

ONLINE SUPPLEMENT

Title: Fluid responsiveness assessment using inferior vena cava collapsibility among spontaneously breathing patients: systematic review and meta-analysis.

Authors:

Luis Carlos Maia CARDOZO JÚNIOR

Guilherme Santos Duarte LEMOS

Bruno Adler Maccagnan Pinheiro BESEN

Contents:

Table S1: Gray zone approach with IVCc cutoffs for sensitivity greater than 90% and cutoffs for specificity greater than 90%.

Table S2: Sensitivity, specificity and Area Under Curve of IVCc as a predictor of fluid responsiveness among the 2 studies that assessed this method under a standardized inspiration.

Figure S1: Pooled sensitivity and specificity of IVCc as a predictor of fluid responsiveness among the included studies sorted by IVCc cutoff.

List S1: List of all studies selected for full review

Table S1 – Gray zone approach with IVCc cutoffs for sensitivity greater than 90% and cutoffs for specificity greater than 90%.

Author and year	N	IVCc cut-off	Sensitivity	Specificity
Corl, 2019	85	> 22%	90%	-
		> 37%	-	90%
Bortolotti, 2018	55	> 11%	90%	-
		>43%	-	90%
Preau, 2017	90	> 13%	90%	-
		> 41%	-	90%

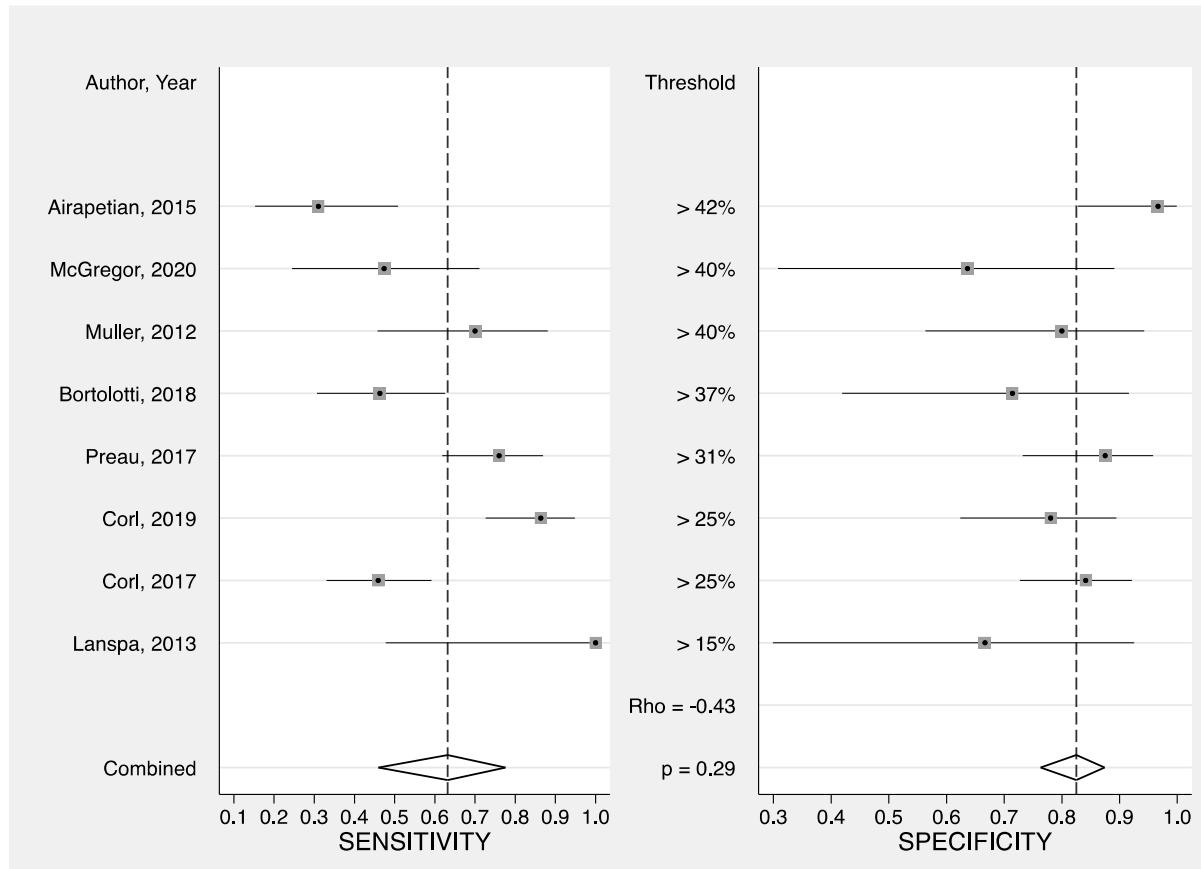
Legend - IVCc: inferior vena cava collapsibility;

