

BET 1: COAGULOPATHY AS A RISK FACTOR IN WARFARINISED HEAD INJURY PATIENTS

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ABSTRACT

A short-cut review was carried out to determine whether the International Normalised Ratio (INR) value was a predictor of the risk of intracranial haemorrhage in patients taking warfarin after head injury. 796 papers were found using the reported search, of which eighteen were directly relevant. The author, date and country of publication, patient group studied, study type, relevant outcomes, results and study weaknesses are shown in the accompanying table. It is concluded that level of the INR correlates poorly with the risk of haemorrhage and that the risk of haemorrhage remains significant even in patients with a sub-therapeutic INR.

CLINICAL SCENARIO

A 72-year-old woman presents with a minor head injury (MHI). Her INR was 2, and she has no amnesia or loss of consciousness, therefore not strictly fulfilling the National Institute for Health and Care Excellence (NICE) criteria for a scan. The radiologist on call does not want to scan the patient unless her INR had been >2.5, and so the request is denied.

You wonder why the radiologist had chosen an INR of 2.5 and want to find out more about relevance of the INR in the WHI patient, and specifically to question the reassurance that a therapeutic or even subtherapeutic INR could bring for the otherwise asymptomatic MHI.

THREE-PART QUESTION

In (elderly warfarinised head injury (WHI) patients) does the (International Normalised Ratio (INR)) influence the likelihood of (intracranial haemorrhage (ICH))?

SEARCH STRATEGY

MEDLINE 1946 to August Week 4 2013 using the OVID interface [(exp Craniocerebral trauma/ OR head injur\$.mp) AND (exp Warfarin/ OR warfarin.mp OR exp Coumarins/ OR exp Anticoagulants/ OR anticoagula\$.mp OR phenprocoumon.mp OR acenocoumarol.mp OR dicumarol.mp OR 4-hydroxycoumarins.mp OR sintrom.mp OR sinthrome.mp OR coumadins.mp)] LIMIT to humans AND english language.

SEARCH OUTCOME

In total, 796 papers were found, of which 778 were irrelevant. The remaining 18 were directly relevant to the three-part question and are summarised in the table 1. The references of these papers were also searched but yielded no additional relevant papers.

Relevant papers were those looking at warfarinised head injuries, together with assessment of the presenting INR and a CT scan for assessment of ICH to give an indicator for bleeding.

COMMENTS

There were no randomised controlled trials, but a mixture of case-controlled studies and cohort studies to give grade B recommendations for our emergency department population. There is good evidence here to demonstrate the deleterious effects of a supra-therapeutic INR (Menditto *et al*, 2012; Major and Reed, 2009; Pieracci *et al*, 2007; Cohen *et al*, 2006; Franko *et al*, 2006), but you would also expect this to accompany clinical signs, a reduced Glasgow Coma Score (GCS) and an increased mortality. It is of more use, though, to examine the impact

