.4 days. All these parameters were higher than for minimally invasive surgery (MIS) in this cohort. Three patients (12%) suffered a postoperative complication, and the rate of complications was not higher than MIS cohort (16%).

Conclusions: Open surgery was most often indicated for large tumors or those located in the inter-aortocaval region. Most such procedures require large incisions and possible hepatic mobilization on the right side. The procedures can be safely completed with few complications.

INTRODUCTION

Pheochromocytomas (PCs) are rare catecholamine producing tumors arising from chromaffin cells and have a highly variable clinical presentation but most commonly present with episodes of headaches, sweating, palpitations, and hypertension.[1] Approximately 10% of PCs are extra-adrenal and are called paragangliomas (PG). Laparoscopic adrenalectomy has replaced the open approach in managing most of the cases with the attendant advantages of lower blood loss, morbidity, hospitalization, and faster recovery.[2,3] While laparoscopic adrenalectomy has become a standard of care with increasing indications for minimally invasive surgery (MIS), open surgery is still required in some cases. We reviewed our database of PC/PG cases to identify patients who required open surgery and determined the indications and outcomes in these patients. We also compared these parameters with patients undergoing MIS in the same cohort.

Access this article online	
Quick Response Code:	Website: www.indianjurol.com
	DOI: 10.4103/iju.IJU_186_19

Received: 17.06.2019, **Accepted:** 02.11.2019

Financial support and sponsorship: Nil.

Conflicts of interest: There are no conflicts of interest.

MATERIALS AND METHODS

Data of patients undergoing surgery for PC/PG in our department from July 2008 to July 2017 was retrieved from our prospectively maintained electronic database and hospital records. All patients provide detailed history; undergo physical examination and investigations necessary to establish the diagnosis. Patients are managed in a multidisciplinary manner involving endocrinology, anesthesia and urology teams. After diagnosis, preoperative preparation and optimization include blood pressure control using a combination of drugs, including alpha-blockers, beta-blockers, calcium channel blockers, and angiotensin receptor blockers. Alpha 1 adrenergic antagonists are gradually titrated and Beta-blockers and other drugs are added as required to optimize blood pressure control. Volume expansion is achieved with increased oral fluid intake. The severity of hypertension and end-organ damage, especially catecholamine-induced cardiomyopathy and cardiac failure are assessed prior to surgery.

For this study, demographic data, data pertaining to preoperative work-up, tumor characteristics, operative and recovery parameters, and complications were retrieved. Patients who had undergone open surgery were identified and evaluated for indications, procedural details, and outcomes and compared with minimally invasive approaches. All patients provided informed, written consent for undergoing the procedures.

Statistical analysis

Data were analyzed using STATA version 14 (StataCorp LLC, Lakeway, Texas, USA) and presented as mean ± standard deviation or median (range). Categorical data were presented as frequency (percentage) and compared using Fisher Exact test. Continuous data were compared using independent *t*-test (for normal data) and Mann–Whitney U-test (for non– normal data). $P < 0.05$ was considered statistically significant.

RESULTS

A total of 106 patients underwent 124 procedures for PC/PG. This included 18 simultaneous bilateral procedures, 102 adrenalectomies, 21 PG excisions including three partial cystectomies for bladder PGs, and one adrenal-sparing PC excision. 95 (76.6%) procedures were performed by minimally invasive methods (Laparoscopy - 83, Robot-assisted - 12) and 29 (23.4%) by open surgery. All three partial cystectomies were performed with robotic-assisted laparoscopy while the adrenal sparing surgery was done laparoscopically. Two laparoscopic procedures had to be converted to open surgery.

Among 106 patients, 25 (23.6%) underwent open surgery, including four patients undergoing bilateral simultaneous adrenalectomies. Twenty-three patients underwent elective open surgeries while two were laparoscopy converted to open surgery. Among these, 15 patients were operated for PCs while eight underwent PG excisions. One patient with left infrahilar PG was converted from laparoscopy to open surgery due to dense adhesions with major vessels, while one case of laparoscopic right adrenalectomy was converted to open due to bleeding from inferior vena cava (IVC).

The most common indication for open surgery was tumor location [13 patients; inter aortocaval or retrocaval, Figure 1] followed by tumor size and characteristics [7 patients; mean 11 cm, Figures 2 and 3]. Other indications were the need for concomitant procedures in 3 patients [Table 1].

