Understanding the management of patients with head injury taking warfarin: who should we scan and when? Lessons from the AHEAD study

Suzanne M Mason,1,2 Rachel Evans,1,2 Maxine Kuczawski1

ABSTRACT
Anticoagulated patients represent an important and increasing proportion of the patients with head trauma attending the ED, but there is no international consensus for their appropriate investigation and management. International guidelines vary and are largely based on a small number of studies, which provide poor-quality evidence for the management of patients taking warfarin. This article provides an overview of the clinical research evidence for CT scanning head-injured patients taking warfarin and a discussion of interpretation of risk and acceptable risk. We aim to provide shop floor clinicians with an understanding of the limitations of the evidence in this field and the limitations of applying ‘one-size-fits-all’ guidelines to individual patients. There is good evidence for a more selective scanning approach to patients with head injuries taking warfarin than is currently recommended by most guidelines. Specifically, patients without any head injury–related symptoms and GCS score 15 have a reduced risk of adverse outcome and may not need to be scanned. We argue that there is evidence to support an individualised approach to decision to CT scan in mild head injuries on warfarin and that clinicians should feel able to discuss risks with patients and sometimes decide not to scan.

CASES
Mrs. A is a 62-year-old woman who presents to the ED with a headache following a fall down the stairs 3 hours earlier. She has a GCS of 15, denies loss of consciousness and has no other injuries. She takes warfarin for a previous pulmonary embolism.

Mr. B is an 89-year-old man who is brought to the ED by his care home staff who report an unwitnessed fall from standing 2 hours ago. He has a laceration to his forehead. Care staff did not see, so are not sure about loss of consciousness. He is confused and apparently more agitated than normal, but has not vomited. He is opening his eyes to voice. He takes warfarin for atrial fibrillation.

Question: Should we scan these patients and if so, when?

INTRODUCTION
Head injury is an increasingly common cause of injury presenting to the ED, responsible for 1.4 million patients attending each year in the UK1 and 2.8 million ED visits, hospitalisations and deaths in the USA in 2013.2 Force applied to the head can result in injuries ranging from superficial scalp lacerations to intracranial haemorrhage. These injuries may disturb brain function and are known as traumatic brain injury (TBI).3 TBI is stratified as mild, moderate or severe, depending on the patient’s level of consciousness as defined by a GCS of 14–15, 9–13 and 8 or less, respectively.

There were 23 million prescriptions of warfarin in the USA in 2014,4 5.4 million in Canada in 20135 and 11.6 million in the UK in 2014.4 Most commonly used for prophylaxis in atrial fibrillation and stroke, and for treatment of pulmonary embolism and deep vein thrombosis,6 its use is likely to have increased from the 8% of over 80s in 2006 as these conditions become more common.9 The main cause of head injury across all age groups is falls10 and the risk of intracerebral haemorrhage is much greater for people taking anticoagulants with head injuries.11

There are multiple varying local or national clinical decision rules (CDRs) for the management of head-injured patients. The widely used Canadian CT head rule (CCHR) and the New Orleans Criteria (NOC) do not apply to anticoagulated patients.12 13 The NEXUS criteria and the American College of Emergency Physicians recommend that patients with a ‘coagulopathy’—into which group patients taking anticoagulant medication fit—should have a CT scan of the head (where CT scan is stated hereafter, this implies CT scan of the head) regardless of other symptoms.14 15 European, Italian and Scandinavian guidelines recommend CT scanning all patients taking anticoagulants, regardless of other symptoms.16–18

The 2014 National Institute for Health and Care Excellence (NICE) for England and Wales specifically refers to warfarin: it recommends that all patients taking warfarin who present to the ED with a minor head injury (i.e., GCS 15) and no other symptoms have a reduced risk of adverse outcome (risk 2.7%; 95% CI 2.1 to 3.6).19 This suggests that routine scanning of these patients may be unnecessary.

