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CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

Dosing of Enoxaparin for Acute Coronary Syndrome: Guidelines

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Authors: Diksha Kumar, Caitlyn Ford

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Research Question

What are the evidence-based guidelines regarding the dosing of enoxaparin in adults with acute coronary syndrome?

Key Findings

Five evidence-based guidelines were identified regarding dosing of enoxaparin in adults with acute coronary syndrome.

Methods

A limited literature search was conducted by an information specialist on key resources including PubMed, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were enoxaparin and acute coronary syndrome. Search filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, or network meta-analyses, and guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents, with no date limit imposed. Internet links were provided, where available.

Selection Criteria

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Adults with acute coronary syndrome
Intervention	Enoxaparin
Comparator	Not applicable
Outcomes	Recommendations regarding the dosing of enoxaparin (e.g., guidance around capping the dose, populations that should receive a reduced dose or who should not be given enoxaparin [e.g., those over a certain body weight threshold])
Study Designs	Evidence-based guidelines

Results

Rapid Response reports are organized so that the higher quality evidence is presented first. Normally, health technology assessment reports and systematic reviews are presented first; however, in reports where guidelines are primarily sought, the aforementioned evidence types are presented in the appendix.

Five evidence-based guidelines[1-5] were identified regarding dosing of enoxaparin in adults with acute coronary syndrome.

Additional references of potential interest are provided in the appendix.

Overall Summary of Findings

Five evidence-based guidelines[1-5] were identified regarding dosing of enoxaparin in adults with acute coronary syndrome.

Guidelines from the European Society of Cardiology[1,2] and American Heart Association/American College of Cardiology[3,4] recommend that enoxaparin be administered subcutaneously at 1 mg/kg twice daily for patients with ST-segment elevation or non–ST-segment elevation acute coronary syndrome. Dosing should be decreased to 1 mg/kg once daily for patients with an estimated glomerular filtration rate of less than 30 mL/min/1.73m^2 or creatinine clearance of less than 30 mL/min.[1-4]

Moreover, the European Society of Cardiology recommends that dosing be decreased to 0.75 mg/kg twice daily for patients with ST-segment elevation aged 75 years and older.[1] Enoxaparin is not recommended for patients with ST-segment elevation and an estimated glomerular filtration rate of less than 15 mL/min/1.73m^2.[1]

The American Heart Association/American College of Cardiology guideline also states that enoxaparin therapy should be continued for the duration of hospitalization or until a percutaneous coronary intervention is performed for patients without ST-segment elevation.[3] At the time of the percutaneous coronary intervention, patients should be administered an additional intravenous dose if they have received fewer than two subcutaneous doses or if the last subcutaneous dose was 8 to 12 hours prior.[3] An intravenous loading dose should be administered to patients who have not received prior anticoagulant therapy.[3]

Similarly, for patients with ST-elevation myocardial infarction undergoing reperfusion with fibrinolytic therapy, the American Heart Association/American College of Cardiology recommends that an anticoagulant such as enoxaparin be administered, first as an intravenous bolus if the patient is under 75 years of age, and then followed in 15 minutes by subcutaneous injection.[4] If the last subcutaneous dose was administered between 8 and 12 hours earlier, additional intravenous enoxaparin dosed at 0.3 mg/kg should be given.[4]

The authors of the last identified guideline[5] recommend that patients with acute coronary syndrome and severe renal impairment be given a decreased dose of low-molecular-weight heparins (such as enoxaparin). Enoxaparin may also be substituted with unfractionated heparin in these patients.[5] Prophylactic doses of enoxaparin may be increased for patients with morbid obesity while therapeutic dosing for patients with obesity should be calculated using total body weight.[5]

References Summarized

Guidelines and Recommendations

1. Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2018 Jan;39(2):119-177. https://academic.oup.com/eurheartj/article/39/2/119/4095042. Accessed 2020 Apr 21. PubMed: PM28886621
   See: Table 9: Recommended doses of antithrombotic agents in the acute care of patients with chronic kidney disease, page 144

2. Roffi M, Patrono C, Collet JP, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute coronary syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). *Eur Heart J*. 2016 Jan;37(3):267-315. PubMed: PM26320110
   See: 5.3.1.2 Low molecular weight heparin, page 288

3. Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC guideline for the management of patients with non–ST-elevation acute coronary syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014 Dec;64(24):e139-e228. http://www.onlinejacc.org/content/64/24/e139. Accessed 2020 Mar 31. PubMed: PM25260718
   See: 4.3.2. Initial Parenteral Anticoagulant Therapy in Patients with Definite NSTE-ACS: Recommendations, page e164; 5.1.2.3. Anticoagulant Therapy in Patients Undergoing PCI: Recommendations, pages e173–e174

4. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2013 Jan;127(4):e362-425. https://www.ahajournals.org/doi/full/10.1161/cir.0b013e3182742cf6. Accessed 2020 Apr 21. PubMed: PM23247304
   See: 5.1.4.2. Adjunctive Anticoagulant Therapy With Fibrinolysis: Recommendations, Class I, Recommendation #1a, page e380; 6.4.2. Anticoagulant Therapy to Support PCI After Fibrinolytic Therapy: Recommendations, Class I, Recommendation #2, page e387

5. Nutescu EA, Spinler SA, Wittkowsky A, Dager WE. Low-molecular-weight heparins in renal impairment and obesity: available evidence and clinical practice recommendations across medical and surgical settings. *Ann Pharmacother*. 2009 Jun;43(6):1064-1083. PubMed: PM19458109

Appendix — Further Information

Systematic Reviews

7. Atiq F, van den Bemt PM, Leebeek FW, van Gelder T, Versmissen J. A systematic review on the accumulation of prophylactic dosages of low-molecular-weight heparins (LMWHs) in patients with renal insufficiency. *Eur J Clin Pharmacol*. 2015 Aug;71(8):921-929.
PubMed: PM26071276

Clinical Practice Guidelines — Methodology Not Specified

8. Unfractionated heparin, low molecular weight heparin and fondaparinux. Whitby (ON): Thrombosis Canada; 2019: https://thrombosiscanada.ca/wp-content/uploads/2019/09/UFH-LMWH-Fonda-4Sep19.pdf. Accessed 2020 Apr 21.
See: Dosing of LWMH, page 2

9. Garcia DA, Baglin TP, Weitz JI, Samama MM. Parenteral anticoagulants: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012 Feb;141(2 Suppl):e24S-e43S. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3278070/. Accessed 2020 Apr 21.
PubMed: PM22315264
See: 1.2.4 Dosing and Monitoring in Special Situations

10. Nova Scotia guidelines for acute coronary syndrome. Halifax (NS): Cardiovascular Health Nova Scotia; 2008: http://www.cdha.nshealth.ca/system/files/sites/documents/nova-scotia-guidelines-acute-coronary-syndromes.pdf. Accessed 2020 Apr 21.
Copy and paste link into web browser
See: Recommendations #15b and #15c, page 11

Review Articles

11. Onwordi EN, Gamal A, Zaman A. Anticoagulant therapy for acute coronary syndromes. *Interv Cardiol*. 2018 May;13(2):87–92.
PubMed: PM29928314

12. Thomson P, Brocklebank C, Semchuk W. Treatment dosing of low-molecular-weight heparins and the dose cap dilemma: considerations for patients in Canada. *Can J Hosp Pharm*. 2009 Sep;62(5):367-374. https://www.cjhp-online.ca/index.php/cjhp/article/view/823. Accessed 2020 Apr 21.
PubMed: PM22478918

13. Duplaga BA, Rivers CW, Nutescu E. Dosing and monitoring of low-molecular-weight heparins in special populations. *Pharmacotherapy*. 2001 Feb;21(2):218-234.
PubMed: PM11213859

Additional References

14. Lovenox (enoxaparin): Enoxaparin sodium solution for injection, manufacturer's standard 100 mg/mL; Lovenox HP: Enoxaparin solidum solution for injection, manufacturer's standard 150mg/mL (high potency) [product monograph]. Laval (QC): sanofi-aventis Canada Inc.; 2019 Dec 19. https://pdf.hres.ca/dpd_pm/00054401.PDF. Accessed 2020 Mar 31.

Correction

The original report, published April 1, 2020, stated: "Three evidence-based guidelines were identified regarding dosing of enoxaparin in adults with acute coronary syndrome."

However, two additional evidence-based guidelines[1,4] have been added to this corrected report. In addition, three clinical practice guidelines with unspecified methodology and one review article have been added to the appendix.