# Laparoscopic Cholecystectomy in the Obese Patient

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The authors' experience with laparoscopic cholecystectomy (LC) in obese (O, n = 96) and morbidly obese (MO, n = 27) patient groups was compared with that in the normal weight (NW, n = 174) group of patients as well as the whole group (WG). There were no operative deaths. There were no significant differences between groups for any of the following: successful intraoperative cholangiography (WG, 52.2%; NW, 52.9%; O, 51.1%; MO, 55.6%), conversion to open cholecystectomy (WG, 9.6%; NW, 9.2%; O, 10.4%; MO, 11.1%), incidence of major complications (WG, 4.1%; NW, 3.4%, O, 5.2%; MO, 0%), incidence of minor complications (WG, 7.4%, NW, 7.5%; O, 6.3%; MO, 3.7%), and length of hospitalization after successful LC (WG, 1.25 days; NW, 1.31 days; O, 1.16 days; MO, 1.13 days). Duration of operation did not differ, except LC in the MO group (136.4  $\pm$  6.9 minutes) was longer when compared with NW patients (123.0  $\pm$  2.9 minutes, p < 0.05). The authors conclude LC is a safe and effective treatment for obese patients with symptomatic cholelithiasis.

APAROSCOPIC CHOLECYSTECTOMY HAS been introduced into the practice of biliary surgery in the United States with remarkable rapidity. The first laparoscopic cholecystectomy (LC) was performed by Philippe Mouret in Lyon in 1987.<sup>1</sup> DuBois et al.<sup>2</sup> published an early series of such procedures performed in France, and Reddick and Olsen<sup>3</sup> authored an early article about the procedure as performed in the United States as recently as 1989. Within the past 2 years, many general surgeons in the United States have incorporated the procedure into their practice. Although the procedure has been documented to be safe and effective,<sup>2-9</sup> its wide application to all patients with cholelithiasis has been the subject of some controversy.

During the introduction of LC into the United States in 1989 and early 1990, training courses frequently inFrom the Department of Surgery, University of Virginia Health Sciences Center, Charlottesville, Virginia

cluded a list of conditions that were relative contraindications for LC. These included previous abdominal surgery, coagulopathy, choledocholithiasis, acute cholecystitis, and obesity. With increasing experience in the performance of LC, however, preliminary reports suggest that these conditions may be only relative contraindications to the performance of LC.<sup>4,10</sup>

We wished to investigate whether obesity posed any relative contraindication to the performance of LC. Based on our initial experience with obese patients, we thought LC was possible in this patient population. This report analyzes our experience to date with LC in obese and morbidly obese patients. Our aim in this retrospective analysis was to determine the excess risk, if any, posed by this condition on the successful and safe performance of LC.

#### Methods

From February 1990 to April 1991, 270 cases of laparoscopic cholecystectomy have been attempted at the University of Virginia Health Sciences Center. Very few cholecystectomies are now performed at our institution using the traditional "open" method. This reported experience therefore represents the great majority of cholecystectomies performed during this period, and represents the combined efforts of five surgeons.

Patients were selected for LC based on clinical and radiographic evaluation showing symptomatic cholelithiasis, or for complications of biliary tract disease including acute acalculous cholecystitis and gallstone pancreatitis. Ultrasound was the diagnostic procedure of choice in virtually all patients. Of the 270 patients, 255 had cholelithiasis diagnosed by ultrasound. In only four cases, oral chole-

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cystography alone was used. Preoperative nuclear scan documented disease in four cases where ultrasound showed no stones, and endoscopic retrograde cholangiopancreatography was used to confirm stones present in two cases. In one case of acute acalculous cholecystitis, the diagnosis was made at laparoscopy.

Operations were all conducted using general anesthesia, with the exception of one patient with severe chronic obstructive pulmonary disease, for whom an epidural anesthetic technique was used. The technique of laparoscopic cholecystectomy was performed as has been previously described,<sup>4</sup> using a four-trochar approach in routine cases (Fig. 1).

Laparoscopic cholecystectomy in the obese patient population was performed generally in the same manner as with average weight patients. For the morbidly obese patient population, however, occasional alterations in technique were found, through experience, to be helpful. One of these included placement of the "umbilical" trocar above the level of the umbilicus if the distance from the umbilicus to the right costal margin was greater than the length of the telescope passed through the trocar (Fig. 2). Otherwise, placement of the trocar in the umbilicus of a patient with a large pannus and a long distance from xyphoid to umbilicus resulted in telescope positioning too far from the gallbladder to allow optimal magnified visualization of the operative dissection. Veress needle placement was still usually done through the umbilicus in morbidly obese patients because of the physical advantage of having a thin area of the body wall in that location for ease and safety of needle insertion. On only rare occasions did we require extra long trocars in the morbidly obese patients. Such items are available as disposable products (U.S. Surgical, Norwalk, CT).