EVIDENCE FOR CT SCANS OF THE HEAD FOR PATIENTS TAKING WARFARIN

In the ED, CT scan is the accepted way to investigate for intracranial injury in patients with head injury. It is a reliable and sensitive way to detect intracranial abnormalities, used in preference to admission and skull radiograph.20 Although MRI may be more

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sensitive to small lesions, it is more costly and time consuming.\textsuperscript{22} Not all patients with a head injury receive a CT scan: it is not necessary nor effective to scan everyone and it costs more than a selective scanning approach.\textsuperscript{23} CDRs have been developed to guide clinician decisions for who to scan and to rationalise the use of CT scanning in order to avoid unnecessary radiation exposure for patients and use healthcare resources judiciously, but few have been adequately validated.\textsuperscript{24} The evidence underpinning their recommendations for CT scanning patients taking warfarin or other anticoagulant medication or with coagulopathy is poor quality.

In order to formulate its head injury guidance for England and Wales, NICE compared the sensitivity and specificity of hand-held electroencephalogram, the NOC, CCHR and the National Emergency X-Radiography Utilisation Study II Rule. These rules mostly have high sensitivity, which is diminished as specificity increases. NICE considers sensitivity to be most important in view of ‘the potentially severe consequences of not detecting clinically important brain injury’.\textsuperscript{25} The 2014 NICE head injury guideline is based on the CCHR (sensitivity 80%, specificity 39%, negative predictive value 88% for clinically important brain injury). The guidance recommends a CT scan for all patients taking warfarin specifically and patients with a ‘coagulopathy’ within 8 hours if they have lost consciousness or have amnesia.\textsuperscript{19}

The study which gave rise to the CCHR, excluded all patients with bleeding disorders or taking anticoagulant medications.\textsuperscript{12} The evidence for other international CDRs for patients taking warfarin is weak: the study underpinning the NOC recruited 1/520 patients with a coagulopathy and the authors specifically comment that ‘since patients with coagulopathy were under-represented in our study we could not evaluate this criterion’.\textsuperscript{13}

Other studies (the NEXUS II study and a synthesis of all head injury CDRs) have found coagulopathy to be poorly predictive of intracranial injury.\textsuperscript{14,26} Results from studies of patients with head injuries while taking warfarin have recruited varying numbers of patients (35–3580) and use different methodologies. Reported proportions of traumatic intracranial haemorrhage are 5.1\%\textsuperscript{32} and 7.9\%\textsuperscript{28} and ORs are reported as 5.48\textsuperscript{29} for abnormal CT and 2.39 for ‘severe head injury’.\textsuperscript{10}

This lack of good-quality evidence pertaining to anticoagulated patients and of international CDR consensus and leaves the shop floor clinician without certainty as to the true risks to their patients and the most appropriate management strategy.

### WHAT DOES AHEAD ADD?

The AHEAD study (2016) was a prospective observational study that recruited 3534 adults taking warfarin with a non-penetrating head injury across 33 EDs in England and Scotland. Of these patients, 59.8\% (n=2114) received a CT scan with findings in 5.4\% displaying an intracranial abnormality likely to be due to the injury. Overall, the adverse outcome rate was 5.9\% (95\% CI 5.2 to 6.7) including patients who required neurosurgery (0.5\%), head injury–related re-admission (1.0\%) and head injury–related death (1.2\%). The full results are published elsewhere.\textsuperscript{20}

GCS <15 was the strongest predictor of adverse outcome. Patients presenting with GCS <15 were uncommon (only 11.1\% of patients) but had a relative risk of adverse outcome of 4.82 (95\% CI 3.66 to 6.35). The highest relative risk of adverse outcome was for patients with GCS ≤12 (RR 10.53; 95\% CI 7.90 to 15.36).

Head injury–associated neurological symptoms (loss of consciousness, vomiting, amnesia) are statistically significantly associated with an increased risk of adverse outcome, even in patients with GCS 15 (see table 2). Headache is more weakly associated, but not statistically significantly when GCS 15, the risk of adverse outcome is reduced (2.7\%; 95\% CI 2.1 to 3.6).

