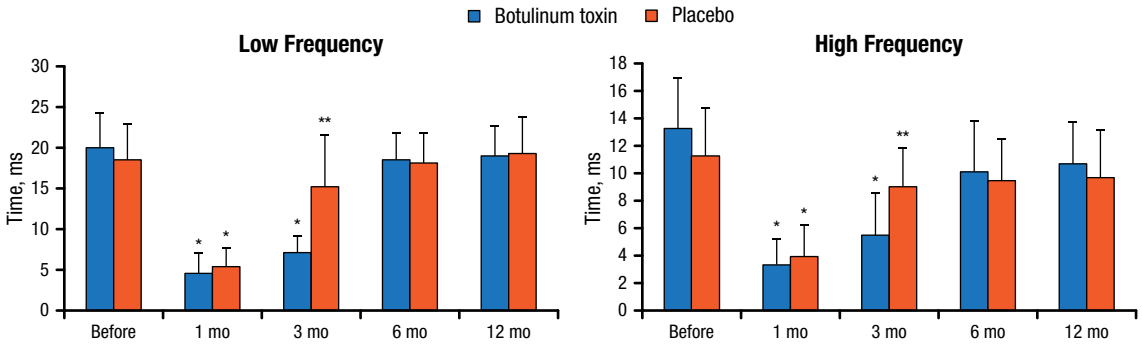
Figure 2. Frequency of Heart Rate Variability



*P<.05 vs baseline; **P<.05 between groups.

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1 month after surgery (P<.05 vs baseline). With botulinum toxin, HRV was significantly lower at 3 months vs baseline (P<.05) and then recovered to near-baseline levels, while HRV recovered to near-baseline levels at 3 months in the placebo group and was maintained. The frequency of HRV in the patients with low and with high frequency was reduced early after surgery with botulinum toxin and placebo, with a similar pattern of rebounding to baseline levels (Figure 2).

According to Dr Steinberg, the alterations in HRV with botulinum toxin suggest there were reductions in parasympathetic and sympathetic activity, but the changes dissipated between 3 and 6 months as expected. Among the limitations of this study are the small number of patients, the lack of data on AF burden prior to surgery, no objective testing to confirm the denervation effect, and no confirmation of functional atrial remodeling or its mechanisms. Although these data suggest botulinum toxin may be a neuromodulator, large-scale trials are required to evaluate its possible value to reduce postoperative AF and in other clinical settings.

Remote Monitoring of Cardiac Rhythm Management Reduced Hospitalization and Costs

Written by Mary Mosley

A retrospective, observational cohort study showed that remote monitoring (RM) added to clinic visits reduced hospitalization, hospital length of stay (LOS), and healthcare costs in patients implanted with any device for cardiac rhythm management (CRM), according to Jonathan P. Piccini, MD, Duke University Medical Center, Durham, North Carolina, USA.

A total of 92 566 patients (mean age, 72 years; 63% men) who had a CRM device implanted between April 1, 2008, and March 31, 2013, were included in the study; of these, 34 259 were in the RM plus clinic visit arm, and 58 307 were in the clinic visit only arm. Patients without any clinic follow-up or whose first clinic or RM follow-up was >4 months after implant were excluded. Each clinic determined the type of follow-up for each patient. The data source was a commercial and Medicare supplemental health insurance database. All outcomes were adjusted using a boosted logistic regression propensity score that included 22 pre-implant comorbidities and age, sex, and geographic location.

More patients who received an implantable cardioverter defibrillator (ICD; 49%) or cardiac resynchronization therapy defibrillator (CRT-D; 51%) were in the RM arm than the pacemaker (PM; 29%) or CRT pacemaker (CRT-P; 27%) groups. The Charlson Comorbidity Index was 3.1 and 3.2 in the RM and no-RM arms, indicating the patients had a similar degree of comorbidity. In the RM arm vs no-RM arm, more patients had a history of heart failure (49.9% vs 44.9%) and ventricular arrhythmia (24.3% vs 15.7%), and fewer patients had atrial fibrillation (42.7% vs 46.7%) and prior cerebrovascular disease (28.1% vs 33.2%). The first clinic visit was 64 and 63 days after the implant in the RM and no-RM arms. The follow-up interval was ≤4 months in >75% of patients.

The primary outcome of all-cause hospitalization for all device types was significantly lower with RM vs no RM (HR, 0.82; 95% CI, 0.80 to 0.84; P<.001). The mean LOS was 5.3 days with RM and 8.1 days with no RM (P<.001). All-cause hospitalization was lower with all device types in the RM vs no-RM arm, but Dr Piccini noted that the magnitude of this difference was greater with ICD (HR, 0.74; 95% CI, 0.71 to 0.77; P<.001) and CRT-D (HR, 0.72;

95% CI, 0.67 to 0.77; $P<.001$), compared with a pacemaker (HR, 0.83; 95% CI, 0.81 to 0.86; $P<.001$) and a CRT pacemaker (HR, 0.84; 95% CI, 0.69 to 1.03; $P=.089$).

