pressure to a comparable degree. Resistance arteries (luminal diameter, 150–350 μm) dissected from gluteal subcutaneous biopsies were studied on a pressurized myograph. Following one year of treatment, the media width to lumen diameter ratio of arteries from losartan-treated patients was significantly reduced (P < 0.01). Arteries from atenolol-treated patients were unchanged. Endothelium-dependent relaxation was normalized by losartan but not by atenolol. Stress-strain relationships of small arteries were shifted to the right by losartan but unchanged in atenolol-treated patients. Thus, treatment for 1 year with the AT1 angiotensin antagonist losartan corrected resistance artery structure and mechanics, and the endothelial dysfunction in hypertensive patients, whereas atenolol had no effect. This vascular protective effect of losartan could contribute to reduce complications of hypertension, which remains to be demonstrated.

Key Words: Small artery remodeling; endothelial dysfunction

Wednesday, May 17, Broadway Ballroom North, 12:30 PM to 2:30 PM
Targeting Blood Pressure Goals and End-Organ Protection: Advances in RAS Blockade
VASCULAR INJURY, VASCULAR HEALING, HYPERTENSION AND THE RENIN SYSTEM
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Alterations in structure and function of blood vessels that occur in hypertensive patients and in experimental hypertensive models may contribute to blood pressure elevation and to the complications of hypertension. Angiotensin II may influence the vasculature in hypertension through its effects on the atherogenic process and on hypertensive vascular disease per se. The actions of angiotensin II on inflammation, smooth muscle cell growth (hypertrophy or hyperplasia) and collagen deposition in blood vessels participate in mechanisms of atherogenesis and hypertensive vascular damage, and are mediated via AT1 receptors, whereas AT2 receptors appear to inhibit growth and stimulate programmed cell death or apoptosis. There is increasing evidence that angiotensin II plays a pivotal role in remodeling of both large and small arteries in experimental and human hypertension. Interruption of the renin-angiotensin system thus appears an interesting approach for the treatment of hypertension in order to correct vascular abnormalities that may contribute to cardiovascular events in hypertension. Treatment of spontaneously hypertensive rats (SHR) with angiotensin converting enzyme (ACE) inhibitors and AT1 angiotensin receptor antagonists results in regression of the altered structure of blood vessels in different vascular beds. Endothelium-dependent relaxation is also improved. Studies in hypertensive patients have now shown that treatment with some ACE inhibitors and more recently AT1 antagonists may induce similar potentially beneficial effects, particularly at the level of small arteries: both structure and endothelium-dependent relaxation are significantly improved. In contrast, treatment with the beta blocker atenolol does not result in any improvement in vascular structure or endothelial function in hypertensive patients with equally well-controlled blood pressure in different studies. It still remains to be determined whether the apparently beneficial vascular effects of blockade of the renin-angiotensin system with ACEI or with AT1 receptor antagonists and their vascular protective properties, beyond blood pressure lowering itself, will result in reduced morbidity and mortality and improved outcomes in hypertensive patients.

Key Words: Vascular remodeling; endothelial dysfunction; resistance arteries

TARGETING HIGH-RISK HYPERTENSIVE PATIENTS WITH RAS BLOCKADE: APPLICATION OF FINDINGS
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High blood pressure is a common clinical illness whose etiology has not been well described. It contributes substantially to the development of cardiovascular disease. Efforts at controlling blood pressure to levels of less than 140/90 mmHg have been limited to some degree by an inexact understanding of the pathophysiology of the disease process as well as its asymptomatic nature. A larger problem may also exist: the maximum benefit of therapy may not be achieved at the goal levels currently targeted in clinical practice.

Epidemiologic evidence supports the need for more intensive control of blood pressure to a systolic less than 130 mmHg in many patients, particularly those with diabetes or target organ damage. Health care providers and patients need to be aware of the overwhelming evidence supporting the need for more intensive blood pressure control and how important this is in reducing cardiovascular morbidity and mortality. Abundant data from the HOT, UKPDS, SHEP, and the Syst-Eur trials demonstrate the need for controlling both systolic, diastolic, and pulse pressure, even in older patients, in order to prevent cardiovascular morbidity and mortality.

Lower levels of blood pressure reduce mechanical stretch, strain, and turbulence within the vascular beds and in the target organs. This reduces the impetus for vascular and target organ production of neurohormones like angiotensin II which leads to maladaptive restructuring and remodeling. Controlling blood pressure may be the critical factor in lessening this risk, and breaking the vicious cycle whereby vascular disease begets higher levels of systemic blood pressure, which begets more vascular disease. Although newer classes of medications which specifically target the renin angiotensin system, like ACE inhibitors or angiotensin type 1 receptor blockers as part of their antihypertensive activity do show some advantage in delaying progression of cardiovascular and renal disease, these agents should not be used as a substitute for intensive blood pressure control, but as an aid in achieving this overall goal. Therapeutic strategies which employ well tolerated medications in lower doses may be the critical strategy to improve blood pressure control in asymptomatic patients.

Key Words: Systolic; diastolic blood pressure; angiotensin II; cardiovascular outcome

Wednesday, May 17, Broadway Ballroom North, 3:00 PM to 5:00 PM