Table S2: Sensitivity, specificity and Area Under Curve of IVCc as a predictor of fluid responsiveness among the 2 studies that assessed this method under a standardized inspiration.

Author and year	N	IVCc cut-off	IVCc - responders	IVCc - non responders	Sensitivity	Specificity	AUC (95% CI)
Bortolotti, 2018	55	> 39%	74%	19%	93%	88%	0.93 (0.86 - 1.00)
Preau, 2017	90	> 48%	55%	18%	84%	90%	0.89 (0.82 - 0.97)

Legend - IVCc: inferior vena cava collapsibility; AUC: *area under curve*; 95% CI: 95% confidence interval; NA: not available.

Figure S1: Pooled sensitivity and specificity of IVCc as a predictor of fluid responsiveness among the eight included studies ordered by the study threshold



Rho (and the p-value) refers to the Spearman correlation coefficient between sensitivity and specificity

List S1: List of all studies selected for full review

Included studies (8) – six studies found in MEDLINE, one found in EMBASE and one found in references of another systematic review

Corl KA, Azab N, Nayeemuddin M, Schick A, Lopardo T, Zeba F, et al. Performance of a 25% Inferior Vena Cava Collapsibility in Detecting Fluid Responsiveness When Assessed by Novice Versus Expert Physician Sonologists. *J Intensive Care Med.* 2019;885066619881123.

Bortolotti P, Colling D, Colas V, Voisin B, Dewavrin F, Poissy J, et al. Respiratory changes of the inferior vena cava diameter predict fluid responsiveness in spontaneously breathing patients with cardiac arrhythmias. *Ann Intensive Care.* 2018;8(1):79.

Corl KA, George NR, Romanoff J, Levinson AT, Chheng DB, Merchant RC, et al. Inferior vena cava collapsibility detects fluid responsiveness among spontaneously breathing critically-ill patients. *Journal of Critical Care.* 2017;41:130-7.

Preau S, Bortolotti P, Colling D, Dewavrin F, Colas V, Voisin B, et al. Diagnostic Accuracy of the Inferior Vena Cava Collapsibility to Predict Fluid Responsiveness in Spontaneously Breathing Patients With Sepsis and Acute Circulatory Failure. *Crit Care Med.* 2017;45(3):e290-e7.

Airapetian N, Maizel J, Alyamani O, Mahjoub Y, Lorne E, Levrard M, et al. Does inferior vena cava respiratory variability predict fluid responsiveness in spontaneously breathing patients? *Crit Care.* 2015;19:400.

Lanspa MJ, Grissom CK, Hirshberg EL, Jones JP, Brown SM. Applying dynamic parameters to predict hemodynamic response to volume expansion in spontaneously breathing patients with septic shock. *Shock.* 2013;39(2):155-60.

Muller L, Bobbia X, Toumi M, Louart G, Molinari N, Ragonnet B, et al. Respiratory variations of inferior vena cava diameter to predict fluid responsiveness in spontaneously breathing patients with acute circulatory failure: need for a cautious use. *Crit Care.* 2012;16(5):R188.

McGregor D, Sharma S, Gupta S, Ahmed S, Harris T. Emergency department non-invasive cardiac output study (EDNICO): an accuracy study. *Scand J Trauma Resusc Emerg Med*. 2020;28(1):8.

