World J Surg (2010) 34:1391–1397
DOI 10.1007/s00268-010-0453-0

World Journal of Surgery

Posterior Retroperitoneoscopic Adrenalectomy for Clinical and Subclinical Cushing's Syndrome

Pier F. Alesina · Silvia Hommeltenberg · Beate Meier · Stephan Petersenn · Harald Lahner · Kurt W. Schmid · Klaus Mann · Martin K. Walz

Published online: 9 February 2010

Abstract
Background Because of co-morbidity, adrenalectomy for adrenal Cushing's syndrome may be associated with an increased complication rate and long operating times. In the present study we report our experience with the posterior retroperitoneoscopic adrenalectomy in a large group of patients with clinical or subclinical Cushing's syndrome.
Patients and methods Between July 1994 and June 2009, 170 patients (17 males, 153 females age 50 ± 13 years; range: 12–78 years) affected by Cushing's syndrome underwent operation via posterior retroperitoneoscopic access. Patients were divided into two groups, those with manifest Cushing's syndrome (mCS) [99 patients: 6 male, 93 female; age 45 ± 13 years] and those with subclinical Cushing's syndrome (sCS) [71 patients: 11 male, 60 female; age: 56 ± 11 years]. The sCS classification was assumed in cases without typical clinical symptoms but with a pathological dexamethasone suppression test. Partial adrenalectomy was performed in 35 cases (24 in the mCS-group and 11 in the sCS-group).
Results Mortality was zero; major complications did not occur. The incidence of postoperative minor complications was 5.3%. Mean operating time was 58 ± 36 min (range: 20–230 min) and did not differ between mCS and sCS patients (58 versus 59 min; p = ns). Postoperative oral steroids supplementation (POSS) was administered in 136 patients (99 mCS, 37 sCS). If POSS was started, mean duration of therapy was 12.3 months (mCS) and 10.3 months (sCS) [$p = 0.08$], respectively. After a mean follow-up of 70.9 ± 46.5 months the cure rate was 99.4%.
Conclusions The posterior retroperitoneoscopic approach is fast and safe even in patients with Cushing's syndrome. Partial adrenalectomy represents a new option in the treatment of cortisol-producing adenomas.

P. F. Alesina (✉) · S. Hommeltenberg · B. Meier · M. K. Walz
Klinik für Chirurgie und Zentrum für Minimal Invasive Chirurgie, Kliniken Essen-Mitte, Akademisches Lehrkrankenhaus der Universität Duisburg-Essen, Henricistrasse 92, 45136 Essen, Germany
e-mail: pieroalesina@libero.it

S. Petersenn · H. Lahner · K. Mann
Klinik für Endokrinologie, Universitätsklinikum Essen, Universität Duisburg-Essen, Hufelandstrasse 55, 45122 Essen, Germany

K. W. Schmid
Institut für Pathologie und Neuropathologie, Universitätsklinikum Essen, Universität Duisburg-Essen, Hufelandstrasse 55, 45122 Essen, Germany

Introduction

Cushing's disease (CD) and Cushing's syndrome (CS) are the result of the overproduction of endogenous cortisol by the adrenal cortex. Approximately 80% of cases are due to ACTH-producing tumors, most often located in the pituitary gland, although very rarely extrapituitary (CD); another 15–20% are due to adrenal adenomas, carcinomas, or bilateral hyperplasia (CS) [1]. Surgical treatment of Cushing's syndrome is a challenging problem for surgeons because of the high incidence of co-morbidities in this group of patients [1]. No more than 20 years ago, morbidity and mortality of adrenalectomy were reported to be 7–13% [2, 3] and 2.3%, respectively [2]. However, the introduction of laparoscopic adrenalectomy in 1992 started a new era in adrenal surgery [4]. In their initial laparoscopic series of 15 patients with 21 adrenalectomies for Cushing's disease and syndrome, Fernández-Cruz et al. [5] reported the lack of any major complication. These

promising data were confirmed by our first study on 29 patients with Cushing's adenoma removed by the posterior retroperitoneoscopic approach [6]. In the present study we summarize our experience with the retroperitoneoscopic treatment of adrenal hypercortisolism in 170 patients.

