

Comparison of the Hemodynamic Parameters of Open and Laparoscopic Adrenalectomy for Pheochromocytoma

William B. Inabnet, M.D.,¹ Joël Pitre, M.D.,² Denis Bernard, M.D.,³ Yves Chapuis, M.D.²

¹Department of General Surgery, Mount Sinai Medical Center, 5 East 98th Street, Box 1259, New York, New York 10028, USA ²Department of General Surgery, Cochin Hospital, CHU Cochin-Port Royal, 27, rue de Fg. St. Jacques, 75674 Paris, France ³Department of Anesthesia, Cochin Hospital, CHU Cochin-Port Royal, 27, rue de Fg. St. Jacques, 75674 Paris, France

Abstract. Laparoscopic adrenalectomy has gained widespread popularity for treating a variety of adrenal disorders including pheochromocytoma, but the effects of pneumoperitoneum on the hemodynamics of patients with catecholamine-secreting tumors are poorly understood. The goal of this study was to compare the effects of carbon dioxide pneumoperitoneum and tumor manipulation on the hemodynamic parameters in two groups of patients with sporadic pheochromocytomas less than 7 cm in size. Group 1 patients (n = 11) underwent lateral transabdominal laparoscopic adrenalectomy, and group 2 (n = 11) underwent adrenalectomy by the open anterior approach. The mean follow-up was 37 months in group 1 (range 26-51 months) and 52 months in group 2 (range 27-72 months). All patients undergoing laparoscopic adrenalectomy experienced intraoperative hypertension (blood pressure \geq 200/90 mmHg), as did 73% with the open approach, but the difference was not significantly different. Intraoperative hypotension (systolic blood pressure < 80 mmHg) occurred in four group 1 patients compared to six patients in group 2. Mean arterial pressure, central venous pressure, and pulmonary capillary wedge pressure were significantly higher in group 1 patients prior to tumor excision, but there was no difference in pulse, cardiac index, or left ventricle work index at any point during the procedure. There were no conversions or complications in the laparoscopic group; one patient in group 2 developed an incisional hernia. Although laparoscopic adrenalectomy for pheochromocytoma is associated with a greater increase in mean arterial pressure, central venous pressure, and pulmonary capillary wedge pressure, the creation of pneumoperitoneum does not significantly change the cardiac index or left ventricle work index. Carbon dioxide pneumoperitoneum is well tolerated in patients with pheochromocytoma.

Since 1992 laparoscopic adrenalectomy (LA) has become the preferred approach for treating a variety of nonmalignant adrenal disorders, including pheochromocytoma [1]. The laparoscopic approach has been shown to be safe and efficacious, resulting in less postoperative pain and shorter hospitalization [1–5]. Adrenalectomy for pheochromocytoma can present special challenges owing to the perioperative medical management, the unique biologic behavior, and the more difficult mobilization of catecholamine-secreting tumors [6].

During laparoscopy it is well known that carbon dioxide (CO_2) insufflation causes an elevation in intraabdominal pressure and an increase in CO_2 absorption, thereby reducing venous return and

increasing peripheral vascular resistance [7]. Generally, these changes are well tolerated by most patients, but in patients with pheochromocytoma the effects of pneumoperitoneum are not completely known. Only a few studies have examined the hemodynamic sequelae of pneumoperitoneum during LA for pheochromocytoma, but these studies are either isolated case reports or have included patients with other pathology such as Cushing's or aldosterone adenoma [8–12]. The purpose of this study was to compare LA to the conventional open approach for treating pheochromocytoma, paying particular attention to the intraoperative hemodynamic changes that occur with each technique.

Materials and Methods

Patients

The goal of the study was to compare the hemodynamic data and outcome of patients undergoing open and laparosocpic adrenalectomy for pheochromocytoma. Between January 1993 and February 1997 a total of 35 patients underwent surgery for sporadic pheochromocytoma at Cochin Hospital in Paris, France. Of these patients, 11 underwent LA. Inclusion criteria for the laparoscopic approach included tumor size less than 7 cm, no evidence of multiple endocrine neoplasia, and an absence of extraadrenal lesions on preoperative localization studies. Altogether 24 patients underwent open adrenalectomy, of whom 11 had a tumor diameter less than 7 cm. To make a meaningful comparison to the laparoscopic group, open adrenalectomy patients with a tumor diameter greater than 7 cm (n = 9; mean diameter 9.4 cm) were excluded from the study. Four additional patients were excluded for having pheochromocytomas located at an extraadrenal site (n = 2) or recurrent disease from surgery performed prior to the beginning of the study period (n = 2).