Table 1 Relevant papers

Author, date, country	Patient group	Study type	Outcomes	Key results	Study weaknesses
Garra <i>et al</i> , 1999, USA	65 anticoagulated (AC) patients suffering minor head injury without LOC or acute neurological abnormality identified from retrospective chart review of electronic records from 6 community hospital EDs, including 1 trauma centre over 2-year period. Only 38 patients had PT assessment (range 12–30.7 s)	Cohort study	Clinically significant intracranial injury	No intracranial injury found in any of the 39 patients who had a CT. Telephone follow-up of the remaining 26 patients revealed no evidence of complications related to their head injuries	Their computer system may not have identified all eligible patients leading to a selection bias. Retrospective. In the 38 patients in whom PT was checked, none was >30 s and almost 1/3 were <14 s, indicating that even though these patients were on warfarin, few were actually AC
Karni <i>et al</i> , 2001, USA	Retrospective review of approx. 2000 patients admitted to trauma service of regional trauma centre between Sept 1998 and May 2000. 278 patients >65 years old with CT-documented TICH. 21 warfarinised but 5 excluded as thought more likely spontaneous ICH. Average age 78, average GCS 11, average INR 3.0	Case-control study	Mortality	Use of FFP and cryoprecipitate to reverse coagulopathy did not impact on mortality. Nearly half of patients studied underwent craniotomy with 67% 30-day mortality. Overall mortality rate in WHI patients was 50% (8/16) compared with 20% (51/256) in those without coagulopathy (p=0.011). In subgroup of patients with INR >3.5, the mortality rate approached 75%	Really no data displayed to appreciate. Inadequate sample size for those with INR >3 (n approx. 8) from which to draw meaningful conclusions. Retrospective
Li <i>et al</i> , 2001, USA	Retrospective chart review from 2 centres, May 1996–May 2000 from 1 and Jan–Dec 1998 from another. 144 WHI patients identified that had CTB. Excluded those with high-risk and moderate-risk findings. Median (IQR) age 83 (77–87)	Cohort study	Clinically important CT injury that results in change in disposition	10 patients found to have such injuries (7%, 95% CI 3% to 11%). No significant demographic or case-characteristic differences between groups with and without CT-identified injuries. Median (IQR) INR 2.1 (1.8–3.0) CT abnormal vs 2.1 (1.6–2.7) CT normal (p=0.6)	Retrospective design using different time periods from 2 centres for an unexplained reason. Selection bias from including only those who had CTB and no follow-up data to ensure no DICH
Mina <i>et al</i> , 2003, USA	Prospective evaluation of all WHI patients seen in ED of level 1 trauma centre between Jan 2001 and Feb 2002 via a 'Coumadin protocol' and compared with a group of age-matched patients over the same time period admitted with head injury but not on warfarin. 94 WHIs, mean age 77±11. Control group mean age 75 ±12 with normal INR values (mean 1.1±0.1)	Case-control study	Demographics ICH Mortality	WHI group: no significant differences between those with and those without ICH in terms of age, gender, INR (3.2 ±1.9 with ICH vs 3.2±2.5 without, p=0.914), or MOI. ISS significantly higher (21.3±8.2 vs 3.4±7.1, p<0.001) and GCS significantly lower (12.0±4.2 vs 14.7±1.6, p<0.001) for patients with ICH. Control group: GCS not significantly different from WHI group but significantly higher ISS than WHI group 25/94 (27%) WHI group. 47/70 (67%) control group. No significant differences in age, gender, ISS, GCS or MOI Significantly higher WHI group 12/25 (48%) vs 5/47 (10%) control group, p<0.001. WHI group: INR similar (3.3±1.6 dead vs 3.0±2.1 survivors, p=0.585). ISS significantly lower and GCS significantly higher in survivors. Control group: ISS not significantly different but GCS significantly higher in survivors	Well designed but no mention of impact of level of anticoagulation with regards to mortality. Apparently, most patients were therapeutic though
Reynolds <i>et al</i> , 2003, USA	32 WHI patients over 7-year period identified from trauma registry database at level 2 trauma centre. Group 1—24 patients (mean age 82.5). All GCS 15. 8 had INR checked (mean 2.45, range 1.6–3.6). Group 2a—4 patients. All GCS 15. Mean INR 2 (range 1.5–2.6). Group 2b—4 patients. All GCS 15 but all became comatose within 6 h. Mean INR 2.5 (range 2.3–3.1)	Cohort study	ICH	Failed to observe a statistically significant difference in mean INR between groups 1 and 2 (p=0.59) although only 8/24 patients from group 1 tested. No statistical difference between subgroups 2a and 2b (p=0.12). Group 1: Only 3 had CTB (all normal). All discharged home from ED. 22 alive 6/12 post-injury without evidence of DICH. 2 patients lost to follow-up. Group 2a: All had evidence of ICH on CTB. 2 had FFP and vitamin K. All treated conservatively and survived to return to their location of origin. Group 2b: All had evidence of ICH on CTB. All had FFP±vitamin K. 3 had craniotomy with decompression (2 died; 1 discharged to nursing/rehab facility) and the 4th declined intervention and subsequently died	Small observational study really with only 8 patients with ICH in 7 years. Retrospective. Would have been more informative if all of group 1 had an INR and CTB. Note that delay to reversal occurred from failure to send appropriate blood samples from patients who appeared neurologically normal after arrival in ED