Missing or inconsistent data (14) – most of these studies did not include information about accuracy or included inconsistent information precluding inclusion in the meta-analysis.

Oord M, Olgers TJ, Doff-Holman M, Harms MP, Ligtenberg JJ, Ter Maaten JC. Ultrasound and NICOM in the assessment of fluid responsiveness in patients with mild sepsis in the emergency department: a pilot study. *BMJ Open*. 2017 Jan 27;7(1):e013465. doi: 10.1136/bmjopen-2016-013465.

Jia M, Yang J, Peng F, Wang Y, Liao G, Gao Y. Analysis of volume management by comparing between critical care ultrasound examination and pulse indicator cardiac output in patients with septic shock. *J Pak Med Assoc*. 2020 Sep;70 [Special Issue](9):51-56.

Brun C, Zieleskiewicz L, Textoris J, Muller L, Bellefleur JP, Antonini F, Tourret M, Ortega D, Vellin A, Lefrant JY, Boubli L, Bretelle F, Martin C, Leone M. Prediction of fluid responsiveness in severe preeclamptic patients with oliguria. *Intensive Care Med*. 2013 Apr;39(4):593-600. doi: 10.1007/s00134-012-2770-2. Epub 2012 Dec 6.

Galang K., Ali S., Singh G. Comparison of noninvasive hemodynamic monitors, respiratory variation in inferior vena cava, and stroke volume variance measured by estimation of finger cuff technology for prediction of fluid responsiveness in septic shock. *Chest* 2020 158:4 Supplement (A2639-).

Sai T.A., Satyanarayana P.V.S. Volume responsiveness after passive leg raising, fluid resuscitation in patients with shock. *Indian Journal of Critical Care Medicine* 2021 25:SUPPL 1.

Hadidy S.E., Albadry A., Radwan W., Metwaly A., Farouk K. Non-invasive hemodynamic monitoring of fluid resuscitation in cirrhotic patients with acute kidney injury. *Open Access Macedonian Journal of Medical Sciences* 2020 8:B (319-323).

Wang S., Gilani A., Santikul D., Vohra A. Noninvasive cardiac output monitoring (nicom) vs caval index ultrasonography: a prospective comparison to predict fluid responsiveness in patients with sepsis. *Chest* 2019 155:4 Supplement.

Sharma V., Hammond N., Li H., Rodriguez J., Gueret R., Bailitz J. A survey of the use of ultrasound based parameters to assess fluid responsiveness Sharma V., Hammond N. *American Journal of Respiratory and Critical Care Medicine* 2018 197:MeetingAbstracts.

Crager S., Amii R., Canders C., Weingrow D., Tseeng S., Chiem A. Agreement between different ultrasound approaches for the assessment of fluid responsiveness. *Critical Care Medicine* 2016 44:12 Supplement 1 (425-).

Fein D., Jordan C., Acquah S., Kory P. A prospective study of inferior vena cava parameters to predict fluid responsiveness. *Chest* 2015 148:4 MEETING ABSTRACT.

Hasanin A., Lotfy A., Abdel-Aal I.R., Elkholey J., El-Adawy A., Mohamed H., Zaghlol A., Salem M., Mukhtar A. Evaluation of ivc and ijk dimensions in prediction of fluid responsiveness in spontaneous breathing patients with septic shock. *Intensive Care Medicine Experimental* 2015 3 Supplement 1 Article Number A594.

Abodorra M.E.M., El Awady S.M., Fayed A.M., El Badawy T.H. A comparison between left ventricular outflow tract velocity time integral and inferior vena cava collapsibility index as a predictor to fluid responsiveness in critically ill septic patients. *Intensive Care Medicine* 2014 40:1 SUPPL. 1 (S202-S203).

