Thromboprophylaxis in obese surgical patients in the Netherlands, current practice and a review of the available guidelines

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Abstract

Background
Obesity is associated with an increased risk of venous thromboembolism. Low-molecular-weight heparins (LMWH) significantly reduce this risk. So far there is no consensus on the optimal dose and duration of LMWH in obese patients. The aim of this study is to assess the current practice of thromboprophylaxis in obese patients in the Netherlands and to describe current guidelines for thromboprophylaxis in obese patients.
Methods
Data on type, duration and dose of thromboprophylaxis for obese patients from all the departments of general surgery (n=90) in the Netherlands were obtained by online questionnaires and telephone interviews. A literature search was conducted to identify available guidelines.
Results
With a response of 93% (n=84) of institutes, 63% reported the use of an in-hospital protocol of thromboprophylaxis for surgical patients. In 77% LMWH dose was adjusted, based on pre-determined total body weight (72%) or body mass index (BMI) (18%). Most hospitals (62%) doubled the standard dose above a pre-determined cut-off limit of body weight. These cut-off limits varied widely ranging from 70-150 kg total body weight or a BMI from 30-50 kg/m^2. In 13% of hospitals obese patients were given thromboprophylaxis for an extended period after discharge, with a maximum of six weeks. None of the identified guidelines in the literature search included advice about dose adjustments or adjustments in duration of thromboprophylaxis for this special group of patients.
Conclusion
There is a wide variety in the current practice of thromboprophylaxis in obese surgical patients in the Netherlands. As current guidelines lack practical dosing advices, further research to identify the optimal dose and duration is mandatory.

Introduction

The prevalence of obesity (body mass index (BMI) > 30kg/m^2) has doubled worldwide in the last two decades, now affecting a global estimate of over 1.7 billion individuals (1, 2). Obesity is associated with multiple co-morbidities, such as type 2 diabetes mellitus and hypertension (2), and a two to three times increased relative risk of venous thromboembolism (VTE) compared to non-obese patients (3).
The administration of low-molecular-weight heparins (LMWH) in surgical patients significantly reduces the incidence of VTE postoperatively (4-6). LMWH derives its antithrombotic activity mainly by binding to anti-thrombin and thereby trapping factor Xa out of the coagulation. LMWH has several benefits over unfractionated heparin, such as a single daily dosing, a more predictable dose-response relationship and a higher effectiveness in the prevention of VTE following bariatric surgery (7, 8).
The increase in the prevalence of obesity introduces new issues in patient care such as the optimal dose and duration of administration of LMWH for this group of patients. Only few studies are available on the optimal dosage of LMWH in patients with (morbid) obesity (9-11), as this patient group is often excluded from clinical trials.
We conducted a survey to analyse the current practice in thromboprophylaxis in obese surgical patients in the Netherlands and conducted a literature search to identify specific guidelines on dosing and duration of thromboprophylaxis in obese patients.

Methods

Questionnaire
The survey was designed using freely available Google™ Docs tools (Google Inc, CA, USA) and was uploaded as a Google™ Docs form. A link to the questionnaire with an introductory cover letter was sent by email to one representative of each department of general surgery (n=90) in the Netherlands. The survey consisted of 10 multiple choice questions and two open questions on thromboprophylaxis in obese patients (Table I). Type of coagulation, duration and dose of thromboprophylaxis in obese patients were assessed, as well as the used definition of obesity and the availability of hospital-based guidelines concerning thromboprophylaxis in obese patients. Data were completed by repeated mailing and telephone interviews with non-responders.

Table I *Questions of survey on prophylactic doses of low-Aolecular weight heparin in obese surgical patients.*

1.Which low-molecular-weight heparin (LMWH) is used in healthy normal-weight and obese patients for thromboprophylaxis?
2.What LMWH dose is used in healthy normal-weight patients for thrombosis prophylaxis?
3.How many days will thromboprophylactic therapy with LMWH be continued after general surgical procedures to prevent venous thromboembolic complications in normal-weight patients with a healthy kidney function (patients without oral anticoagulation)?
4.Will the prophylactic dose of LMWH be adjusted for obese patients?
5.Is there a protocol for prophylactic dose adjustment of LMWH in obesity in your hospital?
6.If so, to what patient groups does this protocol apply?
7.What is the cut-off body weight for LMWH adjustment?
8.Based on what body weight will LMWH doses be adjusted?
9.How will LMWH doses be adjusted in obesity?
10.How many days will LMWH be continued after general surgical procedures to prevent venous thromboembolic complications in obese patients (patients without oral anticoagulation and normal kidney function)?
11.Are anti-Xa levels checked in obese patients receiving venous thromboembolic prophylaxis?
12.Does the surgical department in your hospital perform bariatric procedures?

