BMJ Open

Use and diagnostic value of liver enzyme tests in the emergency department and subsequent heart failure diagnosis: a retrospective cohort study

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To cite: Vasti E, Tabas JA, Hoffman A, *et al*. Use and diagnostic value of liver enzyme tests in the emergency department and subsequent heart failure diagnosis: a retrospective cohort study. *BMJ Open* 2022;**12**:e055216. doi:10.1136/bmjopen-2021-055216

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2021-055216).

Received 06 July 2021
Accepted 04 February 2022

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ABSTRACT

Objectives To determine (1) if liver function tests (LFTs) are ordered in the emergency department (ED) in patients with suspected acute decompensated heart failure (ADHF) and (2) if the pattern of LFT abnormalities are meaningfully associated with a discharge diagnosis of ADHF among patients for whom these tests were ordered.

Setting We conducted a single-centre retrospective cohort study of patients with suspected ADHF who were seen in an academic tertiary ED using electronic medical records.

Participants All ED patients admitted with suspected ADHF from January 2017 to May 2018, defined as any patient who had a brain natriuretic peptide (BNP) ordered.

Primary outcome The primary outcome was ADHF diagnosis at discharge.

Results In 5323 ED patients with suspected ADHF, 60% (n=3184) had LFTs ordered; 34.6% were abnormal. Men comprised 56% of patients with abnormal LFTs and the average age was 67 years. The odds of a final diagnosis of ADHF in the univariate analysis was 59% higher in patients with abnormal LFTs (OR=1.59, (95% CI 1.35 to 1.87) p<0.001) and remained significant though attenuated after adjusting for BNP, race and ethnicity and age (ORadj=1.31 (95% CI 1.09 to 1.57), p=0.004). Likelihood ratios for abnormal and normal LFTs were 1.2 (95% CI 1.21 to 1.28) and 0.76 (95% CI 0.68 to 0.84), respectively.

Conclusions A significant proportion (40%) of patients with suspected ADHF was missing LFTs in their ED workup. Among patients with LFTs, abnormal LFTs are associated with discharge diagnosis of ADHF after accounting for potential confounders, but their diagnostic value was relatively low. Future prospective studies are warranted to explore the role of LFTs in the workup of ADHF.

Strengths and limitations of this study

- ► Liver biochemical tests (LFTs) are commonly ordered in the emergency department (ED); to our knowledge, this is the first study to evaluate the ordering behaviour of providers in the ED in patients with suspected acute decompensated heart failure (ADHF).
- ► The retrospective nature of our study permitted a cost-effective, efficient means of evaluating a major clinical query in a real-world setting to inform management of ED patients.
- ► This cohort analysis allowed for the inclusion of a large number of patients for increased generalisability.
- ► All retrospective study designs are subjected to possible selection biases related to missing data.
- ► Our retrospective study does not evaluate the predictive value of LFTs in terms of outcomes such as all-cause mortality but sets the framework for future investigation of this topic to avoid overuse of LFTs in ADHF in the ED.

INTRODUCTION

Heart Failure (HF) is a leading cause of cardiovascular mortality, affecting 5.7 million Americans over the age of 20 from 2009 to 2012[1]. Projections show that the prevalence of HF will increase by 46% from 2012 to 2030[2 3]. Despite newer treatments, mortality remains high[4–6] and disproportionately affect African Americans.[7 8]

Acute decompensated HF (ADHF) episodes lead to frequent emergency department (ED) visits among patients with HF. ADHF is defined as an exacerbation of underlying systolic or diastolic dysfunction resulting in severe volume overload or low cardiac output.Additionally, readmission rates for ADHF are striking, with studies suggesting that 30-day and 180-day readmission rates approach 20%–25% and 50%, respectively.[9 10] Although brain natriuretic peptide (BNP) has significantly improved the accuracy of ADHF diagnosis in the ED, patients are still misdiagnosed 10%–20% of the time.[11]

Liver function tests (LFTs) are commonly elevated in chronic HF[12] as a result of haemodynamic changes. However, LFTs have only

more recently been studied as a predictor of HF prognosis during hospitalisation for ADHF. The results of these studies have been varied with respect to individual LFT parameters,[13–19] but seem to suggest that elevated LFTs are associated with worse prognosis. All of these studies were conducted in patients with a confirmed diagnosis of ADHF, where baseline LFTs are obtained on admission. Although studies have explored LFT-ordering patterns among ED providers,[20–24] LFTs have not specifically been examined in an ED population with suspected ADHF.

