The Effect of Heparin Therapy in Obese Patients with Venous Thrombembolism

Cara Snyder

University of Wyoming

Introduction

The medication, heparin, is an anticoagulant mainly used intravenously to prevent and/or treat the formation of blood clots caused by venous thromboembolism (VTE) (Labus & Sellers, 2020). Heparin's mechanism of action is to, "accelerate formation of antithrombin III - thrombin complexes and deactivates thrombin, preventing conversion of fibrinogen to fibrin" (Labus & Sellers, 2020). Basically, heparin speeds up the development of antithrombin III, a protein that blocks abnormal blood clots from forming, which inhibits the proteins and enzymes necessary for clotting. Heparin is a very popular anticoagulant used within medicine, especially within the hospital settings of the emergency department (ED), inpatient units such as medical/surgical, and the intensive care unit (ICU). Many providers order heparin for patients diagnosed with venous thromboembolism (VTE) which can be further specified as a pulmonary embolism (PE) or deep vein thrombosis (DVT). The development of VTE can lead to fatal complications such as a collapsed lung and heart failure if left untreated or not treated in a timely manner. The majority of healthcare facilities have a weight-based protocol for the administration of heparin. A patient's weight determines the amount of heparin given in an initial intravenous heparin bolus and in the continuous heparin infusion. Unfortunately, obesity continues to rise at an all time rate not only within the United States, but globally as well (Hosch et al., 2017). Obesity is a direct risk factor for the formation of VTE; obese people are more likely to develop VTE than nonobese people (Hosch et al., 2017). As heparin is the drug of choice for VTE treatment, the anticoagulant is more likely to be used among the obese and morbidly obese population now more than ever. This raises the question: In patients with venous thromboembolism (VTE), what is the effect of heparin therapy in obese patients compared to nonobese patients on anticoagulation within 24 hours of the initial heparin dose?

Heparin has been used as a first-line anticoagulant in the clinical setting, especially in the critically ill patients, for more than 50 years (Myzienski et al., 2010). In a randomized controlled trial executed in 1993, it was demonstrated that heparin weight-based dosing was quicker and more effective than a standard heparin dose unrelated to patient weight (Raschke et al., 1993). Raschke et al. (1993) determined that the anticoagulation is best measured by activated partial thromboplastin time (aPTT) levels. aPTT is used, "to assess the intrinsic system and the common pathway of clot formation" and is used "to monitor heparin therapy" (Pagana & Pagana, 2018). The aPTT is measured in seconds and patients receiving heparin need a longer than normal aPTT to prevent clot formation (Pagana & Pagana, 2018). Furthermore, the Raschke et al. (1993) trial used the heparin weight-based dosage of 80 units/kg for the heparin IV bolus and 18 units/kg/hour for the continuous heparin IV infusion. This unfractionated heparin (UFH) dosing method is still highly used in facilities today. However, many studies, including the Raschke et al. (1993) study, have evaluated therapeutic anticoagulation related to heparin weight-based dosing focusing on the nonobese population diagnosed with VTE. The Raschke et al. (1993) study included a total of 62 patients and only 9 of those patients had a weight greater than 100 kg (Hosch et al., 2017). So, the effect of heparin weight-based dosing in obese patients is not as clear as it is for the nonobese patient. There is controversy behind the use of UFH in the obese population because of the lack of research and the medication's pharmacokinetic properties. Among nonobese individuals, "UFH remains in the intravascular space, with a reported volume of distribution similar to blood volume (0.04 - 0.07 L/kg)" (George et al., 2020). Heparin is cleared by endothelial cells and macrophages breaking down the medication and it is also eliminated via the kidneys (George et al., 2020). The relationship between renal clearance and an increase of adipose tissue is still unknown, but obesity does lead

to a slight increase of blood volume related to sustaining adequate perfusion within the adipose tissue (George et al., 2020). However, adipose tissue does not require as much vasculature as lean tissue, so the distribution of heparin in an obese individual simply varies (George et al., 2020). Finally, it is important to note that several studies, including the infamous Raschke et al. (1993) study, demonstrated an increased risk of VTE recurrence if the patient did not reach therapeutic anticoagulation levels within the first 24 hours of beginning heparin therapy (George et al., 2020). Overall, heparin is widely prescribed by medical providers and is directly administered by nurses; it is essential healthcare workers understand how heparin can be most effective within the obese population.

Obtaining the Outside Evidence

The evidence utilized in this systematic review was obtained from the databases of CINAHL and PubMed. There are two sources included in this review found in the CINAHL database. CINAHL stands for the *Cumulative Index to Nursing and Allied Health Literature*. The database provides literature including journals, studies, trials, and publications for nurses and other healthcare allies and professionals. CINAHL is the largest and most in-depth research database for the nursing profession (Napa Valley College, n.d.). There are five sources included in this systematic review found in the PubMed database. The PubMed database includes millions of scientific and biomedical journals, reviews, and studies with a focus in the improvement of health globally and individually (National Library of Medicine, n.d.). The search for evidence-based sources for this systematic review included keywords such as, “unfractionated heparin therapy”, “obesity”, “therapeutic anticoagulation”, “venous thromboembolism”, and “24 hours”. The evidence obtained related to the history of weight-based heparin use in medicine dates back to the year of 1993. However, the sources

discussed related to this systematic reviews focus question does not fall below the year 2010. The sources are all peer-reviewed and they include one cross-sectional consecutive case series, one case report/literature review, and five retrospective cohort studies related to heparin use in the obesity population.

Discussion of the Evidence

Heparin Prescriptions and Clinical Dosing

The cross-sectional consecutive case series titled, "Dosing of Unfractionated Heparin in Obese Patients with Venous Thromboembolism", focuses on the patterns of providers under prescribing heparin in the obese population (Hurewitz et al., 2010). Individuals with VTE have a 30% risk of developing a recurrence of the disease; VTE is also a risk for the obese population (Hurewitz et al., 2010). Aggressive heparin weight-based dosing is needed to reach proper therapeutic anticoagulation. However, observations from other studies and reports have shown that physicians often deviate from the recommended heparin dosing guidelines, particularly in the obese patient (Hurewitz et al., 2010). Therefore, this study analyzes the time it takes to achieve a therapeutic aPTT of > 60 seconds from the initiation of the heparin therapy in 84 patients who experienced VTE at the Winthrop University Hospital (Hurewitz et al., 2010). Based upon the results of the study, the authors also identified patterns and reasoning behind the under prescribed orders of heparin therapy.

The Winthrop University Hospital heparin protocol recommends the initial bolus of 80 units/kg using the patient's actual body weight (ABW). For the continuous heparin infusion, it recommends the utilization of 18 units/kg/hour related to the patient's ABW. The study compares the suggested heparin dosing to the prescribed and administered heparin. The mean initial bolus patients received in this case series was 6,949 ± 2,560 units (mean ± standard

deviation) or 58 ± 25 units/kg of heparin therapy (Hurewitz et al., 2010). The difference between the above prescribed bolus dose of heparin and the recommended mean dose of heparin was an astounding 37.9% (Hurewitz et al., 2010). As for the continuous infusion rate of heparin given to the patient population, the mean infusion was 1,450 ± 462 units also calculated as 13 ± 4 units/kg/hour (Hurewitz et al., 2010). The mean recommended heparin continuous infusion rate based on the hospital protocol of 18 units/kg/hour was 1,990 ± 478 units/hour (Hurewitz et al., 2010). So, there was a 27.9% difference between prescribed and recommended dosages. This led the authors to conclude that the physicians more often prescribe heparin using a "standard-care" dose of 1,000 units/hour rather than the weight-based dosing (Hurewitz et al., 2010). Overall, "the regression analysis revealed a pattern of initial continuous infusion that fell well below the recommended dose but not far from the final dose that ultimately achieved therapeutic anticoagulation" (Hurewitz et al., 2010, p. 488). The under prescription of heparin increased the amount of time to achieve anticoagulation; with each decrease of 1 unit/kg/hour, the delay of anticoagulation ranged from 0.75 hours to 1.5 hours (Hurewitz et al., 2010).

