Lung ultrasonography in end-stage renal disease: moving from evidence to practice—a narrative review

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Abstract

Traditionally, point of care ultrasonography in nephrology has been used for renal biopsies and dialysis line placement. However, there is an emerging literature supporting the value of point of care lung ultrasonography in the assessment of volume status for dialysis patients. We conducted a review and identified 12 studies that examined the utility of lung ultrasonography in assessing volume status in patients with end-stage renal disease. We conclude that lung ultrasonography can be used to determine volume status in chronic dialysis patients by identifying lung congestion using the B-line score. Incorporating this technique into practice may have significant diagnostic and prognostic value for this high-risk population, as it provides the nephrologist with a useful bedside technique to assess extravascular lung water. Developing competence in lung ultrasonography is straightforward. The nephrology community should consider adding this useful tool into fellowship training, paralleling its broader use in other internal medicine specialties.

Key words: fellowship, lung ultrasonography, lung ultrasonography in nephrology, ultrasonography in dialysis, volume assessment

Introduction

Clinicians in emergency medicine, critical care and internal medicine use point of care ultrasonography to extend the physical examination [1, 2]. Medical schools are incorporating ultrasonography proficiency into their core competencies [3]. Nephrologists have only just begun to incorporate bedside ultrasonography into practice. Currently, ultrasonography is used by nephrologists for dialysis line insertion and

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Lung ultrasonography in ESRD

Understanding the B-line: how to measure and correlate with EVLW

Lung ultrasonography is performed by placing the ultrasonography probe perpendicular to the chest wall in longitudinal scanning axis with the scanning plane directed through an intercostal space. Figure 1 demonstrates the ultrasonography anatomy seen through a rib interspace. The chest wall consists of the epidermis, the underlying soft tissue and the muscle layers external to the rib cage. Below the inner surface of the ribs are the parietal pleura, against which the visceral pleura moves in respirophasic and cardiophasic synchrony. Rib edges form a hyperechoic curvilinear line that results in a shadow artifact deep to each rib. The pleural line is the first horizontal hyperechoic line below the ribs; this represents the interface between visceral and parietal pleura. Normally, there is respirophasic and/or cardiophasic movement of the pleural line that is termed lung sliding or lung pulse. This is a valuable sign that rules out pneumothorax.

Deep to the pleural interface are air-filled alveolar structures within lobules that are surrounded by the interlobular septa. These septa insert into the visceral pleura. They cannot normally be visualized, as their size is below the resolution of standard diagnostic ultrasonography. Normally aerated lung is not visible as a discrete structure, as the ultrasound beams are reflected intensely from the pleural surface. When the interlobular septa or the alveolar compartment underlying the visceral pleura are diseased, distinctive ultrasonography patterns become visible. Depending on the resulting pattern, the examiner discriminates normal from abnormal lung.

Normally aerated lung has a characteristic air artifact termed A-lines. A-lines are horizontally orientated lines that are deep to the pleural line and separated by the same distance as the probe is from the pleural line. When the ultrasound beams meet interlobular septa that is thickened, this creates a reverberation artifact that results in a hyperechoic line perpendicular to the pleural surface (Figure 1). These artifacts are known as B-lines. B-lines have the following characteristics: (i) they arise from the pleural surface; (ii) they move with the pleural line when the pleural line moves; (iii) they are well defined; (iv) they are hyperechoic and spread out without fading; (v) they reach the bottom of the screen; and (vi) they obliterate A-lines [8]. The presence of B-lines indicate the presence of an alveolar or interstitial abnormality such as cardiogenic pulmonary edema, accumulation of EVLW, pneumonia, lymphangitic carcinoma, acute respiratory distress syndrome or pulmonary fibrosis.

B-lines have special interest to nephrologists, as their presence is strongly correlated with EVLW [9]. The reported sensitivity and specificity of diffuse bilateral anterior B-lines for detecting pulmonary edema in the acutely dyspneic patient is 97% and 95%, respectively, when compared with expert clinical review [10]. In dialysis patients, reduction in B-line number following dialysis correlates with volume of ultrafiltration and weight reduction [11].

