Acute Effects of Urinary Bladder Distention on the Coronary Circulation in Patients With Early Atherosclerosis

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OBJECTIVES

We sought to examine whether distention of the urinary bladder, a physiologic stimulus, could induce impaired coronary circulation in patients with early atherosclerosis.

BACKGROUND

Distention of the urinary bladder reflexively causes an increase in sympathetic activity. The effect of such distention on the coronary circulation in patients with early atherosclerosis remains unknown.

METHODS

To assess the effect of bladder distention on coronary dynamic forces, epicardial and microvascular responses were measured with an intracoronary Doppler flow wire in 40 patients with early atherosclerosis (<50% diameter stenosis). Patients were randomized into two groups according to whether they did not (group 1, n = 20) or did have (group 2, n = 20) pretreatment with an alpha1-adrenergic receptor blocker (oral doxazosin, 2 mg). Coronary flow velocity was monitored by quantitative coronary angiography at baseline, during urinary bladder distention and after intracoronary nitroglycerin injection.

RESULTS

Bladder distention significantly decreased the coronary diameter in the stenotic segments (p < 0.001), decreased coronary blood flow (p < 0.001) and increased coronary resistance (p < 0.001), as compared with baseline values, in group 1 patients. In group 2 patients with bladder distention, the angiographic variables did not show significant changes, as compared with baseline values. No significant differences were noted between the groups in the responses of the angiographic variables after nitroglycerin administration.

CONCLUSIONS

The present study shows, for the first time, that urinary bladder distention caused vasoconstriction of coronary conduit and resistance vessels involved mechanisms related to alpha1 adrenoceptors. Pretreated administration of doxazosin reversed the changes toward baseline. Vasoconstriction during bladder distention can be relieved after nitroglycerin administration, suggesting an unchanged responsiveness of vascular smooth muscle cells to such distention. (J Am Coll Cardiol 2000;36:453–60) © 2000 by the American College of Cardiology

The occurrence of transient myocardial ischemia in patients with coronary artery disease during stress is a common problem and has been thought to reflect adrenergic stimulation, with resultant increases in cardiac oxygen consumption. However, adrenergically mediated paradoxic vasoconstriction may also be considered as a possible pathogenetic mechanism in stenotic coronary arteries (1). Other factors, including mental stress (2), smoking (3), isometric handgrip (4), cold-pressor test (5) and supine exercise (6), have been shown to produce adrenergically mediated coronary vasoconstriction. Distention of the urinary bladder has been shown to cause the reflex response of an increase in sympathetic tone (7,8). Electrophysiologic studies have demonstrated that stretching of the bladder wall causes an increase in afferent activity from the pelvic or hypogastric nerves (9). The sensory neurons of the bladder lie in the subepithelial plexus and contain large granulated vesicles typical of the storage sites for neuropeptides (10). The efferent effects of reflexes caused an increase in sympathetic and a decrease in vagal fiber activity (11). Although efferent cardiac nerves are believed to be involved in the reflex changes in coronary blood flow (CBF) (12,13), no studies have demonstrated the vasoconstrictor reflex of the coronary arteries caused by distention of the urinary bladder.

This report describes clinical studies designed to examine whether distention of the urinary bladder, a physiologic stimulus, could induce epicardial and microvascular responses in patients with early atherosclerosis by a combined intracoronary Doppler flow and quantitative coronary angiography measure.

METHODS

Patients. The study was conducted prospectively. Patients were eligible for the present study if they had a single non-flow-limiting stenosis (<50% diameter stenosis) in the proximal or mid portion of one major coronary artery. Exclusion criteria included previous myocardial infarction, unstable angina pectoris, uncontrolled hypertension, ejection fraction <55% by catherization study, valvular heart disease, diabetes mellitus and echocardiographic left ven-
tricular mass index >117 g/m² for men and 104 g/m² for women (14). To make the baseline autonomic system of our study subjects homogeneous, we excluded patients with autonomic dysfunction based on the autonomic reflex evaluation (15). A total of consecutive 40 patients were included. Patients were randomized into two groups on the basis of the use of doxazosin: group 1 (n = 20) had no pretreatment; group 2 (n = 20) had pretreatment with doxazosin (2 mg). The clinical characteristics of the patients are given in Table 1. The study was approved by the Hospital Review Board of National Taiwan University, and all subjects provided written, informed consent before participation. Medications, including calcium channel and beta-adrenergic blockers, were held for 24 h before the study. Most of the study subjects homogeneous, we excluded patients with autonomic dysfunction based on the autonomic reflex evaluation (15). A total of consecutive 40 patients were included. Patients were randomized into two groups on the basis of the use of doxazosin: group 1 (n = 20) had no pretreatment; group 2 (n = 20) had pretreatment with doxazosin (2 mg). The clinical characteristics of the patients are given in Table 1. The study was approved by the Hospital Review Board of National Taiwan University, and all subjects provided written, informed consent before participation. Medications, including calcium channel and beta-adrenergic blockers, were held for 24 h before the study.

