

# Bilateral Adrenalectomy for Cushing's Syndrome

## Anterior *Versus* Posterior Surgical Approach

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### Objective

This study evaluates the intraoperative and postoperative complications in patients with Cushing's syndrome who underwent bilateral adrenalectomy comparing the posterior or anterior operative approach.

### Background

The posterior approach for bilateral adrenalectomy has been advocated over the anterior approach because of rapid recovery and decreased morbidity, but the long-term complications associated with each procedure are not well described.

### Methods

The intraoperative profiles and morbidity in 48 patients undergoing bilateral adrenalectomy for Cushing's disease through either the anterior or posterior approach from 1985 to the present were reviewed comparing the intraoperative complication and early and late postoperative complication rate and morbidity.

### Results

Twenty-seven patients underwent an anterior transabdominal procedure, whereas 21 underwent a posterior retroperitoneal procedure via bilateral incisions. Age, weight, and diagnostic categories of Cushing's syndrome were similar between the two groups as well as serum cortisol and 24-hour urinary cortisol levels. Operative time, estimated blood loss, and transfusion requirements were not different between the groups, even though adrenal glands excised through the anterior approach were significantly larger. Acute morbidity was similar between the groups. However, 17 (81%) of 21 patients who underwent posterior bilateral adrenalectomy suffered from chronic back pain, compared with 2 (7%) of 27 via the anterior approach. Five of these patients in the posterior group considered the pain incapacitating, and the mean time to return to work was significantly longer in the posterior group because of back pain.

### Conclusions

The anterior approach to bilateral adrenalectomy has comparable intraoperative complications and early morbidity compared to the posterior approach. The posterior

approach has a very high incidence of chronic incision-related back pain. The anterior approach is the preferred open surgical technique in most patients undergoing bilateral adrenalectomy for Cushing's syndrome without other contraindications for undergoing laparotomy.

Cushing's syndrome is a clinical condition of excess cortisol production secondary to disorders of the pituitary, adrenal glands, or ectopic production of adrenocorticotrophic hormone (ACTH). The syndrome is manifested by obesity, hypertension, diabetes, amenorrhea, and other symptoms and without recognition and proper treatment can result in substantial morbidity and mortality. For patients who do not respond to treatment directed at pituitary adenomas, have occult ectopic ACTH secreting tumors, or have primary bilateral adrenal disorders such as primary pigmented nodular adrenal disease or macronodular adrenal hyperplasia, bilateral adrenalectomy is effective in curing or controlling hypercortisolism and reversing the signs and symptoms of excess cortisol production.<sup>1,2</sup>

The morbidity associated with bilateral adrenalectomy is not inconsequential, and reported mortality rates range from 2% to 5%.<sup>3-6</sup> In general, patients with Cushing's syndrome are predisposed to infectious or hemorrhagic complications as well as to impaired wound healing. The two open operative approaches for bilateral adrenalectomy are the transabdominal approach through either a midline or bilateral subcostal incision or the posterior approach using bilateral vertically oriented paraspinous incisions. These incisions, also called Hugh-Young incisions, typically require removal of the 12th and frequently the 11th ribs for exposure to the adrenal glands. The posterior approach has the advantage of avoiding entering the peritoneal cavity and is thought to result in a more rapid convalescence.<sup>7</sup> Relative contraindications to a posterior approach are large tumors or pheochromocytomas because of a 10% incidence of extra-adrenal tumors,<sup>8</sup> although these factors typically are not important for patients with Cushing's syndrome. The anterior approach allows a complete abdominal and retroperitoneal exploration and may be most appropriate in patients in whom a coincidental abdominal procedure is contemplated.<sup>9,10</sup>

The posterior approach for bilateral adrenalectomy has become increasingly popular and is advocated because length of hospitalization after operation is shorter compared to the anterior approach.<sup>7</sup> However, there are other factors that may be important in deciding which approach ultimately may be optimal for the patient. In particular, because many of these patients are relatively young at

the time of treatment and return to fully productive lives after surgery, any long-term sequelae of either approach may be important to define. The current study compares the perioperative and long-term outcomes in patients undergoing bilateral adrenalectomy for Cushing's syndrome via either the posterior or anterior approach.