A total of 22 patients had a tumor size less than 7 cm and comprise the patient population of this study. The hospital and operative charts of these patients were reviewed in a retrospective manner, and the following parameters were analyzed: intraoperative hemodynamic data, duration of surgery, transfusion and crystalloid requirements, incidence of intraoperative hypertension, pain medication requirement as measured by the number of days of morphine administration, and the duration of hospital stay.

All patients displayed clinical evidence of excess catecholamine secretion. One or more of the urinary catecholamine values were elevated in each patient. Localization studies included abdominal ultrasonography (n = 11), computed tomography (CT) (n = 21), magnetic resonance imaging (MRI) (n = 14), and ¹²³I metaiodobenzylguanidine (MIBG) scintigraphy (n = 17).

Group 1 patients (n = 11) underwent lateral transabdominal LA. Six of eleven group 1 patients had a history of previous abdominal surgery, including appendectomy (n = 4), excision of ectopic pregnancy (n = 2), hysterectomy (n = 1), and lysis of adhesions (n = 1). In group 1 the age ranged from 32 to 63 years (mean 51.4 \pm 10 years) with three men and eight women. The lesion was located in the right adrenal gland in eight patients and the left gland in three. The mean tumor size was 4.1 ± 1.2 cm (range 2–6 cm).

Group 2 consisted of 11 patients, all of whom underwent open anterior transabdominal adrenalectomy via a subcostal incision. The age of group 2 patients ranged from 16 to 61 years (mean 45.7 ± 14.2 years) with four males and seven females. In contrast to group 1 patients, most of the lesions in group 2 were located on the left side (eight left, three right). The mean tumor size was 4.8 ± 1.2 cm (range 2–7 cm). The mean follow-up was was 37 months in group 1 (range 26–51) and 52 months in group 2 (range 27–72).

Surgery

Twenty of twenty-two patients were prepared for surgery with calcium channel blockers (nicardipine, 60-100 mg/day PO for 7–10 days prior to surgery). In addition, six patients received β -blockers (labetalol 400–800 mg/day) owing to the presence of tachycardia. In two patients the hospital records did not record the preoperative preparation. After induction of general endotracheal anesthesia, a Foley catheter, radial arterial line, and Swan-Ganz central venous catheter were inserted in all patients. Intraoperative hemodynamic data, including pulse, mean arterial pressure, central venous pressure, and pulmonary capillary wedge pressure, were collected during insufflation/incision, gland dissection, and adrenal vein ligation and after tumor excision. The cardiac index and left ventricle work index were calculated.

The lateral transabdominal approach was used in all patients undergoing LA. After carefully positioning and securing the patient in the lateral decubitus position, the open technique was used to insert a 10 mm trocar at the anterior axillary line two fingerbreadths below the costal margin. Pneumoperitoneum was achieved by insufflating CO_2 gas to an intraperitoneal pressure of 12 to 14 mmHg. One additional 10 mm and three 5 mm trocars were inserted. The abdomen was explored laparoscopically to rule out the presence of metastatic disease or additional pathology.

On the right side, complete mobilization of the right lobe of the liver in the cephalad direction and to the left border of the vena cava allowed access to the right adrenal bed. After retracting the liver in the cephalad-medial direction with a laparoscopic hepatic fan retractor (ERBE Medical SARL, Dardilly, France), adrenal gland mobilization was begun. On the left side, the spleen and splenic flexure of the left colon were mobilized. Gentle retraction of the spleen to the right permitted access to the left adrenal bed.

Table 1. Laparoscopic and open adrenalectomy for pheochromocytoma.

