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A Systematic review and meta-analysis of cohorts on enoxaparin dosing regimens in adult hospitalized patients

Heba **Ramadan**[1]

[1] Pharmacy Department, Agamy Medical District, Ministry of Health and Population, Agamy, Alexandria, Egypt

***Corresponding Author**: Heba Ramadan
Pharmacy Department, Agamy Medical District, Ministry of Health and Population, Agamy, Alexandria, Egypt
Email: hebaramadan_24884@yahoo.com

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Abstract

Background: Enoxaparin, a low-molecular-weight heparin, is widely used for hospitalized patients for prevention and situations associated with ischemic complications due to its anticoagulant and anti-inflammatory effects. This study's enoxaparin dosage regimens show adherence to the standard dose in different conditions.

Objective: To review and analyze the adherence to enoxaparin dosage regimens in adult hospitalized patients across various clinical conditions, including COVID-19, and assess the effectiveness and safety of these dosing practices.

Methods: This was applied through searching in Scopus, WOS, and PubMed. A PRISMA checklist was followed, and a quality assessment was checked. Statistical and meta-analysis were conducted using SPSS, Version 28, and the R-4.3.2 package.

Results: Seventeen retrospective cohort studies were included in the final analysis. Eight studies concerned COVID-19 patients. The total number of patients in the non-COVID-19 group studies is 28233; 15421 (49%, 0.4-0.59 95% C.I.) of them received a standard dose. The total number of patients in the COVID-19 group studies is 54099; no patients received a reduced dose, and 38006 (60%, 0.45-0.74 95% C.I.) received a standard dose. For non-COVID-19 studies, there is a significant difference in the means of patient number percentage received standard dose or reduced dose and those received overdose (Sig <0.05, C.I. 95%) in favor of the standard dose or reduced dose and no significant difference in the means of patient number percentage received standard dose and those received reduced dose (Sig. = 0.56, C.I. =95%). For COVID-19 studies, there is no significant difference in the means of patient number percentage received standard dose and those received overdose (Sig. =0.094, C.I. =95%).

Conclusion: Using definite tools to determine the most safe and effective enoxaparin dosage regimens is required.

Keywords: enoxaparin; low-molecular-weight heparin; dosing; hospitalized patients

INTRODUCTION

Enoxaparin is a low-molecular-weight heparin that was first approved in 1993. It has an indirect anticoagulant effect as it binds to ant-thrombin III, forming a complex that irreversibly inactivates factor Xa. Factor Xa is involved in the normal coagulation pathway by cleaving prothrombin to generate thrombin, creating a stabilized cross-linked fibrin clot [1].

Enoxaparin is used for prophylaxis of deep venous thrombosis in patients undergoing surgery, such as hip or knee surgery, abdominal surgery, or patients suffering from conditions that limit their mobility. It can be used for prophylaxis of insufficiency complications of non-ST elevated myocardial infarction and unstable angina. Enoxaparin is also used to treat deep venous thrombosis and ST-elevated and non-ST-elevated myocardial infarction. The enoxaparin dose is varied; in prophylaxis situations, it ranges from 20-40 mg as a fixed standard dose, while in treatment situations, it ranges from 1-1.5 mg/Kg. Also, it varies from 0.75-1 mg/Kg when used in renal patients [1-4].

It has off-label use in pregnancy or the postpartum period for treating venous thromboembolism in those with a high risk of deep venous thrombosis, a history of venous thromboembolism, and a history of fetal loss [5].

During the COVID-19 pandemic, some guidelines, like the American Society of Hematology, advised using supratherapeutic prophylactic doses of enoxaparin due to its antithrombotic and anti-inflammatory effects [6].

Enoxaparin is eliminated by first-order kinetics and excreted primarily in the urine, so its dose is adjusted after screening for Creatinine clearance, especially in renal patients [7].

It is mainly administrated by subcutaneous route, achieving high bioavailability, and it can be administrated intravenously.

Bleeding is a significant adverse effect of enoxaparin. Since enoxaparin is usually prescribed with other anticoagulants with adverse bleeding effects, dosing adjustment is crucial.

Enoxaparin dosage varies according to the situation, patient case, weight, renal function, and age. Anti-Xa level is considered an indicator of the blood level of enoxaparin, and it is advised to continuously measure it to screen if enoxaparin is at a sufficient level or a low or high harmful concentration [8].

