Hypoxic–ischaemic brain injury: imaging and neurophysiology abnormalities related to outcome

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Summary

Background: The outcome for patients with hypoxic–ischaemic brain injury (HIBI) is often poor. It is important to establish an accurate prognosis as soon as possible after the insult to guide management. Clinical assessment is not reliable and ancillary investigations, particularly imaging and EEG, are needed to understand the severity of brain injury and the likely outcome.

Methods: We undertook a retrospective study of 39 patients on an intensive therapy unit (ITU) with HIBI who were referred for MRI. The patients were seen consecutively >57 months. HIBI was due to a variety of insults causing cardiac arrest, hypoperfusion or isolated hypoxia.

Results: The outcome was poor, 29 patients died, 7 were left severely disabled and only 3 made a good recovery. Characteristic imaging changes were seen on MRI. These included extensive changes in the cortex and the deep grey matter present on diffusion-weighted imaging (DWI) and T2-weighted imaging within 6 days of the insult. In other patients, different patterns of involvement of the cortex and basal ganglia occurred. There was no significant difference in the outcome or imaging appearances according to aetiology. A poor prognosis was consistently associated with a non- or poorly responsive EEG rhythm and the presence of periodic generalized phenomena with a very low-voltage background activity.

Conclusion: In this retrospective study of patients with HIBI, MRI and EEG provided valuable information concerning prognosis.

Introduction

Hypoxic–ischaemic brain injury (HIBI) is usually due to cardiac arrest but may follow other causes of hypoxia or hypoperfusion of the brain. The clinical pattern and outcome depends on the severity of the insult, the effectiveness of immediate resuscitation and transfer, and the post-resuscitation management on intensive therapy unit (ITU). Clinical assessment of patients following HIBI is challenging for many reasons. First, the duration and severity of the HIBI are difficult to assess; for example, following out-of-hospital arrests, there is often no clear description of the precipitating event or the duration before paramedics were called. Secondly, the presence of co-existing factors, such as sepsis, renal failure, drug overdose or pre-existing small vessel disease exacerbates any HIBI. Thirdly, the use of sedation, ventilation, hypothermia, neuromuscular blockade and haemodynamic management have rendered the traditional clinical studies of prognosis of less value. Finally, the patient may be unduly susceptible to the effects of hypoxia and ischaemia as a consequence of underlying factors such as peripheral vascular disease, cerebral vascular disease,
embolic source or haematological factors causing thrombophilia.

It is important to recognize that hypoxia and ischaemia are pathologically and clinically distinct patterns of brain injury although they usually coexist.12 Hypoxia refers to a reduction of either oxygen supply or utilization, which develops as a direct consequence of reduced oxygen supply, reduced ambient oxygen pO2, low haemoglobin or impaired tissue utilization following poisoning of the mitochondrial cytochrome enzymes. Ischaemia describes a reduction in blood supply leading to decreased oxygen delivery but, unlike hypoxia alone, there is also limited or no removal of damaging cellular metabolites which therefore accumulate (e.g. lactate, H+, glutamate) leading to severe brain injury.

Assessment of the severity of HIBI is critical in predicting outcome, which in turn guides management on the ICU. The role of ancillary investigations in guiding prognosis remains uncertain because the patterns of brain damage are variable and the significance of varying MRI and EEG appearances is not clearly understood. However, recent papers have suggested that investigation can add valuable information about the severity of the underlying HIBI.9,13–15 In particular, the MRI may show characteristic patterns depending on the severity of HIBI and the timing of imaging. EEG patterns may also suggest the possibility of a good outcome.16–19

In the present series we have retrospectively reviewed 39 patients with HIBI who were resuscitated, admitted to ITU and referred for MRI as part of the neurological assessment.

Methods

We undertook a retrospective review of patients admitted to intensive care between April 2005 and December 2009. These patients were referred for neurological assessment because of suspected hypoxic–ischaemic brain insults. All the patients were seen during their admission by one of the authors and each underwent clinical assessment, appropriate investigation and MR imaging. Twenty-two patients also underwent at least one EEG. The patients were identified from the records of those who underwent MRI scan during the study period. It is likely that some patients with HIBI would have either recovered consciousness or died before being referred for MRI.

