Squatting revisited: comparison of haemodynamic responses in normal individuals and heart transplantation recipients

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Abstract

Background—Squatting produces a prompt increase in cardiac output and arterial blood pressure which is accompanied by an immediate decrease in heart rate and forearm vascular resistance. The rise in cardiac output and blood pressure has been attributed to augmented venous return from compression of leg veins, while the decreases in heart rate and forearm vascular resistance are probably due to activation of cardiopulmonary and arterial baroreflexes. Haemodynamic patterns in nine normal men and six heart transplant recipients during 2 min of squatting were examined to determine the role of cardiac innervation in the mediation of these responses.

Methods—Stroke volume was monitored by ensemble averaged thoracic impedance cardiography and blood pressure was determined with an Ohmeda fingertip plethysmograph. These techniques provided continuous measurements which were capable of detecting transient and non-steady state changes. Forearm blood flow was measured with venous occlusion plethysmography. Measurements were obtained after 3 min of quiet standing, immediately after squatting, and at 20, 60, and 120 s of sustained squatting.

Results—Both groups exhibited similar increases in stroke volume index (normal individuals 10.5 ml/m²; heart transplant recipients 10.3 ml/m²) and mean arterial pressure (normal individuals 8.5 mm Hg; heart transplant recipients 5.0 mm Hg) which were sustained throughout squatting. Each group also showed an initial decrease in peripheral resistance (normal individuals 3.6 units; heart transplant recipients 7.7 units) followed by a return to baseline values after 20 s. Heart rate decreased in normal individuals (10 beats/min) but was unchanged or minimally increased (2 beats/min) in heart transplant recipients. Forearm vascular resistance was conspicuously decreased in normal individuals (47.8 units) but only minimally (20.9 units) and not significantly in heart transplant recipients.

Conclusions—The major haemodynamic responses to squatting (increased cardiac output and blood pressure) are similar in normal individuals and heart transplant

recipients. These responses are primarily due to augmented venous return and are not altered by cardiac denervation. Both groups also exhibited a transient decline in peripheral vascular resistance which is most likely mediated by arterial baroreflexes activated by the acute rise in arterial blood pressure. The absence of a significant decrease in forearm vascular resistance in heart transplant recipients suggests that this response is partially mediated by cardiopulmonary or ventricular baroreflexes or that local forearm flow mediated vasodilatation remains impaired after heart transplantation.

(Br Heart J 1995;74:154-158)

Keywords: squatting; cardiac output; baroreflexes; transplantation

In normal individuals squatting produces a prompt rise in arterial pressure and cardiac output followed closely by moderate slowing of heart rate and an increase in forearm blood flow.¹⁻⁴ The increases in cardiac output and blood pressure are attributed to the combined effects of enhanced venous return and increased vascular resistance due to compression of leg veins and arteries.^{1,2} The decline in heart rate and the forearm vasodilatation are primarily mediated by activation of inhibitory sinoaortic baroreflexes in response to the rise in blood pressure.^{1,2} In addition, cardiopulmonary receptors activated by increased central venous pressure may contribute to forearm vasodilatation.¹

Orthotopic heart transplantation effectively ablates afferent and efferent innervation to the implanted sinus node, atrial cuff, and ventricles. Sinoaortic baroreflexes controlling peripheral resistance remain intact. Thus, the initial haemodynamic responses to squatting due to increased venous return should be largely preserved in heart transplant recipients.⁵ However, baroreflex modulation of heart rate should be absent and the contribution of cardiopulmonary baroreflexes to the control of vascular resistance may be impaired due to denervation of the allograft.^{5,6}

In this study we compared the haemodynamic patterns and reflex responses of normal individuals and heart transplant recipients during squatting to determine the role of cardiac innervation in this postural manoeuvre. We used non-invasive methods which permit continuous determination of cardiac output

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Accepted for publication
4 January 1995

and blood pressure so that transient non-steady state differences in response could be analysed.

Patients and methods

PATIENTS

Nine healthy male volunteers (mean (SE) age 39 (11) years) and six orthotopic heart transplant recipients (mean (SE) age 49 (11)) were studied. Heart transplant recipients were a mean (SE) (range) of 16 (18) (3–48) months from transplantation. Their medications included routine immunosuppressive drugs (cyclosporin, prednisone, and azathioprine). Five of the heart transplant recipients were treated with antihypertensive agents (clonidine (three), enalapril (one), and nifedipine (one)). All medications were maintained during this study.