The safest and most effective dose of enoxaparin is challenging. Many physicians may tend to prescribe reduced doses. In other cases, like in COVID-19 patients, the physicians may tend to prescribe doses higher than the standard doses [6, 9].

In the current study, enoxaparin dosage regimens are examined in different retrospective cohort studies of hospitalized patients with various conditions to demonstrate whether the prescribed dosage regimens usually adhere to the standard dose as specified in the guidelines.

METHODS

This systematic review obeyed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist [10].

Data Sources and Searches

A search was done on January 15, 2024, via Scopus, Web of Science, and PubMed using the search terms "enoxaparin," "dosing," and "cohort study." The included studies of this review are (1) only retrospective cohort studies, as the theory depends on screening what is simultaneously applied to show the behavior of prescribing the dosage regimens. (2) Concerning hospitalized patients who received enoxaparin for different conditions. (3) of adult patients, whose age > 18 years. The excluded studies were (1) not in English. (2) with restricted full text. (3) Duplicates. (4) reviews, prospective, or any predesigned studies. (5) For outpatients, children, and pregnant women.

Study Selection

The eligibility of the search results was assessed in two stages: title and abstract screening, then full-text screening.

Data Extraction and Quality Assessment

The data that were extracted contained the author's name, year of publication, the country where the study was conducted, the journal that published the study, mean age in years, gender (female), monocenter or multicenter, patient condition, total number of patients involved in each study, and number of patients receiving reduced dose, standard dose, and overdose. Quality assessment was checked by a quality scoring system [11]. It included a degree of ascertainment; for the included studies in this analysis, it was retrospective and revised from mono- or multi-center records. All of them involved all patients received enoxaparin in a specific period. The appropriate population was selected, and the size was recorded. The sample size was mentioned and defined. The years of study were recorded. General patient characteristics were recorded. The included studies yielded good quality, with a maximum score of 90 points (supplementary table 1).

Data Synthesis and Analysis

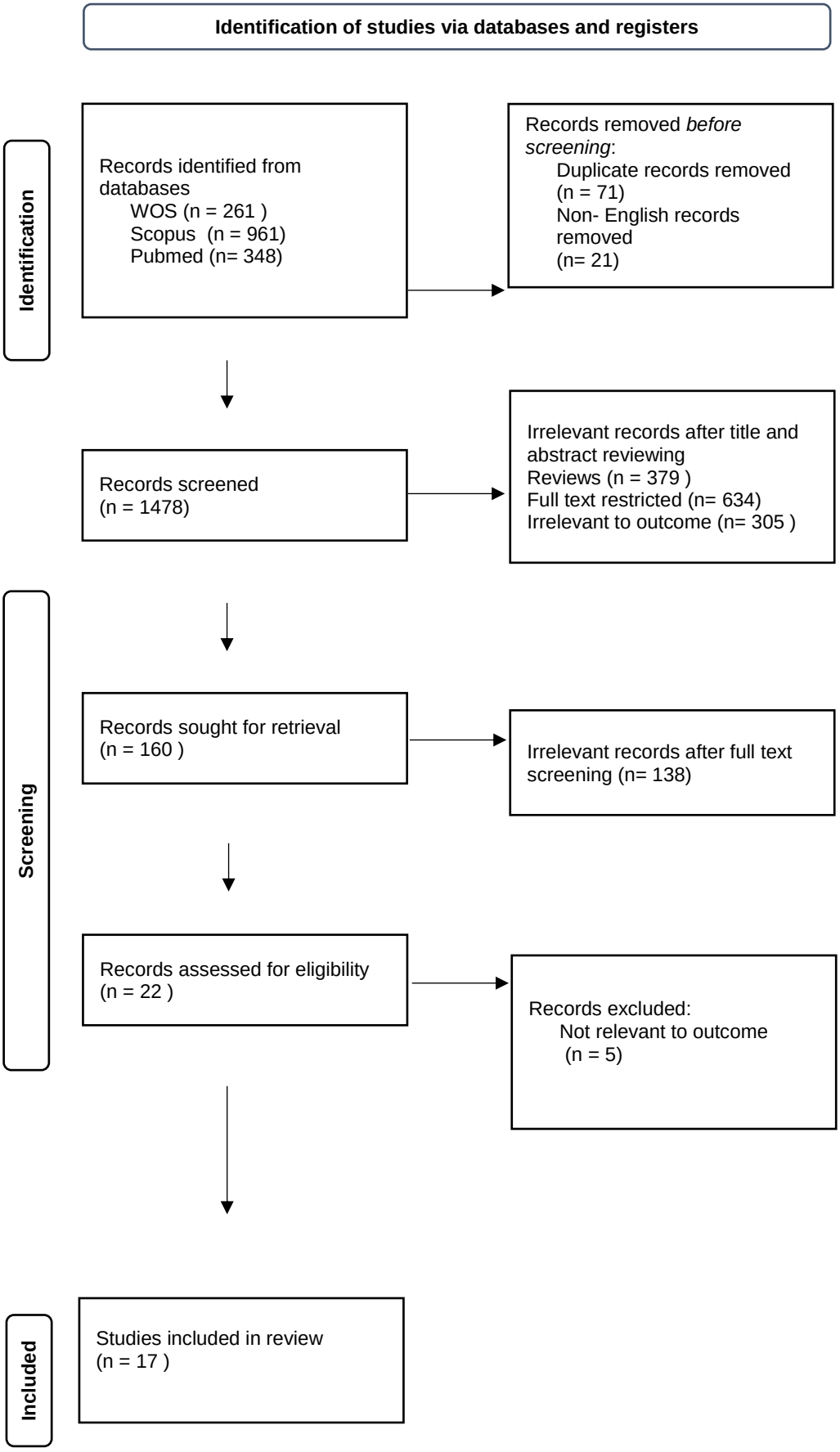
The R-4.3.2 package and SPSS, Version 28, conducted meta-analysis and statistical analysis. The percentage of patients receiving a reduced dose, a standard dose, or an overdose is calculated for each study. A one-way ANOVA and independent samples T-test applied to screen the mean difference between the patient groups receiving reduced dose, standard dose, and overdose. The assumptions of these statistical tests were established.

