Rochester Medical Center, Rochester, New York, USA, was to prospectively assess the effect of CRT-D on long-term survival.

All of the surviving MADIT-CRT trial patients (n=1691) participated in Phase 1 of the long-term follow-up until September 10, 2010. Of these, 854 were included in the Phase 2 registry and followed until September 30, 2013. The primary endpoint was all-cause mortality from MADIT-CRT enrollment until post-trial follow-up. Secondary endpoints included nonfatal HF events and a combined endpoint of a nonfatal HF event or death. The analyses were performed on an intention-to-treat basis and by LBBB status at enrollment.

Overall after 7 years of follow-up, 292 patients (16%) had died and 442 patients (24%) had experienced a nonfatal HF event. Among patients *with* LBBB, the all-cause mortality rate among was 18% in the CRT-D group compared with 29% in the ICD-only group (adjusted HR, 0.59; 95% CI, 0.43 to 0.80; p<0.001; Table 1). Patients in the CRT-D group also had a significantly lower probability of nonfatal HF events than the ICD-only group (adjusted HR, 0.38; 95% CI, 0.30 to 0.48; p<0.001) and the composite endpoint of HF or death (adjusted HR, 0.45; 95% CI, 0.37 to 0.56; p<0.001).

Among patients *without* LBBB, CRT-D provided no benefit (possibly harm) over ICD-only for all-cause mortality (adjusted HR, 1.57; 95% CI, 1.03 to 2.39; p=0.04), nonfatal HF events (adjusted HR, 1.13; 95% CI, 0.80 to 1.60; p=0.48), and the combined endpoint of HF or death (adjusted HR, 1.27; 95% CI, 0.94 to 1.73; p<0.001).

No subgroup with LBBB demonstrated worse survival when treated with CRT-D versus CRT alone. Patients with LBBB benefited from CRT-D regardless of QRS duration (QRS 130 to <150 msec or ≥150 msec), while those without LBBB did not benefit from CRT-D regardless of QRS duration.

Dr. Goldenberg concluded that early intervention with CRT-D compared with ICD-only is associated with a significant long-term survival benefit in patients with mild HF symptoms, left ventricular dysfunction, and LBBB. However, early CRT-D intervention does not benefit patients without LBBB and may be harmful.

Minimal MI Risk With Undetectable hs-cTnT and No ECG Ischemia in ED Patients With Chest Pain

Written by Toni Rizzo

Approximately 15 to 20 million patients visit hospital emergency departments (EDs) in Europe and the United States for chest pain each year [Thygesen K et al. *J Am Coll Cardiol* 2012; Nawar EW et al. *Adv Data* 2007; Goodacre S et al. *Heart* 2005]. However, only 10% to 20% of patients hospitalized for chest pain are diagnosed with myocardial infarction (MI) [Body R et al. *J Am Coll Cardiol* 2011; Than M et al. *Lancet* 2011; Pope JH et al. *N Engl J Med* 2000]. MI is characterized by cardiac troponin elevation in the presence of symptoms, ischemic electrocardiogram (ECG) changes or diagnostic imaging (eg, coronary angiography, echocardiogram) [Thygesen K et al. *J Am Coll Cardiol* 2012]. Traditionally several cardiac troponin measurements are required over hours in order to detect injury indicative of myocardial infarction. Recently developed high-sensitivity cardiac troponin assays, however, can detect increased troponin concentrations hours earlier than older generation assays potentially establishing a diagnosis with a single measurement.

To explore this hypothesis the investigators performed the Undetectable High Sensitivity Cardiac Troponin T Level in the Emergency Department and Risk of Myocardial Infarction study [Bandstein N et al. *J Am Coll Cardiol* 2014], which was presented by Nadia Bandstein, MD, Karolinska University Hospital, Stockholm, Sweden. The investigators hypothesized that all patients presenting with chest pain who have a first undetectable high-sensitivity cardiac troponin T (hs-cTnT), independent of symptom duration, and no signs of ischemia on ECG may be safely discharged from the ED.

The study population included all patients aged ≥25 years who visited the Karolinska University Hospital ED for chest pain and who had at least one hs-cTnT level analyzed between December 10, 2010, and December 31,

Table 1. Multivariate Analysis of Survival Benefit with CRT-D by LBBB Status

			LBBB		No LBBB		
Endpoint	No. of Events	No. of Patients	HR (95% CI)	p Value	HR (95% CI)	p Value	p Value for Interaction
All-cause mortality	267	1681	0.59 (0.43–0.80)	<0.001	1.57 (1.03–2.39)	0.04	<0.001
Nonfatal HF event	405	1681	0.38 (0.30–0.48)	<0.001	1.13 (0.80–1.60)	0.48	<0.001
Nonfatal HF event or death	530	1681	0.45 (0.37–0.56)	<0.001	1.27 (0.94–1.73)	0.12	<0.001

HF=heart failure; LBBB=left bundle branch block; results adjusted for age at enrollment, serum creatinine ≥1.4 mg/dL, smoking, diabetes, etiology of cardiomyopathy, left ventricular end systolic volume, QRS duration ≥150 msec, NYHA Class >II at 3 months prior to enrollment.