It is important to understand the reason of hesitation physicians have while prescribing heparin in the adult obese population diagnosed with VTE. Physicians tend to under prescribe heparin for multiple reasons such as individual clinical experience, concerns regarding bleeding if the patient is given a higher dose of heparin, and the physicians overall comfort with the medication related to the patients weight. According to this cross-sectional consecutive case series, "supratherapeutic partial thromboplastin times do not increase bleeding complications in patients with VTE," whereas, "prompt anticoagulation reduces the risk of [VTE] recurrence" (Hurewitz et al., 2010, p. 490). Although, this statement does differ from a retrospective study by Shlensky et al. (2019) which will be analyzed later in this systematic review. Overall,

physicians and medical residents should prescribe heparin based off of the hospital guidelines rather than under prescribing the anticoagulant. Due to physician uncertainty of heparin dosing in obese patients, the patients included in the study had a delay of therapeutic anticoagulation of > 24 hours and an insufficient heparin dose. The authors recommend physicians to "avoid overcautious behavior" and prescribe the appropriate heparin doses to aggressively treat VTE.

This cross-sectional consecutive case series executed by Hurewitz et al. (2010) correlates with the purpose of this systematic review because it highlights the clinical practice of heparin therapy used in the obese population experiencing VTEs. The study does not focus on the validation of heparin dosing guidelines, like many of the other sources mentioned in this review, rather it simply compares the recommended heparin treatments to the actual prescribed dosing of heparin. The study is paramount in the prescription and administration process of heparin because it reinforces the importance of obtaining therapeutic anticoagulation within 24 hours of initial therapy in the obese population. The study also identifies the flaws in medicine based off of physician preference and practice within the clinical setting. Even though heparin dosing and its guidelines are uncertain within the obese population, this study proves the need for providers to uphold hospital guidelines by following the recommended dosing implemented by the facility. Finally, the study demonstrates the need to reassess the heparin dosing strategies as the obese population continues to increase.

Actual Body Weight and Ideal Body Weight Dosing

The retrospective review, "Comparison of Heparin Dosing Based on Actual Body Weight in Non-Obese, Obese and Morbidly Critically Ill Patients", measures the efficacy of unfractionated heparin (UFH) infusions in the obese population with thromboembolism (Gerlach et al., 2013). As previously mentioned, "obese and morbidly obese patients have a larger blood

volume than normal weight patients due to the additional vasculature required to perfuse the excess adipose tissue. Comparatively, the blood volume of adipose tissue is less than lean tissue" (Gerlach et al., 2013). Therefore, the authors of this review chose to evaluate heparin dosing in obese patients, particularly in the severely ill obese patients, because pharmokinetics such as distribution, metabolism, and protein binding may be more likely to change with these critical aspects (Gerlach et al., 2013). The review analyzed a total of 62 critically ill patients, 21 nonobese (20.0-29.9 kg/m2 BMI), 21 obese (30-39.9 kg/m2 BMI), and 20 morbidly obese patients (> 40.0 kg/m2 BMI) all admitted to surgical and medical ICUs at a tertiary care center who received UFH infusions longer than 24 hours (Gerlach et al., 2013). The facility's heparin protocol does not include a heparin bolus as it is solely based on ABW at an infusion rate of 16 units/kg/hr if nonobese and a rate of 12 units/kg/hr if obese or morbidly obese. The hospital's therapeutic anticoagulation goal was measured via aPTT with a range of 57-84 seconds. The primary goal of the study was to determine the most effective heparin weight-based dosing by comparing ABW (units/kg and units/kg/hr) to IBW (units/kg and units/kg/hr) along with the time to the first therapeutic aPTT (Gerlach et al., 2013). The secondary goal of the review was to achieve a steady state (SS) of three consecutive aPTTs within the therapeutic range; the authors also measured the time to reach a SS aPTT and the percentage of aPTTs in the therapeutic ranges for each BMI cohort (Gerlach et al., 2013).

The results of the study determined that ABW based dosing for heparin therapy is the most effective in all three weight groups. At the time of the first therapeutic aPTT, the IBW dosing (units/kg/hr) for the three weight cohorts were as follows: 14.3 ± 4.8 non-obese, 18.0 ± 5.9 obese, and 30.1 ± 8.4 morbidly obese (Gerlach et al., 2013). At the time of the first therapeutic aPTT, the ABW dosing (units/kg/hr) for the three weight cohorts were as follows:

13.5 ± 4.0 non-obese, 11.7 ± 4.5 obese, and 12.5 ± 2.9 morbidly obese (Gerlach et al., 2013). The achievement of SS using IBW dosing (units/kg/hr) was: 18.1 ± 7.6 non-obese, 17.7 ± 7.0 obese, and 29.0 ± 7.0 morbidly obese (Gerlach et al., 2013). The achievement of SS using ABW dosing (units/kg/hr) was: 16.3 ± 5.3 non-obese, 11.6 ± 5.5 obese, and 11.1 ± 1.2 morbidly obese (Gerlach et al., 2013). It is clear the results of the IBW and ABW dosing strategies differ. The IBW dosing is proportionally related to the weight groups; as the BMI increased, the weight based IBW dosing generally increased. Whereas, the ABW dosing is inversely related to the weight groups; as the BMI increased, the weight based ABW dosing decreased. However, the ABW dosages are more consistently similar to each other than the IBW dosages. The minimal differences found among ABW dosing in the first therapeutic aPTT influenced the hospitals heparin protocol to remain with ABW dosing rather than shift to IBW dosing (Gerlach et al., 2013). Also, the majority of each BMI group using ABW reached therapeutic aPTT levels rather than subtherapeutic or supratherapeutic levels further contributing to the effectiveness of ABW dosing (Gerlach et al., 2013). Approximately 47% of the nonobese group, 45% of the obese group, and 60% of the morbidly obese group all reached therapeutic anticoagulation levels (Gerlach et al., 2013). The results of this study are quite similar to the results of the George et al. (2020) study as Gerlach et al. (2013) determines that patients with significant obesity have improved anticoagulation with the use of reduced ABW doses. Since this study observes the effect of heparin weight based dosages in critically ill patients while also evaluating the heparin doses in different BMI categories, this study gives more insight into heparin therapy practice in critical care settings.

Capped Heparin Dosing

The retrospective audit performed by George et al. (2020) focuses on the current unfractionated heparin practices and whether the dosing strategies lead to insufficient anticoagulation within obese patients. More specifically, the trial questions the effect of capped heparin dosing. Capped dosing, can also be classified as the maximum amount of heparin allowed to administer to a patient. Capped dosing is often used in patients to decrease the risk of bleeding during heparin therapy (George et al., 2020). The study was executed in Queensland, Australia at the Princess Alexandra Hospital (PAH). The PAH heparin protocol used for the treatment of VTE is, "the initial bolus and maintenance dose is capped at 8,000 units for an 80 units/kg bolus (loading) dose and 1,500 units/hour for an 18 unit/kg/hour infusion." (George et al., 2020). The primary objective of this study was to determine the mean absolute heparin infusion dose for the bolus (units/hour) and continuous infusion (units/kg/hour) in order to achieve two therapeutic aPTTs and the median time to achieve this anticoagulation (George et al., 2020). The authors also formed a secondary objective to determine the effect of capped doses on the first aPTT, on the two consecutive therapeutic aPTTs within 24 hours of the UFH infusion, and on the patients who achieved a therapeutic aPTT within the first 24 hours after the infusion began (George et al., 2020). The PAH protocol defined a therapeutic aPTT as 71-110 seconds specifically for the treatment of VTE. A total of 200 patients were included in this randomized controlled trial and 166 of the patients were identified as obese; obesity was defined as > 100 kg. The patients were divided into four separate cohorts based on their weight: 34 patients in the < 100 kg control group, 122 patients in the 100-124.9 kg group, 27 patients in the 125-150 kg group, and 17 patients in the > 150 kg group (George et al., 2020).

