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Venous Stasis and Deep Vein Thrombosis Prevention in Laparoscopic Surgery

Mindaugas Kiudelis, Dalia Adukauskienė and Rolandas Gerbutavičius
*Medical Academy of Lithuanian University of Health Sciences,
 Kaunas,
 Lithuania*

1. Introduction

Laparoscopic surgery – is one of the most progressive minimal invasive surgery branches. About 25–40% of all abdominal operations are performed laparoscopically in our days and this rating is going in ascending order. Laparoscopic operations (cholecystectomy, fundoplication, appendectomy, bypass due to morbid obesity et at.) have rapidly become the operations of choice in abdominal surgery. Several authors reported that deep vein thrombosis (DVT) in the legs developed in 30% of postoperative patients and pulmonary embolism (PE) in 10% of these patients.

Many studies explored the frequency of deep leg vein thrombosis after various open abdominal surgery operations. Some studies (Geerts and al., 1994) determined that deep leg vein thrombosis develops in 55% of polytrauma patients. Clagett & Reisch, 1988; found 25% rate of DVT after open abdominal surgery. Literature data on the incidence of DVT after laparoscopic operations is limited. Patel MI and al., 1996; carried out the prospective clinical study, studying the frequency of DVT after laparoscopic cholecystectomy. The rate of DVT, diagnosed by ultrasound Doppler, was 55%. The incidence of DVT and PE after laparoscopic fundoplications was 1.8% in our prospective randomized study. Lord RV and al., 1998; performed the prospective clinical study and compared the incidence of DVT after laparoscopic or microlaparotomic (open) cholecystectomy. The incidence of DVT was 1.7% after laparoscopic and 2.4% after open cholecystectomy. Nevertheless, many authors states, that the incidence of DVT should be less after laparoscopic surgery when comparing with open one. Laparoscopic operations, in comparison with open ones, have few basic differences:

1. Laparoscopic operation involves a specific manipulation called abdominal insufflation in addition to the routine procedure of general anesthesia. The increased intra-abdominal pressure associated with pneumoperitoneum (12-14 mm Hg) during laparoscopic upper gastrointestinal surgery has the potential to compound any lower-limb venous stasis already present due to general anesthesia by compressing the retroperitoneal vena cava and iliac veins.
2. Most of laparoscopic operations often last more than 1.5 hours and often are performed with patient in the reverse Trendelenburg position. These differences also have the potential for an increased risk of significant venous stasis.

2. Venous stasis and deep vein thrombosis prevention in laparoscopic surgery

Lower – limb venous stasis is one of the major pathophysiological elements involved in the development of intraoperative DVT and postoperative PE. Factors influencing venous return in the healthy subject are left ventricular output, negative intrathoracic pressure during inspiration, the calf's soleal muscle pump, squeezing of the inferior vena cava by increased intra-abdominal pressure during diaphragmatic descent, and the suction effect of the right atrium during systole. Thus, in the anesthetized patient, venous return from the legs depends mainly on the pressure gradient between the venules (12-18 mm Hg) and the right atrium (4-5 mm Hg). It is expected that the introduction of a pressure barrier between legs venules and the right atrium impedes venous return. Venous thrombosis is major causes of morbidity and mortality. Venous thrombosis leads to pulmonary embolism, which can be fatal, and to postphlebotic syndrome. Venous thrombosis occurs when procoagulant stimuli overwhelm natural protective mechanisms. Procoagulant stimuli include the excessive activation of coagulation, particularly when protective pathways are compromised by thrombophilic abnormalities, vessel wall damage, or stasis. Although of less degree than open surgery, laparoscopic surgery may potentially predispose to thrombosis since it alters venous flow and coagulability and cause endothelial injuries.

Little attention has been appointed by the scientists of venous intimal irregularity, as one of the pathogenesis factors of venous thrombosis. Schaub RG and al. 1978; performing experimental studies with dogs, noticed endothelium rupture of small veins, which occurred away from the surgical field and were caused by intra-abdominal surgery. These multiple micro tears often occur in the place of small and large vein (femoral, jugular) fusion sites. Histological studies found that these ruptures are infiltrated with leukocytes and platelets. Comerota AJ and al., 1990; have shown that venous endothelial micro tears occur in dilated veins, which normally are always present during laparoscopic surgery. When the micro tears of endothelium occurs, appeared subendothelial blood vessel collagen stimulates the release of coagulation predisposing factors - thromboplastin and Willebrand factor.