**Study protocol.** Catheterization procedures. Diagnostic left heart catheterization and angiography were performed from a femoral approach. After completion of the diagnostic catheterization, intravenous heparin was supplemented to maintain an activated clotting time of 300 to 350 s, and a 7F Judkins catheter was advanced to the ostium of the left or right coronary artery. A 0.014-in. (0.035-cm) Doppler wire (FloWire, Cardiometrics, Inc, Mountain View, California) was first introduced, through a standard angio-plasty-type Y-connector attached to the angiographic catheter, into the proximal coronary artery that had nonobstructive lesions (<50%): left anterior descending coronary artery (n = 23), circumflex artery (n = 4) and right coronary artery (n = 13). The wire tip was positioned such that characteristics and the stable flow velocity waveform were obtained. Multiple pairs of perpendicular views (90°) of the left and right coronary arteries were obtained. The precise angle, skew rotation and table height of each projection were recorded so that the projection could be duplicated. Serial hand injections were performed at baseline, during urinary bladder distention and after intracoronary nitroglycerin injection. At each interval, intracoronary Doppler flow was recorded, and then coronary angiography was performed.

**Intervention procedures.** All study subjects underwent a postvoiding residual catheterization to empty the bladder. An 8F transurethral catheter was used to fill the bladder with normal saline at room temperature and was then attached to a water-filled line and pressure transducer, which was zeroed to atmospheric pressure. This line measured the intravesical pressure. Aortic blood pressure, heart rate, coronary angiograms, intravesical pressure and intracoronary Doppler velocity were obtained at baseline. Then, normal saline was installed slowly from two 50-ml syringes through the catheter while constantly monitoring the intravesical pressure. If the intravesical pressure reached 20 mm Hg or increased such that there was a risk of leakage into the urethra, normal saline was withdrawn. The pressure level of 20 mm Hg was chosen because the intravesical pressures were at least 17 mm Hg in subjects with normal bladder function during micturition (16). Because the rate of filling influences the bladder’s ability to accommodate an increasing volume and test results (17), the filling rate was controlled at 50 to 100 ml/min. The same measurements were obtained 5 min after the stable conditions of distention of the urinary bladder. Then, 200 μg of nitroglycerin was infused slowly by direct infusion through the catheter into the ostium of the coronary artery of interest during distention of the urinary bladder; all measurements were repeated within 3 min to avoid tachyphylaxis of small vessels for sympathetic stimulation (18). To examine the mechanism of the coronary flow response to distention of the urinary bladder, the patients in group 2 were pretreated with the selective alpha₁ blocker doxazosin (2 mg orally) 4 h before cardiac catheterization. This dose was selected because previous studies used the same dose to obtain alpha-adrenergic blockade (19). There were no complications related to the study.

**Table 1. Clinical and Angiographic Characteristics of the Two Groups**

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (M/F)</td>
<td>15/5</td>
<td>16/4</td>
<td>NS</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>57 ± 9</td>
<td>56 ± 7</td>
<td>NS</td>
</tr>
<tr>
<td>Risk factor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>6 (30%)</td>
<td>8 (40%)</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>5 (25%)</td>
<td>4 (20%)</td>
<td>NS</td>
</tr>
<tr>
<td>Smoking</td>
<td>8 (40%)</td>
<td>9 (45%)</td>
<td>NS</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>184 ± 32</td>
<td>176 ± 42</td>
<td>NS</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dl)</td>
<td>48 ± 12</td>
<td>53 ± 1</td>
<td>NS</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dl)</td>
<td>128 ± 28</td>
<td>116 ± 32</td>
<td>NS</td>
</tr>
<tr>
<td>Triglyceride (mg/dl)</td>
<td>163 ± 72</td>
<td>182 ± 64</td>
<td>NS</td>
</tr>
<tr>
<td>Coronary lesions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD</td>
<td>12 (60%)</td>
<td>11 (55%)</td>
<td>NS</td>
</tr>
<tr>
<td>LCx</td>
<td>2 (10%)</td>
<td>2 (10%)</td>
<td>NS</td>
</tr>
<tr>
<td>RCA</td>
<td>6 (30%)</td>
<td>7 (35%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Patients without pretreatment. †Patients pretreated with doxazosin.

