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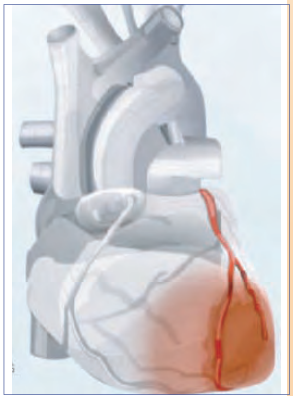
SQUARE PHARMACEUTICALS LTD. BANGLADESH

Efficacy and safety of the low-molecular weight heparin enoxaparin compared with unfractionated heparin across the acute coronary syndrome spectrum: a meta-analysis



Introduction

Antithrombin therapy is an established, guideline recommended treatment, and is central to the management of patients with acute coronary syndromes (ACS). However, the optimal antithrombin agent is still debated. Some, but not all large-scale trials in patients with both ST-segment elevation myocardial infarction (STEMI) and non-ST-elevation ACS (NSTEACS) have shown improved efficacy with the low-molecular weight heparin enoxaparin when compared with unfractionated heparin (UFH), but safety concerns of increased bleeding with enoxaparin have also been reported. The balance between efficacy and safety has been a focus of discussion regarding the choice of optimal antithrombin agent.

The goal of this analysis was to determine whether enoxaparin remains favourable when compared with UFH among patients with ACS when incorporating the efficacy and safety profile of these adjunctive therapies by performing a meta-analysis using a composite net clinical endpoint.

Methods

A PubMed search for randomized clinical trials comparing enoxaparin with UFH among patients with STEMI or NSTEACS. A hand search of references from the original manuscripts and prior meta-analyses was also performed. Inclusion criteria for the analysis were all trials that were: (i) randomized, (ii) compared enoxaparin with UFH, and (iii) were conducted in

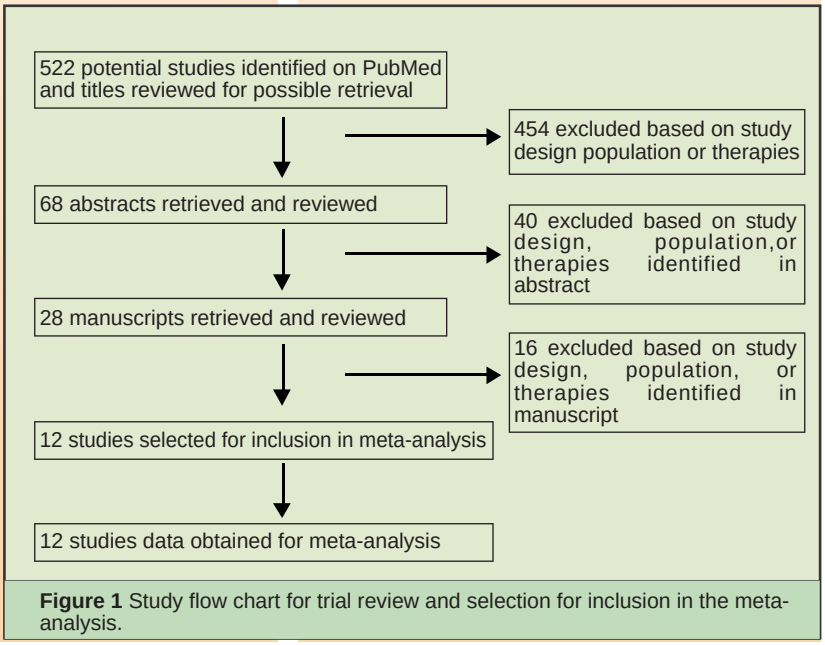


Figure 1 Study flow chart for trial review and selection for inclusion in the meta-analysis.

