Surg Endosc (1999) 13: 35–39

Surgical Endoscopy
Ultrasound and
Interventional Techniques

Surgical treatment of pheochromocytomas

Laparoscopic or conventional?

E. Möbius, C. Nies, M. Rothmund

Department of General Surgery, Philipps-University Marburg, Baldingerstrasse, D-35043 Marburg, Germany

Received: 11 May 1997/Accepted: 20 March 1998

Abstract
Background: The use of minimally invasive techniques in the surgical treatment of pheochromocytoma is controversial because of possible intraoperative excessive hormone release resulting in cardiovascular instabilities.
Methods: Laparoscopic adrenalectomy was performed in nine patients with a total of 10 pheochromocytomas. Conversion was required in two cases. The relevant data were prospectively documented and compared with a historical group of nine patients who had undergone conventional transabdominal adrenalectomy for unilateral pheochromocytoma.
Results: The laparoscopic operations lasted significantly longer than the conventional procedures (median 243 min vs. 100 min, $p < 0.01$). Intraoperative cardiovascular instabilities (tachycardia, hypertension) occurred in seven laparoscopically and eight conventionally treated patients. All were easily controlled. Blood transfusions were necessary in four patients in the conventional and one patient in the laparoscopic group. Postoperative hospital stay and duration of analgetic treatment were significantly shorter after laparoscopic adrenalectomy.
Conclusions: Laparoscopic adrenalectomy is a safe procedure for patients with pheochromocytoma.

Key words: Adrenalectomy — Laparoscopic — Pheochromocytoma

Since the first report on laparoscopic adrenalectomy by Gagner et al. [6] minimally invasive surgery has become the preferred technique for the surgical treatment of benign adrenal tumors in many institutions. As in conventional surgery, a variety of different surgical approaches to the adrenals have been described for minimally invasive adrenalectomy [1, 20]. In principle, the transperitoneal techniques have to be distinguished from the retroperitoneoscopic approaches. The latter require a balloon trocar, which is expanded in the retroperitoneal fat at the beginning of the procedure to create a space similar to that in endoscopic preperitoneal hernia repair [10]. Like many other authors [3, 12, 14, 15, 17, 23, 24], we prefer the laparoscopic transperitoneal techniques. After our first 28 laparoscopic adrenalectomies, which had been performed with the patient in the lithotomy position, we changed our technique to the transperitoneal approach with the patient in the lateral decubitus position as described by Gagner et al. [6].

The most feared complications during adrenalectomy for pheochromozytoma are cardiovascular instabilities due to an excessive intraoperative catecholamine release. Therefore, several authors [22, 26] expressed particular reluctance about using minimally invasive techniques in the surgical treatment of pheochromocytomas. In our series, we have not excluded patients with pheochromocytomas from laparoscopic adrenalectomy. Our results in these patients are compared with the results of those who underwent transabdominal conventional adrenalectomy for pheochromocytoma in the years before the introduction of laparoscopic adrenalectomy in our institution.

Patients and methods

Since June 1993 laparoscopic adrenalectomy is our treatment of choice for benign adrenal lesions. Now the relevant data of all patients requiring adrenalectomy are prospectively documented. Up to January 10, 1997, 33 laparoscopic adrenalectomies have been performed in our institution. A total of 10 adrenals were removed for benign pheochromocytomas in five men and four women (bilateral adrenalectomy in one case). Conversion was required in two cases. The data of these patients were prospectively documented and compared with the retrospectively collected data of nine patients (three men and six women) with unilateral adrenal pheochromocytomas who underwent conventional transperitoneal adrenalectomy between 1987 and 1993.