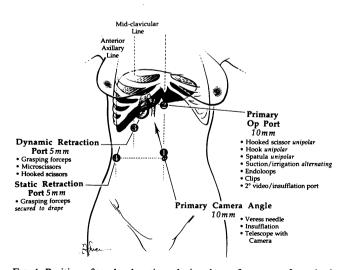


FIG. 1. Position of trochar locations during the performance of standard four-trochar approach laparoscopic cholecystectomy. The usual functions performed through each trochar are given.

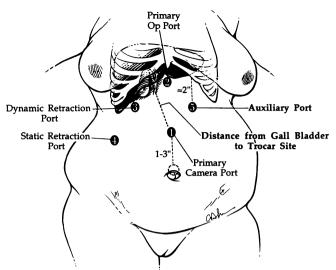


FIG. 2. Placement of trochars in performing laparoscopic cholecystectomy in the morbidly obese patient. The placement of the umbilical trochar may need to be positioned above the umbilicus to allow the telescope to reach the area of dissection in the right upper quadrant. Also, placement of a fifth trochar in the left upper quadrant may be necessary to enhance exposure.

Visualization of the porta hepatis and occasionally the infundibulum of the gallbladder as well can be more difficult in the morbidly obese patient. This is frequently the result of a large amount of omental fat or prominence of the colon or omentum or duodenum. Methods to improve visualization of this area include the use of a 30 degree angled telescope for looking downward at the porta hepatis. Also, we were not hesitant to place a fifth trocar (Fig. 2) in the left upper quadrant to facilitate exposure. A grasper or other blunt instrument kept in the closed position was inserted through this fifth trocar and used to bluntly hold down the duodenum and improve exposure. The reverse Trendelenburg position, with occasional rotation of the patient to the left, were normally used to improve exposure as well.

Patient data were kept in computer data files. Analysis of patient height and weight was performed and patients were categorized into three groups based on a standard height and weight chart. Obese patients (group O) were those patients whose weight was 40% or more above ideal body weight. Morbidly obese (Group MO) patients were those patients who were more than 100 pounds above ideal body weight. Morbidly obese patients were included in the O group, whereas both MO and O were included in the whole group (WG). Normal weight patients (group NW) were those patients whose weight was less than 40% above ideal body weight. Based on these criteria, 96 of the 270 patients were found to be obese, and 27 of those were morbidly obese.

Patient data recorded included age, height, weight, and sex. The number of gallstones, based on preoperative test-

ing (usually ultrasound), were recorded. Patients also were classified according to the American Society of Anesthesiologists<sup>11</sup> categories of operative risk (ASA class).

At the time of operation, successful completion of LC, duration of operation (preparation to dressing), operative findings, and attempted performance and successful completion of intraoperative cholangiography were all recorded. Any attempt to insert a catheter into the cystic duct was considered an attempt at performing cholangiography, no matter how brief.

Cholangiography is done frequently at our institution, although on a somewhat selective basis based on anatomy and other factors at the time of operation. For teaching purposes, cholangiograms are included in the performance of "routine" LC, when easily done, by all of us. Methods of performing cholangiography have differed among surgeons and are often based on available equipment. Cystic duct cannulation was done in most cases, although direct injection of the gallbladder has been done on occasion. Fluoroscopy has been most frequently used recently in our operating rooms for cholangiography, whereas early in our experience plain films were used. We have found the use of plain films adds further to the increase in operative time required to perform cholangiography.

Intraoperative and postoperative complications were recorded, as was length of hospitalization and postoperative use of analgesic medication.

Three patients were excluded from consideration in calculating postoperative recovery and length of hospitalization. Two patients who had successful completion of LC were found to have pelvic pathology by laparoscopy at the time of surgery, and both underwent pelvic operations as soon as LC was completed. One patient, hospitalized status post cardiac transplantation, developed acute acalculous cholecystitis, which was diagnosed at exploratory laparoscopy and treated with successful LC. Her postoperative hospitalization was prolonged for other medical reasons. A fourth patient, also hospitalized with multiple medical problems (including fungal sepsis and Goodpasture's syndrome) was considered to have a 14day postoperative recovery after successful completion of LC, because at that time she underwent laparotomy for persistent abdominal pain. One morbidly obese patient was not included in calculations of ideal body weight because her height was not accurately recorded.

