HOW TO ASSESS LUNG CONGESTION IN DIALYSIS PATIENTS:
LUST AN ERA-EDTA SUPPORTED STUDY
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Slide 1

Disclosure of Interest
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Slide 2
As kidney function declines, the heart becomes bigger and bigger. This is the central paradigm of cardiovascular and renal medicine. In dialysis patients LVH is rampant 80% of patients have LVH and the geometric pattern may be eccentric in half of patients or concentric in the other half.
In functional terms eccentric hypertrophy causes scarce contraction,

Slide 5

scarce emptying whilst in concentric LVH thick walls reduces left ventricular compliance.

Slide 6
However, please note that in both geometric forms the effect is the same, high left ventricular and diastolic pressure.

Slide 7

Now we all know these facts very well but we ignore or do not think enough that the heart is just part of a system, the lung-heart system.

Slide 8
Let's briefly elaborate on this system. Right atrium, right ventricle, pulmonary artery, capillaries and you know how important capillary pressure in the lung is, pulmonary veins and left atrium.

Slide 9

I said capillary pressure is important. In order to measure capillary pressure we should inflate a balloon in the pulmonary artery, in an arteriole of the pulmonary artery. Once the balloon is inflated, the pressure in the pulmonary veins in the atrium equalise with that in the capillaries and this is capillary wedge pressure.

Slide 10
Capillary wedge pressure is high in LV disorder, be it due to systolic or diastolic dysfunctions. This is hemodynamic congestion. The lung may be clean, pulmonary pressure is high but we all know that this may translate also into pulmonary congestion that is the lung may be inundated by water and we know that the frequency of pulmonary oedema in our dialysis patients is quite high.
In part this depends on the fact that permeability in the lung in ESRD, as well as in acute kidney failure, is altered, it is higher than normal.

The fact that there is the propensity to pulmonary oedema in dialysis patients is high is not new. This is a paper from Wallin in 1996. The authors of this paper concluded their investigation by saying that they verified that the oedema, which was removed by dialysis in a group of patients with established renal failure, was not explained solely by high hydrostatic pressure.
But let’s look into some detail at this study and the method they used. They applied stable isotope heavy water and another marker indocyanine green. Therefore, it was a double marker measurement.

Therefore, this was a complex study and for this reason, it was based just on 10 patients.
If it was doable, large-scale measurements of pulmonary water may be useful in clinical practice.

Slide 17

In reality, we can measure pulmonary water based on a simple x-ray of the thorax. As you know, the Kerley B-lines are an expression of water accumulation in the lung. But doing x-rays is complex. You should bring the patient to the radiology department and not only are they complex but they are also risky, you expose your patients to x-rays and you cannot do this as often as you may want.

Slide 18
The novelty is that now you can measure B-lines,

Slide 19

Kerley B lines by ultrasound, by whatever Ultrasound machine you have in your unit. I say whatever, even the probe that you use to do renal biopsy for example, that would be good to get the number of Kerley B-lines by ultrasound.

Slide 20
This is the image of a normal lung.

Slide 21

On the left side you have the ultrasound image, just black. This is due to the fact that the ultrasound beam has no difficulty in passing through the normal interlobular Septa.

Slide 22
This is the picture of pulmonary oedema. You see these are the ultrasound B-lines that are also called lung comets. These comets are formed because the ultrasound beam meets in its way to the lung thickened interlobular sectors and therefore, the beam is reflected back and generates this line.

Now measuring B-lines is easy and fast. This technique can be learned in 2 hours and it takes just 5 minutes to perform the examination.

I will better qualify this statement later on.
But let’s see if ultrasound water B-lines reflect lung water. This slide shows the relationship between lung water measured by thermodilution, standard, the golden standard method and US-B-lines. As you can see, there is a reasonably good correlation.

Slide 25

The shear variance is 16% but the data points are spread. So you may object that the method is not good but you should try to understand why the inter points are so spread.

Slide 26
The reason depends on the golden standard. The golden standard has a 10-15% reproducibility.

while the reproducibility of the new method is 5%.
I said that measuring B-lines is easy and fast. But let’s better qualify this statement.

Francesca Mallamaci from my group did a study and the study started with the validation of the method specifically in dialysis patients as she compared the measurement made by a seasoned technician with that made by a young trainee. The young trainee after just two hours of training.