RESULTS

Literature Search

The initial search recognized 261 studies from Web of Science, 961 studies from Scopus, and 348 studies from Pubmed. 71 studies were excluded as duplicates, and 21 studies were not in English. 1478 studies were screened in the title and abstract screening stage. 379 studies were excluded as reviews, 634 were not available as free full text, and 305 were irrelevant. After the complete text screening stage, 138 were excluded as irrelevant, and 22 studies were assessed for eligibility. The final analysis was applied to 17 included studies (Figure 1).

Figure 1. PRISMA flow diagram



Study Characteristics

Seventeen retrospective cohort studies [12-28] were included in the final analysis. It was published from 2007 to 2023. Eight studies concerning COVID-19 patients receiving enoxaparin during hospitalization were published from 2020 to 2023 [21-28]. Most of the included studies were conducted in the USA by nine studies. The Hospital Pharmacy Journal and the Journal of Thrombosis and Thrombolysis had the most significant contributions, with two studies for each. All studies were applied to adults aged more than 38 years. 10 studies were conducted in mono-centers, and the remaining seven studies were conducted in multi-centers. Patients enrolled in these studies had several conditions and received enoxaparin mainly for ischemic complications prophylaxis during hospitalization (supplementary table 2). The number of patients enrolled in all studies varied from 61 to 50091.

Proportional meta-analysis

The included studies were distinguished into two groups: nine studies concerning several conditions (Table 1) and the remaining eight studies concerning COVID-19 hospitalized patients receiving enoxaparin (Table 2). The R-4.3.2 package applied proportional meta-analysis to display the accurate percentage for prescribing reduced dose, standard dose, and overdose among the different dosage regimens in the non-COVID-19 and COVID-19 groups. A random model was used due to the high heterogeneity between studies, reaching 100%. The heterogeneity in this type of meta-analysis may not be considered. [29]. The total number of patients in the non-COVID-19 group studies is 28233; 8249 (40%, 0.27-0.53 95% C.I.) of them received a reduced dose of enoxaparin (Supplementary figure 1), 15421 (49%, 0.4-0.59 95% C.I.) of them received a standard dose of enoxaparin (Supplementary figure 2), and 4568 (11%, 0.01-0.23 C.I.) of them received an overdose of enoxaparin (Supplementary figure 3). The total number of patients in the COVID-19 group studies is 54099; no patients received a reduced dose; 38006 (60%, 0.45-0.74 C.I.) received a standard dose of enoxaparin (Supplementary figure 4); and 16093 (40%, 0.26-0.55 C.I.) received an overdose of enoxaparin (Supplementary figure 5).

