What's new in ultrasound-based assessment of organ perfusion in the critically ill: expanding the bedside clinical monitoring window for hypoperfusion in shock

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Intensive Care Medicine

ISSN 0342-4642

Intensive Care Med
DOI 10.1007/s00134-019-05791-y

Springer

Intensive Care Med
https://doi.org/10.1007/s00134-019-05791-y

WHAT'S NEW IN INTENSIVE CARE

What's new in ultrasound-based assessment of organ perfusion in the critically ill: expanding the bedside clinical monitoring window for hypoperfusion in shock

Francesco Corradi[1,2*], Gabriele Via[3] and Guido Tavazzi[4,5]

Circulatory shock is defined as a disorder with evidence of both clinical and biochemical tissue hypoperfusion, entailing inadequate oxygen utilization by cells, with or without a systolic blood pressure below 95 mmHg [1]. Its hallmark are signs of hypoperfusion which reflect the global metabolic and circulatory consequences of oxygen transport/demand imbalance.

Clinical signs of shock are generally those detected by looking at three body "windows", namely, skin, kidneys, and brain. Biochemical sensitive and reliable conventional parameters are represented by hyperlactatemia, decreased mixed or central venous oxygen saturation ($SvCO_2$, SvO_2), and an increased veno-arterial carbon dioxide difference (the "pCO_2-gap") [1]. However, the specific evaluation of end-organs perfusion rather than the assessment of downstream consequences of their maladaptation may have relevant implications in treatment guidance.

Echocardiography has been widely adopted to diagnose and monitor cardiac dysfunction leading to hemodynamic instability, and shock pathophysiology in general. However, the echocardiographic information on macro-hemodynamics is partial, especially as being indirect as concerns vascular tone, and not allowing any inference on end-organ perfusion.

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Other ultrasound applications, aiming at the assessment of visceral end-organ perfusion, may offer insights into this facet of shock pathophysiology. Although splanchnic organs account for only 10–12% of total body weight, they receive a substantial proportion (up to 40%) of total cardiac output under resting hemodynamic conditions. This may provide a large "preload reserve" and "perfusion reserve" partially available to support the systemic circulation under hypovolemic or low-output conditions: in the acute phase of shock, blood is in fact mainly diverted to short term perfusion of vital organs. However, the prolonged hypo-perfusion of splanchnic organs may severely affect mid-to-long term outcomes.

How to assess splanchnic perfusion

The evaluation of regional splanchnic hemodynamics by color Doppler resistive index, a measure of pulsatile blood flow reflecting the resistance of microvascular bed to blood flow, provides a useful tool for detecting early hemodynamic abnormalities related to organ dysfunction before the occurrence of biochemical or macro-hemodynamic changes. This is because splanchnic hypo-perfusion alters organ microcirculation by increasing flow resistance and, in turn, Doppler resistive index.

Kidney, liver

The study of renal perfusion by renal Doppler resistive index (RDRI) has been introduced as a tool for assessing changes in renal perfusion in critically ill patients [2] and predicting acute kidney injury in patients with severe sepsis [3] or needing mechanical ventilation [4]. The general concept is that the higher is RDRI, the lower is renal

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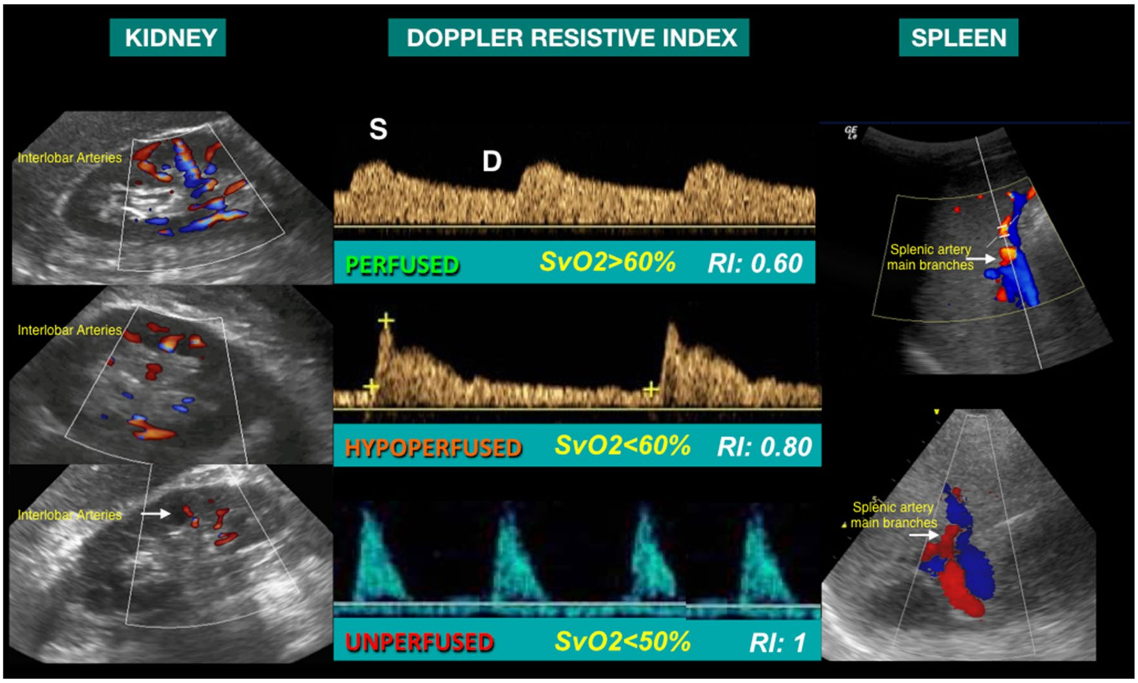


