Effects of Heat Stress on Thermoregulatory Responses in Congestive Heart Failure Patients

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Background—Clinical observations suggest that tolerance to heat stress may be impaired in patients with cardiovascular diseases, particularly those associated with impaired ventricular function and congestive heart failure (CHF). However, thermoregulatory function during a controlled heat stress challenge in patients with CHF has not been studied.

Methods and Results—To test the hypothesis that thermoregulatory responses are attenuated in such patients, we assessed cutaneous vasodilation and sweat rate in patients with stable class II–III CHF and in matched healthy subjects during passive whole-body heating. Whole-body heating induced a similar increase in internal temperature ($\approx 0.85°C$) in both groups. The sweating responses in patients with CHF were not significantly different from that in control subjects. In contrast, the elevation in forearm cutaneous vascular conductance in patients with CHF was reduced by nearly 50% relative to the control subjects (3.8 ± 0.8 versus 6.9 ± 1.0 mL/100 mL tissue per minute per 100 mm Hg, $P=0.04$). Moreover, maximal cutaneous vasodilator capacity to direct local heating in patients with CHF was also significantly lower than in control subjects, suggesting that vascular remodeling may be limiting cutaneous vasodilation during hyperthermia.

Conclusions—These observations suggest that patients with CHF exhibit attenuated cutaneous vasodilator responses to both whole-body and local heating, whereas sweating responses are preserved. Attenuated cutaneous vasodilation may be a potential mechanism for heat intolerance in patients with CHF. (***Circulation***. 2005;112:2286-2292.)

Key Words: blood flow ■ heart failure ■ hemodynamics ■ cardiovascular diseases ■ nervous system, autonomic

Adverse cardiac events occur at a higher frequency during summer months within the United States,[1–3] and patients with congestive heart failure (CHF) may be particularly vulnerable to injury from heat stress.[2] This risk was highlighted during the 1995 heat wave in Chicago in which many reported "excess" deaths occurred in people with a prior "heart condition."[3] These observations suggest that thermal tolerance to heat stress may be altered in patients with CHF.

In patients with CHF, hemodynamic factors influencing the regulation of stroke volume, as well as neurohormonal factors influencing reflex regulation of heart rate and vascular resistance, are deranged.[4,5] These altered responses may contribute to impaired thermoregulatory responses in patients with CHF by limiting the ability to appropriately perfuse the skin during a heat stress, thereby limiting the ability to dissipate a thermal load.

Exposure of healthy individuals to a hyperthermic environment causes a series of physiological responses that are critical for thermoregulation. One of the more pronounced and physiologically important responses is an increase in skin blood flow. In thermal neutral conditions, skin receives 5% to

10% of resting cardiac output, whereas in conditions of heat stress skin blood flow can reach 50% to 70% of resting cardiac output, approaching 8 L/min.[6] To maintain blood pressure, cardiac output must increase; in normal subjects up to 13 L/min during whole-body heating.[7] Although cardiac output in hyperthermic patients with CHF increases,[8] this increase may be lower than that required to adequately perfuse the cutaneous circulation during a heat stress. Therefore, the cardiac reserve may be inadequate to perfuse the skin for thermoregulation while still maintaining sufficient perfusion pressure and blood flow to vital organs.

Alternatively, CHF may directly alter cutaneous vasculature function,[9] which may alter cutaneous vasodilator responses independent of cardiac output. In support of this hypothesis, previous studies showed that maximal peripheral vasodilator capacity to stimuli such as reactive hyperemia[10–12] was impaired, as was endothelium-dependent vasodilator responses in isolated human cutaneous arteries.[13] In addition to cutaneous vasodilation, appropriate sweating responses are necessary for thermal homeostasis during hyperthermic exposure. On the basis of clinical observations and

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TABLE 1. Clinical Findings and Medications for Each of the Patients With Congestive Heart Failure

