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Rapid cardiothoracic ultrasound protocol for diagnosis of acute heart failure in the emergency department

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Abstract

Objectives: The aim of this study was to evaluate the performance of a rapid cardiothoracic ultrasound protocol (CaTUS), combining echocardiographically derived E/e' and lung ultrasound (LUS), for diagnosing acute heart failure (AHF) in patients with undifferentiated dyspnea in an emergency department (ED).

Patients and results: We enrolled 100 patients with undifferentiated dyspnea from a tertiary care ED, who all had CaTUS done immediately upon arrival in the ED. CaTUS was positive for AHF with an E/e' > 15 and congestion, that is bilateral B-lines or bilateral pleural fluid, on LUS. In addition, an inferior vena cava index was also recorded to analyze whether including a central venous pressure estimate would add diagnostic benefit to the CaTUS protocol. All 100 patients had a brain natriuretic peptide (BNP) sample withdrawn, and 96 patients underwent chest radiography in the ED, which was analyzed later by a blinded radiologist. The reference diagnosis of AHF consisted of either a BNP of more than 400 ng/l or a BNP of less than 100 ng/l in combination with congestion on chest radiography and structural heart disease on conventional echocardiography.

CaTUS had a sensitivity of 100% (95% confidence interval: 91.4-100%), a specificity of 95.8% (95% confidence interval: 84.6-99.3%), and an area under the curve of 0.979 for diagnosing AHF ($P<0.001$). The diagnostic accuracy of CaTUS was higher than of either E/e' or LUS alone. Adding the inferior vena cava index to CaTUS did not improve diagnostic accuracy. CaTUS seemed helpful also for differential diagnostics of dyspnea, mainly regarding pneumonias and pulmonary embolisms.

Conclusion: CaTUS, combining E/e' and LUS, provided excellent accuracy for diagnosing AHF.

Introduction

Dyspnea is a common symptom in the emergency department (ED), and acute heart failure (AHF) is a common etiology causing dyspnea in these patients 1,2. Conversely, dyspnea is the main symptom driving patients with AHF through the ED into hospitals 2. Rapid diagnosis of AHF alongside swift differential diagnostics in this patient group could probably improve patient prognosis and streamline ED function 3-5.

Dyspnea in AHF is mainly caused by pulmonary congestion secondary to elevated left atrial filling pressure (LAP) 6. Lung ultrasound (LUS) has emerged as an accurate tool for identifying extravasated lung water (EVLW) as a sign of pulmonary congestion and AHF 7. Although LUS alone has shown great promise in diagnosing AHF 8, differentiating cardiogenic from noncardiogenic EVLW should optimally include evaluation of LAP, either invasively or with echocardiography (echo) 9 E/e' is an echo parameter for evaluating LAP, which is derived by comparing early diastolic left ventricular inflow velocities of blood with early diastolic relaxation velocities of myocardial tissue. E/e' has been studied for determining LAP across a wide variety of patients, including those with atrial fibrillation (Afib) 10-12, a very common finding in patients with AHF 2,13. Furthermore, echo, when available in the ED, is also considered generally useful for diagnosing AHF 3-5.

As E/e' and LUS theoretically complement one another when diagnosing AHF 3, we hypothesized that combining the two could result in improved diagnostic specificity and accuracy compared with either one alone. In this study, we will evaluate a rapid cardiothoracic ultrasound protocol (CaTUS), combining E/e' and LUS, with or without inferior vena cava index (IVCi), for diagnosing AHF. CaTUS will also be compared with E/e' and LUS alone in diagnosing AHF.

Patients and methods

Enrollment

After screening 103 consecutive adult patients with undifferentiated dyspnea in the ED of our tertiary care hospital, of which three patients met the exclusion criteria, we enrolled a convenience sample of 100 patients between July 2014 and January 2015. Patients with unsatisfactory visibility on ultrasound, known pulmonary fibrosis, age less than 18 years, mitral stenosis on echo, or a prosthetic valve in the mitral position were excluded. CaTUS was performed in all patients immediately after arrival in the ED before further investigations. CaTUS was done by an experienced sonographer with several years and more than 1000 examinations experience regarding both echo and LUS. All CaTUS examinations lasted less than 3 min. All enrolled patients also had a brain natriuretic peptide (BNP) sample taken, and in 96/100 patients, a chest radiography done at baseline. Written consent was obtained from all participants, and the study design was approved by the local ethical committee. All ultrasound examinations were done with the Philips CX 50 device (Royal PhilipsAmstelplein 2, Amsterdam, The Netherlands) using the cardiac probe only. All patients had a conventional echo done in the ED as well, with the exact methodology described in the Appendix (Supplemental digital content 1, http://links.lww.com/EJEM/A182).