We reviewed the case notes, imaging and EEG to determine the patterns of change seen and to correlate these with outcome. Outcome was categorized as death, severe residual disability (defined as profound cognitive impairment including persistent vegetative state or minimally area states or severe physical impairment) or good recovery with minimal disability.

Imaging details

All the patients underwent MRI scan after clinical assessment. The timing and protocol varied according to clinical need.

MRI sequences

All patients underwent MRI scanner under GA on a 1.5T Philips MRI scanner, Philips, Amsterdam. The sequences were axial T2-weighted scans, axial FLAIR, coronal T1 with or without contrast, diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) map and depending on clinical details magnetic resonance venography (MRV) and magnetic resonance angiography (MRA).

EEG

Video EEG recordings were performed in a subset of the study population as part of their clinical assessment by the attending anaesthesiologists and neurologists. All video EEGs were recorded bedside in a standard manner, using a Nihon-Kohden Neurofax EEG-1100 portable device (Nihon Kohden Corporation, Tokyo, Japan); Ag/AgCl electrodes were placed on scalp according to the International 10–20 system, linked ear-lobe referenced (A1 and A2) and grounded over FPz, with additional electrodes monitoring ECG and surface EMG from the clinically relevant muscles. Electrode impedance was kept below 5 kΩ during recordings. Video from an analogue camera was synchronized with the EEG sampling, digitized, compressed and stored on computer. All recordings were of at least 30 min duration and, as part of the recording, repeated noxious, tactile, verbal and auditory stimuli were systematically delivered and the reaction of the patient to these was registered. Whenever applicable, administration of anaesthetic agents was discontinued shortly after the beginning of the recording to assess their effect on the EEG.

The EEGs were retrieved from the database of the Department of Clinical Neurophysiology and reviewed by two of the authors (M.K. and I.T.) using the same software system used for the EEG acquisition, with any difference resolved by consensus. A predefined set of EEG parameters was registered during the review and used in data analysis. The primary EEG grading was performed using a modification20 of the original Hockaday scale (HS).21 According to the modified HS the EEG was classified.
into five grades as defined by the presence of dominant normal $\alpha$-activity with or without $\theta$- and $\delta$-activity (Grade I), dominant $\theta$- and $\delta$-activity with detectable normal $\alpha$-activity (Grade II), $\theta$- and $\delta$-activity without $\alpha$-activity (Grade III), $\delta$-activity of low voltage with the possibility of short isoelectric intervals (Grade IVa), dominant, monomorphic, non-reactive $\alpha$-activity (Grade IVb), periodic generalized phenomena with a very low voltage background activity (Grade IVc) and flat to isoelectric EEG with voltage below 20 $\mu$V (Grade V). In addition to the presence or absence of reactivity and spontaneous fluctuations the EEGs also were specifically assessed for characteristic patterns such as periodic lateralized epileptiform discharges (PLEDs), bilateral PLEDs (BiPLEDs), periodic generalized epileptiform discharges (PGEDs), burst-suppression (BS), triphasic waves (TWs) and intermittent rhythmic $\delta$-activity (IRDA). Particular notice was made of seizure activity and changes compatible with non-convulsive status epilepticus. All EEGs were reviewed without knowledge of the clinical outcome or the results of imaging studies.

Data analysis

All EEGs were reviewed, but for subjects who had more than one EEG performed, only data from the first test were used for analysis. The association between selected EEG characteristics and the clinical outcome was assessed by Fisher’s exact test with $P = 0.05$ as the significance level. For the statistical analysis, the EEG grades obtained using the modified HS scale were merged into two categories, one including Grades I, II, III and the other Grades IV and V. Analysis was performed using Stata for Windows (Stata Intercooled 9.2© Stata Corp.).

Results

Thirty-nine patients who had been admitted to ITU >57 months were referred for neurological assessment of presumed HIBI.

There were 27 males and 12 females with a mean age (SD) of 51.7 years [18–80 years (19.0)]. The mean age in the female group was younger [44.1 years (21.4)] than the males [55.0 years (17.7)]. Eighteen patients were below the age of 50 years and seven were above 70 years.