HF is the most common and expensive reason for hospital admission for older Americans.[25] The American Heart Association's scientific statement on approaches to ADHF in the ED[26] recommends that LFTs should be considered in the work up of ADHF in select cases. The authors also emphasise that prior liver disease is an independent risk factor for worse mortality. However, surprisingly little research has been conducted in laboratory testing outside of routine BNP in patients with suspected ADHF in the ED and whether they offer additional diagnostic information. The lack of research in this area could lead to misuse of diagnostic tests, such as LFTs, and missed opportunities for early diagnosis in the ED.

Given the evidence for higher mortality in patients with ADHF and abnormal LFTs, it is necessary to assess if and how LFTs are used in the ED to inform the diagnosis of ADHF. Filling this gap in knowledge could potentially lead to an opportunity for earlier diagnosis, better resource utilisation of laboratory testing and better risk stratification of ADHF. Using LFTs as an adjunct to BNP may also improve triaging of patients from the ED to appropriate levels of care. On the other hand, it is well known that overuse of tests in the ED does not improve outcomes.[27] In general, very little is understood about how ED providers use LFTs in their workup of ADHF in the first place, despite a large body of inpatient literature to suggest that abnormal LFTs can have prognostic value. This study aims to (1) evaluate the ordering patterns of LFTs in the ED in patients with suspected ADHF (2) in patients with LFTs, determine whether LFTs in an abnormal range obtained in the ED are associated with a higher likelihood of subsequent discharge diagnosis of ADHF.

METHODS

We retrospectively identified all unique patient encounters seen in the ED at UCSF Medical Center between January 2017 and May 2018, and identified patients admitted to the hospital with suspected ADHF, defined as patients who had a BNP drawn in the ED. Among those patients, we analysed the association between LFT ordering behaviour and results, and the outcome of ADHF, defined by final discharge diagnosis.

Laboratory measurements

We extracted all measurements of BNP, alanine aminotransaminase (ALT), aspartate aminotransaminase (AST), alkaline phosphatase (AlkPhos), total bilirubin (TBili) and direct bilirubin (DBili) from the electronic health record between January 2017 and May 2018. Each LFT measurement was categorised into ranges representing normal, mild-moderate elevation and significant elevation (or missing completely). These ranges were ALT <34, =34–99, >100 mg/dL or missing, AST<34, =34–99, >100 mg/dL or missing, AlkPhos <123, =123–199, >200 mg/dL or missing and TBili <1.2, =1.2–2.0, >2.0 mg/dL or missing, and DBili was defined as DBili <0.3, =0.3–2.0, >2.0 mg/dL or missing. We also looked at a global LFT measurement, defined as abnormal if any of the LFT measurements were abnormal per patient encounter (ie, any LFT parameter fell into the mild-moderate or significantly elevated categories), missing if all LFT measurements were missing per patient encounter, or normal if all LFT measurements were normal per patient encounter. If patients had more than one LFT parameter measured per unique encounter, we selected the most elevated value per encounter for the analysis.

Other predictors

We examined other predictors including age at ED admission, race and ethnicity. Race and ethnicity were categorised as non-Hispanic Asian, non-Hispanic Black or African American, non-Hispanic white, non-Hispanic other identified race (which included Native American or other Pacific Islander, American Indian or Alaska Native or patients who identified as 'other race'), unknown or declined, or Hispanic, any race. BNP was categorised as high (>700 mg/dL), intermediate high (300–700 mg/dL), intermediate low (100–300 mg/dL) and low (<100 mg/dL).

Outcomes

Because the diagnosis of ADHF is a clinical diagnosis,[26] the final diagnosis given at discharge from the hospital was considered the 'gold standard'. We used any ADHF discharge diagnosis code (not just the first code) to define a final diagnosis of ADHF; see the online supplemental appendix for a listing of ICD-9 and ICD-10 codes we considered to indicate ADHF.[27]

Statistical analysis

Baseline characteristics are presented as mean±SD for continuous variables and as frequencies and percentages for categorical variables. A p value of <0.05 was considered statistically significant and no adjustment was made for multiple comparisons. The data were analysed with the use of commercially available statistical software (Stata, V.15).

To analyse the association between LFTs and ADHF, we first analysed percentage of patients with an ADHF diagnosis according to categories of LFTs (and BNP) measurements. We used χ^2 tests to evaluate these associations. We also calculated likelihood ratios (LRs) with 95% CIs for each category of each predictor.