Agricola et al. [9] compared the number of B-lines to pulmonary capillary wedge pressure (PCWP) and EVLW determined by thermodilution. They demonstrated a direct, statistically significant, relationship between B-lines and both PCWP (r = 0.48, P = 0.001) and EVLW (r = 0.42, P = 0.001) [9]. Trezzi et al. showed that B-line number is statistically significantly reduced after dialysis [12]. Linear regression showed that pre-dialysis B-line number directly correlates to interdialytic weight gain and that B-lines directly correlate with weight loss after dialysis. This study corroborated the earlier study by Noble et al. [11] that showed real-time B-line reduction during hemodialysis (HD).

In 2012, the International Consensus Conference on Lung Ultrasound described a method for quantifying B-lines [13]. Their recommended method for determining B-line pattern requires the operator to scan eight separate intercostal spaces. The presence of three or more B-lines in one intercostal space defines a positive region. A more comprehensive examination includes scanning 28 intercostal spaces and tallying the number of B-lines seen, also known as the B-line score (BLS). For clinical application, the former method is preferred while the latter method has been used in research studies. A quantitative assessment of B-line number may not be required for effective frontline clinical assessment. A pragmatic bedside approach is for the examiner to use a qualitative approach by scanning a number of rib interspaces for rapid assessment of B-line pattern.
using a scan line approach. The ultrasonography probe is moved in cephalad to caudal direction while examining adjacent rib spaces in the midclavicular, anterior axillary and posterior axillary lines for presence and distribution of $B$-lines.

### Evaluation of EVLW with lung ultrasonography—a review of the evidence

There is no objective gold standard to determine target weight and volume status in dialysis patients. Many objective tools have been studied but none has been widely adapted. We conducted a review of the literature on lung ultrasonography to assess EVLW in patients with ESRD with the following objectives: (i) to compare lung ultrasonography to other methods of measuring EVLW and volume status in patients undergoing dialysis and (ii) to describe methods of training clinicians in lung ultrasonography. Searches were conducted in MEDLINE (1946–2016), Embase (1947–2016), Cochrane and Web of Science (1900–2016). An experienced health information specialist developed search strategies using terms to identify studies of ultrasonography use in dialysis patients. Our search strategy is presented in Supplementary Appendix S1.

Studies were eligible if they were cohort studies or randomized controlled trials that described original data with all of the following: (i) five or more adults (age $\geq 18$ years) with ESRD on chronic dialysis, (ii) measured and reported lung ultrasonography findings and (iii) reported another outcome measure of volume status. The exclusion criteria were: (i) the study did not include lung ultrasonography or inferior vena cava (IVC) assessment, (ii) the study did not include exclusively ESRD patients on chronic dialysis, (iii) the population included acute kidney injury (AKI) or chronic kidney disease not on renal replacement therapy, (iv) $n < 5$, (v) the study included children <18 years of age, (vi) the study was a narrative or editorial, (vii) an animal study, (viii) was a duplicate not previously recognized, (ix) there were no extractable or original data or (x) there was no outcome of interest. Citations considered potentially relevant based on the pre-specified inclusion criteria were retrieved in full-text. Full-text article screening was conducted independently and in duplicate (D.W.R. and M.M.A.), with discrepancies resolved by a third reviewer (A.T.M.). A standardized form was used to extract data on number of patients, study duration and definitions of volume status outcomes, as well as lung ultrasonography teaching methodology. The search identified 1249 articles of potential interest. A flow diagram of our search is shown in Supplementary Appendix S1. Twelve articles were designated as appropriate for review.

Table 1 outlines the 12 articles we reviewed [11, 12, 14–23]. Ten of these studies patients undergoing HD; two of these reports studied patients undergoing peritoneal dialysis (PD). Lung ultrasonography to assess EVLW was compared with IVC size in three studies, with bioelectrical impedance analysis (BIA) in eight studies, with brain-natriuretic peptide (BNP) in three studies, with New York Heart Association (NYHA) class in six studies and with subjective dyspnea in one study.