Table 1 Trial designs

Trial	Population	n	Year published	Blinding	Randomization arms		Endpoint description
					Enoxaparin	UFH	
ST-elevation MI							
ASSENT 3	STEMI	4075	2001	Open-label	30 mg bolus; 1 mg/kg bid for ≤7 days	60 U/kg bolus, 12 U/kg/h for 48 h to aPTT 50–70 s	Death 30 days; MI in-hospital; major bleeding (requiring transfusion or intervention due to haemodynamic compromise or ICH) in-hospital
HART II	STEMI	400	2001	Open-label	30 mg bolus; 1 mg/kg bid for ≥3 days	4000–5000 U bolus, 15 U/kg/h for ≥3 days to aPTT 2.0–2.5 X control	Death 30 days; MI 30 days; TIMI major bleeding in-hospital[a]
Baird et al	STEMI	300	2002	Open-label	40 mg bolus, 40 mg tid for 4 days	5000 U bolus, 30 000 U infusion over 24 h for 4 days to aPTT 2.0–2.5 x control	Death 90 days; MI 90 days; major bleeding (clinically significant haemorrhage or ICH) on study drug
ENTIRE-TIMI 23	STEMI	242	2002	Open-label	0 or 30 mg bolus; 1 mg/kg bid for ≤ 8 days	60 U/kg bolus, 12 U/kg/h for ≤ 3 days to aPTT 1.5–2.5 X control	Death 30 days; MI 30 days; TIMI major bleeding 30 days[a]
ASSENT 3 Plus	STEMI	1635	2003	Open-label	30 mg bolus; 1 mg/kg bid for ≤ 7 days	60 U/kg bolus, 12 U/kg/h for 48 h to aPTT 50–70 s	Death 30 days; MI in-hospital; major bleeding (requiring transfusion or intervention because of haemodynamic compromise or ICH) in-hospital
ExTRACT-TIMI 25	STEMI	20 479	2006	Double-blind	30 mg bolus (if age <75); 1 mg/kg bid (if age <75) or 0.75 mg/kg bid (if age ≥ 75) for ≤ 8 days	60 U/kg bolus (omitted if open-label UFH received within 3 h), 12 U/kg/h for ≥ 3 days to aPTT 1.5–2.0 X control	Death 30 days; MI 30 days; TIMI major bleeding 30 days[a]
Non-ST elevation acute coronary syndromes							
ESSENCE	NSTEACS	3171	1997	Double-blind	1 mg/kg bid for ≤ 4 days	5000 U bolus, infusion dose adjusted to aPTT 55–85 s for ≥48 h	Death 30 days; MI 30 days; TIMI major bleeding 30 days[a]
TIMI 11B	NSTEACS	3910	1999	Double-blind	30 mg bolus, 1 mg/kg bid for ≤ 8 days	70 U/kg bolus, 15 U/kg/h for ≥3 days to aPTT 1.5–2.5 X control	Death 30 days; MI 30 days; TIMI major bleeding 30 days[a]
ACUTE II	NSTEACS	525	2002	Double-blind	1 mg/kg bid for ≤ 4 days	5000 U bolus, 1000 U/h for ≤ 4 days to aPTT 1.5–2.5 X control	Death 30 days; MI 30 days; TIMI major bleedin 30 days[a]
INTERACT	NSTEACS	746	2003	Open-label	1 mg/kg bid for 48 h	70 U/kg bolus, 15 U/kg/h for 48 h to aPTT 1.5–2.0 X control	Death 30 days; MI 30 days; major bleeding (retroperitoneal haemorrhage, or bleeding at a specific site accompanied by a 3 g/dL drop in haemoglobin or resulting in death or ICH) 30 days
A to Z	NSTEACS	3618	2004	Open-label	1 mg/kg bid for ≤ 5 days	4000 U bolus, 900 U/h if ≥70 kg; 60 U/kg bolus, 12 U/kg/h if < 70 kg; aPTT 50–70 s	Death 30 days; MI 30 days; TIMI major bleeding through 24 h after tirofiban discontinuation[a]
SYNERGY	NSTEACS	9975	2004	Open-label	1 mg/kg bid	60 U/kg bolus, 12 U/kg/h to aPTT 1.5–2.0 X control or 50–70 s	Death 30 days; MI 30 days; TIMI major bleeding in-hospital[a]

[a]TIMI major bleeding defined as a decrease in haemoglobin of more than 5 mg/dL or intracranial or pericardial bleeding.

patients with STEMI or NSTEACS. Trials conducted exclusively in the STEMI population were restricted to those in which patients were treated with aspirin and fibrinolytic therapy (ASSENT 3, HART II, Baird et al, ENTIRE-TIMI 23, ASSENT 3 Plus, and ExTRACT-TIMI 25). Figure 1 contains the study flow chart for the meta-analysis.

Data were abstracted for each trial from the manuscript and were sent to the corresponding author for verification, as well as clarification of any missing data. When data were not available from the corresponding author, the sponsoring pharmaceutical company was queried for missing data and clarification of data. The primary data sets for ESSENCE, TIMI 11B, ENTIRE-TIMI 23, A to Z, and ExTRACT-TIMI 25, were available at the TIMI Study Group.