Continued

Table 1 Continued

Author, date, country	Patient group	Study type	Outcomes	Key results	Study weaknesses
Gittleman <i>et al</i> , 2005, USA	89 patients being treated with heparin or coumadin who had a head injury and underwent a CTB at a level 1 trauma centre identified over a 4-year period (April 1997–Jan 2002) using hospital information database and neuroradiology case log. 77 taking coumadin, 8 taking heparin and 4 taking both	Cohort study	ICH	7 patients with ICH and all had GCS <15. Included 3 cerebellar haemorrhages that were more suggestive of hypertensive rather than traumatic aetiology. No significant difference found between those with ICH and those without with respect to coagulation profile (INR 2.2 ±1.1 with ICH vs 2.5±1.2 without ICH)	Relatively small numbers and failed to meet sample size required by pretest power calculation. Selection bias from only including those who had CTB. Retrospective. No breakdown of ICH patients to say who was on coumadin or heparin and presumably this could skew the mean INR values of the groups. No mortality data or follow-up data either regarding the possibility of DICH
Ivascu <i>et al</i> , 2005, USA	82 WHI patients identified prospectively between Feb 2003 and April 2007, of which 19 (23%) had evidence of ICH on CTB. Compared with 2 control groups: a group identified during this protocol and a group of historic controls treated before implementation of this protocol to fast-track anticoagulation reversal	Cohort study	Age, sex, MOI, presenting GCS INR ICH Protocol implementation	Not statistically significant between groups with ICH and those without All patients with ICH had therapeutic INR, and there was not a statistically significant difference in degree of anticoagulation between groups. Median INR 2.7 (with ICH) vs 2.5 (without), p=0.350 63 patients without ICH on initial CTB were admitted for 23 h of observation. None subsequently developed ICH, including 12 patients with an INR >3.5 Improved time from hospital presentation to physician evaluation, 50% less time in triage, significant reduction in time to obtain CTB, full anticoagulation reversal with FFP, significant reduction in rates of ICH progression and mortality	The validity of comparing the median INR is questionable, as opposed to the comparison of mean INR. There are minimal details given of the level of coagulopathies, such as range, from which more informed conclusions could be drawn
Cohen <i>et al</i> , 2006, USA	77 patients from 2 trauma databases over 3-year period on warfarin with minor head injury (GCS 13–15). Average age 68. INR obtained in 57% with average 4.4 and values >3 in 47%, range 1.8–9.5. (There was another group of 49 patients who had GCS <8, average age 65. Average INR 6.5, 50% >5. Mortality 87.8%)	Cohort study	Mortality	20 evaluated and sent home from ED. Of these, 35% had CT and all were normal. 18 returned and subsequently diagnosed with significant ICH. 2 patients died at home, 1 with autopsy-confirmed acute SDH. Overall mortality in these 20 patients was 88.8%. 45 patients admitted for observation for head injury± treatment of other injuries. CT obtained before admission in 70%, with only 4 showing any ICH. Within 8–18 h of injury (mean 12 h), 80% deteriorated to GCS <10 with ICH. Mortality in this group 84%. 12 patients presented within h or days of injury with ICH. All underwent emergent craniotomy with a resultant mortality of 83.3%	No matched control group. Majority of patients supra-therapeutically AC, and of those undergoing CT on initial presentation, only slightly more than 30% had any evidence of ICH. Retrospective
Franko <i>et al</i> , 2006, USA	Retrospective analysis of consecutive series of 1493 adult blunt head injury patients between Jan 2001 and May 2005. 159 warfarinised patients identified and were significantly older, with average age 78±10 and average INR 2.4±1.06	Case–control study	ISS LOS ICH Mortality Mortality in those with ICH (n=632) Effect of preinjury anticoagulant level	Significantly greater 14.5±8.4 WHI vs 12.4±9.4 control, p<0.01 Significantly longer 6.7±11.1 WHI vs 4.1±6.3 control, p<0.001 Significantly more likely 96/159 (60.4%) WHI vs 536/1334 (40.2%) control, p<0.001, OR=2.2, 95% CI 1.6 to 3.1 Significantly higher 38/159 (23.9%) WHI vs 66/1334 (4.9%) control, p<0.001, OR=6.0, 95% CI 3.8 to 9.3 Significantly higher 36/96 (37.5%) WHI vs 61/536 (11.4%) control, p<0.001, OR=4.6, 95% CI 2.8 to 7.6 Mortality and occurrence of ICH both significantly increased with increasing INR (Cochran's linear trend p<0.001)	They cite a selection bias through education of AC patients, encouraging the seeking of early medical attention, even after seemingly minimal trauma, and so more of these patients present for evaluation. It is suggested that non-therapeutic users and non-users (NU) had similar results, but they were not compared directly. Retrospective