We then performed logistic regression to estimate the odds of final ADHF diagnosis for abnormal LFTs and each LFT parameter individually. We used normal LFTs as a reference point and included missing LFTs as a separate group from abnormal LFTs. We then adjusted analyses for BNP, age at ED visit and race and ethnicity. We categorised BNP based on the *Breathing Not Properly* trial for the minimal cut-off of BNP 100 mg/dL. We further subdivided into high, intermediate high and intermediate low values of BNP to better assess granular changes in diagnostic accuracy of BNP as a covariate. Minimum values for LFTs were based on institution-specific cut-offs for upper limit of normal and further divided into intermediate values to capture granularity of the data. We felt that this was important to distinguish given that hypoperfusion secondary to low cardiac output causing 'shock liver' can cause extremely elevated LFTs, whereas congestive hepatopathy causes mainly mildly elevated TBili levels. We included previous medical history, which would most commonly present with dyspnoea as a chief complaint, such as Chronic Obstructive Pulmonary Disease (COPD). We stratified other ED diagnoses to include diagnoses of any liver pathology to distinguish patients who might have had liver enzyme elevations from another cause, such as hepatic abscess or acute inflammation. The authors (MP and EV) were responsible for all data cleaning, which was performed exclusively through Stata on the University of California, San Francisco (UCSF)-encrypted desktop.

PATIENT AND PUBLIC INVOLVEMENT

No patient involved.

RESULTS

LFTs were ordered in 60% of patients admitted from the ED with suspected ADHF (n=5323). Baseline characteristics are presented in table 1. We included previous medical history that would be most likely to present with a chief report of dyspnoea. Mean age was 71±16 years in patients with normal LFTs, 67±16 in patients with abnormal LFTs and 68±16 years in patients with missing LFTs. An ED diagnosis of ADHF for patients with normal, abnormal and missing LFTs was 8%, 15% and 13% of patients, respectively. At hospital discharge (obtained per patient encounter), 21% of patients with normal LFTs were diagnosed with ADHF, compared with 30% of patients with abnormal LFTs and 29% of patients with missing LFTs.

Prevalence of LFTs

For patients with suspected ADHF in the ED, LFTs were obtained in 60% of patients; 25% had normal LFTs and 35% had abnormal LFTs (40% were missing). Figure 1 demonstrates LFT-ordering behaviour across BNP subgroups and final diagnosis of ADHF. The likelihood of final diagnosis of ADHF among patients with abnormal LFTs was 1.8% for patients with missing BNP, 3.6% for patients with BNP <100 mg/dL, 15% for patients with BNP 100–300 mg/dL, 37% for patients with BNP 300–700 mg/dL and 54% for patients with BNP >700 mg/dL.

Likelihood ratios

Table 2 demonstrates positive and negative LRs for any abnormal LFT and individual LFT parameters. Positive and negative LRs for abnormal LFTs in patients with suspected ADHF were 1.20 and 0.76, respectively. The LRs were similar for ALT, AST, AlkPhos, TBili and DBili. The positive and negative LRs were stronger for BNP, with LR of 2.95, 1.42, 0.51 and 0.13 for BNP>700, 300–700, 100–300 and <100 mg/dL.

Univariate and multivariate logistic regression

Table 3 demonstrates final diagnosis of ADHF in patients with normal, abnormal and missing LFTs. In the univariate analysis, the odds of a final diagnosis of ADHF were 59% higher in patients with abnormal LFTs than those with normal LFTs (OR 1.59 (95% CI 95% CI 1.35 to 1.87) p=0.000). After adjusting for age, race and ethnicity and BNP, this association remained statistically significant (OR 1.31 (95% CI 1.09 to 1.57) p=0.004).

Individual LFT measurements were also associated with ADHF. For example, abnormal TBili was associated with higher odds (OR 1.41 (CI 1.26 to 1.62) p=0.000) after adjustment, and this was seen at both very high (TBili >2 mg/dL) and slightly elevated (TBili=1.2–2 mg/dL). Missing TBili was also positively associated with the final diagnosis of ADHF (OR 1.39 (CI 1.19 to 1.61), p=0.000). ORs for other individual LFT parameters are found in the Appendix (see online supplemental appendix tables 1–5).

We also conducted an interaction analysis by race and ethnicity variables. No statistically significant interactions were detected.