Additionally, international normalised ratio (INR) had no statistically significant association with adverse outcome and

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### Table 1 Summary of a sample of international guidelines for CT scanning patients with head injury taking anticoagulants

<table>
<thead>
<tr>
<th>Clinical decision rule</th>
<th>Does the rule include ‘coagulopathy’ or ‘taking anticoagulant’ as criteria?</th>
<th>Does presence of coagulopathy or taking anticoagulant medication indicate CT scan of the head is required?</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCHR\textsuperscript{17}</td>
<td>No</td>
<td>Rule does not apply to anticoagulated patients</td>
</tr>
<tr>
<td>NOC\textsuperscript{13}</td>
<td>No</td>
<td>Rule does not apply to anticoagulated patients</td>
</tr>
<tr>
<td>National Emergency X-Radiography Utilisation Study criteria\textsuperscript{14}</td>
<td>Yes</td>
<td>Patients with coagulopathy should have a CT scan regardless of other symptoms</td>
</tr>
<tr>
<td>American College of Emergency Physicians\textsuperscript{15}</td>
<td>Yes</td>
<td>Patients with coagulopathy should have a CT scan regardless of other symptoms</td>
</tr>
<tr>
<td>European Federation of Neurological Societies\textsuperscript{16}</td>
<td>Yes</td>
<td>Patients with coagulopathy or anticoagulant medication should have a CT scan and be admitted for observation</td>
</tr>
<tr>
<td>Italian Society for Neurosurgery\textsuperscript{17}</td>
<td>Yes</td>
<td>Patients with coagulopathy or anticoagulant medication should have a CT scan, be admitted for observation and have a repeat scan prior to discharge</td>
</tr>
<tr>
<td>Scandinavian Neurotrauma Committee\textsuperscript{18}</td>
<td>Yes</td>
<td>Patients with coagulopathy should have a CT scan regardless of other symptoms</td>
</tr>
<tr>
<td>NICE 2007\textsuperscript{26}</td>
<td>Yes</td>
<td>Patients with coagulopathy should have a CT scan within 1 hour</td>
</tr>
<tr>
<td>NICE 2014\textsuperscript{19}</td>
<td>Yes</td>
<td>Patients with amnesia or loss of consciousness and coagulopathy should have a CT scan, and all patients taking warfarin should have a CT scan</td>
</tr>
</tbody>
</table>

CCHR, Canadian CT head rule; NICE, National Institute for Health and Care Excellence; NOC, New Orleans Criteria.

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### Table 2 Univariable analysis results by neurological symptom category, from the AHEAD study\textsuperscript{20}

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Patients</th>
<th>Number of patients</th>
<th>Relative risk</th>
<th>95% CI</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>All</td>
<td>2634</td>
<td>3.94</td>
<td>2.32 to 6.70</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GCS 15 only</td>
<td>2237</td>
<td>3.00</td>
<td>1.68 to 5.41</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Amnesia</td>
<td>All</td>
<td>2070</td>
<td>4.37</td>
<td>3.05 to 6.25</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GCS 15 only</td>
<td>1796</td>
<td>4.90</td>
<td>3.34 to 7.19</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>All</td>
<td>2023</td>
<td>2.11</td>
<td>1.33 to 3.34</td>
<td>0.001</td>
</tr>
<tr>
<td>GCS 15 only</td>
<td>1723</td>
<td>1.78</td>
<td>0.97 to 3.26</td>
<td>0.062</td>
<td></td>
</tr>
<tr>
<td>Loss of consciousness</td>
<td>All</td>
<td>2914</td>
<td>4.14</td>
<td>2.92 to 5.88</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GCS 15 only</td>
<td>2475</td>
<td>3.5</td>
<td>2.26 to 5.41</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>
subgroup analysis showed that the rate of delayed complications (ie, delayed bleeds) is low (1.1% ED re-attendance and 0.06% deaths from head injury–related complications).31

Cost-effectiveness analysis was performed for the CT-all approach as per NICE guidelines compared with a selective scanning approach. This was based on assumptions for patients who died: the probability of survival if a CT scan had been performed, the hypothetical survival Glasgow Outcome Scale (GOS) and the cost of neurosurgery; and for patients who survived: the probability of GOS increase if a CT scan had been performed. This demonstrated that the practice of CT scanning all patients with head injury taking warfarin is associated with an incremental cost-effectiveness ratio (cost per quality-adjusted life year) of £94 895.152. These were robust to sensitivity analyses. Holmes et al previously showed selective CT scanning approaches to be more cost-effective than non-selective approaches in their analysis of all patients with head injury (not just the anticoagulated).153

The AHEAD study is the largest cohort study to date looking specifically at patients taking warfarin with head injuries. It has sufficient power to describe outcomes for these patients and clearly demonstrates a reduced risk of adverse outcome in patients on warfarin with a mild head injury and GCS 15 with no other neurological symptoms.20 This evidence illustrates how there is significant variation between patients with head injury and that general guidelines are not always applicable to the specific patient in front of you.

