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A novel hypothesis comprehensively explains shock, heart failure and aerobic exhaustion through an assumed central physiological control of the momentary cardiovascular performance reserve ☆

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ABSTRACT

Background: Heart failure (HF) and shock are incomprehensively understood, inconclusively defined and lack a single conclusive test. The proceedings that preceded and triggered clinical manifestations are occult. The relationships in between different shock and HF types and between each HF type and its matched shock are poorly understood.

The assumed hypothesis: We suggest that HF and shock are attributed to a momentary cardiovascular performance reserve – "the reserve". The reserve is controlled through an assumed central physiological mechanism that continuously detects and responds accordingly – "the reserve control". The assumed reserve is maximal at rest, and decreases with aerobic activity. When it decreases to a given threshold the reserve control alerts by induces manifestations of dyspnea and fatigue enforcing activity decrease, follow which the manifestations dissolve. HF is a condition of low reserve at baseline; hence, fatigue and dyspnea are frequently experienced following mild activity. Shock is assumed to occur when the cardiovascular reserve deteriorates below a sustainable limit where the reserve control induces a salvage–sacrifice response, preserving vital organ perfusion while impairing microcirculation effective perfusion in non-vital organ in which it causes cellular hypoxia followed by the familiar devastating cascade of events seen in shock.

Discussion and conclusions: The hereby hypothesis may comprehensively explain the heart failure – shock puzzle as no alternative theory had ever succeeded. It provides the missing link between the different types of HF as of shock and in between. The hypothesis poses a great prove challenge but opens new research and clinical possibilities.

Introduction

Heart failure

The current concept considers heart failure (HF) as a physiological state in which cardiac output is insufficient in meeting body needs [1]. This concept raises questions regarding its comprehensiveness and conclusiveness as HF patient are capable to increase cardiac output (e.g., with activity). Different HF types are very different in terms of cardiac output, being either low output heart failure (e.g., cardiac dysfunction or obstructive impairment) and high output heart failure (e.g., hyperthyroidism, sepsis or anemia) [1,2]. Regardless of the specific underlying cause, HF patients share very similar general core manifestations of fatigue and dyspnea (unrelated to respiratory morbidity) either at rest or during activity which may lead to exercise intolerance [1,3,4]. The underlying cause of the fatigue and dyspnea in HF remains debated as both were not conclusively attributed to any hemodynamic, respiratory or metabolic underlying triggering factor [4,5]. Several non-cardiac conditions such as volume depletion and vasculature tone incompetence which reveal the same manifestations are also included in the broader sense of heart failure syndrome [6]. Each HF patient may also carry specific manifestations which are attributable to the specific underling cause of dysfunction (e.g., high output HF due to arterio-venous fistula [5]).

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Shock

Despite the insight that shock is an acute circulatory collapse, shock definition remains inconclusive, general and non-specific as of five decades ago [7]. The current concept explains shock as a cascade of multi system inadequate tissue level perfusion, which leads to cellular hypoxia, anaerobic metabolism, cell death, organ failure and death [8,9]. The main types of shock are cardiogenic or obstructive shock, hypovolemic or hemorrhagic shock and distributive shock [10]. All shock types share similar general core manifestations of multi system cellular hypoxia and exhibits the same devastating cascade of events it induces. All shock types also share excessive sweating (diaphoresis) which appears out of place in a physiological perspective, this is currently explained by high sympathetic activity. All shock types also share decrease in blood pressure and poor prognosis regardless of the specific shock type. Each shock type may also carry specific manifestations attributable to the specific underling abnormality [10,11]. Shock has an interesting similarity with heart failure as different shock types may be either of low output (e.g., cardiogenic or hypovolemic shock) or high output (e.g., septic, anaphylactic and neurogenic shock) [12].

The natural course which preceded tissue level hypo-perfusion is usually occult and poorly understood regardless of the general inconclusive definition of circulation collapse. The underlying cause such as myocardial infarction, infection or trauma is usually known but when and what triggers the exact onset which leads to cellular hypoxia and in turn the cascade of devastating events remains unknown. Accordingly, diagnosis is sometimes delayed until multi organ failure occurs [13]. It is agreed that the underlying mechanism of shock is either a decrease in cardiac output or systemic vascular resistance or both, but a single denominator which preceded or associated with all types of shock was never discovered. It is also well known that while non-vital organs are devastatingly damaged (hypo-perfused), vital organs circulation remains preserved (at least during the initial course) but this sacrifice–salvage mechanism is not entirely understood [14–16].

