



“Flying blind” or “in plain sight”?

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Sepsis is one of the leading drivers of mortality and resource use in the intensive care unit (ICU). Any intervention improving management would be of great help to thousands of patients. Apart from treatment of the underlying cause and appropriate antibiotic treatment a major area in sepsis patients is hemodynamic management. Unfortunately, the amount of evidence to guide the clinician in this difficult topic is very limited.

It may be surprising that in the technology-dominated field of intensive care medicine despite large technological advances in the diagnostic realm including several commercially available continuous hemodynamic monitoring methods and ever more compact and powerful bedside ultrasound imaging devices (1) the mainstay of hemodynamic monitoring is a comparably ancient technique of pressure measurement. *“It was fatal for the development of our understanding of circulation that blood flow is relatively difficult while blood pressure so easy to measure: this is the reason why the blood pressure measurement has gained such a fascinating influence, although most organs do not need blood pressure but blood flow.”* This quote—attributed to Dr. Jarisch (1850–1902)—still holds largely true in today’s ICUs.

Studies on hemodynamic monitoring and echo in shock patients have shown no definite picture but there are several guideline recommendations commenting on this issue. The Guidelines for the Appropriate Use of Bedside General and Cardiac Ultrasonography in the Evaluation of Critically Ill (2) recommend echo in septic patients to evaluate fluid status, left ventricular (LV) and right ventricular (RV) function. The “European Society of Intensive

Care Medicine Task force” (3) recommends to perform echo in patients with circulatory shock initially if further hemodynamic monitoring is needed [‘moderate quality of evidence’—GRADE system (4)] and states that “echo can be used for the sequential evaluation of cardiac function in shock” (no evidence level). Moderate quality of evidence in the GRADE system is defined as “Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate” (4). Therefore, it is clear that the report on Dr. Feng and his colleagues on “Transthoracic echocardiography and mortality in sepsis: analysis of the MIMIC-III database” is a very welcome contribution to the available evidence (5).

Dr. Feng *et al.* performed a retrospective cohort analysis of a large and comprehensive single center ICU database (MIMIC-III). This database was created in a Herculean effort by the Beth Israel Deaconess Medical Center and Massachusetts Institute of Technology (MIT) and includes virtually complete but fully anonymized electronic health records of tens of thousands of ICU patients (6). Randomized controlled trials face inherent difficulties in the ICU field (7) and therefore retrospective analyses of large databases like this are a promising method to increase knowledge where evidence is scarce. Unfortunately, these databases tend to be underutilized by clinical researchers—possibly because of the technical and statistical challenges to get to robust results from ‘real world’ electronic health data.

Dr. Feng and colleagues employed several statistical methods ranging from traditional matching and multivariate regression to more state of the art ‘doubly robust’ methods.

In addition, the authors have made their code available—which will help technically inclined investigators to reproduce results or explore different angles of the data. The study had a hard-primary endpoint: 28-day survival. This is another great feature of the MIMIC-III database: It includes anonymized complete survival data from the “Social Security Death Index”—something very difficult to achieve in plain retrospective chart reviews.

The results show a survival benefit of sepsis patients who underwent echo compared to patients who did not undergo echo (odds ratio for 0.78 for death at 28 days). This result was robust in various statistical analyses and sensitivity analysis. Given a large number of heterogeneous patients [$>3,000$ in both groups, medical intensive care unit (MICU) and surgical intensive care unit (SICU) included] this is a very interesting finding. Secondary outcomes showed increased use of fluids, norepinephrine, and dobutamine in the echo group. Certainly, in a retrospective study there always remain concerns that there are relevant unaccounted confounders, but the authors attempted to vigorously adjust for confounding using 39 variables. Despite the matched groups not being 100% equalized the advanced statistical methods used should adjust for the remainder of imbalance. Therefore, this report is very useful as another piece of evidence to encourage the use of echo in critically ill patients.

Hard evidence considerations aside—anyone who has witnessed the profound and sometimes brisk changes in patient management if an initial echocardiographic evaluation of a patient in shock unexpectedly shows acute mitral regurgitation, severe aortic stenosis, low ejection fraction, enlarged right ventricle, pericardial effusion or (admittedly with low sensitivity) vegetations will be very inclined to agree that there is merit in knowing and recognizing these pathologies.

Another detail in the results shows the challenges ahead when opting for a more frequent use of echo in the ICU: the second strongest predictor of undergoing echo [right after “diagnosis of congestive heart failure (CHF)”] was “hour of ICU admission”. One possible interpretation of this finding is that the expertise to perform echo is not always readily available 24/7. Echo imaging in ICU patients is

inherently difficult—inability to freely position the patient, possibly ongoing positive pressure ventilation impairing the acoustic windows, competing procedures, rapid heart, and respiratory rates to name only a few reasons. This calls for a more widespread adoption of bedside echo training and certification with the aim to make basic level trained ICU providers [as defined in (2)] available independent of the time of the day.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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