Dynamic changes and prognosis of pulmonary congestion by lung ultrasound in hemodialysis patients: a systematic review and meta-analysis

Jianan Zhou, Qi An, Xiukun Hou

The First Affiliated Hospital of Dalian Medical University, Dalian City, Liaoning Province, China

Abstract

Aims: Lung ultrasound (LUS) has been rapidly developed to evaluate pulmonary extravascular fluid. A systematic review was conducted to study the dynamic changes of LUS findings of pulmonary congestion before and after hemodialysis and examine the application of LUS for the prognosis of hemodialysis patients. Material and methods: This study searched online databases for articles on hemodialysis patients that used LUS to evaluate dynamic changes during hemodialysis or prognosis. Articles published in English or Chinese until September 2021 with ≥30 patients were included in this study. Results: Of the 1329 articles, 14 met the inclusion criteria: 9 reported dynamic changes during dialysis in LUS (438 patients), and 5 reported the prognosis of hemodialysis patients in LUS (1274 patients). As indicated by a further meta-analysis, eight studies found that the combined standardized effect size was -0.74. The all-cause mortality rate of the dialysis patient group with high B-line scores was three times that of the dialysis patient group with low B-line scores. In dialysis patients, no difference was found between the LUS guided treatment and the conventional care in reducing the all-cause mortality (HR=0.92 95%CI: 0.67-1.27) and cardiovascular events (HR=0.98 95%CI: 0.72-1.34). Conclusions: LUS can be used to effectively evaluate the volume status of hemodialysis patients in real time. The level of B-line before dialysis is significantly correlated with the poor prognosis. However, compared with the routine nursing group, the treatment of hemodialysis patients with LUS-guided volume management cannot effectively reduce mortality and cardiovascular events.

Keywords: lung ultrasound, hemodialysis, dynamic changes, prognosis

Introduction

Most maintenance hemodialysis patients have been found with fluid retention and chronic volume overload at different degrees for a long time. As indicated by published literature, this volume overload will increase the mortality of patients and become a main cause of death in hemodialysis patients [1]. However, an excessive fluid removal during dialysis can induce symptoms correlated with hypotension, and insufficient tissue perfusion affects residual renal function, and even further fatal cardiovascular and cerebrovascular complications [2]. Accordingly, adjusting the amount of ultrafiltration during dialysis and evaluating patients’ capacity status in real time significantly contribute to the prevention of complications and long-term prognosis of dialysis patients.

The evaluation of patients’ volume status only according to clinical experience is generally inaccurate, and small changes in volume load are difficult to detect [3]. A series of novel technologies for the objective evaluation of volume status have been gradually applied in clinics. To be specific, lung ultrasound can be used to achieve the bedside semi-quantitative evaluation of extravascular lung water in dialysis patients based on B-line, which shows plentiful advantages (e.g., high sensitivity, non-invasiveness, real-time and good repeatability). When pulmonary congestion occurs, the interlobular space will thicken with the increase in water content and form a significant impedance gradient with the gas in the surrounding alveoli. The sound beam is reflected repeatedly at the
interface of the impedance gradient, and the sonogram turns out to be a comet-like tail from the pleural-line strong echo beam, termed B-line. To analyze whether lung ultrasound (LUS) can evaluate the dynamic changes of B-line in real time with the change of patients’ volume status during dialysis, we performed this systematic review objectively summarizing the changes of LUS measurement B-line during dialysis. Moreover, the effect of LUS on the volume status evaluation, or the effect of the guided treatment plan in dialysis patients on the survival and prognosis of patients was further analysed compared with conventional care, and evidence-based medical evidence was provided for further clinical application.

Material and method

Literature search strategy
A computer-based search of research on the application of LUS in dialysis patients was conducted in PubMed, Ebase, Cochrane Library, Chinese Journal Fulltext Database (CNKI), Wanfang Resource Database and Weipu Database. The search period was up to September 2021. The search subject terms included lung, pulmonary, ultrasonography and dialysis, and a combination of subject terms and free words were applied for the search.

