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Adding Chemoprophylaxis to Sequential Compression May Not Reduce the Risk of Venous Thromboembolism in Bariatric Surgery Patients

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Abstract

Background—Anticoagulation, the use of sequential compression devices on lower extremities peri-operatively, and early ambulation are thought to reduce venous thromboembolism (VTE) postoperatively and are recommended to reduce VTE risk. However, the evidence upon which this recommendation is based is not particularly strong. We demonstrate that even a large, multi-center cohort with carefully collected prospective data is inadequate to provide sufficient evidence to support, or refute, this recommendation.

Methods—The Longitudinal Assessment of Bariatric Surgery (LABS) participants from 10 centers in the United States who underwent their first bariatric surgery between March, 2005 and December, 2007 comprise the study group. We examined the ability to address the question of whether anti-coagulation therapy, in addition to sequential compression, reduces the 30 day incidence of VTE or death sufficiently to recommend the use of prophylactic anticoagulation, a therapy that is not without risk.

Results—Of 4416 patients, 396 (9.0%) received sequential compression alone, while the others also received anticoagulation therapy. The incidence of VTE within 30 days of surgery was small (0.25% among those receiving sequential compression alone, 0.47% when anticoagulation therapy was added), and the 30 days incidence of death was also small (0.25% vs. 0.34%, $p = 0.76$, for

sequential compression alone vs. sequential compression plus anticoagulation therapy). Estimates of the number of cases required to address the question of whether there is a difference in outcome related to VTE chemoprophylaxis, or whether the outcome rates are equivalent, range from 13,680 to at least 35,760 patients, depending upon whether superiority or equivalence is being analyzed.

Conclusion—Sufficient evidence from a clinical trial study to determine whether prophylactic anticoagulation added to compression devices further prevents VTEs is not available and such a trial is likely to be impractical. The data presented are insufficient to make a final recommendation concerning prophylactic treatment to prevent VTE in the 30 days following bariatric surgery.

Keywords

bariatric surgery; thromboembolism; pulmonary emboli; chemoprophylaxis; deep vein thrombosis; sequential compression

Introduction

Venous thromboembolism (VTE) is a serious and potentially life-threatening syndrome. Given that emboli develop more frequently in surgical patients than in the non-surgical population, the American College of Chest Physicians (ACCP) recommends use of low-dose unfractionated heparin, low-molecular-weight heparin, or a Factor Xa inhibitor for all moderate-risk general surgery patients ⁽¹⁾. The recommendations for higher-risk general surgery patients with multiple risk factors include combining pharmacologic therapy with graduated compression stockings or intermittent pneumatic compression devices. Given that most bariatric surgery operations are a major procedure, bariatric surgery would be considered at least moderate-risk general surgery ⁽¹⁾.

Specific to patients undergoing bariatric surgery, the American Academy of Clinical Endocrinologists (AACE), The Obesity Society (TOS), and the American Society for Metabolic and Bariatric Surgery (ASMBS) recommend prophylaxis against DVT ⁽²⁾. Furthermore, chemoprophylaxis using various anticoagulant regimens is recommended to be routinely administered to bariatric surgery patients unless contraindicated. The benefit of routine anticoagulation prophylaxis has been documented in surgical populations also at elevated VTE risk, and published statements of expert opinion support the conclusion that anticoagulation be utilized routinely in patients undergoing bariatric surgery unless contraindicated ⁽³⁾.

The extrapolation of recommendations from orthopedic surgery to bariatric surgery, however, might be inappropriate. Despite the rising prevalence of obesity in the general population, the incidence of VTE in general surgery patients has continued to decline since the 1950s ⁽⁴⁾, and this reduction might be a result of the wide-spread use of less invasive surgery techniques, better peri-operative care and shorter hospital stays.

Randomized clinical trials of chemoprophylaxis for VTE in obese surgical patients are lacking, which also casts some doubt on the accepted recommendations, especially in relation to the choice of drug and its dosage. Given that chemoprophylaxis carries a potential for bleeding, a potentially life-threatening risk, and that sequential compression alone has been shown to be safe and effective in terms of VTE prophylaxis in obese surgical patients ⁽⁵⁾, it has been hypothesized that sequential compression alone might provide sufficient VTE prophylaxis. Accordingly, we examined the feasibility of assessing the association between VTE prophylaxis received (sequential compression alone versus sequential compression plus anticoagulation) and the incidence of 30 day VTE or death among bariatric surgery patients in a non-randomized setting.