Fig. 1 Different patterns of splanchnic perfusion inferred by Doppler resistive index: (1) perfused with a clearly visible diastolic phase (top), (2) hypo-perfused with lower diastolic phase (middle), (3) vascularized but unperfused were only the systolic phase of the cardiac cycle is visible without the diastolic (perfusional) phase (bottom). Color and Pulse Doppler Ultrasonography is usually performed with a low frequency probe (sector or convex array transducer) examination with the patient in supine position. Color Doppler is used to target the vessels while pulsed wave Doppler is used to sample the trace. Doppler ultrasound measurements are obtained in the interlobar arteries of the renal cortex or in the main branches of the splenic artery and the average retained for analysis to derive an index for the whole organ in order to minimize sampling error. Waveforms are recorded and Doppler resistive index calculated as the ratio $(S-D)/S$, where "S" and "D" stands for peak systolic and end-diastolic velocities, respectively (yellow crosses). Pulsed wave Doppler spectrum was increased by using the lowest frequency shift range that did not cause aliasing and the wall filter was set at a low frequency (100 MHz) [7, 13]

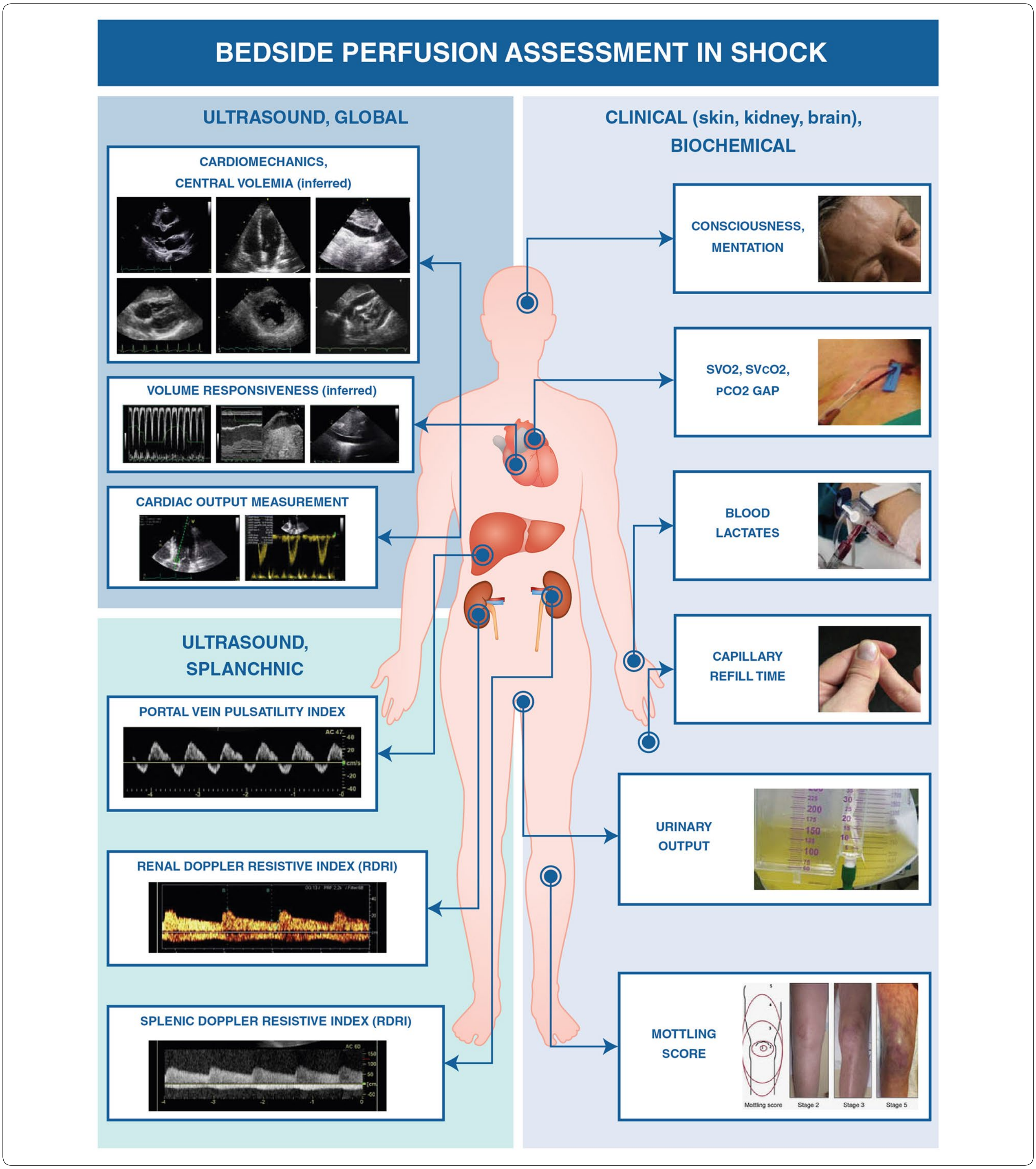
vessel compliance. However, many factors may influence its interpretation [5] such as, arrhythmias, arterial stiffness, intra-abdominal pressure, hypoxia, right heart function, increased parenchymal wedge pressure.

RDRI has shown high sensitivity in: (1) detecting splanchnic occult hypoperfusion due to initial hypovolemia in apparently hemodynamically stable patients [6], (2) estimation of systemic hemodynamics and amine titration to improve renal blood flow and function, and (3) determining the optimal mean artery pressure to improve regional perfusion pressure, avoiding vasoconstriction [2]. RDRI >0.7 may also identify organ-specific supply and demand mismatch when peripheral arterial oxygenation is normal, thus reflecting an early vascular response to systemic tissue hypoxia (Fig. 1) [7]. This hypothesis is in line with findings showing that RDRI was able to mirror mild hypoxemia in ARDS patients while other macro-hemodynamic parameters were not [8].