All patients in both groups had a preoperative α-blockade with phenoxybenzamin. The drug was administered with increasing doses until the patient reported orthostatic symptoms or perioral paresthesias. The first

Correspondence to: E. Möbius

Table 1. Demographic data and clinical presentation of the patients in both groups

	Laparoscopic (n = 9)[a]	Conventional (n = 9)	
Sex (male/female)	5/4	3/6	NS
Age (years) median (range)	48 (25–69)	62 (21–69)	NS
BMI (kg/m^2) median (range)	23.1 (18.7–26.5)	23.8 (21.7–27.2)	NS
Clinical presentation			
Hypertension	8	9	NS
Tachycardia	6	5	NS
MEN-II syndrome	2	0	—

[a] One patient in the laparoscopic group with MEN-IIa syndrome suffered from bilateral pheochromocytomas. NS = not significant.

eight laparoscopic procedures were performed with the patient in the lithotomy position. Depending on the affected side and the patient's stature, four to five trocars were needed. The operative technique has been described in detail elsewhere [18, 20]. The last two transperitoneal laparoscopic adrenalectomies were performed with the patient in the lateral decubitus position. Four trocars were required in both cases. The operative technique also has been precisely described by other authors [6, 13]. In all cases the adrenal vein was clipped and divided before the dissection of the tumor.

Our historic control group consisted only of patients who underwent transabdominal adrenalectomy. In all cases a subcostal incision was used. On the left side, the lesser sac was opened by division of the gastrocolic ligament. The renal vein was exposed, and the tumor was mobilized only after ligation of the adrenal vein. On the right side, Kocher's maneuver was performed and the vena cava exposed. On its right lateral aspect, the adrenal vein was identified and ligated before any further manipulation of the tumor [11].

To characterize the two groups of patients according to age, sex, body mass index (BMI), and clinical presentation as well as tumor size and tumor localization, these data were analyzed. Operative time, number of transfused units of red blood cells, intra- and postoperative complications, postoperative hospital stay, and the duration of analgetic treatment were used for comparison of the two operative procedures. For the evaluation of the intraoperative course, heart rates greater than 100 beats per minute (bpm) were considered as tachycardia. The intraoperative blood pressure was considered hypertensive if the systolic blood pressure exceeded 160 mmHg. The Wilcoxon test and Fisher's exact test were used for statistical comparison. Significance was assumed for values of $p < 0.05$.

Results

Although the conventionally treated patients were slightly older than the patients undergoing laparoscopic adrenalectomy, the two groups were comparable concerning age, sex, BMI, and clinical presentation (Table 1). Two patients in the laparoscopic group were affected by the MEN-IIa syndrome. In one case an asymptomatic unilateral pheochromocytoma was found on routine follow-up. The other patient was the index patient of her family and already had bilateral pheochromocytomas.

The tumors in the patients undergoing conventional adrenalectomy were slightly larger than those in the laparoscopic group (Table 2). Also, the predominance of right-sided pheochromocytomas was more pronounced in the conventional group. However, these differences did not reach statistical significance.

The final dose of phenoxybenzamin required to achieve an adequate preparation of the patient was also comparable in both groups. The laparoscopic group required a median dose of 90 mg/day (range 40–280 mg/day), whereas the conventionally treated patients needed a median dose of 80 mg/day (range 60–140 mg/day).

Table 2. Characteristics of the tumors in both groups

	Laparoscopic (n = 10)	Conventional (n = 9)	
Tumor size (cm) median (range)	3.8 (1.7–7.5)	4.5 (3–7)	NS
Tumor localization right : left	6 : 4	8 : 1	NS

NS = not significant.

In two cases we had to convert from the laparoscopic to the conventional technique. In the first case the reason was a small injury to the renal vein in a right-sided pheochromocytoma. This resulted in a significant bleeding, which could not be controlled laparoscopically. In the second case the operation was performed for a large (7.5 cm) left-sided pheochromocytoma. Due to tumor size, the progress of the operation was inadequate and we opted for an elective conversion. At this time, the adrenal vein had already been controlled and divided.

The laparoscopic procedure required operative times between 125 and 360 min, with a median of 243 min, including the operations requiring conversion. This was significantly longer than the time required to perform the conventional adrenalectomies. These lasted between 85 and 130 min, with a median of 100 min ($p < 0.01$). However, for laparoscopic adrenalectomy we observed a learning curve as with other laparoscopic procedures. The last three adrenalectomies were completed in less than 150 min. There was no correlation between operative time and tumor size.

