ORIGINAL ARTICLE

Incidence of Deep Vein Thrombosis After Laparoscopic vs Minilaparotomy Cholecystectomy

Reginald V. N. Lord, FRACS; Joycelyn J. Ling, MA; Thomas B. Hugh, FRACS; Maxwell J. Coleman, FRACS; Bruce D. Doust, FRACR; Ian Nivison-Smith, MAppSt

Objectives: To determine the frequency of deep vein thrombosis (DVT) associated with minimally invasive cholecystectomy and to determine, using minilaparotomy cholecystectomy as a control operation, the influence of the laparoscopic pneumoperitoneum on DVT formation.

Design: Prospective nonrandomized control trial.

Setting: Tertiary care university hospital.

Patients: One hundred consecutive patients intended to undergo either laparoscopic cholecystectomy (59 patients) or minilaparotomy cholecystectomy (41 patients) with either of 2 surgeons were prospectively enrolled between April 1996 and April 1997. The minilaparotomy cholecystectomy group served as controls to isolate the effect of the pneumoperitoneum. Patient details, operative details, and any thromboembolic or bleeding complications were recorded. The same thromboprophylaxis regimen was prescribed for each group; namely, preoperative and postoperative subcutaneous low-molecular-weight heparin (LMWH), graduated compression stockings, and intraoperative intermittent calf compression.

Intervention: Minimally invasive cholecystectomy.

Main Outcome Measure: Frequency of DVT. Bilateral lower limb venous color duplex scanning was used to detect DVT. Scans were performed on 3 occasions: (1) preoperatively on admission to hospital, (2) on the first postoperative day, and (3) between 2 and 4 weeks postoperatively.

Results: Three patients in the laparoscopic group and 2 patients in the minilaparotomy group underwent conversion to conventional open cholecystectomy. There were no significant differences between patients in the 2 groups for age, sex, body mass index, preoperative white blood cell count, platelet count, prothrombin time, or activated partial thromboplastin time. There were no significant differences between the 2 groups for elective vs emergency operations, public hospital vs private hospital admissions, or consultant vs resident surgeon. Macroscopic gallbladder pathology grades for both groups were not significantly different, and there was no significant difference in the duration of postoperative hospital stay. Operative cholangiography was performed in a significantly larger proportion of laparoscopic cases (86% vs 66% in the minilaparotomy group; χ^2 test, P=.002), and the duration of anesthesia was significantly longer for the laparoscopic operation (118 minutes vs 98 minutes; t test, P=.05). Ninety-seven patients received preoperative LMWH and all patients received graduated compression stockings, intraoperative intermittent calf compression, and postoperative LMWH. Two of the 100 patients had postoperative DVT, 1 after laparoscopic cholecystectomy and 1 after minilaparotomy cholecystectomy. Both DVTs were detected by duplex examination on the first postoperative day. The DVT found after laparoscopic cholecystectomy was in 1 of the 3 patients who did not receive preoperative LMWH. There were no DVTs in any of the 40 patients who had an additional duplex scan between 2 and 4 weeks after operation.

Conclusions: Despite the theoretical risk of thromboembolic disease due to use of the laparoscopic pneumoperitoneum, the frequency of DVT after either laparoscopic cholecystectomy or minilaparotomy cholecystectomy is low if adequate thromboprophylaxis is provided.

Arch Surg. 1998;133:967-973

From the Departments of Surgery (Drs Lord, Hugh and Coleman and Ms Ling), Radiology (Dr Doust), and Statistics/Australian Bone Marrow Transplant Registry (Mr Nivison-Smith), St Vincent's Hospital, Sydney, Australia.

LAPAROSCOPIC cholecystectomy, first performed in a human in 1985,[1] has rapidly become established as the most popular method of gallbladder removal in developed countries. Compared with conventional open cholecystectomy, laparoscopic cholecystectomy provides shorter hospital stay, accelerated recovery, reduced incidence of major wound complications, and possibly reduced intraperitoneal adhesive complications.[2,3]

Laparoscopic surgery in the Western world most commonly involves the use of a pressurized pneumoperitoneum. Raising the intra-abdominal pressure to levels used during laparoscopic surgery has been shown to reduce blood flow through

This article is also available on our Web site: www.ama-assn.org/surgery.

PATIENTS AND METHODS

One hundred consecutive patients who were intended to undergo either laparoscopic cholecystectomy or minilaparotomy cholecystectomy with either of 2 study surgeons were prospectively enrolled between April 1996 to April 1997. Approval for the study was obtained from the ethics committees of St Vincent's Hospital and the University of New South Wales, Sydney, Australia, and written informed consent was obtained from all participating patients. Patient refusal or unavailability of duplex scanning on the first postoperative day were the only reasons for exclusion from the study.

The type of operation performed was determined by the preference of the surgeon. All laparoscopic cholecystectomies were performed by one surgeon or his chief resident under supervison. A standard 4-port laparoscopic method was used, with the members of the surgical team standing on either side of the patient and the patients' legs together on the operating table. All laparoscopic cholecystectomies were performed in the reverse Trendelenburg position, using up to 30° of head-up tilt. The peritoneum was insufflated with carbon dioxide gas to a maximum intra-abdominal pressure of 15 mm Hg. The pneumoperitoneum was deflated at least once during the operation in all cases.