Doppler investigation of renal perfusion also demonstrated a tight link with cardiac function and echo-derived parameters of diastolic dysfunction in heart failure with both preserved and reduced ejection fraction, with findings mirroring a low preload and/or an increased renal afterload, and consistent splanchnic hypo-perfusion [9]. In this context, Doppler detection of a "mirror" decreased venous flow pattern (discontinuous, isolated diastolic flow), has been proposed as a marker of "congestive kidney failure", demonstrating a pathophysiological link with systemic congestion, right atrial and pulmonary pressures [10]. Interestingly, the technically less demanding Doppler assessment of portal vein flow can act as a surrogate for pathological kidney venous flow detection: a portal vein pulsatility index (PVPI) >50% was independently associated with a greater degree of systemic venous congestion, lower arterial diastolic perfusion pressures and greater postoperative acute kidney injury incidence [11].

Spleen

Spleen is a key regulator of body fluid homeostasis under both normal and pathologic conditions. It receives about 10% of cardiac output and nearly two thirds of the


BEDSIDE PERFUSION ASSESSMENT IN SHOCK
ULTRASOUND, GLOBAL
CARDIOMECHANICS, CENTRAL VOLEMIA (inferred)
VOLUME RESPONSIVENESS (inferred)
CARDIAC OUTPUT MEASUREMENT
ULTRASOUND, SPLANCHNIC
PORTAL VEIN PULSATILITY INDEX
RENAL DOPPLER RESISTIVE INDEX (RDRI)
SPLENIC DOPPLER RESISTIVE INDEX (RDRI)
CLINICAL (skin, kidney, brain), BIOCHEMICAL
CONSCIOUSNESS, MENTATION
SVO2, SVCO2, PCO2 GAP
BLOOD LACTATES
CAPILLARY REFILL TIME
URINARY OUTPUT
MOTTLING SCORE
Mottling score
Stage 2
Stage 3
Stage 5

(See figure on previous page.)