	Subjects													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Sex	M	M	F	M	M	M	M	F	M	F	M	M	M	F
Age, y	42	44	38	53	63	59	49	71	76	41	68	33	52	27
LVEF, %	35	30	36	35	30	36	36	35	38	32	16	31	38	27
Medications														
Carvedilol	√							√		√			√	√
Metoprolol succinate		√							√				√	
Atenolol				√										
ACE inhibitor/ARB		√		√	√	√	√			√	√	√		√
Ca^{2+} channel blocker					√				√					
Digoxin			√		√	√	√			√	√	√	√	
Spironolactone									√	√				
Isosorbide nitrate		√					√		√					
α-Blocker									√				√	
Loop diuretic	√		√	√	√	√	√	√		√	√	√		√

LVEF indicates ejection fraction; medications, class of medication each subject was taking; and ACE inhibitor/ARB, angiotensin-converting enzyme inhibitor or angiotensin receptor blocker.

the aforementioned physiological adaptations to CHF, we hypothesized that cutaneous vasodilation and sweating responses during heat stress would be attenuated in patients with CHF.

Methods

Subjects

A total of 14 patients with CHF (10 male, 4 female; age, 51±4 years; height, 177±2 cm; weight, 85±5 kg) and 14 healthy control subjects (10 male, 4 female; age, 51±4 years; height, 176±3 cm; weight, 82±4 kg) matched for age, gender, body mass index, and race participated in this study (Table 1). Thirteen patients with CHF (subjects 1 to 13 in Table 1) and 13 matched control subjects participated in protocol 1. Six patients with CHF (subjects 9 to 14 in Table 1) and 6 control subjects participated in protocol 2. Patients with CHF were eligible on the basis of the following inclusion criteria: (1) New York Heart Association class II–III after stabilization; (2) ejection fraction <0.40 determined by echocardiography, (3) systolic blood pressure ≤140 mm Hg, and (4) no underlying aortic outflow obstruction as assessed by echocardiography. Patients were recruited from the heart failure clinics at Parkland Memorial Hospital and St Paul University Hospital, both teaching hospitals of the University of Texas Southwestern Medical Center at Dallas, as well as from the private practices of 2 major cardiology groups specializing in heart failure care at Presbyterian Hospital of Dallas. Patients with ischemic and nonischemic pathology were considered eligible for this study. Patients with CHF were excluded from the study if they were diagnosed with diseases known to impair thermoregulatory responses, such as diabetes mellitus.[14] Table 1 lists the patients' physical characteristics, ejection fraction, and the medication class each patient was taking. The mean ejection fraction of the healthy control subjects was 64±1%. Most of the patients (12 of 14) reported that they participated in some form of aerobic exercise (eg, walking, biking, and so forth); however, none participated in a structured exercise training program. All subjects refrained from caffeine, nicotine, alcohol, and exercise 24 hours before the study. This study was approved by the institutional review boards of the University of Texas Southwestern Medical Center and the Presbyterian Hospital of Dallas. Written informed consent from each subject was obtained before participation in this study.

Measurements

Internal temperature (Tcore) was measured either by esophageal temperature probe (YSI) with a thermistor placed at a distance of 25% standing height or by an ingestible telemetric temperature pill (HTI Technologies). Both of these methods provide an accurate measurement of internal temperature.[15,16] Mean skin temperature was obtained from the electrical average of 6 thermocouples attached to the skin.[17] The subject was dressed in a tube-lined suit that permitted control of skin temperature by changing the temperature of the water perfusing the suit.[18] Heart rate was obtained from the ECG signal interfaced with a cardiotachometer (CWE). Arterial blood pressure was measured from the upper arm by means of R-wave gated electrosphygmomanometry (SunTech). Mean arterial pressure (MAP) was calculated as diastolic pressure plus one-third pulse pressure. Forearm skin blood flow was measured by means of 2 methods from an area not covered by the tube-lined suit. The first method uses integrating laser-Doppler probes to continuously measure skin blood flow[19,20] from an area of approximately 28 mm². The second method measures forearm blood flow through venous occlusion plethysmography, with the increase in forearm blood flow during heat stress being entirely due to increases in skin blood flow.[21–23] For both methods of skin blood flow assessment, vascular conductance was calculated from the ratio of blood flow to MAP. Forearm sweat rate was measured from 2.83 cm² area by means of capacitance hygrometry (Viasala), as previously described.[18]