Statistical methods
Data analysis was done using SPSS 17.0 (IBM Corporation, NY, USA) for Windows. We compared differences in prescription practice in teaching hospitals (university and non-university) to non-teaching hospitals, and bariatric clinics to non-bariatric clinics using the chi-squared test. The probability level accepted for statistical significance was set at $p < 0.05$ for all comparisons.

Guidelines
A literature search for (inter)national guidelines on thromboprophylaxis in obese patients was performed in Pubmed and SUM Search. The following search terms were used ("Thrombosis"[Mesh] OR "Venous Thrombosis"[Mesh] OR "thrombosis" OR "thromboprophylaxis" OR "thromboembolism") AND ("Heparin, Low-Molecular-Weight"[Mesh] OR "low-molecular weight heparin" OR "LMWH") AND ("Guideline" OR "Guidelines as Topic"[Mesh] OR "Guideline" [Publication Type]).

Results

Questionnaire

Of the 90 contacted surgical departments, questionnaires were completed by 84 hospitals (93% response). The most commonly used LMWH for VTE prophylaxis was nadroparin (n=62, 74%), followed by dalteparin (n=16, 19%) and enoxaparin (n=6, 7%). Of the hospitals that used nadroparin, 74% (n=55) used nadroparin 2,850 IU once daily as standard dose for non-obese patients. Dalteparin was most commonly dosed as 2,500 IU per day (n=13, 81%), although three hospitals (19%) reported a dosage of 5,000 IU for non-obese patients. Enoxaparin was either dosed as 20 mg per day (n=3, 50%) or 40 mg per day (n=3, 50%) for non-obese patients. The majority of the surgical departments continued thromboprophylaxis in non-obese patients until discharge (n=69, 82%). In 12% of hospitals (n=10) thromboprophylaxis was extended in these patients after discharge until the non-obese patient was ambulating well. The duration of thromboprophylaxis was reported to be depending on the surgical procedure in 5% of the hospitals.

Of all institutes, 63% (n=53) reported the use of an in-hospital thromboprophylaxis protocol for obese patients. In 65 hospitals (77%), the prophylactic LMWH doses were adjusted for obese patients. Adjustments were mostly based on total body weight (n=47, 72%) and less commonly on pre-determined BMI (n=12, 18%), individual characteristics (n = 1) or in consultation with the anaesthesiologist (n = 1). Four hospitals (6%) did not report the basis on which the LMWH dose was adjusted. In two hospitals (3%), LMWH dose was only adjusted in (morbidly) obese patients undergoing bariatric surgery.

Cut-off limits for dosing adjustment varied widely, with a median BMI of 33 kg/m2 (range 30 - 50 kg/m^2), and a median total body weight of 80 kg (range 70 - 150 kg). Two hospitals used variable cut-off limits, based on individual characteristics. Most centres adjusted LMWH doses by doubling the dose used in non-obese patients (n=53, 62%). In other hospitals (n=7, 8%), the dose of LMWH was increased with a factor 1.3 - 1.5, resulting for nadroparin in 3,800 IU (n=6) and for dalteparin in 7,500 IU (n=1). Five hospitals (6%) individualized the LMWH by dosing on IU per kilograms. Eleven hospitals (13%) extended the LMWH prophylaxis in patients with obesity, to a duration varying from 1 to 6 weeks postoperative. In 7% (n=6) of the hospitals, anti-Xa levels were measured in individual cases. However, none of these hospitals reported whether and how the dose of LMWH should be adjusted based on these anti-Xa levels.

Comparing teaching hospitals (n=52) with non-teaching hospitals (n=32), we found no significant differences for type of LMWH, adjustment of dose or duration, presence of an in-hospital protocol for obese patients or testing of anti-Xa levels (Table II). Dose adjustment of LMWH did not significantly vary between bariatric (n=27, 32%) and non-bariatric centres (n=57, 68%). Bariatric clinics did more often extend the duration of thromboprophylaxis (33% versus 4%, p<0.005), however in some of these clinics thromboprophylaxis was only extended in patients undergoing bariatric surgery (n=3). Neither the choice of LWMH, nor the existence of a protocol for adjusting LMWH in obese patients, nor the number of hospitals testing anti-Xa levels did significantly differ between bariatric and non-bariatric centres (Table III).

