2:15

820-2 One Year Follow-up of the ESSENCE Trial (enoxaparin Versus Heparin in Unstable Angina and Non-Q-Wave Myocardial Infarction)

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The ESSENCE trial conducted in 3171 patients, demonstrated that enoxaparin plus aspirin is more effective than heparin plus aspirin in reducing recurrent angina (RA), myocardial infarction (MI) or death (D) in patients with unstable angina or non Q wave myocardial infarction in the early (14–30 days) phase. In order to determine whether or not this benefit persists, a one year follow-up survey was prospectively undertaken for each patient enrolled in the ESSENCE study. The status of all patients was to be determined by each site and information regarding the occurrence of endpoints (RA/MI/D), angiography or revascularization procedures and re-hospitalizations were collected. As of August 1997, data have been collected on 1486 patients. At Day 30, the rate of RA/MI/D was 23.3% for heparin and 19.8% for enoxaparin, a relative risk reduction (RRR) of 15%; the rate of MI/D was 7.7% for heparin and 6.2% for enoxaparin, a RRR of 20%. After one year the rate of RA/MI/D was 26.6% for heparin and 22.8% for enoxaparin (RRR 14%), the rate of MI/D was 8.8% for heparin and 7.2% for enoxaparin (RRR 19%), indicating the benefit achieved in the early phase is sustained over one year. All data should be collected by September 1997. Full results of the study will be presented.

2:30

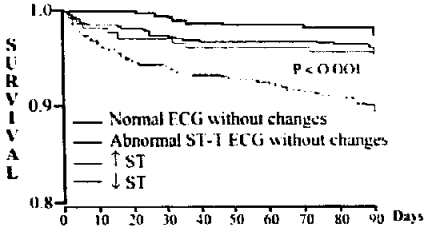
820-3 Prognostic Value of ECG Changes During Chest Pain in Patients With Unstable Angina. Results of the Proyecto de Estudio del Pronostico de la Angina (PEPA)

E. Lopez de Sá, J. López-Sendon, A. Bethencourt, X. Bosch. *The PEPA Investigators; H. Gregorio Marañón, Madrid, Spain*

Background: Repolarization ECG changes during an episode of pain in patients with suspected unstable angina (UA) or non-Q myocardial infarction (N-Q MI) are considered as very specific for myocardial ischemia. However, its prognostic value was not prospectively studied in large series of patients.

Methods: The prognostic value of ischemic ECG changes obtained during the first observed episode of pain as compared to the ECG without pain was prospectively evaluated in 1899 consecutive patients considered to have UA or N-Q MI when first seen by a cardiologist at 16 centers in Spain.

Results: Mortality at 90 days follow-up was higher when ST segment depression ≥0.1 mV was observed during pain and lowest when both ECG (with and without pain) were normal. The figure shows the Kaplan-Meyer survival curves for the different groups.



Conclusion: Downward shift of ST during pain is the variable related with highest mortality in patients with suspected UA.

2:45

820-4 Prognostic Significance of Refractory Ischemia in Unstable Angina Revisited

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Background: Refractory ischemia (RI) in acute ischemic syndromes is associated with a poor prognosis that usually mandates aggressive management. The purpose of this study was to reassess its prognostic significance in the setting of full antithrombotic therapy including aspirin, IV heparin, and a GP IIb/IIIa platelet inhibitor.

Methods: The PRISM-PLUS trial randomized 1,570 patients with unstable angina/non-Q-wave MI to heparin alone (H) or to tirofiban + heparin (T/H). Study drug was administered for 48–108 hours. Angiography ± PTCA was performed if necessary between hours 48 and 96. Aspirin was given to 98% of patients, nitrates to 94%, beta blockers to 79%, and calcium antagonists to 46%. Of the total study population, 84 patients (5.4%) developed RI in the first 48 hours of therapy (5.9% vs. 4.8% in patients receiving H or T/H, respectively).