At this hospital minilaparotomy cholecystectomy involves use of a transverse skin incision less than 6 cm long situated adjacent to the right seventh costal cartilage. Longer transverse incisions are made in the deeper layers, and the rectus muscle is split longitudinally rather than being divided. A special instrument with suction tubing and a halogen light source is held by the assistant to illuminate the operative "well."[40] The process of removing the gallbladder from its bed is similar to that used in conventional open cholecystectomy, although dissection more often begins at the gallbladder fundus. All but 2 minilaparotomy cholecystectomies were performed by the other study surgeon or his resident under supervision; 2 minilaparotomy cholecystectomies were performed by the laparoscopic surgeon in patients with a very small build. Both surgeons have a policy of performing routine operative cholangiography, except in cases in which endoscopic retrograde pancreatocholangiography has been performed or is planned, or if the cystic duct is considered too narrow to admit a 12F cholangiocatheter.

Patient details recorded were age, sex, height, weight, thromboembolic risk factors, results of the preoperative peripheral blood platelet count, white blood cell count, prothrombin time, and activated partial thromboplastin time. To assist in the grading of the difficulty of the procedure, an intraoperative assessment of macroscopic gallbladder pathology was made using the following scale[41]: grade 1, thin-walled gallbladder, no adhesions; grade 2, filmy gallbladder adhesions; grade 3, thick-walled or surrounded by adhesions; grade 4, dense adhesions, attachment of adjacent organs, or empyema of the gallbladder.

The duration of postoperative stay, from the end of anesthesia to time of discharge, was measured. The occurrence of symptoms or signs of thromboembolic disease and any bleeding complications were also recorded.

A standard regimen of thromboprophylaxis was used. This regimen involved the use of knee-length graduated compression elastic stockings for the duration of the hospital stay (TED Anti-Embolism Stockings, Kendall Co Ltd, Sydney), intermittent pneumatic calf compression intraoperatively (SCD Model 5328, Kendall Co Ltd, or Flowtron DVT System, Huntleigh Technology Healthcare Division, Luton, England) and preoperative and postoperative subcutaneous administration of low-molecular-weight heparin (LMWH) (Fragmin heparin sodium 2500 or 5000 U, Fisons Pharmaceuticals Pty Ltd, Sydney, or Clexane enoxaparin sodium 20 mg or 40 mg, Rhone Poulenc-Rorer Pty Ltd, Sydney). The higher LMWH doses were given to patients with thromboembolic risk factors or those who weighed more than 80 kg. The LMWH was given once daily at 10 PM, beginning the night before surgery and continuing until discharge from the hospital. The thromboprophylaxis measures received by each patient were recorded.

Color duplex scanning was used to screen patients for DVT. A preoperative and a day 1 postoperative duplex scan were required for all patients. Patients were also asked to return for a duplex scan examination 2 to 4 weeks after operation. Duplex scanning was performed by a group of experienced dedicated sonographers, who together perform more than 8000 vascular duplex examinations annually. The common and superficial femoral veins, the popliteal veins, the 3 major calf veins, and the venous plexus of the soleus and gastrocnemius muscles were examined in both legs at intervals of a few centimeters. Proximal veins were insonated with the patient in the supine position, with up to 25° reverse Trendelenburg tilt. For examination of calf veins, patients sat with knees flexed and legs dependent. A 5-MHz linear array transducer was used (Acuson 128XP with Acoustic Response Technology and Tissue Contrast Resolution software, Acuson Corp, Mountain View, Calif). Duplex criteria for the diagnosis of DVT included absent flow, either spontaneously or with distal augmentation, in an incompressible venous segment. A completely compressible vein with spontaneous phasic flow was defined as a patent segment, with no evidence of DVT. Normal or diminished flow, either spontaneously or with distal augmentation, in an incompletely compressible vein was defined as partial occlusion. The study protocol included a requirement for patients with equivocal cases to undergo venography to improve diagnostic accuracy, but venography was not needed in any case.

A sample size calculation was made before this study was undertaken. It was calculated that, at an estimated frequency of DVT of 20% in the laparoscopic cholecystectomy group and 5% in the minilaparotomy cholecystectomy group, and allowing for the nonrandomized design of the study, 100 patients would be required in each group to provide greater than 90% power for a type I error rate of 5%. The frequency of DVT found was much lower than the above estimates, however, and the study was stopped after 100 patients had been entered. Comparison of the 2 patient groups and outcomes was made using the χ^2 test of equivalence of proportions and the Student t test for continuous variables.

the inferior vena cava and the renal, splanchnic, and portal venous systems,[4,5] resulting in diminished venous return, decreased cardiac output,[6] and decreased cardiac index.[7,8] The possibility that laparoscopic operations are theoretically associated with an increased risk of deep vein thrombosis (DVT) is suggested by the finding that the raised intraperitoneal pressure caused by the laparoscopic pneumoperitoneum also significantly reduces lower limb venous blood flow.[9-14] A duplex study of 6 patients undergoing laparoscopic cholecystectomy found that creation of a 12 mm Hg pneumoperitoneum caused a significant fall in mean peak systolic venous blood flow velocity, from 20.12 cm/s before insufflation to 12.17 cm/s after insufflation.[9] Other studies reported 8 patients undergoing laparoscopic cholecystectomy in whom creation of a 14 mm Hg pneumoperitoneum resulted in a significant decrease in mean (±SD) peak flow velocities, from 24.9 ± 8.5 cm/s to 18.5 ± 4.5cm/s.[10,11]

