

Platz, E., Merz, A. A., Jhund, P. S. , Vazir, A., Campbell, R. and McMurray, J. J. (2017) Dynamic changes and prognostic value of pulmonary congestion by lung ultrasound in acute and chronic heart failure: a systematic review. *European Journal of Heart Failure*, 19(9), pp. 1154-1163.

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Deposited on: 04 July 2017

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SECTION 1

Literature search strategy

The search was performed with the assistance of two medical librarians and was updated until July 29, 2016 using the following terms:

PubMed Cardiac: ("Ultrasonography"[Mesh] AND "Lung"[Mesh]) OR ("lung ultrasound"[tw] OR "lung ultrasonography"[tw] OR "pulmonary ultrasound"[tw] OR "pulmonary ultrasonography"[tw] OR "pulmonary sonography"[tw] OR "comet tail"[tw] OR "lung comet"[tw] OR "b lines"[tw]) AND ("Heart Failure"[Mesh] OR "cardiac failure" [tw] OR "cardiac insufficiency"[tw] OR "cardial decompensation"[tw] OR "cardial insufficiency"[tw] OR "cardiac insufficiency"[tw] OR "heart failure"[tw] OR "heart decompensation"[tw] OR "myocardial failure"[tw] OR "myocardial insufficiency"[tw]).

PubMed Dyspnea: ("Ultrasonography"[Mesh] AND "Lung"[Mesh]) OR ("lung ultrasound"[tw] OR "lung ultrasonography"[tw] OR "pulmonary ultrasound"[tw] OR "pulmonary ultrasonography"[tw] OR "pulmonary sonography"[tw] OR "comet tail"[tw] OR "lung comet"[tw] OR "b lines"[tw]) AND ("Dyspnea"[Mesh] OR "dyspnea"[tw] OR "dyspnoea"[tw] OR "shortness of breath"[tw] OR "lung edema"[tw] OR "pulmonary edema"[tw] OR "lung oedema"[tw] OR "pulmonary oedema"[tw] OR "lung congestion"[tw] OR "pulmonary congestion"[tw]).

EMBASE Cardiac: (('lung'/exp AND 'ultrasound'/exp) OR 'lung ultrasonography' OR 'lung ultrasound' OR 'pulmonary ultrasonography' OR 'pulmonary sonography' OR 'pulmonary ultrasound' OR 'comet tail' OR 'lung comet' OR 'b lines') AND ('heart failure'/exp OR 'cardiac failure' OR 'cardiac insufficiency' OR 'cardial decompensation' OR 'cardial insufficiency' OR 'cardiac insufficiency' OR 'heart failure' OR 'heart decompensation' OR 'myocardial failure' OR 'myocardial insufficiency').

EMBASE Dyspnea: (('lung'/exp AND 'ultrasound'/exp) OR 'lung ultrasonography' OR 'lung ultrasound' OR 'pulmonary ultrasonography' OR 'pulmonary sonography' OR 'pulmonary ultrasound' OR 'comet tail' OR 'lung comet' OR 'b lines') AND ('dyspnea'/exp OR 'dyspnea' OR

'dyspnoea' OR 'shortness of breath' OR 'lung edema' OR 'pulmonary edema' OR 'lung oedema' OR 'pulmonary oedema' OR 'lung congestion' OR 'pulmonary congestion').

Web of Science Cardiac: TS= ((lung NEAR ultrasonography) OR (lung NEAR ultrasound) OR (lung NEAR sonography) OR (pulmonary NEAR ultrasonography) OR (pulmonary NEAR ultrasound) OR (pulmonary NEAR sonography)) OR TS=("comet tail" OR "lung comet" OR "b lines") AND TS=("Heart Failure" OR "cardiac failure" OR "cardiac insufficiency" OR "cardial decompensation" OR "cardial insufficiency" OR "cardiac insufficiency" OR "heart decompensation" OR "myocardial failure" OR "myocardial insufficiency").

