Anti-FXa levels in patients undergoing laparoscopic sleeve gastrectomy: two different dosing regimens of enoxaparin

כמיליו חול מחזור לשם קבלת תואר דוקטור לרפואה מן הסתם ביה״ש תל אביב-יפו, רמת גן.

עבודת הגמר של התלמיד שאול ג׳ליקס

כמילוי חלק מהדרישות לשם קבלת תואר דוקטור לרפואה מטעם בית הספר לרפואה של האוניברסיטת העברית והדסה, ירושלים.

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Introduction

Approximately two thirds of the adult population in developed countries is categorized as over-weight or obese (BMI>30), and their high propensity for cardiovascular diseases is well established. 1,2 In contrast to diet and medical therapy, bariatric surgery has been shown to be efficient in treating morbidly obese patients (BMI>40 and/or BMI>35 with co-morbidities), resulting in significant weight reduction, and its maintenance. In addition, numerous reports show considerable improvement in obesity-associated co-morbidity (i.e. diabetes, hypertension, hyperlipidemia, etc.). 2,3,4,5,6 Nevertheless, as all major surgical procedures, bariatric surgery harbors potential hazards 2,6; These could be categorized as surgical versus medical complications.

Amid the medical complications, venous thromboembolic events (VTE) are relatively rare, yet potentially lethal; Taken together with the propensity of surgically treated obese patients to develop VTE, perioperative thoromboprophylaxis is mandatory and unequivocally recommended. 7,8 In a recent meta-analysis, pertaining to VTE in laparoscopic bariatric surgery the incidence of screened VTE was 2.0%, whereas that of symptomatic VTE was 0.6%. All patients included in the meta-analysis were treated with some form of thromboprophylaxis. 9

Recently, two relatively large studies, that excluded VTE high risk patients, have concluded that adequate VTE prophylaxis may be achieved with the combination of short operating time, use of pneumatic compression devices, early ambulation, and massive I.V. hydration 10,11; However, to date, most bariatric surgeons still utilize pharmacologic VTE prophylaxis. Low-molecular-weight-Heparins (LMWHs, i.e. Enoxaparin) are widely used in the medical setting for the prevention of VTE. LMWHs are administered subcutaneously and considered to have near 100%
bioavailability, accumulating predominantly in blood and vascular tissue. Since intravascular volume is not linearly linked to total body weight (TBW) concerns have been raised regarding overdosing when administering these drugs based on TBW, thus possibly increasing the risk of bleeding. On the other hand, thromboprophylaxis, using the same fixed doses of LMWHs utilized in the general population, may result in under-dosing in morbidly obese patients undergoing bariatric surgery.

At present, the effectiveness of LMWH therapy is monitored by assessing anti-factor Xa (FXa) activity in the plasma, utilizing the chromogenic assay. The optimal peak anti-FXa level for LMWH prophylactic dose remains unclear and levels around 0.2-0.5 U/ml have been suggested. Data has demonstrated that dosing based on TBW in medically ill obese patients results in appropriate target therapeutic/prophylactic anti-FXa levels.

Several studies have compared different dosing regimens of enoxaparin for VTE prophylaxis in bariatric surgical patients and their results are inconsistent. Rowan et al. compared 30 mg enoxaparin q12h to 40 mg enoxaparin q12h, in 52 patients undergoing laparoscopic bariatric surgery, and the average peak anti-FXa after the third dose was 0.08 U/ml and 0.15 U/ml respectively (P<0.05). Nonetheless, even in the 40 mg group only 41.7% achieved target anti-FXa levels (defined as 0.18-0.44 U/ml by the authors). Simone et al. conducted a similar study, comparing 40 mg enoxaparin q12h to 60 mg enoxaparin q12h, and achieving peak anti-FXa levels, after the third dose, of 0.21 U/ml and 0.43 U/ml, respectively. The percentage of patients with sub-prophylactic levels of anti-FXa (defined as <0.18 U/ml) was 44% and 0% in the 40 mg group and 60 mg group, respectively. The percentage of patients with anti-FXa levels above the prophylactic range (defined as >0.44 U/ml) was 0%
and 57%, respectively. Scholten et al.\textsuperscript{18} compared 30 mg q12h to 40 mg q12h in 481 patients after bariatric surgery (mainly long limb open RYGB) demonstrating clinically evident VTE in 5.4% vs. 0.6% of the patients in the 30 mg group vs. the 40 mg group, respectively (P<0.01). These studies are not randomized, containing several methodological shortcomings, and therefore conclusions should be carefully made.