Table 1. Total number of patients, number of patients receiving a reduced dose, standard dose, and overdose in non-COVID-19 studies

Study ID	Author, year	total number of patients	reduced dose	standard dose	overdose
1	Adisak Weerasaksanti , 2023	602	292	255	55
2	Helena Knox, 2023	419	140	279	0
3	Abigail Nemeth , 2022	171	48	128	0
4	Douglas Buckheit	151	88	63	0

	, 2021				
5	Young R. Lee , 2020	241	16	91	134
6	Byeol Seo , 2018	564	341	221	2
7	Todd W. Costantini , 2014	61	43	18	0
8	Sarah A. Spinler , 2009	15337	4165	8797	2375
9	Nancy M. Allen LaPointe , 2007	10687	3116	5569	2002

Table 2. Total number of patients, number of patients receiving reduced dose, standard dose, and overdose in COVID-19 studies

study ID	Author, year	total number of patients	reduced dose	standard dose	overdose
10	Munyaradzi Stanley Chakabva, 2023	1786	0	398	1388
11	Juan Mora-Delgado, 2023	461	0	369	92
12	Kathleen M. Andersen, 2022	50091	0	36060	14031
13	Ohoud Aljuhani, 2022	565	0	380	185
14	Hasan M. Al-Dorzi, 2022	185	0	104	81
15	Lina H. AlLehaibi, 2022	470	0	373	97
16	Marco G. Mennuni, 2021	436	0	287	149
17	Massimo Mattioli, 2020	105	0	35	70

Statistical analysis

The significance of the difference between all groups was screened by a one-way ANOVA and independent samples T-test, and SPSS, version 28.31, applied this [30].

For non-COVID-19 studies

Patients are classified into 3 groups (1

reduced dose, 2 standard doses, and 3 overdoses) and considered independent categorical variables. In contrast, the dependent variable was the percentage of patients in every study for each group. Assumptions of a one-way ANOVA statistical test 32 were established, the normality of the dependent variable was tested by the Shapiro-Wilk test, and the data distribution appeared normal (Sig. = 0.106). The Levene test tested the homogeneity of the variances of the dependent variable, and the data were considered homogenous (Sig. = 0.524). A one-way ANOVA statistical test indicated a significant difference between groups (Sig.< 0.05, C.I. 95%). The Tukey post hoc test was conducted to explore specific group differences [33].

Standard dose group versus overdose group

There is a significant difference in the means of patient number percentage received standard dose and those received overdose (Sig.<0.05, C.I. 95%) in favor of the standard dose group.

Standard dose group versus reduced dose group

There is no significant difference in the means of patient number percentages who received standard dose and those who received reduced dose (Sig. = 0.56, C.I. =95%).

Reduced dose group versus overdose group

There is a significant difference in the means of patient number percentage received reduced dose and those received overdose (Sig.<0.05, C.I. 95%) in favor of the reduced dose group.

For COVID-19 studies

No patients received reduced doses. Patients are classified into 2 groups (1 standard dose, and 2 overdose) and considered an independent categorical variable, while the dependent variable was the percentage of patients in every study for each group. Assumptions of independent samples T test were established, the normality of the dependent variable was tested by the Shapiro-Wilk test, and the data distribution appeared normal (Sig. =0.148) [34]. The homogeneity of the variances of the dependent variable was tested by the Levene test, and the data were considered homogenous (Sig.> 0.05). There is no significant difference in the means of patient number percentage received standard dose and those received overdose (Sig. = 0.094, C.I. =95%).