General anesthesia has been shown to decrease profoundly lower-limb venous return. In one series, 50% of anesthetized patients developed same degree of venous stasis intraoperatively, similar to that produced by 10-14 days of bed rest. We performed a prospective randomized clinical study in which 72 patients undergoing elective laparoscopic funduplications because of gastroesophageal reflux disease, caused by hiatal hernia were studied. One of our study aims was to evaluate the effect of general anesthesia and the effect of pneumoperitoneum (12 mm Hg) on a femoral venous outflow. Lower extremity venous blood velocity and the femoral vein diameter were evaluated using Doppler ultrasonography. Doppler ultrasound images of the longitudinal section of the femoral vein were obtained at its segment proximal to the bifurcation of the deep femoral artery from the femoral artery.

Our study results demonstrated that both factors - general anesthesia and abdominal insufflation reduced the blood velocity in the femoral vein (figure 1 and 2) and increased cross-sectional area of this vein (figure 3 and 4).

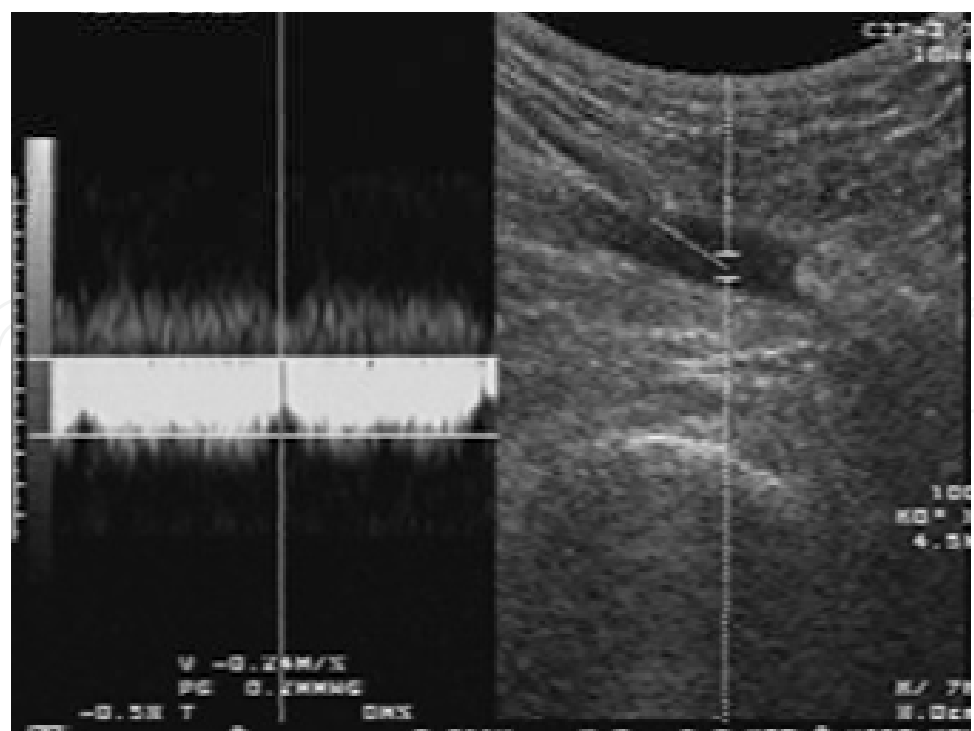


Fig. 1. Ultrasonography of the common femoral vein before the general anesthesia. Figure on the left side shows blood velocity in the femoral vein using doppler ultrasound; the right side shows longitudinal section of the femoral vein.

