Medical and Pharmaceutical Journal

Volume 3 Issue 2

Med. Pharm. J .Review article

A Systematic Review and Meta-Analysis of Cohorts on Enoxaparin Dosing Regimens in Hospitalized Adult 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

DOI: 10.55940/medphar202479
Submitted: 17-Mar-2024
Accepted: 30- Jun -2024
Published: 15-Jul-2024

Abstract

Background: Enoxaparin, a low-molecular-weight heparin, is widely used for hospitalized patients for prevention and treatment of ischemic complications due to its anticoagulant and anti-inflammatory effects.

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: A systematic search was conducted in Scopus, Web of Science (WOS), and PubMed databases following PRISMA guidelines. Quality assessment was assessed, and statistical analyses were conducted using SPSS Version 28 and R-4.3.2 package.

Results: Seventeen retrospective cohort studies were included, with eight studies focusing on COVID-19 patients. In non-COVID-19 studies (n=28,233 patients), 49% (15,421 patients, 95% CI: 0.4-0.59) received the standard dose. In COVID-19 studies (n=54,099 patients), 60% (38,006 patients, 95% CI: 0.45-0.74) received the standard dose, and no patients received a reduced dose. Statistical analysis showed significant differences ($p < 0.05$, 95% CI) in favor of standard or reduced doses versus overdoses in non-COVID-19 studies. In COVID-19 studies, no significant differences were found between standard doses and overdoses ($p = 0.094$, 95% CI).

Conclusion: It is essential to employ reliable tools to determine the safest and most effective enoxaparin dosage regimens. This approach is crucial for providing accurate guidance to healthcare professionals regarding the prescription of enoxaparin.

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 anti-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 elevation myocardial infarction and unstable angina. Enoxaparin is also used to treat deep venous thrombosis and ST-elevation and non-ST-elevation myocardial infarction. The enoxaparin dose varies; in prophylactic situations, it ranges from 20-40 mg as a fixed standard dose, while in treatment situations, it ranges from 1-1.5 mg/Kg. Additionally, it ranges 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, or a history of fetal loss [5].

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

Enoxaparin follows by first-order kinetics and is primarily excreted in the urine, necessitating dose adjustments based on creatinine clearance, particularly in renal patients [7].

It is predominantly administered subcutaneously, offering high bioavailability, but can also be given 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 dosing is tailored based on individual patient factors such as weight, renal function, and age.

Anti-Xa level is considered an indicator of the blood level of enoxaparin, and it is advised to continuously monitor it to screen whether enoxaparin is at a sufficient level or at a low or high harmful concentration [8].

Determining the optimal and safest enoxaparin dose presents a clinical challenge. Physicians often lean towards reduced doses in some cases, while in conditions like COVID-19, higher-than-standard doses may be recommended [6, 9].

In the present study, enoxaparin dosage regimens were examined across various retrospective cohort studies involving hospitalized patients with diverse conditions. The objective is to assess whether prescribed dosages typically adhere to standard guidelines 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 performed on January 15, 2024, via Scopus, Web of Science, and PubMed using the search terms "enoxaparin," "dosing," and "cohort study." The studies included in this review were (1) retrospective cohort studies, as the theory depends on screening what is simultaneously applied to show the behavior of prescribing dosage regimens. (2) Concerning hospitalized patients who received enoxaparin for different reasons. (3) of adult patients aged > 18 years. The excluded studies were (1) not in English. (2) with restricted full text. (3) Duplicates. (4) reviews, prospective studies, 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, and full-text screening.

Data Extraction and Quality Assessment

The data that were extracted included the author's name, year of publication, country where the study was conducted, journal that published the study, mean age in years, proportion of females (%), monocenter or multicenter study, patient condition, total number of patients involved in each study, and number of patients receiving a reduced dose, standard dose, and overdose. The quality assessment was checked by a quality scoring system [11]. It included the degree of ascertainment; for the studies included in this analysis, the data were retrospective and revised from mono- or multi-center records. The studies involved all patients received enoxaparin within a specific time span. The appropriate population was selected, and the size was recorded. The sample size was mentioned and defined. The years of study were recorded. Patient characteristics were recorded. All included studies were deemed of high quality, achieving a maximum score of 90 points (supplementary table 1[36]).

