CHEST

Cardiac Dysfunction After Neurologic Injury

What Do We Know and Where Are We Going?

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VIDEO

Recent literature has implicated severe neurologic injuries, such as aneurysmal subarachnoid hemorrhage, as a cause of cardiac dysfunction, impaired hemodynamic function, and poor outcomes. Mechanistic links between the brain and the heart have been explored in detail over the past several decades, and catecholamine excess, neuroendocrine dysfunction, and unchecked inflammation all likely contribute to the pathophysiologic process. Although cardiac dysfunction has also been described in other disease paradigms, including septic shock and thermal injury, there is likely a common underlying pathophysiology. In this review, we will examine the pathophysiology of cardiac dysfunction after neurologic injury, discuss the evidence surrounding cardiac dysfunction after different neurologic injuries, and suggest future research goals to gain knowledge and improve outcomes in this patient population.

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The idea of an "invisible" link between the brain and heart has been recognized for centuries.[1] For example, although sudden death after severe fright and emotional stress has been reported in ancient texts for centuries, a greater interest in brain-heart interactions has been seen in the medical literature over the past several decades.[2,3] In addition, a growing body of literature has implicated other neurologic injuries, especially aneurysmal subarachnoid hemorrhage (SAH), as a cause of cardiac dysfunction. Although SAH has received the most in-depth study, the body of literature regarding brain-heart interactions in other neurological conditions is more limited.

Some mechanistic links between the brain and the heart have been explored in detail and are considered to be plausible explanations for the observed clinical symptoms. Although cardiac dysfunction has been described in other disease states, including septic shock[4,5] and thermal injuries,[6] there may be a common link regarding catecholamine excess and unchecked inflammation. In this review, we will examine the known pathophysiology of cardiac dysfunction after neurologic injury and suggest a common unifying pathophysiological process, explore the current state of knowledge in various neurologic injury paradigms, and discuss

ABBREVIATIONS: cAMP = cyclic adenosine monophosphate; CBN = contraction-band necrosis; CI/RI = cardiac ischemia/reperfusion injury; NSM = neurogenic stunned myocardium; RWMA = regional wall motion abnormalities; SAH = aneurysmal subarachnoid hemorrhage; TBI = traumatic brain injury; TSM = Takotsubo cardiomyopathy

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future directions for research into these complex disorders.

Neurogenic Stunned Myocardium vs Stress Cardiomyopathy

Cardiac dysfunction after neurologic injury is currently classified either as neurogenic stunned myocardium (NSM) or stress-induced cardiomyopathy (ie, Takotsubo cardiomyopathy [TSM], also known as "broken heart syndrome").[7] Of particular note are the general location (basal in NSM vs apical in TSM) of the myocardial dysfunction, and the predilection toward the female sex, which is more common in TSM[8,9] as compared with NSM.[10] Furthermore, there is debate as to whether NSM and TSM are distinct entities or simply represent different manifestations of a similar underlying pathophysiologic pathway, ultimately resulting in cardiac dysfunction.[11] A review suggested that the clinical and pathophysiologic similarities between the two syndromes suggests a revision of the diagnostic criteria[7]; in fact, the updated Mayo Clinic criteria for diagnosis of TSM includes intracranial hemorrhage.[12] In light of the debate in nomenclature as well as the heterogeneous nature of NSM, we will refer to this state more generally as "cardiac dysfunction" throughout the remainder of this article.

Pathophysiology of Cardiac Dysfunction After Neurologic Illness

A growing body of data is beginning to uncover the complex interactions between the impaired brain and the heart and is summarized in Figure 1, with clinical examples in Videos 1 and 2. Several basic science studies have highlighted the role of the sympathetic nervous system and catecholamine release on cardiac biomarker elevation and histologic evidence of myocardial damage in a variety of animal models.[13-17] Preclinical experiments have been validated by clinical findings of cardiac dysfunction in prospective studies, case series, and case reports. Although SAH[18] and emotional distress[3] remain major disease paradigms in which we draw mechanistic information, cardiac dysfunction has been reported after virtually every major injury to the neurologic system.[7]

Excess catecholamines are central to the pathophysiology of brain-heart interactions. The initial injury to the brain activates pathways of catecholamine release through a variety of mechanisms. Independent of the specific injury type, three key factors are involved at the level of the brain: the location of the lesion, rises in intracranial pressure, and the activation of the lower brain neuroendocrine pathways from the hypothalamus.

A set of experiments by Oppenheimer and Cechetto[19] helped to map the particular areas of the brain with autonomic effects, determining a central role of the

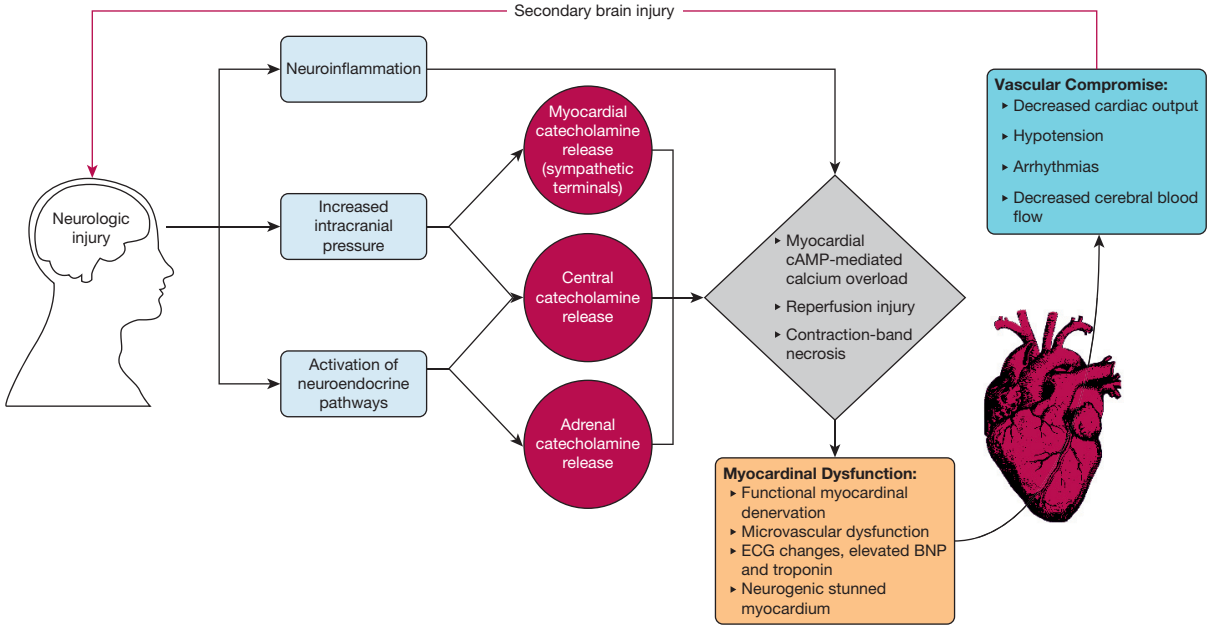

Figure 1 – *Mechanisms and clinical implications of cardiac dysfunction after neurologic illness. BNP = brain natriuretic peptide; cAMP = cyclic adenosine monophosphate.*