Laparoscopic cholecystectomy and some other laparoscopic operations are performed with the patient placed in the reverse Trendelenburg position, causing a further reduction in femoral blood flow velocity during the pneumoperitoneum phase of laparoscopic cholecystectomy operations.[12,13,15] One study found that the combination of an intra-abdominal pressure of 13 to 15 mm Hg and a 30° reverse Trendelenburg position reduced femoral vein peak systolic velocity by 42%.[13]

Another risk factor for venous stasis in patients undergoing laparoscopic cholecystectomy is general anesthesia. General anesthesia may itself cause venous stasis,[16] and DVT is more frequent after general anesthesia than after epidural or spinal anesthesia.[17,18] Patients undergoing laparoscopic operations are thus at risk of DVT formation because of the presence of several factors contributing to lower limb venous stasis.

In addition to venous stasis, the other components of the Virchow triad, hypercoagulability and damage to the vessel wall, may also be present during or after laparoscopic cholecystectomy. A hypercoagulable response has been demonstrated after many types of operations, including open cholecystectomy,[19] probably as a result of activation of coagulation by thromboplastin, together with a failure to clear and inactivate clotting factors and activated platelets from areas of venous stasis.[19] Caprini et al[20] used thromboelastography and measurement of the activated partial thromboplastin time to assess coagulability in a series of 100 patients undergoing laparoscopic cholecystectomy, and found significant hypercoagulability on the first postoperative day compared with preoperative values. Vessel wall injury during laparoscopic cholecystectomy may occur as a result of the significant dilatation of the femoral venous system, which has been observed during this operation when the pneumoperitoneum is created.[9,12,14,15] Damage to the vein endothelium has been found after venous distension in animal studies,[21] and a strong correlation between the degree of venodilatation during operation and the incidence of DVT has been demonstrated in human studies.[21,22]

It is thus likely that 2, and possibly all 3, of Virchow's factors for venous thrombosis are present in patients undergoing laparoscopic cholecystectomy. Despite this, DVT seems to be an uncommon complication of laparoscopic surgery. Although several case reports or series have specifically emphasized the hazard of DVT or pulmonary embolism after laparoscopic cholecystectomy,[23-27] larger studies report a low incidence of thromboembolic disease. A review of the results of 50 427 gynecological laparoscopies found an incidence of DVT and pulmonary embolism of 0.2 per 1000 patients.[28] There were 3 deaths due to pulmonary embolism in a retrospective survey of 77 604 patients undergoing laparoscopic cholecystectomy.[29] Another retrospective review, involving 11 863 patients undergoing laparoscopic cholecystectomy, also reported only 3 deaths due to pulmonary embolus, of a total of 10 postoperative deaths.[30]

Two duplex studies have prospectively examined the risk of DVT associated with laparoscopic cholecystectomy, with very different results. Caprini et al[20] found only 1 DVT (an asymptomatic calf vein DVT) using duplex scanning in a series of 100 consecutive patients undergoing laparoscopic cholecystectomy, while Patel et al[31] found a 55% incidence of DVT in a series of 20 consecutive patients. There was no record of pulmonary embolism in any of the patients in these studies, and Patel et al did not note whether any of the DVTs they detected were symptomatic.

Minilaparotomy cholecystectomy, first described in 1982,[32] is a method of open cholecystectomy through a short incision made directly over the hepatobiliary triangle. No pneumoperitoneum is necessary and there is thus no raised intra-abdominal pressure to resist venous return from the legs or abdomen. The reverse Trendelenburg position is not used.

The suitability of minilaparotomy cholecystectomy as a comparison operation for laparoscopic cholecystectomy is shown by the results of 6 randomized trials that compared the 2 methods.[33-39] A randomized, single-blinded study of 200 patients by Majeed et al[38] found no significant differences between the laparoscopic and minilaparotomy methods for the outcomes of length of postoperative stay, time to return to work, time to full activity, or complication rate. The only significant difference between the 2 groups was operating time, which was longer for the laparoscopic method.[38] The other 5 (nonblinded) randomized trials also found that the results for both operation methods were very similar, although they more commonly found an advantage for the laparoscopic method when any difference was observed.[33-35,39] The results for factors that might most obviously influence rate of DVT formation were that postoperative stay was significantly shorter after laparoscopic cholecystectomy in 3 studies[33-35] and return to normal activities was faster after the laparoscopic operation in 2 studies.[33,35] Duration of operation, which may also influence DVT frequency, was significantly longer for laparoscopic cholecystectomy in 2 of the nonblinded studies,[36,37] as it was in the blinded study, although there was no significant difference in this outcome in other studies.[33,34] These studies indicate that the results of these 2 operations are similar and both may be considered to be minimally invasive procedures when compared with conventional open cholecystectomy. For the purposes of this study, therefore, the significant differences between the 2 procedures were the presence or absence of the pneumoperitoneum and the supine vs head-up position of the patient on the operating table.

