

**CLINICAL SCENARIO**

An elderly woman attends your emergency department (ED) following a mechanical fall. She takes warfarin for atrial fibrillation and has a small occipital haematoma. Her Glasgow Coma Score (GCS) is 15; she has no amnesia and a normal neurological examination but did briefly lose consciousness. The International Normalised Ratio (INR) comes back within the therapeutic range at 2.9 and a CT scan is requested according to the National Institute of Health and Care Excellence (NICE) guidelines.

The scan is reported as normal, and her social circumstances are adequate in that she lives with her husband who can keep an eye on her. You wonder, though, whether it is safe to discharge her or if there is a possibility of delayed intracranial haemorrhage (DICH) due to her coagulopathy, and therefore she should be admitted for a period of neurological observation so that it can be identified and acted upon at the earliest opportunity.

**THREE-PART QUESTION**

In (adult patients on warfarin with a minor head injury) does a (normal CT brain scan) allow (safe discharge home)?

**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 789 were irrelevant or of insufficient quality. The remaining seven were directly relevant to the three-part question and are summarised in the table 3.

**COMMENTS**

There is much debate in the literature as to how best to manage this group of patients. Their risk of immediate traumatic intracranial haemorrhage is increased to about one in six compared with those not warfarinised. The NICE guidelines tell us only to perform a CT scan in the presence of loss of consciousness or amnesia, but tell us nothing about the impact of coagulopathy or about a period of observation, especially if no CT is to be performed. From my research, it is clear that these patients are

**BET 3: OBSERVATION IS UNNECESSARY FOLLOWING A NORMAL CT BRAIN IN WARFARINISED HEAD INJURIES: AN UPDATE**

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**ABSTRACT**

A short-cut review was carried out to determine whether patients on warfarin with a minor head injury can be discharged safely if they have a normal CT scan. 796 papers were found using the reported search, of which seven were considered relevant to the three-part question. 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 the risk of delayed intracranial haemorrhage, at least in patients with an INR <3, is extremely small and discharge of these patients should be considered.

**Table 3** Relevant papers

Author, date, country	Patient group	Study type	Outcomes	Key results	Study weaknesses
Garra <i>et al</i> , 1999, USA	65 anticoagulated 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. 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. 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 anticoagulated.
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 value 4.4 and values >3 in 47%, range 1.8–9.5	Cohort study	Mortality	20 evaluated and sent home from ED. Of these, 35% had CT, all of which were normal. 18 returned to ED and subsequently diagnosed with a significant traumatic intracranial abnormality. 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 traumatic intracranial abnormality—3 contusions and 1 traumatic SAH. Within 8–18 h of injury (mean 12 h), 80% deteriorated to GCS <10 with the following CT abnormalities: acute SDH 31%; contusion 20%; intracerebral haemorrhage 20%; mixed lesions 29%. Mortality in this group 84%. 12 patients presented within hours or days of injury with neurological findings of an intracranial mass and CT evidence of a significant traumatic intracranial abnormality. All underwent emergent craniotomy with a resultant mortality of 83.3%	No matched control group. Majority of patients supra-therapeutically anticoagulated and, of those undergoing CT on initial presentation, only slightly >30% had any evidence of traumatic intracranial abnormality. Conversely, because the majority of patients in this study did not have a CT until clinical deterioration, they may have harboured an intracranial haematoma that 'enlarged' secondary to underlying anticoagulation. Unclear who had reversal of anticoagulation. Again, no estimate of risk possible
Itshayek <i>et al</i> , 2006, Israel	All anticoagulated head injuries are scanned in their level 1 trauma centre and during 2 1/2-year period they describe 4 patients (aged 65–86) presenting following minor head injury. All chronically anticoagulated (3 on warfarin 1 on Enoxaparin and aspirin). INRs of 3 warfarinised patients were 2.99, 3.03 and 3.2. All GCS 15, no LOC, no focal neurological deficit, no evidence of cranial fracture and normal CT on arrival in department	Case report	Development of DASH, morbidity and mortality	3 warfarin patients developed DASH with rapid neurological deterioration within 24 h, the patient on Enoxaparin and Aspirin deteriorated after 3/7. 3 out of 4 patients underwent craniotomy for evacuation of their haematomas. The 2 male patients died after complicated post-operative courses. 1 female patient underwent surgical evacuation and rehabilitation, eventually achieving a GOS of 3. In the 2nd female patient, the haematoma was treated conservatively and she achieved a GOS of 4	Only a small case series, but quantification of risk impossible. We are told that they treat a population of 800 000 but we are not told how many such patients with normal examinations and normal CT scans they saw out of which 4 developed DASH
Kaen <i>et al</i> , 2010, Spain	137 consecutive adult anticoagulated patients with minor head injuries (GCS 14–15) sustained in previous 48 h over 15/12 period with normal initial CT scans. All admitted for 24 h observation with a control CT scan performed before discharge. All warfarinised but 3 also on aspirin	Prospective cohort study	Intracranial bleeding on 2nd CT scan	135 (98.6%) had no evidence of intracranial lesions on control CT and none developed subsequent neurological deterioration or needed neurosurgical intervention during observation period. Only 2 patients (1.4%) (INR 3.1 and 2.88) developed haemorrhagic lesions on control CT. Both patients on both warfarin and aspirin; difference in incidence of bleeding in these 2 cases compared with those only anticoagulated was statistically significant (p=0.01). Likewise, they were among 14 (10%) who had LOC; difference in frequency of bleeding compared with 90% without LOC also statistically significant (p=0.004)	Observational, non- randomised without a control group. Needs larger number of patients to establish definite conclusions