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Table 1 Continued

Author, date, country	Patient group	Study type	Outcomes	Key results	Study weaknesses
			Age-dependent mortality	Mortality of patients >70 significantly higher than that of younger patients ($p<0.001$). In control group mortality significantly higher with age >70 (38/465, 8.2% vs 28/869, 3.2%) $p<0.001$. In WHI group mortality significantly higher with age >70 (34/133, 25.6% vs 4/26, 16.4%) $p<0.001$	
Pieracci <i>et al</i> , 2007, USA	Retrospective study (2004–2006) of all trauma patients aged ≥ 65 ($n=275$) evaluated by a trauma service at a level 1 trauma centre who had a CTB following a head injury, including 40 WHI. 3 cohorts compared: (1) WHI with INR ≥ 2 (therapeutic group (TG)), $n=22$, 11 of whom had INR >3 . Mean INR 3.33, range 2.12–7.28. (2) WHI with INR <2 (non-therapeutic group (NT)), $n=18$. Mean INR 1.51, range 1.00–1.96. (3) Warfarin NU, $n=235$. Mean INR 1.11, range 0.87–4.01	Case-control study	Admission GCS ICH Overall mortality Mortality after ICH	TG 9 patients (40.9%), $p=0.001$; NT 2 patients (11.1%); NU 22 patients (11.9%). OR=5.13, 95% CI 1.97 to 13.39, $p=0.001$ comparing TG to NU group TG 17 patients (77.2%), $p=0.10$; NT 9 patients (50.0%); NU 105 (56.8%). OR=2.59, 95% CI 0.92 to 7.32, $p=0.07$ comparing TG to NU group. Subgroup analysis revealed no difference in likelihood of ICH between those with INR 2–3 (9/11, 81.8%) and INR >3 (8/11, 72.7%) TG 7 patients (31.8%), $p=0.009$; NT 2 patients (11.8%); NU 17 patients (9.4%). OR=4.48, 95% CI 1.60 to 12.50, $p=0.004$ comparing TG to NU group TG 6 patients (35.3%), $p=0.01$; NT 1 patient (12.5%); NU 14 patients (13.7%). OR=3.42, 95% CI 1.09 to 10.76, $p=0.03$ comparing TG to NU group	Relatively small sample size, therefore, unable to fully compare warfarin users with INR 2–3 with those with INR >3 . Results suggest threshold rather than a linear relationship between level of anticoagulation and risk of ICH, which is consistent with exponential scale of INR. However, both a small number of therapeutic users and a relatively narrow range of INRs among them preclude more detailed analysis. Retrospective
Grandhi <i>et al</i> , 2008, USA	Retrospective review of all patients evaluated at level 1 trauma centre between Jan 2000 and Dec 2006, to include patients ≥ 65 coded with a closed head injury. 52/491 (11%) were documented as taking warfarin (AC) and subsequently compared with those not AC (NAC) by 1:3 propensity matching. Mean admission INR in AC group 2.4 ± 1.2	Case-control study	Ventilator LOS (days) ICU LOS (days) Hospital LOS (days) Mortality	2.8 ± 7.9 AC vs 1.5 ± 5.8 NAC, $p=0.08$ 6.4 ± 11.8 AC vs 4.4 ± 7.3 NAC, $p=0.19$ 10.5 ± 13.6 AC vs 9.1 ± 12.1 NAC, $p=0.97$ $19/49$ (38.8%) AC vs $34/147$ (23.1%) NAC, $p=0.04$	Numbers too small to determine if there was a certain level of anticoagulation for which outcomes significantly worsened? type 2 error. Analysis of association between degree of anticoagulation and various measures of morbidity and mortality with larger sample populations may be able to determine a 'cut-off' INR value for which the benefits of anticoagulation are outweighed by its potential complications. Retrospective
Major and Reed, 2009, UK	399 patients presenting to University Hospital ED with head injury and coexistent anticoagulant (warfarin) or antiplatelet (aspirin, clopidogrel or dipyridamole) therapy who were admitted to the hospital over a 3-year period (Jan 2005–Dec 2007), identified through search of electronic patient records	Cohort study	ICH	110 patients (28% had CTB, of which 24 showed ICH. 4 died and 2 had neurosurgical intervention, but none of these were warfarinised. Of 89 patients on warfarin (including 5 also on aspirin), 27 (30%) underwent CTB, with 4 of these (15%) having ICH. There were 63 patients on warfarin who had an INR <3 (2/17 +ve scans) and 26 who had an INR >3 (2/10 +ve scans). The RR of a patient having a +ve CTB with an INR >3 compared with an INR <3 was 1.7 (95% CI 0.3 to 10.3)	Patients discharged from ED excluded leading to a selection bias. Retrospective. Only 44/110 patients scanned had the indication recorded. No information as to whether those with +ve scans were the ones with indications for scanning. May suggest that a significant proportion of this cohort was low risk
Brewer <i>et al</i> , 2011, USA	Retrospective review of trauma registry at level 2 trauma centre. All trauma registry patients with MHI registered between 2004 and 2006 who were taking clopidogrel or warfarin, GCS 15 and had CTB included. Trauma registry includes all patients admitted to or consulted by the trauma service. 141 patients (mean age 79, range 36–101)	Case-control study	ICH	41 patients (29%) diagnosed with ICH. 23/84 (27%) on warfarin. Mean presenting INR with ICH 1.97 ± 0.92 compared with 2.3 ± 1.2 without ICH ($p=0.0987$). 15/36 (41%) on clopidogrel, 3/21 (14%) on combination therapy. 39 (95%) of patients with ICH underwent reversal \pm discontinuation of clopidogrel \pm warfarin. 5 patients required surgical evacuation of ICH. 4 patients died. LOC (Wald=7.468, $\beta=1.179$, $p=0.008$) predicted a +ve CT. Type of medication (warfarin, clopidogrel or aspirin) did not reach statistical significance as a predictor of a +ve CT	Patient population only includes those from trauma registry and may explain a selection bias. Relatively small numbers and retrospective design