## PATIENTS AND METHODS

### Patient Characteristics

The medical records of 48 consecutive patients who underwent bilateral adrenalectomy for treatment of Cushing's syndrome at the National Institutes of Health between 1985 and the present were reviewed. Eighteen patients had Cushing's disease and had not responded to pituitary surgery or radiation therapy or both, 17 had primary bilateral adrenal disease, and 13 had ectopic ACTH production. Three patients in the posterior group died during the follow-up period because of colon cancer (1) or cardiopulmonary disease (2). All patients (or the next of kin for the deceased patients) were contacted by telephone and interviewed to determine any long-term sequelae of their operation. Patients were selected for the anterior or posterior approach based on surgeon's preference, patient's preference, estimated gland size from preoperative computed tomographic or magnetic resonance imaging scan, whether a concomitant intra-abdominal procedure was anticipated, and if there had been prior abdominal surgery. The posterior approach was used in 21 patients and the anterior approach in 27, and patient groups were similar based on demographic and diagnostic data (Table 1). Diabetes was present in five posterior and three anterior patients. Carney's complex was present in three patients from both groups.

### Diagnosis

Biochemical diagnosis of Cushing's syndrome was confirmed by serum and urinary cortisol levels in conjunction with serum ACTH and 17-OH ketosteroid levels. The average morning serum cortisol levels and 24-hour urinary-free cortisol levels were similar between the two groups (Table 1). In patients who had not responded to treatment for pituitary lesions or who had ectopic ACTH production, serum ACTH was equivalent between the posterior and anterior group. Bilateral adrenal disease was confirmed radiographically by a combination of computed

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**Table 1. CLINICAL, BIOCHEMICAL, AND RADIOLOGIC CHARACTERISTICS OF 48 PATIENTS UNDERGOING BILATERAL ADRENALECTOMY FOR CUSHING'S SYNDROME VIA THE ANTERIOR VERSUS POSTERIOR APPROACH**

	Anterior (n = 27)	Posterior (n = 21)
Clinical data		
Age (yr)	39.02 ± 0.3	36.5 ± 0.5
Range (yr)	(10.5–73)	(4.5–68)
Gender (M:F)	10:17	4:17
Weight (kg)	73.3 ± 0.3	72.1 ± 0.6
Diagnosis		
Primary adrenal disease	10	7
Cushing's disease	8	4
Ectopic ACTH	9	10
Diabetes	3	5
Biochemical data		
24-hr urinary cortisol (ng/mL)	1259.0 ± 30.4	1261 ± 44.2
ACTH (ng/mL)*	201.9	191.7
Radiologic data		
Bilateral adrenal enlargement CT	12/23	5/21
Bilateral iodocholesterol uptake	8/8	7/8

ACTH = adrenocorticotrophic hormone; CT = computed tomography.

\* In subgroups with Cushing's disease and ectopic ACTH.

tomographic scans, magnetic resonance imaging scans, or iodocholesterol nuclear medicine scans (Table 1). Overall, bilateral uptake on iodocholesterol scan was seen in 15 (94%) of 16 patients studied, whereas only 17 (39%) of 44 patients had bilateral adrenal enlargement on computed tomographic scan (Table 1).

## Operative Treatment

All anterior operations were performed by a single operating team while for 7 of 21 posterior procedures the initial entry into the retroperitoneum and closures were performed simultaneously by two operating teams. The standard incisions for the posterior approach are two vertical incisions placed approximately 6 to 8 cm from the spinous processes and extending from the 10th or 11th rib to the posterosuperior iliac spine. In the posterior approach, the 12th ribs and frequently the 11th ribs were excised for adequate exposure of the adrenal bed. The incision for the anterior approach was either a midline ( $n = 16$ ) or bilateral subcostal ( $n = 11$ ) incision depending on body habitus. With the anterior approach, a Kocher maneuver and mobilization of the right lobe of the liver was used to gain access to the right adrenal gland. The

**Table 2. INTRAOPERATIVE PARAMETERS FROM PATIENTS UNDERGOING BILATERAL ADRENALECTOMY VIA THE ANTERIOR VERSUS POSTERIOR APPROACH**

	Anterior*	Posterior*	$p_2$ †
OR time (min)	205.2 ± 0.6	200.4 ± 1.2	0.7
EBL (mL)	561 ± 9	678 ± 16	0.49
Fluids (mL)	4453 ± 33	3812 ± 40	0.2
Transfusion (units)	0.92	1.38	0.2
Size of glands (g)			
L	19.9 ± 0.4	9.3 ± 0.1	0.03
R	17.6 ± 0.3	8.9 ± 0.2	

OR = operating room; EBL = estimated blood loss; L = left; R = right.