Table II *Survey results of teaching hospitals versus non-teaching hospitals.*

	Total (n=84) n (%)	Non-teaching (n = 32) n (%)	Teaching (n = 52) n (%)	p-value
LMWH used:				0.058
dalteparin	16 (19)	6 (19)	10 (19)	
enoxaparin	6 (7)	5 (16)	1 (2)	
nadroparin	62 (74)	21 (66)	41 (79)	
Adjusting LMWH dose for obese	65 (77)	38 (73)	27 (84)	0.229
Adjusting LMWH duration for obese	11 (13)	2 (6)	9 (17)	0.145
Existence of hospital protocol for obese	53 (63)	22 (73)	31 (67)	0.582
Anti-Xa tested in obese	6 (7)	1 (3)	5 (10)	0.258

Guidelines

The most recent guideline on thromboprophylaxis is the guideline of the American College of Chest Physicians (ACCP), which has been revised in February 2012. This 9th edition advises to follow manufacturers' recommendation for pharmacological thromboprophylaxis (12-14). The ACCP guideline recognized obesity as a risk factor for VTE in both medical and bariatric surgical patients. It states that even though coagulation monitoring is generally not necessary, monitoring in special patient groups, including obese patients is advised (14). The guidelines of the National Institute for Health and Clinical Excellence (NICE) (15) and the Dutch Institute for Healthcare Improvement (16) also recognize obesity as a risk factor, but do not include advices about adjustments in dose or duration of thromboprophylaxis in obese patients. The guideline of the Scottish

Table III *Survey results of bariatric clinics versus non-bariatric clinics.*

	Total (n=84) n (%)	Bariatric (n = 27) n (%)	Non-bariatric (n = 57) n (%)	p-value
LMWH used:				0.073
dalteparin	16 (19)	8 (30)	8 (14)	
enoxaparin	6 (7)	0 (0)	6 (11)	
nadroparin	62 (74)	19 (70)	43 (75)	
Adjusting LMWH dose for obese	65 (77)	21 (78)	44 (77)	0.952
Adjusting LMWH duration for obese	11 (13)	9 (33)	2 (4)	< 0.05
Existence of hospital protocol for obese	53 (63)	18 (72)	35 (69)	0.764
Anti-Xa tested in obese	6 (7)	2 (8)	4 (7)	0.946

Intercollegiate Guidelines Network (SIGN) does include obesity as a risk factor, but consequently states that patients undergoing bariatric surgery should receive thromboprophylaxis as recommended for those undergoing general surgery. Weight-based dose adjustments are not advised for LMWH according to the SIGN guideline, although it is advised to monitor LMWH activity in patients at extremes of weight (17). The German guideline describes obesity as a moderate risk factor and it recognizes that sometimes weight-based dose adjustments are made, without any specification or appraisal. No specific recommendations regarding dose or duration adjustments are made (18). The guideline of the French Society of Anaesthesiology and Reanimation only advises dose adjustments of prophylactic LMWH in overweight obstetric patients and does not make specific recommendations for surgical patients (19).

Discussion

In this survey we showed that in the majority of hospitals (77%), the LMWH dose is increased for obese patients but various regimens are used in clinical practice both in terms of dosing and duration of antithrombotic treatment. Besides, available guidelines lack practical dosing advices for this special group of patients.

Obesity, defined as a BMI > 30 kg/m^2 or greater, is a known risk factor for venous thromboembolism (VTE) (20) with a more than two times increased relative risk for deep venous thrombosis (DVT) (3) and pulmonary embolism (PE) for hospitalized patients compared to non-obese (21). A linear association between body weight and risk of VTE has been shown with an estimated six-fold increase in the risk of PE in women with a BMI > 35 kg/m^2 (22). With the rising incidence of obesity, health services worldwide are confronted with an ever increasing number of patients undergoing bariatric surgery. Most clinical trials and retrospective analyses on the incidence of VTE in (morbidly) obese patients involve the group of patients undergoing bariatric surgery. The perioperative incidence of VTE, either symptomatic or asymptomatic, after laparoscopic bariatric surgery appears to be relatively low (below 1%), regardless of the antithrombotic prophylaxis regimen (23). This is probably due to short operation times and short immobilization. The incidence of VTE after laparoscopic bariatric surgery for patients receiving thromboprophylactic therapy increases to almost 3% up to 6 months following surgery (24). Within the bariatric population, several contributing risk factors identified for VTE were: previous VTE, age > 55 years, smoking and male sex (24). The risk of postoperative VTE in obese patients undergoing orthopaedic, major gynaecological of oncologic abdominal surgery may be higher, underlining the need for optimal and individualized prophylactic therapy in this special group of patients.

