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Renal Vasodilatory Action of Dopamine in Patients With Heart Failure Magnitude of Effect and Site of Action

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Background—A “renal dose” of dopamine is often used to increase renal blood flow; however, data on the magnitude of effect and site of action in patients with heart failure are scarce.

Methods and Results—Renal effects of intravenous dopamine (1, 2, 3, 5, and 10 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) were evaluated in 13 patients with chronic heart failure. Renal blood flow was calculated from renal artery cross-sectional area measured with intravascular ultrasound and renal blood flow velocity-time integral measured by the intravascular Doppler technique. Cross-sectional area increased and was significantly higher than baseline ($0.30 \pm 0.04 \text{ cm}^2$) at 5 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ($0.36 \pm 0.05 \text{ cm}^2$) and 10 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ($0.38 \pm 0.06 \text{ cm}^2$). The velocity-time integral was significantly higher than baseline ($22 \pm 3 \text{ cm}$) at doses of 3 and 5 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ (both $31 \pm 4 \text{ cm}$). Renal blood flow increased, whereas renal vascular resistance decreased, reaching statistical significance at 2 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ through 10 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. Cardiac output gradually increased, reaching statistical significance at doses of 5 and 10 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ (5.5 ± 0.5 and 6.1 ± 0.7 versus $4.5 \pm 5.2 \text{ L/min}$ at baseline), but the increase in renal blood flow appeared proportionately larger than corresponding increases in cardiac output.

Conclusions—Dopamine is associated with an increase in renal blood flow in patients with heart failure. This effect is due to dilation of both the large conductance and small resistance renal blood vessels. Further evaluation of the efficacy and safety of dopamine for improvement of renal function in hospitalized patients with heart failure is warranted. (*Circulation*. 2008;117:200-205.)

Key Words: heart failure ■ kidney ■ inotropic agents ■ vasodilation ■ blood flow ■ pharmacology

Decreased renal function during hospitalization in patients admitted for heart failure (HF) is common¹ and has been associated with unfavorable outcomes.^{1,2} Further worsening of renal function during treatment of decompensated heart failure, which has been defined as the cardiorenal syndrome,¹ occurs in a substantial number of patients and leads to undesirable consequences, including prolongation of length of stay, increased morbidity, and increased mortality after discharge.^{3,4} Management of the cardiorenal syndrome is difficult because of the lack of effective therapies.²

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Although renal dysfunction is complex and determined by a multiplicity of factors, reduction in renal blood flow (RBF), an important determinant of glomerular filtration rate,⁵ may play an important role. Enhancement of RBF in patients with decompensated HF has been challenging, and commonly used vasoactive drugs, including nesiritide, nitroglycerin,

nitroprusside, and dobutamine, have failed to demonstrate a consistent effect in spite of a considerable increase in cardiac output (CO).^{6–10} Dopamine has been reported both in experimental animals and in a variety of patient populations to enhance RBF by multiple mechanisms, including an increase in CO and local vasodilation due to stimulation of dopamine receptors in renal blood vessels.¹¹ For many years, a small dose of dopamine often has been used by clinicians to enhance RBF in critically ill patients^{12,13}; however, this selective effect of dopamine on the renal circulation may be eliminated or markedly attenuated by other vasoconstrictive mechanisms known to be activated in patients with HF.¹⁴ In addition, the magnitude of its renal vasodilatory effects and site of action in patients with HF have not been clearly defined. The introduction of intravascular ultrasound (IVUS) and Doppler techniques provides an opportunity for further insight, because these techniques allow for an accurate assessment of vascular dimensions and blood flow velocity

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and can be used for evaluation of vasodilatory changes in both the conductance (IVUS) and resistance (Doppler) renal blood vessels.^{15–17} The purpose of the present study, therefore, was to gain further insight into the renal circulatory effect of dopamine in patients with HF using the above-mentioned techniques.