Patients and methods

In the setting of a prospective study (July 1994–June 2009), 170 patients [17 male, 153 female; age 50 ± 13 years (range: 12–78 years)] underwent operation for Cushing's syndrome by the posterior retroperitoneoscopic approach. Patients affected by Cushing's disease were excluded. Patients were divided into two groups, 99 patients (6 male, 93 female; age 45 ± 13 years) with manifest Cushing's syndrome (mCS) and 71 patients (11 males, 60 females; age: 56 ± 10 years) with subclinical Cushing's syndrome (sCS). The diagnosis of CS, performed by several referral endocrinologists, was made on the basis of the results of the available biochemical tests including serum cortisol and plasma ACTH levels, urinary free cortisol, 1 mg overnight or longer low-dose dexamethasone suppression test (DST), together with the presence of classical signs and symptoms [7]; sCS was assumed in cases without typical clinical symptoms but with a pathological dexamethasone (DXM) suppression test (1 mg overnight test with a cortisol suppression threshold set at 3.5 μg/dl). Failure to suppress serum cortisol using at least the overnight DST was considered a mandatory criterion for the diagnosis of sCS. All operations were performed by three surgeons. During the study period, conventional surgery for Cushing's syndrome was performed in 8 patients with obvious adrenal carcinomas; the transperitoneal laparoscopic approach was used in 9 cases. Informed consent was obtained prior to surgery in all cases.

Patients were usually admitted one day before operation. In the early phase of the study patients were generally observed postoperatively for one night in the intensive care unit; later this level of care was used only for patients with high cardiac risk or severe obesity. Mobilization and oral intake were allowed at once, postoperatively. Our actual strategy for corticoid substitution therapy can be summarized as follows: no preoperative or intraoperative corticoid substitution is administered; patients with mCS are substituted postoperatively with oral corticoids; patients with sCS are initially observed without medication. In this group, oral corticosteroid substitution was started if signs of hypocortisolism developed (i.e., hypotension, hypoglycemia, fatigue, signs of confusion or lethargy, fever) (Table 1).

Altogether, 183 adrenalectomies (89 right, 94 left) were performed through the posterior retroperitonescopic approach; 157 patients (11 male, 146 female; age: 49.4 ± 13.6 years) suffered from unilateral adrenal diseases, 13 patients (6 male, 7 female; age: 52.8 ± 14.4 years) suffered from bilateral macronodular hyperplasia (8 mCS, 5 sCS). The surgical technique of posterior retroperitoneoscopic adrenalectomy has been described in detail [6, 8–10]. Recently introduced improvements included increased gas pressures (up to 30 mmHg), dissection of tissue and vessels (including adrenal vein) by bipolar scissors (LigaSure, Covidien) without clips, and single access surgery in selected cases [11]. Total adrenalectomy was the standard operation. Partial adrenalectomy was performed in selected patients with eccentric and/or small tumors.

Table 1 Present strategy of postoperative oral corticosteroid therapy (hydrocortisone in mg)

Days (postoperative)	mCS	sCS
0	50	Observation
1	50–25–0	Observation
2	35–15–0	Observation
3	20–5–0 to 35–15–0	50–25–0[a]
4	20–5–0 to 35–15–0	35–15–0[a]

[a] Started if patients developed signs of hypocortisolism

Data including age, gender, body mass index (BMI), tumor location and size, operating time, intraoperative and postoperative complications, and length of hospital stay were collected prospectively. For the present study a retrospective evaluation of the preoperative co-morbidities including arterial hypertension and diabetes has been performed. The number of drugs necessary to control blood pressure prior to and after surgery, as well as the postoperative BMI (at the time of follow-up), have also been investigated. For the follow-up evaluation (at least 6 months) patients or referring physician were contacted by phone. During the follow-up period the referral endocrinologist strictly followed all patients and an endocrine work-up was performed once a year to exclude recurrence. Recurrence was defined as the evidence of abnormal cortisol levels (urinary or plasma) and/or pathological DST (1 mg overnight) during the follow-up. Data were expressed as mean (range) or mean ± SD as appropriate. Group differences at different time points were examined using Student's *t*-test and Wilcoxon signed rank test; categorical data were analyzed by the chi-square and Fisher's exact test. Statistical significance was set at $p < 0.05$.