Endpoints

The composite endpoint of the analysis was net clinical events, defined as death, non-fatal MI, or non-fatal major bleeding by 30 days, or the closest timepoint available to 30 days. If a subject met more than one part of the composite event, only one event was counted. The components of the net clinical composite endpoint were also evaluated individually. The net clinical endpoint was not available from the ACUTE II trial, but individual components of the endpoint as well as death or MI were available and included in all other analyses. Differences in the timepoints used in the individual trials are noted in Table 1. Eight of the 12 trials used the TIMI major bleeding criteria, defined as observed bleeding with a decrease in haemoglobin of more than 5 mg/dL or intracranial or pericardial bleeding. The definition of major bleeding for the remaining four trials is shown in Table 1. For trials that did not include intracranial hemorrhage (ICH) as part of the major bleeding definition in the main manuscript (INTERACT, Baird et al., ASSENT 3, and ASSENT 3 Plus), data were obtained from the lead authors to include ICH as a major bleeding event in order to provide a more comparable definition of major bleeding as well as a more comprehensive evaluation of safety as part of the net clinical endpoint.

Statistical analysis

A meta-analysis was performed of the relative odds based on random-effects models using the method by Der Simonian and Laird. A test of heterogeneity, which evaluates variability in the treatment effects, was performed using the Mantel–Haenszel method. Results are presented as odds ratios (OR) with their 95% confidence intervals (CIs) and P-values. Event rates for each trial individually and the pooled data are presented as frequencies. A P-value of < 0.05 was considered statistically significant. All statistical analyses were performed using Stata/SE, version 9.0 (StataCorp, College Station, TX, USA).

Results

The design and endpoint descriptions for each of the 12 trials (n = 49,088) are shown in Table 1. Among the STEMI trials (n = 27,131), one (ExTRACT-TIMI 25), involving the majority of subjects (n = 20,479) was double-blind and the remaining five were open-label (Table 1). Use of an enoxaparin bolus and the dosing of the bolus varied across trials (Table 1). Enoxaparin subcutaneous injection dosing was consistent at 1 mg/kg bid, with the exception of the trial by Baird et al. which used a 40 mg tid dose. In the ExTRACT-TIMI 25 trial, the maintenance injection was

Table 2 Baseline characteristics: ST-elevation MI

	ASSENT 3		HART II		Baird et al.		ENTIRE-TIMI 23		ASSENT 3 Plus		ExTRACT-TIMI 25	
	Enox n = 2040	UFH n = 2038	Enox n = 200	UFH n = 200	Enox n =149	UFH n = 151	Enox n = 160	UFH n = 82	Enox n = 818	UFH n = 821	Enox n =10 256	UFH n = 10 223
Age (years)	61 (12)	61 (13)	60	61	62 (12)	62 (10)	57 (10)	57 (10)	62 (13)	62 (13)	60 (12)	60 (12)
Females, n (%)	463 (23)	478 (23)	44 (22)	52 (26)	40 (27)	41 (27)	26 (16)	13 (16)	194 (24)	184 (22)	2415 (24)	2368 (23)
Diabetes, n (%)	381 (19)	363 (18)	31 (15)	23 (11)	16 (11)	13 (9)	24 (15)	13 (16)	115 (14)	128 (16)	1545 (15)	1515 (15)
Heart rate (b.p.m.)	75 (17)	74 (17)	N/A	N/A	N/A	N/A	71 (16)	72 (16)	74 (19)	74 (19)	76 (17)	76 (16)
Systolic blood pressure (mmHg)	134 (22)	133 (23)	N/A	N/A	130 (24)	129 (24)	134 (19)	140 (21)	134 (25)	132 (25)	133 (21)	134 (21)
Fibrin-specific lytic (%)	2012 (99)	2002 (98)	200 (100)	200 (100)	52 (35)	48 (32)	160 (100)	82 (100)	802 (98)	806 (98)	8143 (80)	8141 (80)

Table 3 Baseline characteristics: non-ST-elevation acute coronary syndromes

	ESSENCE		TIMI 11B		ACUTE II		INTERACT		A to Z		SYNERGY	
	Enox n = 1607	UFH n = 1564	Enox n = 1953	UFH n = 1957	Enox n = 315	UFH n = 210	Enox n = 380	UFH n = 366	Enox n = 2026	UFH n = 1961	Enox n = 4993	UFH n = 4985
Age (years)	63 (12)	64 (11)	64 (12)	64 (11)	65 (12)	64 (13)	64[a]	64[a]	60 (11)	61 (11)	68[a]	68[a]
Females, n (%)	528 (33)	531 (34)	677 (35)	701 (36)	108 (34)	69 (33)	121 (32)	112 (31)	580 (29)	564 (29)	1696 (34)	1684 (34)
Diabetes, n (%)	360 (22)	339 (22)	385 (20)	393 (20)	75 (24)	45 (21)	84 (22)	85 (23)	395 (20)	356 (18)	1424 (29)	1502 (30)
ECG changes, n (%)	897 (56)	895 (57)	1611 (83)	1626 (83)	N/A	N/A	88 (23)	79 (22)	1430 (70)	1410 (72)	3904 (78)	3941 (79)
Biomarker positive, n (%)	N/A	N/A	738 (38)	775 (40)	187 (59)	122 (58)	311 (82)	312 (85)	1627 (80)	1563 (80)	4198 (84)	4190 (84)
Cardiac catheterization performed, n (%)	612 (38)	646 (41)	794 (41)	840 (43)	187 (59)	126 (60)	236 (62)	237 (65)	1224 (60)	1210 (62)	4600 (92)	4588 (92)
CABG performed, n (%)	99 (6)	105 (7)	118 (6)	137 (7)	49 (16)	40 (19)	48 (13)	45 (12)	178 (9)	198 (10)	965 (19)	899 (18)
PCI performed, n (%)	161 (10)	206 (13)	243 (12)	271 (14)	89 (28)	66 (31)	103 (27)	111 (30)	528 (26)	514 (26)	2323 (47)	2364 (47)