MEASUREMENTS

Cardiac output indices were measured using the CIC-1000, a computerised impedance cardiograph (version 4.2) (SORBA Medical Systems, Brookfield, Wisconsin). Impedance cardiography has been shown to provide reproducible estimates of absolute^{7,8} as well as relative⁹ values for cardiac output in humans. Stroke volume and cardiac output indicates measured in transplant patients in our laboratory using the CIC-1000 are comparable to reported transplant values determined by radionuclide angiography.¹⁰

The CIC-1000 employs R wave triggering and ensemble averaging which improves the signal to noise ratio by reducing respiratory and motion artefacts and results in a cleaner signal. The accuracy and reliability of this system have been verified in recent studies.^{11–12} Impedance electrodes were placed on the forehead (1), at the left side of the base of the neck (2), the left mid-axillary line at the level of the xiphoid (3), and at the crest of the left hip (4). A phonocardiograph microphone was placed over the left second parasternal region to assist with determination of left ventricular ejection time.

Blood pressure was measured continuously by finger photoplethysmography (Finapres 2300, Ohmeda, Louisville, Colorado). This method provides beat to beat blood pressure values comparable with intra-arterial recordings during postural manoeuvres.¹³

Forearm blood flow was measured by venous occlusion plethysmography using a Silastic strain gauge containing doubled single strand mercury and a rapid cuff inflation system (model E-20) (D E Hokansen, Issaquah, Washington). Continuous monitoring of standard three lead CM5 electrocardiograms was performed.

PROTOCOL

Informed consent was obtained and all participants received instruction in the protocol sequence and the desired position for squatting before performing the study. The study protocol was approved by the University of Wisconsin Medical School Committee on Human Subjects.

Baseline upright measurements were obtained after 3 min of quiet standing with the upper arm maintained on a support stand at estimated right atrial level and the forearm elevated at a slight angle.

Squatting was then performed for a period of 2 min. Body weight was positioned over the heels and a wedge of sponge rubber was placed between the buttocks and heels to prevent possible knee injury due to excessive flexion during squatting. The torso was maintained in a near vertical position, the forearm was held on a supporting stand at the same relative position to the body. Participants were instructed to maintain a normal breathing pattern.

A second trial was performed in each position after 5 min of recovery from the initial squat to assess repeatability.

ANALYSIS OF HAEMODYNAMIC INDICES

Impedance waveforms were continuously recorded and ensemble averaged over 10 s intervals. Stroke volume was determined by computer algorithm based on the Kubicek equation¹⁴:

$$SV = \rho \cdot \frac{L^2 \cdot T}{Z_0^2} (dZ/dt_{\max})$$

where SV = stroke volume, ρ = patient's blood resistivity (assumed constant at 150 Ω cm), L is distance between electrode numbers 2 and 3, T is ventricular ejection time, Z_0 is average baseline impedance, and $dZ/dt_{\max}$ is the peak value of the impedance derivative. Cardiac output was then calculated from the product of stroke volume and mean heart rate in beats/min during the 10 s interval. Cardiac output and stroke volume were automatically converted to cardiac index and stroke index.

We anticipated possible changes in inter-electrode distance and baseline Z_0 during squatting. Small corrections were required for electrode distance (L), but no drift in Z_0 was observed.

The thoracic fluid volume index was calculated as the reciprocal of the transthoracic impedance. This value provides a dynamic indicator of thoracic fluid volume change.¹⁵ Cardiac output and forearm blood flow values were time matched with 10 s averages of beat to beat blood pressure measurement. Mean arterial blood pressure was calculated as diastolic pressure and one third of the pulse pressure value. Total peripheral and forearm vascular resistance were derived from the corresponding ratio between mean arterial pressure and cardiac output or between mean arterial pressure and forearm blood flow.

STATISTICAL ANALYSIS

Data were analysed for intragroup and intergroup differences by repeated measures analysis with post hoc tests performed using Fisher's protected least squares differences. α was set at 0.05. Comparisons were made at standing rest (immediately before squatting), immediately after squatting (5–10 s), and at 20, 60, and 120 s of sustained squatting. All values are expressed as mean (one SE).

Figure 1 Haemodynamic responses to squatting measured at baseline standing (ST), immediately (5–10 s) after squatting (SQ), and at 20, 60, and 120 s of sustained squatting. N, normal individuals; HT, heart transplant recipients; CI, cardiac index; SI, stroke index; TFVI, thoracic fluid volume index; HR, heart rate. Values are mean (SEM). * $P = 0.05$ between groups. † $P = 0.05$ from standing rest.