Methods

Study Population

Patients with a history of chronic HF due to left ventricular systolic dysfunction with moderate to severe HF symptoms (New York Heart Association functional class III or IV) who were undergoing diagnostic cardiac catheterization were included in the study if they agreed and signed a consent form approved by the ethics committee of the Los Angeles County/University of Southern California Medical Center. All patients were undergoing standard therapy for HF.

Measurements of RBF

Changes in RBF were measured in the present study with IVUS and Doppler techniques. These methods were initially validated and used to evaluate coronary anatomy and assess coronary blood flow reserve.^{18,19} More recently, these techniques have also been validated for the measurement of RBF^{20–22} and have been found to provide accurate and reproducible results when used to measure changes in RBF in response to various vasoactive drugs and other vasomotor stimuli in patients with hypertension and renal artery stenosis.^{22,23} Our group has used the technique successfully in the assessment of changes in RBF during various therapeutic interventions in patients with HF.^{16,17}

Study Protocol

Premedication before cardiac catheterization included intravenous metoclopramide (10 mg) and diphenhydramine (50 mg). Nitroglycerin (sublingual, intravenous, or intracoronary) was not allowed during the study. A triple-lumen Swan-Ganz catheter was used for the performance of right heart catheterization. An 8F angioplasty multipurpose catheter or Judkins right coronary artery guiding catheter was placed in the renal artery with the tip positioned in the proximal or middle portion of the main artery. Catheter position in the renal artery was confirmed with a small amount (≈ 3 mL) of angiographic contrast medium (Hexibrix, Mallinckrodt Medical, Hazelwood, Mo). A 0.00018-in (0.045-cm) Doppler guidewire (Flowire, Cardiometrics, Inc, Mountain View, Calif) was then introduced into the guiding catheter through a valved sidearm connector, and its tip was positioned under direct visualization in the main renal artery or 1 of its branches and manipulated to maintain a parallel position to flow and to record the highest possible Doppler flow signal. The wire was then locked to secure a constant position throughout the study. A commercially available 3.5F or 4.3F IVUS catheter (Mansfield, Boston Scientific Corp, Natick, Mass) was then placed through the guiding catheter and positioned under fluoroscopic guidance next to the Doppler wire. Images were obtained with a commercially available intracoronary ultrasound imaging system (Sono Intravascular, Hewlett-Packard, Palo Alto, Calif) at 30 frames per second and recorded on 0.5-in high-quality super VHS videotape for subsequent offline analysis. Renal artery lumen planimetry was performed later from the taped images, and renal artery cross-sectional area (CSA) was determined with specially designed software. Spectral Doppler RBF velocities were recorded. The velocity-time integral (VTI) was measured as the area under the outermost portion of the spectral-velocity envelope. To correct for changes related to respiration and cardiac cycle, 15 to 30 beats were used for VTI, and average values are reported. Renal artery blood flow (mL/min) was calculated as the product of the CSA in the renal artery in which the signal was recorded and the VTI, with the following formula: flow = heart rate (per minute) \times VTI \times CSA. Renal artery blood flow index was calculated for each patient by dividing RBF by the patient's body surface area, and renal vascular resistance

(RVR) was calculated as mean renal artery blood pressure/RBF. Renal arterial pressures were measured directly with the aid of the arterial guiding catheters, fluid-filled pressure tubing, and standard transducers.

After baseline measurements, which included hemodynamic variables, IVUS, and Doppler flow velocity, serial escalating intravenous infusions of dopamine at 1, 2, 3, 5 and 10 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ were begun in each patient for 3- to 5-minute intervals at each dose. Hemodynamic measurements, IVUS, and Doppler flow velocity recordings were obtained at the end of each infusion interval.

Statistical Analysis

Repeated-measures ANOVA was used to compare statistical differences in the various measured or calculated parameters with varying dopamine dose. Significance was determined with the Newman-Keuls post hoc test. The relationship between percentage increase in cardiac index and that of renal artery blood flow index and between the percentage increase in VTI and that of CSA was assessed at each dose of dopamine compared with the baseline by use of the Wilcoxon signed rank test. Results are expressed as mean \pm SD. Probability values < 0.05 were considered statistically significant.