[a]Median.

reduced to 0.75 mg/kg in subjects age ≥75 years and to once daily in patients with creatinine clearance <30 mL/ min. The duration of enoxaparin treatment ranged from 3 to 8 days in the trials. UFH bolus and infusion were constant at 60 U/kg bolus and 12 U/kg/h infusion, with the exception of the HART II trial, which used a 15 U/kg/h infusion.

Among the NSTEACS trials (n = 21,945), three were double-blind and three were open-label (Table 1). Enoxaparin dosing was 1 mg/kg bid in all trials, with the duration of treatment ranging from 2 to 8 days. The UFH dosing varied, with earlier trials having slightly higher bolus and infusion doses.

The majority of patients in the STEMI trials were treated with fibrin-specific lytics (Table 2). Among the NSTEACS trials, SYNERGY, A to Z, and INTERACT trials enrolled the highest risk patients, with more than 80% biomarker positive (Table 3).

Clinical outcomes

The funnel plot shown in Figure 2 demonstrates the treatment effect found in each trial plotted against the size of the trial. The plot shows general symmetry with the exception of the ENTIRE-TIMI 23 trial, which had a small sample size and a strong treatment effect for enoxaparin when compared with UFH. The ExTRACT-TIMI 25 trial was the largest study but did not have a disproportionate treatment effect in relation to the majority of the trials. Although the ENTIRE-TIMI 23 trial was an outlier, the trial was included in the main analysis. A sensitivity analysis in which each of these two trials was excluded showed consistent findings with the main analysis.

Across the entire spectrum of ACS (STEMI and NSTEACS; n = 49,088), the composite efficacy endpoint of death or non-fatal MI was reduced among enoxaparin subjects when compared with UFH subjects (9.8 vs. 11.4%, OR 0.84, 95%

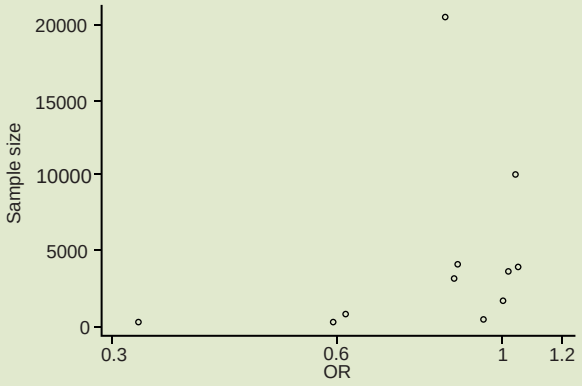


Figure 2 Funnel plot demonstrating the treatment effect found in each trial plotted against the size of the trial. The plot shows general symmetry with the exception of the ENTIRE-TIMI 23 trial, which had a small sample size and a strong treatment effect for enoxaparin compared with unfractionated heparin (UFH). The ExTRACT-TIMI 25 trial was the largest study but did not have a disproportionate treatment effect in relation to the majority of the trials.

CI 0.76–0.92, P< 0.001; Figure 3). The composite net clinical endpoint of death, non-fatal MI, or non-fatal major bleeding also occurred less frequently with enoxaparin when compared with UFH (12.5 vs. 13.5%, OR 0.90, 95% CI 0.81–1.003, P = 0.051; Figure 4). For the net clinical endpoint, evidence of heterogeneity between trials was observed (P = 0.006), as well as heterogeneity between STEMI and NSTEACS syndromes (P = 0.005). Among the STEMI cohort (n = 27,131), the net clinical composite event rate was lower with enoxaparin (11.1 vs. 12.9%, OR 0.84, 95% CI 0.73–0.97, P = 0.018), with no significant evidence of heterogeneity between trials (P = 0.143). The reduction in death, MI, or major bleeding among the STEMI cohort was evident even when excluding individual trials in a sensitivity analysis. When excluding the largest trial, ExTRACT-TIMI 25, consistent results were observed for the net clinical composite event rate (11.5 vs. 13.2%, OR 0.80, 95% CI 0.62–1.04, P = 0.09).