Between the two operative techniques no significant differences were found concerning intraoperative cardiovascular instabilities. In seven of the nine patients in the laparoscopic group, episodes of tachycardia and/or hypertension were observed during the operation. In five patients, short-lasting blood pressure peaks with maximum systolic pressures between 180 and 210 mmHg occurred. In almost all cases, the hypertension was easily controlled with a nitroglycerine drip, which was dosed by effect. Most hypertensive episodes were of short duration. Only one patient had longer lasting periods of hypertension (>3 min). She had a hormonally very active tumor requiring an extensive preoperative α-blockade with 280 mg of phenoxybenzamin per day. Her intraoperative course is shown in Fig. 1.

Intraoperative tachycardia with heart rates between 100 and 140 bpm were seen in four patients in the laparoscopy group. These short episodes either subsided spontaneously or were controlled with a short-acting β-blocking agent. Cardiovascular reactions occurred in eight of the nine conventionally treated patients. In seven cases we observed blood pressure peaks between 170 and 220 mmHg. Three patients had short-lasting phases of tachycardia with heart rates between 100 and 120 bpm. These instabilities were treated in the same way as described earlier and were also quickly and easily controlled.

None of the patients in the laparoscopy group needed intraoperative blood transfusions, including the patient with a 2-cm pheochromocytoma whose operation had to be con-

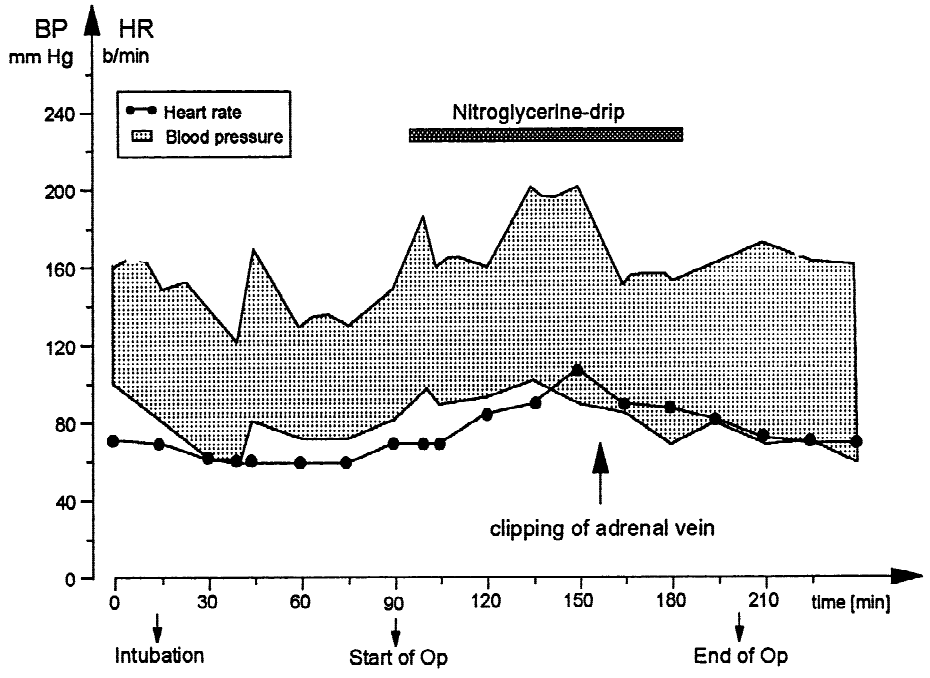

Fig. 1. Intraoperative course in a 46-year-old female patient with a 3.5-cm right-sided pheochromocytoma who had episodes of hypertension and a brief episode of tachycardia despite high preoperative doses of an α-blocking agent. Hypertension was treated with nitroglycerin.

verted to the open technique because of a small injury to the right renal vein. His estimated blood loss was 1,100 ml. One elderly patient developed a postoperative hemorrhage and a consecutive flank hematoma. She required a transfusion of 2 units of packed red blood cells. Four conventionally treated patients (44%) were transfused with 1 to 4 units of red blood cells due to intraoperative hemorrhage. Although this difference is not statistically significant ($p = 0.294$), there is a clear trend in favor of the laparoscopic technique. Except for the case with postoperative retroperitoneal hematoma in a laparoscopic adrenalectomy patient, there was no postoperative complication in either group.