Data are presented as the mean value ± SD or number (%). F = female; HDL = high density lipoprotein; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; LDL = low density lipoprotein; M = male; RCA = right coronary artery.
lands), as previously described (20). The Doppler catheter was positioned ~10 mm proximal to the stenosis, far from any large branching vessel. To determine the cross-sectional area (CSA) of the artery, a 5-mm segment was measured immediately distal to the tip of the Doppler catheter. All injections and projections throughout a given study were performed by the same operator (T.M.L.) to minimize variability in angiographic technique. Three electrocardiographic (ECG) leads were continuously recorded. These were selected to reflect leads showing ST segment changes during bladder distention. Ischemic ECG changes were defined as a horizontal or downsloping ST segment deviation ≥0.1 mV at 60 ms after the J point in any lead. Transient ECG changes that were observed shortly after coronary arteriography were not taken to be positive. During bladder distention, patients were asked to characterize the nature of their chest pain. The degree of segmental vasoactivity to bladder distention and nitroglycerin was expressed as the absolute vessel diameters and percent changes. We have had previous experience with quantitative coronary arteriography (20,21); the intraobserver and interobserver variabilities were 0.18 ± 0.15 mm (5.7 ± 6.2%) and 0.21 ± 0.23 mm (6.7 ± 6.8%), respectively.

**Lactate measurements.** To confirm myocardial ischemic during urinary bladder distention, selective catheterization of the coronary sinus was successfully attempted in the last 10 patients (5 in group 1 and 5 in group 2). Simultaneous samples of the aortic root and coronary sinus at the same speed were obtained for measurements of lactate contents. The myocardial lactate extraction (MLE) ratio was calculated by the following formula: \( \frac{(L_{AO} - L_{CS})}{L_{AO}} \times 100 \), where \( L_{AO} \) and \( L_{CS} \) represent plasma lactate concentrations in the aortic root and coronary sinus, respectively.

**Calculation of volumetric CBF and coronary resistance.** The coronary flow–velocity measurements were obtained with a Doppler ultrasound 0.014-in. guide wire. Digitized spectral peak velocity waveforms were averaged to compute the average peak velocity (APV). The monitor display was continuously recorded on super VHS videotape for off-line analysis. Volumetric CBF was calculated as CBF (ml/min) = CSA (mm²) × APV (cm/s) × 0.5 × 0.6, as validated by Doucette et al. (22). The factor of 0.5 has been empirically validated and corresponds to the correction for a parabolic velocity profile by compensating for the ratio of spectral peak velocity, as measured by the Doppler system, to the spatial average velocity required for the calculation of volumetric flow. Coronary resistance was derived as mean blood pressure divided by CBF.

**Statistics.** The continuous variables are expressed as the mean value ± SD. After testing data for normality, two-way repeated-measures analysis of variance was used to search for the possible effects of intracoronary nitroglycerin and doxazosin on the coronary angiographic measurements. The interaction term of nitroglycerin and doxazosin effects was incorporated into the model. In case of a significant effect, the measurements at each time point were compared, with
P < 0.017 (Bonferroni correction) as significant. The effect of doxazosin on vascular responses between the two groups. Chi-square analysis was used for categoric variables (<5). Probability values are two-tailed, and p < 0.05 was considered to be statistically significant.

RESULTS

There were no baseline characteristics differences between the two groups shown in Table 1. These groups were comparable in terms of gender, age, lipid profile, heart rate and blood pressure. Coronary risk factors for coronary artery disease were evenly distributed among the three groups.

Blood pressure was significantly decreased from 103 ± 5 to 91 ± 5 mm Hg after the doxazosin dose (p < 0.001), as compared with baseline. The baseline MLE ratio was positive and similar in both groups (18 ± 8% in group 1, 22 ± 11% in group 2). The MLE ratio during urinary bladder distention was decreased significantly in group 1 patients (2 ± 12% vs. baseline p = NS), but remained unchanged in group 2 (17 ± 16% vs. baseline, p = NS). Lactate concentrations returned to below the baseline level of 67 ± 17% (from 2.02 ± 0.36 mmol/l to 0.88 ± 0.23 mmol/l in group 1 patients, 15.5 ± 11.3 mmol/l to 7.2 ± 4.6 mmol/l in group 2 patients, and 14.5 ± 15.4 mmol/l in group 3 patients). Changes in heart rate, mean blood pressure and rate–pressure product at rest, during bladder distention and after nitroglycerin were also comparable between the two groups shown in Table 1. These groups were comparable in terms of gender, age, lipid profile, heart rate and blood pressure. Coronary risk factors for coronary artery disease were evenly distributed among the three groups.

