Non-Cardiac Organs Metamorphose Heart
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T he sympathetic and parasympathetic nervous systems regulate heart function. Elevated sympathetic nerve activity exacerbates heart failure (HF) and arrhythmia. Beta-blockers are the current treatment for HF and arrhythmia. Denervation of the cardiac sympathetic nervous system is also effective for electrical storms. Autonomic nerve activities are not easily visualized in usual clinical practice. Electrocardiograms (ECG) are believed to reflect indirectly some sort of imbalance of autonomic nervous system activity.

On the other hand, it is well known that heart diseases change the ECG through autonomic nerve modification. Moreover, several non-cardiac disorders, such as brain hemorrhage, can cause ECG abnormalities by changing autonomic nervous system activity. Therefore, this evidence suggests that non-cardiac organs affect cardiac conditions through autonomic modification.

Chen, et al. reported nonalcoholic fatty liver disease (NAFLD) was a risk factor for arrhythmia after coronary ischemic events. NAFLD increased the incidence of ventricular arrhythmias and sinus arrest among non-ST-segment elevation myocardial infarction (NSTEMI) patients. Their study indicated that we should endeavor to provide more careful management of arrhythmia to AMI patients with NAFLD.

At a glance, it would be hard to believe that liver diseases are connected to heart rhythm formation. However, there have been several reports like that of Chen, et al., that indicated non-cardiac conditions can induce ECG alterations and arrhythmias. For example, intracranial disorders can cause ECG change. In 1947, Byer, et al. first reported the ECG alternation in a patient with subarachnoid hemorrhage (SAH). The features of SAH-provoked ECG changes are diverse, including ST-segment changes, elevation or depression, inverted T wave, U wave, and prolonged QTc interval. To investigate the underlying mechanisms, Rudenhill, et al. compared ECG abnormalities between patients with SAH and ones with brain diseases except SAH, such as intracranial tumors. Brain tumor cases are selected as cranial diseases without cardiac involvement. Only the SAH group showed a higher incidence of T wave abnormalities, the occurrence of U wave, and QTc prolongation. These results implied that the critical driver of brain-induced ECG changes depended on the kinds of intracranial diseases (Figure).

Abdominal diseases have been also reported to shift the ECGs. For example, gastrointestinal distension caused by ileus can yield an AMI-like ECG without coronary stenosis. The AMI-like ST-segment elevation is quickly resolved by nasogastric tube placement and reduction of colon pressure. Other abdominal diseases such as acute cholecystitis, acute pancreatitis, and ulcer can induce ST-segment change and sinus bradycardia or complete atrioventricular block.

What is the mechanism of non-cardiac-driven ECG alterations? As expected, elevated cardiac sympathetic tone and excessive catecholamine production are believed to be central in causing ECG changes. Within the brain, the insular cortex, amygdala, and lateral hypothalamus are core sites for controlling the sympathetic nervous system. Considering the mechanism of central nervous system disorder associated-ECG changes and arrhythmias, the direct or indirect effects on the core sites within the brain are convincing for now. Myocardial damage can be experimentally mimicked by the parenteral administration of catecholamines or by electrical stimulation of a specific brain area. This result mechanistically supports the hypothesis that sympathetic overactivity by brain change affects the heart. Catecholamines have either a direct toxic effect on myocytes or an indirect impact like subsequent myocardial damage through ischemic insult by coronary artery vasoconstriction. Non-cardiogenic myocardial injury after an acute neurologic disease was proven by the elevation of cardiac troponin I level.

In this issue, Chen, et al. reported that the impaired balance of cardiac autonomic function caused the higher incidence of arrhythmia in patients with NAFLD after NSTEMI. Past studies have revealed that hepatic steatosis could cause cardiac autonomic dysfunction. Chen, et al. also showed increased cardiac sympathetic activity and decreased vagal activity, indicated by higher SDNN and lower PNN50, in AMI patients with NAFLD. On the other hand, in the cases of gastrointestinal distension with...
ST-segment elevation, elevated vagal tone by visceral-cardiac reflex is believed to be a possible mechanism.\(^{11}\) Given these reports, the impaired cardiac autonomic function is a source of ECG changes and arrhythmias in patients with non-cardiac disorders.

In 1968, Bonica, et al. reported that human preganglionic cardiac sympathetic output originates from the first to fifth thoracic spinal cord segment.\(^{22}\) Since then, several researchers have tried to prove the level of pre and post-ganglionic sympathetic output regulating heart function.\(^{23,24}\) Despite extensive anatomical research, the route and number of postganglionic nerves remain unclear. Other ganglions, including the superior cervical ganglion, middle cervical ganglion, vertebral ganglion, and inferior cervical ganglion, have often been mentioned to give rise to sympathetic cardiac nerves.\(^{24,25}\) Especially, the inferior cervical ganglion forms stellate ganglion, fused with the first thoracic ganglion. Although the distribution of heart-regulating ganglions and the location of cholinergic and adrenergic nerve fibers are still controversial, several strategies targeting cardiac autonomic innervation have emerged, called neuromodulation.\(^3,26,27\)

Blockade of the right or left stellate ganglion would be a potential treatment for ventricular arrhythmia by reducing QTc prolongation. Owczuk, et al. demonstrated that thoracic epidural anesthesia (TEA), but not lumbar epidural anesthesia, resulted in significant decreases in QTc interval.\(^{26}\) Moreover, TEA and stellectomy significantly reduced the arrhythmia burden in patients with refractory ventricular arrhythmias.\(^{2,26}\) Neuromodulation for atrial fibrillation (AF) could also have the potential to do so. Blockade of the stellate ganglion successfully reduced the atrial effective refractory period and AF duration.\(^{21}\) In addition, according to reports about the effect of neuromodulation on severe HF, TEA over conventional medical treatment could reduce the chamber dimensions and improve systolic function.\(^{20,30}\) Recently, Fossay, et al. reported a very interesting relationship between heart function and spinal cord injury.\(^{31}\) They found that activation of the sympathetic circuitry below the level of spinal cord injury causes an increase in heart systolic function.\(^{31}\)

In conclusion, non-cardiac organs can affect heart activity, and the mechanism is mainly through changes in nervous system activity. Therefore, non-heart organ disorders and their connection to the heart may be potential therapeutic targets of heart diseases.

### Disclosure

**Conflicts of interest:** None.

### References