Methods

The Longitudinal Assessment of Bariatric Surgery (LABS) includes a cohort of unselected participants who underwent bariatric procedures at one of 10 clinical sites in the United States between 2005 and 2007 ⁽⁶⁾. Data were collected pre-surgery, peri-operatively, and 30 days following surgery for the purpose of assessing the short-term safety of bariatric surgeries ⁽⁷⁾.

Data in LABS were collected prospectively according to a standard protocol with common definitions and data collection time points across the clinical sites. However, LABS is an observational study and thus no treatment protocols were implemented. Using a large cohort with prospectively collected data according to rigorous protocol from multiple centers within the United States, LABS was considered as an appropriate source to provide evidence, albeit from an observational study, regarding the additional benefit of chemoprophylaxis over sequential compression alone for preventing VTE within 30 days of bariatric surgery in the United States.

Since VTE, which is comprised of deep vein thrombosis (DVT) or pulmonary embolism (PE), is such an important outcome to measure, LABS included all reported events to be adjudicated by a subcommittee comprised of surgeons and other physicians. Relevant medical records were obtained, de-identified, and distributed by the central Data Coordinating Center (DCC) to adjudication subcommittee members who, by consensus, determined whether the reported event was, in fact, a VTE, if in fact, there were adequate data upon which to base the decision.

Statistical Methods

LABS participant characteristics including demographics, medical history, medication use, surgical characteristics, peri-operative care, and post-operative events were compared between VTE prophylaxis strategy by Student *t*-tests or Wilcoxon non-parametric tests for continuous variables and chi-square test or Fisher's exact test for categorical variables. The incidence and 95% confidence intervals for VTE and other selected 30-day events were calculated using the Kaplan-Meier approach, and unadjusted comparisons of survival curves were performed using the log-rank test. All statistical analyses were performed with SAS version 9.2 (SAS Institute Inc) and all sample size calculations were performed using PASS 2008 (NCSS Kaysville, UT).

Results

LABS includes information about 5107 surgeries performed on 5076 people. Excluded from this analysis are 378 surgeries on participants who had a bariatric or foregut surgery prior to enrolling in LABS and 30 surgeries for which anesthesia was started, but the surgery was subsequently cancelled. An additional 26 surgeries in patients undergoing bariatric surgery were excluded because no VTE prophylaxis was administered. None of these patients had a VTE or died within 30 days of surgery. Also excluded were 252 of the 4673 remaining surgeries (5.4%) because the patients did not receive sequential compression. Of these, 1 participant had a DVT and a PE and another died of a non-VTE related cause within 30 days of surgery. The second surgery for 5 patients was excluded leaving 4416 patients in this analysis of whom 396 (9.0%) received sequential compression alone (S) as VTE prophylaxis while 4020 patients also received chemoprophylaxis for anticoagulation therapy (S+A). Unfractionated (subcutaneous) heparin (5000 units) and low molecular weight heparin (LMWH) accounted for the majority of chemoprophylaxis, with 53.5% of patients receiving only unfractionated heparin, 29.2% receiving only LMWH, and 8.9% receiving both unfractionated and fractionated heparin. A small proportion of patients received other forms

of chemoprophylaxis (0.3%) or a dose other than 5000 units of unfractionated heparin (8.1%)

Those in the S vs. S+A groups did not differ significantly with respect to age, race, ethnicity, or body mass index (BMI) whereas there was a significantly higher percentage of males and of smokers in the S compared to S+A (Table 1). Importantly, there was a site effect with over 68% of those receiving S coming from a single LABS site that contributed less than 0.5% of those receiving S+A.

Before surgery, the prevalence of hypertension, diabetes, congestive heart failure, history of VTE, asthma, ischemic heart disease, and pulmonary hypertension at baseline were not significantly different between the two groups, nor was the ability to walk at least 200 feet (Table 2). However, the prevalence of sleep apnea was significantly ($p<0.001$) higher in the S+A group (51.1%) than in the S group (34.6%).

With respect to medications being taken prior to surgery (Table 3), there were no significant differences in the use of anti-hypertensive medications, beta-blockers, oral diabetic medication or insulin among participants with diabetes, statins or other lipid-lowering agents, or therapeutic anticoagulation medication. However, the prevalence of current narcotic and anti-depressant use was greater in those who ultimately received S+A than S only.