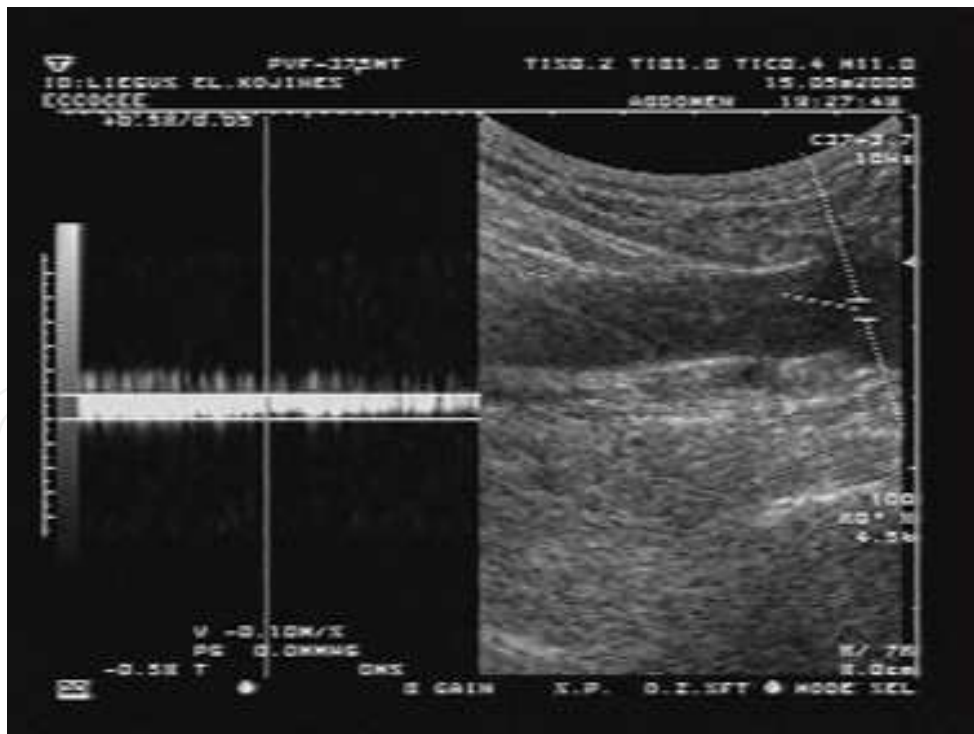


Fig. 2. Ultrasonography of the common femoral vein at the 12 mm Hg insufflation when the patient was placed in the reverse Trendelenburg position (angle 45°). Figure on the left side shows blood velocity in the femoral vein using doppler ultrasound; the right side shows longitudinal section of the femoral vein.



Fig. 3. Ultrasonography of the common femoral vein before the general anesthesia. Figure shows the cross-sectional area of the femoral vein.



Fig. 4. Ultrasonography of the common femoral vein at the 12 mm Hg insufflation when the patient was placed in the reverse Trendelenburg position (angle 45°). Figure shows the cross-sectional area of the femoral vein.

The decrease in the blood velocity of the femoral vein and increase of the cross-sectional area differed significantly between 5-mm Hg insufflation, 10-mm Hg insufflation and 12-mm Hg insufflation. Furthermore, the blood velocity of the femoral vein decreased significantly and the femoral vein cross-sectional area increased significantly when the patient was placed in the reverse Trendelenburg position with the presence of 12 mm Hg pneumoperitoneum. These findings suggest that venous stasis, caused by abdominal insufflation during laparoscopic operations, can be reduced by using lower pressures. Postural changes during laparoscopic operation also greatly affect venous stasis. The large increase in femoral venous blood flow and large decrease in femoral vein cross-sectional area observed after release of the pneumoperitoneum in our study confirmed that venous stasis is present through all laparoscopic operation.

Several other scientists (Ido et al., 1995; Jorgensen et al., 1994; Beebe et al., 1993) also investigated femoral vein blood flow velocities during and after abdominal insufflation in patients, who underwent laparoscopic cholecystectomy, using color Doppler ultrasonography. They also found, that abdominal insufflation reduced the blood velocity in the femoral vein and suggested that abdominal insufflation during laparoscopic operation can cause femoral vein stasis. The femoral vein stasis, which appears in laparoscopic operations, can be minimized by reducing the intraabdominal pressure during operation, and avoiding reverse Trendelenburg position as much as possible.

2.1 Mechanical deep vein thrombosis prevention in laparoscopic surgery

A variety of mechanical techniques and devices has been used in an attempt to reduce the venous stasis, which appears during laparoscopic surgery. Compression bandages, passive exercise, electrical calf stimulation, intermittent pneumatic compression have been employed in reducing venous stasis and the incidence of postoperative DVT.

The other aim of our randomized clinical study was to evaluate the efficacy of mechanical antistasis devices: intermittent pneumatic compression (IPC), intermittent electric calf stimulation (IECS) and graded compression leg bandages (LB) in reducing venous stasis during laparoscopic fundoplication.

