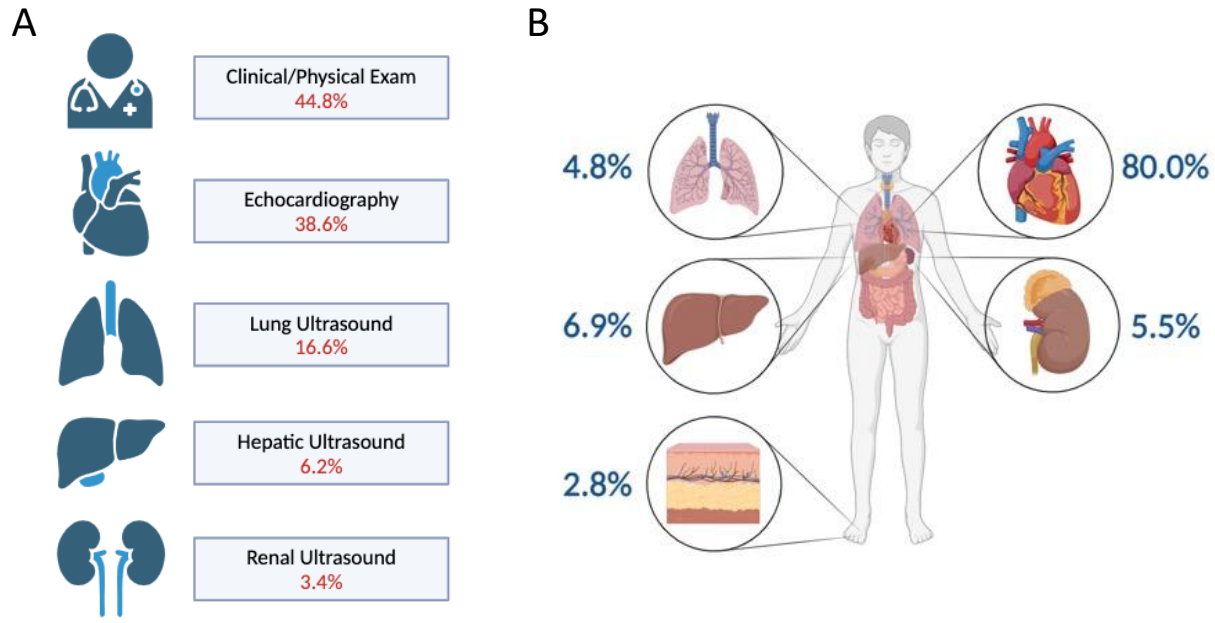
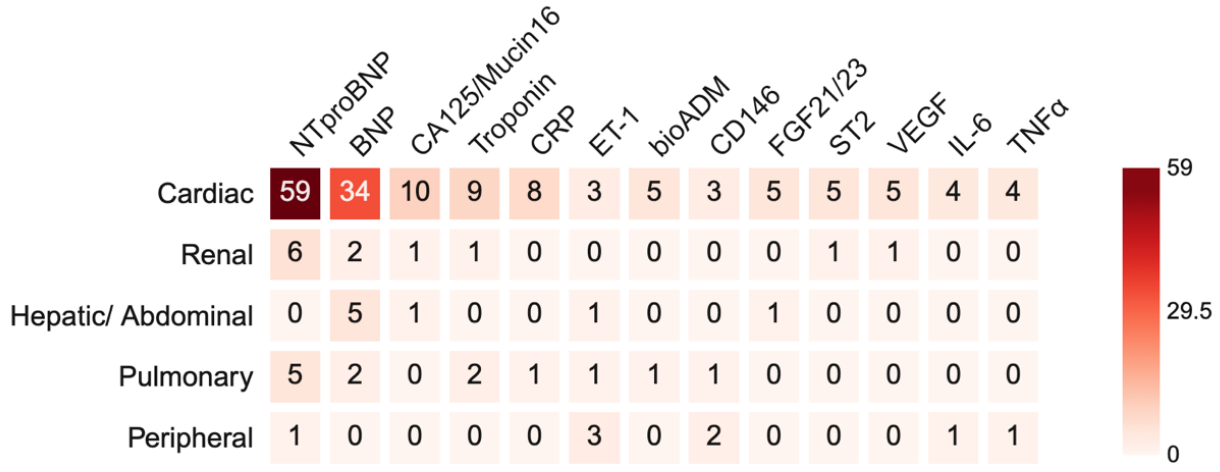


