Time Between Laboratory Tests and Acute Liver and Kidney Injury Diagnosis Codes in CPRD: Are We Doing It Right?

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DISCLOSURES

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BACKGROUND

- In database studies, a 3-month time window around time of diagnosis is commonly used to validate acute kidney injury (AKI) and acute liver injury (ALI), and it is based on clinical criteria defining chronic liver disease and chronic kidney disease (CKD), rather than on specific timing of acute events.

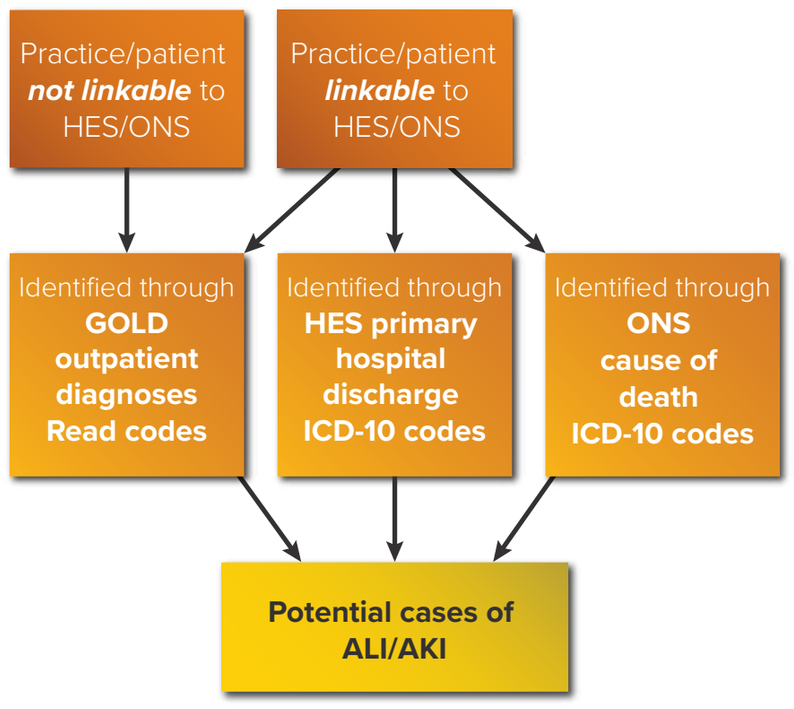
OBJECTIVE

- To evaluate the validity of the 3-month time window used to identify cases of ALI and AKI in the Clinical Practice Research Datalink (CPRD) in the United Kingdom.

METHODS

- Two cohorts of new users of specific oral glucose-lowering drugs for type 2 diabetes (one to evaluate the outcome ALI and one for AKI) were identified (August 2014-September 2017).
- Patients with a previous diagnosis of ALI were excluded from the "ALI cohort," and patients with previous diagnosis of AKI or CKD were excluded from the "AKI cohort." Those with previous abnormal laboratory values were not excluded.
- Cases were identified using codes suggestive of ALI and AKI (Figure 1).
- Among potential cases of ALI/AKI, we evaluated the number of patients who fulfilled the ALI or AKI laboratory criteria for the period extending from 3 months before to 3 months after diagnosis.
- In addition, we assessed the number of patients who fulfilled the laboratory criteria irrespective of being a potential case of ALI/AKI.
- Laboratory criteria were based on the Food and Drug Administration definition for ALI,[1] and the adapted Risk, Injury, Failure, Loss, End-Stage (RIFLE) definition for AKI.[2]

