Calculating the Effective Intravenous Heparin Dose: Comparison between Lean and Actual Body Weight-Based Dosing in Obese Patients

AMR F. ABO EL FOTOUH, M.D.; NADER E. AWAD, M.D.; JANE N.R. ABOULENEIN, M.D. and ASEM Sh. ABD EL KHALIQUE, M.Sc.

The Department of Cardiology, National Heart Institute and Faculty of Medicine, Mansoura University

Abstract

Background: Despite the availability of newer anticoagulants, unfractionated heparin remains a mainstay anticoagulant for atrial fibrillation, acute coronary syndrome with or without percutaneous intervention, treatment and prevention of deep vein thrombosis (DVT), pulmonary embolism (PE), and other thromboembolic disorders.

Aim of Study: The aim of this study is to investigate if intravenous heparin dosing based on lean body weight (LBW) of obese patients would be safe and effective in achieving activated partial thromboplastin time (APTT) within 24 hours compared to the usual practice.

Patients and Methods: This is a case-control study conducted in Cardiology Department Sammanaud General Hospital from May 2017 to May 2018 to investigate if intravenous heparin dosing based on LBW of obese patients would be safe and effective in achieving target APTT within 24 hours compared to the usual practice. The study included 50 obese patients with a diagnosis of atrial fibrillation, suspected or confirmed deep venous thrombosis or pulmonary embolism, unstable angina or Non ST elevation myocardial infarction, or peripheral vascular disease. Patients aged >18 years randomized into two groups (1) and (2).

Results: Studies found that unfractionated heparin dosage adjustments based on the patient's LBW provided therapeutic anticoagulation more rapidly and safely, but protocols based on total body weight increase the risk of a supra-therapeutic PTT.

Conclusion: Unfractionated heparin remains a mainstay anticoagulant for atrial fibrillation, acute coronary syndrome with or without percutaneous intervention, treatment and prevention of deep vein thrombosis (DVT), pulmonary embolism (PE), and other thromboembolic disorders. As lean body weight contributes to approximately 99% of a drug's clearance, it is useful for guiding dosing in obesity. These findings may enhance the utility of LBW as body descriptor instead of TBW in calculating the effective doses of UFH in treatment of thromboembolic disorders.

Key Words: Intravenous heparin dose – Lean body weight-based – Actual body weight-based.

Introduction

DESPITE the availability of newer anticoagulants, UFH remains a mainstay anticoagulant for atrial fibrillation, acute coronary syndrome with or without percutaneous intervention, treatment and prevention of deep vein thrombosis (DVT), pulmonary embolism (PE), and other thromboembolic disorders [1].

For the past two decades, weight-based heparin dosing nomogram has become the standard practice for treatment of thrombosis, as it has been shown to achieve rapid anticoagulation and reduce risk of recurrent thrombosis [2].

Although the guidelines endorse the weight-based strategy, they do not specify what dosing weight should be used or whether a maximum bolus dose or initial infusion rate is recommended for the treatment of DVT, PE, or atrial fibrillation [3-5].

For many years, patients received a standard dosage of unfractionated heparin (UFH), consisting of a 5000-U bolus followed by a 1000-U/hour infusion, for treatment of venous and arterial thrombosis. Later, studies found that UFH dosage adjustments based on the patient's weight provided therapeutic anticoagulation more rapidly [6-8].

Weight-adjusted nomograms have provided an advantage over standard UFH dosing. In one study, a greater percentage of patients achieved an initial APTT greater than 1.5 times the control with weight-based UFH dosing (86%) compared with standard dosing (32%) [9].
Patient management strategies include dosing based on total body weight, ideal body weight (IBW), adjusted body weight, or total body weight with a reduced infusion rate. Protocols based on total body weight increase the risk of a supra-therapeutic APTT; however no increase in bleeding has been reported [10].

The volume of distribution for UFH is similar to that of blood volume, 40-70ml/kg. Although obese patients have a larger blood volume, adipose tissue contains a lower blood volume than lean tissue [11,12].

Lean Body Weight (LBW) is based on the formula by Janmahasatian et al. [13]: Male = [9270 x weight (kg)] / [6680+216 x BMI] Female = [9270 x weight (kg)] / [8780+244 x BMI].