Of the physical methods, simple compression using elastic stockings has been reported to be ineffective. The effectiveness of the graded compression bandage, which we used in the present study, has been noted by several investigators. They found the incidence of deep vein thrombosis 7 % in the graded compression bandage groups and 19 % in the controls groups. In our study we found, that femoral venous blood velocity was significantly increased and cross-sectional area significantly decreased over control values (IPC and IECS groups) before the general anesthesia and after the induction of anesthesia in the supine position. However, after the start of abdominal insufflation (5 mmHg) in the supine position, the difference in venous blood flow velocity and cross-sectional area between LB group and IPC and IECS groups (at that time antistasis devices were not acting on the legs and these groups served as controls) was minimized. These our findings suggest that graded compression leg bandages is effective for patients, undergoing open surgery without abdominal insufflation or postural changes, but it is ineffective in patients undergoing laparoscopic surgery, which involves abdominal insufflation. Ido et al., 1995 also found that this type of bandage is ineffective in patients, undergoing laparoscopic cholecystectomy with abdominal insufflation.

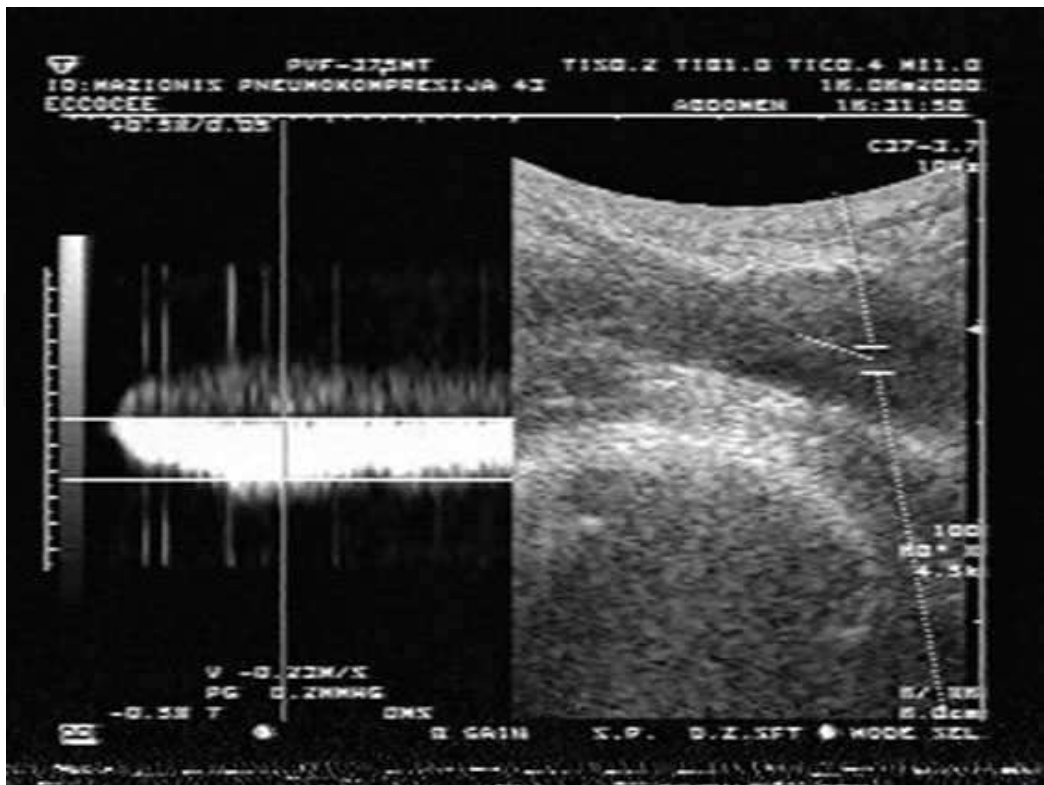


Fig. 5. Venous blood flow velocity at 12 mm Hg insufflation in the reverse Trendelenburg position when intermittent pneumatic compression is acting on the legs.

