

Potential Markers of Remodeling and Function

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Disclosure

- The presenter serves on veterinary advisory boards for CEVA Sante Animale and IDEXX Laboratories

What Are Markers Good For?

- Dogs with MVD
 - Diagnosis and disease severity
 - Diagnosis of CHF vs respiratory disease

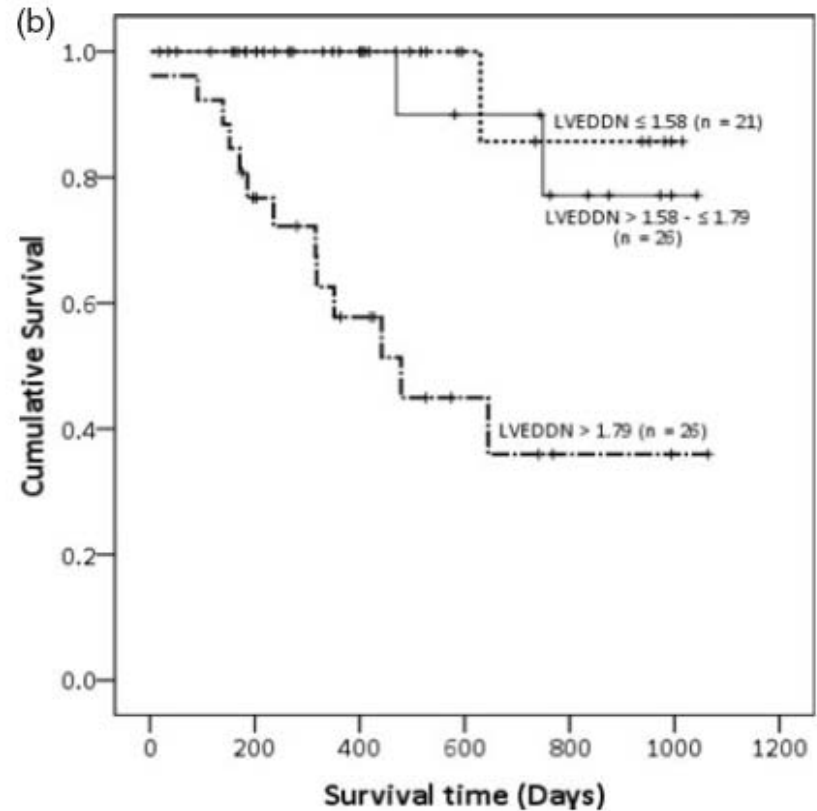
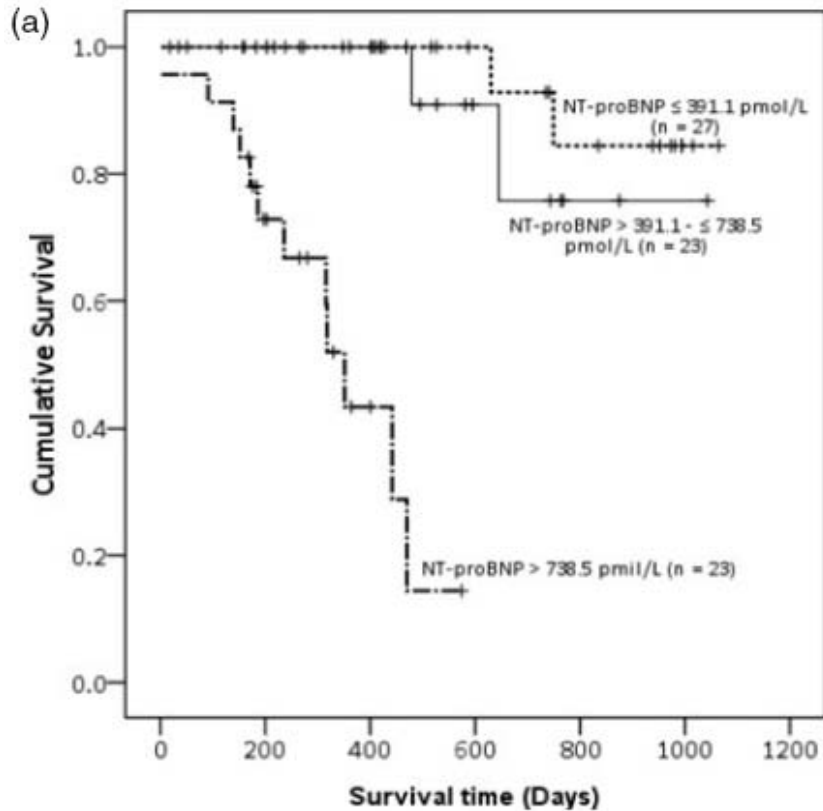
- Risk stratification
 - Mortality
 - First onset of CHF
- Response/guide to therapy