Supplemental Figure 1 Venous Congestion Measurement and Etiology. A) Method of reported measurement of venous congestion is depicted. 65 studies (44.8%) reported on clinical or physical exam features of congestion, 56 studies (38.6%) used echocardiography, 24 studies (16.6%) utilized lung ultrasound, 9 studies (6.2%) used hepatic or abdominal ultrasound, and 5 studies (3.4%) used renal ultrasound. B) Underlying state of venous congestion in reported studies is illustrated. 116 studies (80%) reported congestive measures in the context of cardiac disease, 7 studies (4.8%) in the context of lung disease, 10 studies (6.9%) in the context of liver disease, 8 studies (5.5%) in the context of renal disease, and 4 studies (2.8%) investigated peripheral congestion.



Supplemental Figure 2 Heatmap of Most Frequently Reported Circulating Markers. The cells demonstrate the number of studies (n, reported in cells) that quantified the cardiovascular, endothelial and inflammatory proteins (columns) in Figure 2 in relation to cardiac, renal, hepatic/abdominal, pulmonary or peripheral congestion disease pathology (rows). More frequent studies are depicted in red, and less frequent studies are depicted in white.

Supplemental Table 1: Search Strategy for MEDLINE and EMBASE

Database: Embase Classic+Embase <1947 to 2023 October 02>

Search Strategy:

1 (vein$ or vena$ or blood or vascular or cardiovascular$ or cardio-vascular$ or intravascular$ or intra-vascular$ or vessel or venous$).mp. (8154046)

2 congestion$.mp. (50461)

3 1 and 2 (28430)

4 venous congestion/ (4364)

5 3 or 4 (28430)

6 biological marker/ or biomarker$.mp. or marker$.tw,kw. (1903973)

7 exp *cytokine/ or cytokine$.tw,kw. (1100026)

8 (interleukin-6 or IL-6 or endothelin-1 or ET-1 or angiotensin II or AII or vascular cell adhesion molecule-1 or VCAM-1 or chemokine$ or C-X-C motif$ or CXCL2).tw,kw. (471000)

9 brain natriuretic peptide/ or (NT-proBNP or DELTANT-proBNP$ or (brain$ adj3 natriuretic$ adj3 peptide$)).tw,kw. (58908)

10 angiopoietin 2/ or angiopoietin 1/ or (ang-1 or angiopo?etin-1 or ang1 or ang-2 or angiopo?etin-2 or ang2).tw,kw. (16930)

11 intercellular adhesion molecule 1/ or (inter cellular adhesion molecule-1 or ICAM-1).tw,kw. (55215)

12 endothelial leukocyte adhesion molecule 1/ or (E-selectin or

endothelial$ leukocyte$ adhesion$ molecule-1 or ELAM-1).tw,kw. (17973)

13 (CD146 or CD-146 or cluster$ of differentiation$ 146 or CD62 or CD54).tw,kw. (7843)

14 (CD144 or VE-cadherin$ or (vascular$ adj2 endothelial$ adj2 cadherin) or (CD31 or (platelet$ adj2 endothelial$ cell$ adhesion$ molecule-1) or PECAM-1)).tw,kw. (32558)

15 or/6-14 (3136653)

16 5 and 15 (3758)

17 exp *hospital care/ or exp *hospital/ or *hospitalization/ or exp *"hospital cost"/ or exp *hospital infection/ or exp *hospital patient/ or exp *hospital management/ or (hospital$ or inpatient$ or in-patient$).tw,kw. or Hospital$.in. or (control$ adj5 subject$).tw,kw. (12458397)

18 5 and 17 (14196)

19 *"sensitivity and specificity"/ or *laboratory diagnosis/ or *prediction/ or *"prediction and forecasting"/ or *receiver operating characteristic/ or *roc curve/ or *diagnostic accuracy/ or *diagnostic value/ or *reliability/ or (sensitiv$ or specificity or distinguish$ or differentiat$ or enhancement or identif$ or detect$ or diagnos$ or accur$ or (predictive adj4 value$) or (false adj (positive$ or negative$)) or (receiver operat$ adj (characteristic$ or curve or analysis)) or (ROC or SROC)).tw,kw. [diagnostic filter_EMBASE] (14397102)