Among these 25 subjects, the mean operative time was 217.6 ± 63.8 min (range 120–360), while the average blood loss was 868 ± 734.2 ml (range 100–2800 ml). Eleven patients required packed red blood cell units transfusion. Mean hospital stay was 6.44 ± 2.46 days (range 3–13 days). Three patients (12%) suffered postoperative complications. In comparison, patients undergoing successful MIS had smaller tumors, lower operative time and blood loss, lower requirement of blood transfusions, but similar complication rates (16%) ($P = 0.75$) [Table 2].

DISCUSSION

Despite the wide-spread use and availability of MIS for PCs, we found that open surgery continues to be required in

Table 1: Indications of open surgery

Indications	Patients (*n*=25), *n* (%)
Location	
Interaortocaval PG	8 (32)
Right PC with retrocaval extension	4 (16)
Retro-mesenteric PG	1 (4)
Size or central necrosis	
Unilateral large tumors (mean: 11.02 cm, range: 8-16 cm)	5 (20)
Bilateral large tumors (mean: 8.2 cm, range: 6-10 cm)	2 (8)
Concomitant procedures	
Radical nephrectomy with bilateral PG	1 (4)
Distal pancreatectomy with bilateral PG	1 (4)
PG with large ganglioneuroma excision	1 (4)
Laparoscopic converted to open surgery	2 (8)

PG=Paraganglioma, PC=Pheochromocytoma

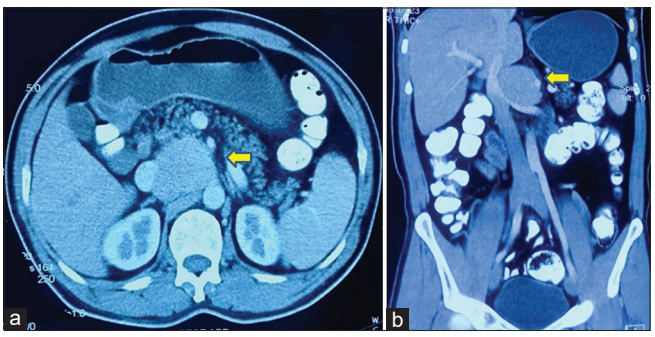

Figure 1: Inter aorto-caval paraganglioma. (a) Axial section, contrast enhanced tomography, (b) coronal reconstruction

Table 2: Operative and recovery parameters of patients undergoing open and minimally invasive surgery for pheochromocytoma/paraganglioma

Parameters	Mean±SD		*P*
	Open surgery (*n*=25)	MIS (*n*=81)	
Tumour size (cm)	6.79±3.28	4.81±1.85	0.005
Operative time (min)	217.6±63.8	139.6±52.6	<0.001
Blood loss (ml)	868±734.2	184.8±186.8	<0.001
Transfusions, *n* (%)	11 (44)	4 (4.9)	<0.001
RBC transfused (units)	1.33±1.68	0.086±0.39	<0.001
Postoperative hospital stay (days)	6.4±2.46	4.17±3.24	<0.001
Complications on Clavien-Dindo scale*, *n* (%)	3 (12)	13 (16)	0.75
Grade 1	1 (ileus)	9 (postoperative fever)	
Grade 2	1 (intestinal obstruction)	1 (blood transfusion)	
Grade 3a	0	3 (abdominal collection requiring pigtail drainage)	
Grade 3b	0	0	
Grade 4a	1 (acute kidney dysfunction requiring dialysis)	0	

*Excluding postoperative inotropic support and routine ICU care. MIS=Minimally invasive surgery, RBC=Red blood cell, SD=Standard deviation

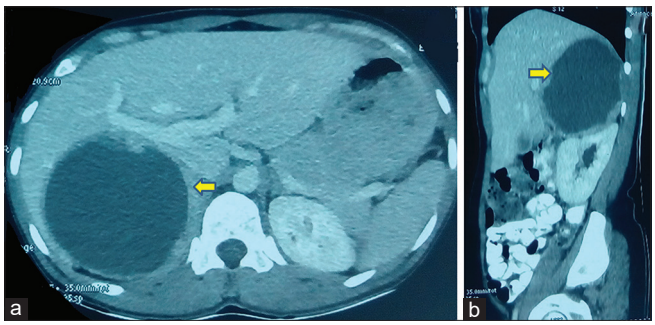

Figure 2: Large right pheochromocytoma with central necrosis. (a) Axial images, contrast enhanced tomography, (b) Sagittal reconstruction