Results

The mortality rate was zero. No major complications were registered intraoperatively. All except one procedure were

completed through the retroperitoneoscopic route. Postoperative complications were minor and included segmental relaxations of the abdominal wall (4 cases), hypoesthesias of the abdominal wall (4 cases) and 1 hematoma treated conservatively. One segmental relaxation of the abdominal wall persisted after 6 months.

Patients affected by mCS ($n = 99$, mean age: 45 ± 13 years) were younger than patients with sCS ($n = 71$, mean age: 56 ± 10 years) ($p < 0.05$). Partial adrenalectomy was performed in 35 cases (24 mCS-group, 11 sCS-group) in unilateral surgery. Thirteen patients with preoperative macronodular hyperplasia underwent bilateral simultaneous surgery (bilateral total [4 mCS, 1 sCS], partial on one side [3 mCS, 3 sCS], partial on both sides [1 mCS, 1 sCS]). Mean intraoperative blood loss was 18 ± 67 ml (range: 0–300 ml) without the need for blood transfusion in any case.

Mean operative time for the 183 procedures (13 bilateral operations) was 58 ± 36 min (range: 20–230 min) and did not differ between right and left procedures (59 ± 37 versus 58 ± 36 min), mCS and sCS (58 ± 37 versus 59 ± 35 min) and between total and partial adrenalectomy (58 ± 38 versus 59 ± 30 min) (p = ns). The learning curve during the overall period of 15 years is demonstrated in Figure 1. Tumor size (< 3 cm versus ≥ 3 cm) as well as the BMI (< 30 versus ≥ 30) did not significantly influence the duration of the procedure (55 ± 39 min versus 59 ± 35 min) and (58 ± 38 min versus 62 ± 34 min), respectively. Male patients ($n = 17$) required a slightly longer operating time when compared with female patients ($n = 153$), but the difference did not reach statistical significance (66 ± 25 versus 58 ± 38 min) ($p = 0.07$). The mean postoperative hospital stay was 4.5 ± 2.2 days (median: 4 days; range: 2–18 days) and did not differ between manifest and subclinical CS (4.3 versus 4.6 days) ($p = 0.3$).

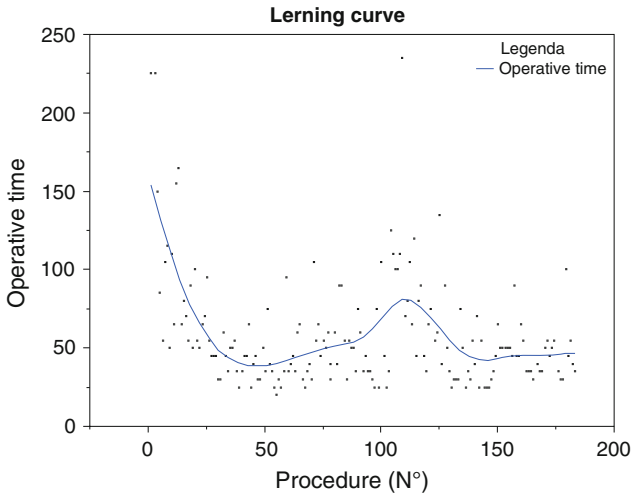

Fig. 1 Effect of learning curve on the operative time after 183 procedures: 1994–2009

Figure 2 summarizes the characteristics of the groups. At the beginning of the experience patients were sent to the intensive care unit for one night (all 4 cases in 1994). With growing experience, only 7 of 166 (4.2%) patients with high cardiac risk or severe obesity were monitored in the intensive care unit.

Histology showed benign lesions in all but one patient with an adrenocortical carcinoma. In one patient no tumor could be found (due to Cushing's disease). Macronodular hyperplasia was identified in 19 cases (10 mCS, 9 sCS), including 13 patients who underwent bilateral surgery. Tumor size ranged from 1 to 10 cm (mean: 3.6 ± 1.4 cm) and was significantly different between mCS (3.4 ± 1.5 cm) and sCS (3.9 ± 1.4 cm) ($p < 0.02$).