The authors had full access to the data and take full responsibility for its integrity. All authors have read and agree to the manuscript as written.

Results

General Information

Thirteen patients were included in the study. There were 10 men and 3 women (22 to 67 years old). The underlying cause of HF was coronary artery disease in 5 patients and nonischemic, dilated cardiomyopathy in 8. All patients had severe depression of left ventricular systolic function as documented by contrast or radionuclide ventriculography or by echocardiography (3 patients). Left ventricular ejection fraction ranged from 14% to 32% (mean $24 \pm 2\%$). Medical therapy included diuretics in all patients, ACE inhibitors in 10, digoxin in 9, β -blocking agents in 7, and organic nitrates in 7. Mean baseline hemodynamic values as measured during cardiac catheterization were as follows: heart rate 86 ± 5 bpm, mean blood pressure 92 ± 4 mm Hg, right atrial pressure 8 ± 1 mm Hg, mean pulmonary artery pressure 31 ± 3 mm Hg, pulmonary artery wedge pressure 20 ± 2 mm Hg, cardiac index 3.3 ± 0.2 L \cdot min⁻¹ \cdot m⁻², stroke volume index 39 ± 4 mL \cdot min⁻¹ \cdot m⁻², and systemic vascular resistance 1158 ± 21 dyne \cdot s⁻¹ \cdot cm⁻⁵.

Systemic Hemodynamics

The dose-dependent systemic hemodynamic effects of dopamine are summarized in the Table. There was no significant change in heart rate, blood pressure, or right atrial pressure at any dopamine dose used in the present study. Mean pulmonary artery pressure showed no significant response to doses between 1 and 5 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ but was significantly increased from 32 ± 4 mm Hg at baseline to 40 ± 4 mm Hg during the infusion of 10 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. CO demonstrated a gradual increase, which reached statistical significance compared with baseline at doses of 5 and 10 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ (5.5 ± 0.5 and 6.1 ± 0.7 versus 4.5 ± 0.5 L/min at baseline). Calculated systemic vascular resistance was reduced significantly compared with baseline at all dopamine doses.

Table. Dose-Dependent Systemic and Renal Hemodynamics of Dopamine

	Dopamine Dose, $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$					
	0	1	2	3	5	10
HR, bpm	90±4	93±5	93±5	89±5	92±6	96±7
SBP, mm Hg	126±7	126±8	121±8	125±8	131±6	137±13
DBP, mm Hg	79±4	76±4	74±5	73±4	77±4	76±7
MBP, mm Hg	96±5	94±5	94±5	97±5	101±3	102±9
RAP, mm Hg	10±1	10±1	10±2	10±1	10±1	10±2
MPAP, mm Hg	32±4	34±3	34±4	34±4	34±4	40±5*
CO, L/min	4.5±0.6	5.2±0.6	5.0±0.3	5.0±0.5	5.5±0.5*	6.1±0.7*†
CI, $\text{L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$	2.5±0.4	2.9±0.4	2.8±0.2	3.0±0.3	3.1±0.3	3.4±0.5*†
SV, mL	52±8	58±8	56±4	62±7	63±7	66±8*†
SVI, mL/m^2	29±5	33±5	31±3	34±4	35±4	36±5*
VTI, cm	22±3	25±3	28±5	31±4*	31±4*	28±4
CSA, cm^2	0.30±0.04	0.32±0.04	0.34±0.04	0.35±0.05	0.36±0.05*	0.38±0.06*†
RBF, mL/min	558±61	677±84	762±94*	831±103*	879±92*	898±131*
RBFi, mL/min	308.2±32.6	373.8±46.2	420.0±50.0	461.7±59.1*	488.3±53.8*	501.1±82.0*
RVR, $\text{dyne} \cdot \text{s}^{-1} \cdot \text{cm}^{-5}$	13615±1317	11681±1384	10200±1310*	10018±1324*	9540±1269*	9408±1620*
SVR, $\text{dyne} \cdot \text{s}^{-1} \cdot \text{cm}^{-5}$	1734±180	1444±137*	1417±129*	1402±122*	1431±131*	1328±200*