**Aim of the work:**

The aim of this study is to investigate if intravenous heparin dosing based on LBW of obese patients indicated for UFH therapy would be safe and effective in achieving APTT within 24 hours compared to the usual practice.

**Patients and Methods**

This is a case-control study conducted in the Cardiology Department Sammanaud General Hospital from May 2017 to May 2018 to investigate if intravenous heparin dosing based on LBW of obese patients would be safe and effective in achieving target aPTT within 24 hours compared to the usual practice.

**Patients:**

The study included 50 obese patients with a diagnosis of atrial fibrillation, suspected or confirmed deep venous thrombosis or pulmonary embolism, unstable angina or non ST elevation myocardial infarction with hemodynamic stability, or peripheral vascular disease. Patients aged >18 years randomized into two groups (1) and (2).

First group (control): Received UFH based on actual body weight at an initial infusion rate of (12-16) units/kg/h.

Second group (cases): Who received UFH based on lean body weight at the same rate.

Serial APTT measured every 6 hours for all patients.

A standardized nomogram is used to achieve a goal APTT of 57-84 sec (normal range, goal APTT 1.5-2.5 x normal) or 57-70 sec (low range, 1.5-2 x normal).

The primary endpoint was UFH dosage and time achieving therapeutic APTT within first 24 hours for each group.

The Secondary endpoint was major bleeding that included documented cerebral, gastrointestinal or retroperitoneal bleeding as well as minor bleeding e.g; ecchymosis, epistaxis, hematoma, hematuria hemoptysis, petechiae or oozing.

**Inclusion criteria:**

- Patients with body mass index greater than or equal to 30kg/m².
- Weight-based intravenous heparin.
- Patient consent.

**Exclusion criteria:**

- Patients with stroke, TIA, or ST elevation myocardial infarction
- Patients who have hemodynamic or cardiopulmonary instability.
- Patients with thrombophilia
- Patients who are pregnant.
- Patients who have been on any oral anticoagulants (Warfarin, rivaroxaban, dabigatran or apixaban), treatment dose of other anticoagulants or intravenous thrombolytics in previous 7 days.
- Patients who have APTT greater than 37 seconds.
- History of heparin-induced thrombocytopenia or allergy to heparin.

**Methods:**

The nature of the study was explained to all participants. An informed consent was taken from all participants in the research and the privacy of the data was greatly considered.

*All patients were subjected to: Clinical assessment:*

Detailed history and clinical examination were performed with special emphasis on:

1. Cardiovascular diseases symptoms:
   - a- Chest pain; typical or atypical, site, nature, duration, radiation, frequency, precipitating factors, relieving factors.
   - b- Palpitation; suspect IHD, AF.
   - c- Dyspnea; relation to exercise, tachypnea.

2. DVT symptoms:
   - Lower limb; pain, swollen, limited mobility.

3. Cerebrovascular Stroke symptoms:
   - Motor deficit, loss of sensation, autonomic neuropathy.
4- Drugs:
Using oral anticoagulants (Warfarin, rivaroxaban, dabigatran or apixaban), treatment dose of other anticoagulants or intravenous thrombolytics in previous 7 days, thrombophilia, hypersensitivity to UFH.

5- Anthropometric measurements:
The following measurements were obtained:
a- Height and weight.
b- Body mass index (BMI): It was calculated using the following formula.
\[
\text{BMI} = \frac{\text{Weight (kg)}}{[\text{height (m)}]^2}
\]
Obesity is defined as BMI ≥ 30Kg/m^2

6- Electrocardiography:
12-lead ECG was done for detection of Coronary artery disease and arrhythmias.

7- Pulmonary CT angiography:
For patients who suspected to have pulmonary embolism.

8- Lower limb duplex:
For patients who suspected to have deep vein thrombosis.

9- Laboratory work-up:
a- Complete blood picture; for detection platelets number.
b- APTT at admission time and every 6 hours.
c- Cardiac enzymes for patients who suspected to have NSTEMI.