A postoperative oral cortisone therapy was administered in all patients affected by mCS and in 32 (of 71) patients with sCS ($p < 0.0001$). Five patients in the sCS group were readmitted due to adrenal insufficiency (5 of 39; 12.8%). Duration of therapy did not differ significantly between the groups (Table 2).

A total of 163 patients (97 patients with mCS: 5 male, 92 female, age 45 ± 13 years; and 66 patients with sCS: 10 male, 56 female, age: 56 ± 11 years) with at least 6 months follow-up were considered for the long-term outcome analysis. The follow-up period (mean: 70.9 ± 46.5, range: 6–179 months) was completed for 110 patients (63 mCS, 47 sCS) (67.5%). During this period six patients (3 mCS, 3 sCS) died, five from unrelated diseases (1 myocardial infarction, 1 urinary tract carcinoma, 1 colorectal carcinoma, 2 unknown) one patient with mCS caused by metastatic adrenocortical carcinoma. The latter, after an uneventful minimally invasive total adrenalectomy for a 7 cm right adrenocortical tumor, developed a locoregional recurrence with lymph node, liver, and peritoneal involvement 6 months after primary surgery. A palliative debulking (including liver resection and interaortocaval lymphadenectomy) was performed and postoperative chemotherapy was started. The patient died several months later from disseminated disease. One patient in the mCS group showed a recurrent/persistent hypercortisolism due to a pituitary adenoma (in this case histology could not identify any tumor in the adrenal gland). No recurrence was observed in any patient who underwent partial adrenalectomy.

Outcome was evaluated on the basis of the following parameters: weight reduction, amelioration or absence of hypertension after the operation, number of antihypertensive medications still required, presence or not of a type II diabetes. A separate analysis was performed for mCS (mean follow-up: 68.8 ± 46.5 months; range: 6–179 months) and sCS (mean follow-up: 73.9 ± 46.7 months;

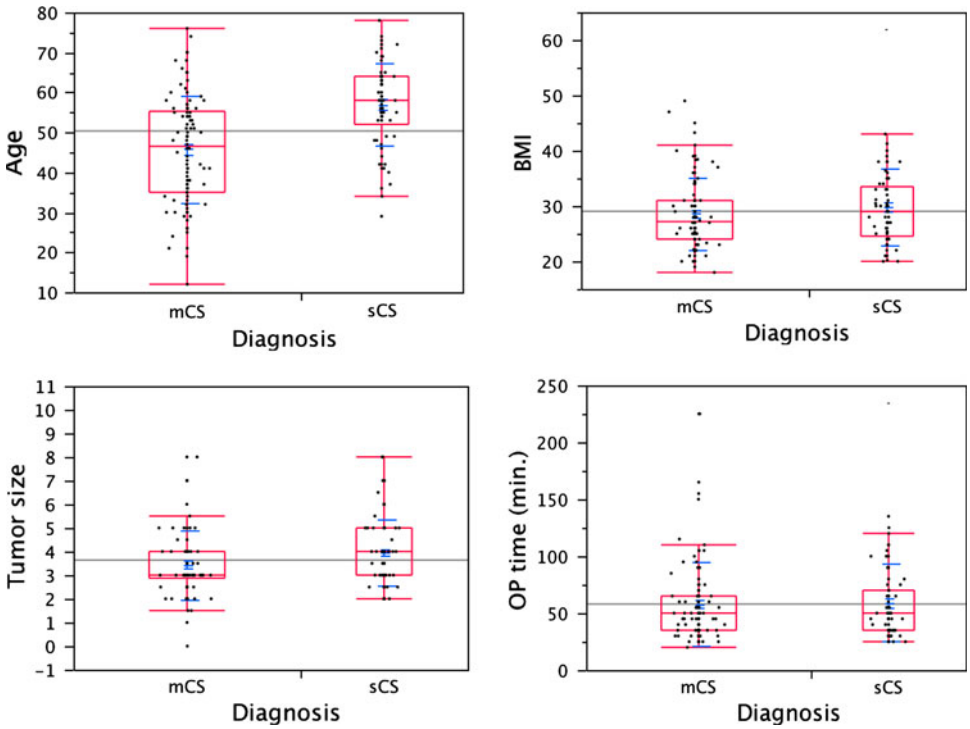

Fig. 2 Comparison between manifest (mCS) and subclinical (sCS) Cushing's syndrome regarding age (45 ± 13 versus 56 ± 10 years) ($p < 0.0001$), body mass index (28.5 versus 29.7) ($p = 0.29$), tumor size (3.4 ± 1.5 versus 3.9 ± 1.4 cm) ($p < 0.02$) and operating time (58 ± 37 versus 59 ± 35 min) ($p = 0.75$)