Surgery was performed laparoscopically for 90.8% of patients overall and did not differ significantly in the two groups defined by VTE prophylaxis used (Table 4). The percentage of patients having either a duodenal switch or sleeve gastrectomy was significantly greater ($p<0.001$) in those in the S group than the S+A group, which reflects the site difference noted above. Perhaps as a result, on average the duration of surgery was 18.3 minutes longer ($p<0.001$) for participants in the S group (140.1 minutes) compared to those in S+A (121.8 minutes). The use of vena cava filter was uncommon-less than 2% overall-and did not differ significantly in the two groups. Blood loss during surgery of at least 50 cc, was higher among the S group as compared to the S+A patients (35.5% versus 27.6%, $p=0.001$). However there was not a significant difference in the amount of blood loss by type of VTE prophylaxis received among those who lost blood (median 100 cc in both groups, $p=0.97$). Transfusions were required for five patients who received chemoprophylaxis and no transfusions were noted in the S group.

With the exception of median length of stay and type of surgical approach (open versus laparoscopic), outcomes were similar in the two groups (Table 5). Length of stay tended to be significantly longer ($p<0.001$) among those who received S (median=3 days) compared to those who had S+A (median=2 days). Participants undergoing open versus laparoscopic surgery experienced a higher incidence of VTE events regardless of prophylaxis (1.73% versus 0.32%, $p<0.001$) and those who received S+A were at highest risk when stratified by surgical approach and prophylaxis received. As can be seen by the confidence intervals, however, the ability to state with reasonable assurance whether the percentages of all events differed, or not, between the prophylaxis groups was limited. Thirty day mortality was only 0.3% overall. Initially, 19 patients were reported undergoing treatment for a suspected VTE within 30 days of surgery (incidence=0.43%). During the adjudication process, one event was adjudicated as something other than a VTE and another 6 could not be confirmed as either a DVT or a PE. Evidence of PE was the adjudicated cause of death for an additional two participants.

When designing LABS, the assumed 30 day incidence of DVT or PE was 0.6% and it was assumed that 20% of the sample would be prescribed LMWH. With these figures, a sample size calculation indicated that it would require 41,306 people to be able to test whether the

risk of VTE for people prescribed LMWH was half, or less, of that for people not prescribed for 90% power and 32,667 for 80% power, assuming a two-sided test with $\alpha=0.05$. LABS was originally designed to include 12,000 participants which would have provided 27% power to detect a halving of risk and 73% power to detect a quartering of risk. Thus, without a very large effect, there was little chance that LABS could identify a benefit of S+A to S alone with respect to preventing VTE within 30 days of surgery. In point of fact, the numbers required to adequately test for reasonable differences in outcome are substantially larger than the final LABS sample of nearly 5000 participants undergoing an initial bariatric surgery. LABS, which is an observational study, was only able to recruit from those participants who underwent evaluation for bariatric surgery from the LABS sites, and the number of surgeries performed was substantially fewer than originally anticipated.

However, in the case of additional prophylaxis, especially one that carries a certain amount of risk such as chemoprophylaxis^(8–10), an equivalence study is warranted. This type of study, in contrast to the more common superiority study, is designed to test whether an alternative therapy is at least as good as the “control” therapy. In this case, if compression stockings alone provide at least the same protection against post-operative VTE as does compression stockings plus chemoprophylaxis, then the treatments would be deemed to be equivalent and the addition of chemoprophylaxis not warranted. If we are willing to accept that risks in the range of from 0.0% to 1.2% for the chemoprophylaxis group are equivalent to a risk of 0.6% in the non-chemoprophylaxis group, then if the true risk of chemoprophylaxis is actually 0.3% higher than sequential compression alone (i.e. 0.9%), total samples of 35,760 and 49,530 are required to have 80% and 90% power, respectively, using an equivalence test with an alpha-level=0.05.

Discussion

Despite including a large unselected cohort of severely obese patients undergoing bariatric surgery from multiple surgical centers in the United States, the LABS cohort is not large enough to provide strong evidence that chemoprophylaxis added to sequential compression is beneficial or harmful with respect to VTE or mortality within 30 days of surgery. Although the point estimate for VTE in the S+A arm is numerically larger than in the S arm, the confidence intervals about these estimates are large enough that it is not possible to determine, with reasonable assurance, whether the true rates are the same or different. The two study groups appeared to be comparable except for a higher percentage of males and smokers in the group receiving compression alone, potential risk factors for VTE. Also, in spite of the longer average anesthesia time among the compression only patients, a known factor for occurrence of DVT, and a longer median hospital stay, the incidence of mortality was also not significantly different.