20 5 and 19 (10952)

21 incidence.sh. or exp mortality/ or exp Morbidity/ or morbidity$.mp. or follow up/ or prognos$.tw. or predict$.tw. or course$.tw. or exp Prognosis/ or (followup or follow-up).mp. or incidence$.tw. or (recurr$ or re-curr$).mp. or death.tw. or mortality$.mp. or surviv$.mp. or exp Survival/ or Survival Analysis/ or risk/ or risk assessment/ or risk factor/ or ep.fs. or risk$.ti. or risk$.ab. /freq=2 [Prognosis filter Maximizes sensitivity EMBASE] (13245132)

22 5 and 21 (13485)

23 16 or 18 or 20 or 22 (22508)

24 limit 23 to english language (20521)

25 24 not ((exp animal/ or nonhuman/) not exp human/) (17221)

26 25 not (animal$1 or mice or rat or rats or cat$1 or cattle$1 or dog$1 or goat$1 or horse$1 or rabbit$1 or sheep$1 or swine$1 or pig$1 or piglet* or canine$1 or feline$1 or porcine$ or calf or primate* or rodent$ or hamster$ or lamb$1 or monkey$1 or murine or veterinar*).ti. (16986)

27 limit 26 to (adult or aged) (9722)

28 limit 26 to (embryo or infant or child) (1288)

29 26 not (28 not (27 and 28)) (16177)

30 29 not (pediatr$ or paediatr$ or child$ or adolescent$ or infan$ or newborn$ or boy$1 or neonat$).ti. (15747)

31 exp case control study/ or (case$ and control$).tw. or exp case study/ or (case$ and series).tw. [EMBASE case series] (1353071)

32 case report/ or case report$.tw,kw. (3122152)

33 30 not (32 not (31 and 32)) (11231)

34 33 not case report.ti. (11157)

35 limit 34 to "reviews (best balance of sensitivity and specificity)" (1886)

36 34 not 35 (9271)

37 limit 36 to yr="2013 -Current" (5705)

38 limit 37 to embase **(3027)**

Database: Ovid MEDLINE(R) ALL <1946 to October 02, 2023>

Search Strategy:

1 (vein$ or vena$ or blood or vascular or cardiovascular$ or cardio-vascular$ or intravascular$ or intra-vascular$ or vessel or venous$).mp. (5412363)

2 congestion$.mp. (22674)

3 1 and 2 (11804)

4 exp Biomarkers/ or biomarker$.mp. or marker$.tw,kf. (1774791)

5 exp Cytokines/ or cytokine$.tw,kf. (982402)

6 (interleukin-6 or IL-6 or endothelin-1 or ET-1 or angiotensin II or AII or vascular cell adhesion molecule-1 or VCAM-1 or chemokine$ or C-X-C motif$ or CXCL2).tw,kf. (340021)

7 Natriuretic Peptide, Brain/ or (NT-proBNP or DELTANT-proBNP$ or (brain$ adj3 natriuretic$ adj3 peptide$)).tw,kf. (25500)

8 exp Angiopoietins/ or (ang-1 or angiopo?etin-1 or ang1 or ang-2 or angiopo?etin-2 or ang2).tw,kf. (9377)

9 Intercellular Adhesion Molecule-1/ or (inter cellular adhesion molecule-1 or ICAM-1).tw,kf. (27250)

10 (E-selectin or endothelial$ leukocyte$ adhesion$ molecule-1 or ELAM-1).tw,kf. (8745)

11 (CD146 or CD-146 or cluster$ of differentiation$ 146 or CD62 or CD54).tw,kf. (5258)

12 (CD144 or VE-cadherin$ or (vascular$ adj2 endothelial$ adj2 cadherin) or (CD31 or (platelet$ adj2 endothelial$ cell$ adhesion$ molecule-1) or PECAM-1)).tw,kf. (19329)

13 or/4-12 (2718271)

14 3 and 13 (1677)

