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EDITORIAL

Monitoring capillary refill time in septic shock

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Capillary refill time (CRT) has been proposed as a marker of tissue hypoperfusion based on physiological and clinical–epidemiological data and is increasingly used as a monitor in shock states and other conditions [1–4]. Indeed, besides being costless and universally available, CRT is a dynamic parameter which changes rapidly in response to hemodynamic interventions, thus making it a suitable bedside tool to monitor and guide septic shock resuscitation [1]. Unfortunately, specific guidelines to standardize how to estimate CRT do not currently exist. This toolbox aims to provide a practical overview of the fundamentals of CRT assessment to facilitate and optimize its use at the bedside.

Technical considerations

CRT measures the amount of time, in seconds, necessary for the skin to return to baseline color after applying a pressure on a soft tissue, generally a fingertip. CRT is influenced by various factors such as room temperature and lighting, skin temperature and color, age, technique quality, and pressure site, and is also subjected to intra-observer and interobserver reliability [2]. Therefore, specific training and standardized measurement techniques are highly relevant for CRT accuracy and reliability. In the absence of training, Alsma et al. reported poor inter-observer agreement on CRT measurements while in centers whose intensivists were trained, reproducibility was good [5].

In routine clinical practice, most operators use just the pressure of their own fingers to get an approximate estimation of CRT; however, standardization for CRT quantification is strongly recommended. In the ANDROMEDA-SHOCK trial, a microscope glass slide was used to compress the ventral side of the index fingertip until blanching occurred, followed by 10 s of compression and the re-coloration time was measured with a chronometer [6] (Fig. 1). Another study employed a 15 s compression over the nail and the pressure standardized as "just enough to remove the blood at the fingertip" [7].

CRT can also be assessed at the earlobe or kneecap but with different predictive cut-offs. Indeed, in septic shock patients the best threshold to predict mortality was 2.4 s in the index fingertip compared to 4.9 s on the knee area [8]. Therefore, a cut off value of 3 s has been adopted in clinical trials. Anyway, repeated measurements should be performed to improve accuracy.

Alternative sites for CRT assessment may be important in some contexts. In fact, CRT measured at the earlobe in semi-recumbent position may represent a valid surrogate when access to the finger is not feasible [9]. A practical guide for CRT assessment is provided in Fig. 1. The use of other promising techniques to assess peripheral perfusion has recently been comprehensively reviewed [1].

CRT monitoring and clinical outcomes

CRT has been related to relevant clinical outcomes in sepsis. In pre-hospital settings, or the emergency department, a prolonged CRT after initial fluid resuscitation was associated with organ failure and increased mortality [1, 10]. Conversely, the rapid normalization of CRT after initial septic shock resuscitation is associated with a two-fold lower mortality compared to patients with persistently abnormal CRT. These data highly support the use of CRT for triage decisions.

The potential role of CRT monitoring in other critical conditions was recently reviewed [1] and some possible uses are shown in Fig. 1.

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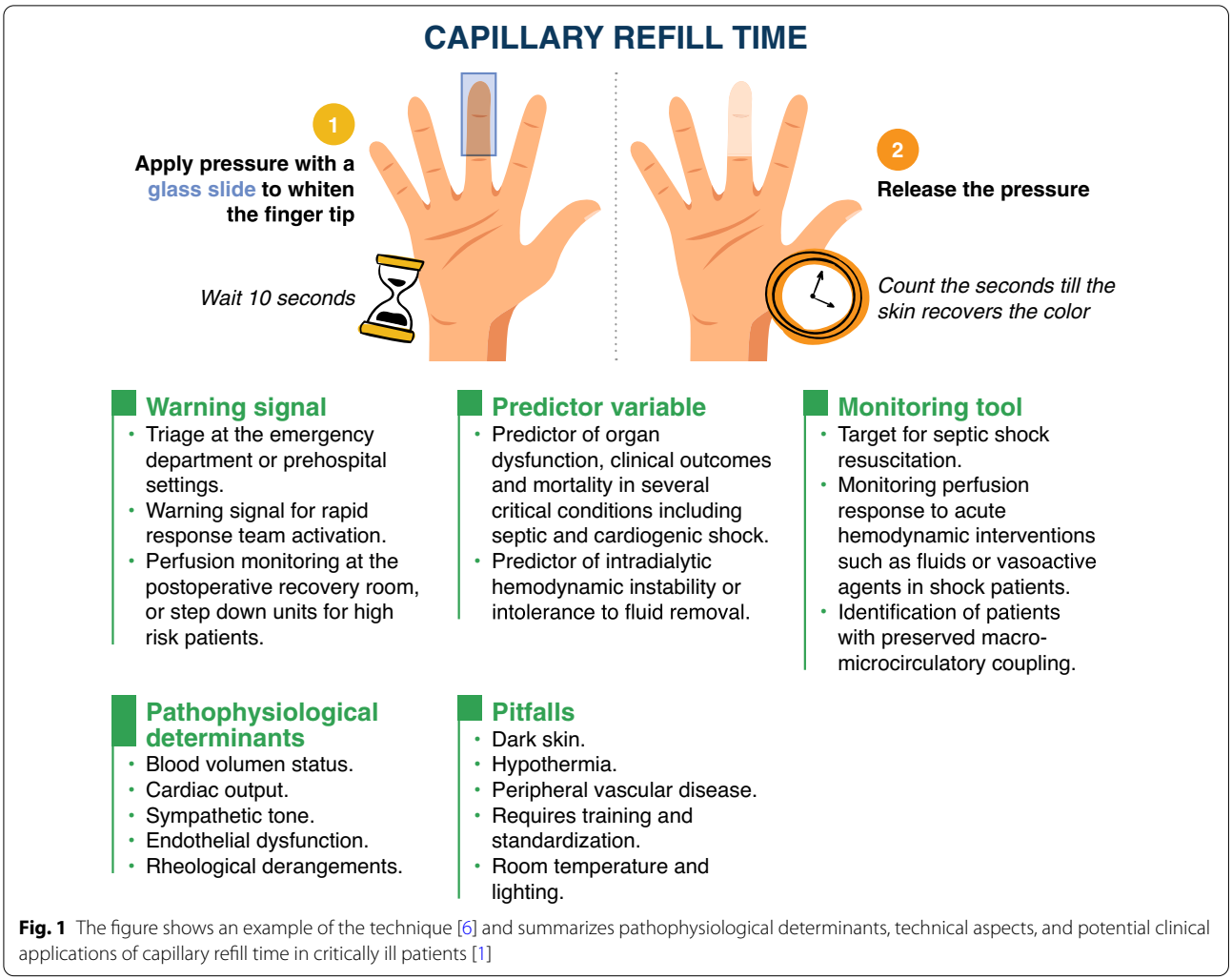