The data were analyzed for differences between the three groups using either one-way analysis of variance, unpaired t test, or chi square analysis where appropriate.<sup>12</sup> Data are represented as mean  $\pm$  standard error, with p values of  $\leq 0.05$  accepted as significant.

## Results

The average age of patients undergoing LC was 44.0  $\pm$  1.0 years (n = 270). Patients who were obese were

younger  $(39.1 \pm 1.3 \text{ years}, n = 96, p < 0.01)$  than both NW patients  $(46.7 \pm 1.2 \text{ years}, n = 174)$  and the group as a whole. Those who were morbidly obese were also significantly younger  $(38.1 \pm 3.0 \text{ years}, n = 27, p < 0.05)$ . There was an increased percentage of female patients in the O group (85.4%) as compared with both the NW group (69.5%) and the WG (75.2%, p < 0.01). The percentage of women in the MO group (81.5%) was higher than NW but not WG. Average weight for O was  $215.5 \pm 4.3$  pounds, and for MO,  $265.7 \pm 7.2$  pounds. The average weight for NW was  $151.6 \pm 2.2$  pounds, and for WG it was  $174.5 \pm 2.8$  pounds.

Most patients had multiple gallstones present on preoperative ultrasound testing (Fig. 3). About 20% of patients tested had a single gallstone, and another 7.4% had only two to three identifiable stones present. There were no significant differences between groups in terms of distribution between these categories.

Thirteen patients in the whole group had acalculous cholecystitis or conditions where no gallstones were present. No morbidly obese patients and two obese patients were in this group, a difference that was not statistically significant.

Other preoperative parameters included ASA classification (Fig. 4). There was a significantly higher average ASA category when comparing O with WG ( $1.97 \pm 0.05$ *versus*  $1.91 \pm 0.04$ , p < 0.05) and with NW ( $1.89 \pm 0.05$ , p < 0.05). The average ASA category for MO ( $2.22 \pm 0.10$ ) was higher than for NW but not for WG. A significantly decreased percentage of MO patients were included in the ASA I category compared with WG (3.7% *versus* 24.8\%, p < 0.01).

There were 49 patients in the WG who had elevated liver function tests (LFTs) before operation, or 18.2% of the group (Table 1). Percentages of patients in O and MO

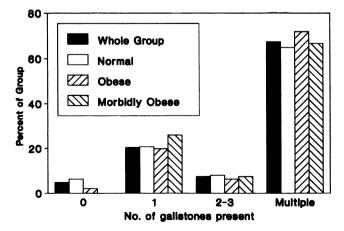


FIG. 3. Percentage of patients with zero, one, two to three, and multiple (more than three) gallstones present by preoperative testing for the whole group as well as the obese and morbidly obese subgroups. There were no differences between groups.

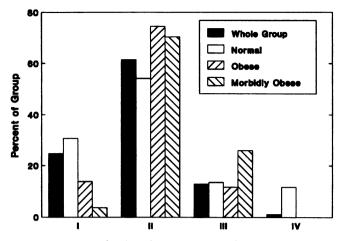


FIG. 4. Percentage of patients in the obese, morbidly obese, and whole group who were represented in each of the ASA classification<sup>11</sup> groups before operation.

with elevated LFTs were not significantly different, nor were the numbers of patients with preoperative pancreatitis or jaundice when compared with WG or NW. Patients confirmed as having acute cholecystitis at operation represented 11.5% of WG, with similar percentages in the NW, O, and MO groups.

Duration of operation was  $126.2 \pm 2.4$  minutes for patients in WG undergoing successful LC. Normal weight patients required  $123.0 \pm 2.9$  minutes. Average duration of operation was not longer for O (131.7  $\pm$  4.1 minutes) compared with WG or NW. Operative time for MO patients (136.4  $\pm$  6.9 minutes) was significantly longer than for NW (p < 0.05), but not for WG. Those patients who were converted to open cholecystectomy during the course of attempted LC had significantly increased durations of operation. Obese patients (n = 10) required  $213.2 \pm 16.9$ minutes for completion of such operations, and MO patients (n = 3) required  $229.3 \pm 27.8$  minutes. The average time for NW patients undergoing conversion to open cholecystectomy was  $187.1 \pm 12.0$  minutes, and for WG it was  $197.2 \pm 9.3$  minutes. There were no differences between groups for duration of operation for patients undergoing conversion to open cholecystectomy.