Data Synthesis and Analysis

The meta-analysis and statistical analyses were performed using the R-4.3.2 package and SPSS, Version 28. For each study, the percentage of patients receiving a reduced dose, standard dose, or overdose of enoxaparin was calculated. A one-way ANOVA and independent samples t-test were applied to assess the mean differences between patient groups receiving different doses. Assumptions required for these statistical tests were established.

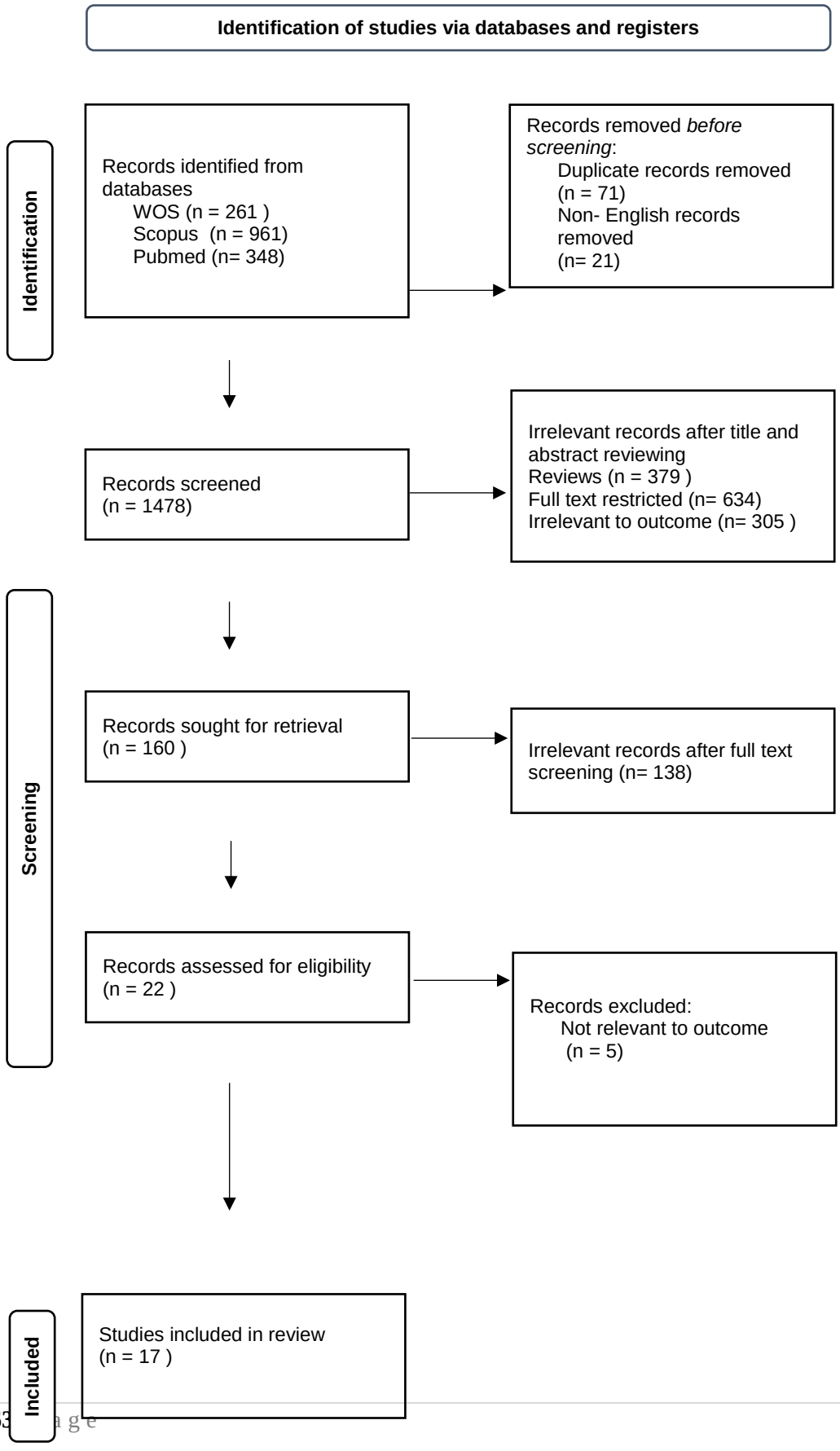
RESULTS

Literature Search

The initial search identified 261 studies from the Web of Science, 961 from Scopus, and 348 studies from PubMed. Seventy-one studies were excluded because they were duplicates, and 21 studies were not in English. A total of 1478 studies underwent title and abstract screening. Among these, 379 reviews and 305 irrelevant studies were excluded. Additionally, 634 studies were unavailable as free full text. After the complete text screening stage, 138 studies were excluded because they were 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], published between 2007 and 2023, were included in the final analysis. Among these, eight studies focused on COVID-19 patients receiving enoxaparin during hospitalization, published from 2020 to 2023 [21-28]. The majority of the included studies (nine studies) were conducted in the USA. 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. Ten studies were conducted in mono-centers, while seven studies were conducted in multi-centers. Patients across these studies presented various conditions and primarily received enoxaparin for prophylaxis against ischemic complications during hospitalization (supplementary table 2). The total number of patients enrolled across all studies ranged from 61 to 50091.

Proportional meta-analysis

The included studies were divided into two groups: nine studies concerning several conditions (Table 1) and eight studies concerning hospitalized patients with COVID-19 receiving enoxaparin (Table 2). Proportional meta-analysis using the R-4.3.2 package was conducted to determine the distribution of reduced doses, standard doses, and overdoses among different dosage regimens in non-COVID-19 and COVID-19 patients. A random-effects model was employed due to high heterogeneity between studies, which approached 100%. The heterogeneity in this type of meta-analysis may not be considered [29]. In non-COVID-19 studies, the total number of patients was 28,233. Among them, 8,249 patients (40%, 95% CI: 0.27-0.53) received