\* Values are mean ± standard error of the mean.

†  $p_2$  calculated by Student's t test.

left adrenal gland typically was approached through the lesser sac and exposed by reflecting the pancreas superiorly. A standard regimen of tapered perioperative stress dose steroids was administered in all patients followed by maintenance hydrocortisone and Florinef (E.R. Squib & Sons, Princeton, NJ) orally.

## Statistical Analysis

Comparison between groups was made using the Student's t test or the Fisher's exact test as indicated. A  $p$  value of 0.05 or less was considered significant.

## RESULTS

There was no difference in operative time between the two groups despite the fact that two teams were used in a portion of the posterior procedures (Table 2). The mean size of the adrenal glands removed via the anterior approach was approximately twice the size of glands removed through the posterior approach (Table 2). Even

**Table 3. POSTOPERATIVE PARAMETERS FROM PATIENTS UNDERGOING BILATERAL ADRENALECTOMY VIA THE ANTERIOR VERSUS POSTERIOR APPROACH**

	Anterior	Posterior	$p_2$ *
Clear liquids (days)	3.3 ± 0.02	1.7 ± 0.02	<0.05
Solids (days)	5.4 ± 0.03	3.4 ± 0.02	<0.05
NG removal (days)	2.1 ± 0.02	0.4 ± 0.01	<0.05
Ambulate (days)	2.1 ± 0.02	1.8 ± 0.01	0.21

NG = nasogastric tube.

\*  $p_2$  calculated by Student's t test.

**Table 4. POSTOPERATIVE ANALGESIC REQUIREMENTS IN PATIENTS UNDERGOING BILATERAL ADRENALECTOMY VIA THE ANTERIOR VERSUS POSTERIOR APPROACH**

	Anterior	Posterior	P <sub>2</sub> *
Epidural (%)	13/27 (50)	7/21 (33)	
IV morphine (mg/patient/day)			
DOS	37	21.6	0.013
POD 1	34.4	28	0.32
POD 2	34	21	0.1
Oral analgesics			
POD 3 (%)	17/27 (63)	15/21 (63)	0.797

DOS = day of surgery; POD = postoperative day; IV = intravenous.  
\* p<sub>2</sub> calculated via Student's t test.

with excising significantly larger adrenal glands via the anterior approach, the operative blood loss was identical with a trend toward a lower transfusion requirement with anterior incisions.

After surgery, the patients operated on via the posterior approach had either no nasogastric suction or at most 1 day after anesthesia, whereas gastric decompression was continued for a mean of 2.1 days for the anterior approach group. In addition, patients in the posterior group were started on a clear liquid diet and advanced to a regular diet more rapidly than were patients in the anterior group (Table 3). Patients in both groups ambulated (defined as independent walking > 50 ft) routinely by the second postoperative day.

One measure of how well a patient tolerates a procedure is the daily dose of pain medication delivered in the immediate postoperative period. The average daily morphine doses per patient on the day of surgery and the first 2 postoperative days were 37.0, 34.4, and 34.0 mg/day in the anterior group and 21.6, 28.0, and 21.0 mg/day in the posterior group, respectively (Table 4). Oral analgesia was used by a majority of patients in both groups by the third postoperative day. Half of the patients in the anterior group compared to a third in the posterior group used continuous epidural catheters for pain control. The lower rate of epidural for the posterior group reflects the difficulty in using this catheter with the bilateral posterior incisions.

The intraoperative and early postoperative complications were similar in both groups. The posterior group incurred three intraoperative complications. One partial hepatic vein tear during removal of a right gland, a vena caval injury, and a superior pole renal infarction due to ligation of an aberrant superior pole artery. The anterior group incurred two operative complications, including splenic injury requiring splenectomy and a reoperation

for postoperative bleeding from the right adrenal bed in a patient with an unappreciated coagulopathy. Superficial wound infections developed in three patients, who were treated by having the wound opened, dressing changes, and antibiotics for healing by secondary intention. Postoperative mechanical ventilation was required in one patient after a posterior adrenalectomy and in three patients in the anterior group, primarily due to severe Cushing's syndrome with muscle weakness.