10- Lean Body Weight (LBW) is based on the formula by Janmahasatian et al.; Male = \[9270 \times \text{weight (kg)}\] / \[6680+216 \times \text{BMI}\] Female = \[9270 \times \text{weight (kg)}\] / \[8780+244 \times \text{BMI}\]. \[13\]

Statistical analysis:
The collected data were coded, processed and analyzed using the SPSS (Statistical Package for Social Sciences) version 22 for Windows® (SPSS Inc, Chicago, IL, USA). \(p<0.05\) was considered to be statistically significant. \(t\): Independent samples \(t\)-test (comparison of normally distributed quantitative data). \(\chi^2\): Chi-square test (Comparison of categorical data). \(Z\): Mann-Whitney test (comparison of abnormally distributed quantitative data).

Results

<table>
<thead>
<tr>
<th>Table (1): Comparison of the demographic data in the two groups.</th>
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<tbody>
<tr>
<td></td>
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<tr>
<td>Age:</td>
</tr>
<tr>
<td>Mean ± S.D.</td>
</tr>
<tr>
<td>Sex:</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Weight Mean ± S.D.</td>
</tr>
<tr>
<td>Height Mean ± S.D.</td>
</tr>
<tr>
<td>BMI Mean ± S.D.</td>
</tr>
</tbody>
</table>

\(t\): Independent samples \(t\)-test (comparison of normally distributed quantitative data). \(\chi^2\): Chi-square test. \((\cdot\cdot\cdot)\): Probability. *: Significant \(p\)-value (<0.05). SD: Standard deviation.

<table>
<thead>
<tr>
<th>Table (2): Comparison of different APTT and different infusion rates in the two groups.</th>
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<tbody>
<tr>
<td></td>
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<tr>
<td>APTT 1 (Sec) Mean ± S.D.</td>
</tr>
<tr>
<td>Rate of infusion 1 (ml/h) Mean ± S.D.</td>
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<tr>
<td>APTT 2 (Sec) Mean ± S.D.</td>
</tr>
<tr>
<td>Rate of infusion 2 (ml/h) Mean ± S.D.</td>
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<tr>
<td>APTT 3 (Sec) Mean ± S.D.</td>
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<tr>
<td>Rate of infusion3 (ml/h) Mean ± S.D.</td>
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<tr>
<td>APTT 4 (Sec) Mean ± S.D.</td>
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<tr>
<td>Rate of infusion 4 (ml/h) Mean ± S.D.</td>
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<tr>
<td>APTT 5 (Sec) Mean ± S.D.</td>
</tr>
</tbody>
</table>

\(t\): Independent samples \(t\)-test (comparison of normally distributed quantitative data) \(P\): Probability. *: Significant \(p\)-value (<0.05). SD: Standard deviation.
Table (3): Comparison between APTT at different time points in control group.

<table>
<thead>
<tr>
<th>APTT</th>
<th>Mean±SD</th>
<th>p1</th>
<th>p2</th>
<th>p3</th>
<th>p4</th>
</tr>
</thead>
<tbody>
<tr>
<td>APTT1</td>
<td>35.2±3.72</td>
<td>&lt;0.0001 *</td>
<td>&lt;0.0001 *</td>
<td>0.013*</td>
<td>0.234</td>
</tr>
<tr>
<td>APTT2</td>
<td>53.6±5.59</td>
<td>&lt;0.0001 *</td>
<td>&lt;0.0001 *</td>
<td>0.118</td>
<td></td>
</tr>
<tr>
<td>APTT3</td>
<td>63.4±5.24</td>
<td>&lt;0.0001 *</td>
<td>&lt;0.0001 *</td>
<td></td>
<td></td>
</tr>
<tr>
<td>APTT4</td>
<td>87.96±23.84</td>
<td>&lt;0.0001 *</td>
<td>&lt;0.0001 *</td>
<td></td>
<td></td>
</tr>
<tr>
<td>APTT5</td>
<td>83.76±14.39</td>
<td>&lt;0.0001 *</td>
<td>&lt;0.0001 *</td>
<td>0.234</td>
<td></td>
</tr>
</tbody>
</table>

p1: Significance relative to APTT1.  
p2: Significance relative to APTT2.  
p3: Significance relative to APTT3.  
p4: Significance relative to APTT4.  
Test used: Paired samples t-test (comparison of normally distributed quantitative data in the same groups at different time points).  
P: Probability.  
*: Significant p-value (<0.05).  
SD: Standard deviation.

Table (4): Comparison between APTT at different time points in cases group.

