Late Breaking Science: Linking Genes to Function in the Heart and Vasculature

Multicenter Randomized Trial Comparing Amiodarone to Implantable Defibrillator in Patients With Nonischemic Cardiomyopathy and Asymptomatic Nonsustained Ventricular Tachycardia: AMIOVIRT Trial

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Introduction. Patients (pts) with nonischemic dilated cardiomyopathy (NIDCM) and asymptomatic (asx) nonsustained ventricular tachycardia (NSVT) are at high risk for sudden cardiac death. Amiodarone or an implantable defibrillator (ICD) may reduce mortality in this patient group. Therefore, the purpose of this multicenter, randomized trial was to compare the total mortality rate associated with amiodarone to ICD therapy in patients with NIDCM and asx NSVT. **Methods.** Pts with NIDCM, left ventricular ejection fraction < 0.35, and asx NSVT were eligible for study participation. 102 pts were randomized to receive either amiodarone or ICD therapy. 75 pts were followed in a study registry. Because there were no identifiable differences in clinical characteristics between randomized and registry pts, all pts were grouped according to initial therapy, irrespective of whether they were randomized or were followed in the study registry. The pts were 59 ± 12 yrs, 29% were women, the left ventricular ejection fraction (LVEF) was 0.22 ± 0.08, 85% had either NYHA Class II or III heart failure, and the mean follow-up was 20.1 ± 12.6 months. The primary study endpoint was total mortality. The study was designed to achieve 80% power to identify a reduction in total mortality from 20% to 10% (219 patients in each group). Stopping rules included a mortality difference associated with a $p < 0.025$, or $p \geq 0.05$ (90% power) when the data were extrapolated to 600 patients. **Results.** The stopping rule for futility was reached, and the study was stopped early. The percent of patients surviving at 2 years (88% vs 89%) and 4 years (85% vs 79%) in the amiodarone and ICD treatment groups, respectively, were similar ($p=0.6$). **Conclusions**. In pts with NIDCM, LVEF <0.35, and asx NSVT the total mortality rate at 4 years is the same in pts treated with Amiodarone or an ICD.

Results of the VMAC Trial: Vasodilation in the Management of Acute Congestive Heart Failure

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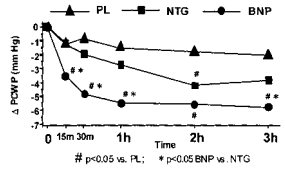
Objective: To compare the efficacy and safety of nesiritide (B-type or brain natriuretic peptide [BNP]), IV nitroglycerin (NTG), and placebo (PL), when added to standard care (may have included IV diuretics, dobutamine, dopamine, and all chronic cardiac therapy). **Methods:** This multicenter, randomized, placebo- and active-controlled trial treated 489 hospitalized patients with dyspnea at rest due to acutely decompensated CHF. Patients with acute coronary syndromes, diastolic dysfunction, arrhythmias, or renal insufficiency were not excluded. Randomization was stratified by use of a right heart catheter ($n=246$) or not ($n=243$). Patients were randomized to PL ($n=142$), NTG ($n=143$), BNP fixed-dose ($n=142$), or BNP adjustable-dose ($n=62$; catheterized patients only). BNP was administered as a 2 μg/kg bolus, followed by a fixed-dose infusion of 0.01 μg/kg/min for 3 hours. After 3 hours, adjustable-dose BNP patients could undergo dose increases to a maximum of 0.03 μg/kg/min, and PL patients crossed over to NTG or BNP fixed-dose. NTG dose was determined by the Investigator and was to be titrated to effect. Primary endpoints were the 3 hour pulmonary capillary wedge pressure (PCWP) and subject's dyspnea evaluation (using a 7-point ordinal scale), comparing BNP to PL. **Results:** BNP significantly reduced PCWP and all PA pressures, compared to NTG and PL, by 15 minutes and through the 3 hour period. At 3 hours, dyspnea was improved by BNP compared to PL ($p=0.034$); the change in dyspnea with NTG was not statistically significant ($p=0.191$).



By 24 hours, symptomatic hypotension occurred in only 4% of BNP patients and 5% of NTG patients, whereas more headache occurred with NTG (20% vs. 8%, $p<0.001$). Fewer adverse events overall occurred in patients treated with BNP than with NTG ($p<0.001$). **Conclusions:** When added to standard care, fixed-dose administration of nesiritide produced a more rapid and greater improvement in hemodynamics than NTG titration or standard care alone (PL). Nesiritide, but not NTG, was associated with significant improvements in dyspnea, compared to standard care alone (PL). Compared to NTG, nesiritide was better tolerated by these acutely ill CHF patients. These data from the VMAC Trial suggest an important role for nesiritide in the treatment of acutely decompensated CHF, with or without invasive monitoring and without the need for dose titration.

The Atlantic C-PORT Trial: A Community-Hospital–Based, Prospective, Randomized Trial Comparing Thrombolytic Therapy With Primary Angioplasty for Treatment of Acute Myocardial Infarction

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453 patients from 11 community hospitals without on-site cardiac surgery were randomly assigned to receive either thrombolytic therapy (TT) or primary percutaneous coronary intervention (PPCI) for treatment of acute myocardial infarction (AMI). The primary outcome was the incidence of the composite adverse event (CAE) endpoint of death, recurrent myocardial infarction (MI) or stroke 6 months after the index MI. The time between emergency room (ER) arrival and first balloon inflation was 107 ± 34 minutes; and the ER to thrombolytic administration time was 53 ± 35 minutes. In an intention-to-treat analysis, at 6 weeks, patients treated with PPCI had a 42% reduction in the incidence of CAE compared with TT (15.4 % vs 8.8 %, $p=0.03$). At 6 months, the CAE was lower with PPCI than after TT by 31 % (15.4 % vs 10.6%, $P=0.13$). In a treatment-received analysis, patients treated with PPCI had significantly improved outcomes at 6 weeks and 6 months compared with patients treated with TT (15.7% vs. 8.1% at 6 wk; 16.9% vs. 10.4% at 6 months, both $p<0.05$). Women benefited from PPCI with nearly 50% reductions in the CAE outcome at 6 weeks and 6 months compared with TT (27.3% vs 10.7% at 6 wks, $p<0.02$; 27.3% vs 13.8 % at 6 m, $p=0.058$). Patients over age 65 also benefited from PPCI compared with TT with 40% reductions in the CAE rate (25.9% vs 13.0% at 6 wk, $p<0.02$; 27.8% vs 15.6%, $p=0.01$). We also noted that outcomes at low volume centers performing fewer than 1 PPCI per month were no better with PPCI than with TT; while outcomes at relatively high volume centers performing an average of 2 PPCI's per month had clearly improved outcomes with PPCI over TT. We conclude that PPCI is at least as good, and in some circumstances is superior to TT for treatment of AMI in community hospitals without on-site cardiac surgery. Access to PPCI can be extended to some, but not all hospitals, without on-site cardiac surgery if the center is committed to the necessary program development and monitoring process, performs a high volume and has PPCI availability 24/7.

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