Significant advantages were found for the laparoscopic technique in terms of postoperative hospital stay and pain (Table 3). Laparoscopic adrenalectomy patients stayed in the hospital for 4 to 9 days after the operation (median, 6 days), whereas the patients in the conventional group were discharged after 8 to 13 days (median, 10 days; $p < 0.01$). However, this comparison has its limitations, because the patients were observed in different time periods. Analgetic drugs were needed by the laparoscopically operated patients for a median of 2 days (range, 1–3 days). In contrast, after conventional adrenalectomy the patients required pain medication for a median of 3 days (range, 2–4 days; $p < 0.01$). The data of the laparoscopy group includes those of the patients requiring conversion.

Discussion

Since the introduction of minimally invasive surgery, increasing experience with these techniques and improvement of laparoscopic instruments has allowed an enlarged spectrum of indications for this type of surgery, which now also includes adrenalectomy [7]. Today, minimally invasive adrenalectomy is the treatment of choice for benign adrenocortical tumors in many institutions. In our department the conventional transperitoneal approach is used only in very few cases. However, the suspicion of adrenal malignancy is considered to be a contraindication for laparoscopic adrenalectomy [6, 15, 19]. Although a large number of endoscopic adrenalectomies for pheochromocytoma have been reported [4, 6, 8, 12, 14, 15, 24, 27], some authors are reluctant to use this technique for the removal of catecholamine-secreting tumors [22, 26]. In our series, pheochromocytoma has been the most frequent indication for laparoscopic adrenalectomy next to primary hyperaldosteronism (Conn's syndrome).

Our results show that pheochromocytomas can be managed safely laparoscopically. Comparing the laparoscopic with the open technique, we did not observe significant differences concerning intraoperative cardiovascular instabilities. The laparoscopic approach allows an excellent exposure of the anatomic region of the adrenals, and the adrenal veins can easily be controlled before the dissection of the tumor itself. Other authors reported similar results. Fernandez-Cruz et al. [5] studied the intraoperative catecholamine secretion and hemodynamic changes in eight patients undergoing conventional and eight patients undergoing laparoscopic adrenalectomy for pheochromocytoma. These authors found hemodynamic instabilities only during conventional operations. As expected, they found the highest catecholamine levels during the manipulation of the tumor, regardless which operative technique was used.

It appears that less manipulation of the tumor is required to identify the adrenal vein if the laparoscopic approach is used. This could explain the results of Fernandez-Cruz et al. [5]. It also supports our concept that the adrenal vein should always be identified and controlled before further manipulations. Guazzoni et al. [8] also emphasized the importance of this principle, which had been uncontradicted in the days of conventional adrenalectomy. However, other groups using retroperitoneoscopic techniques also did not observe an increased number of intraoperative hypertensive or tachycardic upsets, although their techniques do not allow an

Table 3. Intra- and postoperative data of the patients in both groups[a]

	Laparoscopic (n = 9)	Conventional (n = 9)	
Operative time (min), median (range)	243 (125–360)	100 (85–130)	$p < 0.01$
Operation with intraop cardiovascular instabilities	7	8	NS
Tachycardia	4	3	NS
Hypertension	5	7	NS
Patients requiring transfusions	1	4	NS
Duration of analgetic medication (days), median (range)	2 (1–3)	3 (2–4)	$p < 0.01$
Postoperative hospital stay, median (range)	6 (4–9)	10 (8–13)	$p < 0.01$
Postoperative complications	1	0	NS

[a] Operative times of 10 adrenalectomies (one patient had bilateral tumors) are considered. NS = not significant.

early identification of the adrenal vein [9, 28]. Apparently the dissection of an adrenal containing a pheochromocytoma is possible even before ligation of the adrenal vein if the patients are adequately prepared with α-blockers and an atraumatic technique is used.