| Author            | Country | Year | n  | Dialysis modality | Other measurement of volume assessment | Exclusion criteria                                                                 |
|-------------------|---------|------|----|-------------------|----------------------------------------|----------------------------------------------------------------------------------|
| Noble et al. [11] | USA     | 2009 | 40 | HD                | Subjective dyspnea                     | None                                                                             |
| Mallamaci et al. [14] | Italy    | 2010 | 75 | HD                | NYHA Class, BIA                       | None                                                                             |
| Trezzi et al. [12] | Italy    | 2013 | 41 | HD                | IVC                                    | Interstitial lung disease, NYHA class IV                                        |
| Panuccio et al. [15] | Italy    | 2012 | 88 | PD                | NYHA class, BIA                       | None                                                                             |
| Basso et al. [16] | Italy    | 2013 | 30 | HD                | BIA, NYHA, pro-BNP                    | Interstitial lung disease, NYHA class IV                                        |
| Siriopol et al. [17] | Romania | 2013 | 96 | HD                | BIA, NYHA                             | Cancer, pacemakers, cardiac stents, amputation, decompensated cirrhosis         |
| Zoccali et al. [18] | Italy    | 2013 | 392| HD                | NYHA                                  | None                                                                             |
| Vitturi et al. [19] | Italy    | 2014 | 71 | HD                | BIA, IVC                              | Interstitial lung disease, NYHA class III/IV                                     |
| Donadio et al. [20] | Italy    | 2015 | 31 | HD                | BIA, pro-BNP                          | Interstitial lung disease                                                       |
| Paudel et al. [21] | UK      | 2015 | 27 | PD                | BIA, pro-BNP                          | None                                                                             |
| Saad et al. [22]   | USA     | 2015 | 41 | HD                | NYHA class                            | None                                                                             |
| Siriopol et al. [23] | Romania | 2016 | 173| HD                | BIA                                   | Cancer, pacemakers, cardiac stents, amputation, decompensated cirrhosis         |

Table 2 displays results for studies comparing lung ultrasonography with BIA. BIA is a technology where electrodes are placed on a patient’s body and an electrical current is used to assess the patient’s body water composition. Studies comparing lung ultrasonography with BIA in HD patients demonstrate conflicting results. In one study of 75 maintenance HD patients in 2010, Mallamaci et al. [14] found that BLS before HD is not correlated with hydration status determined by BIA. About half of the patients in this study who were ‘normohydrated’ by BIA exhibited signs of severe lung congestion by BLS. Echocardiographic data from this study showed a strong correlation between BLS and left ventricular ejection fraction and pulmonary artery pressure. In contrast to the Mallamaci study, four studies report that higher BLS correlates with hydration status by BIA [16, 17]. The studies by Basso et al. and Siriopol et al. found that patients who are ‘overhydrated’ by BIA are statistically more likely to have higher BLS. Donadio et al. [20] aggregated BIA values pre- and post-dialysis as well as BLS pre- and post-dialysis. They report that extracellular water and total body water, but not intracellular water, are significantly correlated with BLS. It is unclear why the Mallamaci study came out with different results than the other studies listed in Table 2. Sample sizes and patient population were similar to other studies. It should be noted that while these data are suggestive that BIA and BLS are comparable for volume assessment there was marked heterogeneity between studies in how lung congestion and BIA were reported. Two studies compared BIA with lung ultrasonography in PD patients [15, 21]. Both demonstrate that ‘hyperhydration’ by BIA does not correlate with BLS. The results from the two PD studies should be interpreted with caution. The number of B-lines seen in the Paudel study for instance was markedly lower compared with those in the HD studies.

Three studies in HD patients compared BLS with IVC parameters. Trezzi et al. performed lung ultrasonography and IVC measurements.
ultrasonography pre- and post-dialysis [13]. They identified that BLS is reduced after dialysis and that this reduction correlates with weight loss (P < 0.05). The mean number of B-lines before dialysis was 24 and after dialysis was 9 (P < 0.001). Pre- and post-dialysis there was no difference in IVC index. Both IVC diameter and BLS correlated with accumulated interdialytic weight. The reduction in IVC size post-dialysis did not correlate with weight reduction after dialysis, and they reported no relationship between change in IVC size and change in BLS. B-lines and IVC correlated with accumulated weight and volume overload before dialysis. B-lines but not IVC measurements correlated with weight reduction and volume status variation after dialysis. In agreement with these results, Basso et al. [16] found that BLS, BIA hydration status and IVC maximum diameter all correlate pre-dialysis but that only BLS and BIA remain correlated after dialysis.