At present, most VTE prophylaxis guidelines for bariatric surgery patients advocate the administration of LMWH; however, dose and length of therapy vary according to different guidelines, institutional, and surgeon's preference. In a recent survey among Israeli bariatric surgeons we found that the most common regimens used are 40mg/60mg enoxaparin q24h, which are lower than the doses recommended by the aforementioned studies.\textsuperscript{16,17,18} Although frequently prescribed in the world, to the best of our knowledge, the pharmacological efficacy of these doses has never been evaluated.

In this study we examined anti-FXa levels in a cohort of 54 patients undergoing laparoscopic sleeve gastrectomy. These patients were assigned to postoperatively receive one of the two previously mentioned enoxaparin regimens (40mg/60mg q24h). Our main objectives were to determine whether these doses achieve acceptable anti-FXa levels and to determine which of the two regimens achieves preferable anti-FXa levels. We further aspired to identify differences in Anti-FXa levels between patients according to personal characteristics (weight, BMI, gender, etc.) in order to increase the available knowledge towards possible patient specific prophylactic regimens with the goal of avoiding over-treatment and/or under-treatment.
**Methods and Materials**

During the period between November 2013 and September 2014 and after receiving approval from our institutional review board, 62 Adult patients (>18 years old) that were intended to undergo Laparoscopic Sleeve Gastrectomy in our institution were enrolled to participate in the study. Patients with a history of previous VTE, excessive bleeding during surgery (ascertained by the surgeon), IVC filter requirement or known renal failure were excluded from the study. Five additional patients were elected later on to serve as the control group. All of the patients mentioned above were operated on by one of two surgeons (Dr. Guy Lahat – Surgeon 1, Dr. Shai Eldar – Surgeon 2) and had provided written informed consent.

The patients participating in the study were intended to receive 40 mg or 60 mg of enoxaparin once daily beginning at 06:00 the morning after surgery. The surgeons, by means of alternating between the two dosing regimens assigned the patients to one of the two treatment groups. All patients received treatment with postoperative IV hydration and early physiotherapy to promote ambulation. Blood samples were retrieved from the patients, using tubes containing 3.2% sodium citrate, 3-4.25 hours after receiving the third treatment dose. The samples were then transferred to our institutions laboratory where they were centrifuged, stored at -20°C and analyzed utilizing the chromogenic assay in order to determine anti-FXa activity. The laboratory team was blinded to the treatment assignment.

Of the 62 patients in the study group that had provided informed consent, eight were not included in the study analysis. Three of these patients did not receive the intended therapy due to suspected bleeding perioperatively, two patients did not receive treatment according to the intended protocol, one patient refused to wait for the blood
samples to be taken and samples were not taken from two other patients due to staff miss-coordination.

Of the five patients comprising the control group, two patients did not receive enoxaparin at all; these patients were treated postoperatively solely with sequential compression devices, early ambulation and I.V. Hydration and their blood samples were taken preoperatively and on day 3 postoperatively (corresponding to the time when samples were retrieved from the study group). Blood samples were retrieved solely preoperatively from the other three patients in the control group. None of the patients in the control group received preoperative VTE chemoprophylaxis.