Marker-identified
point of intervention



Disease progression →

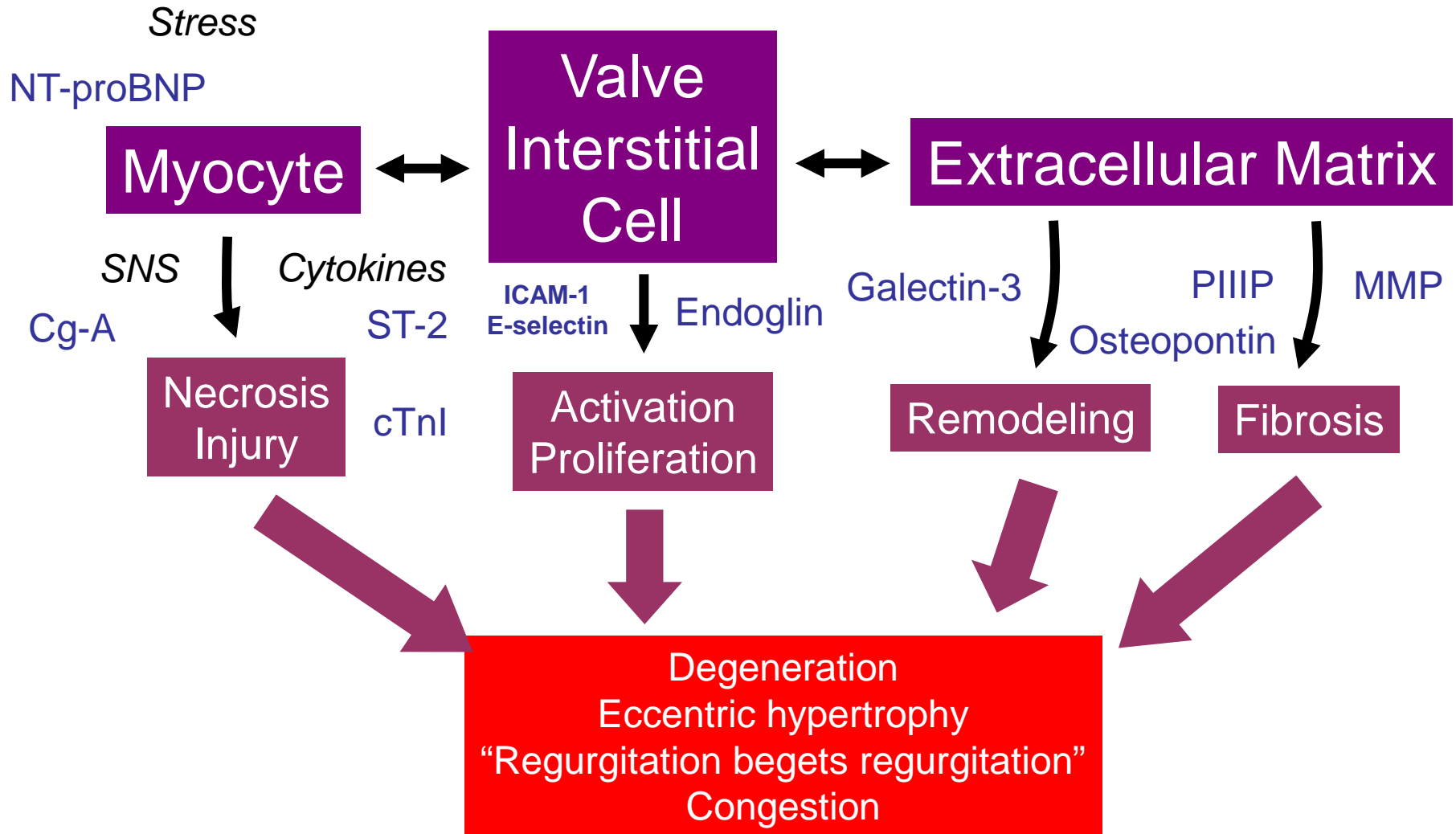
Mortality: Risk Stratification



Cardiac mortality: +100pmol/L BNP = +7% hazard
+0.1 LVIDdN = +20% hazard

73 dogs; Moonarmart et al. JSAP 2010
46 dogs; Serres et al. JVC 2009

Markers and Pathophysiology of MVD

