Putting the Brakes on Cardiac Hypertrophy

Exploiting the NO–cGMP Counter-Regulatory System

George W. Booz

From the Cardiovascular Research Institute, the Texas A&M University System Health Science Center, College of Medicine, Temple, Tex.

Correspondence to George W. Booz, PhD, FAHA, Cardiovascular Research Institute, Texas A&M College of Medicine, 1901 South 1st Street, Bldg 205, Temple, TX 76504. E-mail gbooz@medicine.tamhsc.edu

Abstract. We know a great deal about the receptors and signaling pathways in cardiomyocytes that contribute to hypertrophic growth. Although drugs that target them have proven effective in substantially reducing left ventricular hypertrophy and associated mortality, cardiovascular disease remains the leading cause of death in the West. Another approach may rest with exploiting naturally occurring regulators of maladaptive cardiac hypertrophy that have been identified in the past few years. These endogenous negative regulators can be grouped, for the most part, into those constitutively active but whose activity is decreased by hypertrophic stimulation, and those with little or no baseline activity that are activated by hypertrophic stimulation. Spanning both groups are 4 systems that converge on cyclic guanosine 3', 5'-monophosphate (cGMP) generation, namely natriuretic peptides (ANP and BNP), kinins, nitric oxide (NO), and the angiotensin II type 2 receptor (AT_2). Although holding promise as a means for restricting hypertrophy, each of these signaling molecules has certain limitations that need to be overcome. What follows is an overview of research over the past 2 years, much of it published in *Hypertension*, which has dealt with the antihypertrophic action of this particular group of endogenous signaling molecules. Understanding the function and regulation of the antihypertrophic NO–cGMP system offers the promise of novel therapeutic strategies for treating cardiac hypertrophy and heart failure.

Key Words: adrenergic antagonists • angiotensin II • kinins • natriuretic peptides • nitric oxide synthase • statins

Fibrinogen and other coronary risk factors

Finn Edler von Eybena[a*], Ejvind Aae Mouritsen[a], Jan Holm[b], Paulius Montvilas[c], Georg Dimcevski[d], Inge Helleberg Rasmussen[e], Lisbeth Langholz Kristensen[f], Gabriel Suciu[g], Rie von Eyben[h]

[a]Department of Internal Medicine Herning Hospital, DK-7400 Herning, Denmark
[b]Department of Clinical Chemistry, Herning Hospital, DK-7400 Herning, Denmark
[c]Department of Radiology, Herning Hospital, DK-7400 Herning, Denmark
[d]Department of Clinical Physiology, Herning Hospital, DK-7400 Herning, Denmark
[e]Department of Internal Medicine, Tarm Hospital, DK-6890 Tarm, Denmark
[f]Department of Internal Medicine, Varde Hospital, DK-6800 Varde, Denmark
[g]Institute of Biostatistics, Ohio State University, Columbus, OH, USA
[h]Academic Technology Services, University of California Los Angeles, Los Angeles, CA, USA
Metabolism Clinical and Experimental 54 (2005) 165-170

Abstract. The association between plasma fibrinogen concentration and other coronary risk factors diverged in previous studies, and the impact from complex lipoprotein patterns has not been studied. Our research involved 24 healthy subjects without coronary heart disease (control) and 22 patients who had survived having acute myocardial infarction before the age of 41 years (cases), overall 40 men and 6 women with age range of 34 to 54 years. In multiple linear regression analyses concerning control subjects, family disposition, social class, a score based on serum triglyceride and high-density lipoprotein (HDL) cholesterol concentrations, and fasting capillary blood glucose concentration were significantly associated with plasma fibrinogen concentration ($P < .00005$, $R2 = 0.81$). For case subjects, the ratio between serum low-density lipoprotein cholesterol and high-density lipoprotein cholesterol concentrations was significantly associated with plasma fibrinogen concentration ($P = .0018$, $R2 = 0.39$). Thus, for healthy subjects, 4 coronary risk factors explained three quarters of the variation of plasma fibrinogen concentration, and for patients with a previous acute myocardial infarction, another coronary risk factor explained one third of the variation. In conclusion, the pattern of coronary risk factors associated with plasma fibrinogen concentration differed between those without coronary heart disease and those with a previous acute myocardial infarction.