The aims of this study were to determine the frequency of DVT associated with minimally invasive cholecystectomy and to determine, using minilaparotomy cholecystectomy as a control operation, the influence of the laparoscopic pneumoperitoneum on DVT formation.

RESULTS

One hundred patients were enrolled in the study. When divided on an intent-to-treat basis, there were 59 patients in

Table 1. Patient Data*

	Laparoscopic Cholecystectomy	Minilaparotomy Cholecystectomy	*P*
Mean age, y	51.5	53.6	.54†
Male:female ratio	22:37	14:27	.75‡
Mean body mass index, kg/m^2	25.7	25.6	.89†
Mean white blood cell count, $\times 10^9$/L§	7.8	8	.76†
Mean platelet count, $\times 10^9$/L§	244	253	.52†
Mean APTT, s§	32	30	.53†
Mean PT, s§	10.7	11	.95†
No. of patients with risk factor(s) for DVT/PE	40	29	.75‡

**APTT indicates activated partial thromboplastin time; PT, prothrombin time; DVT, deep vein thrombosis; and PE, pulmonary embolism.*
†Comparison of means using the Student t *test.*
‡Comparison using χ^2 test.
§Preoperative blood test results.

Table 2. Thromboembolic Risk Factors*

Risk Factor	Laparoscopic Cholecystectomy	Minilaparotomy Cholecystectomy	Total
Age >65 y	12	10	**22**
Obesity (body mass index >30 kg/m^2)	6	8	**14**
Current smoker	9	4	**13**
Varicose veins	9	4	**13**
Previous DVT or PE	3	6	**9**
Cardiac failure	3	4	**7**
Oral contraceptive use	4	2	**6**
Cancer†	1	1	**2**
Current pregnancy	0	1	**1**
Total	**47**	**40**	**87**

**Includes all thromboembolic risk factors. Total numbers of risk factors differ from those in Table 1 because some patients had more than 1 thromboembolic risk factor. DVT indicates deep vein thrombosis; PE, pulmonary embolism.*
†Includes patients diagnosed with cancer within last 2 years, or cancer that has not been cured. Excludes patients with minor nonmelanotic skin cancer.

the laparoscopic cholecystectomy group and 41 patients in the minilaparotomy group. Three patients in the laparoscopic group and 2 patients in the minilaparotomy group were converted to conventional open cholecystectomy. Ten patients who underwent either laparoscopic or minilaparotomy cholecystectomy with either of the study surgeons during this period were not included; 3 refused to enter the study and 7 were excluded because of the unexpected unavailability of duplex scanning on the first postoperative day. None of the 10 excluded patients had any unusual prothrombotic states and none had clinical features of thromboembolic disease.

There was no significant difference between patients having either operation for the factors age, male-female ratio, body mass index, preoperative white blood cell count, platelet count, prothrombin time, activated partial thromboplastin time, or proportion of patients with any thromboembolic risk factors in each group (**Table 1**).

Table 3. Operative Data

	Laparoscopic Cholecystectomy	Minilaparotomy Cholecystectomy	*P*
Elective:emergency ratio	46:13	31:10	.99*
Public:private hospital ratio	18:41	12:29	.99*
Consultant:resident ratio	55:4	37:4	.59*
Operative cholangiogram performed (yes:no)	51:8	27:14	.002*
Duration of anesthesia, min	118	98	.05†
Postoperative stay, h	89	82	.81†

**Comparison made using the χ^2 test.*
†Comparison of means using the Student t *test.*

Table 4. Macroscopic Gallbladder Pathology*

Grade	Laparoscopic Cholecystectomy	Minilaparotomy Cholecystectomy
1	10	12
2	28	14
3	15	12
4	6	3

**Intraoperative assessment of severity of gallbladder disease. See "Patients and Methods" section for definitions of grades. Data are given as absolute numbers of patients in each category. The proportions of patients in each operation group are not significantly different (χ^2 test,* P *= .39).*

Some of the patients had more than one risk factor, and there were 87 risk factors for DVT formation among the 69 patients with risk factors (**Table 2**). The ratio of total number of risk factors to number of patients in each group was significantly higher for the minilaparotomy cholecystectomy group (χ^2 test, P=.009).

There was no significant difference between the proportions of patients in each cholecystectomy group who were operated on electively or emergently, who were admitted to the public or the private hospital, or who were operated on by the consultant or the resident (**Table 3**). Significantly more patients in the laparoscopic group had an operative cholangiogram, and the duration of general anesthesia was longer for the laparoscopic cholecystectomy group (Table 3). There was no significant difference between the length of postoperative hospital stay after either operation (Table 3). As summarized in **Table 4**, the proportions of each grade of macroscopic gallbladder pathology were not significantly different in each group (χ^2 test, P=.39).

All patients received graduated calf compression stockings, intermittent pneumatic calf compression, and postoperative subcutaneous LMWH according to the study protocol. Preoperative LMWH was ordered for all patients, but was inadvertently omitted in 3 patients.