RISK IN HEAD INJURY

Risk is the product of this probability multiplied by the severity of the consequence, should the event occur. The probability of an event occurring is how likely it is to occur, measured by the ratio of the cases of interest (in this case adverse outcomes) to the total possible cases (the total head injuries on warfarin). From the AHEAD study, the probability of adverse outcome is roughly 1 in 30. The severity of the consequence can range from a small contusion to a large inoperable bleed and subsequent death. Therein lies the limitations of a compound outcome as used in AHEAD: essential to make the study sample size practicable but does not enable the clinician to stratify the risk for their individual patient.

The level of risk that is acceptable depends on the individual context of this patient’s context. Perhaps, for example, this patient is young, active and a mother of 3. For them, the risk may be higher compared with an elderly, bed-bound care home resident (the severity of the consequences may be increased). Further, the acceptable risk may differ between clinicians and between the patient and the clinician.

Clinicians accept different levels of risk depending on the scenario. For example, clinicians have different thresholds for delaying procedural sedation in the child who has not fasted depending on the child or the urgency,33 and accept varying levels of side effect risk in exchange for treatment benefits.34

Evidence suggests that patients prefer being involved in decisions about their care35,36 and that such patient participation has benefits including increased patient understanding, no adverse effects37 and reduced invasive testing or admissions.38 Patients may be willing to accept a higher risk compared with clinicians.34 For example, most ED clinicians consider an acceptable risk of missed acute myocardial infarction as less than 0.5% (0.1%–1.9%).39 When patients with chest pain were presented with a pre-test probability of 4% (using a decision aid in a shared decision-making approach), some patients declined admission and investigation.38 In this study, there were no reported missed major adverse cardiovascular events or later related admissions despite shorter lengths of stay and reduced tests. This is an important finding in a condition (chest pain) for which ED attendances and morbidity are reducing but the number of tests performed is increasing.40

It is clear that these decisions are not simple, and therefore a simple ‘one size fits all’ clinical decision rule is not always appropriate to apply. We suggest that the clinician should take the individual patient’s situation and preferences into account when considering the need for CT scan. CT scans are now cheap, easy, and quick to perform and therefore represent minimal burden if they are likely to change practice. The radiation risk may even be negligible in older people. However, there must be judicious, considered use of all healthcare resources and there should be clinical justification that the results may change the patient’s course. For warfarinised patients with head injuries who have few or no symptoms, it may be valuable to undertake a more detailed discussion with the patient/family regarding their investigation and management.

Communication about risk between patients and clinicians is notoriously poorly done because of the shared difficulty of explaining and interpreting statistics.41 Risk can be presented as risk reduction (a percentage or proportion) or a natural frequency, but the comprehension can be affected by the negative or positive ‘frame’ in which the statistic is explained and any explanation of uncertainty (ie, how good quality the evidence is supporting that statistic).41

Communication has been enhanced by ‘decision aids’; various media designed to provide information to the patient to enable them to make an informed personalised decision about a treatment or investigation.42 They have already been used in cancers, arthritis and end-of-life care and can improve patient understanding and enable them to make decisions consistent with their values.35 Patients have improved comprehension of risk when presented with personalised risks, calculated with risk tools, such as the QRISK calculator for cardiovascular disease (http://qrisk.org),43 and this may be something to consider in head injury.

IMPLICATIONS FOR PRACTICE

The AHEAD study has shown that GCS and neurological symptoms can predict adverse outcome in patients taking warfarin. The AHEAD study provides good evidence that CT scanning patients with head injury taking warfarin who have GCS 15 and no other symptoms may not be of value and could potentially be avoided.

For patients taking warfarin with head injuries who have few or no symptoms, it may be possible to undertake shared decision-making regarding their investigation and management. It should be emphasised that the aim of involving patients in decision-making is not to reduce resource use but to enable them and avoid paternalism. However, as busy emergency medicine clinicians in urgent care systems under significant strain, we have a duty to use resources judiciously and therefore carefully consider the waiting time, CT scan expense and time, radiographer reporting time and so on, all associated with head injury investigation. Over-investigation carries its own risks of ‘overdiagnosis, over treatment and iatrogenic harm’.44

We strive to practise evidence-based medicine: scientifically rigorous evidence has the potential to improve the care we deliver to patients. In reality, this is not as simple as applying one rule to all patients: this ignores the variation in individual patient histories and presentations. It may not be possible to apply the study population’s characteristics to the patient in front of you or their clinical course may change unexpectedly. We argue that a single guideline for a broad spectrum of patients is no
longer appropriate and clinicians should be encouraged to make management decisions based on the individual patient’s context.

