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LMWH for PE

Clinical bottom line: Fixed dose LMWH is as effective and safe as UFH for the initial treatment of nonmassive PE.

Clinical scenario: 52yo male with h/o recent LE weakness adm with pleuritic chest pain who was found to have PE; hemodynamically stable. Admitted for IV heparin. Could we use lovenox for anticoagulation?

Clinical question: In patients presenting with hemodynamically stable symptomatic PE, is lovenox as effective for anticoagulation bridge as unfractionated heparin?

Search Terms: In PubMed, I used the search terms "LMWH" and "Pulmonary embolism." I limited my search to English language, humans, and 2000-2005.

The Study

Study Design: Meta-analysis using randomized controlled trials meeting study-quality criteria of Schultz et al.—proper generation of randomization, blinding, completeness of follow-up, etc.

--Included patients with objectively diagnosed symptomatic PE or asymptomatic PE with symptomatic DVT

--Compared fixed-dose LMWH with dose-adjusted IV UFH

--Used objective methods to assess recurrent symptomatic VTE, major bleeding, minor bleeding and death.

The Evidence

Recurrent VTE and Death at the End of Treatment

Outcome	LMWH	UFH	Odds Ratio
Any VTE	14/1023 (1.4)	22/928 (2.4)	0.63 (0.33-1.18)
DVT	1/26 (0.1)	7/825 (0.8)	0.47(0.17-1.26)
PE	13/926(1.4)	14/25(1.7)	0.91 (0.45-1.85)
All-cause mortality	14/023 (1.4)	11/28 (1.2)	1.20 (0.59-2.45)

Recurrent VTE and Death at 3 months

Outcome	LMWH	UFH	Odds Ratio
Any VTE	30/988 (3.0)	39/895 (4.4)	0.68(0.42-1.09)
DVT	15/891 (1.7)	19/792 (2.4)	0.64 (0.33-1.25)
PE	16/891 (1.8)	20/792 (2.5)	0.78 (0.41-1.47)
All-cause mortality	46/988 (4.7)	55/895 (6.1)	0.77 (0.52-1.15)

Major and Minor Bleeding

Outcome	LMWH	UFH	Odds Ratio
Major Bleeding	14/1023 (1.4)	21/928 (2.3)	0.67 (0.36-1.27)
Minor Bleeding	67/982 (6.8)	48/874 (5.5)	1.08(0.73-1.59)

Comments:

--Small numbers of events in the trials limited ability to provide precise estimates of incidence and to detect differences in treatment effect.

--Validity analyses: removing individual studies did not alter the results. Funnel plot of effect size vs. study precision was "relatively symmetrical"—consistent with lack of major publication bias. Results of these not shown in paper.

--All results had no statistical evidence of heterogeneity

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Therapy CAT

Clinical Bottom Line: Prophylactic use of levofloxacin in patients with chemotherapy induced neutropenia reduces their risk for developing neutropenic fever.

Appraiser: Franklin Chen, MD Date: 11/9/05

Reference: Bucaneve, G, et. al, Levofloxacin to prevent bacterial infection in patients with cancer and neutropenia. N Engl J Med 2005; 353: 977-987

Clinical Scenario: A 60 year old male was recently diagnosed with AML. He is to undergo induction chemotherapy and is expected to have neutropenia for at least 7 days.

Clinical Question: In patients with neutropenia after receiving chemotherapy, can prophylaxis with oral levofloxacin reduce their risk of developing fever?

Search terms: neutropenic fever, antibiotic prophylaxis

The Study:
This was a prospective, multicenter, Italian, double-blind, randomized placebo controlled, intention to treat study. Prognosis in developing neutropenic fever were similar in the control and experimental group in regards to chemotherapy given, and type of malignancy. Patients, clinicians, outcome assessors were not aware of group allocation.

Experimental therapy: Experimental therapy consisted of levofloxacin 500mg given orally daily with the start of chemotherapy, and until ANC > 1000, or patient until patient was febrile requiring empiric antibiotics.

Control therapy: Control therapy consisted of placebo given orally daily with the start of chemotherapy, and until ANC > 1000, or until patient was febrile and given empiric antibiotics.

Outcomes: Fever developed in 243/375 (65%) of patients prophylaxed with levofloxacin vs. 308/363 (85%) in patients receiving placebo. Also, the experimental group had lower rates of microbiologically documented infection. There was no mortality difference.

The Evidence

Patients	Control Group	Experimental Group
Enrolled	376	384
Analyzed	336	339

Risk in Control	Risk in Treated	Relative risk ratio	Relative risk reduction	Absolute risk reduction	NNT	95% CI
85%	65%	76%	24%	20%	5	-14-26%

Comments: This study has internal validity. However, the fluoroquinolone resistance patterns differ from hospital to hospital and country to country, making it difficult to assess the efficacy of prophylactic levofloxacin in other institutions than the institutions studied. Also, the usage of empiric fluoroquinolones in all chemotherapy induced neutropenic patients may encourage resistance.

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CAT: CCP can be used to diagnose rheumatoid arthritis

Clinical Bottom Line: Anti-CCP antibody can be helpful in the diagnosis of rheumatoid arthritis

Karen Au
Date: November 17, 2005
Reference: Vallbracht I et al. Diagnostic and Clinical Value of Anti-Cyclic Citrullinated Peptide Antibodies Compared with Rheumatoid Factor Isotypes in Rheumatoid Arthritis. *Annals of the Rheumatic Diseases* 2004;**63**: 1079-1084.

Clinical Scenario: 64yo woman with hx of depression presenting with 5 months of multiple bilateral joint pains. She has mild tenderness and swelling in several joints, including bilateral PIPs. Physical exam and plain films of joints are otherwise unremarkable. Will CCP, a new diagnostic test, help us rule in the diagnosis of rheumatoid arthritis?

Clinical Question: Does CCP help in the diagnosis of rheumatoid arthritis in this patient?

Search Terms: In Medline, I searched: "CCP", "rheumatoid arthritis/di [diagnosis]" and limited my search to English language, full text, and humans. This resulted in 27 articles.

The Study:
Clinicians faced diagnostic uncertainty? Yes
Blind comparison between test and an independent gold standard? Yes
Reference standard applied regardless of test results? Yes

Diagnostic Test: CCP (Anti-cyclic citrullinated peptide antibody) by ELISA. Patients also had Rheumatoid Factor IgM, IgA, and IgG tested by ELISA.

Gold standard: 1987 American College of Rheumatology criteria for rheumatoid arthritis

Patients: 295 patients with rheumatoid arthritis, 266 patients with osteoarthritis/gout/other rheumatologic diseases, 154 healthy controls. Study was unclear about the method by which patients were selected for the study.

Details: Compared to rheumatoid factor, CCP is as sensitive and more specific for rheumatoid arthritis.

Evidence:

Test Result	RA present	RA absent	Totals
CCP positive	190	12	202
CCP negative	105	408	513
Totals	295	420	

	Sensitivity	Specificity	LR +	LR -
CCP	64%	97%	22.5	0.37

Comments:
1. CCP was less sensitive for patients with shorter duration of disease or mild disease. Sensitivity dropped to 55% for patients with less than 1 year of disease and 59% for patients with mild disease.
2. Study was done in Germany, a more homogenous population than the United States. Would CCP be as sensitive or specific in African American, Hispanic, or Asian patients?