Many patients were admitted with a known HIBI but, in others, this was only suspected when they were found to be poorly responsive as sedation was weaned.

The underlying cause of HIBI in the 39 patients is shown in Table 1.

### Table 1  Cause of HIBI

<table>
<thead>
<tr>
<th>Cause of HIBI</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>OOHCA</td>
<td>12</td>
</tr>
<tr>
<td>Hypoperfusion associated with surgery</td>
<td>11</td>
</tr>
<tr>
<td>Hypoperfusion associated with sepsis</td>
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<td>Hypoperfusion associated with metabolic encephalopathy</td>
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<tr>
<td>Hypoperfusion associated with trauma</td>
<td>1</td>
</tr>
<tr>
<td>Hanging/CO exposure</td>
<td>2</td>
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</tbody>
</table>

OOHCA, out-of-hospital cardiac arrest.

The history of the precipitating event was often difficult to obtain with certainty and in many critically ill patients multiple factors co-exist. None of the patients underwent hypothermia. This is because hypothermia was restricted to patients who sustained a cardiac arrest due to ventricular fibrillation and all the patients in the series had out-of-hospital asystolic arrests.

Six patients with hypoperfusion following surgery developed cardiogenic shock or had in-hospital cardiac arrest in the perioperative period. However, in the remaining five patients the hypoxic insult arose following prolonged surgery but without clear documentation of a single hypotensive event. Patients with septic or metabolic encephalopathy often had multiple insults associated with septic shock and multi-organ failure leading to an unsuspected reduction in cerebral perfusion. The presence of unsuspected HIBI was diagnosed retrospectively on clinical grounds because the patient failed to regain consciousness in an expected manner. However, the diagnosis was also suggested by characteristic MRI appearances based on previous studies.

When it became clear, on the basis of established clinical criteria, there was no prospect of any meaningful recovery treatment limitation orders were applied in the majority of patients who subsequently died.

Imaging findings

MRI was undertaken in all 39 patients. The time between the HIBI and the imaging of varied between 1 and 150 days. In 18 patients, imaging was undertaken within 5 days of the acute insult and a further eight between 6 and 10 days.

Several characteristic patterns of change were seen on MRI.
Cortical and deep grey matter change
The commonest MRI pattern in this series was the presence of change in both cortical and deep grey matter territory. This was seen in 16 patients. The distribution and pattern of involvement of the cortex, basal ganglia, thalamus and cerebellum varied and this is likely to be due to severity of the initial insult and the timing of the imaging.

In those patients in whom imaging was undertaken within 6 days, there was a consistent pattern of restricted diffusion on DWI and ADC with high signal change on T2 and FLAIR (Figure 1). In the cortex, the changes were mainly seen in the peri-rolandic and parieto-occipital areas and in the deep grey matter, caudate, putamen and globus pallidus and also in the thalamus. Cerebellar involvement was common. In later scans, deep white matter involvement was also seen as a late post-HIBI leuкоencephalopathy. Restricted diffusion was also seen throughout the deep grey matter structures including the lentiform and caudate nuclei and, less frequently, the thalamus. When imaging was undertaken 6 days or later after the HIBI, restricted diffusion was not seen in the deep grey matter but continued to be prominent in the cortical territories, rarely normalizing before 20 days.

Cortical change with little or no deep grey matter change
In seven patients, T2 imaging showed extensive cortical change with hyperintense foci in a parasagittal or superficial cortical distribution, particularly in the occipital, peri-rolandic and cerebellar territories (Figure 2). There was also extensive change in a

Figure 1. T2 (a) and FLAIR (b) MRI scans showing high T2 signal in caudate, putamen and occipital cortex.

Figure 2. T2-weighted MRI showing high signal throughout the cortex but this is more prominently seen in the occipital and peri-rolandic cortex, with relatively less conspicuous change in the deep grey matter.
watershed distribution in the anterior, posterior and tri-vessel territory. The cerebellum was frequently involved. Restricted diffusion corresponding to the T2 changes was prominent in six patients in whom imaging was undertaken up to 12 days after the acute insult (Figures 3 and 4) and was seen in one patient with hypereosinophilic syndrome 30 days after the hypotensive event. In most patients, extensive cortical or watershed change was clearly associated with HIBI but in several patients the occurrence of multiple emboli in a watershed distribution could not be excluded.

