protein (hsCRP), soluble tumor necrosis factor receptor-1 (sTNFR1), and angiopoietin-2.[34] As well, markers of apoptosis including sFas and sFasL, endothelin-1 (marker of neurohumoral axis activation), and procollagen II N-Terminal Pro-peptide (PIINP) as a marker of extracellular matrix turnover are all novel markers under study but not appropriate for routine clinical use.[32]

3.3 | Physical examination

In **Stage A** (*At risk*), patients typically have an unremarkable physical examination often with no signs of volume overload. They are warm, well perfused, with normal mentation. In **Stage B** (*Beginning*), patients have clinical manifestations of elevated right or left sided filling pressures as evidenced by an elevated jugular venous pressure and/or rales on auscultation, or a low BP but preserved end-organ and peripheral perfusion. The hallmark of **Stage C** (*Classic*) and **Stage D** (*Deteriorating / Doom*) is impaired end-organ perfusion. Patients in these categories appear in obvious distress and may exhibit impaired mental status, cold/mottled extremities, volume overload, reduced urine output (<30 mL/h), and/or respiratory failure requiring mechanical ventilatory support. The final **Stage E** (*Extremis*) manifests with cardiovascular collapse with a pulseless (or near pulseless) state and respiratory failure requiring mechanical ventilation.

3.4 | Hemodynamics

3.4.1 | Hemodynamic diagnosis of CS

Although all forms of shock are diagnosed by a relative reduction in systemic blood pressure with tissue hypoperfusion, labeling it *cardiogenic* implies that shock is due to a low cardiac output/index in the absence of hypovolemia. Although CS may be diagnosed clinically, it is often difficult to distinguish it from other forms of shock without invasive hemodynamic monitoring. It is essential to measure intracardiac pressures and cardiac output in patients where the diagnosis of CS is being considered. Intriguing new data suggests that use of PA catheter may be associated with lower mortality in CS patients.[35] Echocardiography may be a valuable adjunct, in particular to identify mechanical complications of myocardial infarction, acute valvular regurgitation and to identify signs of right or left ventricular volume or pressure overload. Other conditions such as pericardial tamponade can also be rapidly identified and may significantly affect management strategies.

3.4.2 | Blood pressure measurements

Systemic hypotension (defined as a sustained systolic blood pressure (SBP) less than or equal to 90 mmHg or a mean arterial pressure at least 30 mmHg lower than baseline) due to CS occurs after a reduction in stroke volume and cardiac output. SBP may be obtained by brachial cuff (cuff measurements in thigh or ankle may be artificially higher or lower), but an arterial line may be preferable to continuously monitor pressure and facilitate frequent arterial blood gas and lactate measurements. However, systolic amplification may occur when measuring arterial pressure in a distal location compared to central aortic pressure. An underestimate of central arterial pressure using a distal arterial line is also possible with peripheral arterial disease or with peripheral vasoconstriction either due to the shock state itself or the vasoactive drugs administered.

3.4.3 | Pulmonary artery catheter measurements

Pulmonary artery (PA) catheters can directly measure right atrial (RA), PA and pulmonary capillary wedge pressures (PCWP), mixed venous oxygenation, cardiac output (CO) and allows calculation of CI, systemic vascular resistance (SVR), pulmonary vascular resistance (PVR), pulmonary artery pulsatility index (PAPI), and cardiac power output (CPO). Recent reviews of the hemodynamics of CS provide further details on the derived values and interpretation of these indices in this setting.[36,37]

Although hemodynamic definitions of CS may vary, the National Cardiovascular Data Registry defines CS as systolic blood pressure ≤ 90 and cardiac index <2.2 L/min/m^2 and/or the requirement for parenteral inotropic or vasopressor agents or mechanical support to maintain BP and CI above these levels.[38] Although classic "cold, wet" CS is associated with low CI and high SVR and PCWP, there are four different common hemodynamic types of CS which are difficult to determine without invasive hemodynamic monitoring, and importantly, the patient may go from one category to another (Figure 2). There are two other uncommon types of CS (approximately 5% of cases): right ventricular shock and normotensive shock.[10]

The use of PA catheters can be critically important to establish the diagnosis of CS versus other causes of shock, unmask normotensive CS in patients with clinical hypoperfusion and SBP >90 mmHg, as well as accurately determining filling pressures. PA catheter hemodynamics are also helpful to assess right ventricular involvement in MI, distinguish classic cardiogenic from a mixed shock picture, assist in choice or titration of vasopressor or inotropic drugs, select patients who may benefit from mechanical circulatory support and guide weaning of pharmacological or mechanical support. Measurement of the saturation of PA blood, as well as CI and CPO are also very helpful to determine prognosis.

Despite these potential benefits, the use of PA catheters remains controversial in the wider setting. A recent analysis of the National Inpatient Sample of 89,718 AMI patients with CS who underwent cardiac catheterization revealed that only 6.1% received a PA catheter.[39] This retrospective report and others have not found a mortality benefit for CS patients who received PA catheters, although interpretation is limited given selection bias to use hemodynamic monitoring in sicker patients. The prospective, randomized ESCAPE trial in patients with decompensated HF showed no benefit, and was stopped early due to safety concerns (infection, ICD firing).[40] However, these patients did not have acute coronary syndromes or CS and all patients were enrolled with clinical equipoise. Accordingly, results of the ESCAPE study do not apply to patients with CS. There is no other randomized trial to evaluate the utility of PA catheters in cardiac patients, especially in those with