Figure 1. Identification of Study Outcomes (ALI/AKI) in CPRD

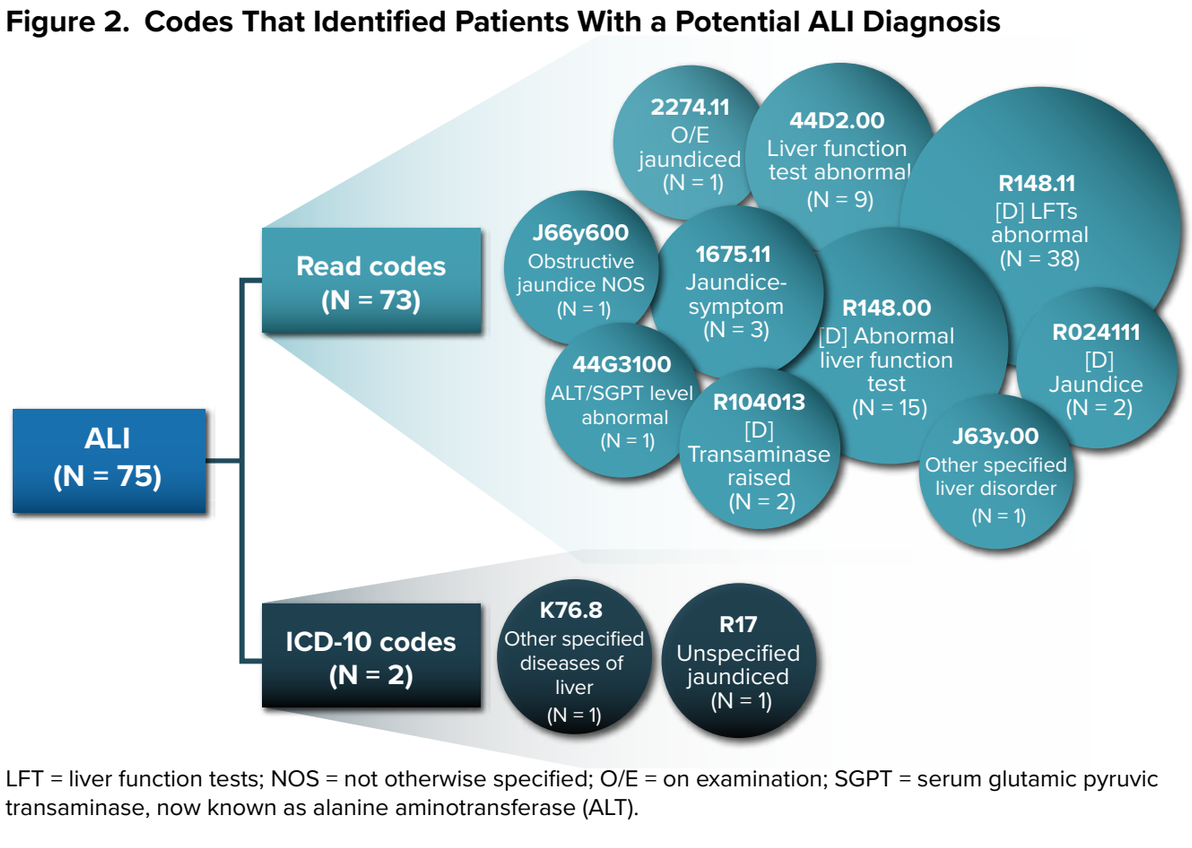


GOLD = General Practitioner Online Database; HES = Hospital Episode Statistics; ICD-10 = International Statistical Classification of Diseases and Related Health Problems, 10th Revision; ONS = Office for National Statistics.

RESULTS

- In the ALI cohort, among 21,621 new users, 75 potential ALI cases were identified (Figure 2); 6 of these fulfilled the laboratory criteria within 3 months of diagnosis (Table 1).
- None of the potential ALI cases had a specific code for ALI (e.g., acute liver failure or acute necrotizing liver disease).
- The majority of the potential ALI cases were identified through nonspecific Read codes indicating "abnormal liver enzymes" or "jaundice" (Figure 2).

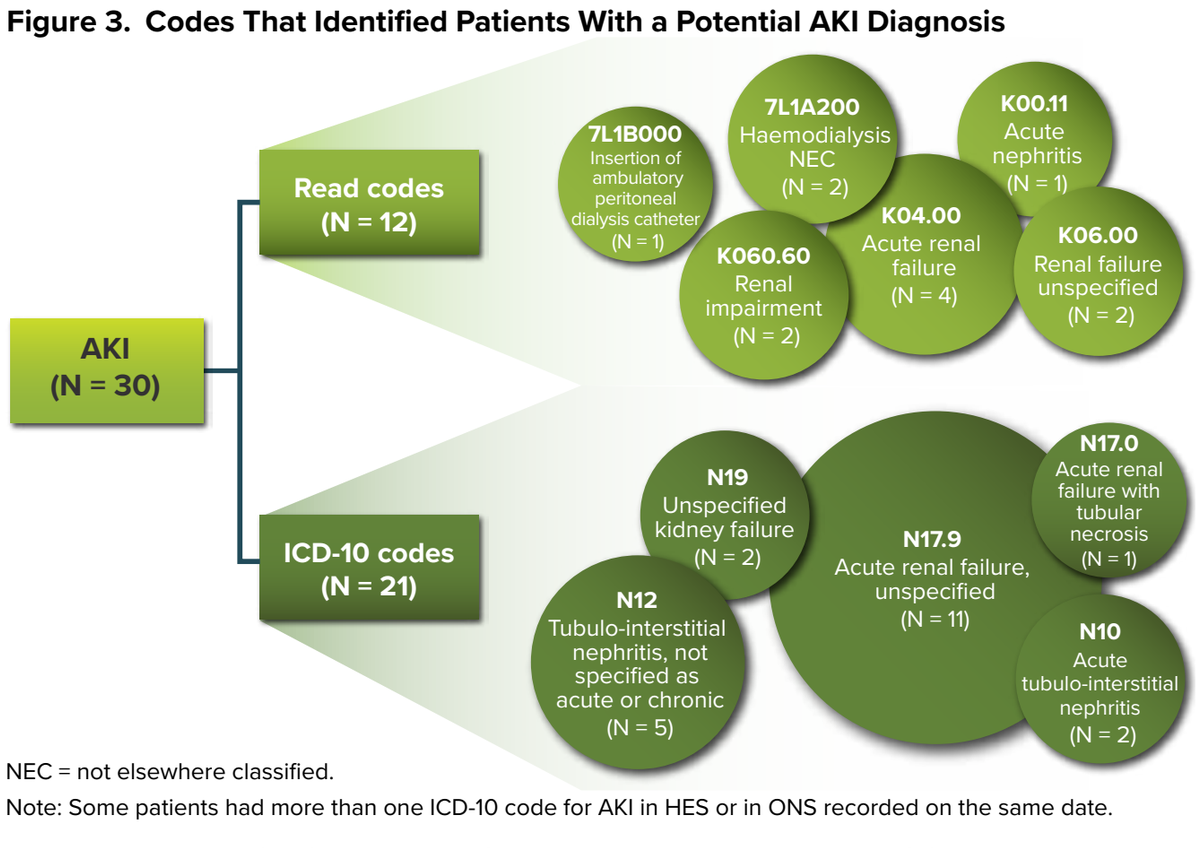
Figure 2. Codes That Identified Patients With a Potential ALI Diagnosis