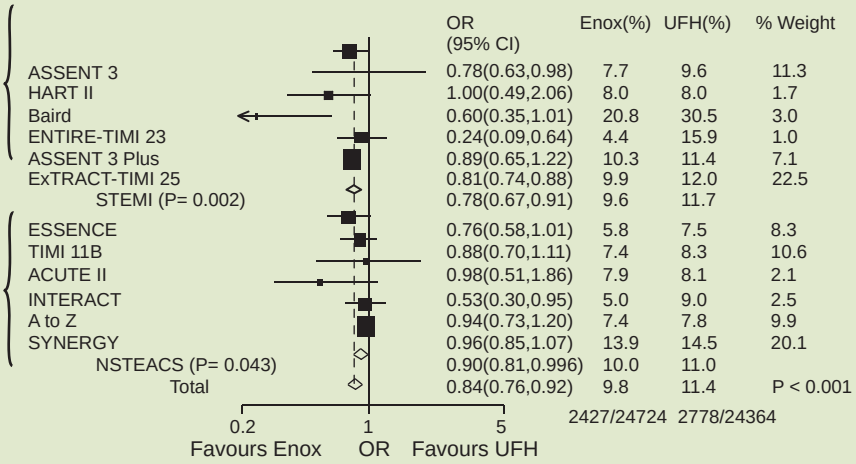


Figure 3 Enoxaparin vs. UFH for the comparison of death or non-fatal myocardial infarction (MI), displayed using a random effects model. Black squares represent odds ratios (ORs), the size of which reflects the statistical weight of a trial in calculating the OR. The horizontal lines represent 95% confidence intervals (CIs). There was evidence of heterogeneity between ST-segment elevation myocardial infarction (STEMI) and non-ST-segment elevation acute coronary syndromes (NSTEACS) (P = 0.005).

There was no difference in the net clinical event rate in the NSTEACS trials (14.1 vs. 14.3%, OR 0.97, 95% CI 0.86–1.09, P = 0.607), with no significant evidence of heterogeneity between trials (P = 0.132).

Individual endpoints

Considering individual endpoints for the entire ACS spectrum, mortality was not significantly different with enoxaparin when compared with UFH (5.0 vs. 5.3%, OR 0.94, 95% CI 0.87–1.02, P = 0.14; Figure 5); MI was significantly lower with enoxaparin (5.5 vs. 6.9%, OR 0.75, 95% CI 0.65– 0.86, P < 0.001; Figure 6); major bleeding was significantly higher with enoxaparin (4.3 vs. 3.4%, OR 1.25, 95% CI 1.04–1.50, P = 0.019; Figure 7).

Results were similar in the STEMI cohort for the comparison of enoxaparin with UFH, respectively, with mortality of 6.6 and 7.1% (OR 0.92, 95% CI 0.84–1.01, P = 0.097); MI 3.4 and 5.1% (OR 0.64, 95% CI 0.52–0.78, P < 0.001); and major bleeding 2.6 and 1.8% (OR 1.45, 95% CI 1.23–1.72, P < 0.001). Death or MI occurred in 9.6% of enoxaparin subjects and 11.7% of UFH subjects (OR 0.78, 95% CI 0.67–0.91, P = 0.002).

In patients with NSTEACS, there was no difference in

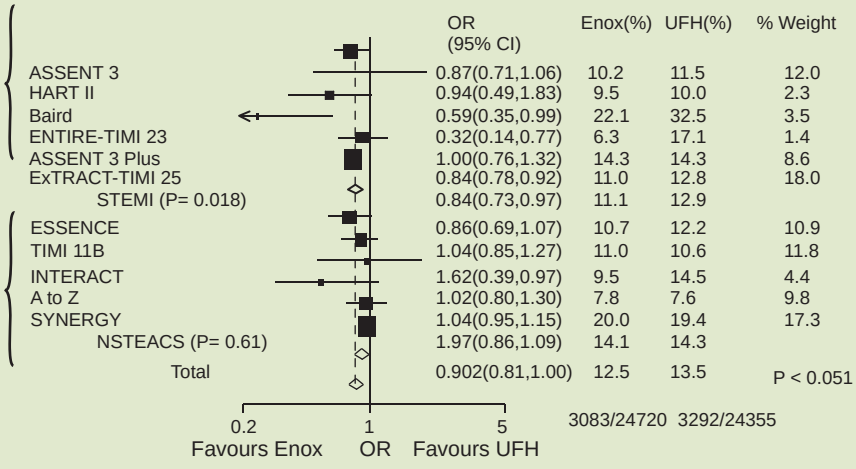


Figure 4 Enoxaparin vs. UFH for the comparison of death, non-fatal myocardial infarction, or non-fatal major bleed, displayed using a random effects model.