Four studies in HD patients and one study in PD patients compared BLS with NYHA class. All studies in HD patients reported a positive correlation between BLS and NYHA class (Table 3) [14, 15, 17, 18, 22]. Three studies compared lung ultrasonography with BNP. Two studies found direct correlation between BNP and BLS, one in PD patients and the other in HD patients [20, 21].

The evidence showed concordance between EVLW determined by BLS and by BIA in HD patients. BLS correlates with symptomatic dyspnea assessed by NYHA class. IVC metrics are informative for assessing pre-dialysis fluid overload but are inferior to BLS for estimating rapid volume status variation. One proposed explanation is that intravascular space takes time to equilibrate. If IVC metrics were rechecked hours after HD they may reflect weight reduction or ultrafiltration volume [21]. We conclude that lung ultrasonography is more useful than IVC ultrasonography for titrating ultrafiltration prescription (Table 4).

Eight studies reported on lung ultrasonography education [11, 12, 14–16, 18, 19, 22]. Table 5 shows that lung ultrasonography was typically performed by trained physicians. Training sessions were between 2 and 3 h [14, 15, 18, 22]. No study showed any difference between novice and expert lung ultrasonographers. The reported time to perform a lung ultrasonography examination was between 6 and 15 min [11, 12, 16].

The studies in our review have limitations. Notably, 10 studies had fewer than 100 patients. There was variability in the way lung

| Author                        | IVC size (mean) | BLS (mean) | Significance                                                   |
|-------------------------------|-----------------|------------|----------------------------------------------------------------|
| Trezzi et al. [12]            | Pre-HD = 1.6 cm  | Pre-HD = 25| AIVC versus ∆BLS, P = 0.28                                      |
|                               | (end expiratory) | Post-HD = 9|                                                                |
| Basso et al. [16]             | Pre-HD = 0.6 cm  | Pre-HD = 20| Pre-HD correlation: r = 0.39, P < 0.05                         |
|                               | (end expiratory) | Post-HD = 13|                                                                |
| Vitturi et al. [19]           | Pre-HD = 1.7 cm  | Pre-HD = 3 | Correlation between B-line reduction IVC reduction: β = 0.28, P < 0.05 |
|                               | (end expiratory) | Post-HD = 1 |                                                                |

Table 2. BIA studies comparing lung ultrasonography to bioelectrical impedance analysis

| Author                      | Hydration status | BLS before HD | Significance |
|-----------------------------|------------------|---------------|--------------|
| Mallamaci et al. [14]       | Hydration status |                |              |
|                             | Overhydrated     | 20            | P = 0.35     |
|                             | Normohydrated    | 17            |              |
|                             | Hypohydrated     | 15            |              |
| Panuccio et al. [15]        | % Overhydrated   |               |              |
|                             | <15              |               |              |
|                             | 15–30            |               |              |
|                             | >30              |               |              |
|                             | % Overhydrated   | 9             | P = 0.79     |
|                             |                  | 15            |              |
|                             |                  | 11            |              |
| Basso et al. [16]           | Hydration status |                |              |
|                             | Overhydrated     | 20b           | P < 0.001    |
|                             | Normohydrated    | 12            | P < 0.05     |
|                             | Hypohydrated     | 9             |              |
| Siriopol et al. [17]        | Mean residual weight |            |              |
|                             | –0.23 kg         | 1 (mean)      |              |
| Vitturi et al. [19]         | Mean residual weight |          |              |
|                             |                   | BLS after HD  |              |
| Donadio et al. [20]         | ECWIc            |               |              |
|                             | Pre-HD = 41 L (mean) |      |              |
|                             | Post-HD = 38 L (mean) |     |              |
| Paudel et al. [21]          | BLS              |               |              |
|                             | 0                | 1–5           | P = 0.19     |
|                             | 0.7              | >5            |              |
|                             | 0.9              |               |              |
|                             | 1.6              |               |              |
| Siriopol et al. [23]        | Relative fluid overload by BIA (%)d |      |              |
|                             | Overhydration (L, mean) |     |              |
|                             |                   | BLS (mean)    |              |

Table 3. IVC studies comparing lung ultrasonography to inferior vena cava size

\[b\]Composite of pre- and post-HD values.
\[c\]Composite of all hydration status pre-HD.
\[d\]Authors also looked at total body water index (TBWI) and intracellular water index (ICWI) and TBWI also correlated with BLS.
ultrasonography was performed. Eleven of 12 studies measured 28 intercostal spaces whereas one study examined 57 intercostal spaces [20]. Exclusion criteria varied by study. Some studies used interstitial lung disease as an exclusion criteria and others did not. Studies where BIA was performed excluded patients with decompensated cirrhosis, mechanical pacemakers and limb amputations. Dialysis patients have multiple comorbidities so studies with rigorous exclusion criteria may have limited generalizability.

