3 years). Support included telephone coaching and home visits, which were arranged based on the patients' clinical stability and their risk profile.

The study identified 5100 high-risk people with cardiovascular disease who had been discharged. Of these, 1059 were eligible for inclusion and 624 were randomized to usual post-discharge care (n=314) or nurse-led home- and clinic-based care (n=310). In total, 611 subjects (standard group, n=310; nurse-led group, n=301) were followed up with for a mean of 1561±240 and 1541±257 days, respectively.

The mean age of the cohort was 66±11 years, and the majority (71%) was male. Of the cohort, 62% were hypertensive; 70% were abdominally obese; 70% had coronary artery disease; 12.4% had asymptomatic left ventricular systolic dysfunction, 56% had asymptomatic HF with preserved ejection fraction, 13% had both cardiac conditions, and 18% had normal function; 83% were receiving antiplatelet therapy, 73% were receiving statin therapy, 71% were receiving angiotensin-converting-enzyme inhibitor or angiotensin receptor blocker, and 52% were receiving β-blockers.

There were 2507 hospital episodes representing 9847 days. Excluding same-day and emergency procedures, there were 827 all-cause admissions and 7824 days of hospitalization (median, 4.0 days; interquartile range, 3.0 to 9.0 days). Cardiovascular-related events included heart disease (n=455), musculoskeletal disease (n=385, of which 178 patients had chest pain), other cardiovascular disease (n=72), peripheral arterial disease (n=64), stroke or transient ischemic attack (n=40), and diabetes (n=22).

At the 3-year time point, there was no significant difference between the nurse-led care group and the usual care group relative to de novo hospitalization for heart failure (p=0.53) or death from any cause (p=0.797; primary end point comparison, p=0.493). More NIL-CHF cases showed reversal and recovery with respect to baseline left ventricular hypertrophy versus normal (39% vs 25%; p=0.047), initial left ventricular systolic dysfunction or HF with preserved ejection fraction versus normal (23% vs 16%; p=0.063), or any cardiac condition versus normal (36% vs 25%; p=0.011; OR, 1.35; 95% CI, 1.04 to 1.76). The nurse-led care produced improvements in many hospitalization-related parameters; however, only the number of emergency hospitalizations reached statistical significance (Table 1).

Study limitations included the single-center design (albeit, an expert tertiary care center) and an open-label design. Nevertheless, the data show the promise of the nurse-led approach in the treatment of patients with CHF and support the further investigation of this strategy.

Table 1. Hospital Admissions and Stay

	Days of Hospitalization/ Patient		
	Usual care	Nurse-led care	p Value
All episodes	1324	1169	0.096
All hospitalizations	733	602	0.087
Emergency hospitalizations	515	302	0.023
Cardiovascular-related hospitalizations	253	197	0.052

Novel Biomarkers Aid in Diagnosis of PPCM

Written by Phil Vinall

Peripartum cardiomyopathy (PPCM) is a potentially life-threatening disease that is manifest as heart failure (HF) with left ventricular systolic dysfunction that occurs toward the end of pregnancy or in the months following delivery. It is associated with significant mortality and morbidity. Although its etiology has recently been the subject of much study, PPCM remains a diagnosis of exclusion. Karen Sliwa, MD, PhD, Hatter Institute for Cardiovascular Research in Africa, University of Cape Town, South Africa, discussed 2 potential biomarkers for PPCM that may improve diagnosis and thus treatment outcomes.

PPCM occurs more frequently in women with preeclampsia and/or multiple gestation [Patten IS et al. *Nature* 2012]. Although the diagnosis of preeclampsia has improved with the recent discovery of the imbalance between substances promoting and antagonizing angiogenesis, there remains a need to identify biomarkers for PPCM, as it can be difficult to differentiate symptomatic HF from physiologic symptoms of pregnancy such as dyspnea, edema, and palpitations.