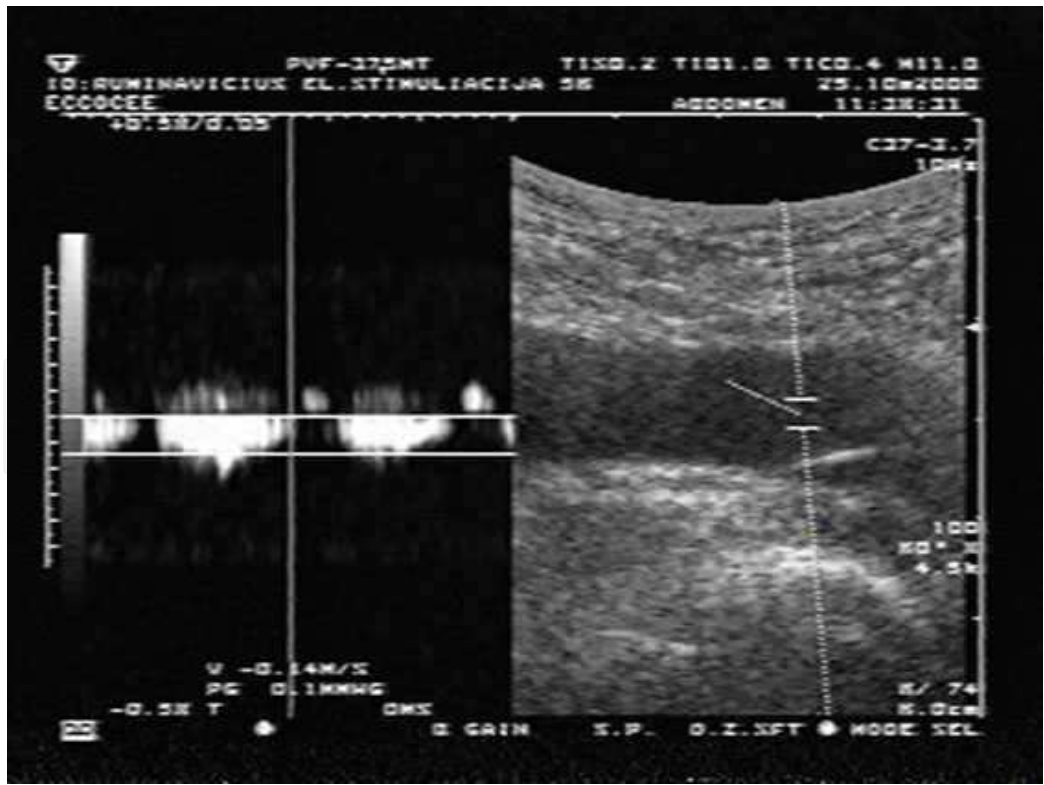
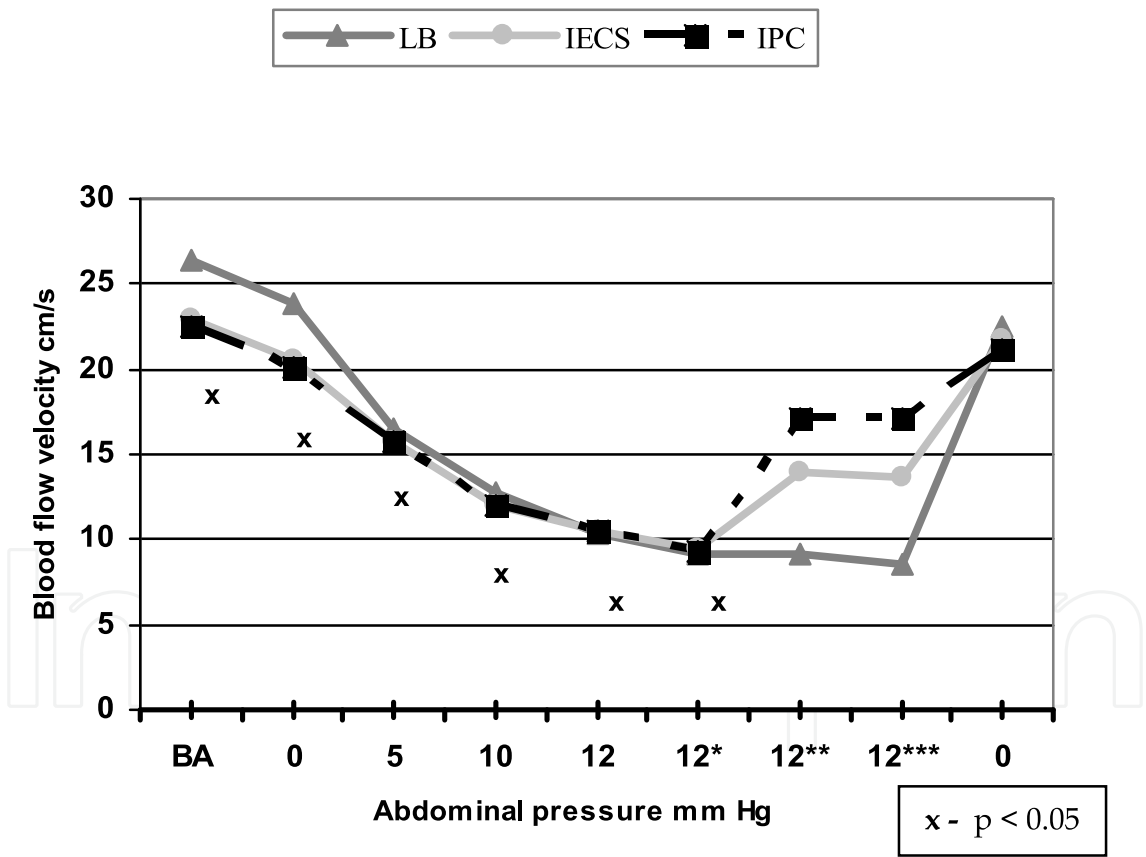