Parameter	Group 1 $(n = 11)$	Group 2 (n = 11)	р
Age	51.4 ± 10.0	45.7 ± 14.0	NS
Gender			NS
Male	3	4	
Female	8	7	
Tumor size (cm)	4.1 ± 1.2	4.6 ± 1.2	NS
Intraoperative hypertension	11	8	NS
Intraoperative hypotension	4	6	NS
Duration of surgery (min)	146 ± 36	153 ± 55	NS
Postoperative morphine requirement (days)	1.3 ± 0.8	2.2 ± 1.2	< 0.05
Duration of hospitalization (days)	5.5 ± 2.2	6.1 ± 1.6	NS
Complications	0	1	NS

The adrenal vein was identified and ligated with two clips as early as possible during the dissection and with minimal gland minipulation. When present, accessory adrenal veins were controlled in a similiar fasion. All cases of intraoperative hypertension, defined as blood pressure $\geq 200/90$, were treated with intravenous infusion of a calcium channel blocker (nicardipine 2.5–7.5 µg/kg/min). Small vessels and lymphatics were controlled with clips or electrocautery as needed. After the specimen had been completely liberated, it was retrieved from the abdominal cavity in a plastic bag.

Statistics

Parametric and nonparametric data were analyzed by the paired Student's *t*-test and the chi-square test. A *p* value ≤ 0.05 was considered statistically significant.

Results

There was no significant difference in age, sex, side of adrenalectomy, or tumor size between groups 1 and 2 (Table 1). An adrenal lesion was successfully localized in all patients by either CT or MRI, but MIBG scintigraphy was negative in 3 of 16 patients, including 2 who underwent LA.

Intraoperative hypertension occurred in all group 1 patients compared to 73% of group 2 patients, but the difference was not statistically significant. All cases of intraoperative hypertension were successfully treated with an intravenous infusion of nicardipine. Four patients in group 1 experienced intraoperative hypotension (systolic blood pressure $\leq 80 \text{ mmHg}$) compared to six in group 2, but the difference was not statistically significant. All patients with intraoperative hypotension responded to volume expansion.

Intraoperative hemodynamic data as collected by a radial arterial line and a pulmonary artery catheter are summarized in Table 2. There was no difference in pulse between the two groups. Mean arterial pressure was significantly higher in group 1 at insufflation but was no different during dissection, vein ligation, or after tumor excision. Central venous pressure was significantly higher in group 1 at the time of insufflation, gland dissection, and adrenal vein ligation. Similarly, group 1 patients experienced an increase in pulmonary capillary wedge pressure at insufflation and gland dissection, but there was no significant difference in cardiac index or

Parameter	Insufflation/incision		Dissection		Vein ligation		Tumor excision	
	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2
Pulse (bpm)	72 ± 24	78 ± 19	94 ± 20	86 ± 21	90 ± 16	94 ± 26	87 ± 12	86 ± 21
MAP (mmHg)	$105 \pm 21^{*}$	$86 \pm 13^{*}$	121 ± 32	115 ± 19	82 ± 10	76 ± 15	83 ± 15	84 ± 14
CVP (mmHg)	$12 \pm 5^{*}$	$8 \pm 3^{*}$	$14 \pm 6^{*}$	$8 \pm 3^{*}$	$12 \pm 6^{*}$	$7 \pm 3^{*}$	10 ± 5	9 ± 2
PCWP (mmHg)	$15 \pm 3^{*}$	$11 \pm 4^{*}$	$20 \pm 6^{*}$	$12 \pm 5^{*}$	15 ± 7	11 ± 3	13 ± 5	13 ± 6
CI (L/min/m ²)	2.6 ± 1.3	3.2 ± 0.7	3.7 ± 1.3	3.9 ± 0.8	3.5 ± 0.8	4.0 ± 0.6	3.2 ± 1.1	4.0 ± 0.8
LVWI (dynes/s/cm ²)	47 ± 22	45 ± 7	52 ± 15	75 ± 23	39 ± 11	43 ± 14	40 ± 11	44 ± 12

 Table 2. Intraoperative hemodynamic data.

MAP: mean arterial pressure; CVP: central venous pressure; PCWP: pulmonary capillary wedge pressure; CI: cardiac index; LVWI: left ventricle work index.

*p < 0.05.

left ventricle work index between group 1 and 2 patients at any point during the procedure. The intraoperative crystalloid requirement was not different between the two groups (4045 ± 1254 vs. 4872 ± 1314 ml), but one patient in group 2 required two units of packed red blood cells during surgery.