Table 2 Cortisone therapy: long-term results

	mCS	sCS	*p* Value
Cortisone therapy	99 (100%)	37 (52.1%)	<0.0001
Duration of therapy[a]	12.3 ± 12.6 (1–60)	10.3 ± 14.1 (1–50)	0.08
Cortisone therapy (at time of follow-up)	16 (25.8%)[b]	3 (6.4%)[c]	0.01

[a] Months: mean ± SD (range)

[b] Including four patients who underwent bilateral adrenalectomy

[c] Including one patient who underwent bilateral adrenalectomy

range: 6–171 months). In the mCS group a significant improvement of the BMI as well as of the hypertension and number of antihypertensive medications was registered after surgery; the same effect could not be demonstrated for type II diabetes (Table 3). In the sCS group the benefits of surgery are controversial. Considering the overall study population, BMI, hypertension, number of medications and type II diabetes are not ameliorated by surgery (Table 3). Nevertheless, by excluding 5 patients who developed hypertension during follow-up (assumed to be due to essential hypertension), arterial hypertension and the number of antihypertensive drugs were significantly reduced after surgery (Table 4).

Discussion

Since the introduction of minimally invasive surgery, adrenalectomy represents an ideal indication. Different techniques have been described (laparoscopic or retroperitoneoscopic), but until now none of these approaches has been demonstrated to be superior [5, 12]. The posterior retroperitoneoscopic route, which we have preferred since 1994, has developed from the familiar open posterior adrenalectomy. In our experience, the retroperitoneoscopic route offers the advantages of a direct view to the retroperitoneum and simple access to the adrenal gland without any need for mobilization of intra-abdominal organs. In previous studies we have demonstrated both safety and short operative time with this approach [6, 10]. In particular the operative time seems to be shorter than with laparoscopic transperitoneal adrenalectomy [13–17].

In the present study—focusing on patients with adrenal hypercortisolism—safety and feasibility of the posterior retroperitoneoscopic approach could again be confirmed. The surgical complication rate was 5.3% and the mean operative time ranged around 1 h. These data had been similar in our previous series of patients with

Table 3 Manifest and subclinical Cushing's syndrome: postoperative outcome (overall study population)

	Manifest Cushing's syndrome		*p* Value	Subclinical Cushing's syndrome		*p* Value
	Preoperative	Postoperative		Preoperative	Postoperative	
Number of patients	97	63 (65%)		63	47 (74.6%)	
With weight gain, *n* (%)	55 (56.7%)			24 (38.0%)		
BMI[a]	28.5 ± 6.5 (18–49)	25.4 ± 5.1 (19–42)	0.0001	29.7 ± 7.0 (20–62)	29.6 ± 7.7 (19–62)	0.79
Improvement		45			21	
No change		12			9	
Worsening		6			17	
Hypertension	68 (70.1%)	30 (47.6%)[b]	0.0009	50 (79.4%)	31 (65.9%)[b]	0.20
Normalization		22			8	
Improvement		16			10	
No change		8			12	
Worsening		5			9	
Number of drugs[a]	1.7 ± 1.4 (1–5)	0.8 ± 1.0 (1–3)	<0.0001	1.5 ± 1.3 (1–5)	1.2 ± 1.2 (1–5)	0.26
Diabetes	12 (12.3%)	4 (6.4%)[c]	0.16	10 (15.9%)	5 (7.9%)[c]	0.46
Improvement		4			2	
No change		2			4	
Worsening		2			1	

[a] Mean ± SD (range)

[b] One mCS patient and 5 sCS patients who developed hypertension after surgery are included in the "worsening group."