2012. The primary analysis group included all patients with an undetectable hs-cTnT (<5 ng/L) and no significant ST-elevation or depression on ECG. The primary endpoint was fatal or nonfatal MI within 30 days. Secondary endpoints included MI at 180 and 365 days and all-cause mortality at 30, 180, and 365 days. The hs-cTnT assay (Roche Diagnostics) has a detection limit of 2 ng/L, a 99th-percentile cutoff point of 14 ng/L, and a coefficient of variation of <10% at 13 ng/L.

A total of 330,821 patients visited the ED within the study period. Of these, 14,636 (4.4%) were aged ≥25 years with chest pain and had at least one hs-cTnT measured. The hs-cTnT was <5 ng/L (undetectable) in 61%, 5 to 14 ng/L in 21% (detectable but <99th percentile), and >14 ng/L (>99th percentile) in 18% of included patients. Patients in the group with undetectable hs-cTnT were younger, more likely to be female, and less likely to have diabetes, prior MI, stroke, or congestive heart failure (Table 1).

Table 1. Patient Characteristics

		hs-cTnT Level (ng/L)		
	All Patients	**<5**	**5 to 14**	**>14**
Number of patients	14,636	8907	3150	2579
Percentage of cohort	100	61	21	18
Age (years)	55	47	63	71
Females (%)	48	53	41	37
Diabetes (%)	10	5	14	21
Prior MI (%)	9	4	14	39
Prior stroke (%)	5	2	7	13
Prior CHF (%)	6	1	8	22

CHF=congestive heart failure; hs-cTnT=high-sensitivity cardiac troponin T; MI=myocardial infarction.

MI was defined according to recent guidelines [Thygesen K et al. *J Am Coll Cardiol* 2012]. Among the patients with undetectable hs-cTnT and no ischemia on the presenting ECG, there were 15 MIs within 30 days (negative predictive value [NPV], 99.8%; 95% CI, 99.7 to 99.9). In comparison, within 30 days there were 97 MIs in the group with hs-cTnT levels of 5 to 14 ng/L (NPV, 96.9%; 95% CI, 96.3 to 97.5) and 676 recurrent MIs in those with hs-cTnT levels >14 ng/L at the index presentation (NPV, 73.8%; 95% CI, 72.1 to 75.5; Table 2).

There were two deaths within 30 days among patients with undetectable hs-cTnT (NPV, 100%; 95% CI, 99.9 to 100). At 1 year, there were 38 deaths in this group, of which 32 were caused by cancer and two were due to cardiovascular disease.

The admission rate for patients with an undetectable first hs-cTnT was 21%. Most patients (89%) had a second hs-cTnT measured and of these, 90% remained undetectable. The authors acknowledge that there may have been patients discharged without a second hs-cTnT measured who would have had an elevated hs-cTnT consistent with an MI if it had been checked; however, they imply that the equivalent 1-year mortality rate in the admitted and discharged populations argues against significant, unrecognized MIs.

Table 2. Absolute Risk and Negative Predictive Value for MI at 30 and 365 Days After ED Discharge

	hs-cTnT Level (ng/L)		
	<5	**5 to 14**	**>14**
Number of patients	8883*	3150	2579
30 Days			
Number of events	15	97	676
Absolute risk % (95% CI)	0.17 (0.09–0.27)	3.08 (2.48–3.68)	26.2 (24.5–27.9)
NPV % (95% CI)	99.8 (99.7–99.9)	96.9 (96.3–97.5)	73.8 (72.1–75.5)
365 Days			
Number of events	54	134	753
Absolute risk % (95% CI)	0.61 (0.45–0.78)	4.25 (3.55–4.96)	29.2 (27.4–31.0)
NPV % (95% CI)	99.4 (99.2–99.5)	95.7 (95.0–96.5)	70.8 (69.0–72.6)

*24 patients with a first hs-cTnT level of <5 ng/L were excluded because they had ECG changes suggestive of MI.

ECG=electrocardiogram; ED=emergency department; hs-cTnT=high-sensitivity cardiac troponin T; MI=myocardial infarction; NPV=negative predictive value.

Overall, the results of this study demonstrated that a first undetectable hs-cTnT level (<5 ng/L) and no signs of ischemia on ECG in patients presenting to the ED with chest pain ruled out MI with a high degree of accuracy, regardless of duration of symptoms, timing of hs-cTnT measurement, prior disease, age, sex, or other risk factors for MI. Dr. Bandstein concluded that use of a single hs-cTnT may prevent unnecessary hospital admissions and shorten ED stays leading to a reduction in ED overcrowding.

Perioperative Aspirin Does Not Reduce Cardiovascular Events in Noncardiac Surgery (POISE-2)

Written by **Brian Hoyle**

Acetylsalicylic acid (aspirin) is ineffective in reducing perioperative heart attacks and death in noncardiac surgery, but increases the risk of bleeding. Results from the Perioperative Ischemic Evaluation-2 trial [POISE-2; Devereaux PJ et al. *N Engl J Med* 2014] were presented by Philip J. Devereaux, MD, PhD, McMaster University, Hamilton, Ontario, Canada.

Patients aged ≥45 years undergoing noncardiac surgery who were at risk of vascular complications were eligible for the Phase 3, randomized, controlled, POISE-2 trial. Exclusion criteria were recent stent implantation (bare-metal stent within 6 weeks or drug-eluting stent within 1 year) and use of aspirin within 72 hours prior to surgery. The