Results: Patients with RI within the first 48 hours had a higher incidence of subsequent death or MI at 30 days vs. patients without RI (15.5% vs. 8.5%, risk ratio [RR] = 1.95, 95% confidence intervals [CI] = 1.10–3.44, p = 0.022). The incidence of death or MI in RI patients receiving H or T/H was 25.5% vs. 13.5%. Revascularization was performed in 89.4% of H patients with RI and in 67.6% of T/H patients with RI (RR = 0.76, CI = 0.59–0.97, p = 0.014). The procedure was performed urgently in 4.4% of patients in the H group and in 3.4% of the patients in the T/H group (RR = 0.77, CI = 0.47–1.26).

Conclusion: Refractory ischemia in unstable angina/non-Q-wave myocardial infarction is associated with severe prognosis despite full medical treatment. Inhibition of the GP IIb/IIIa receptor with tirofiban plus heparin improves prognosis in these patients.

3:00

820-5 Hirudin Reduces Death and Myocardial (Re)infarction at 6-Months: Follow-up Results of the GUSTO IIb Trial

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Background: Longer term follow-up of trials of new antithrombotic therapy for coronary artery disease is important because early treatment effects may not persist or can be accentuated.

Methods: In the GUSTO IIb trial, 12,142 patients presenting within 12 hours of symptom onset of acute coronary syndromes were randomized to a three day infusion of intravenous hirudin or heparin. Follow-up at 6 months and 1 year is 98.0% and 93% complete, respectively.

Results:

	hirudin	heparin	p-value
30 day (re)MI	5.4%	6.3%	0.04
6 month (re)MI	7.1%	8.2%	0.035
30 day death or (re)MI	8.9%	9.8%	0.058
6 month death or (re)MI	12.3%	13.6%	0.039
1 year mortality	9.0%	9.2%	0.68

(*Pearson's chi-square test)

Conclusion: Hirudin is effective at reducing death or MI at 6 months. There is no suggestion of either narrowing or accentuation of the early benefit of hirudin, with the absolute and proportional reduction maintained from 30 days to 6 months.

3:15

820-6 Failure to Achieve Optimal Anticoagulation With Commonly Used Heparin Regimens; A Review of GUSTO II

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GUSTO I data on thrombolytic treated pts on IV heparin demonstrated a clear association of higher aPTT's (75 sec) and death, bleeding and re-MI. AHCPR guidelines recommend a 70 U/kg IV Bolus (B) and a 15 U/kg/hr infusion. We evaluated aPTT's of 5571 pts in GUSTO IIb who received 5000U of heparin IVB and 1000 U/hr with (n = 1543) or without (n = 4028) thrombolytics and divided them into sub-therapeutic (aPTT <50), therapeutic (50–75 sec) and supra-therapeutic (>75 sec) groups. We examined aPTT's of pts who weighed 67–72 kg (approx 70 U/kg IVB and 15 U/kg/hr) and <67 kgs (LBW).

Results: 6 hr aPTT's of pts 67–72 kg were therapeutic in only 21% with 71% supra-therapeutic, similarly LBW pts were overwhelmingly supratherapeutic at 84% with 11% therapeutic. When 67–72 kg pts were divided into thrombolytic and non-thrombolytic groups, 80% and 68% were supra-therapeutic with 15% and 23% therapeutic respectively. The median aPTT at 12 hours was significantly higher in pts with 30 day death and re-MI 69 (52, 95) vs 66 (52, 89), p = 0.029. This remained true in the non-thrombolytic subgroup 69 (54, 93) vs 66 (52, 86), p = 0.023. Moderate/severe bleeding was associated with significantly aPTT's 68 (53, 95) vs 66 (52, 89), p = 0.028.

Conclusion: AHCPR heparin dosing guidelines, and fixed heparin dose (5000/1000) for LBW pts with acute coronary syndromes result in consistent early over anticoagulation regardless of thrombolytic status and this is associated with increased risk of death, bleeding and re-MI.

MONDAY ORAL