Literature inclusion and exclusion criteria
Inclusion criteria: 1. The method of scoring or counting was used to record the complete data of dialysis patients before and after dialysis with lung ultrasonography or a study using lung ultrasonography to make a prognosis of dialysis patients; 2. Full text is available in Chinese or English; 3. Sample Number ≥30 patients. Exclusion criteria: 1. Only abstract, review or case report were included; 2. No valid data or unclear data description; 3. Low quality of the literature.

Quality evaluation and data extraction
Two reviewers independently screened the literature and extracted the literature information in accordance with the literature inclusion and exclusion criteria above. The qualified literature fell into two groups: 1. The dynamic changes of B-line before and after dialysis; 2. The effect of B-line on the prognosis of dialysis patients (analysis of the effect of the baseline B-line value on the prognosis and the use of B-line guidance). Based on the research type, this study employed the NOS literature quality evaluation form and the AHRQ cross-sectional quality evaluation form (supplementary material, Table SI and Table SII, on the journal site).

STATA Version 16 was applied for the statistical analysis of data. The data regarding the application of LUS in the prognosis of hemodialysis patients fell into two groups according to the study type. The HR and 95% CI of the correlation between pulmonary ultrasonography and dialysis patients were extracted. If multiple estimates were proposed in the same article, the most representative one would be selected (multivariate analysis better than univariate analysis). The I² test was performed for heterogeneity analysis, I²<50% indicating no heterogeneity, 50%≤I²<75% indicating mild to moderate heterogeneity, and I²≥75% indicating significant heterogeneity.

Results

Literature retrieval and characteristics of included literature
Overall, 1,329 articles were found using the literature retrieval strategy. The duplicate articles were eliminated, and 65 articles were selected for the full-text review after titles and abstracts were screened. After the further evaluation, fourteen articles were included. nine of them investigated the dynamic changes of the number of B-lines before and after dialysis, and five were concerned with the effect of B-line on the prognosis of dialysis patients (fig 1).

Lung ultrasonography monitors the dynamic changes of B-line
For this analysis, nine studies using B-ultrasound to monitor the real-time dynamic changes of hemodialysis patients before and after dialysis were included [3-11] (Table 1). The average number of B-lines after the hemodialysis of the nine articles included was lower than that before hemodialysis. Two articles reported that the
change of B-line during dialysis was positively correlated with the amount of ultrafiltration during dialysis [6,8]. Two articles concluded that the reduction of B-line during dialysis was closely correlated with weight loss [9,10]. The authors primarily used two methods to count B-line, one directly counting and adding each area, and the other using the scoring method. Furthermore, most articles used the 28-area scoring method.

The heterogeneity of the nine included studies was I²=87.4%>75%, and Q-test p<0.01(fig 2a). Thus, the reasons for heterogeneity were further investigated. Based on the clinical experience, we considered that Torino et al [3] included the high-risk cardiovascular population as the dialysis population. So, the source of heterogeneity was highly suspected. After the Torino et al study [3] was removed, the combined effect size of the meta-analysis changed significantly (fig 2b) and the remaining eight articles had heterogeneity I²=63.3%, which was within an acceptable range. Thus, a random effects model was selected for the meta-analysis. The standardized effect size of the combined eight articles was -0.74, 95%CI (-0.99, -0.48), which was a medium effect size and significant.