The percentage of operations where intraoperative cholangiography was completed successfully, attempted

TABLE 1. Preoperative Data			
	Entire Group	Obese	Morbidly Obese
Elevated liver			
function tests	49 (18.2%)	23 (24.0%)	6 (22.2%)
Pancreatitis	17 (6.3%)	6 (6.3%)	0` ´
Jaundice	7 (2.6%)	1 (1.0%)	1 (3.7%)
Acute cholecystitis	31 (11.5%)	11 (11.5%)	2 (7.4%)

but not completed successfully, or not attempted was similar for all groups (Fig. 5).

Twenty-six of the 270 patients in the entire series (9.6%) required conversion to open cholecystectomy. The most common cause for this was acute cholecystitis, with concurrent inflammation resulting in either poor identification of anatomy, excessively difficult dissection, or other factors that precluded successful completion of LC. Other causes for conversion to open cholecystectomy included hemorrhage from the liver bed or cystic artery, choledo-cholithiasis, excessively short cystic duct, spillage of stones, excessively large stones, or unclear anatomy. There was no significant difference in the percentage of O patients (10.4%) or MO patients (11.1%) requiring conversion to open cholecystectomy when compared with NW (9.2%) or WG.

There have been no operative deaths in the series, and only one life-threatening complication. The latter was a colon perforation in a patient on steroid therapy for Crohn's disease. The perforation occurred 3 days after performance of attempted LC with conversion to open cholecystectomy. At the time of open cholecystectomy, no colon injury was noted. A total of 11 major complications (defined as any adverse event within 30 days after surgery that resulted in either an extension of hospital stay or readmission to the hospital) occurred in the series (4.1%). Five of these occurred in obese patients, and none in morbidly obese patients, with there being no significant differences in the complication rate among groups.

Major complications included the colon perforation, one laceration of the side of the common bile duct (immediately recognized and treated successfully with T-tube insertion), and one laparotomy (which proved negative) for a patient with persistent pain on abdominal exami-

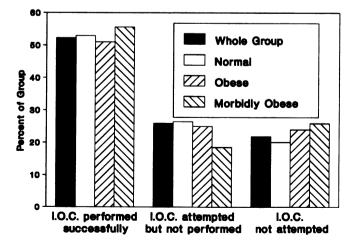


FIG. 5. Percentage of patients in the obese, morbidly obese, and whole group who had intraoperative cholangiography attempted and completed successfully, attempted but not completed, and not attempted. There were no significant differences between groups.

nation 2 weeks after operation. The latter patient later proved to have fungal sepsis among her multiple medical problems.

Eight patients were readmitted to the hospital. One was the patient with severe chronic obstructive pulmonary disease who had an epidural anesthetic. She was readmitted to treat an exacerbation of her pulmonary disease. Other reasons for readmission included wound cellulitis (one), transiently elevated LFTs and abdominal pain (one), abdominal pain similar to preoperative pain (cause never determined), and abdominal pain that proved by endoscopy to be the result of an active peptic ulcer (one). One patient was readmitted for postoperative fever, which resolved within 24 hours. Two patients were admitted with abdominal pain and tenderness, and both responded quickly to intravenous fluids and antibiotics with short 2- to 3-day hospitalizations. None of the patients proved to have evidence for a biliary leak, abdominal abscess, or significant subhepatic fluid collection by ultrasound.

Minor complications numbered 20 for the whole group (7.4%), with no significant difference in the percentages of minor complications in the NW (7.5%), O (6.3%), and MO (3.7%) groups. Minor complications included singlesite wound infections (eight), subcutaneous emphysema (three), pneumoscrotum (two), electrocardiogram changes during operation (two), urinary tract infections (two), arm cellulitis, pulmonary edema, and transient ischemic attack (one each).

Length of hospital stay for patients undergoing successful LC is shown for the all groups in Figure 6. There were no significant differences between groups, with 84.8% of these patients in WG, 84.1% in NW, 86.0% in O, and 87.5% in MO being hospitalized for 1 day or less.