HR indicates heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean arterial blood pressure; RAP, renal artery pressure; MPAP, mean pulmonary artery pressure; CI, cardiac index; SV, stroke volume; SVI, stroke volume index; RBFi, renal blood flow index; and SVR, systemic vascular resistance.

* $P < 0.05$ vs baseline ($0.0 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$).

† $P < 0.05$ vs $1 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$.

Renal Hemodynamics

The renal hemodynamic effects of dopamine are summarized in the Table. There were no significant differences in renal artery pressure with dopamine at any dose. Mean renal artery CSA (Figure 1A) was $0.30 \pm 0.04 \text{ cm}^2$ at baseline before the administration of dopamine and demonstrated a progressive increase with increasing dopamine dose, reaching statistical significance, compared with baseline, at $5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ($0.36 \pm 0.05 \text{ cm}^2$) and at $10 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ($0.38 \pm 0.06 \text{ cm}^2$).

Failure of this parameter to change significantly with lower doses may be related to a type II error due to the relatively small number of patients.

The mean value of VTI (Figure 1B) also showed an increase and was significantly higher than baseline ($22 \pm 3 \text{ cm}$) at doses of 3 and $5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ (both $31 \pm 4 \text{ cm}$). An increase in dopamine dose to $10 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ resulted in a reduction of VTI to $28 \pm 4 \text{ cm}$, a value not statistically different from baseline. The percentage increase in VTI,