Protocol 1: Thermal Response to Whole-Body Heating

In both groups, normothermic baseline data (ie, blood pressure, heart rate, forearm skin blood flow, and sweat rate) were collected, whereas 34°C water perfused the tube-lined suit worn by the subject. After ≈6 minutes, whole-body heating began by elevating skin temperature to ≈38°C by perfusing warm (≈46°C) water through the water-perfused suit. Whole-body heating continued until Tcore increased a minimum of 0.7°C, which is sufficient to cause pronounced cutaneous vasodilation and sweating in healthy individuals.[18,24,25] After this point, for patients with CHF, the heat stress continued until the patient requested the heat stress to be stopped. For the control subjects, the heating was stopped when the increase in Tcore reached the same level as the matched patient with CHF. Plethysmographic forearm blood flows and blood pressure were measured repeatedly throughout whole-body heating. After the heat

TABLE 2.   Hemodynamic and Thermal Responses to Whole-Body Heating in Patients With Congestive Heart Failure

	Patients With CHF		Control Subjects	
	Normothermia	Heat Stress	Normothermia	Heat Stress
MAP, mm Hg	89.8±3.4	84.9±4.0	86.8±2.3	81.5±2.2
HR, bpm	70.0±4.3†	87.3±4.9*	58.2±2.8	80.0±4.3*
Tsk, °C	34.1±0.1	38.0±0.2*	34.1±0.1	38.0±0.1*
Tcore, °C	36.9±0.1	37.7±0.1*	36.8±0.1	37.7±0.1*

MAP indicates mean blood pressure calculated from diastolic pressure plus one-third pulse pressure; HR, heart rate from ECG; Tsk, mean skin temperature; and Tcore, internal temperature.

*$P<0.05$ compared with normothermia; †$P<0.05$ compared with control subjects.

Number of subjects: 13 patients with CHF and 13 control subjects.

stress, a 3-cm-diameter heater element (Perimed), which housed the laser-Doppler flow probe, was engaged to elevate local skin temperature to 42°C. Local temperature was held at this level for 30 minutes to elicit maximal cutaneous vasodilation.[26]

Protocol 2: Maximal Cutaneous Vasodilator Capacity

Cutaneous vasodilation of skin not in contact with the water-perfused suit discussed in protocol 1 occurs through central-mediated reflex mechanisms. This is in contrast to cutaneous vasodilation during direct local heating, which occurs through a different mechanism.[27] Locally induced cutaneous vasodilation may reveal additional information about the responsiveness of the cutaneous vasculature to vasoactive agents (eg, nitric oxide[27]) and/or structural properties of this tissue. However, local heating data from protocol 1 are limited to a very small area sampled by the laser Doppler probe. Thus, to confirm results of the local heating procedure outlined in protocol 1, a second protocol was performed on a subset of subjects in whom vasodilatory responses to whole forearm local heating was assessed. In 6 patients with CHF and 6 control subjects, maximum vasodilation was induced by elevating local temperature surrounding the entire forearm to 42°C for 45 minutes by spraying warm water on the skin with the forearm in an enclosed chamber.[28] This temperature and duration has previously been shown to maximally dilate the cutaneous vasculature[26,29] without altering muscle blood flow.[30] Forearm blood flow was measured within the chamber 3 times per minute by venous occlusion plethysmography.

Data Analysis

Data were sampled at 50 Hz by means of a data acquisition system (Biopac System). Statistical analyses were performed with the use of SigmaStat software (SPSS Science). Thermoregulatory and hemodynamic parameters were statistically analyzed across whole-body heating by means of a 2-way ANOVA. The Tcore thresholds for vasodilation and sweating were identified by an experienced investigator who was blinded as to the subject group. The relation (slope) between Tcore and forearm vascular conductance was obtained by simple linear regression of the points after the Tcore threshold. A similar method was used to obtain the slope between Tcore and sweating rate. These Tcore thresholds and slopes for patients with CHF were compared with control subjects by *t* test. For protocol 2, the maximal cutaneous vasodilator capacity of patients with CHF was compared with control subjects by means of a *t* test. All values are reported as mean±SEM; probability values <0.05 were considered statistically significant.

