Acupuncture in the Treatment of Heart Failure

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Abstract: Few clinical studies evaluating the efficacy of acupuncture in heart failure have been performed. These studies have focused on the acupoint Neiguan (P6) in patients experiencing heart failure and have variably reported either an acute increase in ventricular contractility and/or relaxation or no effect on ventricular contractility and/or relaxation. To date, clinical studies have been hampered by small enrollment, inadequate controls, and unblinded design. Recent scientific studies of animal models of acupuncture support the concept that acupuncture produces release of endogenous opioids in the central nervous system, which in turn could inhibit central sympathetic outflow. Patients experiencing heart failure have markedly elevated sympathetic activity, and those with the greatest sympathetic activation have the worst survival. Preliminary data from our laboratory suggests that acupuncture could be sympatholytic in heart failure. We found that sympathetic activation during acute mental stress was virtually eliminated after acupuncture. More studies defining the efficacy of acupuncture, and its mechanisms, in the treatment of heart failure are warranted.

Key Words: acupuncture, heart failure, sympathetic nervous system, microneurography

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Acupuncture has been used for thousands of years to treat several disorders, including cardiovascular disorders. It has been used to treat chest pain in patients with coronary artery disease and to lower blood pressure in hypertensive patients.[1,2] Furthermore, acupuncture has been used for the treatment of heart failure.[3–5] The Neiguan (P6) point, located between the tendons of palmaris longus and flexor carpi radialis muscles 2 cm above the wrist, is the site most often used to treat cardiac abnormalities. Early studies suggest that acupuncture could be efficacious in heart failure, but conclusive evidence is lacking and potential mechanisms remain unexplored.

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Heart failure is characterized by activation of several neurohumoral systems, including the sympathetic nervous system. Sympathetic nervous system activation has been associated with progression of heart failure, increased sudden death risk, and increased mortality.[6] Pharmacologic treatment of heart failure is focused on interruption of this sympathetic activation with stability or improvement in cardiac function and decreased mortality. Whether the potential benefits of acupuncture are mediated through modulation of the sympathetic nervous system remains an unproven, yet intriguing hypothesis. In this review, we 1) review available evidence that acupuncture is therapeutic in heart failure, 2) develop a rationale for further studies of acupuncture in heart failure, and 3) discuss our experience with acupuncture in patients with heart failure.

PRIOR EXPERIENCE OF ACUPUNCTURE IN HEART FAILURE

In the first study to examine acupuncture in heart failure, Shuxia and colleagues[3] studied patients with 1) hypertrophic cardiomyopathy (n = 24), 2) congestive cardiomyopathy (n = 16), and 3) normal healthy control subjects (n = 12). Acupuncture was compared at 2 sites bilaterally: 1) Neiguan (P6) and 2) Shaofu (H8). Electroacupuncture for 2 minutes was followed by retention of the needles in place for 15 minutes. Echocardiography, apex cardiography, and systolic time interval were used to assess cardiac performance before and after acupuncture. In 2 patients, pulmonary capillary wedge pressure was recorded. In the hypertrophic cardiomyopathy group, acupuncture at Neiguan was associated with an overall worsened cardiac performance. Left ventricular outflow diameter was diminished, stroke volume and cardiac output were diminished significantly, and the pulmonary capillary wedge pressure increased. In contrast, in the congestive cardiomyopathy group, acupuncture at Neiguan improved parameters of cardiac function, specifically contractility. Left ventricular outflow diameter, stroke volume and cardiac output, and pulmonary capillary wedge pressure decreased. The opposite acute effects were seen after stimulation at Shaofu. That is, left ventricular outflow tract diameter increased in hypertrophic cardiomyopathy but decreased in congestive cardiomyopathy; stroke volume and cardiac output increased in hypertrophic but decreased in

congestive cardiomyopathy. Acupuncture had no significant effect in normal subjects. The investigators concluded that acupuncture at the Neiguan point had an overall acute sympathomimetic effect, which could be acutely beneficial in congestive cardiomyopathy, whereas Shaofu appeared to be sympatholytic with similar effects to beta-blockers in hypertrophic cardiomyopathy.

In a small, controlled but unblinded study, the acute effect of electroacupuncture at Neiguan or at an adjacent, nonacupoint site on the heart rate, blood pressure, and echocardiographic findings in 8 patients experiencing congestive heart failure was studied.[4] After Neiguan stimulation, but not control stimulation, left ventricular end diastolic volume and stroke volume increase significantly. Heart rate, blood pressure, and ejection fraction remained unchanged after each type of stimulation. The investigators concluded that acupuncture at Neiguan improved ventricular relaxation, but in contrast to Shuxia's study, contractility was not affected by acupuncture at Neiguan.

In a study of a large, heterogeneous group of cardiac patients (n = 107) and control subjects (n = 100) without cardiac disease, the effects needling at the left Neiguan point on left ventricular function was examined.[5] In normal subjects, heart rate decreased significantly after needling, but other parameters of cardiac function remained unchanged. In cardiac patients, heart rate decreased, contractility increased, but ventricular relaxation remained unchanged.

The explanations for the inconsistent findings in these studies can be found in their limitations of size, inadequate or absent controls, and unblinded design. To date, there are no large randomized, controlled trials of acupuncture in heart failure in which investigators interpreting echocardiographic and/or hemodynamic data are blinded and satisfactory acupuncture controls are used. The effects of chronic acupuncture in patients experiencing heart failure have not been studied.