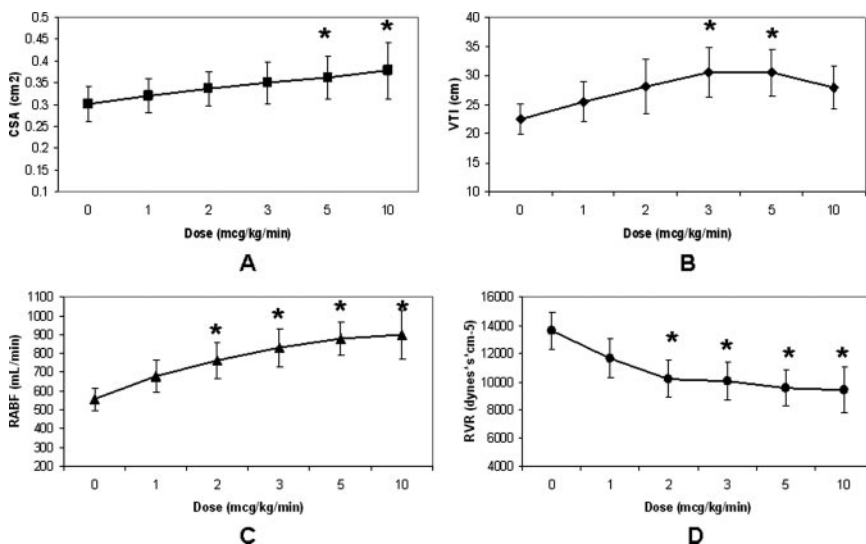


Figure 1. A, Renal artery CSA and dopamine dose. Mean renal artery CSA demonstrated a progressive increase with the up-titration of dopamine dose and reached statistical significance at $5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ($0.36 \pm 0.05 \text{ cm}^2$) and $10 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ($0.38 \pm 0.06 \text{ cm}^2$; $P < 0.05$). B, VTI and dopamine dose. VTI showed a significant increase, which was higher than baseline ($22 \pm 3 \text{ cm}$) at doses of 3 and $5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ (31 ± 4 and $31 \pm 4 \text{ cm}$, respectively). Increase of dose to $10 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ resulted in a reduction of VTI to $28 \pm 4 \text{ cm}$ (not statistically different from baseline). C, RBF and dopamine dose. RBF demonstrated a progressive increase with increasing doses of dopamine. It increased significantly from $558 \pm 60 \text{ mL}/\text{min}$ at baseline to $762 \pm 94 \text{ mL}/\text{min}$ at a dose of $2 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ($P < 0.05$) and achieved its peak level during the infusion of $10 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ($898 \pm 131 \text{ mL}/\text{min}$). There was no significant

difference between values recorded at 2 to $10 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. RBF indicates renal artery blood flow. D, RVR and dopamine dose. RVR was lower than baseline at all doses of dopamine. The fall in RVR reached statistical significance at 2 through $10 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. There was no statistically significant difference in mean values of RVR between 2 and $10 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. * $P < 0.05$.

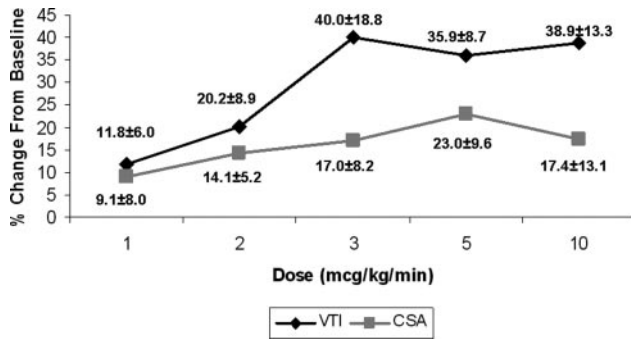


Figure 2. Percentage increase in VTI and CSA with different doses of dopamine infusion. The percentage increase in VTI was generally greater than the corresponding increase in CSA, especially at 3, 5, and $10 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. This difference, however, was not statistically significant.

compared with baseline, was generally greater than the corresponding increase in CSA, especially at 3, 5, and $10 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ (Figure 2); this difference, however, was not statistically significant. Renal artery blood flow (Figure 1C) demonstrated a progressive increase during the infusion of increasing doses of dopamine. It increased significantly from 558 ± 61 mL/min at baseline to 762 ± 94 mL/min at a dose of $2 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ($P < 0.05$) and achieved its maximum during the infusion of $10 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ (898 ± 131 mL/min). There was no statistical difference, however, between values recorded at 2 to $10 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. The percent increase in RBF index, compared with the baseline value, appeared to be greater than the corresponding increase in cardiac index, reaching statistical significance at the dose of $5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ (Figure 3).

Five patients exhibited a maximal increase in RBF at dopamine doses $\leq 3 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$; however, the majority of patients achieved maximal RBF values at doses greater than the usual “renal doses” of dopamine (3 patients at $5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ and 5 patients at $10 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$). RVR (Figure 1D) was lower than baseline at all doses of dopamine. The fall in RVR reached statistical significance, compared with baseline, at 2 through $10 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. There was no statistically significant difference in the mean values of RVR between 2 and $10 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$.

Discussion

The findings of the present study provide new insight into the magnitude and site of action of the renal vasodilatory effect of dopamine and the resulting renal circulatory effects in patients with HF treated with standard HF therapy, including diuretics, neurohormonal blockers, and vasodilators. The present findings show a marked effect of dopamine on RBF. The increase in this parameter started early and became statistically significant at a dose as low as $2 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. RBF continued to rise, achieving its highest value at $10 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, which was the maximum dose used in the present study. Although the difference between RBF values at a dose of $2 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ and higher doses did not reach statistical significance, this may be due to the limited number of patients included in the study. On an individual basis, the present data also demonstrated a high interpatient variability,