Figure 2 Haemodynamic responses to squatting measured at baseline standing (ST), immediately (5–10 s) after squatting (SQ), and at 20, 60, and 120 s of sustained squatting. N, normal individuals; HT, heart transplant recipients; MAP, mean arterial pressure; TPR, total peripheral resistance; FBF, forearm blood flow; FVR, forearm vascular resistance. Values are mean (SEM). * $P = 0.05$ between groups. † $P = 0.05$ from standing rest.

Results

Figures 1 and 2 show the responses to squatting.

STANDING BASELINE MEASUREMENTS

Values for haemodynamic and derived indices were all within the reported range for normal individuals and heart transplant recipients.^{5 6 10} Heart rate was significantly higher and stroke index significantly lower in heart transplant recipients during standing rest. Otherwise, there were no significant differences between groups before squatting.

RESPONSE TO SQUATTING

Cardiac index, stroke volume index, and thoracic fluid volume index increased significantly in both groups after the initial 5–10 s of squatting. The increases in cardiac and thoracic fluid volume indices were similar in normal individuals and heart transplant recipients and the incremental increase in stroke volume index was equal in both groups (normal individuals 10.5 ml/m², heart transplant recipients 10.3 ml/m²). Cardiac and stroke volume indices declined gradually after 20 s of sustained squatting but remained significantly increased in each group at 120 s. The initial increases in thoracic fluid volume index (normal individuals 0.24 units; heart transplant recipients 0.12 units) remained unchanged in both groups throughout the 120 s of sustained squatting.

Heart rate in normal individuals declined (4 beats/min) at the onset of squatting and was significantly decreased (10 beats/min) from 20 s to 60 s. Heart transplant recipients showed a small but significant increase (2 beats/min) in heart rate at the onset of squatting and this increase was maintained for the initial 60 s of squatting.

Mean arterial pressure increased in both groups at the onset of squatting and exhibited a continuous rise from 20 s to 120 s of sustained squatting. The increases in MAP in both groups were significant from 20 s to 120 s.

Total peripheral resistance decreased significantly in both groups (normal individuals 3.6 units; heart transplant recipients 7.7 units) at the onset of squatting and subsequently returned to baseline values after 20 s of sustained squatting.

Forearm blood flow increased promptly (3.4 ml/100 ml/min) at the onset of squatting in normal individuals. These initial changes declined but remained significantly increased at 60 s and returned to baseline at 120 s. Heart transplant recipients showed a delayed increase in forearm blood flow which became significant after 20 s of squatting (1.4 ml/100 ml/min) and was maintained at this level to 120 s.

Forearm vascular resistance noticeably decreased with initial squatting in normal individuals (47.8 units) and remained significantly reduced at 20 s and 60 s. Heart transplant recipients showed a gradual but non-significant decrease (20.9 units) in forearm vascular resistance during squatting.

Coefficients of variation for cardiovascular variables during two trials of squatting

CI	SV	HR	FBF	
Normal individuals	0.055 (0.02)	0.068 (0.02)	0.041 (0.01)	0.30 (0.16)
Heart transplant recipients	0.052 (0.01)	0.052 (0.015)	0.01 (0.007)	0.17 (0.04)

Values are mean (one SD). CI, cardiac index; SV, stroke volume; HR, heart rate; FBF, forearm blood flow.

REPRODUCIBILITY OF RESPONSES

The reproducibility of the two trials of squatting was assessed by determining the coefficient of variation of cardiac index, stroke volume, heart rate, and forearm blood flow for each participant (table). The coefficient of variations for each measurement were normally distributed over time and are expressed as the group mean (one SD).¹⁶

Discussion

The principal findings in this study are that heart transplant recipients and normal individuals exhibit an equivalent pattern and incremental magnitude of increase in cardiac index and mean arterial pressure in response to sustained squatting and also show a similar initial decline in total peripheral resistance. These findings indicate that the circulatory responses (increased cardiac output and arterial blood pressure) to squatting are primarily caused by increased venous return and are not dependent on cardiac innervation.

The increase in cardiac index observed in both groups was fully attributed to increases in stroke volume with no contribution from heart rate. Normal individuals uniformly exhibited a transient bradycardia in response to the acute rise in arterial blood pressure. Heart transplant recipients showed a small but significant rise in heart rate (2 beats/min) which could possibly be explained by mechanical stretch of the sinus node in response to increased venous return.^{6 17 18} It is unlikely that increases in ventricular contractility mediated by sympathetic tone contributed to the initial rise in stroke volume index. If so, the heart transplant recipients should have exhibited a smaller or delayed increase in stroke volume index due to ventricular sympathetic denervation.