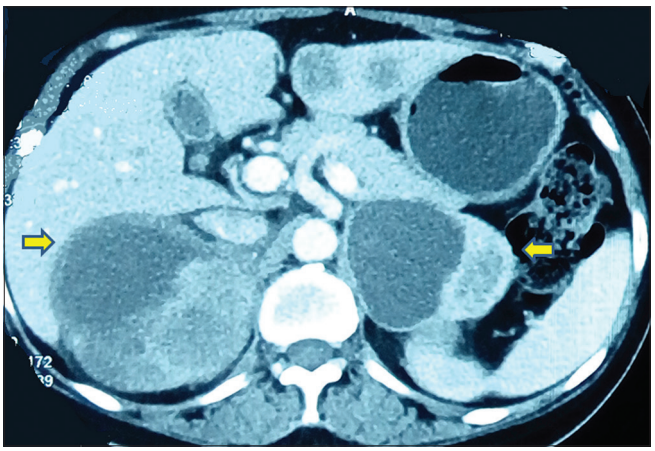

Figure 3: Bilateral large pheochromocytomas with internal necrosis in a patient with MEN 2B syndrome, contrast enhanced tomography

nearly a quarter of all patients. This is most often required for relatively large tumors or those located in difficult-to-access locations. In our series, open surgery resulted in greater blood loss, higher need for blood transfusions and hospital stay but similar overall outcomes as MIS in terms of complications and short-term outcomes.

Despite the improvements in perioperative medical management, anesthesia, and surgical techniques, surgery for PCs continues to carry significant morbidity and mortality.[4] The rarity of these tumors results in few centers having a large experience. Fears of cardiovascular instability due to catecholamine release caused by the pneumoperitoneum and/or laparoscopic dissection cause concerns during laparoscopy, particularly when experience with such surgeries is limited. The decision between open and laparoscopic approach may often thus be difficult. Tumour manipulation has been shown to be the most important intraoperative factor for catecholamine release during both open and laparoscopic adrenal resections.[5-7] Fernández-Cruz *et al.* demonstrated that mean plasma norepinephrine and epinephrine increased 13.7- and 34.2-fold during open tumor manipulation.[8] The key is minimal tumor manipulation with rapid surgery and the open approach is often advocated to achieve this goal.[9,10] However, studies comparing the laparoscopic and open approach did not find the former lacking in safety.[11,12]

The most common indication for open surgery in our cohort was tumor location in relation to major blood vessels. Eight of the patients had inter aortocaval PGs, which are very difficult to access laparoscopically due to location between aorta and IVC and close relation to other major vessels like superior mesenteric artery and renal vessels, particularly the left renal vein [Figure 1]. The mean size of inter aortocaval PGs in our cohort was 6.07 cm (range 4–10 cm), and all were supra-hilar in location. These tumors are supplied by multiple vessels from aorta and drain through multiple venous branches to the IVC. The importance of this location is highlighted by the fact that all other PGs which could be resected laparoscopically ($n = 8$) were in the left para-aortic location, caudal to the renal hilum, where the only important vessel encountered is the inferior mesenteric artery. Brewster and Sundaram[13] have reported a single case of laparoscopic excision of inter aortocaval PG, but the tumor was 2.7 cm in the greatest dimension and infra-hilar in location. Alemanno *et al.*[14] have reported successful laparoscopic resection of

six inter-aortocaval PGs which were located between the renal vessels and aortic bifurcation, and their mean tumor size was 3 cm. The only supra-hilar PG in their series could not be resected laparoscopically and was converted to open surgery. They further analyzed the prognostic factors suggesting the need of open surgery and reported that PGs located above renal hilum, in the inter-aortocaval location, computed tomography evidence of uncertain plane with major vessels, and tumor size >6 cm were more likely to undergo open surgery.

In our series, four adrenal PCs had a significant retrocaval extension. While operating on right-side large tumors or those in the inter aortocaval region, we frequently use a chevron incision with piggyback mobilization of the liver by dividing the coronary and triangular ligaments, similar to that done in liver transplantation. Although a large incision, this allows excellent visualization of the tumor and adequate vascular control. Soejima *et al*.[15] have also reported the use of temporal transaction of infra-hepatic IVC for resection of a large retrocaval PC; where they divided infra-hepatic IVC when piggyback mobilization alone was not adequate, and mobilized the whole liver along with IVC to the left. The IVC was repaired after the resection of tumor.