DISCUSSION

The diagnosis of ADHF in the ED is challenging. Dyspnoea is one of the most common chief complaints assigned to a patient in the ED, however, there is no one piece of history, physical examination, electrocardiographic or radiographic finding to confirm the diagnosis before hospitalisation.[28] Additionally, the final discharge diagnosis is discordant with the initial working diagnosis in the ED in almost 1 out of 4 cases[28]. LFTs are commonly found to be abnormal in patients with ADHF. Certain patterns, such as a small rise in TBili or minimal elevations in intrahepatic enzymes, can suggest congestive hepatopathy. However, extreme elevations of intrahepatic enzymes often suggest shock liver in the setting of hypoperfusion in cardiogenic shock.[16] The aim of this study was to conduct a real-world analysis of the LFT-ordering patterns of providers in the ED and to determine whether abnormal LFTs help to predict ADHF as a final outcome diagnosis. Our study revealed that LFTs are not ordered as part of the workup for a substantial proportion of patients with suspected ADHF in the ED (40%) . The odds of a final diagnosis

Table 1 Baseline characteristics of patients with suspected ADHF in the emergency department

Characteristic	LFTs—normal range N=1342	LFTs—abnormal range N=1842	LFTs—missing N=2139	P value*
Age at ED visit—mean in years±SD	71±16	67±16	68±16	<0.001
Sex identified—number (%)				
Male	633 (47%)	1036 (56%)	1113 (53%)	<0.001
Female	709 (53%)	806 (44%)	1026 (48%)	
Race and ethnicity—number (%)				
Non-Hispanic Asian	303 (23%)	459 (25%)	442 (21%)	<0.001
Non-Hispanic Black or African American	236 (18%)	375 (20%)	401 (19%)	
Non-Hispanic White	546 (41%)	658 (36%)	918 (43%)	
Hispanic, any race	134 (10%)	202 (11%)	181 (9%)	
Other	108 (8%)	132 (7%)	174 (8%)	
Unknown/declined to state	15 (1%)	16 (1%)	20 (1%)	
Insurance† number (%)				
Private	147 (11%)	274 (13%)	295 (14%)	<0.001
MediCal	218 (16%)	382 (21%)	367 (17%)	
Medicare	927 (69%)	1086 (59%)	1357 (64%)	
Other	49 (4%)	23 (1.3%)	117 (5%)	
Diuretics in the ED?				
Yes	250 (19%)	449 (24%)	483 (23%)	0.001
No	1092 (81%)	1393 (76%)	1656 (77%)	
BNP in the ED?				
High BNP (>700 mg/dL)	308 (23%)	636 (35%)	618 (29%)	<0.001
Intermediate high BNP (300–700 mg/dL)	278 (21%)	357 (19%)	441 (21%)	
Intermediate low BNP (100–300 mg/dL)	339 (25%)	376 (20%)	455 (21%)	
Low BNP (<100 mg/dL)	417 (31%)	473 (26%)	625 (29%)	
Past medical history				
History of asthma	251 (19%)	244 (13%)	379 (18%)	<0.001
History of COPD	345 (26%)	412 (22%)	580 (27%)	0.002
History of smoking	699 (52%)	928 (50%)	1129 (53%)	0.012
ED diagnosis‡				
ADHF	107 (8%)	274 (15%)	281 (13%)	<0.001
Pneumonia	175 (13%)	243 (13%)	330 (15%)	0.025
COPD exacerbation	124 (9%)	96 (5%)	235 (11%)	<0.001
Asthma exacerbation	27 (2%)	28 (2%)	68 (3%)	0.001
Acute upper respiratory infection	2 (0.2%)	1 (0.1%)	8 (0.4%)	0.028
Any liver pathology§	12 (1%)	107 (6%)	16 (1%)	<0.001
Final discharge diagnosis¶				
ADHF	283 (21%)	549 (30%)	622 (29%)	<0.001
Not ADHF	1059 (79%)	1293 (70%)	1517 (71%)	