Our data indicate that the increase in mean arterial pressure is due to the maintained rise in cardiac index as total peripheral resistance decreased initially in both groups and subsequently returned towards baseline values. The initial decrease in peripheral vascular resistance observed in each group is most likely explained by activation of sinoaortic baroreflexes in response to the abrupt rise in arterial pressure at the onset of squatting. Previous haemodynamic studies of squatting have not reported indices of systemic vascular resistance.¹⁻⁴ Despite this many authors have concluded that the increase in blood pressure observed during squatting is caused by a rise in peripheral resistance which is attributed to muscular compression of vascular elements in the lower extremities.^{1 2 19-21} Static leg muscle contraction during squatting may also possi-

bly contribute to the sustained rise in arterial blood pressure due to activation of the somatic pressor reflex.^{22 23}

The initial decrease in peripheral resistance may in part be caused by regional vasodilatation in the arm and possibly the splanchnic vasculature.²⁴ In normal individuals there was a prompt increase in forearm blood flow and a corresponding decrease in forearm vascular resistance, whereas heart transplant recipients exhibited a blunted rise in forearm blood flow and a non-significant decrease in forearm vascular resistance. The impairment in forearm vasodilatation in heart transplant recipients is possibly due to the loss of cardiopulmonary and ventricular baroreflexes which are thought to initiate peripheral vasodilatation during squatting or other forms of increased venous return.^{24 25} This interpretation is limited, however, by difficulty in determining the relative contributions of cardiopulmonary and sinoaortic baroreflexes during the squatting manoeuvre.

Several other factors may have contributed to the impaired forearm vasodilatation in heart transplant recipients. Early after transplantation recipients may show a blunted maximal hyperaemic muscle blood flow response after ischaemic arterial occlusion.²⁶ These abnormalities gradually resolve and probably reflect residual impairment of flow mediated vasodilatation which typically occurs in chronic heart failure.^{26 27} We did not measure maximal forearm blood flow responses to ischaemic occlusion; however, previous studies from our laboratory have shown normal forearm vasodilatation responses 16 months after heart transplantation.²⁸ Finally, cyclosporin has been reported to increase sympathetic nervous system activity in heart transplant recipients.²⁹ Cyclosporin may possibly have augmented forearm vasoconstrictor tone and diminished reflex peripheral vasodilatation normally associated with squatting.

LIMITATIONS

A potential limitation of this study is the assumed accuracy of ensemble averaged impedance cardiography for determination of stroke volume during non-steady state haemodynamic responses. We did not verify the measurements of stroke volume and cardiac output by independent methods. Previous studies, however, have reported satisfactory agreement between impedance and thermal or dye dilution methods for determining cardiac output during postural stress,³⁰ Valsalva manoeuvre,⁹ and exercise testing.⁷

Medications were not discontinued in heart transplant recipients due to clinical and logistical factors. Three of these patients were treated with antihypertensive agents which could potentially decrease forearm vascular tone. Forearm blood flow and vascular resistance values in the standing position were similar in both groups so it is unlikely that these agents influenced the observed impairment in forearm vasodilatation during squatting.

Conclusions

The primary haemodynamic responses to squatting are similar in normal individuals and heart transplant recipients. Each group showed a prompt and sustained increase in cardiac output and arterial blood pressure. The rise in arterial blood pressure was mediated by increased cardiac output as peripheral vascular resistance in both groups decreased initially and subsequently returned to baseline values. These findings are in contrast to existing interpretations which have assumed that peripheral resistance *increases* during squatting. Normal individuals exhibit a characteristic bradycardia and forearm vasodilatation during squatting which are attributed to combined activation of cardiopulmonary and sinoaortic baroreflexes in response to increased venous return and arterial blood pressure. Bradycardia is absent in heart transplant recipients due to efferent vagal denervation. Instead, a small increase in heart rate was observed which may be caused by stretch mediated chronotropic mechanisms in the transplanted heart—that is, the Bainbridge reflux. Finally, heart transplant recipients show attenuation of the normal decrease in forearm vascular resistance associated with squatting which may be attributed in part to deafferentation of cardiac baroreceptors or localised impairment of flow mediated vasodilatation.

We are grateful to Ms Sharon Vike for expert word processing and Dr Barbara Morgan, Dr Thomas Ebert, and Jill Barney for constructive comments.

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