Williams K., Ablordeppay E., Theodoro D., Fuller B., Wessman B., Ahrens T., Williams J., Hotchkiss R., Charshafian S., Holthaus C. The diagnostic accuracy of inferior vena cava collapsibility in determining volume responsiveness in emergency department patients with shock. *Critical Care Medicine* 2011 39 SUPPL. 12 (8-).

Zoric L., Mattatia L., Louart G., Lefrant J.Y., Muller L. Ability of respiratory variations of the diameter (RVD) of the inferior vena cava (IVC) to predict fluid responsiveness in patients with spontaneous breathing. *Intensive Care Medicine* 2010 36 SUPPL. 2 (S338)

Without cardiac output measure (10) – these studies did not measure cardiac output, using methods like elevation of arterial blood pressure as standard test.

Bilgin S, Topal FE, Yamanoglu A, Payza U, Karakaya Z, Akyol PY, Tahtaci R, Topal F. Effect of Changes in Intravascular Volume on Inferior Vena Cava and Aorta Diameters and the Caval/Aorta Index in Healthy Volunteers. *J Ultrasound Med.* 2020 Feb;39(2):231-238. doi: 10.1002/jum.15093. Epub 2019 Jul 8.

McGregor D, Sharma S, Gupta S, Ahmad S, Godec T, Harris T. Emergency department non-invasive cardiac output study (EDNICO): a feasibility and repeatability study. *Scand J Trauma Resusc Emerg Med.* 2019 Mar 11;27(1):30. doi: 10.1186/s13049-019-0586-6.

Kaydu A, Gokcek E. Preoperative and Postoperative Assessment of Ultrasonographic Measurement of Inferior Vena Cava: A Prospective, Observational Study. *J Clin Med.* 2018 Jun 10;7(6):145. doi: 10.3390/jcm7060145.

Abahuje E, Munyaneza R, Riviello R, Ntirenganya F. Assessment of hemodynamic response to fluid resuscitation of patients with intra-abdominal sepsis in low- and middle-income countries. *J Surg Res.* 2017 Oct;218:162-166. doi: 10.1016/j.jss.2017.05.061. Epub 2017 Jun 16.

Gui J, Yang Z, Ou B, Xu A, Yang F, Chen Q, Jiang L, Tang W. Is the Collapsibility Index of the Inferior Vena Cava an Accurate Predictor for the Early Detection of Intravascular Volume Change? *Shock.* 2018 Jan;49(1):29-32. doi: 10.1097/SHK.0000000000000932.

Sawe HR, Haeffele C, Mfinanga JA, Mwafongo VG, Reynolds TA. Predicting Fluid Responsiveness Using Bedside Ultrasound Measurements of the Inferior Vena Cava and Physician Gestalt in the Emergency Department of an Urban Public Hospital in Sub-Saharan Africa. *PLoS One.* 2016 Sep 27;11(9):e0162772. doi: 10.1371/journal.pone.0162772. eCollection 2016.

de Valk S, Olgers TJ, Holman M, Ismael F, Ligtenberg JJ, Ter Maaten JC. The caval index: an adequate non-invasive ultrasound parameter to predict fluid responsiveness in the emergency department?. *BMC Anesthesiol.* 2014 Dec 12;14:114. doi: 10.1186/1471-2253-14-114. eCollection 2014.

Kattan E., Ferri G., Ospina-Tascon G., Cavalcanti A.B., Damiani L.P., Estenssoro E., Dubin A., Hurtado J., Friedman G., Castro R., Alegria L., Teboul J.L., Cecconi M., Bakker J., Hernandez G. Fluid responsiveness assessment during early septic shock resuscitation. Secondary analysis of ANDROMEDA-SHOCK trial. *Intensive Care Medicine Experimental* 2019 7 Supplement 3.

Laniado I., You J.Y., Hanumanthu B.K.J., Ataucuri-Vargas J.-B., Reid E.S., Goraya H., Gulani P. Poor concordance between respiratory variation in inferior vena cava and surrogates of cardiac output measurements for determination of fluid responsiveness. *Circulation* 2019 140 Supplement 1.