DISCUSSION

The current study aimed to screen enoxaparin dosage regimens prescribed for adult hospitalized patients, and that was done by demonstrating 17 retrospective cohort studies to see if the physicians adhere to the standard dose or if the fear of bleeding adverse reaction pushes them to prescribe a reduced dose or, in some conditions they may intend to prescribe doses exceeding the standard dose. Eight studies were found concerning COVID-19-hospitalized patients. The total number of patients in the non-COVID-19 group studies is 28233; 8249 (40%, 0.27-0.53 95% C.I.) of them received a reduced dose of enoxaparin, 15421 (49%, 0.4-0.59 95% C.I.) of them received a standard dose of enoxaparin, and 4568 (11%, 0.01-0.23 C.I.) of them received an overdose of

enoxaparin. The total number of patients in the COVID-19 group studies is 54099; no patients received a reduced dose; 38006 (60%, 0.45-0.74 C.I.) received a standard dose of enoxaparin; and 16093 (40%, 0.26-0.55 C.I.) received an overdose of enoxaparin. The significance of the difference between all groups was screened by a one-way ANOVA and an independent samples T test. For non-COVID 19 studies, there is a significant difference in the means of patient number percentage received standard dose or reduced dose and those received overdose (Sig.<0.05, C.I. 95%) in favor of the standard dose group or reduced dose group and no significant difference in the means of patient number percentage received standard dose and those received reduced dose (Sig. = 0.56, C.I. =95%). It goes with a study for acute coronary syndrome patients with basic characters that 42.4% and 48.5% of patients, respectively, received the recommended dose and reduced dose, while only 9.1% received an overdose [12]. Another study applied to critically ill patients receiving enoxaparin for prophylaxis of venous thromboembolism; 33.4% of them received it at a reduced dose, 66.6% of them received it at the standard dose, and no patients received an overdose [13]. On the other hand, a study showed that in morbidly obese patients, 55.6% received an overdose, 6.6% received a reduced dose, and 37.8% received a standard dose [16]. For COVID-19 studies, no patients received reduced doses, and there is no significant difference in the means of patient number percentage received standard dose and those received overdose (Sig. = 0.094, C.I. =95%). It goes with a study, in it the majority of patients received doses exceeded the standard dose by 77.7%.[21] In another study, 66.7% of patients received doses that exceeded the standard dose, and only 33.3% received the standard dose.[27] That is matched with the American Society of Hematology, which advised using supratherapeutic prophylactic doses of enoxaparin due to its antithrombotic and anti-inflammatory effects.[35] on the other hand, a study showed a decreased percentage of patients receiving overdoses versus the standard dose (19.9% versus 79.1%).[22]

The current study showed several limitations, as it was restricted to adults patients, did not involve children, and ignored pregnant women. A huge number of screened studies in the title and abstract step (634 studies) had restricted access and were not involved in the final analysis.

CONCLUSION

Using definite tools to determine the most safe and effective enoxaparin dosage regimens is required to guide the health care professionals about an accurate enoxaparin prescription.

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Ethical issues

Not applicable

Competing interests

Nil

Author's contribution

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REFERENCES

1. Simon SJ, Patell R, Zwicker JI, Kazi DS, Hollenbeck BL. Venous Thromboembolism in Total Hip and Total Knee Arthroplasty. *JAMA Netw Open.* 2023; 6(12): e2345883. doi:10.1001/jamanetworkopen.2023.45883

2. Segon YS, Summey RD, Slawski B, Kaatz S. Surgical venous thromboembolism prophylaxis: clinical practice update. *Hosp Pract (1995).* 2020; 48(5): 248-57. doi:10.1080/21548331.2020.1788893

3. Collet J-P, Thiele H, Barbato E, Barthélémy O, Bauersachs J, Bhatt DL, *et al.* 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: The Task Force for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). *European Heart Journal.* 2020; 42(14): 1289-367. doi:10.1093/eurheartj/ehaa575

4. van Gameren M, Lemmert ME, Wilschut JM, Daemen J, De Jaegere PPT, Zijlstra F, *et al.* An update on the use of anticoagulant therapy in ST-segment elevation myocardial infarction. *Expert Opinion on Pharmacotherapy.* 2018; 19(13): 1441-50. doi:10.1080/14656566.2018.1512583

5. Anonymous. ACOG Practice Bulletin No. 196: Thromboembolism in Pregnancy: Correction. *Obstet Gynecol.* 2018; 132(4): 1068. doi:10.1097/AOG.0000000000002923