The traditional explanation focuses on local, selective decrease in arterial blood supply of the affected organs while vital organs blood supply is relatively preserved [16]. However, this is a simplified explanation which opposes several unfitting clues:

(1) A selective local arterial blood flow was not demonstrated in shock in general and high output shock in particular [17].
(2) It is well known that sweat is derivative of skin blood flow, without which, sweat cannot lasts [18]. The skin is affected early in the course of shock and is believed to be hypo-perfused while diaphoresis is persisting as a core manifestation in shock. While diaphoresis is explained by high sympathetic activity, how does a hypo-perfused tissue produce excessive sweat (with or without sympathetic activity) is debated.
(3) Tissue level hypo-perfusion and in turn cellular hypoxia occurs even in high cardiac output and even when tissue blood flow is proved to be preserved [19]. Moreover the venous oxygen saturation may be either normal or even elevated especially in high output shock states.

The role of the microcirculation in the proceedings that preceded shock had been previously suggested but remains controversial [20–22]. It is well known that some normal tissues (e.g., skin) is wired by two types of capillaries: true (exchange) capillaries – which enable exchange of gases and metabolites with the surrounding tissue cells, and metarteriole thoroughfare channel which are shunting capillaries directly connect the arterial vasculature to the venous bypassing the exchange capillaries [23]. Both capillary types have a pre capillary sphincter on the arterial side by which the nervous system controls the opening or closure of the vessel [24]. A flow shift from exchange to shunt vessels had already been suggested as a specific mechanism explaining mal-perfusion in a high output shock [25].

Shock–HF relationship

Interestingly, each type of heart failure may be matched with its respective shock: e.g., cardiac dysfunction heart failure and cardiogenic shock; hypovolemia (which manifests as HF) and hypovolemic shock; sepsis (which manifests as high output HF) and septic shock, etc. The exact relationship as well as the cutoff between a specific HF type and its respective matched shock is neither conclusive nor sufficiently understood [26]. Several publications had demonstrated conflicting diagnoses on the HF–shock spectrum, such as a diagnosis of heart failure that turns to be an occult shock with more sensitive diagnostic measure and vice versa [27,28]. In the sepsis – septic shock spectrum clinicians had defined a third, intermediate category namely "severe sepsis" [29].

Cardiac output

Under the existing concepts HF and shock manifestations are assumed to be directly mediated and triggered locally through hemodynamic characteristics. Cardiac output, the principle measure of cardiovascular hemodynamic performance, was intensively studied. Numerous attempts were made to develop a precise cardiac output measurement or estimate, either invasively or non-invasive [30–32]. Precise as it may be, cardiac output is prone to be misleading [33]: Firstly, as we had already mentioned, both heart failure and shock have high cardiac output types [34]. Secondly, cardiac output may still be preserved even in a progressive course due to compensatory mechanisms [35]. Thirdly, HF manifestations were proved not to be directly correlated with cardiac output [36].

Both HF and shock lack a comprehensive paradigm which links and combines all the pieces of the puzzle. This is the aim of the novel hypothesis we introduce.

The hypothesis

The hypothesis is composed of three assumed elements:

(1) Reserve
(2) Reserve control
(3) Capillary shunting

The momentary cardiovascular performance reserve – "the reserve"

The term "cardiovascular reserve" has carried diverse connotations in previous publications. Usually "reserve" referred to the global health of the heart rather than a momentary measure [37]. We hereby introduce a new concept – "the momentary cardiovascular performance reserve" or in short "the reserve" which is the momentary global capability of the circulation to increase performance in order to meet intensifying needs of aerobic activity. Generally, the reserve is highest at rest, it reversibly decreases with increased activity. It also decreases (either reversibly or irreversibly) with a diversity of morbid conditions. The reserve is the underlying measure in both HF and shock rather than momentary cardiovascular performance.

Fig. 1 shows the assumed reserve level by morbidity severity and its dynamic with aerobic activity intensity.

It is interesting to note that low frequency heart rate variability (LF-HRV) resembles the assumed reserve characteristics: Firstly, LF-HRV power is highest at rest, and decreases with activity. Secondly, LF-HRV is lower in association with several morbidities