### Table I. Overview of lung ultrasound before and after dialysis: dynamic changes in B-lines

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Age</th>
<th>Zones, n</th>
<th>Method</th>
<th>Dynamic changes in B-lines</th>
<th>Relationship with other findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Torino, 2016 [3]</td>
<td>79</td>
<td>72</td>
<td>28</td>
<td>score</td>
<td>pre: 9 (5-19) post: 5 (2-10)</td>
<td>Poor correlation between B lines and crackles or peripheral edema</td>
</tr>
<tr>
<td>Trezzi, 2013 [9]</td>
<td>41</td>
<td>63±18</td>
<td>28</td>
<td>count</td>
<td>pre: 24.8±25.3</td>
<td>B-lines reduction was significantly correlated with weight loss</td>
</tr>
<tr>
<td>Vitturi, 2014 [10]</td>
<td>71</td>
<td>65±13</td>
<td>28</td>
<td>count</td>
<td>pre: 3.1±3.4 post:1.4±2.5</td>
<td>B-lines reduction correlated with weight loss</td>
</tr>
<tr>
<td>Donadio, 2015 [5]</td>
<td>31</td>
<td>68±11</td>
<td>28+29</td>
<td>score</td>
<td>pre: 12.9±12.5 post:4.5±4.7</td>
<td>B lines correlated with TBWI and ECWI estimated by BIA</td>
</tr>
<tr>
<td>Liang, 2018 [6]</td>
<td>35</td>
<td>58±15</td>
<td>28</td>
<td>score</td>
<td>pre: 10 (0-42) post:4 (0-30)</td>
<td>The reduction of B-line score was negatively correlated with ultrafiltration volume (β=3.3, p=0.002)</td>
</tr>
<tr>
<td>Mohammad, 2020 [8]</td>
<td>38</td>
<td>47±15</td>
<td>28</td>
<td>score</td>
<td>pre: mean10.3±6.2 post:4.4±3.9</td>
<td>CUS% changes and ultrafiltration volume (r=0.74, p&lt;0.01)</td>
</tr>
<tr>
<td>Yang, 2020 [11]</td>
<td>36</td>
<td>&gt;18</td>
<td>28</td>
<td>score</td>
<td>pre: 8 (0-75) post:2 (0-53)</td>
<td>Pre B line score and IVC diameter (r=0.38, p&lt;0.05)</td>
</tr>
<tr>
<td>Miao, 2021 [7]</td>
<td>54</td>
<td>61±16</td>
<td>8</td>
<td>count</td>
<td>pre: 5.2±7.2 post: 3.5±5.8</td>
<td></td>
</tr>
</tbody>
</table>

N: number, CUS%: Lung ultrasound percent changes, TBWI: in total body water index, ECWI: extra-cellular water index, BIA: bioelectrical impedance analysis, IVC: inferior vena cava, NR: not report

Fig 2. Pooled SMD (standardized mean difference) result of dynamic changes of B-line before and after dialysis (a, b)
(z=-5.7, p<0.001). This result demonstrated that the number of B-lines after dialysis decreased significantly. The two subgroups were counted and scored using different counting methods, and the standardized effect sizes were -0.54 and -0.87, both of which were significant.

According to a sensitivity analysis of the standardized effect size (supplementary material, fig S1), after the exclusion of any study, the effect size of the outcome index did not change significantly, which indicated that the results of the meta-analysis were relatively stable and credible. The funnel chart (supplementary material, fig S2) of the eight articles included was basically symmetrical. The egger test result of the funnel chart was p=0.34, which demonstrated that the funnel chart was symmetrical. Accordingly, there was no publication bias in this study.

**The effect of LUS B-line on the prognosis**

Five articles were used for analyzing the prognosis capacity of the LUS findings (Table II). Three papers studied the effect of the baseline B-line value on the prognosis, and two the effect of LUS to guide treatment compared with conventional care on the prognosis of dialysis patients based on Randomized Controlled Trail (RCT) research [12-16]. The results were pooled, and the all-cause mortality rate of the dialysis patient group at a high B-line score was higher than that of the dialysis patient group at a low B-line score (HR=3.01 95%CI: 1.95-4.66 p<0.001, I²=0.0%, p=0.93, fig 3) [12,14,16]. I² value = 0.0%, P value = 0.93; no heterogeneity was found in the study. The remaining two articles respectively added lung ultrasound to dialysis populations at a low cardiovascular risk and at a high cardiovascular risk to guide clinical treatment [13,15]. According to the study, lung ultrasound monitoring guided treatment was not better than conventional care in improving the all-cause mortality (HR=0.92 95%CI: 0.67-1.27, p=0.62 I²=0.0% p=0.72, fig 4a) and cardiovascular events (HR=0.98 95%CI: 0.72-1.34), p=0.91 I²=0.0% p=0.70, fig 4b). I²=0.0% had no heterogeneity.