Changes in Hemodynamic Variables, Angiographic Variables and Coronary Blood Flow in the Two Groups of Patients

Table 2

| Variables | Baseline | Bladder Distention | Bladder Distention Plus NTG | p-Value*
|-----------|----------|--------------------|-----------------------------|--------
| Mean blood pressure (mm Hg) | 99 ± 6 | 77 ± 6 | 74 ± 6 |<0.001
| Heart rate (beats/min) | 67 ± 7 | 82 ± 7 | 89 ± 6 |<0.001
| SBP | 102 ± 5 | 100 ± 5 | 96 ± 6 |<0.001
| HR (rate–pressure product) | 9,401 ± 1,282 | 6,842 ± 1,126 | 8,448 ± 1,623 |<0.001
| Doppler APV (cm/s) | 20.3 ± 4.7 | 13.7 ± 3.7 | 13.0 ± 3.4 |<0.001
| Cross-sectional area (mm²) | 3.20 ± 0.37 | 3.23 ± 0.42 | 3.07 ± 0.49 |<0.001
| HR (rate–pressure product) | 9,401 ± 1,282 | 6,842 ± 1,126 | 8,448 ± 1,623 |<0.001
| Mean coronary resistance (mm Hg/ml per min) | 2.02 ± 0.88 | 1.18 ± 1.18 | 2.38 ± 2.00 |<0.001
| Coronary blood flow (ml/min) | 49.3 ± 15.5 | 37.4 ± 15.4 | 48.0 ± 15.6 |<0.001
| Mean coronary resistance (mm Hg/ml per min) | 2.02 ± 0.88 | 1.18 ± 1.18 | 2.38 ± 2.00 |<0.001
| Coronary blood flow (ml/min) | 49.3 ± 15.5 | 37.4 ± 15.4 | 48.0 ± 15.6 |<0.001

* Patients without pretreatment. † Patients pretreated with doxazosin. ‡ p < 0.05 compared with data from baseline, during bladder distention and after nitroglycerin. § p < 0.05 compared with previous data. Parentheses indicate changes are significant at the p < 0.05 level.

Epicardial Vascular Response. In group 1, bladder distention significantly decreased the epicardial coronary diameter by 19 ± 6% (from 2.03 ± 0.27 to 1.65 ± 0.36 mm, p < 0.001), and decreased CBF by 25 ± 17% (from 49.3 ± 15.5 to 37.4 ± 15.4 ml/min, p < 0.001). In group 2, there were no significant changes in the epicardial coronary diameter during bladder distention, as compared with baseline CBF during bladder distention, as compared with baseline.
After nitroglycerin administration in the presence of bladder distention in group 1, in the stenotic vessel segments, epicardial coronary diameters were significantly increased by 21 ± 14%, epicardial coronary CSA by 45 ± 34% and CBF by 40 ± 48%, as compared with values during bladder distention (Table 2). In group 2, the stenotic epicardial coronary diameter was significantly increased by 9 ± 8%, epicardial coronary CSA by 13 ± 21% and CBF by 16 ± 24% after nitroglycerin administration. No interaction was noted between the effects of nitroglycerin and doxazosin on epicardial angiographic variables.

**Resistance vessel response.** In group 1, bladder distention significantly increased coronary resistance by 68 ± 60% (p < 0.001), as compared with baseline values (Table 2, Fig. 2). In group 2, there was a trend toward increased coronary resistance during bladder distention, as compared with baseline (2.23 ± 0.50 vs. 2.00 ± 0.55 mm Hg/ml per min, p = 0.07). There were significant differences in coronary resistance (p = 0.005) between the two groups during bladder distention.

After nitroglycerin administration in the presence of bladder distention in group 1, coronary resistance was decreased by 32 ± 23% (p < 0.001), as compared with values during bladder distention (Table 2), similar to the changes seen in group 2. There was no interaction between the effects of nitroglycerin and doxazosin on vascular resistance.