*P values based on χ^2 analysis for categorical variables and ANOVA for continuous variables.
†Insurance is categorised as 'Private' (Aetna, Blue Cross, Blue Shield, GCSS/GHP, Capitation, Charity, Commercial, Covered California, Covered California – MediCal, HealthNet, Institutional, and Kaiser), 'MediCal' (Medicaid/MIA/CMSP, MediCal managed care, MediCal pending, MediCal standard) 'Medicare' (Medicare, Medicare Advantage HMO/Senior, Medicare Advantage PFFS) and 'Other' (Self-pay, United Health Care, Worker's compensation).
‡ED Diagnosis was obtained through specification of ICD10 codes for respiratory diagnoses and liver-related diseases.
§Any liver pathology includes ICD10 codes for the following: alcoholic liver disease, toxic liver disease, hepatic failure (not elsewhere specified), chronic hepatitis (not elsewhere specified), fibrosis and cirrhosis of liver, other inflammatory liver diseases, other diseases of the liver, liver disorders in diseases of the liver (classified elsewhere).
¶Final discharge diagnosis of ADHF is based on ICD10 codes for a diagnosis of heart failure named on the discharge summary for a patient's specific encounter.
**Suspected ADHF is defined as patients who had a BNP ordered in the ED.
ADHF, acute decompensated heart failure; ANOVA, analysis of variance; BNP, brain natriuretic peptide; COPD, Chronic Obstructive Pulmonary Disease; ED, emergency department; LFTs, liver function tests.

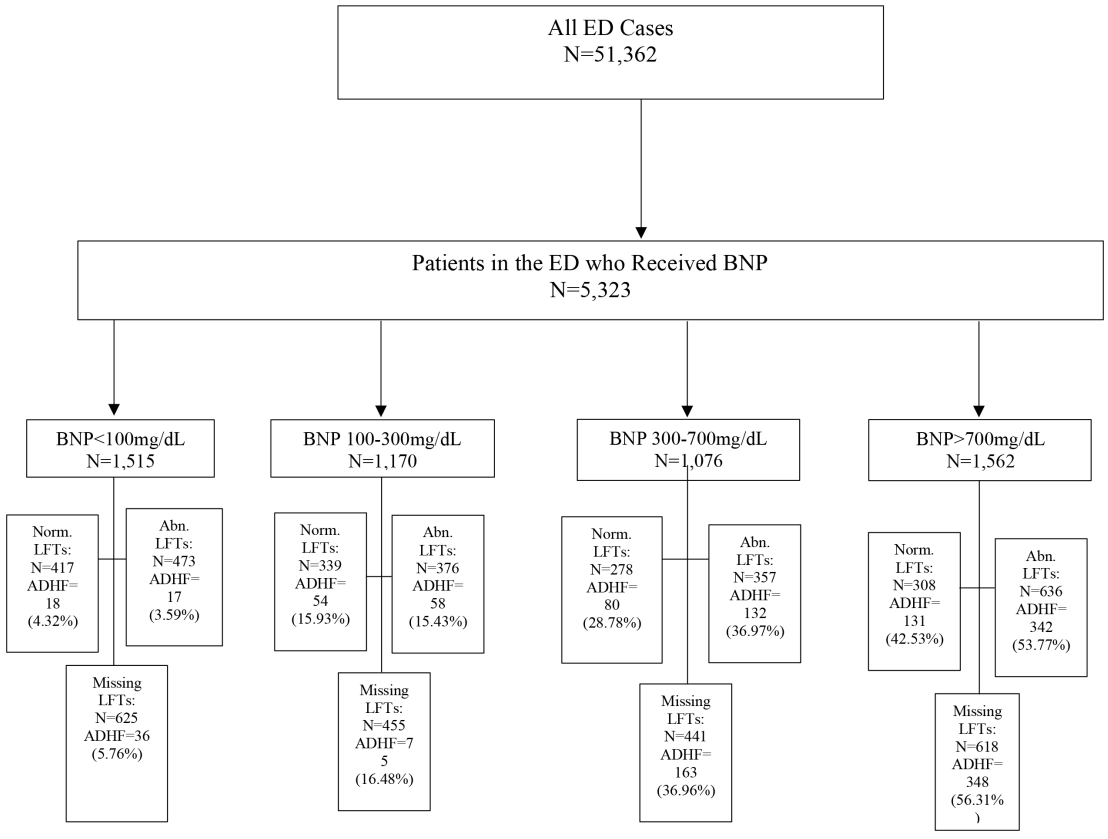

Figure 1 Classification tree. ADHF acute decompensated heart failure; ED, emergency department; BNP, brain natriuretic peptide; LFTs, liver function tests.

of ADHF were positively associated with abnormal LFTs and of the individual LFT measurements, TBili had the highest odds (OR 1.41). Positive LRs for abnormal LFTs, both composite and individual measurements, were in the range of 1.0–1.3 and, thus, unlikely to be of much value for diagnosis of ADHF. We did not detect interactions by demographically defined subgroups.