Bulic S., Cen S.Y., Emanuel B. Inferior Vena Cava point of care ultrasonography in the neuroscience ICU. *Neurocritical Care* 2015 23:1 SUPPL. 1 (S60-).

Review or commentary (11) – studies which were read in full text in attempt to identify additional trials but were reviews or commentary.

Kothekar AT, Patil VP. Transoesophageal echocardiographic thoracic inferior vena caval index: Is it validated and accurate for identifying fluid responders? *Saudi J Anaesth.* 2020 Apr-Jun;14(2):279-280. doi: 10.4103/sja.SJA_50_20. Epub 2020 Mar 5.

Ozakin E, Mert KU. Is caval index an appropriate tool for predicting hypovolemia in stroke. *Am J Emerg Med.* 2020 Nov;38(11):2482. doi: 10.1016/j.ajem.2020.03.014. Epub 2020 Mar 12.

Li Y, Yin W, Kang Y. Is ultrasound assessment of the inferior vena cava for fluid responsiveness unlikely to be helpful, or is it just too early to say? *Can J Anaesth.* 2020 Jun;67(6):783-784. doi: 10.1007/s12630-020-01574-y. Epub 2020 Jan 24.

Seccombe A, McCluskey L, Moorey H, Lasserson D, Sapey E. Assessing Fluid Resuscitation in Adults with Sepsis Who Are Not Mechanically Ventilated: a Systematic Review of Diagnostic Test Accuracy Studies. *J Gen Intern Med.* 2019 Sep;34(9):1874-1883. doi: 10.1007/s11606-019-05073-9. Epub 2019 May 31.

Millington SJ. Ultrasound assessment of the inferior vena cava for fluid responsiveness: easy, fun, but unlikely to be helpful. *Can J Anaesth.* 2019 Jun;66(6):633-638. doi: 10.1007/s12630-019-01357-0. Epub 2019 Mar 27.

Spiegel RJ, McCurdy MT. Inferior vena cava variation predicts fluid responsiveness during dysrhythmias: a rational rearrangement of chairs on The Titanic. *Ann Transl Med.* 2018 Nov;6(Suppl 1):S67. doi: 10.21037/atm.2018.10.36.

Bortolotti P, Colling D, Preau S. Inferior Vena Cava Respiratory Variations: A Useful Tool at Bedside to Guide Fluid Therapy in Spontaneously Breathing Patients. *Shock.* 2018 Feb;49(2):235-236. doi: 10.1097/SHK.0000000000000950.

Long E, Oakley E, Duke T, Babl FE; Does Respiratory Variation in Inferior Vena Cava Diameter Predict Fluid Responsiveness: A Systematic Review and Meta-Analysis. Paediatric Research in Emergency Departments International Collaborative (PREDICT). *Shock.* 2017 May;47(5):550-559. doi: 10.1097/SHK.0000000000000801.

Millington SJ, Koenig S. Ultrasound Assessment of the Inferior Vena Cava for Fluid Responsiveness: Making the Case for Skepticism. *J Intensive Care Med.* 2021 Oct;36(10):1223-1227. doi: 10.1177/08850666211024176. Epub 2021 Jun 25.

Unal Akoglu E., Akoglu H. Does respiratory variation in inferior vena cava diameter predict fluid responsiveness in adult patients? A systematic review and meta-analysis of diagnostic accuracy studies. *Hong Kong Journal of Emergency Medicine* 2021.

Lanspa M.J. Echocardiography is a feasible tool for assessing volume responsiveness *Journal of Thoracic Disease* 2017 9:5 (E477-E479).

Duplicates (11) – studies that were found in both MEDLINE and EMBASE or were original articles that included patients previously included in other trials.

Pereira R.M., Silva A.J.L.C.D., Faller J., Gomes B.C., Silva J.M. Comparative Analysis of the Collapsibility Index and Distensibility Index of the Inferior Vena Cava Through Echocardiography with Pulse Pressure Variation That Predicts Fluid Responsiveness in Surgical Patients: An Observational Controlled Trial. *Journal of Cardiothoracic and Vascular Anesthesia* 2020 34:8 (2162-2168)

Ozakin E, Mert KU. Is caval index an appropriate tool for predicting hypovolemia in stroke. *Am J Emerg Med.* 2020 Nov;38(11):2482. doi: 10.1016/j.ajem.2020.03.014. Epub 2020 Mar 12.