The mean tumor weight in group 1 was 30.4 ± 14 g (range 6–50 g) compared to 56 ± 22 g (range 30-94 g) in group 2 (NS). There were no malignant lesions in the study. The mean operating time was not different between the laparoscopic and open groups (146 ± 36 vs. 153 ± 55 minutes). Patients undergoing LA required less pain medication as measured by the number of days of morphine administration (1.3 ± 0.8 vs. 2.2 ± 1.2 days; p = 0.02), but there was no difference in the duration of hospitalization (5.5 ± 2.2 vs. 6.1 ± 1.6 days). There were no conversions or complications in the laparoscopic group; one patient in group 2 developed an incisional hernia. There was no mortality or recurrence in either group.

Discussion

Despite advances in the perioperative management of patients with pheochromocytoma, the occurrence of intraoperative hypertension is common and remains a valid concern [13–17]. In the current study, the overall incidence of intraoperative hypertension was high, especially in the laparoscopic group; but all cases were successfully treated with an intravenous infusion of nicardipine. We also observed an increase in many of the hemodynamic parameters in patients undergoing LA. Mean arterial pressure (MAP), central venous pressure, and pulmonary capillary wedge pressure, for example, were significantly higher in the laparoscopy group prior to tumor excision. Interestingly, the creation of pneumoperitoneum led to the only significant increase in MAP in the laparoscopic group. These hemodynamic alterations were of little clinical significance, as the cardiac index and left ventricular work index were not compromised at any point during the study.

In most regions of the world, preoperative preparation of patients with pheochromocytoma consists of α -adrenergic blockade with the addition of β -adrenergic blockade if arrhythmias are present. Intraoperative hypertension is typically treated with nitroprusside, adding β -adrenergic blockade for tachyarrhythmias. When β -blockade is desired, the short acting β -blocker esmolol, which has a half-life of 9 minutes, has been efficacious [17].

A few centers in Europe, including ours, use calcium channel blockers as the preferred method of preoperative preparation for patients with pheochromocytoma [9, 14, 17]. In the current study, most patients received a 7- to 10-day course of nicardipine (Loxen) prior to surgery, a calcium channel blocker that induces arterial vasodilatation without the side effects of α -blockade. The occurrence of intraoperative hypertension was transient in most cases and did not cause any adverse sequelae. Calcium channel blockers inhibit calcium influx at the cellular level, thereby modifying hormone synthesis, release, and action [17]. These features make calcium channel blockers an attractive alternative to α -adrenergic blockade when preparing patients with pheochromocytoma for surgery.

During conventional open adrenalectomy for pheochromocytoma, it has been clearly demonstrated that surgical manipulation results in a marked increase in circulating plasma catecholamine levels [13]. With the laparoscopic approach, serum catecholamine levels are also increased during surgery but to a much lesser extent than that seen with the open approach [11]. The greatest increase in plasma catecholamine levels appears to occur during tumor dissection. During LA for pheochromocytoma, Fernandez-Cruz et al. demonstrated a 17.4-fold increase in plasma epinephrine levels during tumor dissection compared to a 34.2-fold increase with the open approach, a difference that was statistically significant [11]. Furthermore, these investigators showed a much higher incidence of hypertension, tachycardia, and cardiovascular instability in patients undergoing conventional open adrenalectomy, an occurrence most pronounced during tumor manipulation. Intraoperative catecholamine levels were not measured in the current study; therefore an association between circulating catecholamines and the occurrence of intraoperative hypertension cannot be made.

With the advent of improved localizing techniques, such as CT, MRI, and more recently MIBG scintigraphy, preoperative localization has become much more accurate than in the past [15]. Our improved ability to localize pheochromocytomas successfully prior to surgery has contributed to the acceptance of the laparoscopic approach in lieu of the conventional transabdominal approach. Nevertheless, some lesions cannot be completely visualized, especially when they are extraadrenal in location. Critics often point out that the sensitivity of MIBG scintigraphy is only around 77% [15]. In the current study, MIBG failed to localize the lesion in 3 of 16 patients, including 2 patients who underwent LA. CT or MRI, on the other hand, successfully localized the lesion in all patients, including the three with negative MIBG scintigraphy. When CT, MRI, and MIBG scintigraphy are combined, the overall acccuracy of preoperative localization approaches 97% [15].