Results

Thermal and Hemodynamic Responses to Whole-Body Heating

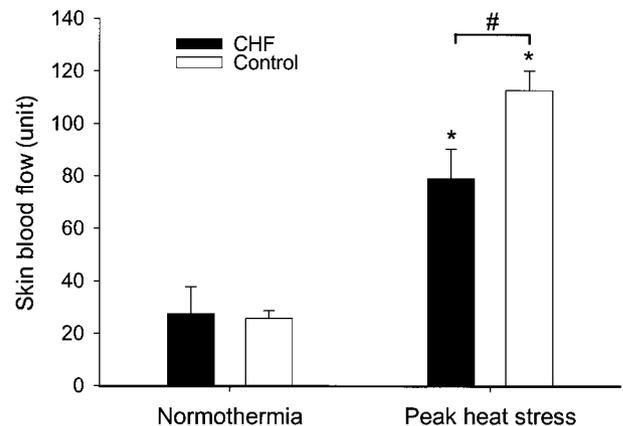Baseline Tcore was not different between groups (Table 2).

Figure 1. Forearm skin blood flow responses before heat stress and at the end of heat stress (peak heat stress). Skin blood flow was measured by means of laser Doppler flowmetry from an area not covered by the water-perfusing suit. Whole-body heating induced significant increases in skin blood flow in patients with congestive heart failure (CHF) and in control subjects. However, the elevation in skin blood flow in patients with CHF was significantly lower than in healthy control subjects. *$P<0.05$ compared with normothermia. #$P<0.05$, difference between groups.

As the result of matching of the increase in Tcore between paired subjects, the elevation in Tcore for the patients with CHF (0.83±0.05°C) was not different relative to the control subjects (0.87±0.05°C, $P=0.51$). This observation, combined with similar skin temperatures throughout the heat stress, demonstrates that the heat stress challenge was similar between groups. During whole-body heating, MAP did not change, whereas heart rate significantly increased in both CHF and control subjects (Table 2).

In the normothermic condition, baseline skin blood flow in patients with CHF, measured with laser Doppler flowmetry, was not significantly different from that in control subjects. However, at the end of the heat stress (peak heat stress), laser Doppler–derived skin blood flow of the patients with CHF was significantly lower relative to the control subjects (Figure 1). Maximum skin blood flow, through discrete local heating as measured by laser Doppler flowmetry, was significantly lower in the patients with CHF (122.8±17.4 U) relative to the control subjects (173.0±12.4 U, $P=0.01$).