The average length of stay for patients requiring con-

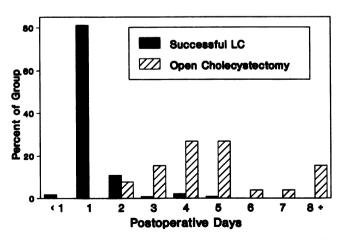


FIG. 6. Distribution of the percentage of patients in the obese, morbidly obese, and whole groups who underwent successful completion of laparoscopic cholecystectomy by length of hospitalization. The distribution was similar for all three groups.

version to open cholecystectomy was longer in all groups when compared with those patients undergoing successful completion of LC. For MO patients requiring open cholecystectomy, this was  $4.7 \pm 1.8$  days (n = 3), for O patients it was  $4.2 \pm 0.6$  days (n = 10), and for NW patients it was  $5.4 \pm 0.7$  days (n = 15). One patient (in the NW group) is still hospitalized with complications of surgery. Excluding this patient, the average length of stay is  $4.9 \pm .5$  days for WG, comparable to the O and MO groups.

Postoperative use of pain medication was recorded from the time patients left the recovery room to discharge. For the whole group, 30.1% of patients undergoing successful completion of LC took no narcotic analgesics during this period. For NW, the percentage was 25.6%, for O it was 38.6%, and for MO it was 41.7%. There were no statistical differences between groups. Patients that did take narcotic analgesics used only oral forms in 28.0% of cases, whereas 36.4% of patients in the whole group undergoing successful LC required parenteral narcotics. In the NW group, 38.5% of patients took parenteral narcotics and 27.6% only oral narcotics. For O patients, 28.6% took oral and 38.1% took parenteral narcotics, whereas in the MO group, 41.7% took oral and 16.7% took parenteral narcotics. Statistical analysis showed there were no significant differences between groups.

## Discussion

Numerous reports of the successful use of laparoscopic cholecystectomy in treating symptomatic gallstones have now been published. Laparoscopic cholecystectomy is, in our opinion, now the treatment of choice for symptomatic gallstones. These reports have frequently referred to the inclusion of obese patients in the overall series, but no distinct analysis has been performed of whether the condition of obesity makes the performance of LC significantly more difficult, or whether LC in the obese patient population is associated with increased morbidity rate or delayed recovery from surgery.

There are several technical aspects of performing LC in the obese, and particularly the morbidly obese, patient population that differ from its performance in the NW population. These have been discussed, and can contribute significantly to the ease with which LC is performed in this patient population. Other technical aspects that can prove beneficial include increasing the level of intraperitoneal pressure. This pressure level, generally kept at 14 to 16 mmHg for most thin patients, has been increased to the 19 to 20 range for the obese patients without experiencing any adverse hemodynamic consequences. The increased pressure is helpful in holding up the heavier abdominal wall and maintaining an adequate working space for instruments.

It is gratifying to substantiate that LC can be performed in MO patients with a similar safety and efficiency as in NW patients, because the technical performance of open cholecystectomy in the MO patient can be a formidable operation, requiring a long incision for adequate exposure and resulting in significant postoperative pain and prolonged recovery in this patient population. Our data show that in the MO patient population there is also an increased operative time requirement when compared with NW patients. Therefore, the increased duration of operation probably reflects the fact that in the severely obese, cholecystectomy is more time consuming and perhaps technically more difficult whether an open or a laparoscopic approach is used. The data on hospitalization times, however, show that, from the patient's perspective, LC is not a procedure that is more difficult to recover from for an obese patient. Actually, the MO patient population tended to show a decreased need for postoperative analgesics.

The O and MO patient populations compared retrospectively in our series appear to be similar with regard to most parameters considered important for increasing morbidity rate or operative time in the performance of LC. We have shown that acute cholecystitis was the only parameter before operation that increased the incidence of conversion to open cholecystectomy,<sup>4</sup> and the incidence of acute cholecystitis was comparable for all groups. Preoperative elevation of liver function tests and the performance of intraoperative cholangiography were found to significantly increase operative time in our series as a whole.<sup>4</sup> The percentages of obese and morbidly obese patients with these conditions, however, were comparable to those of NW patients and those of the group as a whole. The O group was at a higher overall ASA risk category, but they also were younger than the WG. Therefore, the MO and O patient groups were not in any obvious way biased in favor of likely better results by having a lower incidence of any of the proven risk factors for increasing operative morbidity rate or duration of operation.