Ninety-five patients had a preoperative duplex scan, and all 100 patients in the study had a postoperative day 1 scan. The 5 patients who did not have a preoperative duplex scan all had normal postoperative duplex scans. A late duplex scan at 2 to 4 weeks after operation was done in only 40 patients; logistic reasons such as remote residence caused the examination to be omitted in the remainder.

Two of the 100 patients had a postoperative DVT, 1 after laparoscopic cholecystectomy and 1 after minilaparotomy cholecystectomy. Both of these DVTs were identified on scanning on the first postoperative day in patients with normal preoperative duplex scans. One patient was a 60-year-old woman with varicose veins who developed a symptomatic left calf DVT following an otherwise uncomplicated laparoscopic cholecystectomy. Preoperative LMWH had been inadvertently omitted. Color duplex scanning showed a 2-cm fresh thrombus in a medial soleal vein. There was a slightly tender, minimally swollen left calf but no clinical evidence of pulmonary embolism. The second patient, the only postoperative death, was an 86-year-old woman with a history of previous severe cardiac failure. This patient's minilaparotomy cholecystectomy was complicated by the presence of an aberrant segmental bile duct opening directly into the gallbladder fossa from an atrophic area of the liver. The operation was therefore converted to an 8-cm open cholecystectomy. An asymptomatic 1- to 2-cm thrombus in the left peroneal vein was found on routine color duplex examination. This patient died on the fourth postoperative day of cardiac failure and pneumonia. There was no clinical suspicion of pulmonary embolism.

The 2 patients with DVTs diagnosed on postoperative day 1 did not undergo the later duplex scan, and none of the 40 patients who underwent the later duplex scan at 2 to 4 weeks after operation had a DVT.

Three patients had major hemorrhagic complications, with blood loss greater than 500 mL (2000 mL, 1700 mL, and 700 mL). In 2 of these cases, a specific vessel responsible for the bleeding was noted. In the third case, bleeding had ceased when the patient underwent relaparoscopy 4 hours after cholecystectomy, and the cause of the excessive bleeding was not clearly identified. Minor bleeding (<500 mL) was noted in another 14 cases. There were no bile duct injuries. Other complications were not recorded.

The study was stopped after 100 patients were studied, when it had been demonstrated that both cholecystectomy methods were low-risk operations for thromboembolic disease, and when it was apparent that a prohibitively large number of patients would be needed to find a meaningful difference between the 2 operation groups. A power calculation using the frequencies of DVT found in these 100 patients shows that 17 670 patients (8835 in each operation group) would be needed for a study with 90% power for detection of a difference at the .05 significance level.

COMMENT

This study demonstrated that despite the possible presence of all 3 of Virchow's factors for thrombosis formation during the performance of laparoscopic cholecystectomy, DVT detectable by color duplex examination is infrequent (2%) after minimally invasive cholecystectomy by either the laparoscopic or minilaparotomy methods if the thromboprophylaxis regimen used in this study is employed.

This was a nonrandomized study, the type of operation performed being determined by the preference of the participating surgeons. This study design was chosen because each of the surgeons involved has a large experience with, and preference for, one or the other method of cholecystectomy. Referral patterns for both surgeons were largely established in the prelaparoscopic era and referring physicians tend to send all general surgical patients to their preferred surgeon, with no alteration of these referral patterns for a particular operation, such as cholecystectomy. Significant preselection bias by referring physicians is thus minimized. Both operations' patient groups were shown to be very similar. Although there was a significantly greater proportion of risk factors for DVT formation in the minilaparotomy cholecystectomy group, the proportion of patients with any DVT risk factor in each group was not significantly different. There is also no reason to suspect that the 10 excluded patients, who either refused to participate or underwent operation on one of several days after which no first postoperative day duplex scan could be performed, were a select group different in any way from the study group.

A significantly longer duration of anesthesia in the laparoscopic group was the only operation factor that might introduce a bias in the DVT frequency. This bias is toward a higher frequency of DVT in the laparoscopic group, however, strengthening our conclusion that laparoscopic surgery is associated with a low DVT frequency, even with prolonged (median, 118 minutes) general anesthesia.

The findings in this study are similar to those of another prospective duplex study reported by Caprini et al,[20] in which 100 consecutive patients undergoing laparoscopic cholecystectomy had a complete venous duplex scan of both legs on the seventh postoperative day, with only 1 patient (1%) being found to have a DVT. All patients in that study received intermittent pneumatic compression boots from the start of operation until they were fully ambulant, and all patients were also fitted with elastic stockings from before operation until discharge. Heparin prophylaxis was only provided after operation, and was only given to patients determined to be at high risk of thromboembolic disease.

It is difficult to reconcile the low frequency of DVT in these duplex studies and large series of laparoscopic cholecystectomies with the 55% frequency of DVT found by Patel et al.[31] Eight potential reasons for interstudy variations in the frequency of postoperative DVT have been listed by Bergqvist and Lindblad.[42] Of the reasons provided, "diagnostic differences" and "differences in the general care of patients" (especially thromboprophylaxis) may account for the variation in the frequencies of DVT in these studies. Effective prophylaxis was not used in all patients in the study by Patel et al, 2 of the 20 patients were converted to open cholecystectomy, and 2 of the patients with postoperative DVTs did not have preoperative duplex scans.