**Discussion**

This systematic review of the clinical evaluation of hemodialysis patients using LUS achieved three main findings. First, LUS can serve as a powerful tool to evaluate the volume status of hemodialysis patients in real time. Second, the severity of pulmonary edema sig-
Table II. Prognostic value of lung ultrasound in hemodialysis

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Participants</th>
<th>N (A/C)</th>
<th>Mean age</th>
<th>Zone</th>
<th>Method B-line quantification</th>
<th>Intervention</th>
<th>Primary outcomes</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zoccali, 2013</td>
<td>P</td>
<td>HD (≥3M)</td>
<td>392</td>
<td>65±15</td>
<td>28</td>
<td>Score mild (BLS 5-15), moderate to severe (BLS=15–60), very severe (BLS&gt;60)</td>
<td>All-cause mortality and cardiac events</td>
<td>2.1 years</td>
<td></td>
</tr>
<tr>
<td>Siriopol, 2013</td>
<td>P</td>
<td>HD (≥3M)</td>
<td>96</td>
<td>59±14</td>
<td>28</td>
<td>Score none or mild: &lt;16 comets, moderate: 16–30 comets, severe: &gt;30 comets</td>
<td>All-cause mortality</td>
<td>406 days</td>
<td></td>
</tr>
<tr>
<td>Siriopol, 2016</td>
<td>P</td>
<td>HD (≥3M)</td>
<td>173</td>
<td>58 ± 14</td>
<td>28</td>
<td>Score BLS≤22 BLS&gt;22</td>
<td>All-cause mortality</td>
<td>21.3 M</td>
<td></td>
</tr>
<tr>
<td>Siriopol, 2016</td>
<td>RCT</td>
<td>A: HD with low cardiovascular risk C: HD (≥3M)</td>
<td>250 (123/127)</td>
<td>59/59.4</td>
<td>28</td>
<td>Score</td>
<td>HD intensification when BLS&gt;15</td>
<td>All-cause mortality and first cardiovascular events</td>
<td>21.3 M</td>
</tr>
<tr>
<td>Zoccali, 2021</td>
<td>RCT</td>
<td>A: HD with high cardiovascular risk C: HD (≥3M)</td>
<td>363 (183/180)</td>
<td>70/70</td>
<td>28</td>
<td>Score</td>
<td>HD intensification when BLS&gt;15</td>
<td>Composite of death, myocardial infarction, or decompensated heart failure</td>
<td>1.49 years</td>
</tr>
</tbody>
</table>

P: prospective, RCT: Randomized Controlled Trail, M: Months, N(A/C): Numbers (Active arm/Control arm). BLS: B-lines score, HD: hemodialysis
nificantly causes the poor prognosis of hemodialysis patients. Lastly, in hemodialysis patients with high or low cardiovascular risk, LUS-guided treatment is not more effective than conventional care for patient mortality and cardiovascular events.

For ultrasound doctors, it is best for them to take B-line measurements without knowing the dialysis state of the patients (before or after dialysis), but it is difficult to achieve this because of the fixed dialysis time in the dialysis center. Most patients on hemodialysis had asymptomatic pulmonary edema [16,17]. Before dialysis, excessive extravascular lung water was correlated with the amount of fluid accumulated before treatment. The nine articles reported that hemodialysis can rapidly reduce the severity of pulmonary congestion, and the number of B-lines changed significantly after dialysis [3-11]. The results of eight articles after meta-analysis had statistical significance, which demonstrates that LUS can dynamically monitor the volume status of dialysis patients in real time, as an attempt to more effectively assess the effect of dialysis [4-11]. Noble et al in a quantitative analysis of a small sample of patients found that for every 500 ml ultrafiltration, the number of B-lines decreased by about 2.7 [18]. Ngoh et al found that despite the elimination of body fluids, the NT-pro BNP and bioimpedance spectrum index increased inexplicably after dialysis [19]. This means that the current capacity evaluation methods have a reduced ability to detect changes of liquid state after hemodialysis. Meanwhile, the Lung Water by Ultrasound-Guided Treatment in Hemodialysis Patients (LUST) sub-study found that the lung crackles and peripheral edema during auscultation had low sensitivity for judging pulmonary interstitial congestion, and clinical examination had the poor discriminating ability to detect lung congestion [3]. Changes in the B-line dialysis process were correlated with ultrafiltration volume and weight loss [6,8-10]. Furthermore, the B-line level were significantly correlated with other capacity evaluation indicators (e.g., the bioimpedance spectroscopy indicators, inferior vena cava diameter and NT-proBNP) [5,11,19].