All of the patients participating in the study were questioned preoperatively and then again postoperatively regarding baseline characteristics and previous medical history. Furthermore, available medical records were inspected and an effort was made to contact any patient that had missing information. Information was gathered regarding age, gender, weight, height, dietary habits, obesity in 1st degree relatives, previous abdominal/bariatric surgery and existing comorbidities including: diabetes, hypertension, hyperlipidemia, obstructive sleep apnea (OSA, diagnosed at a sleep clinic), orthopedic complaints, cardiac illness, chronic obstructive pulmonary disease (COPD), asthma, gastroesophageal reflux, fatty liver (determined intraoperatively or by ultrasound), cholelitheasis, gastritis, depression, irregular menses/infertility and smoking status.
**Statistical Methods**

In order to compare quantitative variables between two independent groups the T-test as well as the Mann-Whitney non-parametric test were used. The non-parametric test was applied for variables that were not normally distributed. The association between two categorical variables was tested by applying the chi-square test or the Fisher's exact test. The Pearson and the Spearman correlation coefficients were calculated to assess the strength of the linear association between two quantitative variables. The ANCOVA model was applied to test the simultaneous effect of several variables, both quantitative and categorical, on a quantitative dependent variable. All tests applied were two-tailed and a p-value of 0.05% or less was considered statistically significant.
Results

In total, 54 patients were evaluated in the two study groups. 31 patients in group I received enoxaparin 40 mg every 24 hours postoperatively and 23 patients in group II received enoxaparin 60 mg every 24 hours postoperatively. The patients in both groups were similar in terms of baseline demographic characteristics and comorbidities with no statistically significant difference between the groups, as seen in Table 1. Of note is that two patients in the 60 mg group had OSA, two patients in each group had asthma and one patient in the 40 mg group had COPD. The number of absolute cases of these conditions was too small to determine statistical significance.

Table 1: Patient demographic characteristics and comorbidities

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I (40 mg) n=31</th>
<th>Group II (60 mg) n=23</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>36.94 +/- 12.37</td>
<td>39 +/- 11.04</td>
<td>0.529</td>
</tr>
<tr>
<td>Percentage female</td>
<td>67.7%</td>
<td>65.2%</td>
<td>0.846</td>
</tr>
<tr>
<td>Height (meters)</td>
<td>1.68</td>
<td>1.68</td>
<td>0.8</td>
</tr>
<tr>
<td>Weight (Kgs)</td>
<td>120.16 +/- 3.47</td>
<td>125.26 +/- 3.95</td>
<td>0.338</td>
</tr>
<tr>
<td>BMI</td>
<td>42.27 +/- 0.84</td>
<td>44.15 +/- 1.25</td>
<td>0.253</td>
</tr>
<tr>
<td>Comorbidities (% suffering from condition)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>29%</td>
<td>17.4%</td>
<td>0.322</td>
</tr>
<tr>
<td>Hypertension</td>
<td>19.4%</td>
<td>30.4%</td>
<td>0.346</td>
</tr>
<tr>
<td>Gastroesophageal Reflux</td>
<td>25.8%</td>
<td>36.4%</td>
<td>0.409</td>
</tr>
<tr>
<td>Smokers</td>
<td>35.5%</td>
<td>43.5%</td>
<td>0.551</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>41.9%</td>
<td>39.1%</td>
<td>0.836</td>
</tr>
<tr>
<td>Orthopedic complaints</td>
<td>68%</td>
<td>47.1%</td>
<td>0.175</td>
</tr>
<tr>
<td>Fatty Liver</td>
<td>93.5%</td>
<td>87%</td>
<td>0.640</td>
</tr>
<tr>
<td>percentage operated by Surgeon 1</td>
<td>76.7%</td>
<td>78.3%</td>
<td>0.496</td>
</tr>
</tbody>
</table>
The mean anti factor Xa (FXa) level measured after the third dose of enoxaparin in both groups was in the prophylactic range (0.2 – 0.5 U/ml); However, there was a statistically significant difference between the groups: 0.247 U/ml in group I (range: 0.15-0.39) vs. 0.346 U/ml (range: 0.24-0.8) in group II, with a p-value of 0.001. This difference remained statistically significant (0.247 vs. 0.3043 U/ml, p-value 0.001) even after excluding the results of two patients in group II that had extreme levels of anti-FXa activity (0.77 U/ml and 0.8 U/ml, both >2.5 SD from the mean). Overall, in group I there were 6 patients (19.4%) that had anti-FXa levels in the sub-prophylactic range (<0.2 U/ml) whilst none of the patients had levels in the supra-prophylactic range (>0.5 U/ml. In contrast, in group II none of the patients had anti-FXa level in the sub-prophylactic range whereas 2 patients (8.7%) had levels in the supra-prophylactic range (figure 1). Using the cross-tabulation analysis, categorizing the results to three nominal groups (sub-prophylactic, prophylactic and supra-prophylactic), we found that the difference between the two study groups was statistically significant (p-value 0.016).