Whether or not anticoagulation should be added to sequential compression for preventing peri-operative VTE is an important question. Although multiple guidelines strongly recommend thromboprophylaxis, there is little evidence to support the use of this potentially dangerous and expensive therapy in bariatric surgery patients. This study demonstrated that even a study as large as LABS is not large enough to address this question in a prospective rigorous manner. In fact, a randomized clinical trial would require at least 84,000 people to adequately address the issue. Such a study has not been done, and is not feasible.

The perceived high incidence of VTE following surgery is from studies completed when surgery was a major event and performed only by laparotomy. In the current era, surgery is often minimally invasive, hospital stays are generally shorter, and patients are encouraged to ambulate quickly. In fact the incidence of VTE has been decreasing steadily since the 1950s⁽⁴⁾. Lindblad and colleagues in Malmö, Sweden, reported that the incidence of

pulmonary emboli decreased from 0.4% in the 1960s to 0.3% in the 1970s to 0.2% in the 1980s. Of note, there has been an increase in the number of patients operated on who had autopsy confirmed pulmonary embolism and who received thromboprophylaxis.

While there is some thought that obesity is a risk factor for VTE, the data are not consistent. Among 1006 patients consecutively treated for VTE enrolled in MAISTHRO database and studied for recurrent VTE, there was not a significant association between the presence of diabetes, obesity, hypercholesterolemia or smoking with risk of VTE recurrence⁽¹¹⁾. Male sex and arterial hypertension were independently associated with higher risk of recurrent VTE after terminating anticoagulant therapy for the initial VTE event. The development of PE among patients undergoing bariatric surgery was associated with a higher body mass index (57.2 ± 2.4 kg/m² versus 49.9 ± 0.2 kg/m², $p < 0.01$) and remained a significant risk factor after adjusting for other important covariates⁽¹²⁾. The RIETE registry examined the association between BMI and mortality during the first 3 months of therapy for acute VTE⁽¹³⁾. Of the 10,114 patients enrolled as of March 2007: 153 (1.5%) were underweight (BMI < 18.5), 2882 (28%) had a normal weight (BMI 18.5–24.9), 4327 (43%) were overweight (BMI 25.0–30), and 2752 (27%) were obese (BMI > 30). The rate of mortality following PE decreased by BMI and the risk for major bleeding complications was significantly higher among underweight individuals compared to all others. A large autopsy study examining the association between body mass index and antiplatelet therapy reported that morbid obesity was an independent risk factor in cases of sudden death from antiplatelet therapy after the exclusion of previously established clinical, environmental, and molecular risk factors⁽¹⁴⁾.

The true incidence of VTE following weight loss surgery is not well characterized. A study published by Brasileiro reported the incidence of DVT was 0.79% with the use of color Doppler ultrasound performed before and after gastric bypass among patients with no history of DVT⁽¹⁵⁾. This is in contrast to the Murr study of 660 patients of whom 23 (3.5%) developed postoperative VTE events⁽¹⁶⁾.

Laparoscopic surgery poses risk for VTE development because this surgical method requires a pneumoperitoneum at 15 mmHg, which is known to decrease lower extremities venous blood return⁽¹⁷⁾. Still, the potential thrombogenic effect may be overridden by lowering the coagulation cascade activation postoperatively and may still be associated with less VTE risk compared to open surgery, which causes significant abdominal wall trauma.⁽²⁷⁾ The incidence of VTE among super obese patients (BMI > 55 kg/m²) who underwent open gastric bypasses (OGB) compared with a similarly matched group of laparoscopic gastric bypasses (LGB) was 2.1% (four events) versus 0.9% (1 event)⁽¹⁸⁾. The authors observed that despite the theoretical hindrance to venous return and vena caval compression observed with pneumoperitoneum, fewer PEs occurred in the laparoscopic group. Although 90% of obese patients now undergo laparoscopic surgery for weight loss, open surgery was associated with significantly higher incidence of VTE in LABS as compared to those undergoing only laparoscopic surgery (1.73% versus 0.32%, $p < 0.001$). In contrast, a study of 3,861 patients undergoing bariatric procedures at a single institution between 1980 and 2004 reported no difference in the incidence of PE between open (0.84%) and laparoscopic (0.88%) surgery patients⁽¹²⁾. A recent report of 618 patients undergoing laparoscopic Roux-en-Y gastric bypass who received the same thromboprophylaxis regimen were followed with lower extremity color Doppler ultrasonography within the first 24 hours after the surgical procedure⁽¹⁹⁾. The overall rate of DVT in the group of 500 consecutive patients was 0.2%, with no clinically significant pulmonary embolism. The incidence of VTE among patients undergoing laparoscopic gastric banding (LAGB), where the anesthesia time and operative trauma is much smaller, has also been examined. In a review of deaths after LAGB reported in the literature, data from 9,682 patients were collected from 24 articles and 48 (0.51%)

