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CRITICAL CARE

Liver function test abnormalities after traumatic brain injury: is hepato-biliary ultrasound a sensitive diagnostic tool?

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Editor's key points

- Abnormal liver function test results are common among intensive care unit patients with traumatic brain injury.
- This often occurs in the absence of any pre-existing liver dysfunction.
- Hepato-biliary ultrasound scans are frequently requested to exclude treatable causes.
- The authors assessed the diagnostic yield of scans performed for this reason.

Background. This study was to evaluate the usefulness of hepato-biliary ultrasound (HBUS) for the investigation of isolated liver function tests (LFTs) abnormalities.

Methods. We retrospectively reviewed HBUS reports in traumatic brain injury (TBI) patients admitted to our tertiary neuro-critical care unit (NCCU; January 2005–June 2011). We included patients receiving an HBUS for isolated LFTs derangement, excluding pre-existing hepato-biliary diseases or trauma. We assessed the temporal profile of alanine aminotransferase (ALT), bilirubin (Bil), and alkaline phosphatase (ALP).

Results. Of 511 patients, 58 received an HBUS. Of these, 47 were investigated for isolated LFTs derangement; HBUS always failed to identify a cause for these abnormalities. The HBUS was performed on day 18 (range 6–51) with the following mean values: 246 IU litre^{-1} [ALT, 95% confidence interval (CI) 183–308], 24 μmol litre^{-1} (Bil, 95% CI 8–40), and 329 IU litre^{-1} (ALP, 95% CI 267–390); only ALT (72, 95% CI 36–107) and ALP (73, 95% CI 65–81) were deranged from admission values (both $P<0.01$). At NCCU discharge, both ALT (160, 95% CI 118–202) and ALP (300, 95% CI 240–360) were higher than at admission ($P<0.01$). Compared with HBUS-day value, only ALT improved by NCCU discharge ($P<0.05$), while both were recovering by hospital discharge (ALT 83, 95% CI 59–107; ALP 216, 95% CI 181–251; $P<0.01$). At hospital discharge, ALP remained higher than at admission ($P<0.01$).

Conclusions. In TBI patients, HBUS did not appear sensitive in detecting causes for isolated LFT abnormalities. Both ALT and ALP worsened and gradually recovered. Their abnormalities did not prevent NCCU discharge. ALP recovered more slowly than ALT. TBI and its complications, critical illness, and pharmacological strategies may explain the LFTs derangement.

Keywords: critical care; imaging techniques; liver function; ultrasonography

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Patients in intensive care unit (ICU) receive daily blood tests and some abnormal results can be challenging to interpret in the context of deranged physiology and critical illness-induced alteration in pharmacodynamics. Derangement of liver function tests (LFTs) are commonly observed in critically ill patients admitted to ICU;[1] its significance in patients admitted with a primary diagnosis of traumatic brain injury (TBI) and without pre-existing risk factors has not been previously investigated.

A recent study[2] has shown a prevalence of LFT abnormalities on admission to ICU in up to 61% of the patients without pre-existing hepato-biliary disease (HBD). In critically ill patients, these abnormalities can be attributed to multiple factors, such as hepatic ischaemia,[3 4] sepsis,[5] drugs,[6] and artificial nutrition.[7] Even though Thomson and colleagues[2] showed an association of abnormal LFTs with mortality outcomes and clinical events on ICU, this cannot be extrapolated for patients with TBI. In patients with head injury, additional risk factors for LFT abnormalities include hypotension and splanchnic ischaemia, prolonged use of vasopressors–inotropes to sustain cerebral perfusion, and therapeutic agents such as ranitidine,[8] paracetamol,[9] antimicrobials,[10] and phenytoin.[10 11]

The hepato-biliary ultrasound (HBUS) scan is a safe, non-invasive bedside investigation considered as the first-line investigation to detect an obstructive HBD. While the resolution of HBUS is improving over the past decades, the incidence of false positives has not moved forward.[12] Reported sensitivity and specificity ranges of HBUS in detecting acute calculous cholecystitis are 48–100% and 64–100%, respectively.[13–15]

Even though maintaining high specificity (93–94%), the sensitivity of HBUS for detecting acalculous cholecystitis is reported in lower figures (29–50%) and ICU population is at high risk of developing this condition.[16–18]

In a recent study of patients admitted to ICU, almost half (47%) had at least one abnormal HBUS finding, but only one-third of the patients with abnormal bilirubin (Bil) and alkaline phosphatase (ALP) values had an abnormal HBUS.[19]

The aim of this study is to evaluate the usefulness of performing HBUS in ICU, and to add data to the growing body of literature of LFTs abnormalities in ICU. To the best of our knowledge, there is no reported data addressing the yield of HBUS in isolated abnormalities in LFTs in patients with TBI.

Methods

This study was performed after institutional audit department approval (Cambridge University Hospital NHS Foundation trust).