When comparing the percentage of patients achieving appropriate (vs. inappropriate) anti-FXa levels, there was no statistically significant difference between the groups.

**Figure 1. Percentage of patients achieving levels of anti-FXa activity according to designated ranges**

* sub-prophylactic: <0.2 U/ml, prophylactic: 0.2-0.5 U/ml, supra-prophylactic >0.5 U/ml
Due to the extreme deviation, from the mean, of the levels of anti-FXa activity in the blood samples from the two patients mentioned above, we decided to continue the analysis of correlations/associations between different parameters and anti-FXa levels excluding their results. A univariate analysis found a negative correlation between total body weight (TBW) and anti-FXa levels (spearman’s correlation coefficient: -0.283, p-value 0.042), as seen in figure 2; this correlation was not statistically significant in group II (p-value 0.083). No statistically significant correlation was found between anti-FXa levels and age or BMI.

![Figure 2. Correlation between anti-FXa levels and TBW](image)

*TBW: Total Body Weight

Also tested for the association with third day anti-FXa levels, were several of the patients background characteristics, as can be seen in figure 3. A significant association was observed for gender, with females reaching higher anti-FXa levels (0.2831 vs. 0.2435, p-value 0.029). Of note is a strong association between gender and weight with a mean TBW of 115.17 among females and 131.76 among males (p-value 0.001).
Several analyses of covariance on the effect of the different parameters on 3\textsuperscript{rd} day anti-FXa levels were performed. Taking into account both enoxaparin dose and weight, both retained their significant correlation with anti-FXa levels (p-values, <0.001 and 0.033 respectively with an adjusted r-squared of 0.252). When taking into account enoxaparin dose and gender it was also found that both retained their significant correlation with anti-FXa levels (p-values, <0.001 and 0.013 respectively, adjusted r-squared – 0.277). Figure 4 shows the estimated mean third day anti-FXa level according to these two parameters. Finally, an analysis of covariance including dose, gender and TBW found that only enoxaparin dose remained significantly correlated with anti-FXa levels (p-values, <0.001, 0.082 and 0.241, adjusted r-squared – 0.283). Of note is that an analysis of variance in anti-FXa levels including solely the parameter of enoxaparin dose produced an adjusted r-squared of 0.194.
Few adverse events were observed during the Study follow-up. None of the patients developed clinically evident VTE during the first three days postoperatively (the study follow up duration). One patient in group II bled excessively during the operation and received two blood transfusion. It was concluded that this patient had no evidence of residual bleeding at the end of the operation and therefore the patient continued to receive 60 mg enoxaparin q24 hours as intended. This patient was also the only patient in the two groups for whom enoxaparin therapy was continued despite suspected bleeding postoperatively (according to a hemoglobin drop of 2.5 g/dl). The anti-FXa level in this patient's plasma after the third dose of enoxaparin was 0.77 U/ml. As mentioned above three patients that were enrolled to participate in the study did not receive enoxaparin according to the intended protocol due to suspected bleeding.
perioperatively. One of these patients did not receive enoxaparin at all, and the information regarding the doses the other two patients received is lacking.

The anti-FXa levels for the patients in the control group are shown in table 2.