The elevation in forearm cutaneous vascular conductance throughout whole-body heating, as measured by plethysmography, was also substantially attenuated in patients with CHF (Figure 2). The Tcore threshold for vasodilation in the patients with CHF was similar with the control subjects (37.00±0.12 versus 36.96±0.07°C, $P=0.74$). However, the slope of the relation between the elevation in forearm cutaneous vascular conductance relative to the elevation in Tcore was reduced in patients with CHF relative to control subjects (4.9±1.2 versus 9.2±1.4 conductance units/°C, respectively, $P=0.03$). This resulted in an elevation in forearm cutaneous vascular conductance in patients with CHF (3.8±0.8 mL/100 mL tissue per minute per 100 mm Hg) that was significantly lower at the end of the heat stress (peak heat stress) relative to the control subjects (6.9±1.0 mL/100 mL tissue per minute per 100 mm Hg, $P=0.04$). It should be
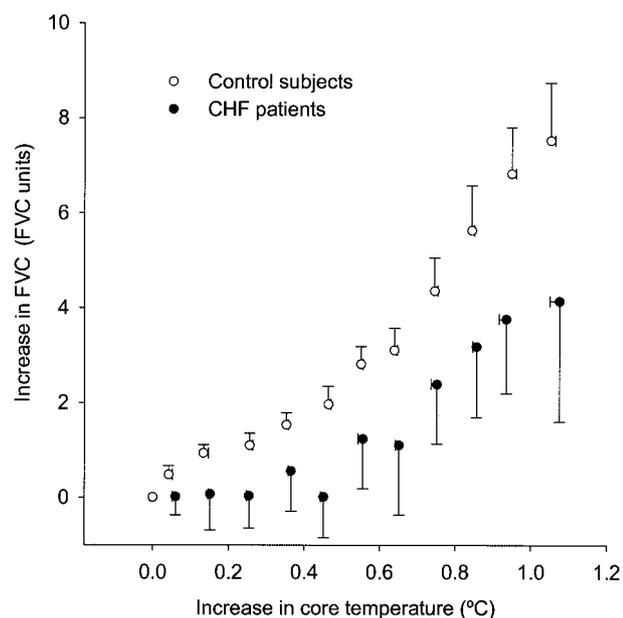
Figure 2. Average increases in forearm cutaneous vascular conductance (FVC) during heat stress for both groups of subjects. FVC was calculated as forearm blood flow (measured by means of limb plethysmography) divided by mean arterial blood pressure×100. The number of subjects in each group gradually decreased after an increase in core temperature of 0.7°C as subjects achieved their level of thermal tolerance in this experimental setting. When this occurred, heat stress was terminated for the matched subject at the same internal temperature elevation (FVC unit: mL/100 mL tissue per minute per 100 mm Hg.
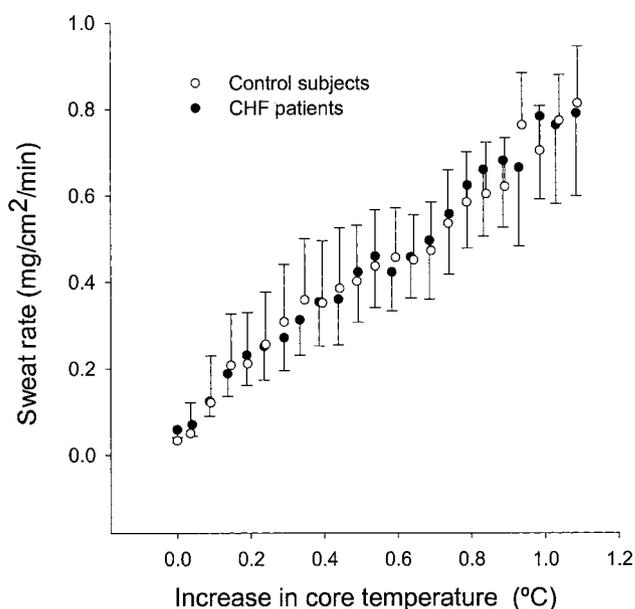

Figure 3. Average increase in forearm sweat rate during heat stress for both groups of subjects. Whole-body heating was sufficient to induced sweating in both groups. The number of subjects in each group gradually decreased after an increase in core temperature of 0.7°C as subjects achieved their level of thermal tolerance in this experimental setting.

noted that in Figure 2, the subject number decreased after Tcore increased ≈0.7°C because some subjects subjectively were unable to tolerate higher core temperatures. However, for each matched control subject, the heat stress was discontinued when Tcore increased to the same magnitude as that which occurred for the matched patient with CHF. Of the 13 patients with CHF, 7 took β-adrenergic–blocking agents. To account for a possible effect of these agents in altering cutaneous vasodilator response during the heat stress,[31,32] the patients with CHF were divided on the basis of the use of this agent, and cutaneous vasodilator data were reanalyzed between these groups. The peak elevation in forearm cutaneous vascular conductance in the group who took β-adrenergic–blocking agents (3.3±1.1 mL/100 mL tissue per minute per 100 mm Hg) was not different relative to the group who did not take β-adrenergic–blocking agents (4.3±1.2 mL/100 mL tissue per minute per 100 mm Hg, $P=0.51$).