Continued

Table 3 Continued

Author, date, country	Patient group	Study type	Outcomes	Key results	Study weaknesses
Peck <i>et al</i> , 2011, USA	Retrospective review of protocol in level 1 trauma centre between 01/01/06 and 31/08/09, whereby those with blunt head trauma and preinjury use of an anticoagulant or antiplatelet agent (ACAP) (defined as warfarin, clopidogrel, heparin, or dipyridamole and aspirin in combination) received an admission CT head (CT1) regardless of symptomatology, and for those without ICH on CT1, a period of observation followed by a routine 2nd CT (CT2) in 6 h. Excluded those solely on warfarin if INR <1.3. Blinded review of CTs by radiologist. Attempts at follow-up across San Diego area. 500 patients qualified for protocol, of which 424 (85%) had -ve CT1. Mean age 75 with almost equal sex distribution, and 84% were a fall from standing. Mean GCS was 14.8. Mean initial INR for 312 warfarinised patients was 2.5 with 22 >4: so largely a therapeutic cohort	Cohort study	Neurological deterioration during observation  CT1 -ve → CT2 +ve  Readmission	15 patients (3.5%) had clear documentation of neurological deterioration; 397 (93.6%) showed no change; 12 (2.8%) had insufficient data. None of the 15 had a +ve CT2 4 patients (1%), all warfarinised with INRs of 2.2, 2.2, 3.9 and 1.7. CT3 was stable or -ve in these cases; 3 were discharged and 1 died of cardiac disease following an orthopaedic procedure, all without intervention 3 (0.6%) of original 500 patients admitted for medical problems. 1 (0.2%) for 'progression of neurological insult,' having trace of intraventricular blood documented on CT3 but resolved on CT4 without intervention or treatment	Retrospective. Neurological examination not clear in all patients. CT2 not performed in 15% of CT1 -ve patients. Platelet inhibition unable to be measured. Clopidogrel and other agents confound the warfarin data of interest here
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  Admission Neurosurgery	19/97 (16%) +ve initial scan 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 was carried out to elicit clinically important outcomes. Warfarin users more aware of risks and so more likely to present with less severe mechanisms of injury

aOR, adjusted OR; DICH, delayed intracranial haemorrhage; ED, emergency department; GCS, Glasgow Coma Score; INR, International Normalised Ratio; ISS, injury severity score; LOC, loss of consciousness; PT, prothrombin time; RR, relative risk; SDH, subdural haematoma; TICH, traumatic intracranial haemorrhage.

managed quite differently even within the same centre, in the absence of robust guidelines. Italian guidelines published in 1999, derived largely from a published case series of two patients, advise a CT scan in all patients with coagulopathy, admission for observation for 24 h and then a second CT prior to discharge. Kaen *et al* here suggest that this second CT may not be necessary, with only 2/137 (1.4%) found to have DICH, both neurosurgically irrelevant. Peck *et al* show that a routine repeat CT after 6 h is also unnecessary.

DICH in this setting, with a normal admission CT and an International Normalised Ratio (INR) not supra-therapeutic, would appear to be a fairly rare occurrence, quoted as <1% in large studies by Nishijima *et al* and Peck *et al*. Indeed, the relative risk of DICH with an INR >3 was found to be 14 (95% CI 4 to 49) by Menditto *et al*. However, more often than not in the literature it is described following a previous discovery of a cranial fracture or following a clinical deterioration in a previously asymptomatic patient that had therefore not been initially scanned.

An important question to ask is whether such findings of DICH really matter? By admitting more patients, and ordering more scans, is outcome improved? Or do we just reveal positive findings of little clinical significance? Furthermore, very few of the DICH found in these studies occurred within 24 h; instead often after several

days. So do we admit these patients for our own false reassurance?

Our practice seems largely to be based on anecdotal evidence, fuelled probably by such case series as presented here, but the larger studies described should reassure us as to the very low risk of DICH, particularly with an initial INR <3 and a normal CT scan. Therefore, it would seem reasonable to discharge these patients, but with robust and clear instructions. Some have even shown the effectiveness of telephone follow-up the following day.

#### Clinical bottom line

- ▶ The risk of delayed intracranial haemorrhage has been quantified as reassuringly small, rather than anecdotally inflated. Therefore, it would seem reasonable to discharge those with an International Normalised Ratio <3 and a normal initial CT scan, ensuring good instructions and follow-up.

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## BET 3: Observation is unnecessary following a normal CT brain in warfarinised head injuries: an update

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