News and Views from the Literature

Patients at Risk

Tricuspid Regurgitation and Survival

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Impact of Tricuspid Regurgitation on Long-Term Survival

Nath J, Foster E, Heidenreich P. J Am Coll Cardiol. 2004:43:405-409.

ricuspid regurgitation (TR) is a common finding on echocardiographic evaluation, observed in up to 90% of imaged patients. With little data available in terms of the implications of tricuspid insufficiency on cardiovascular events, this finding does not result in any significant alteration in the approach to the patient and is generally felt to be benign.

The authors retrospectively studied 5223 patients with a mean age of 66.5 years at three Veterans Affairs medical centers, with a mean follow-up of 498 days. Patients were identified as having normal or elevated pulmonary artery systolic pressure (>40 mm Hg) and normal (≥50%) or reduced left ventricular ejection fraction (LVEF). TR was graded qualitatively using the apical four-chamber and subcostal views and was considered mild if the regurgitant jet/right atrial area was less than 19%, moderate if 20%-40%, or severe if greater than 40%. The right ventricle enlargement was considered mild if it was greater than two-thirds of the left ventricle but less than equal the size, moderate if the right ventricle was equal in size to the left ventricle, and severe if greater in size than the left ventricle. In addition, right ventricular (RV) function was graded as reduced if there was any RV wall motion abnormality or descent of the base less than 2.0 cm. Inferior vena cava (IVC) was characterized as dilated if greater than 2.0 cm.

Features of patients with progressively higher grades of TR include greater age, worsening LVEF, progressive RV dilation, and dysfunction and dilation of the IVC (Table 1).

Patients with moderate or greater TR had higher mortality rates than those with milder TR, regardless of pulmonary artery systolic pressure. In addition, mortality rates were higher for patients with moderate or greater TR whether or not the LVEF was normal or decreased. Patients with moderate and severe TR had a worse prognosis than

Table 1
Features of Patients with Higher Grades of
Tricuspid Regurgitation (TR)

	No TR	Mild TR	Moderate TR	Severe TR
Age, y	62.2 ± 13	66.0 ± 13	71.9 ± 12	71.9 ± 12
LVEF, %	57.3 ± 9	55.4 ± 12	47.1 ± 16	40.4 ± 17
RV dilation, %	8	11	35	66
RV dysfunction, %	3	8	30	61
Dilated IVC, %	6	11	44	71
1-y survival, %	91.7	90.3	78.9	63.9

IVC, inferior vena cava; LVEF, left ventricular ejection fraction; RV, right ventricular.

those with no TR, even after adjusting for age, LVEF, IVC size, RV function, and RV size. Unfortunately, the cause of death in these patients is not defined.

The authors attempt to determine why the severity of TR leads to a worse prognosis independent of the parameters mentioned above. They speculate that the presence of TR may be a more sensitive marker of RV dysfunction than is qualitative inspection on echocardiography, or that TR may "mask the decreased con-

It may be that a more aggressive approach to these patients with surgery such as tricuspid annuloplasty may have a positive effect on the natural history of TR and lead to an improvement in patient survival and quality of life.

tractility of the RV analogous to the effect of mitral insufficiency on the ability to estimate LV contractility from LVEF." Further study is needed in this very large patient population to determine why TR severity has a negative effect on both mortality and morbidity. Indeed, it may be that a more aggressive approach to these patients with surgery such as tricuspid annuloplasty may have a positive effect on the natural history of TR and lead to an improvement in patient survival and quality of life.

Atherosclerosis

Bigger Is Better: High-Density and Low-Density Lipoprotein Particle Size

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therosclerosis was previously thought to be an irreversible process and an inevitable part of aging. Although modern lipid-lowering therapy has resulted in a significant reduction in the risk of cardiac events, this reduction in adverse clinical events has

been associated with only modest degrees of angiographic plaque regression. The salutary effect of lipid-lowering therapy with hydroxymethyl glutaryl coenzyme A inhibitors (statins) on morbidity and mortality is thought to be at least in part conferred by suppression of atherosclerotic plaque inflammation, which results in increased plaque stability. Statin therapy is associated with an average 30% reduction in adverse cardiovascular events. Despite this unquestionable and remarkable beneficial effect, statins still fail to prevent the majority of cardiac events. Other pathogenetic mechanisms, such as local angiogenesis and vascular remodeling, might result in plaque rupture even in the absence of demonstrable inflammation. Indeed, patients with acute coronary syndromes might present with normal levels of C-reactive protein, a marker for vascular inflammation. Further reduction in atherothrombotic events in individuals with established atherosclerosis might require not only plaque stabilization and restoration of normal endothelial function (which can be largely achieved with statin therapy), but also a significant regression in the total atherosclerotic plaque burden. Currently available treatment modalities result in only modest angiographic regression of atherosclerotic arterial obstruction. To achieve more significant regression, not only a reduction in cholesterol influx but also cholesterol efflux from the plaque must be achieved. The key to plaque regression seems to reside in high-density lipoprotein (HDL) size.

In a small village in northern Italy lives a family with a naturally occurring variant of apolipoprotein A-I, known as ApoA-I Milano. Individuals with ApoA-I Milano are characterized by very low levels of HDL, ranging from 10 to 30 mg/dL. Life expectancy, however, is not adversely affected, and atherosclerosis is uncommon. ApoA-I Milano is characterized by a substitution of cysteine for arginine in position 173, thus allowing HDL dimerization and the formation of large HDL particles, which are particularly active in reverse cholesterol transfer. Esperion Therapeutics (Ann Arbor, MI) has formulated recombinant ApoA-I Milano into a complex (ETC-216) with naturally occurring phospholipids to mimic the properties of nascent HDL. Preliminary data derived in animals demonstrated objective plaque regression as quickly as 48 hours after a single infusion.1

Effect of Recombinant ApoA-1 Milano on Coronary Atherosclerosis in Patients with Acute Coronary Syndromes—A Randomized Controlled Trial

Nissen SE, Tsunoda T, Tuzcu EM, et al. JAMA. 2003:290:2292-2300.