As shown by others and confirmed in our study, patients who undergo LA experience less postoperative pain and shorter hospital stays [1–5]. There is definitely a learning curve with the laparoscopic approach, but as experience becomes more widespread the duration of surgery should continue to decrease. For extended laparoscopic procedures, helium pneumoperitoneum may be used as an alternative to CO_2 [16, 18]. Although not statistically significant, in the current study LA took less time than the open approach, but this may have been due to patient selection and the small mean tumor size in this series of patients. The length of hospital stay was longer in this series than in recent publications, but the immediate postoperative management of patients with pheochromocytoma is often more complex than that for other adrenal lesions [8]. Furthermore, the French health care delivery system allows longer hospital stays than do other Western countries.

Conclusions

Laparoscopic adrenalectomy can be safely performed for pheochromocytomas less than 7 cm in size. Pneumoperitoneum is well tolerated in these patients, despite the frequent alterations in mean arterial pressure, central venous pressure, and pulmonary capillary wedge pressure. Calcium channel blockers may be safely used as an alternative to α -adrenergic blockade. In patients with pheochromocytomas larger than 7 cm, we recommend the open approach because of the more difficult mobilization of large lesions.

Résumé

Fond du problème: La popularité de la surrénalectomie laparoscopique pour traiter une large gamme de maladies de la corticosurrénale y compris le phéochromocytome, ne cesse d'augmenter, mais les effets du pneumopéritoine sur l'hémodynamique des patients ayant une tumeur sécrétant des catécholamines ne sont pas bien connus. Objectives: Le but de cette étude a été de comparer les effets du pneumopéritoine à l'oxyde de carbone et la manipulation tumorale sur l'hémodynamique chez deux groupes de patients ayant un phéochromocytome sporadique de moins de 7 cm. Méthodes: Les patients dans le groupe 1 (n = 11) ont eu une surrénalectomie par laparoscopie transabdominale alors que ceux du groupe 2 (n =11) ont eu une surrénalectomie par laparotomie antérieure. Le suivi moyen a été de 37 mois dans le groupe 1 (extrêmes 26-51) et de 52 mois dans le groupe 2 (extrêmes 27-72). Résultats: Tous les patients ayant eu une surrénalectomie laparoscopique avaient une hypertension peropératoire (TA > 200/90 mmHg) comparés à 73% ayant une laparotomie mais cette différence n'était pas statistiquement significative. L'hypotension peropératoire (< 80 mm Hg de pression artérielle systolique) s'est produite chez 4 patients dans le groupe 1 comparé à 6 patients dans le groupe 2. La pression artérielle moyenne, la pression veineuse centrale et la pression pulmonaire dans l'artère pulmonaire bloquée étaient significativement plus élevées dans le groupe 1 avant l'ablation de la tumeur. Cependant, on n'a noté aucune différence en ce qui concerne la fréquence cardiaque, l'index cardiaque ou l'index de travail cardiaque pendant l'acte chirurgical. On n'a noté aucune conversion ou complication dans le groupe laparoscopique, alors qu'un patient dans le groupe 2 a développé une éventration. Conclusions: Bien que la surrénalectomie laparoscopique soit associée à une augmentation plus importante de la pression artérielle moyenne, de la pression veineuse centrale et de la pression dans l'artère pulmonaire bloquée, la création d'un pneumopéritoine ne modifie pas de façon significative l'indexe cardiaque ou le travail du ventricule gauche. Le pneumopéritoine à l'oxyde de carbone est bien toléré chez le patient ayant un phéochromocytome.

