



**HAL**  
open science

## Prognostic Value and Therapeutic Utility of Lung Ultrasound in Acute and Chronic Heart Failure

Tripti Rastogi, Erwan Bozec, Pierpaolo Pellicori, Antoni Bayes-Genis, Stefano Coiro, Mar Domingo, Luna Gargani, Alberto Palazzuoli, Nicolas Girerd

► **To cite this version:**

Tripti Rastogi, Erwan Bozec, Pierpaolo Pellicori, Antoni Bayes-Genis, Stefano Coiro, et al.. Prognostic Value and Therapeutic Utility of Lung Ultrasound in Acute and Chronic Heart Failure. *JACC: Cardiovascular Imaging*, 2022, 15 (5), pp.950-952. 10.1016/j.jcmg.2021.11.024 . hal-03698090

**HAL Id: hal-03698090**

**<https://hal.univ-lorraine.fr/hal-03698090>**

Submitted on 17 Jun 2022

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial - NoDerivatives | 4.0  
International License

# **Prognostic value and therapeutic utility of lung ultrasound (LUS) in acute and chronic heart failure: a meta-analysis**

**Short Title:** LUS in heart failure: a meta-analysis

Tripti Rastogi M.D.<sup>a</sup>, Erwan Bozec Ph.D.<sup>a</sup>, Pierpaolo Pellicori M.D.<sup>b</sup>, Antoni Bayes Genis M.D., Ph.D.<sup>c</sup>, Stefano Coiro M.D., Ph.D.<sup>d</sup>, Mar Domingo M.D., Ph.D.<sup>c</sup>, Luna Gargani M.D., Ph.D.<sup>e</sup>, Alberto Palazzuoli M.D., Ph.D.<sup>f</sup>, Nicolas Girerd M.D., Ph.D.<sup>a</sup>

<sup>a</sup> Université de Lorraine, Centre d'Investigations Cliniques Plurithématique 1433, Institut Lorrain du Cœur et des Vaisseaux Louis Mathieu, CHRU de Nancy, INSERM DCAC, F-CRIN INI-CRCT, Nancy, France

<sup>b</sup> Robertson Institute of Biostatistics and Clinical Trials Unit, University of Glasgow, Glasgow, UK

<sup>c</sup> Department of Medicine, Autonomous University of Barcelona, Barcelona, Spain

<sup>d</sup> Cardiology Department, Santa Maria della Misericordia University Hospital, Perugia, Italy.

<sup>e</sup> Institute of Clinical Physiology, National Research Council, Pisa, Italy

<sup>f</sup> Cardiovascular Diseases Unit Department of Internal Medicine, University of Siena, Siena, Italy

## **Corresponding author:**

Nicolas Girerd

Centre d'Investigation Clinique Pierre Drouin -INSERM - CHRU de Nancy, Institut lorrain du cœur et des vaisseaux Louis Mathieu, Nancy, France.

4, rue du Morvan. 54500 Vandœuvre-Lès-Nancy

E-mail: n.girerd@chru-nancy.fr

Phone: +33383157496

Fax: +33383157324

**Acknowledgements:**

Dr Girerd is supported by the French National Research Agency Fighting Heart Failure (ANR-15-RHU-0004), by the French PIA project Lorraine Université d'Excellence GEENAGE (ANR-15-IDEX-04-LUE) programs, and the Contrat de Plan Etat Région Lorraine and FEDER IT2MP and reports honoraria from AstraZeneca, Bayer, Boehringer, Lilly, Novartis, and Vifor. Dr Gargani is supported by Italian Ministry of Health and Regione Toscana and reports personal fees from GE Healthcare, Phillips Healthcare and Caption Health. Dr Bayes-Genis reports grant and non-financial support from Boehringer-Ingelheim and personal fees from Abbott, AstraZeneca, Bohringer-Ingelheim, Novartis, Vifor, Roche Diagnostics, Critical diagnostics. Tripti Rastogi, Erwan Bozec, Pierpaolo Pellicori, Mar Domingo, Alberto Palazzuoli declared no conflict of interest.