After the authors were able to analyze the data of the 200 participants, the primary objective was determined. The mean heparin doses for the IV bolus (units/hour), starting with an

80 unit/kg calculation, is described based on the specific weight cohort: 1,229 ± 316 in the < 100 kg group, 1,673 ± 523 in the 100-124.9 kg group, 2,031 ± 596 in the 125-150 kg group, and 2,146 ± 846 in the >150 kg group (George et al., 2020). This data expresses a proportional relationship between the heparin bolus and the patients total body weight (TBW), also known as actual body weight. As the weight increases, so does the heparin bolus dose needed to obtain two consecutive therapeutic aPTT values (Figure 1). As for the mean heparin doses for the continuous IV infusion (units/kg/hour), the appropriate doses related to the weight cohorts is as follows: 16 ± 4.1 in in the < 100 kg group, 15.1 ± 4.8 in the 100-124.9 kg group, 14.9 ± in the 125-150 kg group, and 11.6 ± 4.2 in the > 150 kg group (George et al., 2020). The results of the continuous IV infusion differs from the initial heparin bolus as the continuous infusion shows an inverse relationship to the patients TBW. To summarize, as weight increases, the recommended units/kg/hour continuous heparin IV infusion decreases in order to meet therapeutic anticoagulation (Figure 1).

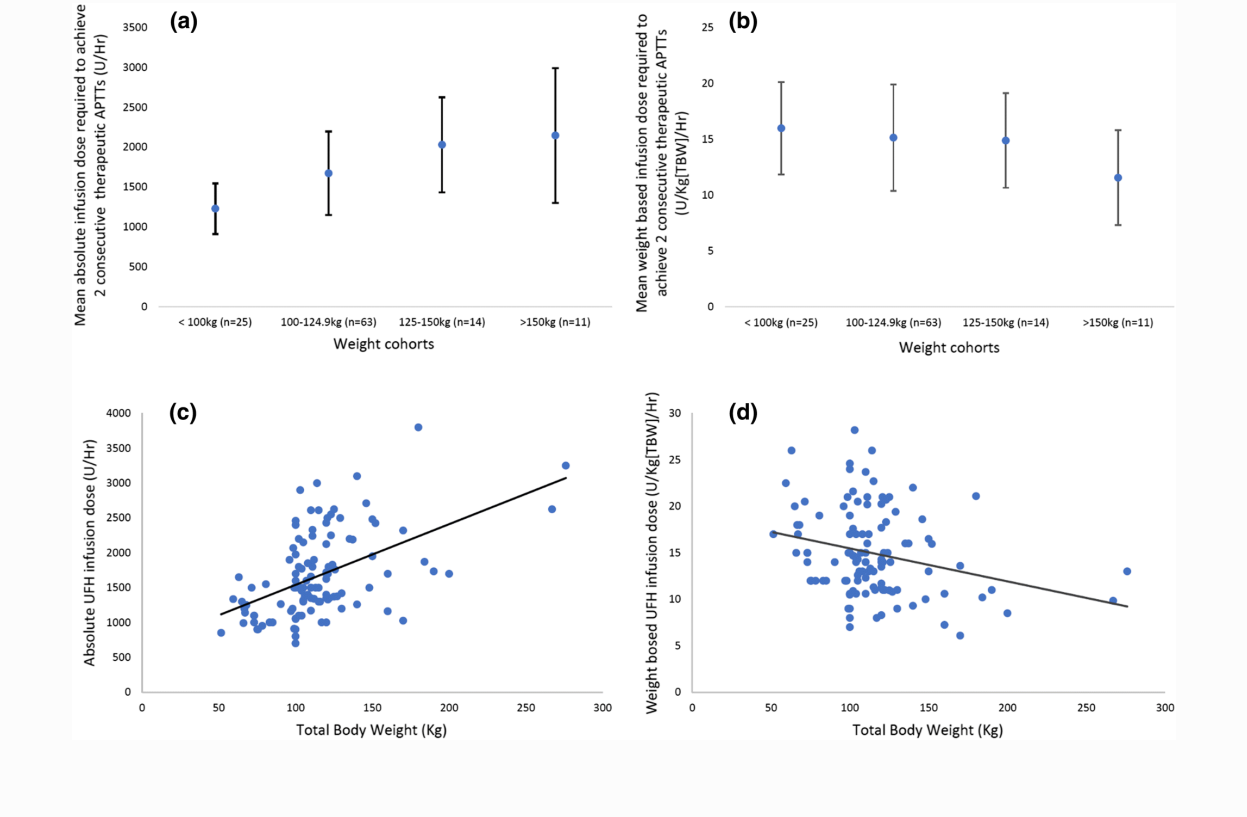

Figure 1: "Differing analyses of doses required to achieve 2 consecutive therapeutic Activated Partial Thromboplastin Times (APTTs), with; a as—mean ± standard deviation absolute infusion dose (U/h) b as—mean ± standard deviation weight based infusion dose (U/kg[TBW]/h) c as—absolute infusion dose (U/h) required to achieve 2 consecutive therapeutic APTTs d as—weight based infusion dose (U/kg[TBW]/h)"

Last, the primary objective also focuses on the timing outcomes of the patients obtaining two consecutive therapeutic aPTTs. It was found that the median time to attain the two consecutive therapeutic aPTTs was 47 hours for nonobese patients (< 100 kg) and 39 hours for the obese patients (> 100 kg) (George et al., 2020). Ultimately, neither weight population reached the reviews goal of achieving appropriate anticoagulation within 24 hours; it took at least 36 hours for 50% of the patients to reach the therapeutic aPTT range (George et al., 2020).

The secondary objective focuses on the effect of capped heparin doses related to the two consecutive achieved aPTTs with a greater focus among those who achieved anticoagulation within 24 hours. As noted above in the primary objective regarding the timing outcomes, the study shows poor attainment of anticoagulation in the appropriate 24 hours from when the heparin infusion started (George et al., 2020). The study only resulted in 15% of the patients achieving two consecutive therapeutic aPTTs within the 24 hour window (George et al., 2020). Therefore, it can be determined that dosed capping is not very effective in the obese population. The patients need greater heparin infusion doses above the initial recommendation of the 8,000 units cap for an 80 units/kg bolus and a 1,500 units/hour cap for an 18 unit/kg/hour continuous infusion (Figure 2).

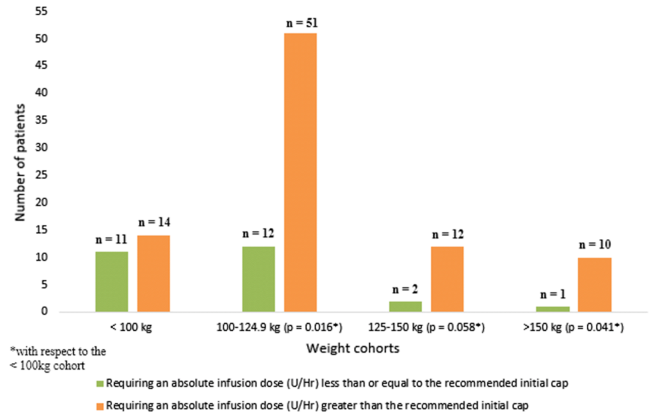

Figure 2. Shows the number of patients needing an absolute infusion bolus dose greater than the recommended initial cap of heparin.