[c] Data are not available for four patients in each group, two from the mCS-group and one from the sCS-group, respectively, had no diabetes before surgery

Table 4 Subclinical Cushing's syndrome: postoperative outcome (differentiated analysis of BMI and hypertension according to the preoperative symtoms)

	Subclinical Cushing's syndrome		*p* Value
	Preoperative	Postoperative	
Weight gain, *n* (%)	24 (38.0%)	a	
Improvement		7	
No change		3	
Worsening		8	
BMI[b] (calculated for patients with weight gain)	31.6 ± 8.1 (23–62)	32.6 ± 8.6 (25–62)	0.69
Hypertension (excluding patients who became hypertensive during the follow-up period)	50 (79.4%)	26 (55.3%)	0.02
Number of drugs (excluding patients who became hypertensive during the follow-up period)	1.7 ± 1.3 (1–5)	1.1 ± 1.0 (1–4)	0.05

[a] Data are not available for 6 patients

[b] Mean ± SD (range)

pheochromocytoma [18] and hyperaldosteronism [19], demonstrating that patients affected by Cushing's syndrome do not represent a high-risk group as reported in historical series [20]. This is emphasized by the low proportion of patients (11 of 170; 6%) who had to be monitored postoperatively in an intensive care unit.

The cure rate in our series is 99.4% (169 of 170 patients). In one case a recurrent/persistent hypercortisolism was observed after surgery. The histological examination of the operation specimen failed to detect adrenal hyperplasia or neoplasia. In this case adrenalectomy was performed, misinterpreting Cushing's disease that was treated later on by trans-sphenoidal hypophysectomy. As expected and according to previous reports [21–24], there is no doubt that surgery is mandatory for patients with mCS. In our series we were able to demonstrate a significant reduction of the BMI from 28.5 to 25.4, improvement of hypertension in 60.3%, and reduction of antihypertensive medications. Diabetes type II was cured in 4 of 12 patients.

Partial adrenalectomy was performed in selected patients, none of whom showed persistent or recurrent hypercortisolism postoperatively. These data demonstrate that even in patients affected by Cushing's syndrome due to unilateral adenomas, partial adrenalectomy can be safely performed, as already shown for pheochromocytoma or Conn adenomas [18, 19, 25, 26]. In Cushing's syndrome associated with macronodular bilateral hyperplasia partial resection offers a new option. In our series of 13 patients we performed partial adrenalectomies in 8 cases. All 8 patients beneficiated from surgery, with disappearance or improvement of hypertension, and all but one needed no steroid therapy at the time of follow-up. Similar data were reported by Iacobone et al. in seven cases [27] and Young and colleagues in 10 patients [28], all of whom were treated by less than bilateral adrenalectomy on the basis of tumor diameter and guided by the adrenal venous sampling, respectively.

Postoperative corticosteroid supplementation is considered mandatory in patients with manifest or subclinical Cushing's syndrome [29]. Beside the principal indication of treatment, appropriate levels of perioperative and postoperative doses remain questionable. In earlier studies high dosages of corticoids (about 300 mg hydrocortisone/day initially) were used as a standard, sometimes causing severe infectious complications [29]. In our experience those doses are not necessary. Based on the idea of minimized perioperative stress by minimally invasive surgery, we did not use preoperative or intraoperative cortisone administration and started with lower dosages (50 mg hydrocortisone given orally) on the day of surgery, followed by 75 mg on the first postoperative day. The dosage was reduced to 50 mg for the next days until discharge. Using this supplementation strategy we did not observe any phase of hypocortisolism. Moreover, none of these patients was readmitted due to Addisonian crisis. Additionally we found that (in contrast to mCS) about half of our patients with sCS did not require cortisone therapy postoperatively. The selection of those patients is based on clinical findings during the first postoperative days. If signs of hypocortisolism were absent, patients were discharged after detailed description of Addiosonian symptoms. With this strategy, 5 patients had to be readmitted with mild symptoms of hypocortisolism in the second week after surgery, and oral hydrocortisone therapy was started. However, compliance of patients is essential for application of this concept.

