COLUMBIA UNIVERSITY MEDICAL CENTER

DIVISION OF GENERAL MEDICINE

Senior Medicine Rotation: Evidence-Based Medicine Project

Resident Name: **Rajiv Singh** **Block:** **Date: 1/26/05**

Case SIGNOUT:

Adm SRMed 1/14

62F 1mos s/p LLE foot sx adm LLE DVT/PE. HD stable, TTE(-)RV strain. Ortho following. **Awaiting therapeutic INR**.

NKDA
MEDS: Lovenox 50 SQ q12, Coumadin 5 qhs, Tyl #3 PRN

Clinical Question: Is an initial 10mg loading dose of coumadin superior to 5mg in terms of decreased LOS without major complications?

Search Strategy

Database:	PUBMED
Search:	coumadin dosing comparison
Limits:	English, Human, RCT

Items 1 - 6 of 6 One page.

Comparison of 10-mg and 5-mg warfarin initiation nomograms together with low-molecular-weight heparin for outpatient treatment of acute venous thromboembolism. A randomized, double-blind, controlled trial.
Ann Intern Med. 2003 May 6;138(9):714-9.
PMID: 12729425 [PubMed - indexed for MEDLINE]

A randomized, crossover comparison of warfarin products in the treatment of chronic atrial fibrillation.
Ann Pharmacother. 2000 Sep;34(9):981-8.
PMID: 10981241 [PubMed - indexed for MEDLINE]

Comparison of an age adjusted warfarin loading protocol with empirical dosing and Fennerty's protocol.
Aust N Z J Med. 1999 Oct;29(5):731-6.
PMID: 10630656 [PubMed - indexed for MEDLINE]

Comparison of 5-mg and 10-mg loading doses in initiation of warfarin therapy.
Ann Intern Med. 1997 Jan 15;126(2):133-6.
PMID: 9005747 [PubMed - indexed for MEDLINE]

Pharmacokinetic and pharmacodynamic evaluation of warfarin and nefazodone coadministration in healthy subjects.
J Clin Pharmacol. 1995 Jul;35(7):730-8.
PMID: 7560254 [PubMed - indexed for MEDLINE]

Initiation of warfarin therapy: comparison of physician dosing with computer-assisted dosing.
J Gen Intern Med. 1987 May-Jun;2(3):141-8.
PMID: 3295148 [PubMed - indexed for MEDLINE]

Senior Medicine Rotation: Based Medicine Project (Cont)

Group	Criteria or definition	n
Population screened.	Consecutive Canadians from single hospital thrombosis unit	?
Inclusion criteria	Anticoagulation indicated for INR 2-3	53+?
Exclusion criteria	Anticoagulation contraindicated, distance from hospital	?
10mg group		21
5mg group		32

Primary endpoints: Proportion with INR 2-3 on 2 consecutive days within 5 days
Secondary endpoints: Proportion without INR values > 3 within 5 days

- Are the Results of the Trial Valid? Yes
  - Randomized? Yes (imbalanced)
  - All patients accounted for at end? Yes (removed: 1 5mg dropouts: 3 10mg, 2 5mg)
  - Intention to treat? Yes (worse-case scenario)
  - Blinding? Yes, partially (lab tech, patient?)
  - Groups similar at start of trial? Yes
  - Equal treatment of groups? Yes
  - Did randomization work? Yes
- Are the Results of the Trial important? Yes
  - Size of treatment effect? Yes
  - Precision of the estimate of the effect? No (low N, wide CI)

Endpoint	Result	Significance	ARR	NNT
5mg reaching INR 2-3	21 of 32 (66%)	RR=2.22 (CI=1.3 – 3.7)		
10mg reaching INR 2-3	5 of 21 (24%)	P<.003	22%	5
Morbidity	**Result**	**Significance**	**ARI**	**NNH**
5mg superseding INR >3	2 of 30 (7%)	RR=0.82 (CI=.63–1.06)		
10mg superseding INR >3	5 of 21 (24%)	P=.11	17%	6

- Can I apply these results to my patient? Yes
  - Comparison of my patient to trial patients. Yes (lower wt, no LMWH)
  - All clinically important outcomes considered. No (but are likely considered)

CONCLUSION

There is no evidence that a 10mg loading dose decreases LOS, and a trend towards added harm.

21Jan05 08:55	40.3		3.94	Coumadin Clinic
18Jan05 05:50	28.2	45.7 *	2.50	D/C on Day 5
17Jan05 05:30	26.5	49.2 *	2.31	5mg
16Jan05 06:10	17.6	39.1 *	1.37	5mg
15Jan05 06:09	16.6	36.4 *	1.28	10mg x1
14Jan05 11:02	15.9	56.9 *	1.21	5mg

Senior Medicine Rotation: Based Medicine Project (Cont)

Group	Criteria or definition	n
Population screened.	Consecutive Canadians visiting thrombosis clinics at 4 tertiary academic medical centers over 1year (out patients)	210
Inclusion criteria	Confirmed DVT/PE	210
Exclusion criteria	**INR>1.4** Plt<50 age<18 **require hospitalization** **anticoagulation < 2wks** contraindication to bleeding *abnormal Cr/inability to administer LMWH*	9
10mg group		104
5mg group		97

Primary endpoints: Days to INR >1.9
Secondary endpoints: Proportion of patients with INR 2-3 by Day 5
Number of DVT/PE recurrences within 90days
Number of major bleeding episodes within 28 days
Number of INR results >5
Number of INR assessments needed in 28 days
Survival at 90 days

- Are the Results of the Trial Valid? Yes
  - Randomized? Yes
  - All patients accounted for at end? Yes
  - Intention to treat? Yes
  - Blinding? Double
  - Groups similar at start of trial? More men in 10mg
  - Equal treatment of groups? Yes
  - Did randomization work? Yes
- Are the Results of the Trial important? Yes
  - Size of treatment effect? Yes
  - Precision of the estimate of the effect? Yes

Table 2. **Comparison of the 10-mg and 5-mg Nomogram Groups***

Results			
Mean time to INR >1.9 +/- SD, *d*	4.2 +/- 1.1	5.6 +/- 1.4	(P<0.001)
Patients therapeutic by day 5, *n* (%)	86 (83 [74–89])	45 (46 [36–57])	(P<0.001)

- Can I apply these results to my patient? Yes (characteristics are out-patient like)
  - Comparison of my patient to trial patients. Smaller weight, female
  - All clinically important outcomes considered. Yes (but not sufficiently powered)
  - Likely benefits outweigh potential harms and cost? No

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