Web of Science Dyspnea: TS= ((lung NEAR ultrasonography) OR (lung NEAR ultrasound) OR (lung NEAR sonography) OR (pulmonary NEAR ultrasonography) OR (pulmonary NEAR ultrasound) OR (pulmonary NEAR sonography)) OR TS=("comet tail" OR "lung comet" OR "b lines") AND TS=(Dyspnea OR dyspnoea OR "shortness of breath" OR "difficulty breathing" OR "lung edema" OR "pulmonary edema" OR "lung oedema" OR "pulmonary oedema" OR "lung congestion" OR "pulmonary congestion").

Data synthesis

Abstracts and manuscripts were reviewed by 2 investigators (AAM and EP). Discrepancies were resolved by a third reviewer (RTC). Data were tabulated by two investigators (EP, AAM) and authors of studies were contacted in two instances in order to clarify their study methodology.

SECTION 2

Table S1. Metaanalysis of observational studies in epidemiology (MOOSE) checklist

Section/topic	Checklist item	Reported where?
Reporting of background		
	Problem definition	Introduction
	Hypothesis statement	Introduction
	Description of study outcome(s)	Methods
	Type of exposure or intervention used	Methods
	Study population	Methods
Reporting of search strategy		
	Qualifications of searchers	Supplements
	Search strategy, incl. time period included in the synthesis and keywords	Methods & Supplements
	Effort to include all available studies, incl. contact with authors	Supplements
	Databases and registries searched	N/A
	Search software used, name and version, including special features	Methods & Supplements
	Use of hand searching	N/A
	List of citations located and those excluded, incl. justification	References & Figure 1
	Method of addressing articles published in languages other than English	Methods
	Method of handling abstracts and unpublished studies	Methods
	Description of any contact with authors	Supplements
Reporting of methods		
	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	Methods
	Rational for the selection and coding of data	Methods
	Documentation of how data were classified and coded	Methods
	Assessment of confounding	Tables S2 & S3
	Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results	Results & Tables S2 & S3
	Assessment of heterogeneity	Methods
	Description of statistical methods in sufficient detail to be replicated	Methods
	Provision of appropriate tables and graphics	Tables & Figures
Reporting of results		
	Graphic summarizing individual study estimates and overall study estimate	Figure 2
	Table giving descriptive information for each study	Tables 1-3

	included	
	Results of sensitivity testing (e.g. subgroup analysis)	Figure 2
	Indication of statistical uncertainty of findings	Results & Figure 2
Reporting of discussion		
	Quantitative assessment of bias	Methods
	Justification of exclusion	Methods
	Assessment of quality of included studies	Discussion
Reporting of conclusions		
	Consideration of alternative explanations for observed results	Discussion
	Generalization of the conclusions	Discussion
	Guidelines for future research	Discussion
	Disclosure of funding source	Funding

Table S2. Potential sources of confounding and bias (I)

Author (year)	Cohort: Exclusion or reporting of conditions which may impact B-line number	B-line quantification: Blinding of assessors to clinical findings	B-line quantification: Real-time or off-line	B-line quantification: Temporal blinding of assessors
Monitoring: Dynamic changes in B-lines with HF therapy				
Volpicelli (2008) ²¹	<u>Excluded:</u> Any acute lung disease or chronic pulmonary fibrosis	Yes (blinded to CXR, BNP level, and auscultation)	<i>Not reported</i>	<i>Not reported</i>
Vitturi (2011) ²²	Exclusion criteria: <i>Not reported</i>	Yes (blinded to clinical diagnosis)	<i>Not reported</i>	<i>Not reported</i>
Gargani (2015) ²³	<u>Excluded:</u> Pulmonary fibrosis, pneumothorax, fibrothorax, lung cancer; <u>Reported:</u> Creatinine	<i>Not reported</i>	<i>Not reported</i>	<i>Not reported</i>
Facchini (2016) ²⁴	<u>Excluded:</u> Patient weight >120 kg, pleural effusion, creatinine clearance <25 ml/min, interstitial lung disease, severe COPD	<i>Not reported</i>	<i>Not reported</i>	<i>Not reported</i>
Cortellaro (2016) ²⁵	<u>Excluded:</u> Interstitial lung disease, pneumonia, dialysis; <u>Reported:</u> Kidney failure (n=13)	Yes (blinded to NT-proBNP and chest X-ray results)	<i>Not reported</i>	<i>Not reported</i>
Monitoring: Dynamic changes in B-lines in HF with other interventions				
Frasure (2014) ¹⁰	<u>Excluded:</u> Dialysis, active lung cancer, prior pleurodesis, current pneumothorax; <u>Reported:</u> Creatinine; temperature >100.4F	Yes	Off-line (6 sec. clips)	Yes