None of these DVT frequency studies was designed to assess the effectiveness of different methods of thromboprophylaxis, and no statistical analysis is possible with such small numbers of patients and thromboses. Nevertheless, the thromboprophylaxis protocol used for this present study can be endorsed on the basis of our results. The study by Caprini et al,[20] in which preoperative heparin was not given, suggests that a combination of elastic stockings and pneumatic compression used from the start of operation until patients are fully ambulant may be sufficient thromboprophylaxis. In contrast, the possibility that preoperative heparin may have a significant benefit is at least suggested by this present study and the study by Patel et al.[31] In the study by Patel et al, all of the 4 patients who did not receive preoperative heparin developed a DVT, while in this study 1 of the 3 patients who did not receive preoperative heparin developed a DVT.

Several studies involving patients undergoing laparoscopic cholecystectomy have examined the effect of mechanical thromboprophylaxis devices on lower limb venous blood flow, although the effect of these devices on thrombosis formation has not been directly investigated. In a randomized study, graduated compression stockings were shown to effectively counteract the resistance to venous return caused by the laparoscopic pneumoperitoneum, with similar venous capacitance and outflow measurements in the stockinged group before and after establishment of a pneumoperitoneum.[43] In a similar study, graded compression bandages were of no benefit when the pressurized pneumoperitoneum was created.[15] The use of intermittent pneumatic compression devices completely reversed the reduction in mean femoral venous peak systolic velocity caused by the laparoscopic pneumoperitoneum in another study.[13] Pneumatic compression devices have been shown to activate the fibrinolytic system,[44] and placing these devices on the arms of patients during operations was shown to reduce the incidence of leg DVT by more than half.[45] Pneumatic compression devices, therefore, have a likely benefit in decreasing both venous stasis and hypercoagulability, and it seems reasonable to recommend their use for all patients undergoing laparoscopic procedures.

Venous duplex color flow imaging was used to screen for DVT in this study. Ascending venography remains the diagnostic standard for DVT surveillance in asymptomatic postoperative patients, but the test is invasive and uncomfortable, interpretation variability is reported, and the contrast agents may cause allergic reactions, renal toxic effects, and venous thrombosis. The sodium iodide I 125 fibrinogen uptake test, which has been widely used for DVT surveillance studies, is no longer available in this country or in the United States because of the risk of virus transmission from the blood donors. Duplex scanning is noninvasive, and experienced examiners report only marginally inferior results for duplex scanning compared with venography for symptomatic cases, especially for femoropopliteal segment DVT.[46-48] Asymptomatic DVTs are mostly small, hemodynamically insignificant calf thromboses, however, which may be missed by duplex scanning even if color duplex is used.[49] Although the specificity of color duplex for the detection of asymptomatic below-knee thrombi is greater than 95% in some reports,[46,49,50] the sensitivity of this test for symptomless calf DVT ranges from only 33% to 88%.[49,51] Even allowing for the possibility that the number of undiagnosed DVTs in this surveillance study was as many as 2 or 3 times the number diagnosed, laparoscopic and minilaparotomy cholecystectomy remain procedures with a low risk of thrombosis if the thromboprophylaxis measures used in this study are employed.

Future studies could investigate the effectiveness of various thromboprophylaxis measures using the outcome of venous thrombosis rather than femoral vein flow. Such a study would probably require a very large number of patients and considerable funds, however, and its usefulness might be questioned in view of the low rate of clinical thromboembolic disease reported in large reviews of laparoscopic cholecystectomy. Until such studies are reported, the thromboprophylaxis protocol of preoperative and postoperative LMWH, graduated compression stockings, and intraoperative intermittent pneumatic calf compression can be recommended for patients undergoing minimally invasive cholecystectomy.

This study was supported in part by funding from the St Vincent's Clinic Foundation, Sydney, Australia.

Corresponding author: Reginald V. N. Lord, FRACS, Department of Surgery, Level 17, O'Brien Bldg, St Vincent's Hospital, Victoria Street Darlinghurst, Sydney, Australia 2010.