Fig. 1 The figure shows an example of the technique [6] and summarizes pathophysiological determinants, technical aspects, and potential clinical applications of capillary refill time in critically ill patients [1]

Capillary refill time as a potential resuscitation target

The ANDROMEDA-SHOCK trial found that targeting CRT during early septic shock resuscitation was associated with less organ dysfunction at 72 h, and a trend to lower 28-day mortality [6]. A post hoc Bayesian analysis supported the superiority of CRT-targeted resuscitation in mortality and organ dysfunction compared to lactate-guided resuscitation [11]. Another post hoc analysis was focused on patients with normalized CRT at 2 h, irrespective of initial allocation [12]. Interestingly, in the lactate-arm, patients received significantly more interventions such as fluid boluses, and vasoactive drugs, and exhibited a significantly higher mortality. These data support the relevance of assessing CRT to provide a more rational resuscitation avoiding detrimental over-resuscitation.

The ongoing ANDROMEDA-SHOCK-2 trial (NCT 05057611) will randomize 1500 septic shock patients to a CRT-targeted resuscitation strategy based on hemodynamic phenotyping or standard care, providing further insights into the impact of CRT monitoring on patient-centered outcomes.

Kinetics of response of CRT to acute hemodynamic interventions

Macro-to-microcirculatory coupling refers to the relationship between systemic macrohemodynamics and microcirculatory flow during resuscitation [13]. The relevance of coupling is that pushing more fluids and/or vasoactive agents may be useful in patients with preserved coupling but could induce harm and potentially worsen microcirculatory abnormalities in those who lost it.

Some recent data support the use of CRT response to a short-term hemodynamic intervention as a fluid bolus or a transient increase in mean arterial pressure (MAP) to disclose the status of macro-to-microcirculatory coupling in septic shock patients. Jacquet-Lagreze et al. found that passive leg raising-induced CRT changes

accurately predicted CRT response to a fluid bolus in shock patients [14]. Raia et al. evaluated CRT response kinetics after a fluid challenge in 40 septic patients [7]. Among responders, CRT exhibited a significant decrease at 6–8 min that was maintained at 30 min. Fage et al. investigated the impact of a fluid bolus and an increase in norepinephrine dose on CRT in septic shock patients [15]. Significant changes in CRT were observed only in patients with abnormal CRT at baseline but response was highly heterogeneous.

On the other hand, the ANDROMEDA-SHOCK trial introduced a vasopressor test, transiently raising MAP levels to 80–85 mmHg in chronically hypertensive, fluid-unresponsive septic shock patients and persistent hypoperfusion, with a CRT response in > 40% [6]. Criteria for defining CRT response were also variable among studies but a decrease in CRT of > 0.5 s is likely to be clinically relevant.

Take-home message

A growing body of evidence supports the role of CRT assessment as a relevant monitoring tool for septic shock and other critically ill patients. CRT exhibits a rapid response to hemodynamic interventions and thus may be useful to tailor fluid and vasoactive drug administration, and eventually to disclose the status of macro- to microcirculatory coupling. Its use as a resuscitation target in septic shock was supported by ANDROMEDA-SHOCK trial and is being further addressed by an ongoing major trial. However, training and standardization of the acquisition technique are mandatory to accurately measure CRT and use it to guide resuscitation.

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Declarations

Conflicts of interest
None declared.

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