Different dosing strategies for LMWH in obese patients have been proposed but most reports are inconclusive on how to individualize the LMWH dosing regimen (9-11). Retrospective subgroup analyses from large VTE prophylaxis trials using a similar standard dose of LMWH in obese and non-obese hospitalized patients show no significant difference in postoperative VTE in both groups (25, 26). Prospective studies on different dosing regimens for VTE prophylaxis in morbidly obese subjects, mostly involving patients undergoing bariatric surgery, show equivocal results. Kalfarentos et al. comparing two doses of nadroparin (5,700 IU vs. 9,500 IU) in a randomized study among morbidly obese patients undergoing Roux-en-Y gastric bypass surgery, reported no VTE events in both groups. However, the higher dose resulted in two major haemorrhages while no major bleeding event occurred in patients receiving the lower dose (27). A higher dose of 40 mg enoxaparin showed to reduce non-fatal VTE compared to 30 mg for obese patients (0.6% vs. 5.4%) without increased incidence of bleeding complications (28). Singh et al. found no VTE events in 170 morbidly obese patients (BMI 40-59 kg/m^2) using a BMI-stratified enoxaparin dosing schedule, with doses ranging for 30 to 60 mg (29). These results support the evidence to increase the LMWH dose for obese patients, although the optimal dose is still unknown.

As there are currently no evidence-based dosing guidelines available for prophylactic LMWH therapy in obese patients, monitoring of anti-Xa levels

four hours after the first dose is often recommended (30). No therapeutic range has been defined for obese patients, but it seems rational to aim for the prophylactic range in non-obese patients of 0.2-0.5 IU/mL at four hours after administration of LMWH (11). Most studies have focused on the effect of increased LMWH doses on anti-Xa levels. Rowan et al. achieved a higher percentage of therapeutic anti-Xa levels (9% vs. 41.7%) for 40 mg enoxaparin compared to 30 mg enoxaparin (31). Although therapeutic levels were not reached in over 50% of patients, no VTE events were reported. In another study less subtherapeutic levels (0% vs. 40%) were achieved with a higher dose of 60 mg enoxaparin compared to 40 mg enoxaparin, without increasing the number of bleeding complications (32). Both studies involved patient groups with a mean BMI of 48 kg/m^2 (31, 32). Although results of some of the aforementioned studies may seem inconclusive, it appears that a standard dose of LMWH as used in the non-obese population is insufficient in the (morbidly) obese population and dose adjustments are warranted. A recent review by Nutescu et al. recommended a 30% higher dose for morbidly obese patients, as well as monitoring anti-Xa levels in individuals weighting over 190 kilograms (11).

In a previous study among bariatric patients we showed that after a double dose of nadroparin compared to non-obese patients, still 50% of the morbidly obese patients showed peak anti-Xa levels below the recommended range. These peak anti-Xa levels correlated with lean body weight and therefore lean body weight was proposed as dosing scalar for thromboprophylaxis with LMWH nadroparin (33). In addition, peak anti-Xa levels in morbidly obese patients were not found to correlate with total body weight or BMI (34). As LMWH distribute mainly to the intravascular compartment, instead of tissues and body fat, these findings might be explained by the non-linear increase of plasma volume with the increase in total body weight (35).

The currently available guidelines do not specifically advise dose adjustment of LMWH in morbidly obese patients, and most recommend to use product labels (12-19). This advice is often ignored, as proven by Barras et al., showing that 96% of questioned hospitals had a LMWH strategy that contravened with product labels (9). In clinical practice in Dutch hospitals, 62% of the hospital doubled the LMWH dose for thromboprophylactic therapy in obese patients. However, the cut-off point for body weight above which the LMWH dose was increased differed between hospitals.

Beside the optimal dose, there is debate about the duration of prophylaxis after surgery. Our study shows that extended duration of prophylaxis is not yet common practice in the Netherlands. Only 13% of respondents indicate to adjust duration of prophylaxis in obese patients. Significantly more surgical departments performing bariatric surgery (33%, $p<0.05$) extended the duration of thromboprophylaxis after discharge. The benefits of extended duration of prophylaxis have been studied in bariatric populations and showed a reduced incidence of thromboembolic complications in patients receiving prophylaxis up to ten days post-discharge (10, 36, 37). To date, guidelines do not include this evidence.