Resumen

Objetivo: En la actualidad, la adrenalectomía laparoscópica es una técnica habitual en el tratamiento quirúrgico de diversas afecciones de las glándulas suprarrenales. Sin embargo, se desconocen los efectos del neumoperitoneo en la hemodinámica de pacientes con tumores productores de catecolaminas. Métodos: El objetivo de este estudio fue comparar los efectos del neumoperitoneo con dióxido de carbono así como, los de la manipulación tumoral, sobre parámetros hemodinámicos en dos grupos de pacientes con feocromocitomas menores a 7 cm. de diámetro. En el grupo 1 (n = 11) los pacientes sufrieron una adrenalectomía mediante una vía de acceso laparoscópica lateral transabdominal. En el grupo 2 (n = 11) la adrenalectomía se efectuó mediante laparotomía anterior. El tiempo medio de seguimiento fue de 37 meses (rango 26-51) para el grupo 1 y 52 meses (rango 27-72) para los pacientes del grupo 2. Resultados: En todos los pacientes adrenalectomizados por vía laparoscópica se registró, durante la operación, una hipertensión superior a 200/90 mm Hg. Sólo el 73% de los pacientes adrenalectomizados mediante laparotomía presentaron hipertensión en el transcurso de la operación (no existen diferencias significativas entre ambos grupos). Hipotensión arterial intraoperatoria con presión sistólica menor a 80 mm Hg se observó en 4 pacientes del grupo 1 y en 6 del grupo 2. La presión arterial media, la presión venosa central y la presión de enclavamiento pulmonar fueron significativamente más altas en los pacientes del grupo 1, antes de la extirpación del tumor, que en el grupo 2. Sin embargo, no se registraron diferencias significativas entre ambos grupos, por lo que al pulso, gasto cardiaco y volumen sistólico de eyección se refiere. No hubo necesidad de efectuar reconversión alguna en los pacientes del grupo 1, no registrándose tampoco complicación alguna. Por el contrario en el grupo 2, un paciente se eventró. Conclusiones: Aunque la adrenalectomía laparoscópica por feocromocitoma origina un marcado incremento de la presión arterial media, presión venosa central y presión de enclavamiento, el neumoperitoneo no modifica significativamente ni el gasto cardiaco, ni el volumen de eyección sistólica. Los pacientes con feocromocitoma toleran bien el neumoperitoneo con dióxido de carbono es bien tolerado.

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Invited Commentary

Clive S. Grant, M.D.

Department of Surgery, Mayo Clinic, Rochester, Minnesota, USA

The study by Chapuis' group, comparing hemodynamic changes in patients undergoing excision of adrenal pheochromocytoma using laparoscopic versus open techniques, is interesting and provides scientific support for the clinical impressions of many groups employing laparoscopic adrenalectomy. Their primary aim focused on the hemodynamic effects of CO_2 pneumoperitoneum in patients with adrenal catecholamine-secreting tumors. Equally important are the other observations contained in their manuscript.

To compare and contrast hemodynamics specifically consequent to CO_2 pneumoperitoneum requires accurate measurements taken *after* induction of anesthesia but *prior* to tumor manipulation or dissection in the laparoscopic (LA) and open adrenalectomy (OA) groups. This was well demonstrated. Moreover, because this was a retrospective analysis and not a randomized prospective study, other confounding variables, such as type of anesthetic, medications used for preoperative preparation, or preexisting cardiopulmonary conditions or medications should have been noted to be equivalent and consistent in the two groups. Whereas patients undergoing LA and OA were operated during the same time period and were prepared utilizing the same medications, few other preoperative data for the two groups is furnished. Even recognizing the inclusion of 11 patients in each of two groups of the rare pheochromocytomas, the prospect for a type 2 error in statistical comparisons is possible. That a 27% Mazze, R.I., Lomoy, E.: Hypertensive responses during operation for phaeochromocytoma: a study of plasma catecholamine and haemody-namic changes. Eur. J. Anaesth. 2:257, 1984

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difference in intraoperative systolic hypertension above 200 mmHg does not reach statistical significance may reflect this limitation.

Nevertheless, although the CVP, MAP, and pulmonary capillary wedge pressure were higher in the LA group, the cardiac index was not compromised and there were no cardiopulmonary complications. This bears testimony to the safety of LA for managing this disease and other less volatile-behaving adrenal lesions.

Additional data presented serve to reinforce our understanding of pheochromocytomas.

- Despite extended preoperative preparation, the release of tumor catecholamines cannot be totally prevented and impressive intraoperative hypertension is common. In our recent LA experience with pheochromocytomas, 8 of 15 patients had blood pressures at least transiently over 200 mmHg intraoperatively. In anticipation of this occurrence, nitroprusside is used with any early indication of hypertension.
- 2. Conversely, following tumor excision, preoperative chronic vasoconstriction is suddenly reversed and exacerbated by α -blockade medication, resulting in the need for considerable fluid infusion to restore the blood pressure. This excess fluid is then rapidly excreted over the next few days as the vascular system restores normal tone.
- 3. The length of postoperative hospitalization is influenced by so many socioeconomic factors as to render comparisons from one center to another nearly meaningless. Even though recognized as clear medical advances, even dramatically for such operations as laparoscopic cholecystectomy, adrenalectomy, and antireflux procedures, data regarding return to work or "normal" activity may be similarly compromised.