Traditionally, CO_2 is used to create the pneumoperitoneum, which is needed for laparoscopic operations. Because CO_2 can cause hypercapnia, respiratory acidosis, increased vascular resistance, decreased cardiac index with elevated O_2-consumption of the myocardium, and increased mean arterial pressure [21], it has been questioned whether CO_2 is the appropriate gas to be used in surgery for pheochromocytomas. Helium does not cause hypercapnia and acidosis. Fernandez-Cruz et al. [5] used helium for pneumoperitoneum in such tumors. It was well tolerated by the patients. However, studies comparing CO_2 and helium are still pending.

Brunt et al. [2] reported a highly significant lesser operative blood loss in laparoscopic adrenalectomy than with the conventional transabdominal and retroperitoneal approaches. Their endoscopic adrenalectomy patients had a lower incidence of perioperative blood transfusion, as did our patients with pheochromocytomas in the laparoscopic group. This indicates that minimally invasive adrenalectomy allows a more precise dissection than the conventional techniques, which is particularly important in patients with pheochromocytomas.

The significantly longer operative time is a major disadvantage of laparoscopic adrenalectomy. However, this appears to be a question of experience. As with other laparoscopic operations, there is a typical learning curve. Today operative times of 2 hours and less are realistic for laparoscopic adrenalectomy, even in patients with pheochromocytomas [4, 6, 16].

It should be emphasized that the prerequisite for an uncomplicated intra- and postoperative course is an experienced team. Because pheochromocytomas are relatively rare tumors, laparoscopic adrenalectomy for pheochromocytoma should remain an operation that is performed in centers with particular interest in endocrine disorders and laparoscopic surgery.

We favor the laparoscopic approach in patients with pheochromocytomas as well as in patients with all other benign adrenal lesions up to a size of 6 to 8 cm. It is a safe procedure and compares favorably with the conventional technique. Besides the advantages mentioned earlier (reduced postoperative stay, reduced need for analgetic drugs), the patients have the advantage of a superior functional and cosmetic result.