Late complications differ between the two groups with the greatest point of distinction being chronic back pain. Only 7% of the anterior procedure group reported mild back pain, whereas 81% of the posterior group had some level of chronic back pain (Table 5). Eight patients (38%) in the posterior group subjectively rated their pain as severe and four patients required long-term weekly narcotics to manage the back discomfort. This late complication translated into a significantly prolonged time to return to work after the operative procedure (Table 6, p<sub>2</sub> < 0.05). Three patients operated on via the posterior approach were unable to return to work, specifically claiming disability due to chronic back pain despite curative treatment of their Cushing's syndrome.

Another late complication that was noted in the anterior procedure group was a high rate of incisional hernia of 11% versus no late hernias in the posterior operative group. Other complications that were fairly minor but noted were incisional numbness and chronic fatigue. These symptoms are reported in both groups but were higher with a twofold difference in incidence in the posterior group (Table 5).

**DISCUSSION**

In this study, we reviewed the intraoperative and short-term and long-term postoperative outcomes of two groups

**Table 5. PERIOPERATIVE AND LATE COMPLICATIONS FROM PATIENTS UNDERGOING BILATERAL ADRENALECTOMY VIA THE ANTERIOR VERSUS POSTERIOR APPROACH**

Anterior Group		Posterior Group	
Type of Complication	n (%)	Type of Complication	n (%)
<b>Acute</b>			
Incidental splenectomy	1 (4)	Upper pole renal infarction	1 (5)
Reoperation (bleeding)	1 (4)	Vascular injury	2 (10)
Wound infection	3 (11)	Wound infection	3 (14)
<b>Late</b>			
Chronic back pain	2 (7)	Chronic back pain	17 (81)
Incisional numbness	3 (11)	Incisional numbness	6 (29)
Chronic fatigue	2 (7)	Chronic fatigue	6 (29)
Incisional hernia	3 (11)		

**Table 6. DETAILED ANALYSIS OF CHRONIC BACK PAIN FOLLOWING BILATERAL ADRENALECTOMY IN TERMS OF SUBJECTIVE SYMPTOMS, MEDICATION REQUIREMENT, AND RETURN TO WORK**

	Anterior n (%)	Posterior n (%)
Description of subjective back pain		
None	25 (93)	4 (19)
Mild	2 (7)	9 (43)
Severe	0	8 (38)*
Medication needed for back pain		
None	24 (89)	4 (19)
Weekly NSAIDs	3 (11)	13 (62)
Weekly narcotics	0	4 (19)
Time from operation to return to work (wk)		
Mean	6.6 ± 0.8	10.4 ± 1.8
Range	(4–24)	(6–24)
No. disabled due to back pain	0	3

\*  $P_2 = 0.036$ .

NSAIDs = nonsteroidal anti-inflammatory drugs.

of patients undergoing bilateral adrenalectomy through either an anterior or posterior approach for Cushing's syndrome. Patients in both groups were similar with respect to age, weight, pathologic diagnoses, and severity of hypercortisolism (serum cortisol, urinary cortisol). One difference was that the mean weight of adrenal glands removed via the anterior approach was twice that of the posterior group because larger gland size is one of the factors that influences an anterior approach. Despite the potential technical difficulties in removing larger glands in patients undergoing adrenalectomy via the anterior approach, there was no significant difference between the groups with respect to operative time, estimated blood loss, or transfusion requirements.