Overall, it is extremely concerning that the heparin dosing protocol used in PAH is poor and ineffective for the majority of nonobese and obese patients within 24 hours of heparin therapy. There are limitations worthy of note in this study that could have moderately affected the anticoagulation outcome. Some limitations include the small nonobese cohort (34 patients). A small nonobese cohort minimizes the control group of the study which can affect the results of the nonobese population and the comparison to the >100 kg groups. The study also included patients treated with heparin diagnosed with VTE and acute coronary syndrome (ACS) (George et al., 2020). ACS heparin treatment is not the primary focus of this systematic review. There are other unknown patient factors that could have affected the patients ability to reach therapeutic anticoagulation in a timely manner (George et al., 2020). It is essential for other future studies to continue to analyze aPTT values and clinical outcomes among the obese population experiencing VTE. The study concludes that, "the currently used nomogram for IV UFH [capped dosing] is not adequate for dosing in obesity. "Larger absolute doses (units/hour) of IV UFH but reduced uncapped TBW based doses (units/kg/hour) should be considered in obese patients" (George et al., 2020). As the obese population continues to rise, further research

studies are needed to analyze heparin dosing and therapeutic aPTT timing outcomes in the future.

Safety and Efficacy of Total Body Weight and Adjusted Body Weight Dosing

The retrospective observational cohort study, "Intravenous Unfractionated Heparin Dosing in Obese Patients Using Anti-Xa Levels", analyzes the efficacy of heparin treatment in the obese population by measuring the anti-Xa blood levels, rather than the aPTT levels (Ebied et al., 2020). Anti-Xa is a lab value that directly monitors plasma heparin and can be used to adjust UFH therapy (Pagana & Pagana, 2018). Even though aPTT usually measures UFH therapy, in some cases, the measurement of plasma anti-Xa levels has proven to be more accurate in its assessment of anticoagulation (Pagana & Pagana, 2018). This study differs from the other sources included in this systematic review due to the anti-Xa measuring tool rather than aPTT levels. Even with this difference, this study is still useful in determining the efficacy heparin has among the obese population by specifically evaluating the safety of using different heparin dosing strategies (Ebied et al., 2020). The study claims that its ultimate purpose, "was to determine the efficacy and safety of a standard unfractionated heparin (UFH) protocol in obese patients based on total body weight (TBW) or adjusted body weight to reach two consecutive therapeutic anti-Xa levels" (Ebied et al., 2020). In comparison to the other studies mentioned in this systematic review, total body weight is simply another term equivalent to actual body weight (ABW) and adjusted body weight is equivalent to dosing weight (DW) or dosing body weight (DBW). This retrospective observational cohort study was conducted at the University of Florida Health Shands Hospital. The patient population consisted of 131 patients who were treated with UFH for many medical situations; the study did not only include patients experiencing VTEs. The patients were further separated into three categories based on their

TBW: 100-124.9 kg, 125-149.9 kg, and ≥ 150 kg (Ebied et al., 2020). The hospital's heparin protocol was based on UFH levels which were further measured by anti-Xa levels (Figure 3). The target anti-Xa level was 0.3-0.7 units/mL. The initial bolus was calculated by 80 units/kg and the initial continuous infusion rate was calculated by 18 units/kg/hr as suggested by the Raschke et al. (1993) trial. Furthermore, the heparin protocol includes titratable instructions based on the results of the anti-Xa levels; nurses would be alerted to titrate the heparin infusion rates based on the protocol (Figure 3) (Ebied et al., 2020). Last, the protocol suggests that patients weighing 125 kg or more be prescribed their heparin infusion using the adjusted body weight equation: IBW + 0.4(TBW-IBW) (Ebied et al., 2020).

Initial bolus: 80 units/kg		**Initial infusion rate: 18 units/kg/h**		**Goal anti-Xa level: 0.3–0.7 units/mL**
Anti-Xa level (units/mL)	Bolus dose	Hold (min)	Rate change	Repeat UFH level†
< 0.2	80 units/kg	None	Increase by 4 units/kg/h	6 h
0.2–0.29	40 units/kg	None	Increase by 2 units/kg/h	6 h
0.3–0.7	Therapeutic			6 h or next AM labs‡
0.71–0.8	None	None	Decrease by 1 unit/kg/h	6 h
0.81–0.9	None	30	Decrease by 2 units/kg/h	6 h
≥ 0.91	None	60	Decrease by 3 units/kg/h	6 h

Figure 3. The University of Florida Health Shands Hospital heparin protocol using anti-Xa levels to assess therapeutic anticoagulation.

The primary outcome of the study was to determine the time to obtain two consecutive therapeutic levels of heparin measured by anti-Xa levels using the TBW or adjusted body weight

dosages (Ebied et al., 2020). The secondary outcome of the study was to compare and contrast the time it took to reach two consecutive therapeutic levels within the three weight categories and whether a heparin bolus was given prior to the continuous heparin infusion (Ebied et al., 2020). The average weight of the patients who were given heparin based on TBW was 127.4 ± 19.4 kg (Ebied et al., 2020). The average weight of the patients who were given heparin based on adjusted body weight was 151.1 ± 26.5 kg (Ebied et al., 2020). Of the 131 patients included in this study, 109 of them obtained two consecutive therapeutic anti-Xa levels within 96 hours of the start of heparin therapy (Ebied et al., 2020). On average, the patients who were administered heparin based on TBW achieved therapeutic levels at 29.4 hours and the adjusted body weight patients achieved therapeutic levels at 27.6 hours (Ebied et al., 2020). As for the secondary outcome, the mean time it took for the weight groups to attain two consecutive therapeutic UFH levels are as listed: 29.3 hrs in the 100-124.9 kg group, 27.5 hrs in the 125-149.9 kg group, and 29.9 hrs in the ≥ 150 kg group (Ebied et al., 2020). Also, 89 of the 131 patients included in the study did not receive a heparin bolus before the initial heparin infusion (Ebied et al., 2020). It was evaluated that the 89 patients who did not receive a bolus reached the primary outcome of a therapeutic anti-Xa level quicker than those who did receive a heparin bolus.

Based off of the results, it was determined by the authors that both TBW and adjusted body weight heparin dosing are recommended in the obese patient. Between the two different dosing strategies, the average time it took to achieve two consecutive therapeutic UFH levels was 28.6 hrs (Ebied et al., 2020). Unfortunately, this average time still exceeds the appropriate 24 hour time limit in which VTEs may recur and does not completely align with the overall goal of this systematic review. Although, this study did identify a need for change in the hospital's protocol. A heparin bolus is simply not needed for obese patients undergoing heparin therapy

because not administering a bolus allows for a quicker achievement of therapeutic anticoagulation. The fact that only 42 of the 131 patients received a heparin bolus also provides more insight into real clinical practice; the majority of patients do not receive a heparin bolus even if it is recommended in the protocol which could be due to multiple clinical, real life factors (Ebied et al., 2020). The results of the study also suggest that a lower infusion rate, lower than the 18 units/kg/hour rate, of TBW or actual body weight dosing heparin can be applied to obese patients, this finding also correlates with other studies such as Gerlach et al. (2013) and George et al. (2020) (Ebied et al., 2020). There is an inverse relationship as weight increases, the appropriate heparin dose needed for therapeutic anticoagulation decreases. In conclusion, this study shows very similar, safe, and effective outcomes with TBW and adjusted body weight dosages as they were both able to achieve therapeutic UFH levels with anti-Xa measurements. More research is encouraged to be conducted related to initial heparin boluses and anti-Xa levels as there is limited research in both of these factors.