A number of reports support laparoscopic adrenalectomy as the standard of care for most PCs with size limit varying from 6 to 15 cm.[16-21] This variability in tumor size limits is possibly related to surgeon experience more than size alone. Our own data of over 100 patients show that tumors up to 9.5 cm in size were successfully treated laparoscopically. However, the mean size of tumors treated by open surgery, at 11 cm, was greater than the largest tumor treated laparoscopically, suggesting that size will be a limitation even with experience. As an overall experience, we found that, as the learning curve improved, larger tumors were treated by a laparoscopic approach, and open surgery for size alone seemed to decline. However, there has been no change in the numbers of open surgery for inter aortocaval PGs and retrocaval tumors. However, it would require a randomized trial to assess the superiority of one approach over another.

In addition to size alone, we preferred open surgery for large tumors with central necrosis due to a fear of tumor rupture during dissection [Figures 2 and 3]. There is limited literature on the management of PC with central necrosis which are also called cystic PCs and are included in pseudocyst category of cystic adrenal masses. According to Schmid *et al*.,[22] open surgery should be preferred for cystic adrenal masses >8 cm and wherever there is a suspicion of malignancy. Further, large right-sided tumors with central necrosis were considered better suited for open surgery due to anticipated difficulties in separating them from the liver and the IVC without injuries and the possible need of liver mobilization. It would thus seem that size alone may not be a contraindication. Rather a combination of size, location, and tumor characteristics would help determine the need for open surgery.

Three patients were planned for elective open surgeries due to the need for concomitant procedures. While adjacent organ involvement is not common in PCs, PGs, at times, surround renal vessels, and a concomitant nephrectomy may be required. Patients with syndromic tumors such as the Von-Hippel Lindau syndrome may have concomitant pancreatic tumours as did one of our patients who required a simultaneous distal pancreatectomy along with bilateral adrenalectomy.

Despite the greater blood loss and transfusion rate, our cohort of patients undergoing open surgery did not suffer any greater complications compared to the minimally invasive group. This suggests that open surgery is safe, and although it prevents the benefits of MIS to the patient, it should be used whenever the surgeons feel it would be the preferred approach. We recently reported our prospective evaluation of blood pressure, sugar, and quality of life outcomes in such patients which further suggests that this surgery results in long-term benefits for the patients.[23]

Our study is limited by its retrospective nature and the fact that surgeons of differing laparoscopy experience contributed to it, which could have affected patient selection for the open approach. However, it is one of the larger series on the subject, and this would have helped minimize the impact of individual variations. The almost nonoverlapping characteristics of the open and minimally invasive groups also suggest that individual surgeon preference may not have impacted the data.

CONCLUSIONS

While the majority of patients with PCs are candidates for minimally invasive approaches, open surgery may be indicated in one-fourth of all patients. Large tumors, tumors located in the supra-hilar, inter aortocaval region or those requiring concomitant procedures are the most frequent candidates for open surgery. Open surgery requires large incisions, larger blood loss, higher transfusion rate and hospital stay but has similar overall outcomes as MIS.

REFERENCES

1. Lenders JW, Eisenhofer G, Mannelli M, Pacak K. Phaeochromocytoma. Lancet 2005;366:665-75.
2. Gagner M, Lacroix A, Bolté E. Laparoscopic adrenalectomy in Cushing's syndrome and pheochromocytoma. N Engl J Med 1992;327:1033.
3. Assalia A, Gagner M. Laparoscopic adrenalectomy. Br J Surg 2004;91:1259-74.
4. Werbel SS, Ober KP. Pheochromocytoma. Update on diagnosis, localization, and management. Med Clin North Am 1995;79:131-53.
5. Flávio Rocha M, Faramarzi-Roques R, Tauzin-Fin P, Vallee V,