Table 2. Control group preoperative and postoperative anti-FXa levels

<table>
<thead>
<tr>
<th>Control patient</th>
<th>Preoperative anti-FXa levels</th>
<th>Anti FXa levels 3 days postoperatively</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0.02</td>
<td>0.04</td>
</tr>
<tr>
<td>B</td>
<td>0.04</td>
<td>0.05</td>
</tr>
<tr>
<td>C</td>
<td>0</td>
<td>----</td>
</tr>
<tr>
<td>D</td>
<td>0</td>
<td>----</td>
</tr>
<tr>
<td>E</td>
<td>0</td>
<td>----</td>
</tr>
</tbody>
</table>
**Discussion**

Although this study was not formally randomized, the similarity between the study groups in regards to baseline patient characteristics and comorbidities points at an unbiased assignment of patients to each one of the study groups. The two dosing regimens tested in the current study are markedly lower than those tested in similar previous studies, in which enoxaparin was given in a twice daily regimen.\(^{16,17}\)

Interestingly, despite this difference, both groups in the current study achieved appropriate mean anti-FXa levels after the third dose of enoxaparin. The discrepancy between our results and the results of previous studies may be due to the pharmacological properties of enoxaparin. Peak anti-FXa levels when administering this drug in obese individuals have been shown to be achieved approximately 4 hours after administration. More relevant is the slower decline in anti-FXa levels, especially after 15 hours from administration.\(^ {19}\) This slow decline in anti-FXa activity suggests that the peak levels of anti-FXa reached after the third dose of enoxaparin may be similar whether a once-daily or rather a twice-daily dosing strategy is used. That being said, the 'appropriate' peak anti-FXa level for venous thromboembolism prophylaxis defined in the current study is based upon the suggestion of authors of different papers.\(^ {8,15}\) This suggestion is not well validated and it is quite possible that the target peak anti-FXa levels are different for a twice daily dosing regimen and a once daily regimen. Another feasible explanation for the discrepancy between the results is the lack of standardization between different laboratories in the testing of anti-FXa levels. The control group in our study served as a means of verifying our laboratories reliability. The three patients that had been tested solely for preoperative anti-FXa levels indeed had levels equal to zero, as would be expected in patients not receiving anticoagulation. The fact that the two other patients in the control group (that were tested for both
preoperative and postoperative anti-FXa levels) had levels above zero with a small increase between preoperative and postoperative levels, despite not receiving anticoagulation, points at a possible deviation in our laboratory's measurements which might also simply reflect a normal random error.

There was no significant difference between the groups in the percentage of patients achieving appropriate anti-FXa levels. A high proportion of the patients achieved appropriate levels: 80.6% and 91.3% in groups I (40mg every 24 hours) and II (60mg every 24 hours) respectively. Nonetheless, there was a significant difference between the groups. Patients in the 60 mg group reached higher levels compared with patients in the 40 mg group. This was expressed in that more patients in the 40 mg group had sub-prophylactic levels as opposed to more patients in the 60 mg group that had supra-prophylactic levels.

In the analysis of correlations/associations of different parameters with anti-FXa levels the data of two patients from group II who had exceptionally high anti-FXa levels (almost twice as high as the next highest level and >2.5 SD from the mean), was excluded. The rationale behind their exclusion was the assumption that their results might be a result of a laboratory and/or other error, and the fact that both of these patients' operations were on the same day strengthens this assumption. In the current study, a negative correlation between TBW and anti-FXa levels was observed; this correlation was not statistically significant for group II, presumably because of the smaller sample size. Also observed was an association between female gender and higher anti-FXa levels with mean levels higher by approximately 0.04 IU/ml among females. The thought that this association was merely the result of the strong association between lower total body weight and female gender was refuted in a multivariate analysis examining the effects of enoxaparin dose, total body weight and gender on
anti-FXa levels. This analysis found that only enoxaparin dose remained significantly correlated with anti-FXa levels. Furthermore, gender was a variable nearly reaching statistical significance with a p-value of 0.082, whereas total body weight was not (p-value 0.241). Overall, it was found that enoxaparin dose alone explained 19.4% of the variance in anti-FXa levels, and adding both gender and total body weight to the equation improved this by 8.9%, while gender alone improved this by 8.3%.