Heat stress induced significant increases in sweating in both groups (Figure 3). The Tcore threshold for sweating in the patients with CHF was similar to that in the control subjects (37.00±0.13 versus 36.97±0.07°C, $P=0.84$). Moreover, the slope of the relation between the elevation in sweat rate relative to the elevation in Tcore in patients with CHF was similar to that in control subjects (1.09±0.25 versus 1.26±0.25 mg/cm² per minute per °C $P=0.65$). At the end of heat stress (peak heat stress), sweat rate of the patients with CHF (0.62±0.13 mg/cm² per minute) was not significantly different from the control subjects (0.77±0.11 mg/cm² per minute, $P=0.39$).

Maximal Cutaneous Vasodilator Capacity

Local heating of a forearm with the water spray device did not alter MAP or heart rate in either group. At the end of local heating with this device, the increase in forearm blood flow in patients with CHF (5.9±1.2 mL/100 g tissue per minute) was significantly less relative to that in control subjects (10.2±1.9 mL/100 g tissue per minute). This resulted in a significant attenuation in the calculated increase in forearm cutaneous vascular conductance in the patients with CHF during this mode of local heating (Figure 4). Moreover, the increase of cutaneous vasculature conductance in each CHF patient was consistently less relative to that person's matched control subject. As outlined above, similar findings were observed with the discrete local heating protocol.

Discussion

The major novel finding of the present study is that cutaneous vasodilator responses to both whole-body and local heating are significantly reduced in patients with CHF, whereas sweating responses are not impaired in these patients. These observations suggest that impaired cutaneous vasodilation may be a key mechanism for heat intolerance in patients with CHF.

A number of studies report that adverse cardiac events occur at a higher frequency when environmental temperature is elevated,[1–3] which suggests that thermal tolerance may be reduced in patients with cardiovascular disease. Patients with heart failure may be at particularly high risk because of their compromised hemodynamics and limited cardiac output reserve. However, before the present study systemic thermal regulatory responses to a heat stress challenge had not been investigated in patients with CHF. The present data clearly show that cutaneous vasodilation during whole-body heating
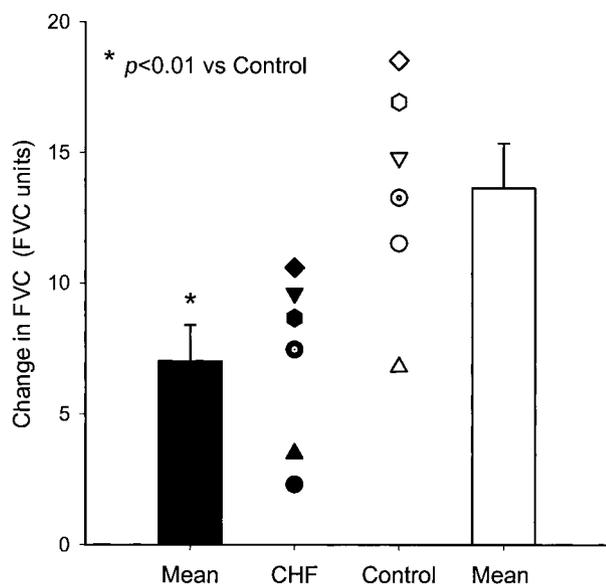
Figure 4. Maximum increases in forearm cutaneous vascular conductance (FVC) caused by local heating of the entire forearm to 42°C for 45 minutes by means of the forearm being enclosed in a water spray device. FVC was calculated as forearm blood flow (from limb plethysmography) divided by mean arterial blood pressure×100. Small symbols represent individual data from patients with CHF (closed) and from control subjects (open). Similar symbols represent matched subjects. *Significantly less than control subjects (FVC unit: mL/100 mL tissue per minute per 100 mm Hg).

is reduced in patients with CHF. On the other hand, sweat responses during the heat stress were not different between patients with CHF and control subjects (see Figure 3), suggesting intact temperature sensing, efferent sympathetic cholinergic innervation, and sweat gland function. Taken together, the present data suggest that the function of cutaneous vasodilation but not sweating is altered with CHF, and thus heat dissipation to a hyperthermic challenge will be attenuated in these patients.