6. Cuker A, Tseng EK, Nieuwlaat R, Angchaisuksiri P, Blair C, Dane K, *et al.* American Society of Hematology living guidelines on the use of anticoagulation for thromboprophylaxis in patients with COVID-19: January 2022 update on the use of therapeutic-intensity anticoagulation in acutely ill patients. *Blood Advances.* 2022; 6(17): 4915-23. doi:10.1182/bloodadvances.2022007561

7. Shaikh SA, Regal RE. Dosing of Enoxaparin in Renal Impairment. *P T.* 2017; 42(4): 245-9.

8. Crowther MA, Warkentin TE. Bleeding risk and the management of bleeding complications in patients undergoing anticoagulant therapy: focus on new anticoagulant agents. *Blood.* 2008; 111(10): 4871-9. doi:10.1182/blood-2007-10-120543

9. Sebaaly J, Covert K. Enoxaparin Dosing at Extremes of Weight: Literature Review and Dosing Recommendations. *Annals of Pharmacotherapy.* 2018; 52(9): 898-909. doi:10.1177/1060028018768449

10. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, *et al.* The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ.* 2021; 372: n71. doi:10.1136/bmj.n71

11. Al-Jader L, Newcombe R, Hayes S, Murray A, Layzell J, Harper P. Developing a quality scoring system for epidemiological surveys of genetic disorders. *Clinical genetics.* 2002; 62(3): 230-4.

12. Weerasaksanti A, Siwamogsatham S, Kunlamas Y, Bunditanukul K. Factors associated with bleeding events from enoxaparin used for patients with acute coronary syndrome. *Bmc Cardiovascular Disorders.* 2023; 23(1). doi:10.1186/s12872-023-03278-9

13. Knox H, Edwin SB, Giuliano C, Paxton RA. Venous Thromboembolism Prophylaxis in Low Body Weight Critically Ill Patients. *Journal of Intensive Care Medicine.* 2023. doi:10.1177/08850666231217693

14. Nemeth A, Isherwood M. Safety and Effectiveness of Reduced Dose Versus Standard Dose Enoxaparin Venous Thromboembolism Prophylaxis in Underweight Medically Ill Patients. *Hospital Pharmacy.* 2023; 58(2): 178-82. doi:10.1177/00185787221123220

15. Buckheit D, Lefemine A, Sobieraj DM, Hobbs L. Venous Thromboembolism Prophylaxis in Underweight Hospitalized Patients. *Clinical and Applied Thrombosis/Hemostasis.* 2021; 27. doi:10.1177/10760296211018752

16. Lee YR, Palmere PJ, Burton CE, Benavides TM. Stratifying Therapeutic Enoxaparin Dose in Morbidly Obese Patients by BMI Class: A Retrospective Cohort Study. *Clinical Drug Investigation.* 2020; 40(1): 33-40.

doi:10.1007/s40261-019-00855-9

17. Seo B, Yang Y-M, Choi EJ. A retrospective study of enoxaparin dosing in cancer patients based on renal function in South Korea. *Yakhak Hoeji*. 2018; 62(2): 109-17.

18. Costantini TW, Min E, Box K, Tran V, Winfield RD, Fortlage D, *et al.* Dose adjusting enoxaparin is necessary to achieve adequate venous thromboembolism prophylaxis in trauma patients. *The journal of trauma and acute care surgery*. 2013; 74(1): 128.

19. Spinler SA, Ou FS, Roe MT, Gibler WB, Ohman EM, Pollack CV, *et al.* Weight-based dosing of enoxaparin in obese patients with non-ST-segment elevation acute coronary syndromes: results from the CRUSADE initiative. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*. 2009; 29(6): 631-8.

20. LaPointe NMA, Chen AY, Alexander KP, Roe MT, Pollack CV, Lytle BL, *et al.* Enoxaparin dosing and associated risk of in-hospital bleeding and death in patients with non–ST-segment elevation acute coronary syndromes. *Archives of internal medicine*. 2007; 167(14): 1539-44.