<table>
<thead>
<tr>
<th>APTT</th>
<th>Mean±SD</th>
<th>p1</th>
<th>p2</th>
<th>p3</th>
<th>p4</th>
</tr>
</thead>
<tbody>
<tr>
<td>APTT1</td>
<td>33.6±4.23</td>
<td>&lt;0.0001 *</td>
<td>&lt;0.0001 *</td>
<td>0.032*</td>
<td>0.001</td>
</tr>
<tr>
<td>APTT2</td>
<td>46.6±6.5</td>
<td>&lt;0.0001 *</td>
<td>&lt;0.0001 *</td>
<td>&lt;0.0001 *</td>
<td></td>
</tr>
<tr>
<td>APTT3</td>
<td>46.4±5.69</td>
<td>&lt;0.0001 *</td>
<td>&lt;0.0001 *</td>
<td>&lt;0.0001 *</td>
<td></td>
</tr>
<tr>
<td>APTT4</td>
<td>49.08±5.63</td>
<td>&lt;0.0001 *</td>
<td>&lt;0.0001 *</td>
<td>&lt;0.0001 *</td>
<td></td>
</tr>
<tr>
<td>APTT5</td>
<td>62.36±5.84</td>
<td>&lt;0.0001 *</td>
<td>&lt;0.0001 *</td>
<td>&lt;0.0001 *</td>
<td></td>
</tr>
</tbody>
</table>

p1: Significance relative to APTT1.  
p2: Significance relative to APTT2.  
p3: Significance relative to APTT3.  
p4: Significance relative to APTT4.  
Test used: Paired samples t-test (comparison of normally distributed quantitative data in the same groups at different time points).  
P: Probability.  
*: Significant p-value (<0.05).  
SD: Standard deviation.

Table (5): Comparison between infusion rates at different time points in control group.

<table>
<thead>
<tr>
<th>Infusion rate</th>
<th>Mean±SD</th>
<th>p1</th>
<th>p2</th>
<th>p3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infusion rate 1</td>
<td>2.92±0.32</td>
<td>0.572</td>
<td>0.215</td>
<td>0.026*</td>
</tr>
<tr>
<td>Infusion rate 2</td>
<td>2.94±0.29</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infusion rate 3</td>
<td>2.86±0.24</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infusion rate 4</td>
<td>2.79±0.21</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

p1: Significance relative to infusion rate 1.  
p2: Significance relative to infusion rate 2.  
p3: Significance relative to infusion rate 3.  
Test used: Paired samples t-test (comparison of normally distributed quantitative data in the same groups at different time points).  
P: Probability.  
*: Significant p-value (<0.05).  
SD: Standard deviation.

Table (6): Comparison between infusion rates at different time points in cases group.

<table>
<thead>
<tr>
<th>Infusion rate</th>
<th>Mean±SD</th>
<th>p1</th>
<th>p2</th>
<th>p3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infusion rate 1</td>
<td>1.81±0.24</td>
<td>0.001 *</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infusion rate 2</td>
<td>2.06±0.32</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infusion rate 3</td>
<td>2.06±0.32</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infusion rate 4</td>
<td>2.09±0.36</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

p1: Significance relative to infusion rate 1.  
p2: Significance relative to infusion rate 2.  
p3: Significance relative to infusion rate 3.  
Test used: Paired samples t-test (comparison of normally distributed quantitative data in the same groups at different time points).  
P: Probability.  
*: Significant p-value (<0.05).  
SD: Standard deviation.

Table (7): Comparison between achievements of the target APTT (57-83 sec) within 24 hours in the two study groups.

<table>
<thead>
<tr>
<th>Group 1 (Control group)</th>
<th>Group 2 (Cases)</th>
<th>Test of significance</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Achieved (N=25)</td>
<td>15 (60%)</td>
<td>25 (100%)</td>
<td>χ² =12.5</td>
</tr>
<tr>
<td>Not-achieved (N=25)</td>
<td>10 (40%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
</tbody>
</table>

χ²: Chi-square test. (Comparison of categorical data).  
P: Probability.  
*: Significant p-value (<0.05).
Discussion

Despite the availability of newer anticoagulants, unfractionated heparin remains a mainstay anticoagulant for atrial fibrillation, acute coronary syndrome with or without percutaneous intervention, treatment and prevention of deep vein thrombosis (DVT), pulmonary embolism (PE), and other thromboembolic disorders [1].