Heparin Dosing Body Weight

This retrospective cohort study conducted by Hosch et al. (2017) evaluates the unfractionated heparin dosing protocol for VTE therapy in nonobese, obese, and severely obese patients. The main goal of the study was to determine the time and dose needed to achieve therapeutic aPTT within these weight cohorts. The patients were separated into the following weight cohorts based off of body mass index (BMI): patients with a BMI < 30 kg/m2 in the nonobese group, patients with a BMI of 30-39.9 kg/m2 in the obese group, and patients with a BMI > 40 kg/m2 in the severely obese group (Hosch et al., 2017). The authors also looked into using multiple forms of dosing weights in order to identify the most effective weight-based heparin dosing for obese patients. The study compared ABW to dosing body weight (DBW) by

determining if each patient met their IBW (Figure 4). If a patient's ABW was over 20% the IBW, the patient would be given the DBW for the heparin bolus dose and infusion (Hosch et al., 2017).

Table 2. Dosing Definitions.

IBW (kg)	• Males: 50 + (2.3 × Height in inches > 60 inches) • Females: 45.5 + (2.3 × Height in inches > 60 inches)
DBW (kg)	IBW + [0.4 (ABW − IBW)]

Abbreviations: ABW, actual body weight; DBW, dosing body weight; IBW, ideal body weight.

Figure 4. The dosing calculations for IBW and DBW.

The hospital's heparin dosing protocol used in this study is specifically pharmacist-directed (Figure 5). According to other heparin studies in the past, "pharmacist-directed heparin adjustments lead to an increased number of patients within therapeutic range compared with physician adjustments" (Hosch et al., 2017). It is important to note that the initial bolus and initial infusion both have a cap for the amount of heparin that can be administered, regardless of patient weight (Figure 5). The capped dosing strategy is not always utilized in facilities when treating VTE, typically capped dosing is mainly used in treating ACS.

Table 1. Pharmacy Dosing Protocol.

Initial Bolus	Bolus Cap	Initial Infusion Rate	Initial Infusion Cap	Goal aPTT
80 U/kg	10 000 U	18 U/kg/h	2500 U/h	57-96 sec
aPTT	**Bolus Dose**	**Hold (minutes)**	**Rate Change**	**Repeat aPTT[a]**
<45	60 U/kg	0	Increase by 4 U/kg/h	6 hours
45-56	40 U/kg	0	Increase by 2 U/kg/h	6 hours
57-96		Therapeutic range		Next AM labs[b]
97-115	0	0	Decrease by 1 U/kg/h	6 hours
116-150	0	30	Decrease by 2 U/kg/h	6 hours
151-163	0	60	Decrease by 3 U/kg/h	6 hours
>163	0	90	Decrease by 4 U/kg/h	6 hours

Abbreviation: aPTT, activated partial thromboplastin time.
[a]aPTT repeated 6 hours after dose change.
[b]aPTT will be repeated every 6 hours until 2 consecutive therapeutic range PTT results are measured; then, frequency will change to once daily with morning labs.

Figure 5. The pharmacy-directed capped heparin protocol used in this retrospective cohort study.

The primary outcome of the trial was to recognize the time (hours) and dose needed to reach a therapeutic aPTT from the start of the heparin bolus; the authors defined therapeutic aPTT as 57-96 seconds per the institutions protocol (Figure 5) (Hosch et al., 2017).

There were a total of 294 patients involved in this retrospective cohort study. The median time (hours:minutes) to achieve therapeutic aPTT did not substantially differ between the three BMI groups: 15:00 nonobese group, 15:40 obese group, and 15:22 severely obese group (Hosch et al., 2017). The authors chose to further analyze the heparin dosages used upon the 140 patients who achieved at least three consecutive aPTTs (60 nonobese, 52 obese, and 28 severely obese). The mean ± standard deviation ABW and DBW heparin infusion rates for each cohort were: 17.2 ± 5 U/kg/h based on ABW and 18.4 ± 5.6 U/kg/h based on DBW in the nonobese group, 15.9 ± 4.4 U/kg/h based on ABW and 20.2 ± 5.7 U/kg/h based on DBW in the obese group, and 13.9 ± 3.9 U/kg/h based on ABW and 20.8 ± 6 U/kg/h based on DBW in the severely obese group (Hosch et al., 2017). The ABW continuous infusion dosing depicts a clear inverse relationship between the heparin dosing and BMI; as the patient's BMI increases, the ABW dosing decreases. On the other hand, the DBW continuous infusion dosing shows a proportional relationship between the heparin dosing and BMI; as the patient's BMI increases, the DBW dosing increases. Overall, out of the 140 patients further analyzed, "a total of 29 patients (55.8%) and 13 patients (46.4%) in the obese and severely obese groups, compared with 21 (35%) in the nonobese group, required an infusion rate above the initial dose of 18 U/kg/h to achieve consecutive therapeutic aPTT values." (Hosch et al., 2017). This data proves that a larger continuous heparin infusion rate using the DBW rather than the 18 U/kg/h ABW is necessary for the obese and severely obese patients to reach three consecutive therapetuic aPTT values.

The results of this study encourages the use of DBW heparin bolus and initial infusion dosing. It shows this strategy to be very effective within the obese population being treated for VTE. In fact, "a pharmacist-managed heparin dosing protocol using a DBW for patients weighing greater than 20% over their IBW resulted in a therapeutic aPTT within approximately 15 hours of infusion initiation for nonobese, obese and severely obese patients" (Hosch et al., 2017). Due to the average therapeutic aPTT being achieved below the preferable 24 hours, it is likely these patients will not have recurrent VTE which leads to better patient health outcome. The main take away from this study is the effectiveness of using DBW in the obese and severely obese populations, especially if the individual's ABW is 20% over their IBW (Hosch et al., 2017). Last, because the DBW is more complex than the ABW, it will be paramount for the patient's provider and nurse to collaborate with a pharmacist to confirm the dosing calculation and administration.

A Case Report and Dosing Body Weight Recommendation

A case report and review of the literature presented by Myzienski et al. (2010) analyzes a case of a 388 kg morbidly obese patient treated with heparin therapy. The authors also reviewed other research related to the effect heparin weight-based dosing has on the anticoagulation in the obese population within this publication (Myzienski et al., 2010). This case report claims that even though "obese patients have a larger blood volume, adipose tissue contains a lower blood volume than lean tissue" (Myzienski et al., 2010). Therefore, throughout the report and review of the literature, the authors try to determine the difference between ABW heparin dosing compared to IBW dosing; they believe that ABW may "provide too much heparin whereas infusion rates based on IBW could underestimate heparin requirements" (Myzienski et al., 2010). Much of the literature included in this systematic review focuses on the concern that obese

patients with VTE are unable to achieve therapeutic aPTT levels related to heparin dosing recommendations. The purpose of the Myzienski et al. (2010) report was to identify the most effective heparin dosing strategy within the obese population by observing a morbidly obese patient case and other scientific literature.

The case report discusses a 32 year old man weighing 388 kg (BMI 134 kg/m2), with an ideal body weight of 66.1 kg (Myzienski et al., 2010). The patient came to the institution's ED complaining of an intermittent cough, worsening chest pain, and shortness of breath for approximately nine days (Myzienski et al., 2010). The patient's medical history included morbid obesity related to his weight and BMI, obstructive sleep apnea, probable chronic obstructive pulmonary disease most likely caused by the patient's excessive 60-pack-year history of tobacco use, venous stasis, and hypoventilation. The patient presented to the ED with bilateral leg swelling and bilateral wheezes and rhonchi in the lungs (Myzienski et al., 2010). The initial diagnostic tests and labs identified bilateral air space disease, possible vascular congestion, and a low suspected PE. Ultimately, the patient was intubated and admitted for acute respiratory failure secondary to obesity hypoventilation syndrome (Myzienski et al., 2010). The patient's admitting diagnosis was related to the diagnostic findings, abnormal arterial blood gas, an oxygen saturation of 80% on 3L of oxygen, and a poor ABG response to the BiPAP. Even with a low suspected PE, the patient was prescribed and administered heparin to treat the PE and/or prevent a PE from developing.