In an in-depth analysis of LFTs in suspected ADHF in the ED, our study makes several important observations that can inform future practice. First, a significant number of patients with suspected ADHF had missing LFTs at this large tertiary centre. A review[29] of the evaluation and management of ADHF in the ED indicates that testing should include LFTs, as these tests are found to be abnormal in approximately 75% of patients and are associated with worse mortality. The authors conclude that, in some ways, liver and renal function tests can be more helpful than even BNP, given their additional prognostic value. Even despite the American Heart Association (AHA's) scientific statement indicating that patients presenting with symptoms of ADHF should have LFTs considered, nearly 40% of patients in our study with suspected ADHF did not have LFTs ordered. Therefore, our study reveals a surprising and remarkable contrast to prior reviews and society guidelines. This could be for a number of reasons, including lack of prior liver disease in the medical history to prompt ED providers to obtain LFTs or that sufficient diagnostic information was obtained through clinical history, imaging or BNP alone. Regardless of the reason, our study importantly suggests that despite the association of abnormal LFTs to higher mortality in patients with ADHF, ED providers are not routinely ordering LFTs in this subset of patients.

Second, in our analysis of patients who had LFTs, we discovered a positive association between abnormal LFTs and the odds of final diagnosis of ADHF in patients with suspected ADHF. These results are comparable to several landmark HF trials, which examine prognosis in ADHF. The Acute Study of Clinical Effectiveness of Nesiritide in Decompensated Heart Failure trial (ASCEND-HF), the largest study to date to explore this question, evaluated the relationship of baseline LFTs to 30-day and 180-day mortality in patients admitted for ADHF. Similar to our study, only 59% of patients had baseline LFTs. Elevated TBili was associated with a 24% and 30% increase in 30-day and 180-day mortality, respectively.[30] The authors found no association with AST or ALT. Another study found that abnormal ALT and AST values, as well as low albumin, have been associated with a combined end point of mortality or rehospitalisation at 60 days.[18] Similarly, patients with ADHF had a high prevalence of abnormal LFTs at admission and was significantly associated with lower cardiac index and more elevated central venous pressures and Model for End-Stage Liver Disease - Excluding INR (MELD-XI) scores.[16] However, both studies of baseline LFTs were inadequately powered to

Table 2 LFTs, BNP and acute decompensated heart failure at discharge in ED patients with suspected ADHF (n=5323)

Characteristic	N	% with ADHF diagnosis at discharge	P value*	LR (95% CI)
LFTs				
Abnormal LFTs	1842	30	0.000	1.20 (1.13 to 1.28)
Normal LFTs	1342	21		0.76 (0.68 to 0.84)
Missing LFTs	2139	29		–
Alanine transaminase (ALT)				
ALT≥100 mg/dL	168	27	0.017	1.03 (0.74 to 1.44)
ALT 34–99 mg/dL	684	30		1.19 (1.03 to 1.37)
ALT<34 mg/dL	2310	25		0.95 (0.90 to 1.00)
Missing ALT	2161	29		–
Aspartate transaminase (AST)				
AST≥100 mg/dL	246	24	0.000	0.87 (0.66 to 1.16)
AST 34–99 mg/dL	1070	30		1.22 (1.10 to 1.35)
AST<34 mg/dL	1864	24		0.90 (0.84 to 0.97)
Missing AST	2143	29		–
Alkaline phosphate (AlkPhos)				
AlkPhos≥200 mg/dL	249	22	0.004	0.81 (0.60 to 1.08)
AlkPhos 123–199 mg/dL	420	31		1.26 (1.04 to 1.53)
AlkPhos<123 mg/dL	2451	26		0.98 (0.94 to 1.02)
Missing AlkPhos	2203	29		–
Total bilirubin				
Total bilirubin>2 mg/dL	323	32	0.000	1.32 (1.06 to 1.65)
Total bilirubin 1.2–2 mg/dL	501	36		1.59 (1.35 to 1.88)
Total bilirubin <1.2 mg/dL	2314	23		0.85 (0.81 to 0.90)
Missing total bilirubin	2185	29		–
Direct bilirubin				
Direct bilirubin >2 mg/dL	18	22	0.007	0.62 (0.22 to 1.75)
Direct bilirubin 0.3–2 mg/dL	48	48		1.99 (1.32 to 3.00)
Direct bilirubin <0.3 mg/dL	51	20		0.53 (0.30 to 0.93)
Missing direct bilirubin	5206	27		–
BNP				
High BNP (>700 mg/dL)	1562	53	0.000	2.95 (2.72 to 3.19)
Intermediate high BNP (300–700 mg/dL)	1076	35		1.42 (1.28 to 1.59)
Intermediate low BNP (100–300 mg/dL)	1170	16		0.51 (0.44 to 0.59)
Low BNP (<100 mg/dL)	1515	5		0.13 (0.10 to 0.17)