According to WHO, obesity is defined as a BMI $\geq 30$ kg/m$^2$ [14,15], obesity rates have nearly doubled since 1980. In 2008, an estimated 1.5 billion adults over the age of 20 years (35%) were overweight, and 500 million (11%) were obese [16].

Studies found that UFH dosage adjustments based on the patient's weight provided therapeutic anticoagulation more rapidly [6-8]. Although the guidelines endorse the weight-based strategy, they do not specify what dosing weight should be used [3-5].

To our knowledge, this is the first study that has explored calculating of the effective intravenous heparin dose by comparison between lean body weight-based dosing and actual body weight based dosing in obese patients; our study group consisted of 50 patients divided into two groups:

- Group 1 (control): 25 obese patients indicated for receiving UFH; received UFH at Actual Body Weight-based Doses.
- Group 2 (cases): 25 obese patients indicated for receiving UFH; received UFH at Lean Body Weight-based Doses.

We noticed that the count of patients who achieved the target APTT (57-83 sec) within 24 hours in group 2 was 25 (100%) while in control group the count of patients who achieved the target APTT within 24 hours was 15 (60%).

The infusion rates at different time points in group I; the infusion rate 1 Mean ± SD was 2.92 ± 0.32, infusion rate 2 Mean ± SD was 2.94 ± 0.29, infusion rate 3 Mean ± SD was 2.86 ± 0.24, infusion rate 4 Mean ± SD was 2.79 ± 0.21.

The infusion rates at different time points in group II; the infusion rate 1 Mean ± SD was 1.81 ± 0.24, infusion rate 2 Mean ± SD was 2.06 ± 0.32, infusion rate 3 Mean ± SD was 2.06 ± 0.32, infusion rate 4 Mean ± SD was 2.09 ± 0.36.

In our study it is clear that, by using the LBW in cases group instead of TBW in control group for calculating the therapeutic doses of UFH, we achieved the targeted APTT in all (100%) patients effectively, safely, with less infusion rates and no increase in risk of bleeding or cause supra therapeutic range, while in control group we achieved the targeted APTT only in 60% of patients with increasing risk of bleeding and being supra therapeutic range.

Due to the varying anticoagulant response of UFH among patients, UFH therapy is monitored and the dose is adjusted based on these results. The test most often used to monitor heparin is the activated partial thromboplastin time (APTT).

An APTT ratio between 1.5 and 2.5 (calculated by dividing the reported therapeutic APTT range by the control value for the reagent) was associated with a reduced risk for recurrent VTE in a previous large retrospective registry. Using total body weight assumes that the pharmacokinetics of the drug are linearly scalable from normal-weight patients to those who are obese, this is inaccurate; For example, we cannot assume that a 150kg patient eliminates a drug twice as fast as a 75kg patient and therefore double the dose so clinicians are alert to toxicities with higher doses, for example bleeding with anticoagulants [17,18,19].

In concordance with our results Hanley et al., reported that drug clearance is correlated to lean rather than adipose weight as adipose tissue has little metabolic activity and as clearance determines a drug’s maintenance dose, clinicians should consider how lean body weight, rather than total body weight, impacts dosing. When lean body weight increases there will be a corresponding increase in drug clearance and an increased dose may be required [17].

Hanley et al., also concluded that using a lean body weight metric encompasses a more scientific approach to weight-based dosing. Lean body weight reflects the weight of all ‘non-fat’ body components, including muscle and vascular organs such as the liver and kidneys. As lean body weight contributes to approximately 99% of a drug’s clearance, it is useful for guiding dosing in obesity. 

Pai et al., reported that hydrophilic drugs e.g. heparins typically remain in extracellular fluid and their volume of distribution correlates with lean mass, this implies that the distribution of hydrophilic drugs should not be significantly influenced by excess adipose tissue [18].