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Table 1 Continued

Author, date, country	Patient group	Study type	Outcomes	Key results	Study weaknesses
Claudia <i>et al</i> , 2011, Italy	Medical records of 1554 adult patients with MHI evaluated by a University Hospital ED between Jan 2007 and Feb 2008 analysed retrospectively. 1410 patients (mean age 57) had at least 1 risk factor and so underwent CTB. 75 patients (5.2%) on warfarin	Case-control study	ICH Risk factors significantly associated with ICH INR	89 patients in total (12 warfarinised) Anticoagulation (OR=2.69, 95% CI 1.36 to 5.3, $p<0.005$) multiple linear regression: coefficient β 0.078, $t=2.841$, $p=0.005$ Mean INR for warfarinised patient 2.37 ± 1.04 and was significantly associated with ICH after head injury ($r=0.37$, $p<0.005$). INR values analysed using ROC curve, AUC 0.76 (95% CI 0.62 to 0.91), $p<0.05$. Showed that most effective INR cut off value was 2.43, with sensitivity of 92%, specificity of 66%, and PPV and NPV of 33% and 97%, respectively	Small sample size—12/75 with ICH. Retrospective
Menditto <i>et al</i> , 2012, Italy	97 prospectively enrolled consecutive warfarinised (for at least 1/52) patients ≥ 14 years old in Level 2 trauma centre without ICH on 1st CT after minor head injury (any head trauma, other than superficial injury to face, presenting with GCS 14 or 15), regardless of presence of absence of LOC, within 48 h of injury, with ISS <15 between Jan 2007–Mar 2010. Structured clinical pathway implemented, comprising 24-h period of observation and 2nd CT prior to discharge	Case series	Immediate TICH Death DICH Admission Neurosurgery	19/97 (16%) +ve initial CT scan No deaths reported 5/97 (6%) (95% CI 1% to 11%). Only 1 showed signs of neurological deterioration during observation period, 2/5 were discharged anyway as ICH regarded as minimal. 2 discharged after completing study protocol with –ve CT admitted 2/7 and 8/7 later with symptomatic SDH; neither required surgery. 2/5 with DICH at 24 h had initial INR >3 as did both beyond 24 h (RR DICH with INR >3 was 14 (95% CI 4 to 49)). 10 refused 2nd CT and were well during 30/7 follow-up 3 hospitalised 1 craniotomy	None had GCS 14 or received concomitant antiplatelet therapy. Only 5 developed ICH by 2nd CT—therefore lacking statistical power to analyse multivariate predictors of such haemorrhage. Not designed to investigate optimal period of observation before repeat CT
Nishijima <i>et al</i> , 2012, USA	Prospective observational study at 2 trauma centres and 4 community hospitals' EDs in California of patients ≥ 18 with blunt head trauma (most commonly ground level fall (83.3%)), regardless of LOC/amnesia and preinjury warfarin or clopidogrel use (but not both) within previous 7/7 between Aug 2009–Jan 2011. Followed for 2/52 by review of in-patient electronic medical record or by telephone survey if already discharged. 1064 patients enrolled (768 warfarin (72.2%) and 296 clopidogrel (27.8%)). 364 (34.2%) from level 1 or 2 trauma centres and 700 (65.8%) community hospitals. 