Figure 3. ADC (a) and DWI (b) showing restricted diffusion most prominently seen in the posterior parietal and occipital cortex.

Figure 4. ADC (a) and DWI (b) showing restricted diffusion in the occipital cortex.
Deep grey matter nuclei with little or no cortical change
In seven patients, imaging changes were seen in the deep grey matter but were not present in the cortex (Figure 5). In four, imaging was undertaken within 5 days of the onset and in each of these patients, there was striking T2 change in the caudate nucleus, putamen and thalamus but restricted diffusion was only seen in one patient. In those patients in whom imaging was undertaken later than 10 days, there was extensive T2 high signal in the caudate, lenticuliform nuclei and occipital cortex but no residual restricted diffusion.

Multiple emboli
The cause of brain injury was not always certain but in four patients the distribution of MRI change suggested multiple infarction due to presumed emboli. The mechanism was different in each patient but the distribution of infarction on both DWI and T2 was predominantly in watershed territories. In each patient, there was evidence of multiple areas of discreetly impaired perfusion or focal T2 hyperintensity suggesting contemporaneous emboli rather than hypoperfusion.

Other patterns
Several other patterns were seen on imaging suggesting different mechanisms of HIBI.
In one patient, MRI was normal following an out-of-hospital arrest. He made a full recovery because effective resuscitation was instituted immediately by trained bystanders, presumably, limiting the extent of cerebral damage. In a patient with hypoxia related to metabolic encephalopathy (cerebral lupus), MRI showed posterior reversible leucoencephalopathy, which resolved >2 weeks. In another patient, imaging undertaken after a prolonged period on ICU, following a severe hypotensive insult due to septic shock, showed long-established changes of bilateral occipital, parietal and parasagittal gliosis with periventricular white matter changes. Finally, a 28-year-old woman who sustained a severe HIBI as a result of smoke and carbon monoxide inhalation in a domestic fire, extensive white matter change was seen in a scan undertaken 10 days after the event. There was high signal on T2 and restricted diffusion throughout the deep white matter, predominantly posteriorly. T2 changes were also present in the basal ganglia and cerebellar hemispheres but there was no associated DWI change suggesting post-hypoxic leucencephalopathy rather than HIBI.

Table 2 shows the pattern of imaging change and the aetiology. Extensive cortical and deep grey

![Figure 5. FLAIR MRI showing high signal in the deep grey structures.](https://academic.oup.com/qjmed/article-abstract/105/6/551/1561295/03March2019)

<table>
<thead>
<tr>
<th>Imaging appearance</th>
<th>OOHCA</th>
<th>Post-operative</th>
<th>Sepsis</th>
<th>Metabolic</th>
<th>Others</th>
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<tr>
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<td>1</td>
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<tr>
<td>Deep grey matter nuclei with little or no cortical change</td>
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<td>2</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Multiple emboli</td>
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<td>1</td>
<td></td>
<td>1</td>
<td></td>
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<tr>
<td>Total</td>
<td>12</td>
<td>11</td>
<td>7</td>
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</table>

OOHCA, out-of-hospital cardiac arrest.
matter change were seen in 9 of 12 patients following out-of-hospital cardiac arrest, but in patients with other causes of HIBI, the imaging changes were variable.

**Outcome**

*Correlation of aetiology with outcome*

The outcome for these patients was poor regardless of the underlying aetiology (Table 3). Twenty-nine patients died without being discharged, 13 of these died while still on the ITU and a further 16 patients died despite having been weaned from ventilatory support, extubated and discharged to the ward. Of the 10 patients who survived, 5 were left in either a persistent vegetative state or a minimally conscious state. Five had only mild or no cognitive impairment, of the latter group one had a T4 paraplegia and one remained on ventilatory support. In each of the three patients who made a complete recovery, there was considerable uncertainty about the nature and severity of the initial HIBI.

*Correlation of imaging appearances with outcome*

The outcome was poor for most patients regardless of the aetiology or imaging appearances. All the patients in whom there was extensive cortical involvement, whether or not the deep grey matter structures were involved, did very poorly. A good outcome was only seen if there was isolated deep grey matter involvement or minimal change (Table 4).