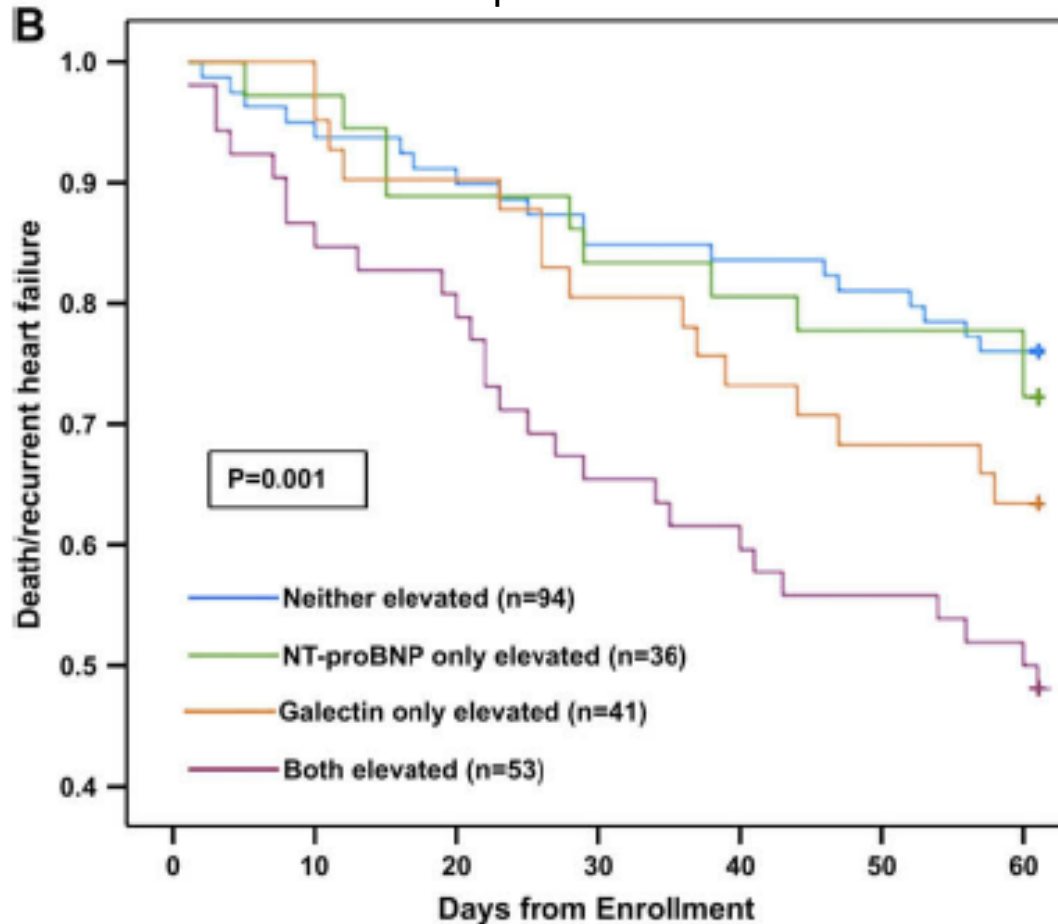


Objectives

- Present a selection of candidate markers based on data from canine and human studies
- Show pilot results of 9 different markers in dogs with spontaneous heart disease
- Show marker-based stratification of risk for first-time CHF in dogs with MVD