Cardiothoracic ultrasound protocol

The CaTUS protocol included LUS and a medial E/e'-ratio on focused echo, and it is illustrated in Fig. 1. CaTUS result was considered positive for AHF if presenting with both an E/e' of more than 15 and a congestive LUS as defined later. In addition to CaTUS, an IVC index was also recorded.

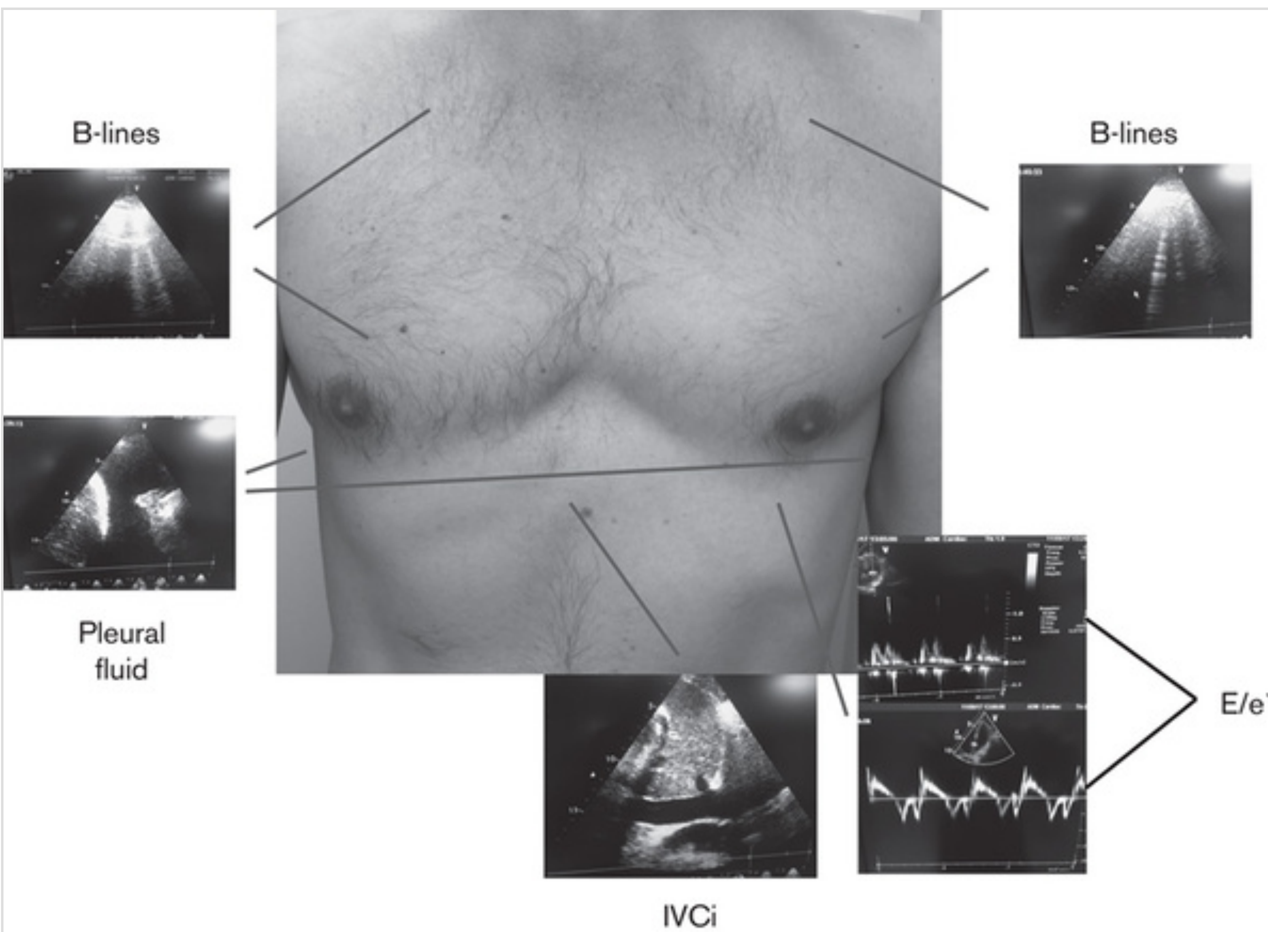

Fig. 1. An overview of the cardiothoracic ultrasound protocol protocol and the inferior vena cava index (IVCi) in addition.

