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Activation of the renin-angiotensin-aldosterone system in arterial hypertension can lead to remodeling of the myocardial collagen network, with progressive collagen accumulation in the cardiac interstitium. This reactive myocardial fibrosis, which is not secondary to myocyte necrosis, appears to be an important determinant of diastolic dysfunction and thus of pathologic hypertrophy. To examine the effects of the aldosterone antagonist spironolactone on myocardial fibrosis, we analyzed interstitial fibrosis in 7 different models of arterial hypertension in rats: 2 kidney, 1 clip model of renovascular hypertension (RHT); continuous subcutaneous aldosterone (0.75 micrograms/hr) infusion; RHT and aldosterone models treated with 20 mg/kg per day of subcutaneous spironolactone; uninephrectomized rats on a high sodium diet; and age- and sex-matched controls with or without spironolactone treatment. Systolic arterial pressure was comparably elevated in RHT and aldosterone models; it was modestly lowered but not normalized by 8 weeks of spironolactone treatment at the low doses used. Such treatment also failed to prevent left ventricular hypertrophy (LVH) in all experimental groups with hypertension. Spironolactone, however, was able to prevent myocardial fibrosis in RHT and aldosterone models of acquired arterial hypertension irrespective of the development of LVH and the presence of hypertension. These findings provide further evidence that elevated aldosterone levels play an important role in the adverse remodeling of the myocardium in arterial hypertension. The antifibrotic effects of spironolactone, if confirmed in human studies, may be a valuable strategy in treating hypertensive heart disease.