Fig. 6. Venous blood flow velocity at 12 mm Hg insufflation in the reverse Trendelenburg position when intermittent electric calf stimulation is acting on the legs.

The creation of pulsatile venous blood flow is thought to be crucial for the function of mechanical antistasis devices. This pulsatile blood flow episodically flushes activated clotting factors from stagnant soleal sinuses, thereby preventing thrombosis. Both IPC and IECS were able to achieve pulsatile blood flow with a pneumoperitoneum (figure 5 and 6).

The maximum blood velocity generated by the IPC when a pneumoperitoneum (12 mm Hg) was present and the patient was placed in the reverse Trendelenburg position was significantly greater than the maximum blood velocity generated by the IECS. The femoral vein cross-sectional area decreased 25 % when IPC was acting on the legs, when pneumoperitoneum (12 mmHg) was present and the patient was placed in the reverse Trendelenburg position, while the femoral vein cross-sectional area decreased only 3 % when IECS was acting on the legs during laparoscopic operation. The femoral vein cross-sectional area changes received by IPC were significantly greater than changes received by IECS when the pneumoperitoneum (12 mm Hg) was present. These findings show that IPC is more effective than IECS in reducing venous stasis induced by the pneumoperitoneum and the reverse Trendelenburg position. Graded compression leg bandages is totally ineffective in patients, undergoing laparoscopic operations (figure 7).



BA - Before the general anesthesia, * - the patient placed in the reverse Trendelenburg position (angle 45°), ** - the patient placed in the reverse Trendelenburg position, when the mechanical antistasis devices is acting on the legs, *** - the patient placed in the reverse Trendelenburg position, when the mechanical antistasis devices is acting on the legs and 1 h after the beginning of the operation

Fig. 7. Mean blood flow velocity changes in the relationship with pneumoperitoneum, reverse Trendelenburg position and antistasis devices.

With a pneumoperitoneum in place, neither device is able to return the depressed blood flow velocity to the values recorded without a pneumoperitoneum. The incidence of DVT and PE after laparoscopic funduplications was 1.8% in our study.

2.2 Pharmaceutical deep vein thrombosis prevention in laparoscopic surgery

Methods that have conventionally been used to prevent postoperative deep vein thrombosis during laparoscopic surgery include not only mechanical techniques or devices (compression bandages, electrical calf stimulation, passive exercise, intermittent pneumatic compression), but also drug therapy (low-dose heparin, low-molecular-weight-heparin).

Stasis alone does not cause thrombosis, but the combination of stasis, hypercoagulability, and endothelial damage allows thrombus to develop. Some studies demonstrated that laparoscopic operations lead to postoperative activation of the coagulation system, which is one of the factors for postoperative thromboembolic complications.

We performed other prospective randomized clinical study and the aim of this study was to evaluate the hypocoagulation effect of intermittent pneumatic compression (IPC) or combination of low molecular weight heparin (LMWH) and IPC during and after laparoscopic funduplication. The patients were randomized in to two groups – 10 patients in each group. The first group received IPC during laparoscopic funduplications. The second group received 40mg LMWH enoxaparin subcutaneous 1h before operation and IPC during laparoscopic funduplication.

A series of highly sensitive and specific immunochemical tools has been developed that can quantitate the levels and activities of various steps of the haemostatic mechanism in vivo at the sub abnormal level. These include prothrombin F1+2, which measures the cleavage of prothrombin molecule by factor Xa and thrombin –antithrombin complex (TAT) reflecting the in vivo thrombin generation process. The increases in plasma prothrombin fragment F1+2 and thrombin – antithrombin complex indicate increased formation of thrombin. In this study plasma prothrombin fragment F1+2 and TAT were used as markers of coagulation pathway activation. Our study results demonstrated that hypercoagulable state is present during and after laparoscopic funduplication when using IPC alone for deep-vein thrombosis prevention (tables 1 and 2).