Corl K., Abbasi A., Azab N., Nayeemuddin M., Schick A., Lopardo T., Baird G., Merchant R., Levy M.M., Blaivas M. Implementation of an inferior vena cava collapsibility cutoff of 25[percent] detects fluid responsiveness in spontaneously breathing critically ill patients. *American Journal of Respiratory and Critical Care Medicine* 2019 199:9.

Bortolotti P., Colling D., Colas V., Voisin B., Dewavrin F., Poissy J., Girardie P., Kyheng M., Saulnier F., Favery R., Preau S. Respiratory changes of the inferior vena cava diameter predict fluid responsiveness in spontaneously breathing patients with cardiac arrhythmias. *Annals of Intensive Care* 2018 8:1 Article Number 79.

Corl K.A., George N.R., Romanoff J., Levinson A.T., Chheng D.B., Merchant R.C., Levy M.M., Napoli A.M. Inferior vena cava collapsibility detects fluid responsiveness among spontaneously breathing critically-ill patients. *Journal of Critical Care* 2017 41 (130-137).

Preau S., Bortolotti P., Colling D., Dewavrin F., Colas V., Voisin B., Onimus T., Drumez E., Durocher A., Redheuil A., Saulnier F. Diagnostic Accuracy of the Inferior Vena Cava Collapsibility to Predict Fluid Responsiveness in Spontaneously Breathing Patients with Sepsis and Acute Circulatory Failure. *Critical Care Medicine* 2017 45:3 (e290-e297).

Bortolotti P., Colling D., Colas V., Voisin B., Dewavrin F., Onimus T., Girardie P., Saulnier F., Preau S. Diagnostic accuracy of the inferior vena cava collapsibility to predict fluid responsiveness in spontaneously breathing patients with cardiac arrhythmia
Annals of Intensive Care 2017 7:1 Supplement 1 (92-93).

Corl K., George N., Romanoff J., Levinson A., Merchant R., Levy M., Napoli A. IVC collapsibility shows promise in detecting fluid responsiveness among critically ill patients. Critical Care Medicine 2016 44:12 Supplement 1 (154-).

Muller L., Bobbia X., Toumi M., Louart G., Molinari N., Ragonnet B., Quintard H., Leone M., Zoric L., Lefrant J.Y. Respiratory variations of inferior vena cava diameter to predict fluid responsiveness in spontaneously breathing patients with acute circulatory failure: Need for a cautious use. Critical Care 2012 16:5 Article Number R188

Corl K., Napoli A.M., Gardiner F. Bedside sonographic measurement of the inferior vena cava caval index is a poor predictor of fluid responsiveness in emergency department patients. EMA - Emergency Medicine Australasia 2012 24:5 (534-539).

Corl K., Napoli A. Bedside sonographic measurement of IVC caval index is a poor predictor of fluid responsiveness. Academic Emergency Medicine 2011 18:5 SUPPL. 1 (S108-).

Included patients mechanically ventilated (6) – studies excluded because included patients on mechanical ventilation.

Pereira RM, Silva AJLCD, Faller J, Gomes BC, Silva JM Jr. Comparative Analysis of the Collapsibility Index and Distensibility Index of the Inferior Vena Cava Through Echocardiography with Pulse Pressure Variation That Predicts Fluid Responsiveness in Surgical Patients: An Observational Controlled Trial. J Cardiothorac Vasc Anesth. 2020 Aug;34(8):2162-2168. doi: 10.1053/j.jvca.2020.02.007. Epub 2020 Feb 12.

Kaçar CK, Uzundere O, Yektaş A. A Two Parameters for the Evaluation of Hypovolemia in Patients with Septic Shock: Inferior Vena Cava Collapsibility Index (IVCCI), Delta Cardiac Output. Med Sci Monit. 2019 Oct 29;25:8105-8111. doi: 10.12659/MSM.919434.

