Hepatocyte Growth Factor and Cardiomyopathy in Dialysis Patients

To the Editor:

Hepatocyte growth factor (HGF) is a pleiotropic cytokine with cardioprotective properties. In an elegant study published in the May issue of Hypertension, Okayama et al. demonstrated in transgenic mice that HGF reduced cardiac fibrosis by inhibiting endothelial-mesenchymal transition and the transformation of fibroblasts into myofibroblasts. The amount of cardiac fibrosis significantly decreased in pressure-overloaded HGF-transgenic mice compared with pressure-overloaded nontransgenic controls, particularly in the perivascular region. This pattern was accompanied by a reduction in the expression levels of fibrosis-related genes and by significant preservation of echocardiographic measurements of cardiac function in the HGF-transgenic mice.1 These intriguing experimental data suggest that an increased expression of HGF may limit myocardial fibrosis in human cardiomyopathies with a relevant pressure-overload component. Pressure-overload and volume expansion are pervasive in patients with kidney failure on dialysis, a population with an exceedingly high risk for death and cardiovascular events, particularly heart failure. Left ventricular hypertrophy has 70% to 80% prevalence in dialysis patients, and excessive myocardial fibrosis is a hallmark in cardiomyopathy in experimental models of kidney failure2 and in cardiomyopathy in this population as well.3 Arterial and cardiac remodeling proceed in parallel in dialysis patients,3 and we demonstrated that circulating HGF associates with cardiac3 and vascular remodeling and predicts survival.4 In our study published in Hypertension,3 HGF was directly associated with the muscular component of the left ventricle (mean wall thickness and concentric remodeling of the left ventricle) and inversely with the cavitary component (left ventricular end diastolic volume), suggesting a compensatory mechanism aimed at limiting cardiac fibrosis in these patients. Experimental data by Okayama et al.1 showing that HGF limits myocardial fibrosis in a pressure-overload model suggests that the direct association of circulating HGF with concentric left ventricular geometry observed in our study may underlie resistance to the cardioprotective effect of HGF. Resistance to potentially protective endogenous factors plays a role in cardiomyopathy in kidney failure. Indeed, myocardial capillary rarefaction is another fundamental component of left ventricular hypertrophy in experimental models of kidney failure, underlies vascular endothelial growth factor resistance, and high vascular endothelial growth factor predicted mortality in another study in dialysis patients by us.5 Studies aimed at clarifying molecular mechanisms underlying resistance to endogenous HGF may unravel new opportunities for counteracting the progression of cardiomyopathy in patients with kidney failure and improve the dim health prospects of this very high risk population.

Disclosures

None.

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Hypertension, 2012;60:e24; originally published online August 6, 2012;
doi: 10.1161/HYPERTENSIONAHA.112.198424
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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World Wide Web at:
http://hyper.ahajournals.org/content/60/3/e24

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