Lung ultrasonography as a prognostic tool

BLS reliably estimates EVLW and patients with higher BLS have more severe symptoms. Two studies reported an association between BLS and mortality [18, 23]. Zoccali et al. followed patients for a median of 2.1 years and report that patients with severe lung congestion (BLS >60) have a 4.2-fold increased risk of death compared with those without severe congestion. In a multivariate analysis, NYHA symptomatic class was not associated with mortality, while severe lung congestion had a statistically significant association [hazard ratio (HR) 3.04; 95% confidence interval (CI) 1.73–5.35; P-value <0.001]. Seventy percent of patients with moderate to severe lung congestion (BLS >15) did not have significant symptoms. It is possible that B-lines detect sub-clinical EVLW that still confers risk. Siriopol et al. [23] studied 173 HD patients for a median of 1.8 years. After adjusting for NYHA class, diabetes, high sensitivity C reactive protein (hs-CRP) and left ventricular mass index (LVMI), EVLW (BLS >22) carried an increased risk of death (HR = 2.72; 95% CI 1.19–6.16).

Zoccali et al. [18] reported a significant risk reclassification for cardiac events of 10% when BLS is added to a model

| Author                  | Lung congestion on ultrasound | Degree | Significance |
|-------------------------|-------------------------------|-------|-------------|
| Mallamaci et al. [14]   | NYHA III or IV                | Mild  | 11%          |
|                         |                               | Moderate | 23%          |
|                         |                               | Severe | 48%          |
| Panuccio et al. [15]    | NYHA III or IV                | Mild  | 15%          |
|                         |                               | Moderate | 10%          |
|                         |                               | Severe | 24%          |
| Siriopol et al. [17]    | NYHA III or IV                | Mild  | 28%          |
|                         |                               | Moderate | 21%          |
|                         |                               | Severe | 75%          |
| Zoccali et al. [18]     | NYHA III or IV                | Mild  | 24%          |
|                         |                               | Moderate | 29%          |
|                         |                               | Severe | 51%          |
| Saad et al. [22]        | NYHA                          | Data not presented | |

Table 4. Studies comparing lung ultrasonography to New York Heart Association Class

| Author                  | Performed lung ultrasound | Interpreted lung ultrasound | Training course | Inter-observer agreement | Intercostal sites examined | Minutes to perform |
|-------------------------|----------------------------|-----------------------------|-----------------|--------------------------|----------------------------|-------------------|
| Noble et al. [11]       | Emergency medicine physicians with >1-year experience | Not stated | Not stated | Only one performer | 28 | 10–15 |
| Mallamaci et al. [14]   | Not stated | One nephrology trainee | 2-h practical training course | Concordance index = 0.83 (95% CI 0.60–0.93) | 28 | Not stated |
| Trezzi et al. [12]      | Two physicians trained in lung ultrasound | Two physicians trained in lung ultrasound | Not stated | Inter-observer variability 0.96 (P < 0.01) | 28 | <10 |
| Panuccio et al. [15]    | Not stated | One operator at each center | 2-h practical training course | Not reported | 28 | Not stated |
| Basso et al. [16]       | Two nephrologists | Two nephrologists | Not mentioned | Inter-observer variability 0.991 (P < 0.001) | 28 | Average 6.4 |
| Siriopol et al. [17]    | Not stated | Not stated | 2 to 3-h training course | Not stated | 28 | Not stated |
| Zoccali et al. [18]     | Nephrologists | Blinded observer | Not stated | Estimates between nephrologists were within 10% | 28 | Not stated |
| Vitturi et al. [19]     | Two physicians | A third trained physician | Not stated | Not stated | 28 | Not stated |
| Donadio et al. [20]     | Not stated | Not stated | Not stated | Not stated | 57 | Not stated |
| Paudel et al. [21]      | Not stated | Not stated | Not stated | Not stated | 28 | Not stated |
| Saad et al. [22]        | Internal medicine and emergency medicine residents | Residents and emergency medicine physicians | Not stated | No significant difference between residents and attendings | 28 | Not stated |
| Siriopol et al. [23]    | Not stated | Not stated | Not stated | Not stated | 28 | Not stated |