All CaTUS measurements were done with the patient in a supine position, with the upper body slightly elevated for maximum patient comfort. Slight leftward rotation of the patient was allowed only if necessary for sufficient visualization, to avoid postural alteration of cardiac filling pressures. LUS included bilateral examination of two pulmonary fields per side, the apical and mammillary region in a mid-clavicular line, for evaluating B-lines. Additionally, the lower basal regions in an axillary line bilaterally were evaluated for pleural effusion (Fig. 1). B-lines were positive for one region if presenting at least three B-lines within one intercostal space 7,14, and a positive region for B-lines bilaterally was defined as a B-profile. Pleural fluid was defined as more than 5 mm of dependent fluid seen in the interpleural space. LUS was considered congestive within the CaTUS protocol if presenting either bilateral B-lines or bilateral pleural fluid.

The E-wave was recorded using pulse wave doppler at the tips of the opened mitral valve. If the patient was in sinus rhythm, or any other regular rhythm, three consecutive cycles at end expiration were recorded, and the average of these three E-waves was registered. If the patient was presenting with an irregular rhythm, such as atrial fibrillation or extra-systolia, five consecutive cycles and the average of these five E-waves were registered. Sweep speed was adjusted to fit a proper number of cardiac cycles into one picture frame. The e'-wave was measured using tissue pulse wave doppler with the sample volume placed at the medial mitral annulus. The E/e' was obtained in the four-chamber window using minimal angulation. Gain settings were optimized to obtain a crisp, clear signal without signal aberration. The IVC index was graded on a scale from 1 to 3, with grade 1 representing a maximum diameter of less than 21 mm and a respiratory variation of greater than 50%, grade 3 representing a maximum diameter of at least 21 mm and a respiratory variation of less than 50%, and grade 2 either/or 15. IVC measurements were performed 1-2 cm caudally of the first hepatic vein 15.

LUS and E/e' measurements were validated on 10 randomly assigned patients, using blinded experienced validators. Regarding congestion on LUS, the validation resulted in an interobserver agreement of 100% and thus a *[kappa]*-coefficient of 1.0. Regarding E/e', the mean interobserver coefficient of variation was 9.99%. Thirty randomly assigned patients were also referred for a blinded cardiologist review using patient data, and CaTUS reached a sensitivity of 95.8% and a specificity of 97.8% compared with this cardiologist's review.

Reference diagnosis

Patients were classified as having AHF if two criteria were fulfilled: (i) structural heart disease on conventional echo and (ii) either a BNP of more than 400 ng/l or a BNP of more than 100 ng/l in combination with congestion on chest radiography, as evaluated by a radiologist working in the radiology department, blinded to CaTUS findings, laboratory results, or the final diagnosis of the patient.

Statistical analysis

All statistical analyses were done using the SPSS, version 23 software (IBM Corp., Armonk, New York, USA). Continuous variables were presented as mean values including SD, except for BNP, which were presented as median values with 25-75% interquartile ranges displayed. Grouping variables were presented as frequencies. Differences between groups were determined using the *t*-test for mean values, the Mann-Whitney *U*-test for median values regarding continuous variables, and the Pearson *[chi]*^{2}-test for grouping variables. Hazard ratios were reported inclusive of 95% confidence intervals.

Results

Baseline characteristics of the enrolled 100 patients, of which 52 were classified as having AHF, and 48 as not, as can be seen in Table 1. Patients with AHF were older and more comorbid, whereas patients without AHF had more pulmonary disease. Laboratory and imaging results of the patients can be seen in Table 2, displaying a clear difference in AHF-associated parameters between the groups.