Remodeling: Galectin-3

Risk stratification when combined with NT-proBNP

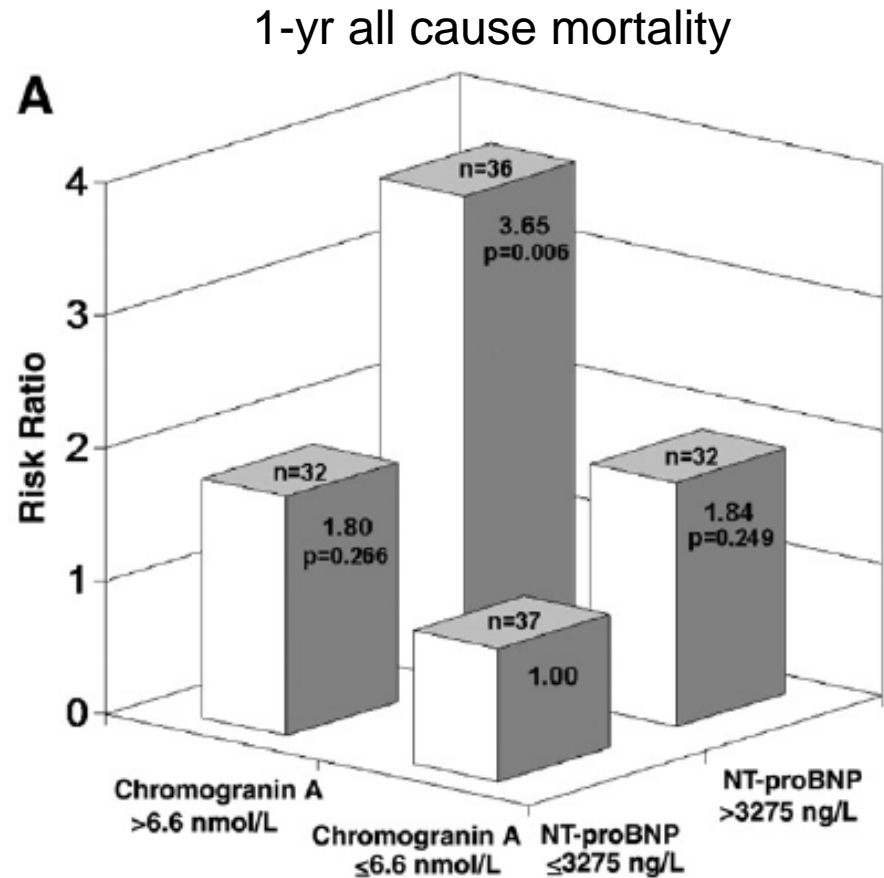


- B-galactoside-binding lectin produced by activated macrophages
- Myocardial fibroblast proliferation, fibrosis
- Enhances risk stratification when combined with BNP

van Kimmendade JACC 2006;48:1222

SNS Activation: Chromogranin-A

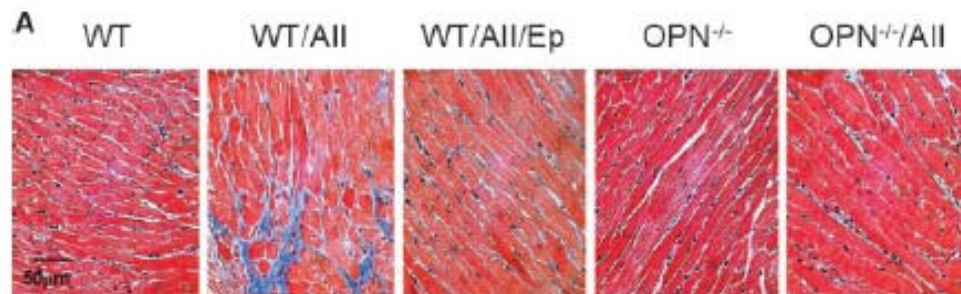
- Precursor of vasostatin, catestatin, inhibits catecholamine release
- Released from secretory granules in central and peripheral neurons and cholinergic nerve terminals
- Enhances risk stratification when combined with BNP



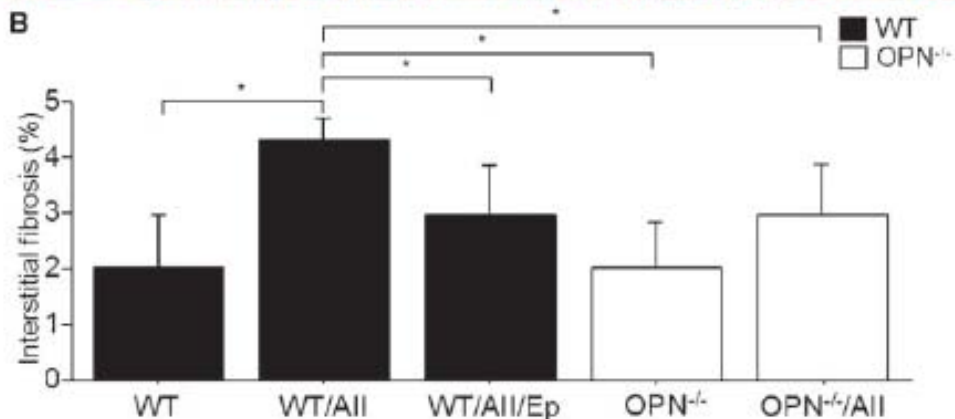
Dieplinger B et al. Clin Chim Acta 2009;400:95