Hospitalization costs were significantly lower ($12 423 vs $8720; $P<.001$) with RM vs no RM for all devices (by 30% per patient-year) and for each type of device (by 31% to 45% per patient-year). The greatest difference in hospitalization cost was observed for CRT-D, where hospitalization cost per patient-year was nearly $10 000 (45%) lower with RM vs no RM, followed by a nearly $7000 (43%) reduction for ICD with RM vs no RM.

RM vs no RM was associated with reduced hospitalization for heart failure in patients with a history of heart failure (HR, 0.76; 95% CI, 0.71 to 0.81; $P<.001$) and for stroke in patients with atrial fibrillation (HR, 0.78; 95% CI, 0.67 to 0.91; $P<.001$). The shorter mean LOS for stroke hospitalization (2.9 vs 3.3 days with RM and no RM) translated into a 44% reduction in mean costs per patient-year. Rehospitalization for heart failure was lower with RM at 30, 90, and 180 days for all devices and for each type of device; there was a 7% absolute difference in patients with a CRT in the RM vs no-RM arms.

The limitations of being a retrospective analysis, which can show correlation but not causality, and evaluating only hospital costs are balanced against the strengths of being a large nationwide cohort that was adjusted for 22 clinical conditions and the inclusion of all device manufacturers.

The investigators estimated that based on the study results, for every 100 000 patient-years, RM would be associated with 9810 fewer hospitalizations, 119 000 fewer hospital days, and $370 270 000 lower hospital payments. Confirmation in a broader trial is needed.

BAT Improves Clinical Status Preferentially in Patients Not Undergoing CRT

Written by Wayne Kuznar

Baroreflex activation therapy (BAT) improved quality of life and exercise capacity in patients with heart failure and reduced ejection fraction, with a more pronounced impact in patients who had not undergone cardiac resynchronization therapy (CRT). Data from a randomized, phase 2 trial of BAT were presented by Michael Zile, MD, Medical University of South Carolina, Charleston, South Carolina, USA.

BAT acts through a central integrated mechanism to both decrease sympathetic tone and increase parasympathetic tone, rebalancing the autonomic imbalance present in patients with heart failure, explained Dr Zile. The procedure involves surgically implanting a 2 mm lead at the coronary sinus and connecting it to a pulse generator, which is placed in the subcutaneous space. Initial studies demonstrated a positive effect of carotid baroreceptor stimulation on ventricular remodeling, vasodilation, and renal function [Abraham WT et al. *JACC Heart Fail.* 2015]. Whether the positive response to BAT is uniform across all patients, particularly those who receive guideline-directed medical therapy, is not known.

In the prospective multinational trial, 140 patients with NYHA functional class III heart failure were randomized 1:1 to optimal medical and device therapy alone (control group) or BAT plus optimal medical and device therapy. To be eligible, patients had to have a left ventricular ejection fraction ≤35% and a 6-minute hall walk distance of 150 to 400 m. They had to be on stable medical therapy for at least 4 weeks prior to baseline assessment and, if indicated, device therapy for at least 6 months. Of the 140 patients, 45 had undergone CRT.

The primary safety end point was system- or procedure-related major adverse neurological or cardiovascular events at 6 months; the event-free rates were 100% in the CRT group and 96% in the no-CRT group, attesting to the safety of BAT.

In patients without CRT, the Minnesota Living with Heart Failure Quality of Life score improved by 21.6 points from baseline to 6 months in the BAT group, compared with a 3.5-point decrement in the control group ($P<.001$). In patients with CRT, there was no significant difference in this score between the BAT group and controls ($P=.23$). The difference in response to BAT between the CRT and no-CRT groups was statistically significant (P-interaction = .04).

In patients without CRT, 6-minute walk distance improved by 85.5 m in the BAT group vs a 3.6-m improvement in the controls ($P=.003$). No such difference between the BAT groups and controls emerged in the CRT patients ($P=.38$). Again, the difference in response to BAT on this end point between the CRT and no-CRT groups was significant (P-interaction = .01).

Left ventricular ejection fraction, an exploratory end point, improved significantly from baseline to 6 months in the no-CRT patients who received BAT vs controls ($P<.03$), with no such difference in the CRT group ($P=.71$). The difference in response to BAT between the CRT and no-CRT groups was statistically significant (P-interaction = .02).

The observations need to be confirmed in an adequately powered, prospective, randomized clinical outcomes trial, which is scheduled to begin in September 2015, said Dr Zile.