The short-term postoperative recovery as assessed by pain medication requirements and resolution of ileus favors the posterior approach. The posterior cohort had a lower narcotic requirement on the day of surgery and earlier bowel recovery based on the length of postoperative nasogastric decompression and subsequent initiation of diet. However, the analgesic requirements were not significantly different on all subsequent postoperative days, although the posterior group tended to use fewer narcotics. The timing of conversion to oral analgesics was not significantly different between the two groups. The longer period of nasogastric decompression observed in the anterior approach group of patients may reflect a bias that patients require longer nasogastric decompression after laparotomy. Current management based on recent reports of the lack of utility of nasogastric tubes in gen-

eral<sup>11</sup> is that patients undergoing posterior bilateral adrenalectomy do not have a postoperative nasogastric tube and for the anterior approach, they either have no tube or typically 1 day of gastric decompression. The slightly increased time to begin clear liquids and advance to a regular diet reflects a longer ileus after a transabdominal procedure *versus* a retroperitoneal one. Patients in both groups were ambulating on average by the second postoperative day. Length of hospitalization was not considered an appropriate endpoint of comparison as many patients remain hospitalized at our institution after surgery for a brief period for research purposes or because they have considerable distances to travel home.

The intraoperative complications and the acute postoperative morbidity were similar between the groups. The vascular injuries in the posterior group occurred in obese patients undergoing explorations via relatively small incisions but caused no secondary problems for these patients. The reported wound infection rate after bilateral adrenalectomy ranges from 4% to 23%,<sup>7</sup> and the overall infection rate of 12% (6 of 48 patients) in this series is not inconsistent with previous results. Late morbidity, however, was dramatically different between the groups. All patients were contacted by telephone and asked to describe any chronic symptoms relating to the procedure. Eighty-one percent of patients in the posterior group reported chronic back pain and 8 patients described it as being incapacitating, that is, preventing them from pursuing their full range of desired activities. The responses from a similar telephone interview of the patients who had undergone anterior operations were distinctly different. Therefore, the difference in back pain cannot be attributed to osteoporosis or muscle injury due to the cortisol excess of Cushing's syndrome, but rather is a direct result of the paraspinous incisions used for the posterior approach. To remove the adrenal glands posteriorly in these patients with truncal obesity, the 12th rib virtually is always removed and the accompanying neurovascular bundle is ligated. The paraspinous muscles in the lumbar region are retracted medially to allow the necessary exposure to excise the adrenal. The retraction on the paraspinous muscle is quite vigorous and may be a contributing factor to the chronic back pain we have observed with this approach. The only significant late complication in the anterior group was incisional hernia in 3 of 27 patients. This high rate of hernia (11%) may be explained by poor wound healing due to cortisol excess and the obesity associated with this disease.

During the past few years, there has been considerable interest in the use of laparoscopic adrenalectomy.<sup>12–14</sup> However, the utility of laparoscopic bilateral adrenalectomy has not yet been clearly shown, particularly in patients with Cushing's syndrome who almost uniformly have significant truncal obesity and significant retroperi-

toneal fat. Several distinct potential drawbacks of this procedure may be the technical difficulties in removing large lesions, the longer operative time, and the carbon dioxide intoxication.<sup>15</sup> The use of the laparoscopic approach has not been advocated for patients with tumors greater than 70 g or those with central obesity.<sup>13</sup> Some investigators think that the posterior approach to bilateral adrenalectomy allows recovery nearly equivalent to that expected with bilateral laparoscopic adrenalectomy. This bias that the posterior approach is a better-tolerated procedure in the opinion of most endocrine surgeons reflects observations made in the immediate postoperative period while patients are recovering in the hospital.<sup>7,9</sup> Our data support this impression, but the differences between the anterior approach and the posterior approach are not as dramatic as may be intuitively expected, particularly with the widespread use of epidural catheters for postoperative pain control after laparotomy. The impression of a fast recovery with less pain using the posterior approach is overshadowed by the very significant incidence of chronic pain reported in our series. Unless the operating surgeon continues to observe these patients who are typically managed long term by an endocrinologist, this late complication may not be appreciated.

We conclude that both the posterior and anterior approaches to bilateral adrenalectomy are safe techniques for the treatment of Cushing's syndrome. However, many patients are relatively young at the time of treatment (the mean age in this series was younger than 40 years of age) and will return to full and productive lives after surgery. The data presented here show that the majority of patients who undergo posterior bilateral adrenalectomy will have long-term incisional pain, which can be severe and incapacitating in some. Therefore, we think the posterior approach should be reserved for patients in whom the anterior approach may pose some technical difficulties, such as for patients who have had multiple prior laparotomies or extreme truncal obesity.

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