a reduced dose of enoxaparin (Supplementary Figure 1), 15,421 patients (49%, 95% CI: 0.4-0.59) received a standard dose (Supplementary figure 2), and 4,568 patients (11%, 95% CI: 0.01-0.23) received an overdose (Supplementary Figure 3). For COVID-19 studies encompassing 54,099 patients, no patients received a reduced dose, while 38,006 patients (60%, 95% CI: 0.45-0.74) received a standard dose of enoxaparin (Supplementary Figure 4), and 16,093 patients (40%, 95% CI: 0.26-0.55) received an overdose (Supplementary figure 5).

Table 1. Total number of patients, and the 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 , 2021	151	88	63	0
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, and the number of patients receiving a 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 differences between all groups was assessed using a one-way ANOVA [30] and independent samples t-test, conducted with SPSS, Version 28 [31].

For non-COVID-19 studies

Patients were classified into three groups (1 reduced dose, 2 standard doses, and 3 overdoses). This classification served as the independent categorical variable, while the dependent variable was the percentage of patients in every study across the groups. Assumptions for conducting a one-way ANOVA [32] were established, the normality of the dependent variable was assessed using the Shapiro-Wilk test, indicating a normal data distribution ($p = 0.106$). The Levene test tested the homogeneity of the variances of the dependent variable, and the data were considered homogenous ($p = 0.524$). The one-way ANOVA revealed a statistically significant difference between the groups ($p < 0.05$, 95% CI). Subsequently, a Tukey post hoc test [33] was conducted to further explore specific differences between the groups.

Standard dose group versus overdose group

There was a statistically significant difference in the mean percentage of patients who received a standard dose compared to those who received an overdose ($p < 0.05$, 95% CI), favoring the standard dose group.

Standard dose group versus reduced dose group

There was no statistically significant difference in the mean percentage of patients who received the standard dose compared to those who received the reduced dose ($p = 0.56$, C.I. =95%).

Reduced dose group versus overdose group

There was a statistically significant difference in the mean percentage of patients who received a reduced dose compared to those who received an overdose ($p < 0.05$, 95% CI), favoring the reduced dose group.