deaths were reported ⁽²⁰⁾. Pulmonary embolism was the most frequent cause of death, in 11 (22.9%) patients, with an incidence at 0.11%, or 1 in every 1000 patients. The guidelines for VTE prophylaxis in the “open surgery” era may no longer apply in an era where the majority of surgery is performed laparoscopically.

The advantages of sequential compression without antiplatelet therapy include lowering the risks of post-operative hemorrhage associated with chemoprophylaxis, and avoiding heparin-induced thrombocytopenia ⁽²¹⁾. Intermittent pneumatic compression has been shown to decrease the risk of DVT by 62% ⁽²²⁾. Furthermore, sequential compression alone may be sufficient to decrease VTE in obese surgical patients, in today’s modern surgical era. In fact several reports involving cohorts of obese surgical patients treated with sequential compression alone have observed a low incidence of postoperative VTE. Among 380 patients who underwent laparoscopic gastric bypass with peri and postoperative intermittent pneumatic compression followed by early ambulation over a 3 year period, nine patients had clinical evidence of severe, chronic venous disease pre-operatively and one patient (0.26%) experienced a clinically evident DVT limited to the popliteal vein on duplex ultrasonography ⁽²³⁾. No clinically evident pulmonary thromboembolism occurred in this study group. A retrospective chart review of 107 patients who underwent gastric bypass reported no incidence of VTE during hospitalization, and only one patient developed a symptomatic DVT after discharge when external compression devices and ambulation orders were used ⁽²⁴⁾.

Given that there are inherent and potentially serious risks to the use of chemoprophylaxis to prevent VTE, perhaps a better strategy is to administer chemoprophylaxis to high-risk subgroups, such as those with a history of VTE, hypercoagulable state, or profound immobility, rather than the entire obese surgical population

To date, there have been few direct comparisons of VTE strategies in the obese population and among those undergoing bariatric surgery. Rocha and colleagues published a review article of VTE and thromboprophylaxis among hospitalized obese patients ⁽²⁵⁾. Of 37 publications, only 6 studies evaluated prophylactic methods (unfractionated heparin, LMWH, and sequential compression devices). Given the small sample size of each study and the low incidence of VTE events, none of the studies provided a definitive conclusion about the most effective and safe VTE prophylactic method for obese patients.

Despite the fact that evidence-based clinical practice guidelines for VTE prevention continue to be updated and re-published ⁽¹⁾, physicians do not appear to be incorporating the guidelines in their clinical practice. A recent publication reported an overall compliance rate of 13% with ACCP guidelines among a review of 123,304 hospital admissions ⁽²⁸⁾. Appropriate dosing related to weight is difficult, as is duration of chemoprophylaxis in bariatric surgery; there is a significant incidence of VTE that occur post discharge. The incidence of VTE is actually quite low, and sequential compression devices alone may be sufficient to prevent VTE without adding the hemorrhagic risks of chemoprophylaxis.

There are some limitations to this investigation. It was based on an observational registry of consecutive patients undergoing bariatric surgery and not a randomized trial. Selection of the VTE prophylaxis was the choice of the surgeon and thus it is possible there was an unmeasured selection bias toward the use of compression devices alone and that lower-risk patients were selected to receive compression only. However, the baseline characteristics show that the two groups are relatively similar with males and smokers being relatively more common in the group receiving compression devices alone than in the group also receiving chemoprophylaxis. It is also possible that VTE events could have been missed

because screening via ultrasound was not mandated. This scope of this study is limited because the sample size was not adequately powered to compare VTE treatment options.

Conclusion

In conclusion, the overall incidence of VTE (0.45%) or all-cause death (0.34%) in LABS was small. The addition of anticoagulation therapy to the use of sequential compression devices may, or may not, lower the rate of VTE following bariatric surgery; the sample size in LABS was inadequate to address this question with a reasonable error rate, unless the effect of adding anticoagulation was extremely large. While further study of this topic is warranted, obtaining sufficient evidence whether prophylactic anticoagulation or compression devices prevent VTEs is likely to be beyond the resources available for a reliable prospective study.