	All (*N*=100)	AHF (*n*=52)	Non-AHF (*n*=48)	*P*
Baseline characteristics				
Age [mean (SD)] (years)	71.4 (14.8)	76.4 (10.3)	65.8 (16.9)	**<0.001**
Diabetes (%)	34.0	42.3	25.0	0.091
Previous renal failure (%)	30.0	44.2	12.7	**0.001**
Hypertension (%)	70.0	84.6	54.2	**0.001**
Coronary artery disease (%)	39.0	53.8	22.9	**0.002**
History of heart failure (%)	41.0	63.5	16.7	**<0.001**
Obstructive pulmonary disease (%)	34.0	23.1	45.8	**0.021**
Parenchymal pulmonary disease (%)	4.0	0	4	**0.050**
Clinical parameters on admission				
Respiratory rate [mean (SD)] (/min)	23.4 (6.10)	25.0 (6.47)	21.6 (5.14)	**0.005**
Rales on auscultation (%)	28.0	36.5	18.8	0.074
Obstruction on auscultation (%)	22.0	23.1	45.8	**0.021**
Sinus rhythm (%)	62.0	47.2	77.1	**0.004**
QRS interval >120 ms (%)	28.0	46.2	8.3	**<0.001**
Systolic blood pressure [mean (SD)] (mmHg)	140 (33.7)	143 (35.8)	137 (31.3)	0.339
Atrial fibrillation/flutter (%)	32.0	40.3	22.9	0.086
Heart rate [mean (SD)] (/min)	85.7 (21.9)	83.6 (24.4)	88.0 (18.7)	0.308

AHF, acute heart failure.
Bold values statistically significant.

Table 1 Baseline characteristics and clinical parameters on admission

	All (*N*=100)	AHF (*n*=52)	Non-AHF (*n*=48)	*P*
Laboratory				
BNP [median (range)] (ng/l)	367 (121–919)	842 (381–1822)	117 (33.0–286)	**<0.001**
BNP>100 ng/l (%)	75.0	100.0	47.9	**<0.001**
BNP>400 ng/l (%)	50.0	75.0	22.9	**<0.001**
eGFR [mean (SD)] (ml/min/1.73 m^2)	62.1 (27.2)	51.1 (21.6)	74.6 (27.6)	**<0.001**
Imaging (ultrasound+radiography)				
Bilateral B-lines on LUS (%)	59.0	96.2	18.8	**<0.001**
Bilateral pleural fluid on LUS (%)	39.0	69.2	6.3	**<0.001**
E/e′ [mean (SD)]	15.9 (6.8)	21.3 (4.2)	9.99 (3.1)	**<0.001**
IVC index [mean (SD)]	1.88 (0.77)	2.27 (0.69)	1.45 (0.62)	**<0.001**
Left ventricular EF [mean (SD)] (%)	46.1 (16.1)	42.4 (16.0)	51.8 (11.2)	0.130
RV dysfunction (%)	32.0	34.6	29.2	0.560
Congestion on chest radiograph	51.0	90.4	8.3	**<0.001**

AHF, acute heart failure; BNP, brain natriuretic peptide; E/e′, medial ratio of early diastolic E-wave to e′-wave; EF, ejection fraction; eGFR, estimated glomerular filtration rate; IVC, inferior vena cava; LUS, lung ultrasound; RV, right ventricular; radiograph, thoracic radiograph.
Bold values statistically significant.

Table 2 Imaging and laboratory characteristics on admission

E/e' and congestive findings on LUS correlated well. The *[kappa]*-coefficient for E/e' with a cutoff of 15 for predicting congestion on LUS was 0.796 (*P*<0.001). The area under the curve for E/e' in identifying congestion on LUS was 0.95. The diagnostic performance of CaTUS, as well as the other ultrasound parameters in diagnosing AHF, can be seen in Table 3.