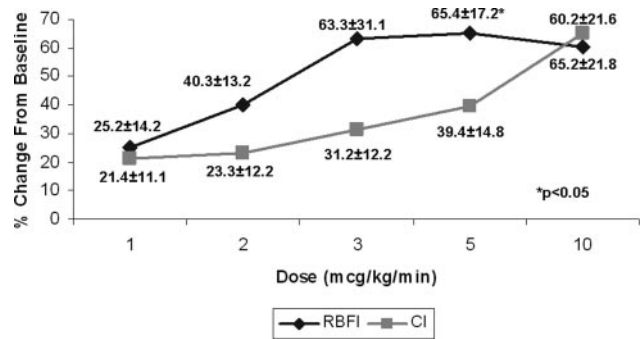


Figure 3. Percentage increase in RBF index (RBFi) and cardiac index (CI). The percentage increases in RBFi appeared to be greater than those of CI at different doses, reaching statistical significance at $5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$.

with a number of subjects achieving maximum response at doses greater than 1 to $3 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, a dose range traditionally used by clinicians to augment RBF. These findings support previous reports indicating that the dose of dopamine that produces the maximal increase in RBF in patients with HF is higher than the dose commonly thought of as the low “renal” dose.^{12,24,25}

The present results reflect the known pharmacology of dopamine, which has been shown to exhibit a graded pharmacological response, with a dose-dependent predominant activation of dopaminergic receptors, β -receptors, and α -receptors.^{11,26} Generally, at doses $< 3 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, dopamine has been found to activate dopamine A1 receptors, which cause vasodilation of the renal arteries and other vascular beds, including mesenteric, coronary, and cerebral beds. In addition, there is stimulation of dopamine A2 receptors that leads to inhibition of norepinephrine release from sympathetic nerve endings.²⁶ Activation of dopamine A1 and A2 receptors also results in a decline in systemic vascular resistance and an increase in RBF, which was observed in the present study. Dopamine infused at approximately 3 to $5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ activates β_1 - and β_2 -adrenergic receptors, conferring a positive inotropic effect that is responsible for the increase in CO. At a dose $> 5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, dopamine has been reported to exert clinically relevant activation of α_1 - and α_2 -adrenergic receptors, which results in arterial vasoconstriction. In the present study, however, the use of $10 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ did not result in apparent vasoconstriction, possibly because of the short duration of the infusion.

The dopamine-mediated increase in RBF has been reported to be multifactorial¹¹ and includes renal vasodilatation due to activation of dopamine receptors in the renal vasculature, augmentation of CO due to β -adrenergic activity that leads to both inotropic and chronotropic effects, and peripheral vasodilatation mediated by stimulation of dopamine receptors in the systemic vasculature. The present study provides information regarding the magnitude and site of dopamine action in the renal circulation. Intravenous infusion of dopamine resulted in an early vasodilatory effect on the small resistance renal arteries, as reflected by a significant fall in RVR and an increase in RBF velocity. At the same time, a gradual dose-dependent increase in renal artery CSA indicated a

concomitant vasodilatory effect of dopamine on the large conductance blood vessels, especially with the use of larger (5 and 10 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) doses, which may also contribute to an increase in RBF. This increase in CSA may be due to the direct effect of dopamine but could also represent a flow-mediated, endothelium-derived vasodilation.

An increase in CO with either vasodilators or inotropes is often assumed by clinicians to augment RBF in hospitalized patients with acute decompensated HF; however, a marked increase in CO with drugs such as nitroglycerin, nitroprusside, and nesiritide has resulted in small or even no effect on RBF.^{6–10} The present study demonstrates a dopamine-mediated increase in both CO and RBF. The change in RBF, however, appeared to be proportionally larger than the change in CO, which suggests that dopamine-mediated renal vasoregulation in patients with HF is predominantly due to its local vascular action rather than its central hemodynamic effect.