The list of absolute and relative contraindications to the performance of LC is shrinking with increasing experience in the use of this procedure. A list of absolute and relative contraindications is suggested in Table 2. As with all procedures and their indications, however, the community of general surgeons must be cautious about advocating the use of LC in these special circumstances until it can be proven that the same benefits to the patient will result as have been shown for the use of LC in the low-risk patient population. Our report documents the fact that obesity can safely be removed from the risk of relative contraindications. Our series of morbidly obese patients, 27 in number, weighing an average of 265.7 pounds, with the heaviest patient weighing 365 pounds,

 TABLE 2. Contraindications to Performing

 Laparoscopic Cholecystectomy

Requirement	for concomitant upper abdominal incision
Septic shock	
Pregnancy	
Cirrhosis	
Inability to to	olerate general anesthesia*
Coagulopath	
Choledochol	ithiasis*
Acute cholec	vstitis*
Previous abd	ominal surgery*
Obesity*	<i>.</i>
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\* Successfully performed laparoscopic cholecystectomy at the University of Virginia in a patient with this problem.

confirms the safety of LC in our hands in this patient population. Whether LC can be performed safely and efficiently in those occasional patients weighing in excess of 400 pounds is a matter not addressed by our data.

At our institution, we have safely performed LC for patients with the conditions marked with an asterisk in the list in Table 2. The numbers of these patients are small, however. For example, we have performed LC for one patient with severe lung disease by using epidural anesthesia. We have successfully performed LC in two patients with coagulopathy, both of whom had severalday hospitalizations for observation. Acute cholecystitis is no longer a contraindication, but certainly our conversion rate to open cholecystectomy is much higher than in the group as a whole.<sup>4</sup> Therefore, as in all operations, the patient with increased risk factors should be informed of those factors and the likelihood they will increase operative morbidity and even mortality rates. Until larger numbers of such patients with "relative contraindications" are treated, we will be uncertain as to whether LC is indeed a better procedure for their symptomatic gallstones as compared with traditional cholecystectomy or, in some extremely high-risk patients, nonoperative and nondefinitive treatment options. Therefore, although LC probably physically can be performed for all the conditions in Table 2, the wisdom of doing so is as yet unproven. Certainly it is hard to conceive that LC is warranted in any patient undergoing a concomitant upper abdominal procedure requiring an open incision.

Laparoscopic cholecystectomy has achieved the position as the treatment of choice for most patients with symptomatic cholelithiasis. In the obese patient population, LC can be performed with the same efficiency, morbidity rate, mortality rate, and length of hospitalization as in the average weight population. Other relative contraindications that have been proposed for the use of LC should undergo similar scrutiny, and LC should be objectively proven to be safe and efficient in those conditions as well.

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#### References

- 1. Perissat J, Vitale GC. Laparoscopic cholecystectomy: gateway to the future. Am J Surg 1991; 161:408.
- Dubois F, Icard P, Berthelot G, Levard H. Coelioscopic cholecystectomy: a preliminary report of 36 cases. Ann Surg 1990; 211: 60-62.
- Reddick E, Olsen D. Laparoscopic laser cholecystectomy: a comparison with mini-lap cholecystectomy. Surg Endosc 1989; 3:44– 48.
- Schirmer BD, Edge SB, Dix J, et al. Laparoscopic cholecystectomy: treatment of choice for symptomatic cholelithiasis. Ann Surg 1991; 213:665-677.
- 5. Meyers WC, Aghazarian SG, Albertson DA, et al. A prospective

analysis of 1518 laparoscopic cholecystectomies performed by southern U.S. surgeons. N Engl J Med 1991; 324(16):1075-1078.

- Peters JH, Ellison EC, Innes JT, et al. Safety and efficacy of laparoscopic cholecystectomy: a prospective analysis of 100 initial patients. Ann Surg 1991; 213(1):3–12.
- Zucker KA, Bailey RW, Gadacz TR, Imbembo AL. Laparoscopic guided cholecystectomy. Am J Surg 1991; 161:36–44.
- Berci G, Sackier JM. The Los Angeles experience with laparoscopic cholecystectomy. Am J Surg 1991; 161:382-384.
- Voyles CR, Petro AB, Meena AL, et al. A practical approach to laparoscopic cholecystectomy. Am J Surg 1991; 161:365–370.
- Flowers JL, Bailey RW, Scovill WA, Zucker KA. The Baltimore experience with laparoscopic management of acute cholecystitis. Am J Surg 1991; 161:388–392.
- American Society of Anesthesiologists: Classification of physical status. Anesthesiology 1963: 24:111.
- Snedecor GW, Cochran WG. Statistical Methods, 6th Edition. Ames, IA: Iowa State University Press, 1967.
- Cushieri A, Dubois F, Mouiel J, et al. The European experience with laparoscopic cholecystectomy. Am J Surg 1991; 161:385– 387.
- Reddick, EJ, Olsen D, Spaw A, et al. Safe performance of difficult laparoscopic cholecystectomies. Am J Surg 1991; 161:377-381.