This study was underpowered to detect differences in the amount of adverse events (i.e. bleeding or venous thromboembolic events (VTE). Furthermore, the data collected included only those events that occurred during the first three days postoperatively. None of the patients had clinically evident VTE during the aforementioned days and only one patient, from the 60 mg group, had suspected bleeding. Regarding this topic, the data from the Bariatric Longitudinal Database, revealed that 73% of VTEs occurred after hospital discharge.\textsuperscript{20} Hamad et al. performed a retrospective study comparing venous thromboembolic events and bleeding in 668 patients that had undergone bariatric surgery at five different centers, each center utilizing a different enoxaparin regimen. It was observed that all VTEs occurred after cessation of VTE chemoprophylaxis.\textsuperscript{21} These findings raise the idea that maybe more important than the specific chemoprophylaxis regimen given is the duration of prophylaxis.

\textbf{Limitations}

Our study has several limitations. Firstly, as mentioned above the study was underpowered for detecting differences in adverse events (VTE or bleeding). Moreover, data is missing regarding patients who had bled postoperatively and therefore stopped receiving anticoagulation, causing an under presentation of bleeding events in the study groups. Also mentioned above, is the fact that the 'appropriate' prophylactic peak anti-
FXa level defined is merely an assumption not well validated and therefore conclusions according to these levels should be made with caution. Another limitation is in that our study is a single-center study and we did not test the reproducibility of our laboratory's results in different laboratories. Lastly, stands the exclusion of two patients from part of the analysis due to the assumption that the anti-FXa levels reported for them are a result of an error of some sort. This was discussed above and of note is the fact that the statistically significant difference between the mean anti-FXa levels in each group was not affected by the exclusion of these patients.

Conclusions

We conclude that in the absence of sufficient data regarding the clinical efficacy and safety of different dosing regimens, both dosing regimens studied are reasonable choices for VTE prophylaxis after bariatric surgery, with the emphasis on extending the duration of treatment beyond hospital discharge. Both regimens resulted in high proportions of patients achieving the assumed target anti-FXa activity. When deciding on which regimen to use an effort must be made to weigh the risk of under-treatment vs. that of overtreatment. The evidence found in this study is that the most important factor found to be associated with anti-FXa levels was the enoxaparin dose. Decisions regarding the administration of higher doses of enoxaparin to male patients and/or patients with higher total body weight should be made with caution as in the current study gender and total body weight were not shown to be significantly associated with anti-FXa levels in a multivariate analysis of covariance. Further randomized, prospective studies including large study populations are required to test the clinical efficacy and safety of different enoxaparin dosing regimens for the prophylaxis of venous thromboembolic events in patients after bariatric surgery.
Summary

The current study is the first of its kind to be performed on a population of patients undergoing laparoscopic sleeve gastrectomy, not including other forms of bariatric surgery. These patients, being morbidly obese patients undergoing surgery, are considered to be at higher risk of developing venous thromboembolic events and are therefore commonly treated with anticoagulation postoperatively. In this study a comparison was performed between the levels of anti factor Xa achieved after three days of treatment with one of two different treatment regimens of the anticoagulant enoxaparin (40 mg every 24 hours or 60 mg every 24 hours). These levels are an indicator of the level of activity of the medication in the patients' plasma and they were tested at a time intended to reflect peak levels. Worth mentioning is that the treatment regimens tested in this study have not been tested in similar previous studies. Nonetheless, according to fellow bariatric surgeons these regimens are widely used as standard therapy after bariatric surgery.