ECM Remodeling: Osteopontin

- Cytokine Eta-1
- Remodeling, immunity, inflammation, recruitment of macrophages and T cells



OPN mediates AII-related interstitial fibrosis
Blocked by eplerenone



Matsui Y et al. Hypertension 2004;43:1195.

Cytokines: Soluble ST-2

- Soluble isoform of IL-1 receptor (sST2)
- Cardioprotective if membrane bound (ST2L)
ST2L \leftrightarrow sST2

- Enhances risk stratification when combined with BNP

Pascual-Figal et al. JACC 2009;54:2174

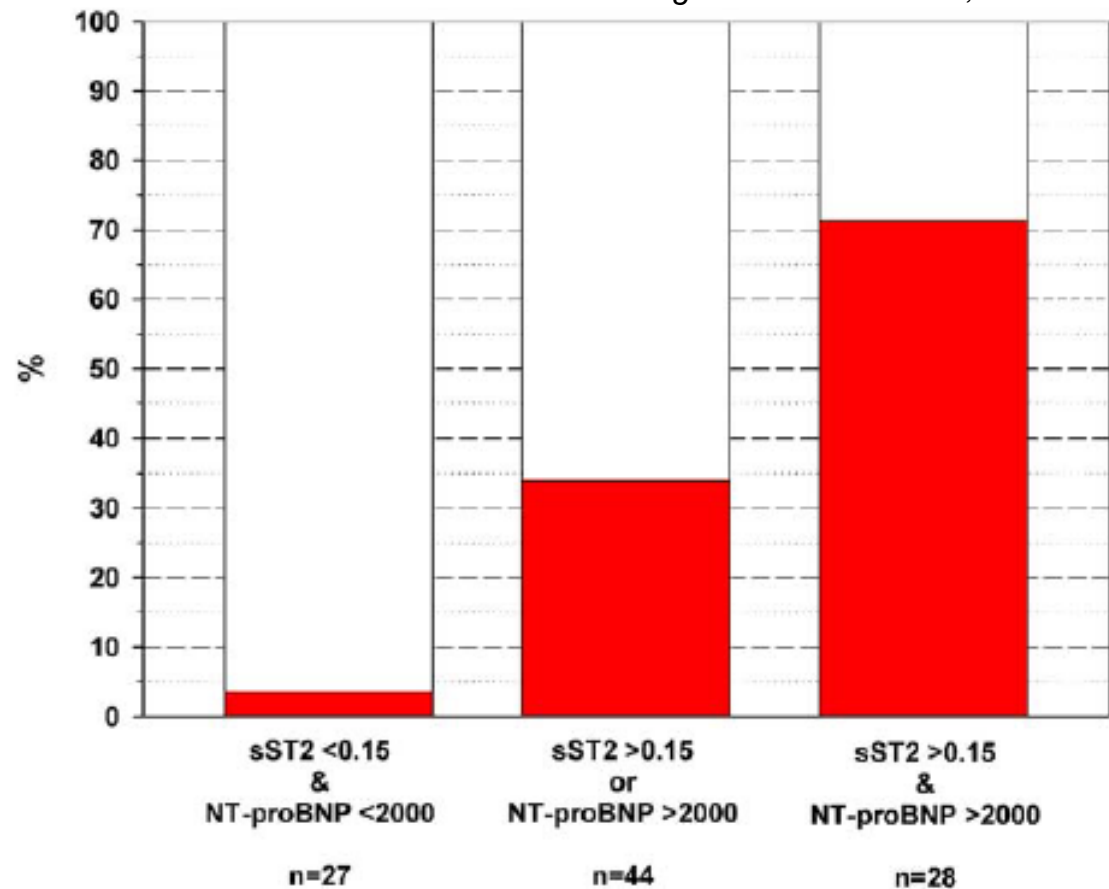


Figure 3

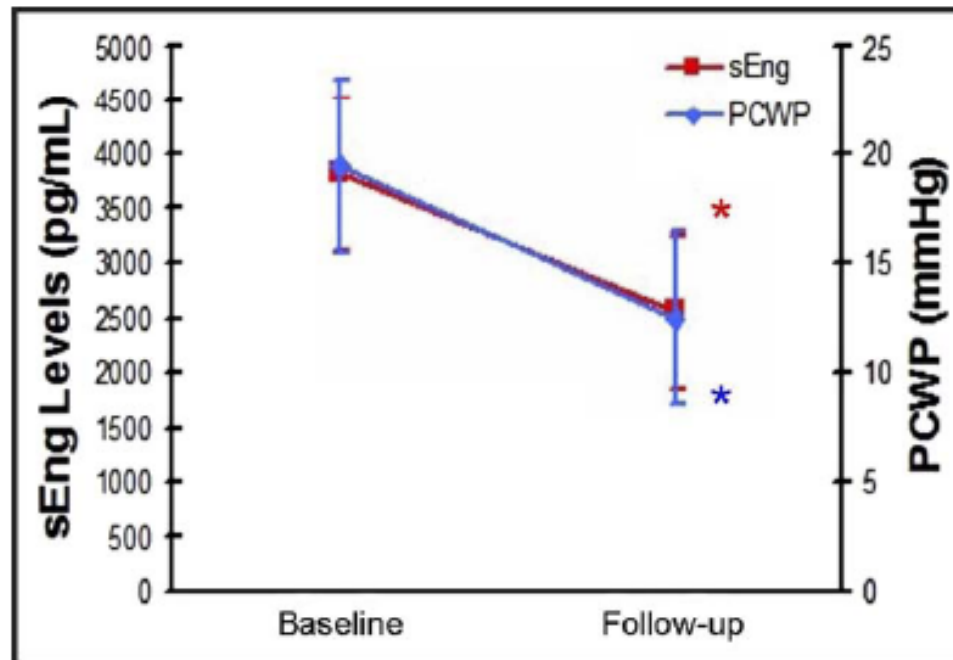
Events According to the Presence of None, Either, or Both sST2 >0.15 ng/ml and NT-proBNP >2,000 ng/l

Red bars = sudden cardiac death;
open bars = survivors. Abbreviations as in Figure 1.