The mechanism(s) for impaired vasodilator responses in patients with CHF remains speculative. At least 3 hypotheses may explain this observation: altered neural control of the cutaneous circulation, altered responsiveness to vasodilator neurotransmitters, and/or structural changes of the cutaneous vasculature. With regard to the first, control of human skin blood flow occurs through 2 distinct sympathetic pathways. The first, through sympathetic vasoconstrictor nerves, releases norepinephrine and causes cutaneous vasoconstriction,[25,33] whereas the second system is a nonadrenergic sympathetic active vasodilator system.[6,25] The neurotransmitter responsible for cutaneous active vasodilation remains unknown, although this neurotransmitter probably is a peptide coreleased with acetylcholine from sympathetic cholinergic nerves.[34] In healthy individuals, on exposure to a warm/hot environment, the initial increase in skin blood flow occurs through withdrawal of cutaneous vasoconstrictor activity.[25] As internal temperature continues to increase, the cutaneous active vasodilator system is engaged,[25] and this system mediates 85% to 95% of the rise in skin blood flow in nonglabrous (ie, hairy) skin during whole-body heating.[35]

Patients with CHF are characterized by an increase in sympathetic activity[4,5] and increased plasma norepinephrine.[4,5,8] Given these observations, attenuated cutaneous vasodilator responses during heat stress in patients with CHF could be due to enhanced cutaneous vasoconstrictor neural activity and/or reduced cutaneous active vasodilator activity, perhaps through a baroreflex mediated response.

In healthy individuals, skin blood flow can increase upward to 8 L/min during pronounced whole-body heating.[6] To maintain blood pressure in the face of a large reduction in vascular resistance that occurs with heat stress, cardiac output must increase. For example, Rowell et al[7] have shown that during whole-body heat stress, cardiac output is capable of doubling (up to 13 L/min) in healthy individuals. Although cardiac output in patients with CHF exposed to heat stress has been shown to increase up to ≈3.6 L/min per m²,[8] if this increase in cardiac output is insufficient to offset the reduction in vascular resistance, blood pressure will decrease. Such a reduction in blood pressure will evoke baroreflex mediate responses that have been shown to attenuate cutaneous vasodilation[24,36] without altering sweating.[18] Consistent with this hypothesis is the observation that blood pressure was well maintained in patients with CHF during the heat stress. Thus, attenuated cutaneous vasodilation may be necessary to prevent a reduction in blood pressure in patients with CHF with limited cardiac output reserve during heat stress, although this occurs at the expense of thermal regulatory control.

Instead of, or in combination with the aforementioned mechanism, altered nitric oxide–mediated mechanisms in patients with CHF may also impair cutaneous vasodilator responses to heating. It has been shown that production, release, and vascular responsiveness to nitric oxide is abnormal in patients with CHF,[37–40] whereas studies have shown that ≈30% of the elevation in cutaneous vascular conductance during indirect whole-body heating is mediated by nitric oxide–dependent mechanisms.[41,42] Therefore, if nitric oxide production, release, and/or responsiveness are similarly attenuated in the skin of patients with CHF, this could explain a component of the observed reduction in cutaneous vasodilation during the whole-body heat stress.