The 32 year old, 388 kg patient was first heparin bolus dose was capped at 5,000 units (12.9 units/kg of ABW) and 1,500 units/hr intravenous infusion (3.9 units/kg ABW/hr) (Myzienski et al., 2010). The patient's aPTT was closely evaluated during the first 24 hours of the heparin therapy. At 7 hours of heparin treatment, the aPTT was subtherapeutic at 27 seconds.

At 24 hours of heparin treatment, the aPTT still remained subtherapeutic at 29.4 seconds with a target range of 55-89 seconds. Since the patient's aPTT level did not reach the target aPTT range of 55-89 seconds within the first 24 hours of treatment, the heparin infusion rate was dramatically increased past the 1,500 units/hr initial infusion cap (Myzienski et al., 2010). Finally, at a heparin infusion rate of 3,650 units/hr (9.4 units/kg ABW/hr), more than double the initial infusion rate, the first therapeutic aPTT was achieved 55 hours after starting heparin therapy (Myzienski et al., 2010). The heparin treatment was discontinued at day 6 due to concerns related to heparin-induced thrombocytopenia and risk of bleeding with a 50% decrease of platelets (Myzienski et al., 2010). On the patient's tenth day in the hospital, the heparin therapy was restarted because of persistent refractory hypoxemia and greater suspicion of a PE. The healthcare team approached this heparin prescription differently. An immediate 10,000 unit bolus (25.8 units/kg ABW) and a 3,000 units/hr initial infusion rate (7.7 units/kg ABW/hr) was prescribed (Myzienski et al., 2010). The infusion rate eventually increased to 3,550 units/hr (9.1 units/kg ABW/hr) which assisted the patient in reaching a therapeutic aPTT level in 48 hours from starting the second round of heparin therapy. The second round of heparin therapy was discontinued on day 14 due to bloody pulmonary secretions. The focus of the patient's care turned towards his development of refractory hypotension and need to be placed on vasopressor therapy. Later on day 14, the patient became even more hypoxic and hypotensive and developed pulseless electrical activity of the heart (Myzienski et al., 2010). The patient was a full code, so advanced cardiac life support was initiated but the patient's life could not be saved. The 32 year old, 388 kg man, treated with heparin therapy for the majority of his time in the hospital, died on day 14.

The authors further analyzed other heparin weight-based dosing research studies and case reports. The main area of concern with each study and case report mentioned was the ABW dosing in the obese and morbidly obese population. The authors noticed a pattern of ABW heparin dosing causing a risk of overanticoagulation or supratherapeutic aPTT especially in the morbidly obese patient when using a 15 unit/kg/hour or 18 unit/kg/hour initial infusion heparin rate (Myzienski et al., 2010). In several sources of literature, the studies recommended using heparin dosing weight (DW) (also known as DBW) and IBW in obese patients. The specific heparin dosing strategy recommended for optimal dosage for obese patients is, DW = IBW + 0.4[ABW-IBW]. In fact, the ABW based infusion rate that reached therapeutic anticoagulation in the 388 kg patient very closely resembles the DW equation (Myzienski et al., 2010). If the institution would have initially used the DW dosing strategy calculation for this morbidly obese patient's heparin dosing, the dose would not have needed to be dramatically adjusted and the time to attain therapeutic anticoagulation could have been reduced from the 55 hours ABW therapeutic time. To summarize, the 1,500 units/hr capped initial heparin infusion rate to treat VTE in the morbidly obese patient was too timid which resulted in a prolonged time of 55 hours to achieve therapeutic aPTT. Ultimately, the capped ABW dosing strategy placed the patient at an increased risk of recurrent VTE and likely contributed to the negative outcome. The authors of this case report and review of literature determined, "institutons with maximum [capped] initial heparin rates for treatment of VTE (with the intention of avoiding overanticoagulation in obese patients) are encouraged to develop a special provision for initial dosing in morbid obesity, as limitations on initial infusion rates may greatly increase time to achievement of therapeutic anticoagulation in this population" (Myzienski et al., 2010). Last, it is recommended by Myzienski et al. (2010) that a trial is conducted to further analyze the effect the DW heparin

strategy has especially in the morbidly obese population as this review believes this strategy would have been highly effective in the 388 kg patient.

Uncapped Dosing and Heparin Boluses

The authors, Shlensky et al. (2019), conducted a retrospective cohort, single-center study evaluating ABW UFH dosing without dose capping in patients with VTE. This study's primary focus was to compare the weight-based UFH doses without a capped dose in BMI categories classified as nonobese (< 30 kg/m2), obese (30-39.9 kg/m2), and morbidly obese (> 40 kg/m2) patients (Shlensky et al., 2019). The primary endpoint of the study was to compare the time to the first therapeutic aPTT, defined as 70-120 seconds, in all three BMI cohorts using the hospital's high-intensity heparin nomogram (HIHN) which is described in figure 6 (Shlensky et al., 2019). The secondary endpoint of the study was to determine if a subtherapeutic, therapeutic, or supratherapeutic aPTT was attained at 10 and 24 hours from the start of the heparin therapy (Shlensky et al., 2019). The authors also chose to analyze the bleeding complications within the patient population and the number of dose adjustments needed to achieve a therapeutic aPTT.

Table 1. High-intensity heparin dosing nomogram parameters.

aPTT Level	IV push loading dose	Infusion	IV rate change (units/hour)	Repeat aPTT
< 45 seconds	80 units/kg	Continue	Increase 4 units/kg/hour	6 hours
45–59 seconds	40 units/kg	Continue	Increase 2 units/kg/hour	6 hours
60–69 seconds	0	Continue	Increase 2 units/kg/hour	6 hours
70–120 seconds	0	No change	No change	Next morning
121–139 seconds	0	Stop for 1 hour	Decrease 2 units/kg/hour	6 hours after heparin resumed
140–180 seconds	0	Stop for 1 hour	Decrease 3 units/kg/hour	6 hours after heparin resumed
> 180 seconds	0	Stop for 2 hours	Decrease 4 units/kg/hour	6 hours after heparin resumed

Initial loading dose: 80 units/kg IV push.
Heparin IV infusion: 25,000 units/250 mL (100 units/mL) at 18 units/kg/hour.
Decision for the initial bolus was made by the ordering clinician. The protocol was nurse-driven by the above parameters.
aPTT, activated partial thromboplastin time; IV, intravenous.

Figure 6. The Mayo Clinic's High-Intensity Heparin Dosing Nomogram Parameters Used in the study.

The study was conducted among patients admitted and diagnosed with an acute VTE at the Mayo Clinic Hospital in Rochester, Minnesota (Shlensky et al., 2019). There were 423 patients (230 nonobese, 146 obese, and 47 morbidly obese patients) included in the study and the majority of the patients were given a heparin bolus at 80 units/kg, at the physician's discretion, and a heparin infusion would follow at 18 units/kg/hr per the Raschke et al. (1993) recommendation (Shlensky et al., 2019). Then, most of the patients began the Mayo Clinic's HIHN protocol. The first aPTT level would be drawn after the first 6 hours of beginning the heparin treatment and then based on the 6 hour aPTT blood draw, "further heparin dose adjustments were made by the registered nurses using the protocol directions" (Shlensky et al., 2019).