Study Limitations

In the present study, we used the antiemetic drug metoclopramide for premedication before cardiac catheterization. Metoclopramide possesses a dopamine A2 receptor antagonistic effect and has been shown to slightly attenuate the effect of dopamine on renal plasma flow in healthy volunteers but not in patients with renal failure²⁷ and only at high doses in patients receiving chemotherapy.²⁸ Although no information is available on the effect of metoclopramide on RBF at the dose used in the present study in patients with heart failure, it is possible that the effect of dopamine on RBF was somewhat attenuated by metoclopramide.

In addition, the dose of dopamine was increased at 3- to 5-minute intervals without washout periods between the doses. Although the half-life of the drug is relatively short, a carryover effect of the previous dose to the next, and thus augmentation of effect, cannot be excluded. At the same time, however, it is possible that the relatively short duration of infusion of each dose did not allow enough time for equilibration and achievement of maximum effect.

The method used in the present study was not designed to accurately measure total RBF or RVR but rather to assess the relative changes in these parameters. Because it is not always possible to position the tip of the Doppler wire in the main renal artery owing to early artery division, and because positioning of the flow wire absolutely parallel to blood flow is not always possible, especially in larger vessels such as the renal artery, the method used here is likely to often underestimate total RBF. However, this method provides accurate and reproducible information and is highly suitable for assessment of changes in renal hemodynamics, which are likely to be proportional to the change in total RBF.^{15,22,23} The study was performed in clinically stable HF patients as part of diagnostic cardiac catheterization, with an unknown effect of contrast used on the vascular effect of dopamine. For all these reasons, the present findings may not be completely applicable to patients with acute decompensated HF who are treated with renal-dose dopamine.

The present study was also limited to evaluation of the magnitude and site of vasodilatory action of various doses of

dopamine on the renal vasculature and was not designed to assess renal function. Although RBF is an important determinant of glomerular filtration rate,⁵ more information will be needed to determine whether the rise in RBF documented in the present study may also influence parameters of renal function in patients with HF. In addition, the study cannot provide safety information related to a potential effect of the drug on either short- or long-term outcome. Tachycardia, cardiac arrhythmias, myocardial ischemia, and infarction are well-documented potential side effects of dopamine. Blunting of hypoxic ventilatory drive, increasing pulmonary shunt fraction, and gut ischemia have also been described in critically ill patients receiving dopamine.²⁹ Recent studies have demonstrated a detrimental effect of other inotropes used for the hemodynamic improvement in hospitalized patients with HF on both short- and long term outcome.^{30,31}

In summary, the present study demonstrated a significant increase in RBF with intravenous dopamine in patients with HF. This effect was due to dilatation of both the large conductance renal blood vessels and the small resistance vessels, although the latter appeared to be affected earlier. The increase in RBF appeared proportionally larger than the increase in CO, which indicates that augmentation of flow is mainly due to reduction in RVR mediated by the local vasodilatory effect of dopamine. These data, coupled with previous reports indicating a lack of RBF response to other vasoactive medications and an increased risk of both short- and long-term outcomes with other inotropic drugs, suggest that further evaluation of the efficacy and safety of dopamine for improvement of renal function in hospitalized patients with acute decompensated HF is warranted.

Disclosures

None.

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CLINICAL PERSPECTIVE

Decreased renal function is common in hospitalized patients with heart failure, and attempts to improve it with a number of vasoactive medications have not resulted in a consistent favorable effect. A “renal dose” of dopamine has been used by clinicians for many years to enhance renal function in critically ill patients. The renal circulatory effect of dopamine, however, has not been well studied in patients with heart failure. The results of the present study demonstrated a significant vasodilatory effect of dopamine in doses between 2 and 10 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ on both resistance and conductance renal arteries. This effect resulted in a significant reduction in renal vascular resistance and a rise in renal blood flow. In addition, intravenous dopamine resulted in a marked effect on cardiac output. These beneficial effects of intravenous dopamine both on the systemic and renal circulation are encouraging and suggest that further research on the effect of dopamine on renal function and outcome in hospitalized patients with heart failure is warranted.

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