mortality between enoxaparin and UFH (3.0% each, OR 0.99, 95% CI 0.83–1.18, P = 0.890). MI occurred significantly less frequently in the enoxaparin group (8.0 vs. 9.1%, OR 0.87, 95% CI 0.79–0.96, P = 0.005), as did the composite of death or non-fatal MI (10.0 vs. 11.0%, OR 0.90, 95% CI 0.81–0.996, P = 0.043). Major bleeding did not differ between treatment groups (6.3% with enoxaparin vs. 5.4% with UFH, OR 1.13, 95% CI 0.84–1.54, P = 0.419).

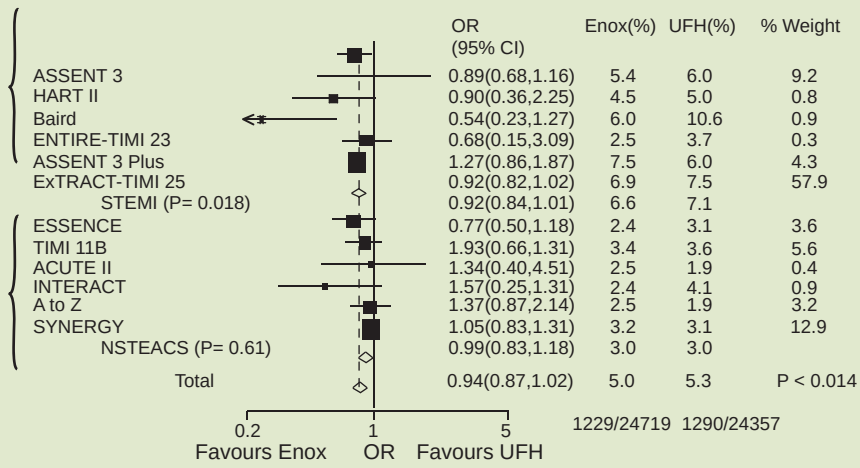


Figure 5 Enoxaparin vs. UFH for the comparison of death, displayed using a random effects model.

Discussion

When compared with UFH, enoxaparin was associated with superior efficacy as adjunctive antithrombin therapy among more than 49,000 patients across the ACS spectrum. Although major bleeding was increased with enoxaparin, this increase was offset by a significant reduction in death or non-fatal MI.

Antithrombotic therapy acts in part by reducing the risk of reocclusion of initially successfully reperfused infarct arteries in the setting of STEMI and preventing further thrombus formation in NSTEACS by inhibiting thrombin generation and/or activity. Enoxaparin intervenes more proximally in the coagulation cascade to a greater extent than UFH (greater anti-factor Xa to anti-factor IIa activity), presumably resulting in a reduction in the amount of thrombin generated in the culprit artery. In addition, enoxaparin offers a more stable level of anticoagulation, which eliminates the need for aPTT monitoring and allows for subcutaneous dosing rather than intravenous infusions, making it a more convenient strategy that may also reduce the cost of care.

Prior meta-analyses have examined individually the efficacy and safety of enoxaparin when compared with UFH in STEMI, and in NSTEACS, but the present analysis is the first to (i) evaluate a net clinical endpoint; (ii) assess the entire ACS spectrum; and (iii) include the ExTRACT-TIMI 25 trial, thereby increasing the total population of patients available for analysis by 72% (from n = 28,609 to n = 49,088). Given the consistent efficacy of reduced death or MI with enoxaparin, use of a net clinical endpoint incorporating bleeding can be justified to characterize the clinical profile of the therapy; had no efficacy been observed, use of a net clinical endpoint would not be warranted.