	95% CI			
Protocols	Sensitivity (%)	Sepcificity (%)	AUC	*P*
CaTUS	100 (91.4–100)	95.8 (84.6–99.3)	0.979	<0.001
BL-profile on LUS alone	96.2 (86.8–99.5)	81.3 (67.4–91.1)	0.887	<0.001
E/e′>15 alone	100 (91.4–100)	84.9 (71.9–92.8)	0.925	<0.001
CaTUS+(IVC ≥ group 2)	86.5 (73.6–94.0)	97.1 (88.8–99.5)	0.918	<0.001
CaTUS+(IVC ≥ group 3)	40.4 (27.3–54.9)	100 (93.3–100)	0.702	<0.001

AUC, area under the curve; BL-profile, bilateral B-lines in at least one scanning zone bilaterally; CaTUS, cardiothoracic ultrasound protocol; CI, confidence interval; E/e′, medial ratio of early diastolic E-wave to e′-wave; IVC, inferior vena cava; LUS, lung ultrasound.

Table 3 Diagnostic accuracy of CaTUS, LUS and E/e' alone, as well as CaTUS in combination with the IVC index

The CaTUS protocol, as such, presented a significantly higher specificity and diagnostic accuracy for diagnosing AHF compared with either E/e' or B-profile on LUS alone. Combining the IVCi with CaTUS in turn resulted in a worse total diagnostic accuracy as compared with CaTUS alone, despite slightly enhanced specificity, especially when using the at least class 3 IVCi criteria.

In an additional analysis of patients without congestion on LUS, CaTUS detected focal B-lines on LUS in four out of five patients diagnosed with pneumonia, and visually estimated right ventricular pressure overload on echo in four out of five patients with pulmonary embolism. One type A aortic dissection causing pericardial tamponade, and one chordae rupture of the mitral valve causing cardiogenic shock through severe mitral regurgitation were also revealed as incidental findings.

Discussion

In this study, CaTUS resulted in excellent accuracy in diagnosing and excluding AHF. Although both LUS and E/e' did very well in diagnosing AHF, the combination of the two within CaTUS resulted in improved specificity and total diagnostic accuracy compared with either parameter alone, without compromised sensitivity. Although not a primary focus in this study, CaTUS also seemed useful for differential diagnostics in patients with dyspnea, a finding well reported earlier as well. Importantly, a small, mainly hypertensive portion of AHF patients had an IVCi of zero, which resulted in a decreased sensitivity and total accuracy when combining the IVCi with CaTUS. E/e' and LUS as such thus seemed like the optimal combination for diagnosing AHF, and the hypertensive patients with a nonplethoric IVC probably represented a 'vascular' phenotype of AHF [4].

Previous studies combining echo and LUS for diagnosing AHF or cardiogenic pulmonary edema in an ICU or ED setting are summarized in Table 4 [13,16-20]. The diagnostic accuracies reported in these studies were inferior to that achieved with CaTUS in this present study. This study, however, is to our best knowledge the first study using E/e' in all patients for evaluating LAP, thus allowing uniform evaluation of patients in nonsinus rhythm as well. Furthermore, including the pleural fluid criterion as a sign of congestion within CaTUS also allowed for increased sensitivity, despite combination with echo. Of the studies in Table 4, the number of patients with Afib and the exact methodology for echocardiographic estimation of LAP in these patients were only reported in the study by Gallard and colleagues, where 49% of the patients with AHF had Afib, and these patients were completely excluded from LAP estimation and solely evaluated using LUS. As Afib is very common in AHF [2,13] and most echocardiographic LAP parameters other than E/e' are nonfeasible in Afib, methodological issues might have greatly reduced diagnostic accuracy in these studies. Furthermore, LUS alone presented a sensitivity and specificity of more than 90% for diagnosing AHF in a large meta-analysis [8], and thus combining two robust methods like echocardiography and LUS should expectedly result in good accuracy. Compared with the aforementioned studies with LAP evaluation, our methodology, including only six lung zones and one uniform echo parameter for evaluating LAP, was also significantly faster. As simpler LUS protocols have yielded good accuracy regarding AHF as well [7,14], such faster protocols might be more suitable for the ED.

	Diagnostic accuracy					
References[a]	Sensitivity (%)	Specificity (%)	AUC	Duration (min)	Methodology for estimating LAP in Afib	LAP evaluation
Kajimoto *et al.* [16]	94.3	91.9	–	< 1	Unclear	–
Silva *et al.* [17]	–	–	0.93	12 ± 4	Unclear	+
Bataille *et al.* [18]	100	91	–	9 ± 2	Unclear	+
Sekiguch *et al.* [19]	[b]		–	< 10	Unclear	+
Gallard *et al.* [13]	83	83	–	12 ± 3	Afib patients excluded	+
Russel *et al.* [20]	93	86	–	Not reported	Unclear	+

Afib, atrial fibrillation; AUC, area under the curve; LAP, echocardiographically estimated left atrial filling pressure.
[a]Exact references in text.
[b]Cutoff analysis using R-package found E/e′, ejection fraction, inferior vena cava index and left-sided pleural effusion significant for differentiating cardiogenic pulmonary edema and acute respiratory distress syndrome.