As bariatric procedures are exponentially increasing worldwide this patient group could be a target population for the study of perioperative thromboprophylaxis regimen in the subset of obese patients. As the incidence of post-operative VTE appears to be rather low in the bariatric population, future studies should focus on risk groups within this population, i.e. patients within the highest ranges of BMI or comorbidities. Prospective studies should identify the optimal dosing schedules for the obese patients and clarify the benefit of extended prophylaxis. The increasing numbers of obese surgical patients and the current wide variety in the practice of thromboprophylaxis demonstrate the necessity of uniform guidelines for LMWH prophylaxis in obese patients.

References

1. Deitel M. Overweight and obesity worldwide now estimated to involve 1.7 billion people. Obes Surg. 2003;13(3):329-30.
2. Kopelman PG. Obesity as a medical problem. Nature. 2000;404(6778):635-43.
3. Stein PD, Beemath A, Olson RE. Obesity as a risk factor in venous thromboembolism. Am J Med. 2005;118(9):978-80.
4. Alikhan R, Cohen AT. Heparin for the prevention of venous thromboembolism in general medical patients (excluding stroke and myocardial infarction). Cochrane Database Syst Rev. 2009(3):CD003747.
5. Mismetti P, Laporte S, Darmon JY, Buchmuller A, Decousus H. Meta-analysis of low molecular weight heparin in the prevention of venous thromboembolism in general surgery. Br J Surg. 2001;88(7):913-30.
6. Rasmussen MS, Jorgensen LN, Wille-Jorgensen P. Prolonged thromboprophylaxis with low molecular weight heparin for abdominal or pelvic surgery. Cochrane Database Syst Rev. 2009(1):CD004318.
7. Geerts WH, Pineo GF, Heit JA, Bergqvist D, Lassen MR, Colwell CW, et al. Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest. 2004;126(3 Suppl):338S-400S.
8. Birkmeyer NJ, Finks JF, Carlin AM, Chengelis DL, Krause KR, Hawasli AA, et al. Comparative Effectiveness of Unfractionated and Low-Molecular-Weight Heparin for Prevention of Venous Thromboembolism Following Bariatric Surgery. Arch Surg. 2012;147(11):994-8.
9. Barras MA, Kirkpatrick CM, Green B. Current dosing of low-molecular-weight heparins does not reflect licensed product labels: an international survey. Br J Clin Pharmacol. 2010;69(5):520-8.
10. Borkgren-Okonek MJ, Hart RW, Pantano JE, Rantis PC, Jr., Guske PJ, Kane JM, Jr., et al. Enoxaparin thromboprophylaxis in gastric bypass patients: extended duration, dose stratification, and antifactor Xa activity. Surg Obes Relat Dis. 2008;4(5):625-31.
11. Nutescu EA, Spinler SA, Wittkowsky A, Dager WE. Low-molecular-weight heparins in renal impairment and obesity: available evidence and clinical practice recommendations across medical and surgical settings. Ann Pharmacother. 2009;43(6):1064-83.
12. Garcia DA, Baglin TP, Weitz JI, Samama MM. Parenteral anticoagulants: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e24S-43S.
13. Gould MK, Garcia DA, Wren SM, Karanicolas PJ, Arcelus JI, Heit JA, et al. Prevention of VTE in Nonorthopedic Surgical Patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e227S-77S.
14. Douketis JD, Spyropoulos AC, Spencer FA, Mayr M, Jaffer AK, Eckman MH, et al. Perioperative management of antithrombotic therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e326S-50S.
15. Hill J, Treasure T. Reducing the risk of venous thromboembolism in patients admitted to hospital: summary of NICE guidance. BMJ. 2010;340:c95.
16. CBO. Diagnostiek, preventie en behandeling van veneuze trombo-embolie en secundaire preventie arteriële trombose (Dutch). Utrecht: CBO; 2009.
17. SIGN. Prevention and management of venous thromboembolism. A national clinical guideline. Edinburgh, Scotland: 2011.
18. AWMF. Leitlinie Prophylaxe der venösen Thromboembolie (VTE). Marburg, Germany: 2010.