CASE REVIEW: WHO SHOULD I SCAN?

Patients A and B represent familiar cases in our EDs. Under most international guidelines, they both would receive a CT scan. Patient A has a headache and no head injury–related injuries, but she takes an anticoagulant medication. All aforementioned head injury guidelines would recommend that she has a CT scan because of anticoagulant use even though she has no other symptoms or signs (see table 1). CCHR and NOC cannot apply to this patient. Patient B is confused but his eyes are open (GCS eye score 4/4) and assuming he is obeying commands to move his limbs (GCS motor score 6/6), he has a GCS 14. Although care staff may report that this is normal for him, strictly he has a GCS <15 at 2 hours postinjury and you the clinician cannot be sure if the new agitation is relating to an intracranial injury. Although he has ‘within 8 hours’ criteria according to NICE guidance—he is over 65 and taking warfarin—he should have the scan performed and reported within 1 hour because of his GCS. Other international guidelines (except CCHR and NOC as mentioned) would also recommend scanning him.

With GCS 15 and no other neurological symptoms, patient A is at reduced risk for adverse outcome. 20 The AHEAD study suggests that you may be able to make a time-saving and cost-saving decision by giving her good verbal and written head injury advice and discharging her. You may consider it good practice to check her anticoagulant use, as there has been shown to be a higher prevalence of non-treatment errors in patients presenting to the ED than in the community. 45 However, the AHEAD study found no association between INR and outcomes in patients with GCS 15, 20 so in this case the value will not affect her risk of intracranial injury. Based on the AHEAD data, there is no justification to admit and/or observe this patient in case of a delayed bleed. 22

Patient B is different: he is difficult to assess because of the unclear history and cognitive impairment. His GCS is not 15 therefore his relative risk of poor outcome is 4.82. The AHEAD study did not consider the baseline GCS of included patients and therefore the GCS must be taken at face value (even though in this case, it is unchanged). This is illustrative of the point that evidence cannot always be applied to the patient in front of you. His CT scan eventually shows no acute intracranial abnormality. Therefore, you are safe to clean and dress the facial wound and discharge him back to the care home. Admission of patients with a normal CT scan is not cost-effective, 22 and as noted above, the risk of delayed bleeding is minimal. These patients should be discharged with good advice for the patient and/or carer. Whether this patient should be taking warfarin at all is a discussion outwith the scope of this article.

CONCLUSION

Clinicians treating a warfarinised patient with a mild head injury face an emotive dilemma: they must weigh up the risk of missing a potentially devastating intracranial injury with the risk of radiating to the patient and the use of time and resources. CDRs based on good-quality evidence are valuable to support the ED clinician in choosing which patients to scan or not but are not currently helpful with warfarinised patients. Recommendations to scan all patients taking warfarin are based on poor-quality evidence. This article summarises how contemporary relevant evidence advocates a more considered and individualised approach to decision to CT scan in head injuries. Specifically, consideration of the individual patient context for decisions to CT scan patients taking warfarin who have GCS 15 and no other symptoms is appropriate and of value.

Acknowledgements The authors thank the AHEAD study team, Richard Jacques for statistical support and all departments involved in the study.

Contributors SMM was responsible for the conception of the work and devising the angle which it promotes. She also reviewed draft copies of the article and gave final approval of the main document. RE was responsible for summarising and critiquing the literature, drafting the article and re-drafting following comments. She also did the majority of writing the article and gives approval for the final copy of the article. She managed the submission and comments for the article. MK was responsible for managing the initial AHEAD study and providing the data for the article. She also reviewed and commented on drafts of the article including giving approval for the final copy after comments. All authors gave final approval to the version submitted for publication.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent None required.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement There are further data available from the AHEAD study, which are currently being analysed. These data items include the CT findings and the mechanisms of injury of the patients involved. We aim to publish these findings separately in due course. There are no further unpublished data specifically relating to this review article.

REFERENCES