*P values are based on χ^2 test.
ADHF, acute decompensated heart failure; BNP, brain natriuretic peptide; ED, emergency department; LFTs, liver function tests.

perform a multivariable analysis and did not account for other factors such as BNP. In the ED setting, making the diagnosis of ADHF is crucial to expediting treatment and, thus, reducing length of hospital stay and mortality.[31]

Thus, to explore the true diagnostic value of these tests, we performed LRs, which showed that the diagnostic value of these associations was relatively limited after adjustment for age, race and ethnicity and BNP level, with LRs near 1.0. The LRs for BNP were strong: 2.95, 1.42, 0.51 and 0.13 for BNP >700, 300–700, 100–300 and <100 mg/dL. BNP and N-terminal pro-BNP have been shown to be effective in diagnosing ADHF because of their negative LRs, ranging from 0.1 to 0.14[28]. The LRs for BNP in our study were consistent with previous systematic reviews. To our knowledge, this is the first study to examine how LFTs predict ADHF in terms of LRs. The positive LR of 1.20 for abnormal LFTs and negative LR of 0.76 for normal LFTs that we found in our study are likely to have minimal

Table 3 Univariate and multivariate logistic regression analysis of high LFTs and final diagnosis of ADHF in patients with suspected ADHF in the ED (n=5323)

	Univariate analysis		Multivariate analysis*	
Characteristic	OR (95% CI)	P value	OR (95% CI)	P value
Abnormal LFTs	1.59 (1.35 to 1.87)	0.000	1.29 (1.08 to 1.55)	0.006
Missing LFTs	1.53 (1.31 to 1.80)	0.000	1.42 (1.19 to 1.71)	0.000
Normal LFTs	Reference	Reference	Reference	Reference
BNP†				
High BNP (>700 mg/dL)	22.53 (17.41 to 29.17)	0.000	22.53 (17.35 to 29.28)	0.000
Intermediate high BNP (300–700 mg/dL)	10.88 (8.31 to 14.24)	0.000	11.10 (8.45 to 14.60)	0.000
Intermediate low BNP (100–300 mg/dL)	3.87 (2.91 to 5.14)	0.000	4.00 (3.00 to 5.33)	0.000
Low BNP (100 mg/dL)	Reference	Reference	Reference	Reference
Race and ethnicity‡				
Non-Hispanic Asian			0.81 (0.65 to 1.01)	0.062
Non-Hispanic Black or African American			Reference	Reference
Non-Hispanic White			0.93 (0.77 to 1.12)	0.438
Other, Non-Hispanic			1.06 (0.80 to 1.41)	0.695
Hispanic, any race			0.97 (0.74 to 1.26)	0.809
Unknown/declined to state			0.52 (0.21 to 1.25)	0.144
Age at ED visit, per year			1.00 (0.99 to 1.00)	0.395
Male sex			1.21 (1.06 to 1.39)	0.006

*Multivariate analysis adjusted for BNP, age at ED visit, race and ethnicity.
†BNP in the multivariate analysis reflects analysis of high LFTs, race and ethnicity and age at ED visit.
‡Univariate analyses of 'Race and ethnicity' and 'Age at ED visit' were not performed.
ADHF, acute decompensated heart failure; BNP, brain natriuretic peptide; ED, emergency department; LFTs, liver function tests.

diagnostic impact, especially when compared with the LRs for BNP.