21. Chakabva MS, Polina S, Brauner M, McGuire M, Brown Z, Akthar T, *et al.* Comparison of Standard Versus Intermediate Prophylaxis Dose for Venous Thromboembolism Prophylaxis in Patients Hospitalized With COVID-19 Infection. *Hospital Pharmacy*. 2023. DOI:10.1177/00185787231194997

22. Mora-Delgado J, Lojo-Cruz C, Marín PR, Campos EMM, Michán-Doña A. Enoxaparin Posology According to Prothrombotic Status and Bleeding Risk in Hospitalized Patients with SARS-CoV-2 Pneumonia. *Journal of Clinical Medicine*. 2023; 12(3). DOI:10.3390/jcm12030928

23. Andersen KM, Joseph CS, Mehta HB, Streiff MB, Betz JF, Bollinger Jr RC, *et al.* Thromboprophylaxis in people hospitalized with COVID-19: Assessing intermediate or standard doses in a retrospective cohort study. *Research and Practice in Thrombosis and Haemostasis*. 2022; 6(5): e12753.

24. Aljuhani O, Al Sulaiman K, Hafiz A, Eljaaly K, Alharbi A, Algarni R, *et al.* Comparison between standard Vs. Escalated dose venous thromboembolism (VTE) prophylaxis in critically ill patients with COVID-19: A two centers, observational study. *Saudi Pharmaceutical Journal*. 2022; 30(4): 398-406. DOI:10.1016/j.jsps.2022.01.022

25. Al-Dorzi HM, Alqirnas MQ, Hegazy MM, Alghamdi AS, Alotaibi MT, Albogami MT, *et al.* Prevalence and Risk Factors of Venous Thromboembolism in Critically Ill Patients with Severe COVID-19 and the Association between the Dose of Anticoagulants and Outcomes. *Journal of Critical Care Medicine*. 2022; 8(4): 249-58. DOI:10.2478/jccm-2022-0023

26. AlLehaibi LH, Alomar M, Almulhim A, Al-Makki S, Alrwaili NR, Al-Bassam S, *et al.* Effectiveness and Safety of Enoxaparin Versus Unfractionated Heparin as Thromboprophylaxis in Hospitalized COVID-19 Patients: Real-World Evidence. *Annals of Pharmacotherapy*. 2023; 57(4): 361-74. DOI:10.1177/10600280221115299

27. Mennuni MG, Renda G, Grisafi L, Rognoni A, Colombo C, Lio V, *et al.* Clinical outcome with different doses of low-molecular-weight heparin in patients hospitalized for COVID-19. *Journal of Thrombosis and Thrombolysis*. 2021; 52(3): 782-90. DOI:10.1007/s11239-021-02401-x

28. Mattioli M, Benfaremo D, Mancini M, Mucci L, Mainquà P, Polenta A, *et al.* Safety of intermediate dose of low molecular weight heparin in COVID-19 patients. *J Thromb Thrombolysis*. 2021; 51(2): 286-92. DOI:10.1007/s11239-020-02243-z

29. Barker TH, Migliavaca CB, Stein C, Colpani V, Falavigna M, Aromataris E, *et al.* Conducting proportional meta-analysis in different types of systematic reviews: a guide for synthesisers of evidence. *BMC Medical Research Methodology*. 2021; 21: 1-9.

30. Quirk TJ, Quirk TJ. One-way analysis of variance (ANOVA). *Excel 2007 for Educational and Psychological Statistics: A Guide to Solving Practical Problems*. 2012: 163-79.

31. Kim H-Y. Statistical notes for clinical researchers: the independent samples t-test. *Restorative Dentistry & Endodontics*. 2019; 44(3).

32. Sheng Y. Testing the assumptions of analysis of variance. *Best practices in quantitative methods*. 2008: 324-40.

33. Ruxton GD, Beauchamp G. Time for some a priori thinking about post hoc testing. *Behavioral ecology*. 2008; 19(3): 690-3.

34. Kim TK, Park JH. More about the basic assumptions of t-test: normality and sample size. *Korean journal of anesthesiology*. 2019; 72(4): 331-5.

35. Cuker A, Tseng EK, Nieuwlaat R, Angchaisuksiri P, Blair C, Dane K, *et al.* American Society of Hematology living guidelines on the use of anticoagulation for thromboprophylaxis in patients with COVID-19: January 2022 update on the use of therapeutic-intensity anticoagulation in acutely ill patients. *Blood Advances*. 2022; 6(17): 4915-23. DOI: 10.1182/bloodadvances.2022007561.

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