The patients with subclinical Cushing's syndrome represent an interesting subgroup of our study population. The optimal therapy of patients with sCS is an emerging problem due to the constant increase of incidentally discovered adrenal masses ("incidentalomas") in which the incidence of subclinical Cushing is reported to range from 12 to 24% [30, 31]. However, because of the low number of patients (between 5 and 11) included in published studies, only limited data are available from the literature dealing with the outcome of this group of patients after adrenal surgery [30–32]. Nevertheless, the authors suggest an improvement of arterial hypertension [30–32], permanent weight loss in obese subjects [30, 31], as well as a better metabolic control of diabetes [30, 32] in the majority of patients. Recently, a randomized study [33] comparing surgical (22 cases) versus conservative (23 cases) treatment of sCS concluded that in the surgical group, diabetes normalized or improved in 62.5% of patients (5 of 8), hypertension in 67% (12 of 18), hyperlipidemia in 37.5% (3 of 8), and central obesity in 50% (3 of 6), although a significant improvement was achieved only for the blood pressure ($p = 0.046$). Erbil et al. [32] also reported an improvement in the frequency of hypertension in their series of 11 patients.

To our knowledge the present report represents the largest series of sCS treated by surgery at a single institution. According to our experience, the effect of surgery on weight reduction and disappearance of type II diabetes is rather controversial, and therefore adrenalectomy remains questionable in patients with those clinical symptoms. In the group of patients with preoperative weight gain (24 cases) a positive effect of adrenalectomy was observed in 7 cases (29.2%); disappearance of diabetes was registered in 2 (20%). Nevertheless, we demonstrated a significant improvement of hypertension ($p = 0.02$) and decrease of patients requiring medications ($p = 0.05$).

We present our 15 years of experience with patients operated for Cushing's syndrome by retroperitoneoscopic adrenalectomy. Surgery could be performed with minimal morbidity and achieved an excellent outcome. Partial adrenalectomy has to be considered a novel option for the treatment of cortisol-producing adenomas. In the subgroup of patients with sCS, surgery should be considered for patients with arterial hypertension.

References

1. Arnaldi G, Angeli A, Atkinson AB et al (2003) Diagnosis and complications of Cushing's syndrome: a consensus statement. J Clin Endocrinol Metab 88:5593–5602
2. Sarkar R, Thompson NW, McLeod MK (1990) The role of adrenalectomy in Cushing's syndrome. Surgery 108:1079–1084
3. Scott HW Jr, Abumrad NN, Orth DN (1985) Tumors of the adrenal cortex and Cushing's syndrome. Ann Surg 201:586–594
4. Gagner M, Lacroix A, Bolté E (1992) Laparoscopic adrenalectomy in Cushing's syndrome and pheochromocytoma. N Engl J Med 327:1033
5. Fernández-Cruz L, Saenz A, Benarroch G et al (1996) Laparoscopic unilateral and bilateral adrenalectomy for Cushing's syndrome. Transperitoneal and retroperitoneal approaches. Ann Surg 224:727–734 (discussion 734–736)