Wang Y, Jiang Y, Wu H, Wang R, Wang Y, Du C. Assessment of fluid responsiveness by inferior vena cava diameter variation in post-pneumonectomy patients. *Echocardiography*. 2018 Dec;35(12):1922-1925. doi: 10.1111/echo.14172. Epub 2018 Oct 18.

Trifi A, Abdellatif S, Daly F, Nasri R, Touil Y, Ben Lakhel S. Ultrasound stroke volume variation induced by passive leg raising and fluid responsiveness: An observational cohort study. *Med Intensiva (Engl Ed)*. 2019 Jan-Feb;43(1):10-17. doi: 10.1016/j.medint.2017.11.002. Epub 2017 Dec 16.

Theerawit P, Morasert T, Sutherasan Y. Inferior vena cava diameter variation compared with pulse pressure variation as predictors of fluid responsiveness in patients with sepsis. *J Crit Care*. 2016 Dec;36:246-251. doi: 10.1016/j.jcrc.2016.07.023. Epub 2016 Aug 13.

Basbous A., Ledoux D., Canivet J.-L. Respiratory variation in IVC cross-sectional surface to predict fluid responsiveness-a prospective study. *Annals of Intensive Care* 2019 9 Supplement 1.

Without fluid expansion (4) – in these studies patients did not receive fluids and passive leg raising was used as standard test.

Haliloğlu M, Bilgili B, Kararmaz A, Cinel İ. The value of internal jugular vein collapsibility index in sepsis. *Ulus Travma Acil Cerrahi Derg*. 2017 Jul;23(4):294-300. doi: 10.5505/tjtes.2016.04832.

Güney Pınar S, Pekdemir M, Özturan İU, Doğan NÖ, Yaka E, Yılmaz S, Karadaş A, Ferek Emir D. Assessment of end-tidal carbon dioxide and vena cava collapsibility in volume responsiveness in spontaneously breathing patients. *Med Klin Intensivmed Notfmed*. 2020 Oct 25. doi: 10.1007/s00063-020-00749-1.

Corl K, Napoli AM, Gardiner F. Bedside sonographic measurement of the inferior vena cava caval index is a poor predictor of fluid responsiveness in emergency department patients. *Emerg*

Med Australas. 2012 Oct;24(5):534-9. doi: 10.1111/j.1742-6723.2012.01596.x. Epub 2012 Sep 7.

Haliloglu M., Bilgili B., Kararmaz A., Cinel I. Internal jugular vein versus inferior vena cava collapsibility index for fluid responsiveness. Critical Care Medicine 2016 44:12 Supplement 1 (124-).

Other (3) – one study was a randomized controlled trial, one was retrospective and the last one was post-hoc analysis.

Musikatavorn K, Plitawanon P, Lumlertgul S, Narajeenron K, Rojanasarntikul D, Tarapan T, Saoraya J. Randomized Controlled Trial of Ultrasound-guided Fluid Resuscitation of Sepsis-Induced Hypoperfusion and Septic Shock. West J Emerg Med. 2021 Feb 10;22(2):369-378. doi: 10.5811/westjem.2020.11.48571.

Caplan M, Durand A, Bortolotti P, Colling D, Goutay J, Duburcq T, Drumez E, Rouze A, Nseir S, Howsam M, Onimus T, Favory R, Preau S. Measurement site of inferior vena cava diameter affects the accuracy with which fluid responsiveness can be predicted in spontaneously breathing patients: a post hoc analysis of two prospective cohorts. Ann Intensive Care. 2020 Dec 11;10(1):168. doi: 10.1186/s13613-020-00786-1.

Blaivas M., Blaivas L.N., Tsung J.W. Deep learning algorithm performance compared to experts in visual evaluation of interior vena cava collapse on ultrasound to determine intravenous fluid need in dehydration management. Signa Vitae 2021 17:5 (34-41)