**DISCUSSION**

The present study demonstrates, for the first time, that distention of the urinary bladder decreases the coronary diameter of the stenotic segments and CBF and increases coronary resistance in a homogeneous group of patients with similar severities of coronary atherosclerosis. These angiographic changes resulted in myocardial ischemia, as assessed by net lactate production. Such changes are not related to smooth muscle cell alteration because the vaso-motor response was similar between the two groups after nitroglycerin administration. Doxazosin administration reversed the myocardial ischemia, reflecting the mechanism of coronary vasoconstriction, and a concomitant increase in coronary vascular resistance was mediated by alpha1 adrenoceptors during bladder distention.

**Conduit vessels.** Our results showing that vasoconstriction of conduit vessels evoked by urinary bladder distention were consistent with previous reports showing that sympathetic activation dilates normal coronary arteries but constricts atherosclerotic vessels (23). The constriction of coronary conduit vessels in response to bladder distention may be due to an exaggerated response to sympathetic activation and, in part, endothelial function.

Distention of the urinary bladder induces sympathetic release, which evokes an increase in heart rate, blood pressure, myocardial oxygen demand and myocardial isch-
emia, as assessed by sinus lactate production. Distention of hollow viscera has been shown to stimulate receptors located in their walls (8,24), which may reflexively affect the coronary circulation. For instance, distention of the stomach has been reported to elicit reflex increases in heart rate and blood pressure and has been related to postprandial angina (25).

The mechanism of coronary vasoconstriction is mediated by \( \alpha_1 \) adrenceptors. Epicardial coronary arteries are innervated with sympathetic nerve fibers and have \( \alpha_1 \) and \( \alpha_2 \)-adrenergic receptors (26). Baran et al. (26) have shown that \( \alpha_1 \) receptors are involved in vasoconstriction of large coronary arteries during exercise. The increased vascular \( \alpha_1 \) tone can explain epicardial coronary vasoconstriction during bladder distention. Furthermore, an \( \alpha_2 \)-adrenergic antagonist has been shown in our study to limit coronary vasoconstriction during bladder distention, which was consistent with the finding of Collins et al. (27) that indoramin, a selective \( \alpha_2 \)-adrenergic antagonist, has been shown to limit exercise-induced angina pectoris.

Besides, vasoconstriction of the coronary arteries in response to bladder distention could also be caused by impaired endothelial function. Endothelial dysfunction may play a central role in precipitating altered vasomotion in the coronary artery. Hypersensitivity of vascular smooth muscle in the region of endothelial dysfunction (atherosclerotic plaque) may produce paradoxic vasoconstriction. Nabel et al. (28) have demonstrated that sympathetic stimulation dilates normal and constricts atherosclerotic coronary arteries, which was inconsistent with our finding that vasoconstriction was noted in stenotic segments but remained unchanged in “normal reference” segments. However, a “smooth” appearance of the lumen surface on the coronary angiogram does not exclude the presence of intimal involvement with atherosclerosis. The presence of functioning endothelium in normal reference segments may attenuate urinary bladder distention-induced vasoconstriction.

**Increased microvascular resistance.** Distention of the urinary bladder causes an increase of coronary vascular resistance in patients with early atherosclerosis. In patients with coronary disease, coronary resistance increases during sympathetic stimulation because the vasodilatory reserve has been exhausted such that alpha adrenoceptor-mediated vasoconstriction is unopposed (29). The failure of CBF to increase during bladder distention may suggest either endothelial dysfunction or exaggerated sympathetic vasoconstriction at the level of resistance, leading to uncoupling between increased metabolic demand and coronary flow. Although atherosclerotic lesions are confined to epicardial vessels, the functional consequences of atherosclerosis may extend to the microvessels. The failure of endothelial cells to produce or release adequate quantities of nitric oxide occurred in resistance vessels devoid of atheroma.

**Effect of nitroglycerin.** Nitroglycerin has different effects on the epicardial and microvascular coronary circulation. Nitroglycerin causes endothelium-independent epicardial vasodilation by the formation of exogenous nitric oxide within vascular smooth muscle cells (30). Nitric oxide will dilate coronary artery size, even at the segments of impaired endothelial function (30). Sudhir et al. (31) demonstrated that nitroglycerin predominantly influences coronary conductance arteries and has large effects on increased CSA, with minimal effects on coronary resistance, which is not consistent with our finding that there was a similar effect of nitroglycerin on conduit (CSA increased by 45%) and resistance vessels (vascular resistance decreased by 32%). A possible explanation may be the different doses of nitroglycerin used. Previous reports (32,33) have suggested that large vessel tone is diminished by low concentrations of nitrates and small vessels dilate only by higher nitrate concentration. In fact, the dose of 200 \( \mu \)g of intracoronary nitroglycerin that we used could dilate resistance vessels (32,33).