Remodeling/Hemodynamics: Endoglin

- Type III TGF- β 1 co-receptor
- Present in myocardial fibroblasts

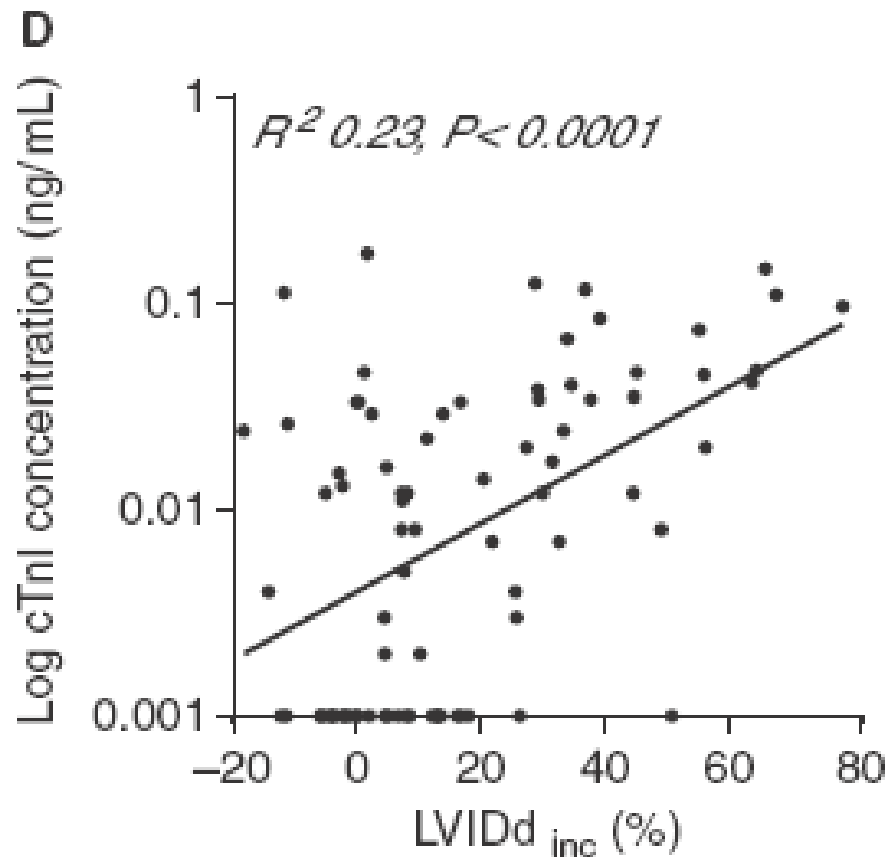
Tracks changes in PCWP after treatment



Kapur NK et al. Am J Cardiol 2010;106:1770

Cell Injury: Cardiac Troponin-I

- Necrosis, cell membrane damage

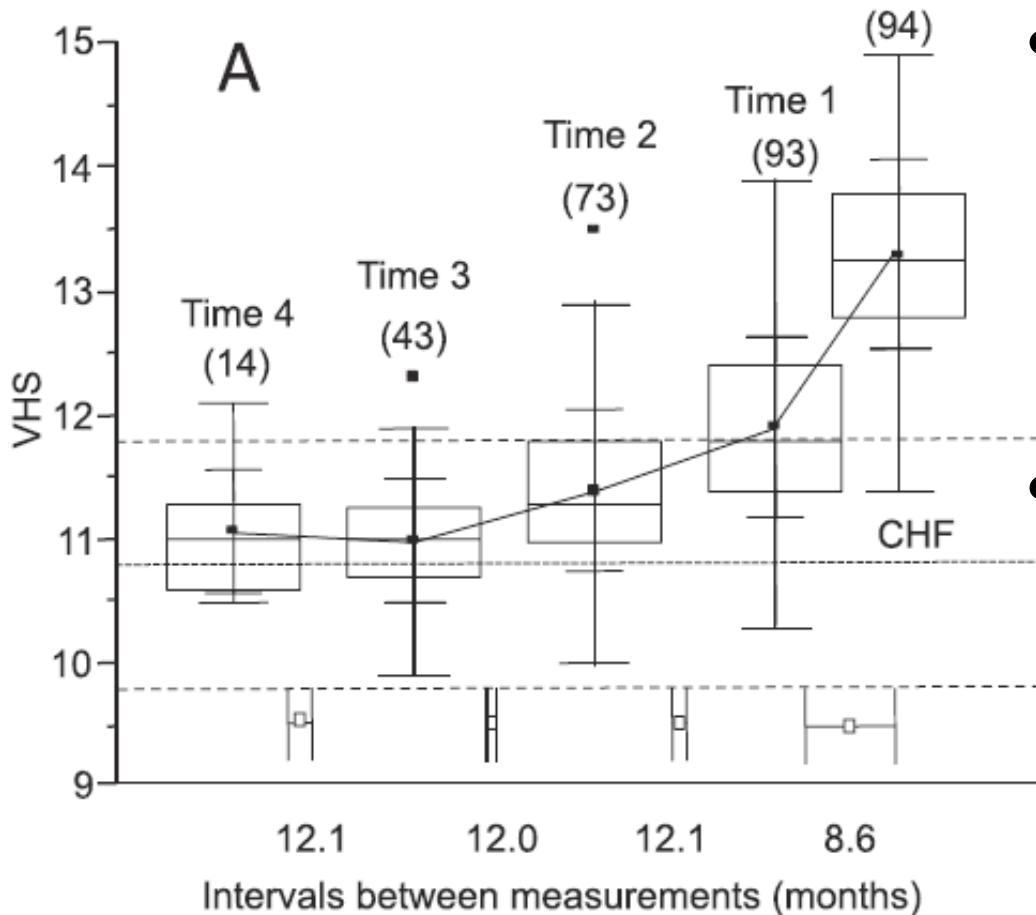


cTnI correlated to increases in LVIDd

Ljungvall I et al. JVIM 2010;24:153

Radiographic Risk Stratification

Lord P et al. *JVIM* 2011; epub before press

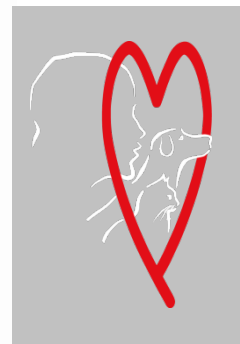


- VHS prior to CHF
 - If ≥ 12.3
 - 4.9x more likely to experience future CHF
- Change in VHS
 - If $\geq 0.08/\text{month}$
 - 15x more likely to experience CHF

Thank You!

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