**Abbreviations:**

CV, cardiovascular

HF, heart failure

LUS, lung ultrasound

LVEF, left ventricular ejection fraction

RR, risk ratio

Congestion drives the risk of hospitalization in heart failure (HF). Accurate and early identification and quantification of congestion could improve management, thereby leading to lower risk of poor outcomes (1). Lung ultrasound (LUS) is a quick and reliable imaging technique, based on the counts of B-lines, to assess clinical and subclinical pulmonary congestion. In this meta-analysis, we studied the prognostic value of B-lines and the treatment effect of LUS-guided therapy on cardiovascular (CV) outcomes in HF.

We conducted a systematic search of the published data in PUBMED/Medline using the keywords “lung ultrasound” AND “heart failure” AND “prognosis” for the period from 2010 to May 2021. Twelve studies assessing the prognostic value (2,293 patients) and three trials (493 patients) evaluating LUS-guided management in HF were finally included (mean LVEF range: 30 to 60%) (Figure 1(A)). Thereafter, studies on prognosis were grouped according to the clinical setting: 1) out-patient clinic, 2) at admission, and 3) at discharge for HF hospitalizations (Figure 1(B)). Clinical trials assessing LUS-guided therapy were analysed separately (Figure 1(C)).

We conducted a fixed-effect meta-analysis. Based on recommendations of available published literature, the following cut-offs for pooling the risk estimates were used:  $\geq 15$  in 28 zones ( $\sim 0.5$  B-line/zone);  $\geq 3$  in 5-8 zones ( $\sim 0.4$  B-line/zone);  $\geq 4$  in 4 zones (1 B-line/zone) LUS (1,2). Additionally, the RR for studies reporting 8 or more zone LUS was calculated to assess the effect size when maximizing the congruence of the thresholds of B-lines per zone in the discharge group. Authors were contacted for RR associated with pre-selected cut-offs if needed. In the clinical trials, B-lines  $\geq 3$  using 8 zone method was considered as significant for congestion in two studies (Figure 1(C)).

For most of the studies, the primary outcome was a composite of hospitalization for HF and all-cause mortality; two studies also reported urgent visits for worsening of HF. LUS-

guided treatment effect was evaluated by pooling the adjusted RR of primary outcome and hospitalization for HF from clinical trials. All analyses were conducted in R (v4.0.3).

A higher number of B-lines was associated with an increased risk of primary outcome irrespective of the setting (out-patient clinic: RR=1.66, 95%CI: 1.28-2.15,  $p=0.0001$ ,  $I^2=57.5\%$ ; at admission: RR=2.32, 95%CI: 1.46-3.70,  $p=0.0004$ ,  $I^2=50.92\%$ ; at discharge: RR= 2.46, 95%CI: 1.56-3.86,  $p=0.0001$ ,  $I^2=0.00\%$ ) (Figure 1(B)). In sensitivity analysis, we included all the tertiles from Platz et al., study in discharge group and the results did not change (RR=2.60, 95%CI: 1.77-3.83,  $p<0.001$ ,  $I^2=0.00\%$ ). When 8 or more zones were used to assess B-lines at discharge, the increase in the risk of hospitalization for HF or death was similar (RR=2.47, 95%CI: 1.55-3.93,  $p<0.0001$ ,  $I^2=3.50\%$ ).

In clinical trials, the pooled RR for the primary outcome (urgent visits for worsening of HF, hospitalization for HF and mortality) and for hospitalization for HF was 0.50 (95%CI: 0.35-0.72,  $p=0.001$ ,  $I^2=0.00\%$ ) and 0.62 (95%CI: 0.40-0.87,  $p=0.007$ ,  $I^2=41.01\%$ ), respectively (Figure 1(C)). The lower risk of primary composite outcome was reported to be largely driven by a reduction in urgent visits for worsening HF in the studies that included urgent visits in primary outcome.

This analysis provides inclusive results of available literature regarding LUS, combining results from different LUS techniques (4 to 28 zones), study design (cohorts and trials) and settings (out-patient and hospitalized patients). We expand the results of the previous meta-analysis by Platz et al., and Wang et al., by the inclusion of 8 zones LUS and the assessment of the prognostic value of LUS conducted at the time of admission (2,3). Wang et al., reported higher RR compared to our results possibly because of the absence of adjustment for clinically relevant variables (age, sex, NYHA class/LVEF, renal function, NT-pro-BNP and others). The fact that the number of B-lines persisted as a significant prognostic factor even after adjustment further emphasizes the clinical utility of LUS.