REFERENCES

1. Mühe E. Die erste cholezystektomie durch das laparoskop. *Langenbecks Arch Chir.* 1986;369:804.
2. Berggren U, Gordh T, Grama D, Haglund U, Rastad J, Arvidsson D. Laparoscopic versus open cholecystectomy: hospitalization, sick leave, analgesia and trauma responses. *Br J Surg.* 1994;81:1362-1365.
3. Sanabria JR, Clavien PA, Cywes R, Strasberg SM. Laparoscopic versus open cholecystectomy: a matched study. *Can J Surg.* 1993;36:330-336.
4. Ho HS, Gunther RA, Wolfe BM. Intraperitoneal carbon dioxide insufflation and cardiopulmonary functions: laparoscopic cholecystectomy in pigs. *Arch Surg.* 1992;127:928-933.
5. Ishizaki Y, Bandai Y, Shimomura K, Abe H, Ohtomo Y, Idezuki Y. Changes in splanchnic blood flow and cardiovascular effects following peritoneal insufflation of carbon dioxide. *Surg Endosc.* 1993;7:420-423.
6. Safran D, Sgambati S, Orlando R III. Laparoscopy in high risk cardiac patients. *Surg Gynecol Obstet.* 1993;176:548-554.
7. Westerband A, Van De Water JM, Amzallag M, et al. Cardiovascular changes during laparoscopic cholecystectomy. *Surg Gynecol Obstet.* 1992;175:535-538.
8. Portera CA, Compton RP, Walters DN, Browder IW. Benefits of pulmonary artery catheter and transesophageal echocardiographic monitoring in laparoscopic cholecystectomy patients with cardiac disease. *Am J Surg.* 1995;169: 202-207.
9. Jorgensen JO, Lalak NJ, North L, Hanel K, Hunt DR, Morris DL. Venous stasis during laparoscopic cholecystectomy. *Surg Laparosc Endosc.* 1994;4:128-133.
10. Beebe DS, McNevin MP, Crain JM, et al. Evidence of venous stasis after abdominal insufflation for laparoscopic cholecystectomy. *Surg Gynecol Obstet.* 1993; 176:443-447.
11. Goodale RL, Beebe DS, McNevin MP, et al. Hemodynamic, respiratory, and metabolic effects of laparoscopic cholecystectomy. *Am J Surg.* 1993;166:533-537.
12. Ido K, Suzuki T, Kimura K, et al. Lower-extremity venous stasis during laparoscopic cholecystectomy as assessed using color doppler ultrasound. *Surg Endosc.* 1995;9:310-313.
13. Millard JA, Hill BB, Cook PS, Fenoglio ME, Stahlgren LH. Intermittent sequential pneumatic compression in prevention of venous stasis associated with pneumoperitoneum during laparoscopic cholecystectomy. *Arch Surg.* 1993;128:914-918.
14. Sobolewski AP, Deshmukh RM, Brunson BL, et al. Venous hemodynamic changes during laparoscopic cholecystectomy. *J Laparoendoscopic Surg.* 1995;5:363-369.
15. Ido K, Suzuki T, Taniguchi Y, et al. Femoral vein stasis during laparoscopic cholecystectomy: effects of graded elastic compression leg bandages in preventing thrombus formation. *Gastrointest Endosc.* 1995;42:151-155.
16. Coleridge-Smith PD, Hasty JH, Scurr JH. Venous stasis and vein changes during surgery. *Br J Surg.* 1990;77:1055-1059.
17. Modig J, Hjelmstedt A, Sahlstedt B, Maripuu E. Comparative influences of epidural and general anesthesia on deep venous thrombosis and pulmonary embolism after total hip replacement. *Acta Chir Scand.* 1981;147:125-130.
18. Davis FM, Laurenson VG, Gillespie WJ, Wells JE, Foate J, Newman E. Deep vein thrombosis after total hip replacement: a comparison between spinal and general anesthesia. *J Bone Joint Surg Br.* 1989;71:181-185.
19. Caprini JA, Arcelus JI. Prevention of postoperative venous thromboembolism following laparoscopic cholecystectomy. *Surg Endosc.* 1994;8:741-747.
20. Caprini JA, Arcelus JI, Laubach M, et al. Postoperative hypercoagulability and