RATIONALE FOR FURTHER STUDIES OF ACUPUNCTURE IN HEART FAILURE

Studies of acupuncture-like stimulation have been performed in animal models.[7,8] Li and colleagues[7] studied a feline model of electroacupuncture at the Neiguan point, in which the median nerve was stimulated with low frequency (5 Hz) to mimic electroacupuncture. Type III and IV sensory fibers were stimulated. Myocardial ischemia induced by reflex activation of the cardiovascular system was improved after 30 minutes of electroacupuncture, consistent with a sympatholytic effect. Yao and colleagues[8] used acupuncture-like stimulation of the sciatic nerve in Wistar-Kyoto normotensive rats (WKR). After 30 minutes of acupuncture, blood pressure and heart rate fell significantly and remained depressed for 12 hours. Type III afferent nerve stimulation was essential to the depressor response. Furthermore, recordings of efferent splanchnic nerve efferent discharge demonstrated a simultaneous fall in sympathetic activity, consistent with the hypothesis that the depressor response was mediated through attenuation of the sympathetic nervous system. These findings are consistent with the concept that the depressor effect of acupuncture is mediated through activation of peripheral sensory nerves, including type III nerves, which lead to attenuation of efferent sympathetic nerve activity.

Recent scientific studies in acupuncture analgesia support the concept that acupuncture produces release of endogenous opioids in the central nervous system.[9–12] Experimental evidence supports the concept that opioids in the central nervous system, in addition to modulating acupuncture analgesia, could also play a role in sympathetic neural regulation of the cardiovascular system. The depressor effect of acupuncture in WKRs, discussed previously, is abolished by intravenous naloxone.[8] Similarly, in the feline model of acupuncture, naloxone administered intravenously or microinjected into the rostral ventrolateral medulla (rVLM) inhibits the antiischemic effect of electroacupuncture.[13] The rVLM, where opioid receptors have been localized, is an important cardiovascular center as well.[14] It is possible that acupuncture is sympathoinhibitory in humans through activation of muscle sensory neurons, which then trigger central nervous system opioid release (Fig. 1).

The nucleus tractus solitarius (NTS) is the site of integration of visceral sensory information and modulates sympathetic outflow. Interestingly, in rabbits, extracellular recordings made with glass microelectrodes positioned in the NTS demonstrate convergence of activation in the NTS during Neiguan stimulation and during acute myocardial ischemia.[15] These findings are consistent with the hypothesis that Neiguan stimulation affects the cardiovascular reflex

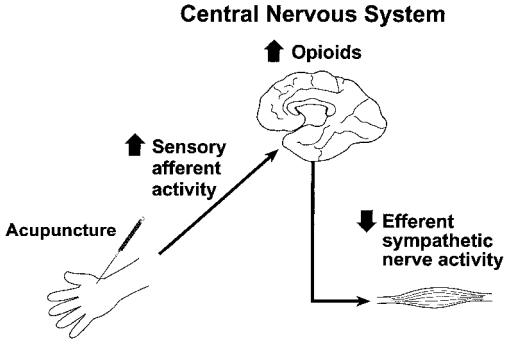

FIGURE 1. Hypothesized mechanism of acupuncture modulation the sympathetic nerve activity in heart failure. Acupuncture needles stimulate sensory neurons located in muscles at conventional acupuncture sites. Activation of these type III nerve fibers induces release of endogenous opioids in the central nervous system. Increased central sympathetic opioid levels directly suppress central sympathetic neural outflow.

changes that occur during cardiac ischemia and could be involved during other cardiac conditions such as heart failure. Imaging studies support this hypothesis. Using positron emission tomography and functional magnetic resonance imaging during acupuncture at sites traditionally used for analgesia, hypothalamic and subcortical centers involved in autonomic neural regulation are activated.[16–18] The Neiguan acupoint has not yet been studied.

ACUPUNCTURE IN PATIENTS WITH HEART FAILURE

Preliminary evidence from our laboratory is consistent with a sympatholytic effect of acute acupuncture in patients experiencing chronic heart failure.[19] Ten patients with advanced heart failure underwent acute mental stress testing before and after "real" acupuncture at Neiguan (P6), Hegu (Li4), and Taichong (Liv3). Acupuncture needles were inserted and manually stimulated to achieve the De Qi sensation of heaviness, fullness, or soreness, and then left in place for 15 minutes. In 2 control protocols, 1) needles were placed at nonacupoints and were stimulated in 10 patients experiencing heart failure; or 2) empty needle holders were tapped against the skin outside the patient's field of view, but subjects were not told that no needles had actually been inserted (n = 10). Mental stress was produced by having the patient perform mental arithmetic and answer aloud or by the color–word conflict test. In this test, names of colors were written in a different color ink than the printed word. Patients were instructed to rapidly name the color, not read the word. Sympathetic nerve activity (MSNA) directed to the muscle vasculature was directly recorded from the peroneal nerve using the technique of microneurography. Resting MSNA was not different before and after acupuncture. During mental stress, MSNA increased by approximately 25%. This increase in sympathetic activity was eliminated after real acupuncture, but sympathetic activity remained unchanged nonacupoint or no-needle acupuncture, eliminating the possibility of a placebo or time effect.

In summary, acupuncture remains an intriguing yet understudied therapeutic modality in patients with advanced heart failure. Animal data supports the hypothesis that acupuncture at specific sites could attenuate sympathetic nerve activation. Preliminary data in humans is consistent with the hypothesis that acupuncture could activate cardiovascular centers in the central nervous system, which directly modulate central sympathetic neural outflow. Direct sympathetic nerve recordings in patients with heart failure lend further support to the sympatholytic potential of acupuncture. Because the most effective pharmacologic therapies in heart failure are known to work through interactions with the autonomic nervous system, further studies of acupuncture efficacy and its mechanisms in heart failure are mandated.

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