The results of the study related to the primary outcome of the time to the first therapeutic aPTT are as follows: a median of 16.4 hours for the non-obese cohort, 16.6 hours for the obese cohort, 17.1 hours hours for the morbidly obese cohort (Shlensky et al., 2019). The majority of each BMI cohort reached a therapeutic aPTT within 24 hours from the initial heparin bolus and/or infusion as 70.7% of the nonobese, 69.9% of the obese, and 61.7% of the morbidly obese cohort achieved effective anticoagulation (Shlensky et al., 2019). There are no significant differences between the cohorts and their ability to achieve therapeutic aPTT. However, there was a difference found in the secondary endpoint of the BMI cohorts in relation to the subtherapeutic and supratherapeutic aPTTs within the 24 hour time limit. The difference was found among the nonobese and morbidly obese populations. 43.9% of the nonobese and 17% of the morbidly obese groups achieved a subtherapeutic aPTT in 24 hours of heparin therapy (Figure 7) (Shlensky et al., 2019). Whereas, 42.2% of the nonobese and 61.7% of the morbidly

obese groups achieved a supratherapeutic aPTT in 24 hours of heparin therapy (Figure 7) (Shlensky et al., 2019).

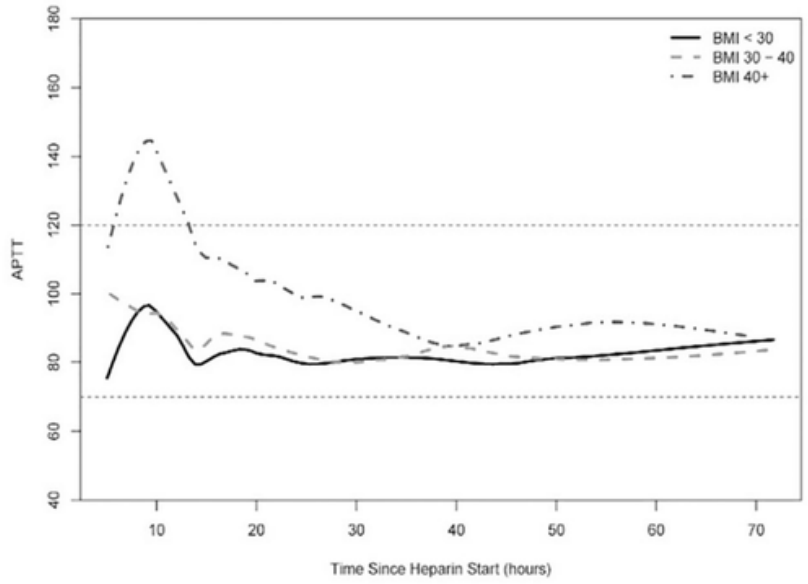

Figure 7. Average aPTT values, per BMI group, over time.

Also, there were a total of 27 bleeding events among the 423 patients in all three cohorts. The majority of the patients who had a bleeding complication measured to have a supratherapeutic aPTT value. There was no difference between the BMI groups and the 27 bleeding complications (Shlensky et al., 2019). There was also no significant data found between the three cohorts and the need to adjust the dose of heparin administered to the patients to achieve the target aPTT. However, there was an interesting result related to the administration of a heparin bolus. A heparin bolus was not given to 37.6% of the patients and "for those who received a bolus, obese patients were at a higher risk than non-obese patients of having a major bleed" (Shlensky et al., 2019). There was also a slight difference between those who received a bolus to those who did not receive a heparin bolus; "the median time to first therapeutic aPTT was 17 hours for those who received a bolus and 16 hours for those who did not receive a bolus" (Shlensky et al., 2019).

Overall, this study shows that ABW heparin dosing without a cap is safe and effective among the three different weight groups. It is important to note that the morbidly obese patient population recieving heparin treatment had a higher incidence of supratherapeutic aPTT which has a higher chance of leading to heparin induced bleeding complications (Figure 7) (Shlensky et al., 2019). This study has some limitations such as the number of morbidly obese (47) patients is quite less to the number of nonobese (230) patients included in this study. This unequal number of patients representing their assigned BMI categories could have affected the ultimate primary or secondary outcomes. Another limitation to note is some of the patients admitted to the Mayo Clinic began their heparin therapy on the hospital's "intermediate-intensity heparin nomogram (IIHN)" rather than the HIHN parameters (Shlensky et al., 2019). The patients who started heparin treatment on IIHN did not receive the 80 unit/kg bolus. This difference of heparin bolus administration effects the controlled results. Although, if all patients started on HIHN, the authors may have not identified the notable difference between time to therapeutic aPTT and the bleeding events that occurred in the study. Even with these limitations, this study determined that heparin dosing based on ABW without a dose cap is safe and effective in patients with ranging BMIs (Shlensky et al., 2019). More studies and trials are suggested to simply compare the results of this study to another study examining ABW without a dosing cap or analyze an adjusted weight dosing or a heparin capped dosing strategy (Shlensky et al., 2019).

Gaps in the Body of Evidence

The sources identified in this systematic review are all credible and correlate with the PICOT question. Despite the applicability of these sources, there are a few gaps and limitations with the sources that are worthy to mention for acceptable understanding of this systematic review. There are five retrospective cohort studies included and they each have similar evidence

barriers. The studies only evaluate the impact weight has on UFH dosing, they did not go into detail of other factors, besides weight, that could have affected the heparin efficacy in obese patients. Other uncontrolled variables of the patient population analyzed in each study could have had a positive or negative impact on the effect of heparin therapy. Many of the following variables were not analyzed by the authors of the studies including, "age, race, gender, renal function, tobacco use, indication and history of diabetes mellitus or thyroid disease may all potentially contribute to variability in UFH dosing" (Gerlach et al., 2013). Another limitation affecting the results of each of the seven sources is they each only observed one institution's heparin protocol. None of the sources reviewed the difference among two or multiple hospital heparin practices. Each source focuses solely on their specific protocol which limits the ability to juxtapose different heparin practices in one single study. For an example, the study conducted by Shlensky et al. (2019) uses a high-intensity heparin nomogram protocol specific to the Mayo Clinic's research and clinical practice. Whereas, the George et al. (2020) study uses the hospital protocol of 80 unit/kg capped at 8,000 units for a bolus and 18 unit/kg/hour continuous infusion capped at 8,000 units. The work of contrasting the results of heparin protocols has to be done by evaluating multiple peer review sources as it is difficult to find a source analyzing several opposing heparin protocols within different facilities in a single study. Last, while the seven sources analyze the effect heparin therapy has within the obese population, not every source defines the term "obesity" equally. The George et al. (2020) retrospective cohort study defines obesity as a weight greater than 100 kg, whereas the Hosch et al. (2017) and Shlensky et al. (2019) studies define an obese patient as having a BMI of 30-39.9 kg/m2. The Ebied et al. (2020) study does not even define obesity, it simply divides the patients into three separate cohorts based on weight and only suggest that the larger weight patients fulfilled the obese and

morbidly obese categories. The sources included in this systematic review each have their own limitations which ultimately affected their results and conclusions. Even with these gaps of evidence, the collection of the resources in this systematic review contribute to the answer of the PICOT. The outcomes of the sources could affect the practice of heparin in the obese patient with VTE.