**Study limitations.** This study could be criticized because heart rate was uncontrolled by cardiac pacing and the rate–pressure product was not held constant during the study. Although the patients were not paced during bladder distention, the degrees of changes in the rate–pressure product between the two groups were similar. Thus, the changes in the rate–pressure product could not be a major factor of vasoconstriction during bladder distention.

Another limitation of the present study was a lack of normal control data for ethical reasons. The invasive nature of the study made it impractical to have a normal control group. Instead, each patient serves as his or her own control.

The third limitation of the present study was the poor sensitivity of the surface ECG to detect myocardial ischemic during bladder distention. Sutton et al. (34) reported on the electrical focus, causing the ST segment changes to be a localized area of myocardium, and therefore may not be apparent on the leads of a surface ECG. Besides, the relatively short bladder distention time may not produce ischemia sufficient to develop ST–T segment changes. We did not measure intracoronary ECG and regional wall motion abnormalities, as assessed by echocardiography, which has been proved to be more sensitive for detecting myocardial ischemia (35). Thus, although the supplied flow was only about one-half of the metabolic flow demand, as indicated by the decrease of coronary flow (24%) and the concomitant increase in metabolic demand (32%), as compared to predistention values, only 30% of the patients in group 1 demonstrated symptoms and signs of ischemia.

The fourth limitation refers to the possibility that the alpha-adrenergic antagonist used in this study provided an insufficient dose. However, this is unlikely because the mean blood pressure reduction after complete blockade of the alpha-adrenergic pressor effects was 13 mm Hg, as reported by Guth et al. (36), which is similar to our level of 12 mm Hg.

Finally, although previous studies have used \( \alpha_2 \)-adrenergic blockers to demonstrate the role of adrenergic receptors in mediating coronary vasoconstriction effects, we did not use these because they would increase circulating...
norepinephrine and myocardial oxygen consumption (37). Such adverse myocardial effects will increase the complexity of effects of alpha₂-adrenergic blockers on coronary vaso-
motor function.

Clinical implications. Urinary bladder distention in this study constitutes a physiologic form of stress and therefore may have relevance to the clinical setting. During bladder distention, the reflex coronary vasconstriction would limit the expected coronary vasodilation, which is secondary to the concomitant reflex increases in heart rate and arterial blood pressure. Traditionally, the relation of bladder disten-
tion to myocardial ischemia has been related to an increased rate–pressure product, an index of myocardial oxygen de-
mand. From this study, another potentially important con-
tributing mechanism is the reflex coronary vasoconstriction. Such a vasoconstriction response of resistance vessels distal the stenosis could further limit the blood supply to the myocardium and contribute to myocardial ischemia during bladder distention.

The effects of alpha₁ adrenergic blockade on the treat-
ment of benign prostatic hyperplasia have been extensively documented (38). The study suggested that the alpha₁ adre-
nergic blocker is unique among drugs for benign prostatic hyperplasia in that it has a beneficial effect on CBF during bladder distention. Particularly, patients with benign prostatic hyperplasia may coexist with coronary atherosclerosis.

Large volumes of bladder irrigation fluid during trans-
urethral resection of the prostate can produce a complication known as transurethral resection syndrome. The pathophys-
iological characteristics are complex, including transient hy-
pervolemia from the absorption of electrolyte-free irrigation fluid, dilutional hypoalbuminemia, toxicity from glycine and impaired renal function (39). However, chest pain, with an incidence of 2% (38) in transurethral resection syndrome, could not be explained by these mechanisms. The chest pain during transurethral resection may be explained in part by the sudden increase in intravesical pressure, which in turn results in a decrease in CBF (decreased blood supply) and an increase in the rate–pressure product (increased oxygen consumption). Thus, the problem may be raised whether it is necessary to screen for the possibility of coronary artery disease before performing transurethral resection, especially in elderly people.

Conclusions. The present study shows that urinary bladder distention caused a reflex reduction in CBF, even in patients with early coronary atherosclerosis. The response involved effenter sympathetic mechanisms related to alpha₁ adreno-
ceptors. Pretreatment with doxazosin reversed the decreased CBF during bladder distention toward baseline. The reflex reduction in CBF can be relieved after nitroglycerin admin-
istration.

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