In an era where value-based care is a major priority across hospital systems, it is important to critically assess the value of testing in the ED prior to admission. Studies such as the Reducing Unnecessary Coagulation Testing in the Emergency Department (REDUCED) trial[22] have examined the effects of uncoupling coagulation tests in the ED and found that implementing systemic changes to the order panel resulted in fewer tests ordered without a negative effect on patient outcomes. However, a clinical review[23] of the management of elevated LFTs in the ED suggested that severely elevated LFTs suggest injury secondary to cardiorenal syndrome and should prompt physicians to evaluate for ADHF. Although we found that the diagnostic utility of abnormal LFTs was relatively low, a significant proportion of patients with suspected ADHF did not have LFTs ordered. This might have impacted the diagnostic value of abnormal LFT findings in the ED setting. The presence or absence of a lab test itself has been shown in prior studies to be predictive of survival. In an analysis of all tests ordered between 2005 and 2006 at two hospitals, researchers found that the presence of a lab test order itself was significantly associated with the odds of survival in more than 80% of lab tests, regardless of specific information related to the lab test itself.[32] This relates to our study in its key finding: the predictive value of healthcare process variables (guidelines, hospital metrics, the culture of how providers order tests at their institutions) might be more predictive of survival than the results of those tests themselves. We should undeniably strive to reduce unnecessary resource utilisation in the ED. However, in ADHF, the high degree of mortality and costs related to advanced diagnostics such as echocardiogram renders further investigation of initial LFTs in the ED to inform guideline-directed practice. The use of LFTs in the ED for patients admitted with ADHF may serve as an important baseline for a patient's trajectory during their hospitalisation. Given that abnormal LFTs are associated with worse mortality in ADHF during hospitalisation, obtaining these tests prior to any intervention in the ED can further inform prognosis after receiving treatment. Prospective studies must be conducted to evaluate which patients would benefit from LFTs in terms of earlier diagnosis and risk stratification.

Our study has several limitations. First, this was a retrospective analysis of ED patients at a single site, which are susceptible to inherent limitations in data collection and study design. Additionally, our study used data from a single tertiary clinical medical centre, which may not be generalisable to other EDs in other academic or community settings. We do not have baseline LFTs for this group of patients, so it is possible that patients with chronic HF had pre-existing abnormal LFTs. We also did not

have baseline renal function for patients in our data set, which represents a group where BNP might be elevated in the absence of overt HF. However, the intention of our analysis was to capture real-world ED setting, where this information might not always be accessible. We did not systematically obtain LFTs for all potentially eligible patients, and a substantial number of patients did not have LFTs obtained in the ED. Patients with missing LFTs had higher odds of final ADHF diagnosis at discharge, similar to patients with abnormal LFTs. A plausible explanation for this finding is that ED clinicians were less likely to order LFTs if they had a high degree of certainty that a patient was presenting with ADHF. This finding makes it difficult to interpret the outcome in patients with missing LFTs, because these patients potentially might have had abnormal LFTs if the tests were obtained. [33]However, other studies, such as Acute Decompensated Heart Failure Registry Emergency Module (ADHERE-EM), had similar proportions LFTs to our study. This finding in itself is interesting in that it suggests that providers may have been relying more heavily on other forms of diagnostic testing, such as echocardiogram, when LFTs might have given a more cost-effective insight into volume status or effective circulating volume. An important study done by Vyskocilova *et al* examined a large repository of patients with ADHF across nine university hospitals and five regional healthcare facilities in the Czech Republic. They found that abnormal LFTs were found in 76% of patients with ADHF and patients with cardiogenic shock were more likely to have abnormal LFTs than those with mild ADHF or pulmonary oedema.[34] They found that abnormal LFTs were highly suggestive of more severe ADHF and reflected worse New York Heart Association (NYHA) class. They argued that it is crucial to assess LFTs in the initial diagnostic investigation of ADHF as it informs management and stratifies patients based on severity. Although patients with missing LFTs were similarly diagnosed with ADHF to those with abnormal LFTs, it is possible that LFTs performed in the ED would have facilitated any additional workup performed after admission.

On the other hand, our study has important strengths, especially in contrast to prior analyses. First, we studied a large sample of patients seen in the ED prior to admission, where an initial suspicion for ADHF is most crucial to guide early evidence-based diagnosis and management. For these reasons, the study is generalisable to patients presenting to the ED with similar reports and available lab tests. Second, our study was powered to adjust for BNP, which is known to be a strong predictor of ADHF. Third, our study estimated LRs, a key step in translating diagnostic test findings to clinical practice.

Our real-world analysis of patients admitted from the ED with suspected ADHF found that LFTs were not ordered for 40% of patients. Among patients who had LFTs ordered, abnormal LFTs in the ED are associated with a final ADHF diagnosis, the LRs indicate their limited diagnostic value, particularly in contrast with BNP. To balance the risks of overuse of tests and high inpatient mortality associated with abnormal LFTs, it is imperative to prospectively evaluate LFTs in the workup of ADHF and incorporate recommendations in society guidelines for clinical practice.

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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 for publication Not applicable.

Ethics approval Data were de-identified so research ethics approval was not required for this study.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available.

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