Table 5. How lung ultrasound was taught
The importance of teaching lung ultrasonography

Table 3 shows that lung ultrasonography can be reliably taught to learners. Saad et al. trained internal medicine and emergency medicine residents. In their study, they found that there was no difference between experts and residents. Mallamaci et al. gave a 2-h teaching session to a nephrology fellow and reported a high concordance between trainee and expert. In preparation for the LUST trial, Gargani et al. [24] (published after literature review) taught physicians to perform lung ultrasonography and quantify B-lines. Thirty physicians were educated using a web-based curriculum. Their ability to count B-lines is accurate compared to an expert sonographer (r = 0.979, P < 0.0001).

Point of care lung ultrasonography training is an ACGME requirement for critical care fellows and medical schools are following their lead. A consensus of 34 medical educators identified 90 core clinical milestones for ultrasonography allopathic and osteopathic students before graduation. Lung ultrasonography performance and interpretation are included in those core competencies. As emergency medicine physicians, intensivists and graduating medical students rely more on lung ultrasonography, nephrologists will need to ‘speak the same language’. In our institution, Northwell Health, lung ultrasonography is practiced routinely in the intensive care unit and affects decision-making around need for ultrafiltration. Based on our experience, we encourage nephrology fellowship program directors to incorporate ultrasonography into fellowship training.

Using collaborative expertise from nephrology and critical care faculty, we have developed a 4-h practical training course on lung ultrasonography for nephrology fellows and faculty members of the nephrology division. In our experience, this short course is sufficient to attain basic proficiency, and we advocate refresher courses on a yearly basis to retain and hone ultrasonography skills.

Future directions

The optimal method to train the attending nephrologists and nephrology fellows in lung ultrasonography has not been determined. Based on our experience, a 4-h course that includes pre-course cognitive preparation, a didactic lecture and training in image acquisition/interpretation are sufficient to give the learner a strong foundation in both lung ultrasonography and renal ultrasonography. These two subjects are productively combined into one introductory course. The course alone is not sufficient to provide competence. Competence in lung ultrasonography and renal ultrasonography requires additional bedside scanning of patients under the supervision of capable faculty. Ultrasonography is still nascent in nephrology practice in the USA. This provides the opportunity to develop a standardized curriculum that could be developed at a national level round-table meeting by professional societies. This would assure a uniform standard for competence, and avoid the situation where each training program developed its unique training sequence. Use of a standardized approach to training and a uniform definition of competence allows for derivative research on the best design of the course, requirements for follow-through point of care training and development of formal testing of competence.

The role of lung ultrasonography in nephrology practice requires further research regarding its clinical applications.
(i) What is the role of lung ultrasonography in the management of AKI in the intensive care unit? Could it be used as an endpoint for continuous renal replacement therapy?
(ii) Given the association of mortality with the presence of B-lines in the chronic dialysis population, what is the role of lung ultrasonography in the management of the patient on chronic HD? Could B-lines be used to guide need for increased ultrafiltration and would this change long-term outcome?
(iii) Could lung ultrasonography be used to guide diuretic therapy in patients with chronic cardiorenal syndrome?
(iv) As B-lines detect subclinical volume expansion, could lung ultrasonography be useful in differentiating hypervolemic from euvolemic hyponatremia?

Conclusions

Lung ultrasonography can be used to assess EVLW in chronic dialysis patients; quantifying lung congestion by BLS has prognostic value. These have clinical implications for management of patients with ESRD. Teaching lung ultrasonography to our nephrology trainees is an important step to improve care collaboration with our critical care and emergency medicine colleagues. We favor development of a standardized approach to training the nephrology community in lung ultrasonography and renal ultrasonography, as this would facilitate widespread competence in the field and would facilitate research to better define clinical applications of ultrasonography in nephrology practice.

Supplementary data

Supplementary data are available online at http://ckj.oxfordjournals.org.

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Conflict of interest statement

None declared.

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