Conclusion:

Unfractionated heparin remains a mainstay anticoagulant for atrial fibrillation, acute coronary
syndrome with or without percutaneous intervention, treatment and prevention of deep vein thrombosis (DVT), pulmonary embolism (PE), and other thromboembolic disorders. Hydrophilic drugs (e.g., heparins) typically remain in extracellular fluid and their volume of distribution correlates with lean mass. This implies that the distribution of hydrophilic drugs should not be significantly influenced by excess adipose tissue. As lean body weight contributes to approximately 99% of a drug’s clearance, it is useful for guiding dosing in obesity. These findings may enhance the utility of LBW as body descriptor instead of TBW in calculating the effective doses of UFH in treatment of thromboembolic disorders.

References


حساب جرعة الهيبارين الفعالة في الوريد:
مقارنة بين الجرعة القائمة على وزن الجسم الخالى من الدهون والجرعة القائمة على وزن الجسم الفعلي في المرضى الذين يعانون من السمنة

مقدمة: بالرغم من توافر مضادات تخثر أخرى إلا أن الهيبارين سيظل أساسية في حالات الوفيات الأثنية ومتلازمة الشريان التاجي الحاد وجلطات الأوردة العميقة والسدة الرئوية.

طبقاً للدراسات تثبيت تقوية البروتوكول المستند إلى وزن المريض على البروتوكول المعتاد وتضمنت استراتيجيات العلاج محاولات لاستخدام الوزن الكلى للجسم والوزن الكلبي والوزن الجسدي ولكن كان النتائج السلبية وحيث أن حجم إنتاج الهيبارين مساله لحجم الدم (V) (0-37 مللي/كم) ويتراوح أن مرضى السمنة يمكن أن حجم دم أكبر ولكن النسيج الدهني يحتوي على دم أقل من النسيج الخارجي من الدهون. وجد أنه من الأفضل استخدام وزن الجسم السائد من الدهون.

الهدف من البحث: التحري ما إذا كانت جرعات الهيبارين المستند إلى وزن المريض الخارجي من الدهون آمنة وفعالة لتحقيق التأثير الدوائي المطلوب مقارنة بالممارسات المعتادة المستخدمة على الوزن الكلي للجسم.

طريقة البحث: إنشاء هذا البحث على 60 مريضا مقتسم إلى مجموعتين:
المجموعة الأولى (A) مريض تعاطي الهيبارين بجرعات مستندة إلى الوزن الفعلي.
المجموعة الثانية (B) مريض تعاطي الهيبارين بجرعات مستندة إلى الوزن الخارجي من الدهون.

تم شرح طبيعة البحث وأخذ موافقة من جميع المرضى.

تم عمل الألي لكل مريض في هذه الدراسة:

1- تأخذ تاريخ مريضي وفحص إكلينيكي قبله بإلاتكز على أعراض قصور القلب الناجمة والتنظيم القلبي والهولوس الدوائي خاصة.

2- تم قياس الوزن الكلي وحساب الوزن الخارجي من الدهون طبقاً للمعادلة الأثية:
الذكور: تساوي (7200 + 860 * وزن الجسم (كم))
الإناث: تساوي (6400 + 780 * وزن الجسم (كم))

3- تم سحب عينات الدم من مفرع زمن الترموميلاسين الجسري النشط عند الدخول ودف ست ساعات بعد تدشين تتراوح الهيبارين

طبقاً النتائج.

وقد أظهرت الدراسة هذه النتائج:

1- أنه في المجموعة الأولى (A) حققت زمن الترموميلاسين الجنسي النشط المستهدف في 10/2 من المريضي فقط بالإضافة إلى زيادة مخاطر التوقف وتحقيق زمن أعلي من المحلول.

2- في المجموعة الثانية (B) حققت زمن الترموميلاسين الجنسي النشط المستهدف بكفاءة وأمان في جميع المرضى المستخدمين وزن الجسم الخارجي من الدهون.

وقد وجد أنه عند مدى فعالية وأمان استخدام وزن الجسم الخارجي من الدهون بدلاً من الوزن الكلي لحساب جرعات الهيبارين المستخدمة لعلاج إضطرابات التخثر الدمى سواء الوريدي أو الشرياني.

ملاحظات البحث: صغر حجم عينة الدراسة، إقتصر الدراسة على استخدام وزن الجسم الخارجي من الدهون فقط دون غيره من الأجزاء المختلفة، دراسة الأثر قصيرة المدى فقط وعدم توفر الوقت اللازم لإجراء المعادلات الحسابية للحصول على الوزن الخارجي من الدهون.