For COVID-19 studies

No patients received reduced doses. Patients were classified into 2 groups (1 standard dose, and 2 overdose), serving as the independent categorical variable, while the dependent variable was the percentage of patients in every study across the groups. Assumptions of an 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 ($p =0.148$) [34]. The homogeneity of the variances of the dependent variable was tested by the Levene test, and the data were considered homogenous ($p > 0.05$). The independent samples t-test showed no statistically significant difference in the mean percentages of patients who received the standard dose compared to those who received an overdose ($p = 0.094$, 95% CI).

DISCUSSION

The present study aimed to screen enoxaparin dosage regimens prescribed for hospitalized adult patients, and that was done by demonstrating 17 retrospective cohort studies to determine adherence to standard doses,

consideration of reduced doses due to fear of bleeding adverse reactions, or potential prescription of doses exceeding standard recommendations. Among these studies, eight focused on hospitalized COVID-19 patients.

In the non-COVID-19 studies, involving a total of 28,233 patients, 8,249 patients (40%, 95% CI: 0.27-0.53) received a reduced dose of enoxaparin, 15,421 patients (49%, 95% CI: 0.4-0.59) received a standard dose, and 4,568 patients (11%, 95% CI: 0.01-0.23) received an overdose. For COVID-19 studies encompassing 54,099 patients, no patients received a reduced dose, 38,006 patients (60%, 95% CI: 0.45-0.74) received a standard dose, and 16,093 patients (40%, 95% CI: 0.26-0.55) received an overdose of enoxaparin.

Statistical analyses, including one-way ANOVA and independent samples t-test, were employed to assess differences between groups. In the non-COVID-19 studies, a significant difference was observed in the mean percentages of patients receiving a standard dose or reduced dose compared to those receiving an overdose ($p < 0.05$, 95% CI), favoring the standard dose or reduced dose groups. However, there was no significant difference in the mean percentages of patients receiving a standard dose versus a reduced dose ($p = 0.56$, 95% CI). It goes with a study on acute coronary syndrome patients reported that 42.4% and 48.5% of patients received the recommended and reduced doses, respectively, while only 9.1% received an overdose [12].

Another study applied to critically ill patients receiving enoxaparin for prophylaxis against venous thromboembolism reported that 33.4% of them received a reduced dose, 66.6% received the standard dose, and no patients received an overdose [13].

Conversely, a study involving morbidly obese patients indicated that 55.6% received an overdose of enoxaparin, 6.6% received a reduced dose, and 37.8% received the standard dose [16].

In COVID-19 studies, no patients received reduced doses, and there was no significant difference in the mean percentage of patients receiving the standard dose compared to those receiving an overdose ($p = 0.094$, 95% CI). It goes with a study reported that the majority of patients (77.7%) received doses exceeding the standard dose [21]. Similarly, another study found that 66.7% of patients received supratherapeutic doses, while only 33.3% received the standard dose [27]. These findings align with recommendations from the American Society of Hematology advocating for supratherapeutic prophylactic doses of enoxaparin due to its antithrombotic and anti-inflammatory effects [35]. On the other hand, another study indicated a lower percentage of patients receiving overdoses compared to those receiving the standard dose (19.9% versus 79.1%) [22].

The current study has several limitations. It focused exclusively on adult patients and did not include children or pregnant women. Additionally, a significant number of studies screened during the title and abstract review (634 studies) were excluded due to restricted access and were therefore not included in the final analysis.

CONCLUSION

It is essential to employ reliable tools to determine the safest and most effective enoxaparin dosage regimens. This approach is crucial for providing accurate guidance to healthcare professionals regarding the prescription of enoxaparin.

ACKNOWLEDGMENT

Nil

Ethical issues

Not applicable

Competing interests

Nil

Author's contribution

One author conducted the manuscript

Funding

Nil

Supplementary Data

All Data are available under Creative Commons Attribution- (CC BY) 4.0[36] contains the Supplementary table and figures

REFERENCES

1. 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.

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.

36. Ramadan. supplementary materials. Zenodo; 2024.DOI:10.5281/zenodo.13200786

How to cite this article:
Ramadan H. A Systematic review and meta-analysis of cohorts on enoxaparin dosing regimens in adult hospitalized patients. Medical and Pharmaceutical Journal. 2024; 3(2): 60-70.
DOI: 10.55940/medphar202479
Available from: http://pharmacoj.com/ojs/index.php/Medph/article/view/79