Table 4 Previous studies combining echocardiography and lung ultrasound within a single protocol for diagnosing acute heart failure or cardiogenic pulmonary edema

In this study, including the pleural fluid criterion as a sign of congestion within CaTUS also allowed for increased sensitivity despite combination of echo to the protocol, compared with B-lines alone. Compared with the aforementioned studies, our methodology was also simpler. We included only six lung zones on LUS and one uniform echocardiographic parameter for evaluating LAP, making this protocol significantly faster. Simpler LUS protocols have yielded excellent results as well 7,14, and we find simpler protocols more suitable for an ED setting.

Echo and LUS in an ED setting are also useful for diagnosing other cardiopulmonary conditions than AHF 21,22, and CaTUS also presented a significant differential diagnostic yield in this study. Nevertheless, despite the proven accuracy of LUS in diagnosing pneumonia 21, the ability of CaTUS to detect focal B-lines in 4/5 patients with pneumonia in this study was perhaps surprising, considering that the protocol uses only six lung zones in total. Thus, faster LUS protocols might also be able to diagnose pulmonary conditions with reasonable accuracy.

The operator in this presents study was experienced in both echo and LUS. Nevertheless, echo and LUS, which are powerful diagnostic tools in the ED 8,21,22, can both be learned with a steep learning curve 23,24. Estimation of LAP with tissue Doppler imaging has also been implemented by ED physicians successfully and has been proven to be feasible and especially useful for diagnosing AHF 25,26. Thus, although the exact learning curve regarding CaTUS remains to be investigated, such a protocol could probably be implemented into an ED setting after consideration of sufficient training and quality assessment 25.

Conclusion

Combining LUS and E/e' into a rapid ultrasound protocol resulted in very good diagnostic accuracy regarding AHF, and such a protocol seems helpful regarding differential diagnostics as well. Larger future studies are needed to confirm the findings of this small single-center study.

Limitations

This study has several limitations. This was a single experienced investigator, single-center study with a limited population size. The operator performing the CaTUS exams could not be 100% blinded to clinical gesture or vital signs of the patients in the ED. However, both LUS and echocardiographic evaluation of cardiac filling pressures were validated, and the blinded cardiologist's review also confirmed good correlation of AHF diagnosis compared with CaTUS.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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Keywords: acute heart failure; dyspnea; echocardiography; lung ultrasound

IMAGE GALLERY

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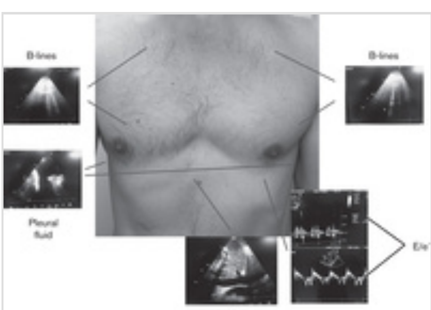
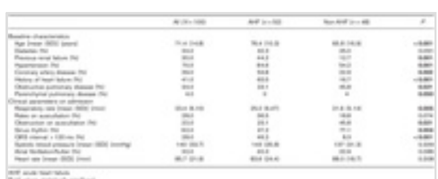


Fig. 1



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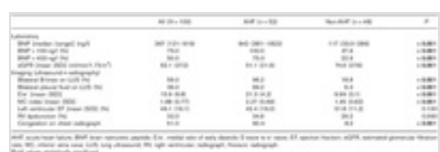

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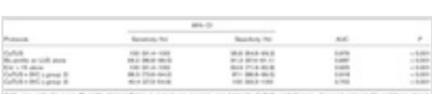

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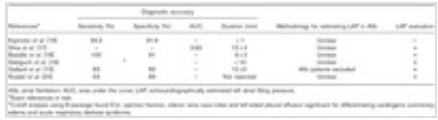

Table 4

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