Cardiovascular Volume Reserve in Patients with Heart Failure and Reduced Ejection Fraction

Nijst, Petra; Martens, Pieter; Verbrugge, Frederik H.; Dupont, Matthias; Tang, W. H. Wilson; Mullens, Wilfried

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The total number 12-week hospital days was 60 vs. 121 days, with an average number of hospital days of 5.45 [3.88] vs. 11.00 [6.74] (p=0.028) among those hospitalized in the groups with an increase vs. no increase in salt taste sensitivity, respectively (Figure 1). KCCQ-CSS at 12-weeks trended higher in the group with an increase in salt taste sensitivity: (64.24 [23.06] vs. 56.25 [24.80], p=0.195). **Conclusions**: Changes in salt taste sensitivity occurred in some but not all subjects in a 12-week period following hospitalization for HF. Subjects with increased salt taste sensitivity over this time period were rehospitalized for fewer days. Improved salt taste sensitivity may represent a novel prognostic factor in post-discharge patients with HF.

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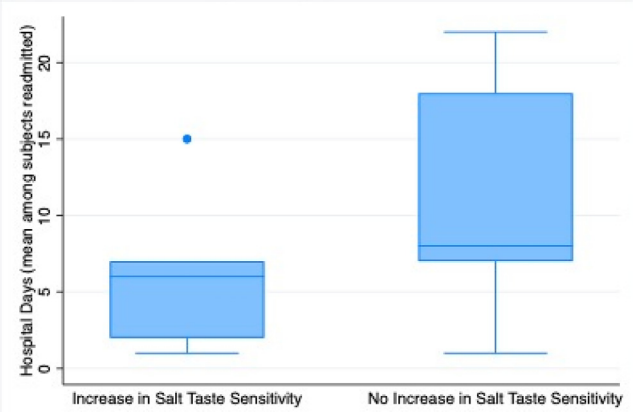

Figure 1. Hospital readmissions by change in salt taste sensitivity over 12-week post-discharge period.

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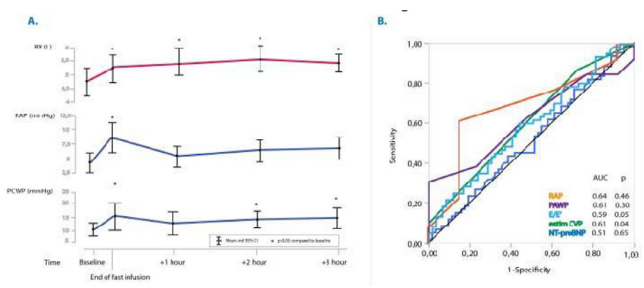
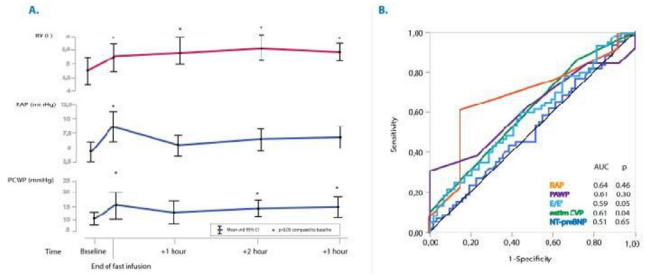
Petra Nijst[1], Pieter Martens[1], Frederik H. Verbrugge[1], Matthias Dupont[1], W.H. Wilson Tang[2], Wilfried Mullens[1]; [1]Ziekenhuis Oost Limburg/UHasselt, Genk, Belgium; [2]Cleveland Clinic Foundation, Cleveland, OH

Background: Volume overload is a hallmark feature of HF. The pressure-based assessment of volume status has gained popularity in HF with the use of implantable devices, yet its accuracy to detect early intravascular volume expansion is unclear. **Objectives**: To study the relationship between intravascular volume and intra-cardiac filling pressures in the setting of stable HFrEF. **Methods**: 40 euvolemic HFrEF patients (10 subjects with a PAC), underwent intravascular volume expansion with 1 liter hydroxyl-ethyl-starch over 3 hours with coinciding intravascular volume measurements (technetium (^{99}Tc)-labeled red blood cell technique). **Results**: Intravascular blood volume increased from 5.0±1.0 L to 5.7±1.0 L (p<0.0001). No change in clinical status or NT-proBNP levels (670[225;1383] ng/L vs 615[217;521] ng/L; p=0.86) was observed. No significant changes in echocardiographic indices of cardiac filling pressures were present (Fig 1). Invasively measured RAP and PAWP increased significantly immediately after start of infusion (4±2 mmHg to 8±4 mmHg; p=0.01 and 10±3 mmHg to 15±6 mmHg; p=0.01), decreased afterwards and remained stable for 3 hours (6±2 mmHg and 14±4 mmHg), indicative of cardiovascular volume reserve (Fig 2A). The accuracy of cardiac filling pressure (estimates) to predict intravascular volume expansion was very low (all AUC <0.65; fig 2B). **Conclusion**: Euvolemic HFrEF patients can tolerate an intravascular volume expansion of 0.7L without signs and symptoms of HF. Due to this cardiovascular volume reserve, estimates of cardiac filling pressures might be of limited value to reliable assess intravascular volume changes.