Relaxin-2 is a naturally occurring peptide that is important to the hemodynamic and renal adjustments required during pregnancy. Myocardial expression of relaxin-2 is upregulated in congestive HF [Dschietzig T et al. *FASEB J* 2001]. Serelaxin is a relaxin-2 analogue that has recently been shown to improve clinical symptoms, organ function, and survival when administered intravenously to hospitalized patients admitted with nonperipartum acute HF [Teerlink JR et al. *Lancet* 2013].

The objective of the study presented by Professor Sliwa was to assess whether plasma angiogenesis and

relaxin-2 are altered in women with PPCM. The study population included 160 peripartum women (77 with PPCM, 75 healthy breastfeeding mothers, and 8 with stable non-PPCM cardiac disease) and 94 nonperipartum participants (29 healthy women and 65 men and women with acute HF; Table 1).

Cardiovascular (N-terminal pro–brain natriuretic peptide, copeptin, midregional proadrenomedullin, and soluble ST2) and angiogenic (placenta-inhibiting growth factor, vascular endothelial growth factor, soluble fms-like tyrosine kinase 1, relaxin-2, etc) biomarkers were measured.

Compared with the other groups, subjects with PPCM had significantly higher levels of N-terminal pro–brain natriuretic peptide and lower levels of plasma relaxin-2 (Table 2). Plasma relaxin-2 was much lower among women with PPCM compared with healthy breastfeeding mothers (Table 2) and undetectable in 50% of patients with PPCM compared with 4% of healthy breastfeeding mothers.

The ratio of soluble fms-like tyrosine kinase 1 to placenta-inhibiting growth factor was lower among women with PPCM (1.3; range, 0.9–2.8) compared with the group of healthy breastfeeding mothers (52.8; range, 20.6–116.2). Receiver operating characteristic curve analysis confirmed that the lowest level of plasma relaxin-2 or soluble fms-like tyrosine kinase 1/placenta-inhibiting growth factor ratio and the highest level of plasma N-terminal pro–brain natriuretic peptide were all associated with PPCM, with areas under the curve of about 0.95. Combining these biomarkers for the diagnosis of PPCM in peripartum women had specificity of 0.75, sensitivity of 0.74, positive predictive value of 0.92, and negative predictive value of 0.82.

These results suggest that angiogenic and relaxin-2 pathways are altered in patients with PPCM, providing a novel biomarker strategy to aid in diagnosis. These findings also raise the question of whether women with PPCM may benefit from adjunctive therapy with serelaxin in addition to standard care.

Table 1. Clinical Characteristics

	Peripartum			Nonperipartum	
Characteristic	**PPCM (n=77)**	**Healthy (n=75)**	**Stable Non-PPCM CVD (n=8)**	**Healthy (n=29)**	**AHF (n=65)[a]**
Age, years	29	30	25	28	54
LVEF, percent	30	60	—	60	30
Parity, number	2	1	—	3	—
SBP, mm Hg	112	117	119	120	128
DBP, mm Hg	72	69	68	70	77

AHF=acute heart failure; CVD=cardiovascular disease; DBP=diastolic blood pressure; LVEF=left ventricular ejection fraction; PPCM=peripartum cardiomyopathy; SBP=systolic blood pressure.

[a]45% women.

Table 2. Biomarker Comparison[a]

	Peripartum			Nonperipartum
Biomarker	**PPCM (n=77)**	**Healthy (n=75)**	**Stable Non-PPCM CVD (n=8)**	**AHF (n=65)[b]**
NT-proBNP, pmol/L	4071 (136–7379)	94 (28–168)	2284 (1827–2845)	3156 (706–6175)
Relaxin-2, pg/mL	0.4 (0–4.5)	957.2 (250.5–1984.4)	371 (341.2–471.9)	0 (0–1.1)

AHF=acute heart failure; CVD=cardiovascular disease; NT-proBNP=N-terminal pro–brain natriuretic peptide; PPCM=peripartum cardiomyopathy.

[a]Data are expressed as median (interquartile range).

[b]45% women.