15 exp Hospitalization/ or exp hospital units/ or exp hospitals/ or patients/ or inpatients/ or outpatients/ or pharmacy service, hospital/ or exp Drug Prescriptions/ or hospital$.mp. or (patients$ or inpatient$ or outpatient$ or in-patient$ or out-patient$ or tertiary$ or (out$ adj2 hospital$) or ambulat$ or same day or same-day or admission$ or admitted$).tw,kf. or Hospital$.in. or (control$ adj5 subject$).tw,kf. (11174390)

16 3 and 15 (7079)

17 exp "Sensitivity and Specificity"/ or false negative reactions/ or false positive reactions/ or diagnostic errors/ or (sensitiv$ or specificity or distinguish$ or differentiat$ or enhancement or identif$ or detect$ or diagnos$ or accur$).tw,kf. or (predictive adj4 value$).tw,kf. or (false adj (positive$ or negative$)).tw,kf. or (receiver operat$ adj (characteristic$ or curve or analysis)).tw,kf. or (ROC or SROC).tw,kf. or exp *"diagnostic techniques and procedures"/ or exp *early diagnosis/ [diagnostic filter_MEDLINE] (12466747)

18 3 and 17 (4821)

19 incidence.sh. or exp mortality/ or follow-up studies.sh. or prognos$.tw,kf. or predict$.tw,kf. or course$.tw,kf. or exp Prognosis/ or (followup or follow-up or followed).tw,kf. or incidence$.tw,kf. [Prognosis filter Maximizes sensitivity MEDLINE] (7117493)

20 3 and 19 (4268)

21 14 or 16 or 18 or 20 (9546)

22 limit 21 to english language (8538)

23 22 not (exp Animals/ not (Human/ and exp Animals/)) (6918)

24 23 not (animal$1 or mice or rat or rats or cat$1 or cattle$1 or dog$1 or goat$1 or horse$1 or rabbit$1 or sheep$1 or swine$1 or pig$1 or piglet* or canine$1 or feline$1 or porcine$ or calf or primate* or rodent$ or hamster$ or lamb$1 or monkey$1 or murine or veterinar*).ti. (6671)

25 limit 24 to "all adult (19 plus years)" (3481)

26 limit 24 to "all child (0 to 18 years)" (954)

27 24 not (26 not (25 and 26)) (6262)

28 27 not (pediatr$ or paediatr$ or child$ or adolescent$ or infan$ or newborn$ or boy$1 or neonat$).ti. (6191)

29 exp case-control studies/ or (case$ and control$).tw. or (case$ and series).tw. [Medline case series] (2042744)

30 case reports/ or case report$.mp. (2458234)

31 28 not (30 not (29 and 30)) (4848)

32 31 not case report.ti. (4818)

33 limit 32 to "reviews (best balance of sensitivity and specificity)" (923)

34 32 not 33 (3895)

35 **limit 34 to yr="2013 -Current" (2209)**

Supplemental Table 2: Circulating Markers Identified In Studies With Reported Measures Of Venous Congestion

Protein name	Number of Studies n (%)
N-terminal pro B-type natriuretic peptide (NTproBNP)	71 (48.9)
B-type natriuretic peptide (BNP)	43 (29.7)
Cancer antigen 125 (CA-125/Mucin16)	12 (8.3)
Troponin (Tn)	12 (8.3)
C-reactive protein (CRP)	9 (6.2)
Endothelin-1 (ET-1)	8 (5.5)
Adrenomedullin/bioactive adrenomedullin (bioADM)	6 (4.1)
Cluster of differentiation 146 (CD146)	6 (4.1)
Fibroblast growth factor 21/23 (FGF21/23)	6 (4.1)
Suppression of Tumorgenicity (ST2)	6 (4.1)
Vascular endothelial growth factor (VEGF-A/C/D)	6 (4.1)
Interlekin-6 (IL-6)	5 (3.4)
Tumor necrosis factor alpha (TNFα)	5 (3.4)
Alkaline Phosphatase (ALP)	4 (2.8)
Aspartate Aminotransferase (AST)	3 (2.1)
Cystatin C	3 (2.1)