Applications to Nursing

This systematic review includes several sources analyzing UFH practice in the clinical setting and specific UFH dosing and its efficacy in obese patients. After closely analyzing each source and its findings, the following clinical recommendations were determined:

- Providers should not under prescribe heparin to obese patients. Under prescription can lead to inadequate heparin dosing which delays therapeutic anticoagulation greater than 24 hours. Providers need to follow facility heparin guidelines (Hurewitz et al., 2010).
- Providers and nurses should utilize a pharmacist in the calculation and verification of UFH dosing. Pharmacist-directed UFH adjustments leads to a greater number of patients achieving target aPTT levels rather than physician-directed adjustments (Hosch et al., 2017).
- Hospitals should consider adding or changing their heparin protocol based on the below dosage recommendations for patients with VTE:
    - Heparin doses should be based on uncapped actual body weight (ABW) for all weight cohorts. Uncapped ABW heparin dosing has been proven safe and effective, whereas capped ABW dosing only prolongs the time to attain proper aPTT levels which ultimately leads to an increased risk of VTE recurrence (George et al., 2020; Shlensky et al., 2019; Myzienski et al., 2010).

- If a facility chooses to utilize ABW dosing, an inverse relationship to weight and ABW continuous infusion dosing should be observed before heparin administration. As weight increases, the ABW dose (units/kg/hr) should decrease (Ebied et al., 2020; Gerlach et al., 2013; George et al., 2020; Hosch et al., 2017).
- If a facility decides to utilize DBW heparin, the DBW equation, IBW + [0.4(ABW-IBW)]), can be used at the discretion of the provider, pharmacist, and nurse in the obese and/or morbidly obese patient population. The DBW method has a proportional relationship with weight, so this may require a continuous infusion dose above 18 units/kg/hr as weight increases (Ebied et al., 2020; Myzienski et al., 2010; Hosch et al., 2017).
- Heparin boluses should be excluded from the protocol in obese patients with VTE. Heparin IV boluses slow down the achievement of therapeutic anticoagulation and leads to a greater chance of bleeding complications related to supratherapeutic aPTT levels in the obese patient (Ebied et al., 2020; Shlensky et al., 2019).

It is the nurses role to enforce the clinical recommendations listed above. The nurse is the healthcare worker who should be involved in the heparin calculation and administration process from start to end. Whether the above recommendations of heparin dosing are implemented into hospital protocol, the nurse has the competency to determine if the provider is prescribing the correct heparin value based on the patient's current weight and the specific institution's heparin protocol. The nurse should verify the providers heparin dosage calculation. The nurse could also request to perform the calculation with the provider if available; this would allow for minimal to no risk of medication administration error. An even better solution would

be to include the pharmacist in the heparin calculation process. The nurse can act as an advocate for the three professionals, the nurse, provider, and pharmacist, to collaborate. Appropriate communication between the three health care workers will lead to the correct amount of heparin to be administered and should hopefully contribute to a positive patient outcome of achieving therapeutic anticoagulation within 24 hours or less. Not only is it extremely vital the patient is given the right heparin dose so VTE does not recur, but the right heparin dosage is needed to prevent further health complications. It may also be the nurses job to titrate the heparin dosing if therapeutic aPTT levels are not met with the first heparin continuous infusion dose. Last, the findings in this systematic review apply to the nurse because the nurses scope of practice includes monitoring, reassessing, and evaluating the patient's reaction to heparin therapy. This role is highly significant as adequate patient-care includes analyzing lab values and communicating with the patients health care provider depending on the patient response. It is absolutely crucial nurses understand the importance of heparin therapy, the dosing of heparin, and the effect it has in the obese population with VTE.

Conclusion

The findings of this systematic review proved that in patients with venous thromboembolism, heparin therapy can lead to therapeutic anticoagulation within 24 hours in obese patients. This systematic review supports the current heparin practice of uncapped actual body weight dosing in all weight cohorts. The review also supports the use of dosing body weight in the obese and morbidly obese population with VTE, but it is preferable to have more research concerning DBW. Right now, the research suggests that heparin dosing somewhat differs in the obese patient from the nonobese patient, especially when trying to achieve proper anticoagulation in 24 hours. The utilization of uncapped actual body weight dosing for all

weight categories has proven to be effective. In the obese and morbidly obese patient, the alternative of dosing body weight can be utilized and may be more successful in the clinical practice setting as well. More research is needed to fully understand the safety and effect the dosing body weight has in the achievement of therapeutic anticoagulation in obese patients, especially regarding the 24 hour time frame. Current evidence shows that the heparin bolus leads to supratherapeutic aPTT levels and slower therapeutic aPTT. Additional research is recommended to prove that heparin boluses are not useful in the obese and morbidly obese population with VTE. Overall, as obesity continues to increase in the United States, more research should be conducted to evaluate the effect weight-based heparin therapy has in the obese patient with venous thromboembolism.

References

Ebied, A. M., Li, T., Axelrod, S. F., Tam, D. J., & Chen, Y. (2020). Intravenous unfractionated heparin dosing in obese patients using anti-Xa levels. *Journal of Thrombosis and Thrombolysis, 49.* **https://doi.org/10.1007/s11239-019-01942-6**

George, C., Barras, M., Coombes, J., & Winckel, K. (2020). Unfractionated heparin dosing in obese patients. *International Journal of Clinical Pharmacy, 42*. **https://doi.org/10.1007/s11096-020-01004-5**

Gerlach, A. T., Folino, J., Morris, B. N., Murphy, C. V., Stawicki, S. P., & Cook, C. H. (2013). Comparison of heparin dosing based on actual body weight in non-obese, obese and morbidly obese critically ill patients. *International Journal of Critical Illness & Injury Science, 3*(3). **doi: 10.4103/2229-5151.119200**

Hosch, L. M., Breedlove, E. Y., Scono, L. E., & Knoderer, C. A. (2017). Evaluation of an unfractionated heparin pharmacy dosing protocol for the treatment of venous thromboembolism in nonobese, obese, and severely obese patients. *Annals of Pharmacotherapy.* **https://doi.org/10.1177/1060028017709819**

Hurewitz, A. N., Khan, S. U., Groth, M. L., Patrick, P. A., & Brand, D. A. (2010). Dosing of unfractionated heparin in obese patients with venous thromboembolism. *J Gen Intern Med, 26*(5): 487-491. **https://doi.org/10.1007/s11606-010-1551-2**

Labus, D. & Sellers, E. (Eds). (2020). *Nursing 2020 drug handbook*. Philadelphia, PA: Wolters Kluwer.

Myzienski, A. E., Lutz, M. F., & Smythe, M. A. (2010). Unfractionated heparin dosing for

venous thromboembolism in morbidly obese patients: Case report and review of the literature. The Journal of Human Pharmacology and Drug Therapy, 30(3). **https://doi.org/10.1592/phco.30.3.324**

Napa Valley College. (n.d.) *An introduction to using CINAHL*. Retrieved from http://www.napavalley.edu/Library/Documents/CinahlGuide.pdf

National Library of Medicine. (n.d.). PubMed Overview. Retrieved from https://pubmed.ncbi.nlm.nih.gov/about/

Pagana, K. D., & Pagana, T. J. (2018). *Mosby's manual of diagnostic and laboratory tests* (6th ed.). St.Louis, MO: Mosby Elsevier.

Raschke, R. A., Reilly, B. M., Guidry, J. R., Fontana, J. R., & Srinivas, S. (1993). The weight-based heparin dosing nomogram compared with a "standard care" nomogram. A randomized controlled trial. *Annals of Internal Medicine, 119*(9). **https://doi.org/10.7326/0003-4819-119-9-199311010-00002**

Shlensky, J. A., Thurber, K. M., O'Meara, J. G., Ou, N. N., Osborn, J. L., Dierkhising, R. A., Mara, K. C., Bierle, D. M., & Daniels, P. R. (2019). Unfractionated heparin infusion for treatment of venous thromboembolism based on actual body weight without dose capping. *Society for Vascular Medicine*. **https://doi.org/10.1177/1358863X19875813**