deep-vein thrombosis after laparoscopic cholecystectomy. *Surg Endosc*. 1995; 9:304-309.
21. Comerota AJ. Operative venous dilatation and postoperative deep vein thrombosis. In: Bergqvist D, Comerota AJ, Nicolaides AN, Scurr JH, eds. *Prevention of Venous Thromboembolism*. Nicosia, Cyprus: Med-Orion; 1994:9.
22. Stewart GJ, Lachman JW, Alburger PD, Ziskin MC, Phillips CM, Jensen K. Intraoperative venous dilatation and subsequent development of deep vein thrombosis in patients undergoing total hip or knee replacement. *Ultrasound Med Biol*. 1990;16:133-140.
23. Jorgensen JO, Hanel K, Lalak NJ, Hunt DR, North L, Morris DL. Thromboembolic complications of laparoscopic cholecystectomy. *BMJ*. 1993;306:518-519.
24. Mayol J, Vincent-Hamelin E, Sarmiento JM, et al. Pulmonary embolism following laparoscopic cholecystectomy: report of two cases and review of the literature. *Surg Endosc*. 1994;8:214-217.
25. Bentolila S, Samama M, Lumbroso M, Andreassian B. Thrombose veineuse profonde au decours d'une cholecystectomie par laparoscopie. *Presse Med*. 1994; 23:1832.
26. Bailey RW, Zucker KA, Flowers JL, Scovill WA, Graham SM, Imbembo AL. Laparoscopic cholecystectomy: experience with 375 consecutive patients. *Ann Surg*. 1991;214:531-541.
27. Femandez RM, Lasierra CJ. Utilizamos racionalmente la tromboprofilaxis en la cirugia minimamente invasiva por laparoscopia? *Rev Esp Enferm Dig*. 1996;88: 573-575.
28. Chamberlain G, Brown JC. *Gynaecological Laparoscopy: The Report of a Working Party in a Confidential Enquiry of Gynaecological Laparoscopy*. London, Engand: Royal College of Obstetricians and Gynaecologists; 1978.
29. Deziel DJ, Millikan KW, Economou SG, Doolas A, Ko S-T, Airan MC. Complications of laparoscopic cholecystectomy: a national survey of 4,292 hospitals and an analysis of 77,604 cases. *Am J Surg*. 1993;165:9-14.
30. Scott TR, Zucker KA, Bailey RW. Laparoscopic cholecystectomy: a review of 12,397 patients. *Surg Laparosc Endosc*. 1992;2:191-198.
31. Patel MI, Hardman DT, Nicholls D, Fisher CM, Appleberg M. The incidence of deep venous thrombosis after laparoscopic cholecystectomy. *Med J Aust*. 1996; 164:652-656.
32. Dubois F, Barthelot G. Cholecystectomie par minilaparotomie. *Presse Med*. 1982; 11:1139-1141.
33. Barkun JS, Barkun AN, Sampalis JS, et al. Randomised controlled trial of laparoscopic versus mini cholecystectomy. *Lancet*. 1992;340:1116-1119.
34. Kunz R, Orth K, Vogel J, et al. Laparoskopische cholecystektomie versus minilap-cholecystektomie: ergebnisse einer prospektiven, randomisierten studie. *Chirurgia*. 1992;63:291-295.
35. McMahon AJ, Russell IT, Baxter JN, et al. Laparoscopic versus minilaparotomy: a randomised trial. *Lancet*. 1994;343:135-138.
36. McMahon AJ, Russell IT, Ramsay G, et al. Laparoscopic and minilaparotomy cholecystectomy: a randomised trial comparing postoperative pain and pulmonary function. *Surgery*. 1994;115:533-539.
37. McGinn FP, Miles AJ, Uglow M, Ozmen M, Terzi C, Humby M. Randomized trial of laparoscopic cholecystectomy and mini-cholecystectomy. *Br J Surg*. 1995; 82:1374-1377.
38. Majeed AW, Troy G, Nicholl JP, et al. Randomised, prospective, single-blind comparison of laparoscopic versus small-incision cholecystectomy. *Lancet*. 1996; 347:989-994.
39. Coelho JC, de Araujo RP, Marchesini JB, Coelho ICMM, de Araujo LRR. Pulmonary function after cholecystectomy performed through Kocher's incision, a mini-incision, and laparoscopy. *World J Surg*. 1993;17:544-546.
40. Merrill JR. Minimal trauma cholecystectomy (a "no touch" procedure in a "well"). *Am Surg*. 1988;54:256-261.
41. Hugh TB, Chen FC, Hugh TJ, Li B. Laparoscopic cholecystectomy: a prospective study of outcome in 100 unselected patients. *Med J Aust*. 1992;156:318-320.
42. Bergqvist D, Lindblad B. Incidence of venous thromboembolism in medical and surgical patients. In: Bergqvist D, Comerota AJ, Nicolaides AN, Scurr JH, eds. *Prevention of Venous Thromboembolism*. Nicosia, Cyprus: Med-Orion; 1994:9.
43. Wilson YG, Allen PE, Skidmore R, Baker AR. Influence of compression stockings on lower-limb venous haemodynamics during laparoscopic cholecystectomy. *Br J Surg*. 1994;81:841-844.
44. Tarnay TJ, Rohr PR, Davidson AG, Stevenson MM, Byars EF, Hopkins GR. Pneumatic calf compression, fibrinolysis, and the prevention of deep venous thrombosis. *Surgery*. 1980;88:489-496.
45. Knight MTN, Dawson R. Effect of intermittent compression of the arms on deep venous thrombosis in the legs. *Lancet*. 1976;2:1265-1268.
46. Nicolaides A, Kalodiki E. Duplex scanning in postoperative surgical patients. *Haemostasis*. 1993;23(suppl 1):72-79.
47. Miller N, Satin R, Tousignant L, Sheiner NM. A prospective study comparing duplex scan and venography for diagnosis of lower extremity deep vein thrombosis. *Cardiovasc Surg*. 1996;4:505-508.
48. Lensing AW, Hirsh J, Buller HR. Diagnosis of venous thrombosis. In: Colman RW, Hirsh J, Marder VJ, Salzman EW, eds. *Hemostasis and Thrombosis: Basic Principles and Clinical Practice*. 3rd ed. Philadelphia, Pa: JB Lippincott; 1994: 1297-1321.
49. Grady-Benson JC, Oishi CS, Hanson PB, Colwell CW Jr, Otis SM, Walker RH. Postoperative surveillance for deep venous thrombosis with duplex ultrasonography after total knee arthroplasty. *J Bone Joint Surg Am*. 1994;76:1649-1657.
50. Mattos MA, Londrey GL, Leutz DW, et al. Color-flow duplex scanning for the surveillance and diagnosis of acute deep vein thrombosis. *J Vasc Surg*. 1992;15: 366-376.
51. Lensing AW, Doris CI, McGrath FP, et al. A comparison of compression ultrasound with color Doppler ultrasound for the diagnosis of symptomless postoperative deep vein thrombosis. *Arch Intern Med*. 1997;157:765-768.