Progression from Hypertension to Heart Failure: Mechanisms, Epidemiology, and Prevention

MMPs and TIMPs: An Aspect of Pathophysiology

Michael Zile, MD, Medical University of South Carolina, discussed the HTN-HF continuum, focusing on matrix mettalloproteinases (MMPs) and tissue inhibitors of metalloproteinases (TIMPs). Research conducted at his own institution measured plasma profiles of MMPs and TIMPs in HF patients and age-matched healthy people. "We know that inflammatory cytokines induce MMP expression in vitro," Dr. Zile said. The South Carolina investigators detected MMP/TIMP ratios elevated as high as 16-fold in hypertensive patients with HF.

Whether routine measurement of MMP/TIMP ratios might someday serve as a biomarker or a diagnostic tool in HF remains unclear. But "cytokine activity was linked to changes in MMP levels," Dr. Zile said, "and it's evident that MMP proliferation is related to the ventricular non-compliance that can ultimately degrade to florid HF."

The Framingham Perspective

"We wanted to identify risk factors that contributed to—and connected—HTN and HF," said Dan Levy, MD, Director, Framingham Heart Study. Study participants included original Framingham Heart Study and Framingham Offspring Study participants between 40 and 89 years of age who had no HF.

Over a 14-year follow-up investigators found that 91% of patients who ultimately developed HF had a history of HTN, according to Dr. Levy. "The risk of developing HF after HTN as compared with normotensive individuals was about 2-fold in men and 3-fold in women."

Post-MI Progression

"When any of us has a heart attack we bring all our baggage with us," said Marc A. Pfeffer, MD, PhD, Harvard Medical School. Hypertension, diabetes, obesity—whatever the risk factor, "we carry it with us into the MI and beyond."

"The most sensible recommendation any doctor can offer is: Don't have the MI to begin with," Dr. Pfeffer said. "Or, if you're going to have one, make it the smallest infarct possible."

Dr. Pfeffer noted compelling emerging evidence for genetic factors that dictate how any given individual heart handles the stress of infarction. "Some of us appear to have better intrinsic repair capacity than others. But until we know a great deal more about the genomics of CV disease, no one can afford to ignore risk factor modification."

Barry Greenberg, MD, Director, Heart Failure/Cardiac Transplantation Unit, University of California, observed that "the road from an MI to HF is metabolically treacherous. Post-MI patients are very likely to remodel and go on to HF. Neurohormonal activation is a major factor in this pathway."

Dr. Greenberg recommended neurohormonal blocking agents (e.g., ARBs, ACEIs). "Is it possible to attenuate the pathological changes that follow in the wake of MI? The answer is a resounding yes."

Valvular Disease: from Recognition to HF

Blase Carabello, MD, Professor, Baylor College of Medicine, offered a crisply delineated approach to valvular heart disease (VHD) and HF: VHD is a mechanical problem that demands a mechanical solution. "It's a given that any valve disease that creates increased load on the heart might eventually go on to HF," Dr. Carabello said.

"Any symptoms at all in a person with VHD is a turn for the worse," said Dr. Carabello. "We need to remember the 'melanoma metaphor'—we never say that a person has 'just has a little melanoma'. We should approach VHD the same way. The earliest symptoms mark the time to consider surgery in appropriate patients who can tolerate it."