**Early imaging**

Imaging was undertaken within 5 days in 21 patients. In 14 of these patients, there were extensive changes in the cortex and basal ganglia. In 11 patients, there was severely restricted diffusion but also extensive high signal on T2 and FLAIR imaging. In the three patients in whom imaging was undertaken 5 days after the insult, there was a consistent pattern of high signal in the deep grey matter and cortex on T2 and FLAIR with restricted diffusion in the cortex but apparently normal diffusion in the deep grey matter (pseudo-normalization). Three of these patients survived but each was profoundly impaired. In three patients, changes were restricted to the basal ganglia without evidence of cortical involvement but there was restricted diffusion in only one of these patients. The remaining two patients survived and one made a good recovery. Two patients showed a pattern of multiple emboli, one extensive white matter change in a watershed distribution and one generalized atrophy. Each of these patients died.

**Late imaging**

Imaging was undertaken later than 6 days in 18 patients. There was a much wider variation in the imaging appearances in this group.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Outcome according to aetiology</th>
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<tr>
<td>Cause</td>
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<tr>
<td>Out-of-hospital arrest</td>
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<tr>
<td>HIBI associated with surgery</td>
<td>11</td>
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<td>HIBI associated with trauma</td>
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<td>Hanging/CO exposure</td>
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<td>Total</td>
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</tr>
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</table>

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Outcome according to imaging characteristics</th>
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</thead>
<tbody>
<tr>
<td>Imaging appearance</td>
<td>Total</td>
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<tr>
<td>Cortical change</td>
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<tr>
<td>Cortical and deep grey matter change</td>
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<tr>
<td>Deep grey matter nuclei with little or no cortical change</td>
<td>7</td>
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<tr>
<td>Multiple emboli</td>
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<tr>
<td>Other patterns</td>
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</tr>
<tr>
<td>Total</td>
<td>39</td>
</tr>
</tbody>
</table>
In two patients, there were T2 and FLAIR changes in the basal ganglia and cortex but in both patients diffusion had normalized in the basal ganglia. In four patients, there were isolated T2 changes in the basal ganglia and deep grey matter alone with no associated restriction of diffusion. One of these patients made a good recovery and one patient survived with severe disability. Two patients showed imaging evidence of multiple emboli following cardiac surgery and cardiogenic shock, one patient survived with severe disability.

Six patients showed exclusively cortical change with involvement of the watershed territories and also peri-rolandic cortex. In five of these patients, there was restricted diffusion in the same regions even in scans undertaken up to 30 days after the insult. This latter patient survived but with severe disability.

One patient who survived with a good outcome had a normal MRI scan undertaken 1 day after collapse from an out-of-hospital arrest.

**Good outcome**

Three patients had a good outcome and were able to leave hospital with minimal impairment. Two patients, who were rapidly resuscitated from out-of-hospital cardiac arrests, had either, a normal MRI or imaging showing isolated T2 changes in the basal ganglia up to a month after the event. The remaining patient had a prolonged episode of septic encephalopathy associated with an in-hospital cardiac arrest. He was slow to wean. Bang imaging at one day showed limited T2 high signal in the basal ganglia, which may have been long-standing, but there was no restricted diffusion.

**EEG**

EEG was performed on a mean range (SD) of 5 days after admission to ICU [2–14 (3)] and was generally preceded by imaging studies, as it was on average performed 1 day after CT (±3) and 2 days (±7) after MRI. The majority of EEGs were classified into Grades II (6), III (6) and IVc (6). A single patient had a normal EEG.

Among EEG features assessed, the EEG reactivity to external stimuli (P=0.039) and the presence of spontaneous fluctuations in the EEG (P=0.003) were significantly associated with a favourable outcome on hospital discharge. Assessment of specific EEG patterns showed a significant association of PGEDs with an unfavourable outcome on hospital discharge (P=0.037). Classification into HS Grades IV and V was significantly associated with an unfavourable outcome (P=0.012).