In addition to altered responsiveness to vasoactive agents, structural changes in the cutaneous vasculature of patients with CHF may result in attenuated vasodilator responses to a heat stress. Sustained local heating causes cutaneous vasodilation through nitric oxide–dependent mechanisms.[27,43] The present and previous[10,44] findings show that local heating-induced cutaneous vasodilation is attenuated in patients with CHF. These observations are consent with those of others showing that patients with CHF exhibit attenuated endothelium-dependent vasodilation of the peripheral circulation,[38,45,46] including skin.[47] However, it is recognized that the present results do not permit the discrimination between altered responsiveness to vasodilator agents, such as nitric oxide, from possible structural changes in the cutaneous vasculature with CHF, previously shown in these patients. With regard to the latter, in patients with CHF, structural alterations of cutaneous terminal arterioles have been reported, and these alterations may decrease distensibility and

increase stiffness of the cutaneous microvascular bed.[9] Taken together, these findings suggest that attenuated vascular responsiveness to vasodilator agents and/or structural changes in the cutaneous vasculature may at least partially explain the observed attenuated vasodilator responses to whole-body heating.

Study Limitations

Like all treated patients with CHF, patients in the present study were taking a variety of cardiovascular medications. Patients in the present protocol did not take diuretics from when they woke up in the morning through the end of the study, but no other medications were withheld. This approach was selected because of concerns of the risk of exposing a patient with CHF to a severe heat stress in the absence of appropriate medical therapy. Thus, we cannot exclude the possibility that a drug or a combination of drugs may attenuate cutaneous vasodilator responses to the heat stress. β-Blockers in particular, which were taken by 7 of the patients, may have restrained the rise in cardiac output, necessitating the increased vasoconstriction to maintain blood pressure. Consistent with this hypothesis, others have shown attenuated cutaneous vasodilation during exercise in healthy subjects taking β-blockers.[31,32] However, in the present study, the magnitude of cutaneous vasodilation in the patients taking β-blocking agents was not different from the subjects not taking a β-blocker. Nevertheless, it is difficult to identify whether altered cutaneous vasodilatory responses in patients with CHF was attributed to CHF, medications used to treat this illness, or a combination of both. Importantly, regardless of the mechanism leading to the observed responses, patients with CHF who are treated for this disease will be at a higher risk for a heat-related injury because of altered cutaneous vasodilation during heat stress. Finally, studying patients receiving modern therapy, including ACE inhibitors/angiotensin receptor antagonists and β-blockers, allows the extrapolation of the results of this study to the broader population of patients with compensated CHF exposed to environmental heat stress.

The severity of the symptoms associated with CHF probably will change along the course of the illness. In the present study, the duration from the onset of the illness to the thermal assessment was not controlled (average, 45 ± 10 months; range, 4 to 108 months). It is possible that variations in cutaneous vasodilator responses between patients with CHF could be explained on the basis of duration from the onset of the illness. To investigate this question, we assessed the magnitude of the elevation in forearm cutaneous vascular conductance relative to the duration from the onset of the illness and found that the correlation coefficient was very low ($R = 0.03$) This finding strongly suggests that the magnitude of cutaneous vasodilatory impairment was unrelated to the duration of the illness. Exercise training improves thermoregulatory responses,[48,49] enhances endothelial function in healthy individuals,[50] and even can reverse systemic endothelial dysfunction in patients with heart failure.[40,51] Thus, the exercise habits of the subjects might affect cutaneous vasodilatory response to whole-body and local heat stresses. Twelve of the 14 subjects with CHF self-reported participat-

ing in aerobic exercise, averaging 2.9 ± 0.6 days per week, although none were in a structured exercise program and the duration of exercise training, as well as the duration and intensity of each exercise bout, are unknown. It remains speculative whether these bouts of exercise provide protection against further decrements in cutaneous vasodilatory responses during whole-body and local heating. On the other hand, although patients with CHF reported participating exercise, it is likely that the level of physical activity in these patients is reduced, relative to healthy subjects. Thus, it is possible that factors associated with physical inactivity may contribute to attenuated vasodilation responses in patients with CHF, although normal sweating responses between groups of subjects argue against this hypothesis.

In conclusion, data from the present study clearly demonstrate that cutaneous vasodilator responses to whole-body and local heating are impaired in patients with CHF treated with modern medical therapy. Conversely, sweating responses are preserved in these individuals. Attenuated cutaneous vasodilation may increase the risk of these individuals having a heat-related illness when they are exposed to hyperthermic conditions.

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