This retrospective study included patients admitted with diagnosis of TBI to our neuro-critical care unit (NCCU) in a tertiary level hospital, in the period between January 2005 and June 2011. We included in our analysis only those patients receiving an HBUS for isolated LFTs abnormalities (detected on daily routine investigations) during the NCCU stay. To capture patients with hepato-biliary injury due to critical illness, we excluded patients with suspected or proven hepato-biliary trauma and known chronic liver diseases.

At our institution, all the HBUS scans in ICU or NCCU are performed and reported by a radiologist, and reports are available and accessed through electronic records. The decision to investigate isolated LFTs derangement with HBUS scan was decided by the attending NCCU consultant in charge for the day. Over the period of study, there was no protocol for investigating LFTs abnormalities in our NCCU. Three authors (F.S., T.V., C.S.V.) independently screened each report looking for any abnormal finding, regardless of the relationship with the LFTs derangement.

The daily LFTs profile investigated in our unit includes: alanine aminotransferase (ALT, normal range 0–50 IU litre^{-1}), Bil (normal range 0–17 μmol litre^{-1}), and alkaline phosphatase (ALP, normal range 30–135 IU litre^{-1}).

In the population of study who underwent an HBUS, the temporal change of LFTs was investigated at admission, on the day of HBUS, on discharge from NCCU, and on the day of hospital discharge. We also recorded the peak values of each LFT, length of stay on the day of HBUS, and length of stay on the day of peak liver function abnormalities. In patients receiving more than one HBUS, we decided to consider only the length of stay and the LFTs values recorded on the day of the first HBUS.

To address the question of 'which LFT triggers a request of HBUS investigation', a subgroup analysis was performed, arbitrarily considering as triggers for requesting HBUS only values of ALT, Bil, or ALP $\geq$1.5 times their normal upper limit.

Statistical analysis

Statistical analyses were performed using IBM® SPSS® Statistics 17 for windows. The Kolmogorov–Smirnov test, histograms, and normal quartile plots were examined to test for the normality assumption of continuous variables. Continuous variables are presented as the mean and range or 95% confidence interval (95% CI), and categorical variables as number and percentage (%). The non-parametric Friedman test for related samples was performed for the analysis of the course of the LFTs. A Wilcoxon signed-rank test was then used to detect differences among a couple of samples. All tests were two-sided and a result of $P<0.05$ was considered statistically significant. All P-values are quoted after the Bonferroni corrections (where appropriate), and corrected P-values of <0.05 were considered significant.

Results

During the 66 months of this retrospective study, 511 patients were admitted with TBI and 58 of them (11.3%) were investigated with an HBUS (Fig. 1). In this cohort, 47 patients (81, 9.2% of all the TBIs) were included in the study as receiving HBUS for isolated LFTs derangement. One of them received three further HBUS investigations, with a total of 50 HBUSs in the population of study. Eleven patients, with a total of 12 HBUS scans, were excluded from the analysis because of traumatic injury to the liver ($n=4$) or for pre-existing liver diseases ($n=7$, one of them receiving a repeated HBUS). In Table 1 is shown the distribution of the HBUS performed over the period of study.

The mean age of the group analysed was 41 (range 20–73) yr, 64% were male, and the mean APACHE score on admission was 12 (range 3–30). The mean lengths of stay in NCCU and in hospital were, respectively, 29 (range 9–98) and 53 (9–230) days. Forty-five patients were discharged from hospital (95.7%).

The mean day for the HBUS investigation was 18 (range 6–51). Of the 50 HBUS scans investigating isolated LFTs derangement, no one revealed obstructive causes or suggested a rationale for the biochemical abnormality. In eight reports (16%), the radiologist reported that a limited vision was

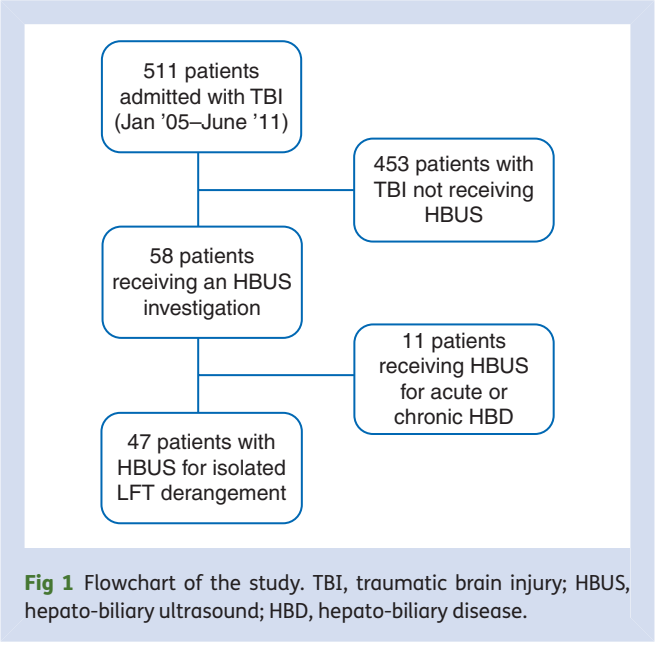

Fig 1 Flowchart of the study. TBI, traumatic brain injury; HBUS, hepato-biliary ultrasound; HBD, hepato-biliary disease.