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Table 1

Baseline characteristics

	All (n=4416)	Chemoprophylaxis and sequential compression (n=4020)	Sequential compression only (n=396)	p- value
Median (and range) age (y)	45.0 (36,53)	45 (36, 53)	44 (34, 53)	0.09
% Male	20.8	19.9	29.5	< 0.001
% Caucasian	87.9	88.0	86.3	0.31
% Hispanic	5.3	5.1	7.6	0.039
Median (and range) weight (lbs)	286 (254, 330)	286 (254, 330)	289 (255, 333)	0.37
Median (and range) body mass index (kg/m ²)	46.5 (42.2, 52.4)	46.5 (42.1, 52.4)	46.2 (42.3, 52.4)	0.89
Current smoking %	3.6	3.4	6.6	0.001

Table 2

Prevalence of comorbidities (%) prior to bariatric surgery

	All (n=4416)	Chemoprophylaxis and sequential compression (n=4020)	Sequential compression only (n=396)	p-value
Hypertension	55.0	55.0	54.8	0.92
Diabetes	33.4	33.7	30.3	0.17
Congestive heart failure	2.3	2.3	1.8	0.49
Asthma	22.7	23.0	19.9	0.17
Prior DVT/PE	3.3	3.4	2.5	0.36
Sleep apnea	49.7	51.1	34.6	<0.001
Coronary artery disease	5.3	5.3	5.8	0.67
Pulmonary hypertension	1.2	1.2	0.8	0.62
Functional status				0.20
Walk 200 feet unassisted	93.4	93.1	95.4	
Walk 200 feet assisted	4.9	5.0	3.5	
Unable to walk 200 feet	1.7	1.8	1.0	

Table 3

Medication use at baseline (%)

	All (n=4416)	Chemoprophylaxis and sequential compression (n=4020)	Sequential compression only (n=396)	p- value
Anti-hypertensive	48.2	48.6	44.8	0.15
Beta-blocker	18.0	18.1	17.2	0.65
Oral diabetic medication or insulin *	85.3	85.0	88.3	0.32
Statin or other lipid lowering agent	26.7	26.4	29.8	0.15
Therapeutic anticoagulation	4.4	4.5	4.0	0.69
Narcotic	16.3	16.9	10.6	0.001
Anti-depressant	40.6	41.2	34.4	0.009

* Among participants reporting diabetes mellitus

Table 4

Peri-operative care

	All (n=4416)	Chemoprophylaxis and sequential compression (n=4020)	Sequential compression only (n=396)	p-value
Laparoscopic %	90.8	90.6	92.2	0.32
Vena cava filter %	1.6	1.5	2.0	0.47
Surgery received				<0.001
Roux-en-Y gastric bypass	72.3	73.4	61.4	
Adjustable band	24.9	25.9	15.1	
Sleeve gastrectomy	1.7	0.4	15.4	
Duodenal switch	0.8	0.1	7.8	
Operative time (min)	123.5	121.8	140.1	<0.001
Blood loss (> 50 cc) %	28.3	27.6	35.5	0.001

Table 5

Post-operative events within 30 days following bariatric surgery

	All (n=4416)	Chemoprophylaxis and sequential compression (n=4020)	Sequential compression only (n=396)	p-value
Median length of stay (days)	2.0	2.0	3.0	<0.001
Mortality % (95% CI [*])	0.34	0.35 (0.21 – 0.59)	0.25 (0.04 – 1.78)	0.76
Re-hospitalization % (95% CI [*])	5.57	5.67 (5.00 – 6.43)	4.58 (2.91 – 7.17)	0.35
Abdominal re-operation % (95% CI [*])	2.52	2.54 (2.10 – 3.08)	2.28 (1.19 – 4.33)	0.75
Treatment for cardiac event % (95% CI [*])	0.16	0.18 (0.08 – 0.38)	0.0 (0 – 0)	0.40
Incidence of VTE % (95% CI [*])	0.45	0.47 (0.30 – 0.74)	0.25 (0.04 – 1.78)	0.53
Open surgery	1.73	1.87 (0.90 – 3.89)	0.0 (0 – 0)	<0.001
Laparoscopic surgery	0.32	0.33 (0.19 – 0.60)	0.27 (0.04 – 1.93)	

^{*}
CI: Confidence interval