The included articles in this study primarily applied 28 regional schemes for measurement, whereas the simplified 4-area and 8-area schemes in actual clinical applications were recommended for the international consensus LUS guidelines to evaluate pulmonary congestion [20]. The measured values of Area 4, Area 6 and Area 8 are highly consistent with the measured values of dialysis patients diagnosed with pulmonary congestion using Area 28 method [21,22]. Moreover, the consistency of the scores of the B-line between observers was relatively high, and there was no obvious difference in the B-line detection results of different types of ultrasound equipment [7]. LUST’s sub-study aimed at clinicians who can master the B-lines measurement method quickly and effectively after online video training, as well as at nurses who can successfully evaluate B-lines for the differential diagnosis of acute dyspnoea with high accuracy [23]. The findings above made the application of LUS more convenient for clinical promotion. Although LUS has high performance in capacity evaluation, it is noteworthy that it cannot differentiate a dry from a “too dry” patient. The LUS for primary lung diseases can also show considerable B-lines, so we cannot rely too much on LUS in clinic, but comprehensively analyze multiple indicators.

According to the effect of LUS on the prognosis, the all-cause mortality of the dialysis patient group with a high B-line score was three times higher compared to the dialysis patient group with a low B-line score [12,14,16]. Saad et al [24] had similar results but, because no valid data could be extracted, the paper was not included in this meta-analysis [24]. In addition to the prediction of all-cause mortality, it was found that people with high B-line scores had a higher incidence of cardiovascular events [16,24]. However, we have seen the results of the Extravascular Lung Water Monitoring by Combined Bioimpedance and Ultrasonography as a Guide for Treatment in Hemodialysis Patients (BUST) and LUST studies that the application of pulmonary ultra-guided therapy to reduce pulmonary congestion was not effective in reducing the mortality and the incidence of cardiovascular events in the dialysis population compared with the conventional care group [13,15]. Likewise, according to a meta-analysis of 493 patients with heart failure included in LUS guided volume management compared with routine physical examination, LUS management may not reduce the patient all-cause mortality and heart failure hospitalization rate, whereas it could reduce urgent visits for worsening symptoms of heart failure [25]. However, the multi-center LUST study also found that LUS-guided therapy can recur recurrent episodes of decompensated heart failure and cardiovascular events [15]. In a LUST sub-study including non-high-risk hypertensive patients who received hemodialysis, a LUS-guided strategy could safely reduce 48 h ambulatory blood pressure [26]. Although the existing research results reveal that LUS-guided patient volume management does not significantly impact long-term mortality and cardiovascular events, it still helps improve other clinical outcome indicators and enable patients to obtain certain clinical benefits.

Several limitations are found in this study (e.g., the small number of cases in some articles, the lack of standardization of chest zone, and the inconsistent risk factors
for the study subjects). In addition, some articles investigating the dynamic changes of the number of B-lines before and after dialysis expressed the B-line level using the median form, and our study referred to the statistical method of Wan et al to convert the median form into the forms of mean plus and minus standard deviation for the meta-analysis, which caused a certain error [27]. However, we consider that the systematic review of this study presented hypothetical data capable of suggesting the future treatment of HD patients.

**Conclusion**

As indicated by the meta-analysis of this study, LUS can evaluate the volume status of hemodialysis patients in real time. The level of B-line before dialysis is significantly correlated with the poor prognosis of patients. Compared with the conventional care group, LUS intervention-guided therapy had no significant effect on reducing the mortality and cardiovascular events of hemodialysis patients whether at a high cardiovascular risk or a low cardiovascular risk. Subsequently, multicenter randomized clinical trials should have larger sample sizes and longer follow-up periods to validate LUS guidance strategies for treating hemodialysis patients.

**Conflicts of interest:** none

**References**