Baseline characteristics

variable	total cohort of HFrEF subjects	HFrEFsubjects with PAC
n	40	10
age (years)	65+/-12	68+/-11
Male gender	88%	80%
ischemic heart disease	83%	80%
BMI (kg/m2)	28+/-4	30+/-4
LVEF (%)	36+/-4	37+/-4
echocardiograpic estimated CVP (mmHg)	7+/-2	8+/-0
E/E'	12+/-5	12+/-5
serum creatinine (mg/dl)	1.4+/-0.6	1.6+/-0.7
NTproBNP (ng/L)	670(225;1383)	1135(521;1527)
PAP systolic (mmHg)		33+/-11
PAP mean (mmHg)		21+/-7
RAP (mmHg)		4+/-2
PAWP (mmHg)		10+/-3
CI (L/min/m2)		2.1+/-0.4
intravascular blood volume (L)	5.0+/-1.0	4.7+/-0.7

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Predictive Prognostic Value of Ventilatory Inefficiency across the Spectrum of Heart Failure

Jingyi Gong[1], Renata R.T. Castro[1], Jesse P. Caron[1], Camden P. Bay[1], Jon Hainer[1], Alexander R. Opotowsky[2], Mandeep R. Mehra[1], Anju Nohria[1], Bradley A. Maron[1], Marcelo F. Di Carli[1], John D. Groarke[1]; [1]Brigham and Women's Hospital, Boston, MA; [2]Boston Children's Hospital, Boston, MA

Background: Minute ventilation-carbon dioxide production relationship (VE/VCO2 slope), as assessed by cardiopulmonary exercise testing (CPET), strongly predicts outcomes in heart failure (HF). High VE/VCO2 slope can indicate ventilatory inefficiency. A single VE/VCO2 slope threshold defining abnormal of ≥ 34 to 36 is used clinically across HF categories; however, this threshold has been validated largely in patients with reduced left ventricular ejection fraction (LVEF). **Objectives**: To examine the associations between VE/VCO2 slope categories and a composite outcome of all-cause mortality and HF hospitalization across the spectrum of HF patients defined by LVEF. **Methods**: Single-center retrospective cohort study of 1347 patients with heart failure (60.5% male, age 58.0±14.6 years, LVEF 42 ± 17%) clinically referred for CPET between 2010 and 2016. LVEF was obtained from echocardiogram (n=1309) or cardiac MRI (n=38). All-cause mortality was determined using Partners Research Patient Data Registry, which is linked to National Death Index. HF hospitalization data were adjudicated by review of electronic medical record. Patients with HF were categorized based on LVEF into heart failure with reduced (HFrEF, LVEF <40%), mid-range (HFmrEF, 40% ≤ LVEF<50%) and preserved (HFpEF, LVEF ≥50%) ejection fraction. VE/VCO2 slope was divided into four ventilatory categories (VC) - VC-I: VE/VCO2≤29, VC-II: 29<VE/VCO2<36, VC-III: 36≤VE/VCO2<45, VC-IV: VE/VCO2 ≥45. **Results**: At two-year follow-up post CPET, there were 197 composite events (64 deaths and 133 HF hospitalizations). Across the entire cohort, increases in VC category were associated with increasing risk of two-year composite outcome in unadjusted and adjusted models. Compared to patients in VC-I, patients in VC-II were at increased risk of having two-year composite outcome in both HFrEF and HFpEF cohorts. Patients in VC III and IV had incremental increases in the likelihood of two-year composite outcome across all three HF cohorts (Table). **Conclusions**: Higher VE/VCO2 slope categories are associated with increased risk of the two-year composite outcome of all-cause mortality and HF hospitalization across the spectrum of HF defined by LVEF. A VE/VCO2 slope between 29 and 36, often considered borderline in clinical practice, is associated with increased risk of this composite outcome in patients with HFrEF and HFpEF. Identifying a wider VE/VCO2 slope associated with increased risk in HF may have important implications on risk stratification clinically.