1000 received head CT in ED. Both warfarin and clopidogrel groups had similar demographics and clinical characteristics, although concomitant aspirin use more prevalent among clopidogrel group. Enrolled after screening by treating physician (16.7% missed by screening failure, but these had similar characteristics and outcomes). Repeat CT was at clinicians' discretion. Excluded patients with known injury transferred in as their injuries would falsely inflate prevalence of TICH. 78.5% had INR checked, median 2.5; IQR 2.0–3.3	Cohort study	Immediate TICH In-hospital mortality after immediate TICH Neurosurgical intervention after immediate TICH DICH (TICH within 2/52 after initially normal CT in absence of further head trauma)	37/724 (5.1%) (95% CI 3.6% to 7.0%). Follow-up of 63/64 not undergoing initial CT showed no subsequent diagnosis of TICH. Majority of patients (62.2%) had GCS 15, and 4/37 (10.8%) had no LOC, GCS 15 and no evidence of trauma above clavicles 8/37 (21.6%) (95% CI 9.8% to 38.2%) 5/37 (13.5%) (95% CI 4.5% to 28.8%) 4/687 (0.6%) (95% CI 0.2% to 1.5%). 2 were inoperable and died from extensive TICH	Observational—not everyone scanned initially for ethical reasons, or routinely before discharge. Clinical follow-up though to elicit clinically important outcomes. Warfarin users more aware of risks and so more likely to present with less severe mechanisms of injury

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Table 1 Continued

Author, date, country	Patient group	Study type	Outcomes	Key results	Study weaknesses
Nishijima <i>et al</i> , 2013, USA	Secondary aims from previously published study data (see below). Those without initial CT however excluded, leaving 982 patients on warfarin (72.7%) or clopidogrel. Mean age 75 with almost equal sex distribution. 83.6% were ground level falls and 89.5% were GCS 15	Cohort study	Immediate TICH In-hospital mortality after immediate TICH Neurosurgical intervention after immediate TICH Factors associated with immediate TICH identified by multivariate logistic regression	60 patients (6.1%; 95% CI 4.7% to 7.8%). None of 65 without initial CT were later diagnosed with TICH although 2 were lost to follow-up. 31/60 warfarinised. RR of warfarin 0.40 (95% CI 0.25 to 0.65) 10/60 (16.7%; 95% CI 8.3% to 28.5%) 12/60 (20%; 95% CI 8.3% to 28.5%) Vomiting (aOR 3.68; 95% CI 1.55 to 8.96) and abnormal mental status (aOR 3.08; 95% CI 1.60 to 5.4.) However, these 2 variables were absent in a substantial number of those with TICH	In addition to comments for the previous paper, there were relatively few patients meeting primary outcome of immediate TICH, however, including more patients with TICH would not resolve the fact that many patients with immediate TICH appeared to have no risk factors for TICH beyond age and anticoagulant use. Also limited ability to conduct subgroup analyses by medication type (warfarin or clopidogrel) or by INR level
Rendell and Batchelor, 2013, UK	82 WHI patients identified from 3338 CT scans requested by the ED over 2-year period (Jan 2008–Dec 2009) 72/82 (88%) patients had their INR checked	Cohort study	ICH Neurosurgical intervention Death	12/82 (15%). RR of ICH for INR subgroups calculated: INR <2 (RR 1.89; 95% CI 0.65 to 5.55); INR 2–3 (RR 0.84; 95% CI 0.27 to 2.64); and INR >3 (RR 0.53; 95% CI 0.13 to 2.29). The greatest proportion of those with ICH (42%) had a sub-therapeutic INR. 2/12 (17%) found to have ICH despite not meeting criteria for a CT scan according to NICE. Results of INR subgroup analysis suggest that a sub-therapeutic INR may not be protective against ICH following a minor head injury 4/12 3/12	Retrospective review so never easy to capture all patients. However, a random trawl of notes over a 2-month period coded as head injury revealed no further patients. Small, but comparatively equivalent sample size, did not allow statistically significant conclusions, but did, however, yield interesting conclusions