19. SFAR. Prévention de la maladie thromboembolique veineuse périopératoire et obstétricale. Recommandations pour la pratique clinique. Nancy, France: 2005.
20. Geerts WH, Bergqvist D, Pineo GF, Heit JA, Samama CM, Lassen MR, et al. Prevention of venous thromboembolism: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest. 2008;133(6 Suppl):381S-453S.
21. Stein PD, Matta F, Goldman J. Obesityand pulmonary embolism: The mounting evidence of risk and the mortality paradox. Thromb Res. 2011. Epud 2011/11/15
22. Kabrhel C, Varraso R, Goldhaber SZ, Rimm EB, Camargo CA. Prospective study of BMI and the risk of pulmonary embolism in women. Obesity (Silver Spring). 2009;17(11):2040-6.
23. Becattini C, Agnelli G, Manina G, Noya G, Rondelli F. Venous thromboembolism after laparoscopic bariatric surgery for morbid obesity: clinical burden and prevention. Surg Obes Relat Dis. 2012;8(1):108-15.
24. Steele KE, Schweitzer MA, Prokopowicz G, Shore AD, Eaton LC, Lidor AO, et al. The long-term risk of venous thromboembolism following bariatric surgery. Obes Surg. 2011;21(9):1371-6.
25. Alikhan R, Cohen AT, Combe S, Samama MM, Desjardins L, Eldor A, et al. Prevention of venous thromboembolism in medical patients with enoxaparin: a subgroup analysis of the MEDENOX study. Blood Coagul Fibrinolysis. 2003;14(4):341-6.
26. Kucher N, Leizorovicz A, Vaitkus PT, Cohen AT, Turpie AG, Olsson CG, et al. Efficacy and safety of fixed low-dose dalteparin in preventing venous thromboembolism among obese or elderly hospitalized patients: a subgroup analysis of the PREVENT trial. Arch Intern Med. 2005;165(3):341-5.
27. Kalfarentzos F, Stavropoulou F, Yarmenitis S, Kehagias I, Karamesini M, Dimitrakopoulos A, et al. Prophylaxis of venous thromboembolism using two different doses of low-molecular-weight heparin (nadroparin) in bariatric surgery: a prospective randomized trial. Obes Surg. 2001;11(6):670-6.
28. Scholten DJ, Hoedema RM, Scholten SE. A comparison of two different prophylactic dose regimens of low molecular weight heparin in bariatric surgery. Obes Surg. 2002;12(1):19-24.
29. Singh K, Podolsky ER, Um S, Saba S, Saeed I, Aggarwal L, et al. Evaluating the safety and efficacy of BMI-based preoperative administration of low-molecular-weight heparin in morbidly obese patients undergoing Roux-en-Y gastric bypass surgery. Obes Surg. 2012;22(1):47-51.
30. Harenberg J. Is laboratory monitoring of low-molecular-weight heparin therapy necessary? Yes. J Thromb Haemost. 2004;2(4):547-50.
31. Rowan BO, Kuhl DA, Lee MD, Tichansky DS, Madan AK. Anti-Xa levels in bariatric surgery patients receiving prophylactic enoxaparin. Obes Surg. 2008;18(2):162-6.
32. Simone EP, Madan AK, Tichansky DS, Kuhl DA, Lee MD. Comparison of two low-molecular-weight heparin dosing regimens for patients undergoing laparoscopic bariatric surgery. Surg Endosc. 2008. Epud 2008 Jul 2
33. Diepstraten J, Hackeng CM, Van Kralingen S, Zapletal J, Van Dongen EP, Wiezer MJ, et al. Anti-Xa levels 4 hours after subcutaneous administration of 5700 IU nadroparin strongly correlate with lean body weight in morbidly obese patients. Obes Surg. 2012;Epub 1 feb.
34. Rondina MT, Wheeler M, Rodgers GM, Draper L, Pendleton RC. Weight-based dosing of enoxaparin for VTE prophylaxis in morbidly obese, medically-Ill patients. Thromb Res. 2010;125(3):220-3.
35. Lemmens HJ, Bernstein DP, Brodsky JB. Estimating blood volume in obese and morbidly obese patients. Obes Surg. 2006;16(6):773-6.
36. Hamad GG, Choban PS. Enoxaparin for thromboprophylaxis in morbidly obese patients undergoing bariatric surgery: findings of the prophylaxis against VTE outcomes in bariatric surgery patients receiving enoxaparin (PROBE) study. Obes Surg. 2005;15(10):1368-74.
37. Raftopoulos I, Martindale C, Cronin A, Steinberg J. The effect of extended post-discharge chemical thromboprophylaxis on venous thromboembolism rates after bariatric surgery: a prospective comparison trial. Surg Endosc. 2008;22(11):2384-91.