Fatty Acid Binding Protein 1/4 (FABP1/4)	3 (2.1)
Growth differentiation factor 15 (GDF15)	3 (2.1)
Gamma-glutamyl transferase (GGT)	3 (2.1)
Midregional proatrial natriuretic peptide (MRproANP)	3 (2.1)
7S domain collagen type IV (P4NP7S)	3 (2.1)
Herceptin 2/4 (HER2/4)	2 (1.4)
Hepatocyte growth factor (HGF)	2 (1.4)
Insulin Growth Factor Binding Protein 7 (IGFBP7)	2 (1.4)
Kallikrein (KLK)	2 (1.4)
Neutrophil gelatinase-associated lipocalin (NGAL)	2 (1.4)
Stem Cell Factor (SCF)/Kit ligand (KITLG)	2 (0.7)
Tumor necrosis factor receptor 1 (sTNFR1/TNFRSF1A)	2 (1.4)
Vascular cell adhesion protein 1 (VCAM-1)	2 (1.4)
Adiponectin (ADIPOQ)	1 (0.7)
Albumin	1 (0.7)
Alanine Aminotransferase (ALT)	1 (0.7)
Angiopoeitin-2 (ANGPT2)	1 (0.7)
AnnexinA1 (AnxA1)	1 (0.7)
Aminopeptidase-N (AP-N)	1 (0.7)
B-arrestin 2 (ARRB2)	1 (0.7)
Bone morphogenetic protein 6 (BMP6)	1 (0.7)
Brother of CDO (BOC)	1 (0.7)
C-telopeptide for type I collagen (CTX-1)	1 (0.7)
Cluster of differentiation 16 (CD16)	1 (0.7)
Cluster of differentiation 44 (CD44)	1 (0.7)
Carcinoembryonic antigen-related cell adhesion molecule 1 (CEACAM1)	1 (0.7)
Copeptin (CT-proAVP)	1 (0.7)

Carboxypeptidase A1 (CPA1)	1 (0.7)
Carboxypeptidase B1 (CPB1)	1 (0.7)
Carboxypeptidase E (CPE)	1 (0.7)
CXCL12	1 (0.7)
CXCL2	1 (0.7)
Epidermal growth factor (EGF)	1 (0.7)
Endocan (ESM1)	1 (0.7)
C-terminal proEndothelin-1 (CTproET1)	1 (0.7)
Fibroblast growth factor binding protein 1 (FGF-BP1)	1 (0.7)
Furin	1 (0.7)
Glycated hemoglobin (HbA1c)	1 (0.7)
High-density lipoprotein cholesterol (HDL-C)	1 (0.7)
Hepcidin	1 (0.7)
Hyaluronic Acid (HA)	1 (0.7)
Immunoglobulin A (IgA)	1 (0.7)
Interleukin-1β (IL-1B)	1 (0.7)
Interleukin-33 (IL-33)	1 (0.7)
Insulin	1 (0.7)
Kidney injury molecule 1 (KIM1)	1 (0.7)
Kit ligand (KITLG)	1 (0.7)
Lactate dehydrogenase (LDH)	1 (0.7)
Low-density lipoprotein cholesterol (LDL-C)	1 (0.7)
Leptin (LEP)	1 (0.7)
Mac2 Binding protein (Mac2-BP)	1 (0.7)
Macrophage inflammatory protein 1B (MIP1B)	1 (0.7)
Midregional Proadrenomedullin (MRproADM)	1 (0.7)
Paraoxonase-3 (PON3)	1 (0.7)
Pro-collagen III N-terminal peptide (P3NP)	1 (0.7)

Parathyroid hormone (PTH)	1 (0.7)
Relaxin-2 (RLN2)	1 (0.7)
Soluble neprilysin (sNEP)	1 (0.7)
Receptor for Advanced Glycation Endproducts (sRAGE)	1 (0.7)
Tumor growth factor alpha (TGFα)	1 (0.7)
Tumor growth factor beta 1 (TGF β1)	1 (0.7)
Angiopoeitin-1 receptor (Tie-2)	1 (0.7)
Tumor necrosis factor receptor 2 (sTNFR2)	1 (0.7)
Vimentin (Vim)	1 (0.7)

Studies shaded in yellow represent the markers reported in at least 5 studies (>3% of the publications).