Fig. 2 Organ perfusion assessment in the shocked patient. Right side of the diagram describes established clinical indices of global perfusion, entailing the exam of the 3 "clinical windows" for perfusion assessment: brain (degree of consciousness, mentation), skin (assessment of the mottling score and of capillary refill time), kidney (urinary output monitoring). Left side of the diagram describes current ultrasound applications providing information on: global perfusion (upper half, left side of the diagram), in contrast with the ones aiming at splanchnic district perfusion (lower half, left side of the diagram). Echocardiography, when not used to measure cardiac output, allows only to infer indirect information on the adequacy of global body perfusion: when normal cardiac mechanics (normal right and left ventricular function, valvular integrity, absence of pericardial hemodynamically relevant pathology) and adequate cardiac filling (2D signs ruling out severe central hypovolemia, negative echo-based indices of volume responsiveness such as superior vena cava collapsibility, inferior vena cava distensibility, LVOT flow respiratory variations, LVOT flow response to passive leg raising) are ascertained, one can assume that cardiac output is reasonably not defective. By means of PW Doppler sampling of LVOT flow, echocardiography allows then measurement and trending of stroke volume, providing an estimate of global perfusion. Doppler sampling of kidney's interlobar arteries and splenic artery flows allow for calculation of respectively the renal Doppler resistive index (RDRI) and the splenic Doppler resistive index (SDRI), which provide insight into state of splanchnic perfusion. The Doppler sampling of renal interlobar veins and of portal vein flows (especially its degree of pulsatility) add information on the existence and degree of splanchnic venous congestion

splanchnic blood (i.e., >800 ml) can be auto-transfused into the systemic circulation within seconds through the β_2 and α-adrenergic receptor activation in the splanchnic vasculature in case of shock. The sympathetic splenorenal neural reflex in response to a reduction of blood pressure, mediates the renin-angiotensin axis acting as endogen vasoconstrictor to restore a adequate perfusion pressure. The over expression of renin has been identified as an initiating factor in the development of cardiovascular dysregulation in conditions of shock [12]. Beside the important role of venous reservoir and pressure mediator, the spleen has demonstrated to be also an early indicator of tissue hypoperfusion.

Splenic vascularization, evaluated by means of the splenic Doppler resistive index (SDRI), has been linked to cardiovascular function with significant prognostic implications concerning fluid responsiveness. SDRI percentage reduction ≥4% provides evidence that improvement in splanchnic circulation occurs in the presence or absence of a positive fluid challenge response and is representative of active vasodilation in the splanchnic circulation. This is confirmed by its correlation with arterial lactate levels and central venous oxygen saturation changes [13]. Moreover, SDRI >0.71 is very sensitive in detecting occult hypovolemic shock and is able to titrate the adequacy of resuscitation targeting persistent occult hypoperfusion (Fig. 1), also when arterial lactates are still normal [14].

These indices are potentially applicable whenever cardiovascular homeostasis is jeopardized (such as in trauma, sepsis, cardiogenic shock) and in different clinical contexts (from prehospital and emergency department, to anesthesia and intensive care), due to the portability and nowadays increasingly ubiquitous availability of point-of-care-ultrasound. Similar to brain ultrasound, ultrasound-based splancnic perfusion assessment can indeed be easily integrated into the whole-body-approach to complex scenarios such as trauma [15] and allow simultaneously the evaluation of global and regional blood flow (Fig. 2).

The goal of the therapy in circulatory shock is to achieve and maintain an adequate end-organ perfusion. Currently available variables for the assessment of peripheral hypo-perfusion rely merely on macro-hemodynamics and established non-specific, although sensitive, clinical-biochemical signs. The Doppler evaluation of splanchnic organ perfusion and its response to therapy, so far only partially explored, has a potential to represent in clinical settings a more sensitive diagnostic and monitoring tool for the comprehensive assessment of cardio-vascular interactions at the bedside.

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Compliance with ethical standards

Conflicts of interest

Francesco Corradi has no conflict of interest to declare. Gabriele Via has no conflict of interest to declare. Guido Tavazzi has no conflict of interest to declare.

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Received: 18 August 2019 Accepted: 17 September 2019
Published online: 25 October 2019

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