There was a consistent efficacy benefit of reduced death or

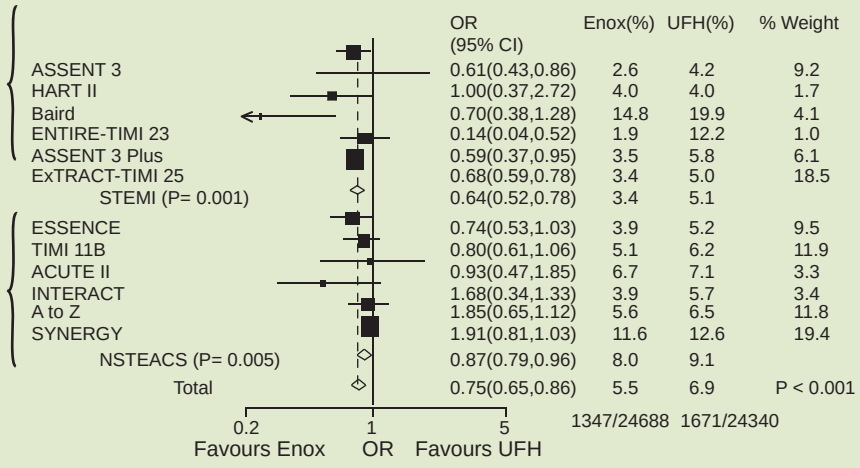


Figure 6 Enoxaparin vs. UFH for the comparison of myocardial infarction, displayed using a random effects model.

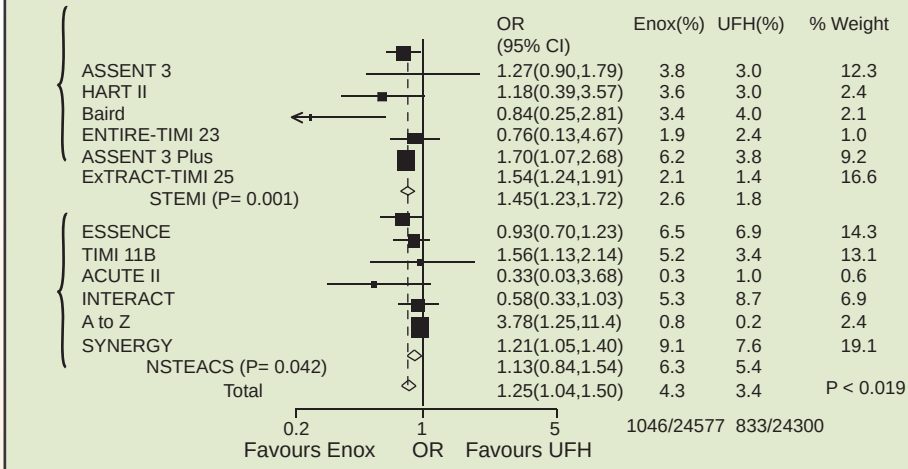


Figure 7 Enoxaparin vs. UFH for the comparison of major bleed, displayed using a random effects model.

MI with enoxaparin in both STEMI and NSTEACS trials. Net clinical benefit was evident among the STEMI population and was neutral among the NSTEACS population. Several factors may have contributed to these findings. In the NSTEACS trials, the major bleeding rate was higher overall than in the STEMI trials (5.8% in NSTEACS trials vs. 2.2% in STEMI trials), and therefore contributed more events to the net clinical endpoint. Although the absolute major bleeding event rate was higher in the NSTEACS trials than the STEMI trials, there was no significant relative increase in major bleeding between enoxaparin and UFH in the NSTEACS trials (OR 1.13, P = NS) in contrast to the STEMI trials. Conversely, the relative reduction in death or MI was somewhat greater in the STEMI trials (OR 0.78) than in the NSTEACS trials (OR 0.90). These differences in both efficacy and bleeding may be explained in part by the greater use of revascularization procedures in the NSTEACS trials, differences in concomitant therapies such as thienopyridines and pre-randomization antithrombin use, and different durations of enoxaparin therapy in the trials. In addition, NSTEACS patients tend to be a more heterogeneous population than STEMI patients, with therapies often showing different degrees of efficacy and safety in unstable angina patients and in NSTEMI patients. Additional trials evaluating lower doses of enoxaparin in certain populations at high-risk for bleeding, including the elderly and those with reduced renal function, should be considered to improve the safety profile of enoxaparin. Another consideration to reduce bleeding rates in the ACS population undergoing PCI is increased use of radial artery catheterization, where studies have shown reductions in major bleeding when compared with femoral access.

Limitations

As with all meta-analyses, differences in trial designs should be considered when interpreting the overall results. Timing and definitions of endpoints for MI and major bleeding varied somewhat across trials, as did the use of adjudication of events. However, point estimates for MI consistently fell to the left of the line of unity (favouring enoxaparin). Point estimates for major bleeding are more varied, but the majority of trials fell to the right of the line of unity (favouring UFH). Duration and dose of study drugs also differed between trials, as did the use of concomitant therapies, revascularization, and risk profiles. Given the heterogeneity in the analysis of the entire ACS spectrum for the net clinical endpoint, the results of the STEMI and the NSTEACS cohorts are reported individually as well as pooled. Patient-level data were not available for all 12 trials, so additional subgroup analyses could not be performed. Long-term data beyond 30 days were not available in most trials so late mortality was not evaluated.