aOR, adjusted OR; AUC, area under the curve; CTB, CT brain; DICH, delayed intracranial haemorrhage; ED, emergency department; FFP, fresh frozen plasma; GCS, Glasgow Coma Score; ICU, intensive care unit; INR, International Normalised Ratio; ISS, injury severity score; LOC, loss of consciousness; LOS, length of stay; MHI, minor head injury; MOI, mechanism of injury; NICE, National Institute for Health and Care Excellence; NPV, negative predictive value; PPV, positive predictive value; PT, prothrombin time; ROC, receiver operator curve; RR, relative risk; SDH, subdural haematoma; TICH, traumatic intracranial haemorrhage; WHI, warfarinised head injury.

of the INR in the low risk patient: one who is asymptomatic with GCS 15. Cohen *et al* (2006) highlight significant inconsistencies in the management of this group of patients even in a single centre, particularly with respect to measuring the INR, obtaining a CT scan and indeed the timing of this scan. They suggest routine measurement of the INR in all those warfarinised and consideration of routine CT scanning. There is much to suggest, though, that there is not a great causal significance in the level of coagulopathy in the low-risk WHI patient (Rendell and Batchelor, 2013; Nishijima *et al*, 2012). Nishijima *et al* (2013), Nishijima *et al* (2012), Gittleman *et al* (2005) and Li *et al* (2001) demonstrate the high incidence of ICH in anticoagulated patients following seemingly trivial injury without high-risk features. Furthermore, Rendell and Batchelor (2013), Brewer *et al* (2011) and Reynolds *et al* (2003) found no statistical difference in INR between those with positive compared with negative scans, Mina *et al* (2003) between those that died compared with survivors and Reynolds *et al* (2003) between those with ICH who remained stable compared with those who subsequently deteriorated. Rendell and Batchelor (2013) and Ivascu *et al* (2005) conclude that neither the GCS nor the level of anticoagulation can reliably predict the presence of ICH, even that a sub-therapeutic INR appears to offer no protection, and that urgent scanning combined with prompt reversal can reduce ICH progression and improve mortality. Therefore, both the clinical picture and the INR have not shown to be effective at ruling out ICH in the asymptomatic WHI patient. It is, nevertheless, an important investigation in this setting, as an early check has been shown to allow rapid time to reversal of the INR with ICH. Importantly, Nishijima *et al* (2013) and Rendell and Batchelor (2013) found that there was no 'low-risk group' of warfarinised head injury patients safely managed without CT despite their apparent well-being. In the presence of a normal CT scan, it would appear to be prudent to admit a patient with a supra-therapeutic INR for at least a period of observation, and perhaps consideration given to short-term reversal of anticoagulation, as advocated by Cohen *et al* (2006).

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Emerg Med J 2014;31:331-337.
doi:10.1136/emered-2014-203646.1



BET 1: Coagulopathy as a risk factor in warfarinised head injury patients

Emerg Med J 2014 31: 331-337
doi: 10.1136/emered-2014-203646.1

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