In clinical trials, LUS-guided therapy was consistently associated with lower risk of CV events perhaps due to a better optimization of HF therapy in LUS-guided group. However, a recent pilot study BLUSHED-HF did not identify a benefit from LUS-guided therapy versus standard care in acute HF (4). How to best use LUS-guided therapy in HF still needs to be defined.

Our study has two main limitations. First, the number of studies in each setting is limited. Second, significant heterogeneity exists across studies, possibly due to the grouping of different B-lines thresholds from different LUS protocols (different transducer orientation, scoring/counting methods), statistical adjustment and differences in post-discharge care. This heterogeneity reinforces the need for a standardized approach to assess B-lines according to a cut-off specific to each setting.

In conclusion, findings from this meta-analysis support the use of LUS for evaluating the risk of adverse outcome in patients with HF regardless of the clinical setting, and provide evidence in favour of a beneficial effect of LUS-guided management in out-patients.

## References:

1. Girerd N, Rossignol P. Performing lung ultrasound at rest and/or after an exercise stress test to better identify high-risk ambulatory patients with heart failure. *Eur J Heart Fail* 2017;19:1479-1482.
2. Platz E, Merz AA, Jhund PS, Vazir A, Campbell R, McMurray JJ. Dynamic changes and prognostic value of pulmonary congestion by lung ultrasound in acute and chronic heart failure: a systematic review. *Eur J Heart Fail* 2017;19:1154-1163.
3. Wang Y, Shi D, Liu F, Xu P, Ma M. Prognostic Value of Lung Ultrasound for Clinical Outcomes in Heart Failure Patients: A Systematic Review and Meta-Analysis. *Arq Bras Cardiol* 2021.
4. Pang PS, Russell FM, Ehrman R et al. Lung Ultrasound-Guided Emergency Department Management of Acute Heart Failure (BLUSHED-AHF): A Randomized Controlled Pilot Trial. *JACC Heart Fail* 2021;9:638-648.

## Figure Legend

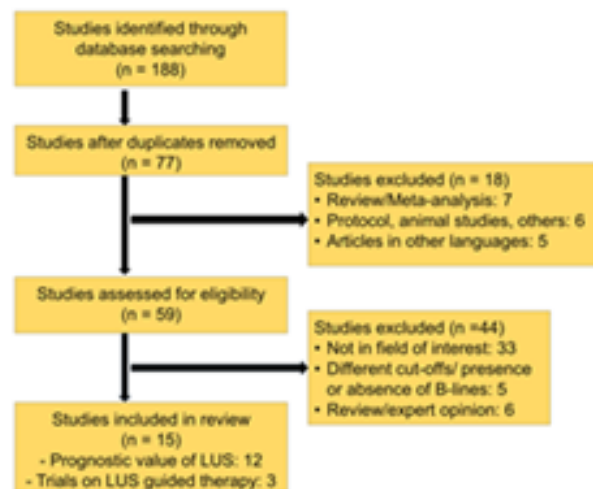
### **Figure 1: Prognostic value of B-lines and therapeutic utility of LUS-guided therapy in patients with HF.**

(A) Literature search results with exclusion criteria (B) Baseline characteristics and pooled risk estimates of the prognostic value of B-lines according to clinical setting of LUS. (C) Baseline characteristics and pooled risk estimates of the primary outcome in patients treated with LUS-guided therapy in clinical trials.



**Figure 1: Systematic review and meta-analysis of Prognostic value and Therapeutic utility of LUS in Heart Failure**

**A**



**C**

Author year	Criteria for significant congestion	FU	Total N	Number in each group	Total events	Death	HHF	Urgent visits	HR/RR (CI)
<b>Clinical trials</b>									
Rivas-Lasarte 2019	≥ 3 in 8 zones	6m	123	control (n=62) LUS (n=61)	25 14	2 3	13 14	13 3	0.518 (0.268-0.998)
Araiza-Garayzorbil 2020	≥ 3 in 8 zones	6m	126	control (n=63) LUS (n=63)	30 20	6 9	8 4	25 9	0.55 (0.30-0.99)
Marini 2019	LUS score based on B-line visualization in each field	3m	244	control (n=117) LUS (n=127)	25 12	4 5	25 12	NA NA	0.44 (0.23-0.84) (RR for HHF)
<b>Overall</b>									0.50 (95% CI: 0.35-0.72) p=0.001, I <sup>2</sup> :0.00%