The graph that you see here is a standard Altman-Bland graph and as you know, the data point in order for the method to be defined ‘good’ should be within the two standard deviations.
These are the data points, just two points outside the two standard deviations and the concordance index was 0.96 which is considered very high.

But I also said that you can do the examination with whatever machine you have in your department, either the ultrasound machine you use for doing renal biopsy or a sophisticated machine you use for doing Doppler studies. When we compared probes, the concordance was even higher, 0.98.
Therefore, I think that this proves that the technique is reliable and as far as reproducibility goes, it makes sense to apply it in clinical practice.

But let's see in the lung congestion dialysis patients. In this paper lung congestion was classified as moderate and severe based on the number of lung comets.
35 patients had moderate lung congestion, as much as 28% had severe lung congestion.
Let's look now at the relationship between B-lines and the hydration status as measured by BIA.

As you can see no relationship. Hypo, normal and hyper hydrated patients had a similar number of lung comets. This lack of correlation clearly suggests that left ventricular dysfunction is a fundamental driver of lung congestion in end stage kidney disease patients. I will show a slide later on proving this statement.
Post-dialysis. Post-dialysis, the number of lung comets or B-lines, call them as you want, went down. It halved the prevalence of moderate and severe lung congestion, halved but please note that the prevalence was higher than the prevalence you may find in normal healthy subjects.

Slide 39

Now lung congestion is a reversible phenomenon.

Slide 40
You can remove water by dialysis but lung congestion is also a predictable phenomenon. In fact, lung comets change across dialysis depending on pre-dialysis lung comets. The more comets, B-lines you have before dialysis, the more water is removed from the lung.

Of course, you expect lung congestion to be linked to symptoms and to impaired physical performance.
Giuseppe Enia, also from my group, looked into this problem in peritoneal dialysis patients and found that there is a strong association between the two but the study was small, 51 patients.

Therefore, these authors expanded their observation to haemodialysis. This study is much larger, 270 patients.
This is the association between the number of lung comets and physical performance as measured by the kidney disease quality of life instrument.

Slide 45

The higher the number of lung comets, the lower the physical performance. You may object but lung comets depend on left ventricular dysfunction and so you are showing just an association between lung comets and heart failure.

Slide 46
In reality, as you may expect, when we looked at the association between New York Heart Association Class and physical performance, we found an inverse relationship. So heart failure may be a confounder for the interpretation of lung comets or B-lines, call them as you want. Therefore, you need to make adjusted analysis to see whether the association is independent or not from NYHA class. Here as you can see we made multivariate logistic regression and found that ultrasound B-line predicts physical performance independent of NYHA class and it was the fourth factor in rank explaining reduced physical performance.

Now why do B-lines predict physical performance? Because they convey information about left ventricular function.
In fact, the number of B-lines at echocardiography is inversely associated to left ventricular systolic function. The higher the number the lower the ejection fraction. Similar associations, but positive of course, were found with atrial volume and pulmonary pressure.

But a biomarker needs to be useful also for prognosis. For this reason, we performed a multicentre cohort study in 11 nephrology units and the results were published early this year in JASN.
As you can see the higher the number of B-lines the lower survival and the lower survival free from cardiovascular events time.

Slide 51

Now let’s look at the same problem that is prognosis with the ROC curve analysis. A model based on classical risk factors Enia explained 76% of the prognostic power in dialysis patients.

Slide 52
When we added to these factors also lung comets, the power went up to 78%, just a small gain but statistically significant. Other independent analyses based on reclassification showed that we gain 10% in reclassification when we analyse, when we measure lung comets and try to make a prognosis. 10% is not trivial at all. So this analysis indicated that validating lung comets in a clinical trial would be a truly worthy undertaking.

Slide 53

EURECA-m have designed a trial. In this trial 500 high risk patients will be randomised to treatment guide by lung ultrasound and standard treatment. Patients will be followed up for 2 years. The study endpoints are based on a composite endpoint of death, myocardial infarction and heart failure, hospitalisation and also on echocardiographic
changes of critical echocardiographic variables like left ventricular volume, systolic, diastolic function and left ventricular mass.

Let’s now give a summary and conclusion.
Pulmonary congestion commonly occurs both in asymptomatic and symptomatic dialysis patients. Lung ultrasound provides reliable information on the degree of pulmonary congestion and may be useful to prevent and treat cardiopulmonary congestion in these patients. Finally, the usefulness of this technique cannot be taken for granted, for this reason it is being tested in a clinical trial. Thank you for your attention.