**Discussion**

Clinical assessment of patients with HIBI is difficult and often depends on the support of ancillary investigations to guide prognosis and management. In the present series, we have assessed the role of imaging and EEG in predicting outcome. Although we present a heterogeneous population it is an accurate reflection of clinical practice for a neurologist on a general ITU.

MRI is infrequently undertaken following HIBI because patients may require sedation, ventilation and airway protection and often, in the UK, because it is not available. However, MRI may be particularly helpful in showing important information about the extent of cerebral damage. A number of studies report imaging appearances following cardiac arrest but few describe other mechanisms of HIBI as are discussed in the present report.

There is a greater vulnerability of grey matter to ischaemia and hypoxia. This primarily affects the basal ganglia, thalamus, cerebral cortex (in particular the sensorimotor and visual cortices), cerebellum and hippocampus. The grey matter is preferentially affected because it is metabolically more active than white matter as it contains a large number of synapses, which are vulnerable to HIBI, which leads to glutamate excitotoxicity.

The imaging findings depend on the aetiology of HIBI, the severity of the event (i.e. the circumstances and the effectiveness of resuscitation), the relative component of ischaemia and hypoxia, the duration of the event, the underlying brain and the presence of co-morbidities.

The sequence of brain damage which occurs after HIBI is characterized by brain swelling, cortical laminar necrosis, hypersignal in the basal ganglia, delayed white matter degeneration and atrophy. It is suggested that the MRI findings in HIBI follow corresponding phases: acute (<24 h after insult), early subacute (1–13 days), late subacute (14–20 days), chronic (>21 days). However, the present series suggests this view of sequential change is simplistic and potentially misleading as different patterns may be seen at varying intervals after the HIBI.

In the acute stages (first few days) after severe HIBI, diffusion-weighted images show widespread hyperintensity initially involving the basal ganglia, caudate, striatum and thalamus with similar changes developing in the cortex (particularly peri-rolandic and occipital) cerebellum and hippocampus and, occasionally, subcortical white matter. In the present series, similar changes were seen following cardiac arrest, prolonged hypotension and primary hypoxic insults. It is previously reported that, in the acute stages, T2-weighted imaging is normal;
However, in the present series established changes on T2 and FLAIR sequences were seen much sooner after HIBI than previously described with high signal being present within 3 days of the event.

The early appearance of diffusely abnormal findings on DWI and fluid-attenuated inversion recovery correlate with a poor outcome and the use of ADC mapping adds greater precision with severe reduction in whole-brain ADC predicting a poor outcome. In the present series, extensive early change on DWI and ADC was also associated with a poor prognosis.

In the subacute phase (7–20 days), there is progressive resolution of brain oedema with disappearance of DWI hyperintensity (pseudo-normalization). However, extensive grey matter change affecting basal ganglia, cortical and hippocampal grey matter change is seen in FLAIR and T2-weighted images and white matter hyperintensity may also develop. In the present series, restricted diffusion on DWI and ADC were generally present in both cortical territories and deep grey matter on early imaging, but there was apparent normalization of diffusion in the basal ganglia within the first 6 days while changes persisted in the cortex for much longer, being prominent in six patients in whom imaging was undertaken up to 12 days after the acute insult and in one with hyper-eosinophilic syndrome, 30 days after the hypotensive event. It has been suggested that white matter change occurs early (<6 days) with restricted DWI lesions being prominent throughout the white matter in the periventricular region, the corpus callosum and the internal capsule. This was not noted in the present series.

In the chronic phase, there is diffuse atrophy. T1 and T2 sequences may show cortical laminar necrosis (i.e. cell death involving layers III and IV of the cortical mantle). Lesions were also seen in hippocampus and basal ganglia. In the present series, extensive diffuse gliosis and cortical change were seen in the one patient in whom late imaging was undertaken.

Border zone infarction is particularly associated with hypotension, often due to prolonged cardiac bypass, but it may also occur with multiple emboli, particularly after aortic procedures. Although the characteristic imaging appearances of border zone infarction may be seen after cardiac arrest, it is relatively unusual. The distribution and severity of border zone infarction is determined by the extent of the hypoxic–ischaemic insult and the underlying atheromatous involvement of the carotid and cerebral vessels; for example, unilateral watershed infarction may develop with severe stenosis or occlusion of an internal carotid artery. Characteristic clinical syndromes may occur if the hypoperfusion is reversed before extensive hemispheric infarction evolves. In the present series, border zone infarction could occur in isolation, in association with extensive cortical involvement or with involvement of the deep grey matter. These patterns reflect the severity of the initial insult and extensive change was associated with a poor outcome.