References

1. Bonjer HJ, Lange JF, Kazemier G, Bruining HA (1996) Optimal minimally invasive approach to adrenals: transperitoneal or retroperitoneal. [Abstract] Surg Endosc 10: 591
2. Brunt LM, Doherty GM, Norton JA, Soper NJ, Quasebarth MA, Moley JF (1996) Laparoscopic adrenalectomy compared to open adrenalectomy for benign adrenal lesion. J Am Coll Surg 183: 1–10
3. Constantino GN, Mukalian GG, Vincent GJ, Kliefoth WL (1993) Laparoscopic adrenalectomy. J Laparoendosc Surg 3: 309–311
4. Deans GT, Kappadia R, Wedgewood K, Royston CMS, Brough WA (1995) Laparoscopic adrenalectomy. Br J Surg 82: 994–995
5. Fernandez-Cruz L, Taura P, Saenz A, Benarroch G, Sabater L (1996) Laparoscopic approach to pheochromocytoma: hemodynamic changes and catecholamine secretion. World J Surg 20: 762–768
6. Gagner M (1996) Laparoscopic adrenalectomy. Surg Clin North Am 76: 523–537
7. Gagner M, Lacroix A, Bolte E (1992) Laparoscopic adrenalectomy in Cushing's syndrome and pheochromocytoma. N Engl J Med 327: 1033
8. Guazzoni G, Montorsi F, Bocciardi A, Da Pozzo L, Rigatti P, Lanzi R, Pontiroli A (1995) Transperitoneal laparoscopic versus open adenalectomy for benign hyperfunctional adrenal tumors: a comparative study. J Urol 153: 1597–1600
9. Heintz A, Junginger T (1994) Die endoskopische, extraperitoneale Adrenalektomie. Chirurg 65: 1140–1142
10. Kieturakis MJ, Nguyen DT, Vargas H, Fogarty TJ, Klein SR (1994) Balloon dissection facilitated laparoscopic extraperitoneal hemioplasty. Am J Surg 168: 603–608
11. Kiffner EM, Schildberg FW (1991) Eingriffe in Retroperitonealraum. In: Durst J, Rohen JW (eds) Chirurgische Operationsiehre. Schattauer, Stuttgart, New York, pp 601–611
12. Lepsien G, Neufang T, Lüdtke FE (1994) Laparoscopic resection of pheochromocytoma. Surg Endosc 8: 906–909
13. Marescaux J, Mutter D, Wheeler MH (1996) Laparoscopic right and left adrenalectomies: surgical procedures. Surg Endosc 10: 912–915
14. Meurisse M, Joris J, Hamoir E, Hubert B, Charlier C (1995) Laparoscopic removal of pheochromocytoma: Why? When? and Who? Surg Endosc 9: 431–436
15. Meyer G, Schardey HM, Schildberg FW (1995) Die laparoskopische transperitoneale Adrenalektomie. Chirurg 66: 413–418
16. Miccoli P, Iacconi P, Conte M, Goletti O, Buccianti P (1995) Laparoscopic adrenalectomy. J Laparoendosc Surg 5: 221–225
17. Naito S, Uozumi J, Ichimiya H, Tanaka M, Kimoto K, Takahashi K, Ohta Y, Tanaka M, Kumazawa Y (1994) Laparoscopic adrenalectomy: comparison with open adrenalectomy. Eur Urol 26: 253–257
18. Nies C, Bartsch D, Schäfer U, Rothmund (1993) Laparoskopische Adrenalektomie. Disch Med Wochenschr 118: 1831–1836
19. Nies C, Möbius E, Rothmund M (1997) Laparoskopische Nebennierenchirurgie. Chirurg 68: 99–106

20. Nies C, Rothmund M (1995) Endoskopische Adrenalektomie: Indikation, Technik und erste Ergebnisse. Acta Chir Austriaca 27: 256–262
21. Noirot D, Joris J, Legrand M, Lamy H (1992) Hemodynamic changes during laparoscopic cholecystectomy. Anesth Analg 76: 1067–1071
22. Pemegger C, Keller A, Deisenhammer C, Mayr R (1993) Laparoskopische Therapie von Nebennierentumoren. Minim Invasive Chir 3: 82–86
23. Robertson CS, Chung SC, Bouchier-Hayes D, Cockram CS, Li AK (1995) Laparoscopic left adrenalectomy: a new approach. Aust N Z J Surg 65: 619–620
24. Stuart RC, Chung SCS, Lau JYW, Chan ACW (1995) Laparoscopic adrenalectomy. Br J Surg 82: 1498–1499
25. Suzuki K, Kageyama S, Ueda D, Ushiyama T, Kawabe K, Tajima A, Aso Y (1993) Laparoscopic adrenalectomy: clinical experience with 12 cases. J Urol 150: 1099–1102
26. Takeda M, Go H, Imai T, Nishiyama T, Morishita H (1994) Laparoscopic adrenalectomy for primary aldosteronism: report of initial ten cases. Surgery 115: 621–625
27. Vogelbach P, Kocher T, von Flue M, Oertli D, Harder F (1995) Laparoskopische Adrenalektomie beim Phäochromozytom. Schweiz Med Wochenschr 125: 1735–1739
28. Waiz MK, Peitgen K, Hoermann R, Giebler RM, Mann K, Eigler FW (1996) Posterior retroperitoneoscopy as a new minimally invasive approach for adrenalectomy: results of 30 adrenalectomies in 27 patients. World J Surg 20: 769–774