Table S3. Potential sources of confounding and bias (II)

Author (year)	Cohort: Exclusion or reporting of conditions which may impact B-line number	B-line quantification: Blinding of assessors to clinical findings	B-line quantification: Real-time or off-line	Outcomes: Blinding of outcome assessors to LUS findings	Outcomes: Criteria for endpoint adjudication (HF hospitalization)
Prognosis: Acute dyspnea					
Frassi (2007) ²⁷	Exclusion criteria: Not reported; <u>Reported</u> : Chronic kidney failure (n=34)	Yes (blinded to echo data)	<i>Not reported</i>	<i>Not reported</i>	At least 1 criterion: Worsening of NYHA class, new hospitalization for worsened or decompensated HF, or ICD implantation
Wang (2014) ²⁸	None	No	<i>Not reported</i>	<i>Not reported</i>	N/A
Prognosis: Acute heart failure					
Gargani (2015) ²³	<u>Excluded</u> : Pulmonary fibrosis, pneumothorax, fibrothorax, lung cancer; <u>Reported</u> : Creatinine	<i>Not reported</i>	<i>Not reported</i>	<i>Not reported</i>	Framingham criteria, with corroborative information*
Coiro (2015) ¹⁶	<u>Excluded</u> : Pulmonary fibrosis, significant pleural effusion, severe emphysema, previous pneumectomy or lobectomy, pulmonary cancer or metastases; <u>Reported</u> : Creatinine clearance	Yes	Real-time (3 sec. clips)	<i>Not reported</i>	2014 ACC/AHA Key data elements and definitions for cardiovascular endpoint events in clinical trials
Cogliati (2016) ²⁹	<u>Excluded</u> : Pneumonia, interstitial lung disease, pleural effusion more than moderate at time of discharge; <u>Reported</u> : Chronic kidney disease (24.2%)	Yes	<i>Not reported</i>	<i>Not reported</i>	<i>Not reported</i>

Author (year)	Cohort: Exclusion or reporting of conditions which may impact B-line number	B-line quantification: Blinding of assessors to clinical findings	B-line quantification: Real-time or off-line	Outcomes: Blinding of outcome assessors to LUS findings	Outcomes: Criteria for endpoint adjudication (HF hospitalization)
Prognosis: Chronic heart failure					
Gustafsson (2015) ¹¹	Exclusion criteria: Not reported; <u>Reported</u> : Renal failure (n=24)	<i>Not reported</i>	<i>Not reported</i>	<i>Not reported</i>	<i>Not reported</i>
Platz (2016) ³⁰	<u>Excluded</u> : Recent chest trauma, current pneumonia, current cancer involving lung or pleura, dialysis; <u>Reported</u> : Interstitial lung disease (n=2); eGFR	Yes	Off-line (2 sec. clips)	Yes	Definitions based on draft standardized data collection criteria for cardiovascular trials (FDA)

*Corroborative information: clinical diary, information on hospital course, response to diuretics and other drugs, haemodynamic monitoring, ECG, chest X-ray, echocardiography, natriuretic peptides, results of subsequent cardiac testing, including nuclear medicine or MRI. For patients with a diagnosis other than HF, confirmation was attempted using the following variables: normal chest X-ray (lack of heart enlargement and signs of pulmonary congestion), normal systolic and diastolic heart function by echocardiography, normal valve function at echocardiography, normal natriuretic peptides, hospital clinical course.