Variable	Before operation (Baseline)	1 h after introduction of laparoscope	10 min after extubation
IPC group (n = 10)	1.07 (0.89-1.23)	1.0 (0.73-1.26)	1.85 (1.31-5.36) ^{ab}
IPC + LMWH group (n = 10)	1.11 (0.83-1.94)	1.01 (0.77-1.93)	1.44 (0.89-2.17)

Values are expressed as median (range)

^a p < 0.0001 vs baseline

^b p < 0.0001 vs 1h after introduction of laparoscope

Table 1. Changes of prothrombin fragment F1+2 plasma levels (nmol/L) in the IPC and IPC + LMWH groups.

Variable	Before operation (Baseline)	1 h after introduction of laparoscope	10 min after extubation
IPC group (n = 10)	1.5 (1.2-2.5)	6.5 (2.7-9.5) ^a	9.1 (1.4-45.2) ^{bc}
IPC + LMWH group (n = 10)	2.5 (1.2-7.3)	4.8 (1.3-20.1)	4.7 (1.3-7.1)

Values are expressed as median (range)

^a p < 0.0001 vs baseline

^b p < 0.0001 vs baseline

^c p < 0.0001 vs 1h after introduction of laparoscope

Table 2. Changes of thrombin – antithrombin complex plasma levels (µg/L) in the IPC and IPC + LMWH groups.

Coagulation is regulated at several levels. Key inhibitors include tissue factor pathway inhibitor, antithrombin, and the protein C pathway. The inhibition of the factor VIIa/tissue factor complex (extrinsic coagulation pathway) is effected by TFPI. TFPI acts in a two-step manner. In the first step, TFPI complexes and inactivates factor Xa to form a TFPI/factor Xa complex. The TFPI within this complex then inactivates tissue factor-bound VIIa as the second step. Because the formation of the TFPI/factor Xa complex is a prerequisite for the efficient inactivation of factor VIIa, the system ensures that some factor Xa generation occurs before factor VIIa-mediated initiation of the coagulation system is shut down. In this study plasma free tissue factor pathway inhibitor as marker of hypocoagulation effect was used. Our study results demonstrated that a combination of LMWH and IPC generates hypocoagulation effect and are more effective than IPC alone to prevent deep-vein thrombosis after laparoscopic fundoplication (table 3).

Variable	Before operation (Baseline)	1 h after introduction of laparoscope	10 min after extubation
IPC group (n = 10)	13.7 (7.2-22.3)	13.7 (7.3-20.1)	11.3 (7.9-15.2)
IPC + LMWH group (n = 10)	13.4 (8.3-20.4)	27.9 (20.6-43.6) ^a	21.3 (11.5-32.3) ^b

Values are expressed as median (range)

^a p < 0.001 vs baseline

^b p < 0.05 vs baseline

Table 3. Changes of free tissue pathway factor inhibitor plasma levels (ng/ml) in the IPC and IPC + LMWH groups.

The antithrombotic effect of IPC is thought to be the result of increased venous velocity and stimulation of endogenous fibrinolysis. However, the results of several studies on the enhancement of hypocoagulation effect by an IPC have been controversial. Cahan et al., 2000; showed that external pneumatic compression devices did not enhance systemic fibrinolysis or prevent postoperative shutdown either by decreasing plasminogen activator

inhibitor-1 activity or by increasing tissue plasminogen activator activity. Their data suggest that external pneumatic compression devices do not prevent deep venous thrombosis by fibrinolytic enhancement; effective prophylaxis is achieved only when the devices are used in a manner that reduces lower extremity venous stasis. Jacobs et al., 1996; reported that sequential gradient intermittent pneumatic compression induces prompt, but short-lived, alterations in both fibrinolytic function, and the values quickly reverted to baseline on termination of compression. Okuda et al., 2002; reported that intermittent compression boot did not prevent increased intravascular thrombogenesis and platelet activation through significant increases of plasma D-dimer and β -thromboglobulin after laparoscopic cholecystectomy. Killewich et al., 2002; also reported that enhanced regional fibrinolysis in the lower extremities could not be detected with the use of external pneumatic compression devices, as measured with tissue plasminogen activator and plasminogen activator inhibitor-1 activity in common femoral venous blood samples in patients undergoing abdominal surgery. On the other hand, Comerota et al., 1997; reported that external pneumatic compression devices induced a significant decrease in plasminogen activator inhibitor-1 activity in normal volunteers.