LFT = liver function tests; NOS = not otherwise specified; O/E = on examination; SGPT = serum glutamic pyruvic transaminase, now known as alanine aminotransferase (ALT).

- In the AKI cohort, among 18,107 new users, 30 potential AKI cases were identified (Figure 3); 6 patients fulfilled the laboratory criteria within 3 months of diagnosis (Table 1).
- Most of the potential cases had a specific code for AKI (e.g., acute renal failure) and indicated that the kidney event was acute (Figure 3).
- Among potential cases of ALI or AKI classified as not fulfilling laboratory criteria, most had laboratory values within 3 months of the diagnosis (Table 2).

Figure 3. Codes That Identified Patients With a Potential AKI Diagnosis



NEC = not elsewhere classified.

Note: Some patients had more than one ICD-10 code for AKI in HES or in ONS recorded on the same date.

Table 1. Time Between Laboratory Criteria Related to Diagnosis Codes by Outcome Cohort

Characteristic	ALI Cohort (N = 21,621)	AKI Cohort (N = 18,107)
Patients with a diagnosis code	75	30
Patients fulfilling laboratory criteria	21[a]	305[b]
With no diagnosis code	15	296
At least 1 diagnosis code	6	9 (6 within 3 months and 3 beyond 3 months)
Patients by number of days in between fulfilling laboratory criteria and diagnosis code		
0-7 days	5 (83.33%)	4 (44.44%)
8-15 days	1 (16.67%)	1 (11.11%)
16-30 days	0 (0.00%)	1 (11.11%)
31-90 days	0 (0.00%)	0 (0.00%)
91-180 days	0 (0.00%)	1 (11.11%)
181-270 days	0 (0.00%)	1 (11.11%)
271-365 days	0 (0.00%)	1 (11.11%)

[a]For ALI if the patient had: (1) an elevation of the serum concentration of alanine aminotransferase (ALT) or AST of at least three times the ULN and (2) a contemporaneous (within 30 days of the ALT or AST elevation) elevation of the serum bilirubin concentration of at least two times the ULN during a time period extending from 3 months before to 3 months after the ALI diagnosis

[b]For AKI if the patient had: (1) at least a twofold increase in serum creatinine from the lowest baseline value recorded at any time before the index date and the value is above the ULN or (2) an increase in serum creatinine to at least two times the ULN in the absence of a recorded baseline value during a time period extending from 3 months before to 3 months after the AKI diagnosis.

Table 2. Characterization of Potential Cases of ALI or AKI Not Fulfilling Laboratory Criteria by Outcome Cohort

Characteristic	ALI Cohort (N = 21,621)	AKI Cohort (N = 18,107)
Patients with a diagnosis code and not fulfilling laboratory criteria	69	24
Patients not fulfilling laboratory criteria within 3 months of a diagnosis code[a]	60 (86.96%)	14 (58.33%)
Patients with no laboratory values within 3 months of a diagnosis code	7 (10.14%)	3 (12.50%)[b]
No laboratory values during the whole follow-up	0 (0.00%)	5 (20.83%)
Missing ULN values	2 (2.90%)	2 (8.33%)

ULN = upper limit of the normal range.

[a]Patients had laboratory values within 3 months of a diagnosis code but did not fulfil the laboratory criteria for AKI or ALI.

[b]Patients fulfilled the laboratory criteria but beyond 3 months of a diagnosis code.

CONCLUSIONS

- Of patients who had a diagnosis code and fulfilled the laboratory criteria, 83% in the ALI cohort and 44% in the AKI cohort fulfilled the laboratory criteria within 1 week of the diagnosis code, bringing into question the relevance of using a 3-month time window in database studies.
- A high number of patients in the AKI cohort fulfilled the laboratory criteria but did not have a code suggestive of an acute event. These patients may have CKD.
- Evaluation of repeated renal laboratory test results may help identify patients with undiagnosed CKD.

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