**B**

Author year	Total	FU*	Lung fields	B-lines >15; >3; >45*	B-lines <15; <45*	Total events	Event details Death HHF	Adjusted HR/RR (CI)*
<b>Out-patients (B-line thresholds: ≥15 in 28 zones; ≥ 3 in 5-8 zones)</b>								
Curbelo 2019	99	12 m	8	NA	NA	36	12 35	1.8 (0.8-4.0)
Dwyer, 2018	119 HF (total=230)	12 m	8	49	70	28 (patients with HF)	10 21	2.62 (1.15-5.96)
Pellicori 2019	342	7.8 m (4.5±11.7)	28	106	236	60	25 35	1.54 (0.68-3.48)
Platz 2016	195	6 m	8	59	126+10 incomplete data	50	15 48	4.08 (1.95-8.54)
Domingo 2020 <sup>1</sup>	577	31±7.1	8	/	/	157	111 74	1.26 (0.89-1.77)
<b>Overall</b>								1.66 (95%CI: 1.28 - 2.15) p=0.0001, I <sup>2</sup> : 57.5%
<b>Admission (B-lines threshold: ≥ 45 in 28 zones)</b>								
Gargani 2015	100	6 m (5.3 ±1.6)	28	NA	NA	14	4 14	4.87 (0.88-27.06)
Coiro 2016	50 (total 110)	3 m	28	19	31	33 in whole cohort	16 26	9.20 (1.82-46.61)
Gargani 2021 <sup>1</sup>	296 (HF) (total=1021)	14.4 m	28	NA	NA	82	40 42	1.90 (1.14-3.16)
<b>Overall</b>								2.32 (95%CI 1.46 - 3.70) p= 0.0004, I <sup>2</sup> :50.92%
<b>Discharge (B-lines thresholds: ≥15 in 28 zones; ≥ 3 in 5-8 zones; ≥ 4 in 4 zones)</b>								
Coiro 2015; 2016	60	3 m	8 & 28	NA	NA	18	10 15	4.1 (0.95-14.63)
Gargani 2015	100	6 m	28	40	60	14	4 14	11.74 (1.3-106.16)
Rivas-lasarte 2020	100 (total 123)	6 m	8	41	59	28	3 19	2.63 (1.08-6.41)
Platz 2019	132 (total 349)	3 m	4&8	71	61	42	13 32	1.45 (0.6-3.46)
Rueda-Camino 2020	103	3m (2.4±0.9)	28	29	74	28	1 27	2.46 (1.11-5.46)
<b>Overall</b>								2.46, 95%CI: 1.56 - 3.86) p=0.0001, I <sup>2</sup> :0.00%

Curbelo DOI: 10.1080/03007995.2018.1519502; Dwyer DOI: 10.1016/j.cardfail.2018.02.004; Pellicori DOI: https://doi.org/10.1002/ehf.1383; Platz DOI: 10.1093/eurheartj/ehv745; Domingo DOI: 10.1016/j.rec.2020.07.006; Gargani DOI: 10.1186/s12947-015-0033-4; Coiro DOI: 10.1038/srep39426; Gargani DOI: 10.1002/ehf2.13206; Coiro DOI: 10.1002/ehf.344; Rivas-lasarte DOI: 10.1002/ehf2.12842; Platz DOI: 10.1016/j.jchf.2019.07.008; Rueda-Camino DOI: 10.1016/j.medcl.2020.03.012; Rivas-Lasarte DOI: 10.1002/ehf.1604; Araiza-Garayzorbil DOI: 10.1016/j.ahj.2020.06.003; Marini DOI: 10.1136/heartjnl-2019-316429

(A) Study flow chart (B) Description of studies included in the review to assess prognostic value of LUS (C) Clinical trials comparing LUS guided treatment in comparison to standard treatment in HF patients. \*B-lines more than 15 in 28 zones LUS or ≥3 in 8 zones LUS in out-patients and discharge patients studies and B-lines ≥45 in admission LUS studies. (\* FU mean or median duration reported in parenthesis; a adjusted hazard ratio presented for selected cut-offs; \$