In our study, the IPC used alone during laparoscopic fundoplication, did not prevent increased intravascular thrombogenesis through significant increases of plasma F1+2 and TAT during and after laparoscopic fundoplication.

Giddings et al., 1999; reported that IPC led to highly significant falls in factor VIIa, associated with increased levels of tissue factor pathway inhibitor in non-smoking volunteers. Chouhan et al., 1999; investigated the effect of IPC on the tissue factor pathway in 6 normal subjects and 6 patients with postthrombotic venous disease. Their study results demonstrated that IPC results in an increase in plasma TFPI and decline in FVIIa in both groups. Authors speculated that inhibition of tissue factor pathway, the initiating mechanism of blood coagulation, is a possible mechanism for the antithrombotic effect of IPC. Our study results demonstrate that IPC used alone did not increase TFPI in plasma and didn't produce hypocoagulation effect during laparoscopic fundoplication.

Most circulating TFPI is bound to lipoproteins. TFPI is also found in platelet α -granules and on the endothelium cell surface. TFPI bound to the endothelium is released with therapeutic doses of heparin or low molecular weight heparin, suggesting that TFPI binds to endogenous glycosaminoglycans on the endothelium wall surface.

Our clinical data suggest that LMWH, administered 1 h before operation, together with IPC induce more favorable hypocoagulation profile compared with LMWH alone. However, clinical data, comparing the rate of DVT between these two prophylactic methods are still lacking. On the other hand, alone LMWHs have been evaluated in a large number of randomized clinical trials and have been shown to be safe and effective for the prevention and treatment of venous thrombosis in laparoscopic or in open surgery.

Our recommendation is LMWH, administered 1 h before operation, together with IPC against postoperative venous thromboembolism in laparoscopic operations. Of course, this recommendation has to be proved in future prospective randomized clinical trials, comparing the incidence of DVT between these two prophylactic methods.

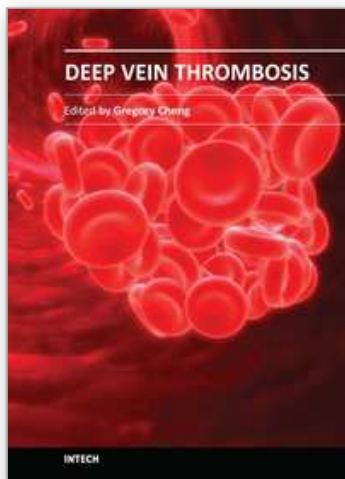
3. Conclusions

1. Venous stasis, which appears in laparoscopic operations, can be minimized by reducing the intraabdominal pressure during operation and avoiding reverse Trendelenburg position as much as possible.
2. IPC is more effective than IECS in reducing venous stasis induced by the pneumoperitoneum and the reverse Trendelenburg position.
3. Graded compression leg bandages is ineffective in patients, undergoing laparoscopic operations with pneumoperitoneum.
4. With a pneumoperitoneum in place, neither mechanical device is able to return the depressed blood flow velocity to the values recorded without a pneumoperitoneum.
5. Hypercoagulable state is present during and after laparoscopic fundoplications when using IPC alone for deep-vein thrombosis prevention: the IPC, used alone, did not prevent increased intravascular thrombogenesis through significant increases of plasma F1+2 and TAT during operation.
6. A combination of LMWH and IPC generates hypocoagulation effect and can be more effective than IPC alone to prevent deep-vein thrombosis after laparoscopic operations.
7. Our recommendation is LMWH, administered 1 h before operation, together with IPC against postoperative venous tromboembolism in laparoscopic operations.

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Deep Vein Thrombosis

Edited by Dr. Gregory Cheng

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This book provides a comprehensive review of deep vein thrombosis. There are chapters on risk factors for DVT, post thrombotic syndrome and its management, vena cava malformation as a new etiological factor and thrombosis in the upper limbs. DVT is usually seen in patients undergoing major surgeries. The guidelines for thrombo-prophylaxis in orthopaedic patients, radical pelvic surgeries, laparoscopic operations and risks versus benefits in regions with a low prevalence of DVT are thoroughly addressed. Cancer and its treatment are recognized risk factors for VTE and extended prophylaxis in ambulatory cancer patients is reviewed. The role of imaging and endovascular therapies in acute DVT, hypercoagulability in liver diseases and the challenges in developing countries are discussed.

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Phone: +385 (51) 770 447
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Phone: +86-21-62489820
Fax: +86-21-62489821

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