Clinical implications

Compared with UFH, adjunctive antithrombin therapy with enoxaparin was associated with significantly superior efficacy benefit across the ACS spectrum among more than 49,000 patients. Among STEMI patients, death or MI events were prevented for every 1,000 patients treated with enoxaparin, at the cost of an increase of four non-fatal major bleeds; among NSTEACS patients, nine death or MI events were prevented for every 1,000 patients treated with enoxaparin, at the cost of an increase of eight non-fatal major bleeds. These data provide evidence in favour of enoxaparin adjunctive antithrombin regimen to support ACS therapy over the standard strategy of UFH, especially among STEMI patients.

Ref: *European Heart Journal (2007) 28, 2077-2086*

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Cardiology News

Statins May Reduce Renal Complications of Elective Surgery

Statins may protect against renal complications after major elective surgery, according to the results of a population-based, retrospective cohort study. The study cohort consisted of 213,347 older patients from 211 hospitals in Ontario, Canada, who had major elective surgery, including cardiac, thoracic, vascular, intra-abdominal, and retroperitoneal procedures between 1995 and 2008. Acute renal injury occurred in 4020 patients (1.9%) during the first 14 postoperative days, and 1173 patients (0.5%) required acute dialysis. At 30 days after surgery, 5974 patients (2.8%) had died. Nearly one third (32%) of patients were being treated with a statin before surgery. Statin use was associated with 16% lower odds of acute kidney injury, 17% lower odds of acute dialysis, and 21% lower odds of mortality, after statistical adjustment for patient-related and surgical factors. There appeared to be evidence of a dose-effect, in that patients receiving higher-potency statins had less kidney injury. Statin use also appeared to be beneficial regardless of whether treatment was started more than 90 days or less than 30 days before surgery. Limitations of this study include observational design, precluding causal inference; possible confounding by indication; and concern about the accuracy of diagnostic codes used.

Soc Nephrol. Published online April 14, 2011.

Gene Therapy Might Help in Heart Ischemia

In patients with refractory heart ischemia, percutaneous intramyocardial transfer of bicistronic vascular endothelial growth factor/fibroblast growth factor (VEGF/FGF) plasmid appears to show some benefit, but more research is needed. Refractory ischemic disease is one of those conditions and the researchers sought to achieve therapeutic angiogenesis and perfusion improvement with plasmid injected into ischemic myocardium using a percutaneous, catheter-based technique. Dr. Kukula of the Institute of Cardiology, Warsaw, and colleagues randomized 52 patients to receive VEGF/FGF plasmid or placebo. The VEGF-A165/basic FGF plasmid had not previously been studied in cardiology patients. At 5 months, there was no difference between groups in perfusion defects whether at rest or stress induced. However, at 5 and 12 months, Canadian Cardiovascular Society functional class improved significantly in the active treatment group. As measured by the electrocardiographic treadmill exercise test, their exercise tolerance also improved, with significant increases in maximum work load and total test distance. There was also an increase in total exercise time. Although there was no improvement in perfusion. In addition, at 1 year there were no apparent adverse effects.

Am Heart J 2011;161:581-589.

Delay Elective Surgeries After Heart Attack

After a myocardial infarction (MI), waiting at least two months before an elective surgery is linked to a lower risk of dying or having a second heart attack. Researchers analyzed outcomes for more than half a million people in a California hospital who had undergone non-cardiac elective surgeries, such as hip replacement or gallbladder removal. About 3% had also had a heart attack within the year before the surgery. The risk of a postoperative heart attack declined dramatically the longer a patient waited before elective surgery - from 32.8% between 0-30 days, to 18.7% at 31-60 days, 8.4% at 61-90 days, and 5.9% at 91-180 days. Thirty-day mortality rates followed a similar pattern: 124.2% at 0-30 days, 11.5% at 31-60 days, 10.5% at 61-90 days, and 9.9% at 91-180 days. Also, the authors report, patients with an MI within 30 days before an operation had risk ratios for a postoperative MI that ranged from 9.98-44.29 for the 5 procedures. Their risk ratios for 30-day mortality ranged from 1.83-3.84 and from 1.56-3.14 for one-year mortality.

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Editorial Note

Dear Doctor,

We are happy to present the 21st issue of "Insight Heart". It is a small endeavor to provide you compiled & updated information on cardiovascular diseases and its management. This issue is focused on " ***Efficacy and safety of the low-molecular weight heparin enoxaparin compared with unfractionated heparin across the acute coronary syndrome spectrum: a meta-analysis***". We will appreciate your thoughtful comments.

Thanks and regards.