Leitao de Vasconcelos PR, Ballanger P, *et al.* Laparoscopic surgery for pheochromocytoma. Eur Urol 2004;45:226-32.
6. Fernández-Cruz L, Sáenz A, Taurá P, Sabater L, Astudillo E, Fontanals J. Helium and carbon dioxide pneumoperitoneum in patients with pheochromocytoma undergoing laparoscopic adrenalectomy. World J Surg 1998;22:1250-5.
7. Marty J, Desmonts JM, Chalaux G, Fischler M, Michon F, Mazze RI, *et al.* Hypertensive responses during operation for phaeochromocytoma: A study of plasma catecholamine and haemodynamic changes. Eur J Anaesthesiol 1985;2:257-64.
8. Fernández-Cruz L, Taurá P, Sáenz A, Benarroch G, Sabater L. Laparoscopic approach to pheochromocytoma: Hemodynamic changes and catecholamine secretion. World J Surg 1996;20:762-8.
9. Carter YM, Mazeh H, Sippel RS, Chen H. Safety and feasibility of laparoscopic resection for large (≥6 CM) pheochromocytomas without suspected malignancy. Endocr Pract 2012;18:720-6.
10. Conzo G, Pasquali D, Della Pietra C, Napolitano S, Esposito D, Iorio S, *et al.* Laparoscopic adrenal surgery: Ten-year experience in a single institution. BMC Surg 2013;13 Suppl 2:S5.
11. Lodin M, Privitera A, Giannone G. Laparoscopic adrenalectomy (LA): Keys to success: Correct surgical indications, adequate preoperative preparation, surgical team experience. Surg Laparosc Endosc Percutan Tech 2007;17:392-5.
12. Toniato A, Boschin IM, Opocher G, Guolo A, Pelizzo M, Mantero F. Is the laparoscopic adrenalectomy for pheochromocytoma the best treatment? Surgery 2007;141:723-7.
13. Brewster JB, Sundaram CP. Laparoscopic resection of an interaortocaval paraganglioma: Diagnosis following a needle biopsy. JSLS 2007;11:502-5.
14. Alemanno G, Bergamini C, Somigli R, Prosperi P, Bruscino A, Valeri A. Abdominal paragangliomas: A quantitative prognostic score as predictive factor of the feasibility of the laparoscopic approach. Updates Surg 2017;69:509-15.
15. Soejima Y, Yoshizumi T, Ikegami T, Harimoto N, Ito S, Harada N, *et al.* Surgical resection of giant pheochromocytomas arising behind the retrohepatic inferior vena cava. Anticancer Res 2017;37:277-80.
16. MacGillivray DC, Whalen GF, Malchoff CD, Oppenheim DS, Shichman SJ. Laparoscopic resection of large adrenal tumors. Ann Surg Oncol 2002;9:480-5.
17. Wang DS, Terashi T. Laparoscopic adrenalectomy. Urol Clin North Am 2008;35:351-63, vii.
18. Novitsky YW, Czerniach DR, Kercher KW, Perugini RA, Kelly JJ, Litwin DE. Feasibility of laparoscopic adrenalectomy for large adrenal masses. Surg Laparosc Endosc Percutan Tech 2003;13:106-10.
19. Brunt LM, Doherty GM, Norton JA, Soper NJ, Quasebarth MA, Moley JF. Laparoscopic adrenalectomy compared to open adrenalectomy for benign adrenal neoplasms. J Am Coll Surg 1996;183:1-0.
20. Gagner M, Pomp A, Heniford BT, Pharand D, Lacroix A. Laparoscopic adrenalectomy: Lessons learned from 100 consecutive procedures. Ann Surg 1997;226:238-46.
21. de Cannière L, Michel L, Hamoir E, Hubens G, Meurisse M, Squifflet JP, *et al.* Multicentric experience of the belgian group for endoscopic surgery (BGES) with endoscopic adrenalectomy. Surg Endosc 1997;11:1065-7.
22. Schmid H, Mussack T, Wörnle M, Pietrzyk MC, Banas B. Clinical management of large adrenal cystic lesions. Int Urol Nephrol 2005;37:767-71.
23. Prakash P, Ramachandran R, Tandon N, Kumar R. Changes in blood pressure, blood sugar, and quality of life in patients undergoing pheochromocytoma surgery: A prospective cohort study. Indian J Urol 2019;35:34-40.

How to cite this article: Prakash P, Ramachandran R, Tandon N, Kumar R. Open surgery for pheochromocytoma: Current indications and outcomes from a retrospective cohort. Indian J Urol 2020;36:21-5.