This study strongly suggests that attempts to present a uniform sequence of MRI imaging changes following HIBI are unreliable because of the great variability. The presence of PGEDs and classification into Grades IV and V of the modified HS were inversely significantly associated with an unfavourable outcome. The EEG has been widely used over many years to assess the level of consciousness and to guide prognosis after HIBI. The appearances are influenced by confounding factors (including medication, metabolic derangements and sepsis) that bear upon the level of arousal, duration of coma and interval between resuscitation and EEG recording. In the initial stages following resuscitation, there may be electrical silence, but distinct rhythms may gradually evolve which guide prognosis.

A number of patterns suggest a poor prognosis. These include: generalized electrical suppression or burst suppression; unresponsive α-, θ- or δ-rhythms; periodic patterns (periodic lateralized, bilateral or synchronous epileptiform discharges); the presence of electrocerebral silence or generalized voltage suppression below 10 μV for >24 h in normothermic patients who are free of toxic ingestion or pharmacological sedation is the only reliable indicator that there is no chance of meaningful recovery.

The study showed a significant association between reactivity and spontaneous fluctuations in the EEG and a favourable outcome on hospital discharge. The presence of PGEDs and classification into Grades IV and V of the modified HS were conversely significantly associated with an unfavourable outcome. Due to the small number of subjects, the results of EEG analysis should be interpreted with caution.
This is particularly true with regard to the lack of association between specific EEG patterns and the outcome. However, the results of the study seem to confirm previous reports concerning the prognostic value of the HS and the significance of reactivity and spontaneous fluctuations in the EEG in assisting prognosis.

A larger study would allow not only a better interpretation of EEG findings for prognosis, but also a correlation of EEG characteristics to the results of imaging studies and clinical parameters with the purpose of establishing more valid markers to assist clinical decision making for this important and resource demanding patient population.

There are a number of limitations with this retrospective, observational study. First, in those patients with out-of-hospital cardiac arrest, the history was often fragmentated and it was difficult to establish the timing and effectiveness of resuscitation, the underlying rhythm of the arrest and the duration before paramedics arrive. Secondly, a number of factors complicate the assessment of patients who have hypotensive insults during cardiac surgery. In many cases, surgery is undertaken with acute indications, often when there is significant myocardial dysfunction and widespread vascular disease. Similarly, the timing and recognition of HIBI following sepsis or metabolic encephalopathy is often difficult. Thirdly, the timing of imaging and EEG were highly variable. In practical terms, it would be almost impossible to establish a rigid proactive protocol allowing imaging and EEG to be undertaken a set time after HIBI. The practical difficulties of clinical care, co-existing factors preventing the transfer of patients, such as sepsis and haemodynamic instability would mitigate against a formalized prospective study.

Importantly, we must be concerned to ensure that definitive comments concerning the importance of individual or combinations of prognostic features do not become ‘self-fulfilling’ prophesies. Decisions concerning the escalation of support in these patients are necessarily driven clinical assessment supported by ancillary investigations. However, in patients for whom a poor prognosis is suggested, it is important to recognize differences in outcome that will depend on multiple factors relating to the underlying state of the patient, the severity of the insult, resuscitation and the acute management, the mechanism of transfer and the ITU care. These can never be entirely correlated even with the most complex multivariate analysis. In clinical practice, this means that great care and caution must be exercised before a poor prognosis is delivered by the attending neurological team.

Finally, studying a heterogeneous group of patients with varying underlying aetiology may make it difficult to recognize unifying factors relevant to individual conditions but it does accurately reflect clinical practice.

The findings suggest that ancillary investigations play an important role in the assessment and have traditionally been underused. In particular, MRI and EEG provide detailed, accurate and reliable information about the distribution and severity of HIBI.

Conflict of interest: None declared.

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