During the study duration, 62 patients that had undergone the aforementioned operation were enrolled to participate in the study. These patients were divided into two different treatment groups (according to the regimens mentioned above). 54 of these patients successfully received treatment according to the study protocol, had blood samples retrieved from them and were included in the study analysis. The main study objective was to determine whether each one of the treatment regimens achieves anti factor Xa levels considered appropriate for venous thromboembolism prophylaxis. Furthermore, the difference in anti factor Xa levels between the two study groups was examined and correlations between several patient characteristics (age, gender, total body weight, BMI, etc.) and these levels were ascertained.
The study analyses revealed that both treatment groups achieved mean anti factor Xa levels in the range deemed appropriate, with a high proportion of patients in each group that had reached levels in this range. Nevertheless, a higher proportion of patients in the 40 mg group achieved levels beneath the desired range as opposed to a higher proportion of patients in the 60 mg group that achieved levels above the desired range. This difference was statistically significant. Univariate analyses performed found that enoxaparin dose, female gender and low total body weight were associated with higher anti factor Xa levels. A multivariate analysis including these variables found that enoxaparin dose remained the only variable significantly associated with anti factor Xa levels, with gender being slightly short of statistical significance.

The conclusion of this study is that in the absence of sufficient data regarding the clinical efficacy and safety of various treatments, both treatment regimens studied are reasonable choices for venous thromboembolism prophylaxis in patients undergoing bariatric surgery. The decision on which treatment regimen to use should take into consideration the risk of over-treatment vs. that of under-treatment. Seeing as in a multivariate analysis gender and total body weight were not found to be significantly associated with anti factor Xa levels, caution should be exercised when trying to adjust treatment doses according to these variables.
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 SUMMARY

 This work is the first of its kind dealing with patients after surgery of ovaries only. These patients, being overweight patients undergoing surgery, are considered to have a higher risk of developing postoperative bleeding. Therefore, it is common practice to treat them in postoperative bleed wards.

 In the current study, a comparison is made between the levels of anti-factor Xa levels after three days of treatment in one of two different dosing schedules of enoxaparin (40 mg/day or 60 mg/day). These levels reflect the activity of the anticoagulant in the blood of the patients and are taken at a time intended to reflect the levels of 'peak'. It should be noted that the dosing schedules examined in this study were not examined in previous similar studies. However, according to discussions with colleagues in the field, they were used in the treatment of patients after bariatric surgery.

 In order to conduct the study, 62 patients underwent the mentioned surgery and were divided into two treatment groups, where each group received treatment in one of the mentioned dosing schedules. Out of 62 patients, 54 completed treatment according to the study protocol, blood tests were taken and they were included in the analysis.

 The objective of the study was primarily to examine whether the treatment of the dosing schedules examined successfully reached levels of anti-factor Xa considered suitable for preventing excess bleeding. Moreover, in addition to the differences in the levels obtained in each of the treatment groups, the relationship between various patient characteristics (age, gender, BMI, etc.) and these levels was examined. In the study, it was found that both treatment groups achieved an average level of anti-factor Xa within the desired range and that a higher percentage of patients in both groups reached levels within this range. However, there was a significant statistical trend for a higher percentage of patients with levels below the desired range among patients receiving 40 mg/day compared to a higher percentage of patients with levels above the desired range among patients receiving 60 mg/day. In the analysis of individual variables, it was found that a greater dosing, female gender and lower weight were associated with higher levels of anti-factor Xa. A detailed statistical analysis found that only the dosing of the medication remained the only significant association with anti-factor Xa levels when appropriate. It should be noted that the gender variable was on the edge of statistical significance.
מסקנה מחקר זה שבירה של מיקודמחקרים, אוסף עדויות על חיונות ובדיות
ridor ביומטרים, ושיפורים ממושכים,

טרופילום פוגע במגמות וארעויות קיימות החברות והולמים לאחרים וייחודיים. השיפורים ממושכים

המגמות שביחה בבריאות הובלים יוני מתכונת על תועות, בהתחלטת באיד אמית מושך מפגש מנגנון להשתתפות יש לשקל את

האםシアטרו והכוננות והציבור בהפרכים הטרופילום בבריאות הנושעים. במתחבר בבריאות הנושעים, באיזו מחנה בבריאות, ומגמות

המגמות והמערקות לא נמצאו במתחם בבריל קרזר מובאות ממסכים על המגמות אולMIC פאquito Xa יש לשקל

בניכור הלחימה מבית הטרופילום על פ"ע מתחמות עם
References