6. Walz MK, Peitgen K, Walz MV et al (2001) Posterior retroperitoneoscopic adrenalectomy: lessons learned within five years. World J Surg 25:728–734
7. Nieman LK, Biller BM, Findling JW et al (2008) The diagnosis of Cushing's syndrome: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 93:1526–1540
8. Walz MK, Peitgen K, Krause U et al (1995) Dorsal retroperitoneoscopic adrenalectomy—a new surgical technique. Zentralbl Chir 120:53–58
9. Walz MK, Peitgen K, Hoermann R et al (1996) Posterior retroperitoneoscopy as a new minimally invasive approach for adrenalectomy: results of 30 adrenalectomies in 27 patients. World J Surg 20:769–774
10. Walz MK, Alesina PF, Wenger FA et al (2006) Posterior retroperitoneoscopic adrenalectomy—results of 560 procedures in 520 patients. Surgery 140:943–948 (discussion 948–950)
11. Walz MK, Alesina PF (2009) Single access retroperitoneoscopic adrenalectomy (SARA)—one step beyond in endocrine surgery. Langenbecks Arch Surg 394:447–450
12. Lombardi CP, Raffaelli M, De Crea C et al (2008) Endoscopic adrenalectomy: is there an optimal operative approach? Results of a single-center case-control study. Surgery 144:1008–1014 (discussion 1014–1015)
13. Henry JF, Sebag F, Iacobone M et al (2002) Lessons learned from 274 laparoscopic adrenalectomies. Ann Chir 127:512–519
14. Gagner M, Pomp A, Heniford BT et al (1997) Laparoscopic adrenalectomy: lessons learned from 100 consecutive procedures. Ann Surg 226:238–246 (discussion 246–247)
15. Kazaryan AM, Marangos IP, Rosseland AR et al (2009) Laparoscopic adrenalectomy: Norwegian single-center experience of 242 procedures. J Laparoendosc Adv Surg Tech A 19:181–189
16. Bjornsson B, Birgisson G, Oddsdottir M (2008) Laparoscopic adrenalectomies: a nationwide single-surgeon experience. Surg Endosc 22:622–626
17. Lezoche E, Guerrieri M, Crosta F et al (2008) Perioperative results of 214 laparoscopic adrenalectomies by anterior transperitoneal approach. Surg Endosc 22:522–526
18. Walz MK, Alesina PF, Wenger FA et al (2006) Laparoscopic and retroperitoneoscopic treatment of pheochromocytomas and retroperitoneal paragangliomas: results of 161 tumors in 126 patients. World J Surg 30:899–908
19. Walz MK, Gwosdz R, Levin SL et al (2008) Retroperitoneoscopic adrenalectomy in Conn's syndrome caused by adrenal adenomas or nodular hyperplasia. World J Surg 32:847–853
20. Priestley JT, Sprague RG, Walters W et al (1951) Subtotal adrenalectomy for Cushing's syndrome: a preliminary report of 29 cases. Ann Surg 134:464–475
21. Meyer A, Behrend M (2004) Cushing's syndrome: adrenalectomy and long-term results. Dig Surg 21:363–370
22. Iacobone M, Mantero F, Basso SM et al (2005) Results and long-term follow-up after unilateral adrenalectomy for ACTH-independent hypercortisolism in a series of fifty patients. J Endocrinol Invest 28:327–332
23. Mishra AK, Agarwal A, Gupta S et al (2007) Outcome of adrenalectomy for Cushing's syndrome: experience from a tertiary care center. World J Surg 31:1425–1432
24. Sippel RS, Elaraj DM, Kebebew E et al (2008) Waiting for change: symptom resolution after adrenalectomy for Cushing's syndrome. Surgery 144:1054–1060 (discussion 1060–1061)
25. Cheng SP, Saunders BD, Gauger PG et al (2008) Laparoscopic partial adrenalectomy for bilateral pheochromocytomas. Ann Surg Oncol 15:2506–2508
26. Kok KY, Yapp SK (2002) Laparoscopic adrenal-sparing surgery for primary hyperaldosteronism due to aldosterone-producing adenoma. Surg Endosc 16:108–111
27. Iacobone M, Albiger N, Scaroni C et al (2008) The role of unilateral adrenalectomy in ACTH-independent macronodular adrenal hyperplasia (AIMAH). World J Surg 32:882–889
28. Young WF Jr, du Plessis H, Thompson GB et al (2008) The clinical conundrum of corticotropin-independent autonomous cortisol secretion in patients with bilateral adrenal masses. World J Surg 32:856–862
29. Shen WT, Lee J, Kebebew E et al (2006) Selective use of steroid replacement after adrenalectomy: lessons from 331 consecutive cases. Arch Surg 141:771–774 (discussion 774–776)
30. Reincke M, Nieke J, Krestin GP et al (1992) Preclinical Cushing's syndrome in adrenal "incidentalomas": comparison with adrenal Cushing's syndrome. J Clin Endocrinol Metab 75:826–832
31. Rossi R, Tauchmanova L, Luciano A et al (2000) Subclinical Cushing's syndrome in patients with adrenal incidentaloma: clinical and biochemical features. J Clin Endocrinol Metab 85:1440–1448
32. Erbil Y, Ademoğlu E, Ozbey N et al (2008) Evaluation of the cardiovascular risk in patients with subclinical Cushing syndrome before and after surgery. World J Surg 30:1665–1671
33. Toniato A, Merante-Boschin I, Opocher G et al (2009) Surgical versus conservative management for subclinical Cushing syndrome in adrenal incidentalomas: a prospective randomized study. Ann Surg 249:388–391