unexpected safety findings in patients with resistant hypertension. (ClinicalTrials.gov: NCT03541174).

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Key Words: Resistant hypertension Endothelin Blood pressure Clinical trials Renal function

**19697**

### Effect of Radiofrequency Renal Denervation on Blood Pressure in the Presence of Antihypertensive Drugs: 6-Month Primary Results From the SPYRAL HTN-ON Med Expansion Randomized Trial

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**Background:** Results from the randomized SPYRAL HTN-OFF MED Pivotal and HTN-ON MED proof-of-concept trials demonstrated that radiofrequency (RF) renal denervation (RDN) significantly lowered blood pressure (BP) in patients with uncontrolled hypertension (HTN) in the absence and presence of prescribed antihypertensive (AH) medications, respectively. We will report the primary endpoint results from the SPYRAL HTN-ON MED Expansion randomized trial. **Methods:** SPYRAL HTN-ON MED Expansion trial is a prospective, multi-center, randomized, sham-controlled, blinded study conducted internationally to evaluate BP reduction after RF RDN compared with sham control in patients on AH medications. The first 106 patients were randomized 1:1 to undergo RDN or a sham procedure. As a prespecified Bayesian analysis, a subsequent 231 patients were randomized 2:1 to undergo RDN or the sham procedure for a total of 337 randomized patients. Trial recruitment was paused and re-started in 2020 due to COVID-19 pandemic. Eligible patients had an office systolic BP >=150 mmHg and <180 mmHg, an office diastolic BP >=90 mmHg, and were prescribed 1-3 AH medications, including a diuretic. The primary endpoint is the comparisons of change in 24-hour ambulatory systolic blood pressure at 6 months between groups using ANCOVA analysis to adjust for baseline blood pressure. **Results:** Six-month, efficacy and safety results from the SPYRAL HTN-ON MED Expansion trial will be presented for the first time at AHA 2022, including analyses related to the COVID 19 impact on patient randomization and follow-up. **Conclusions:** The primary endpoint efficacy and safety outcomes comparing RDN with sham control in HTN patients on AH medications will be presented at AHA 2022.

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Key Words: Hypertension; essential Renal denervation Hypertension; resistant

# Heart Failure and Cardiomyopathies

## In-depth and Fresh Look in Heart Failure Trials

**19512**

### The Effect of Percutaneous Revascularization on Arrhythmic Risk in Ischemic Left Ventricular Dysfunction

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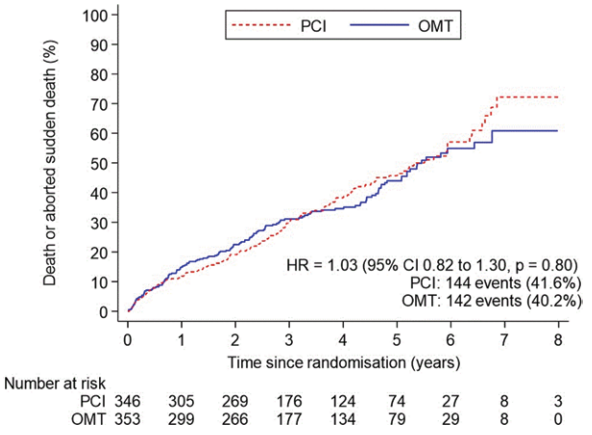
**Background** Coronary artery disease is the most common cause of severe left ventricular systolic dysfunction. The mortality rate in this population is high, largely due to ventricular arrhythmias. The effect of revascularization on the incidence of potentially fatal ventricular arrhythmias, compared to medical therapy alone, has never been assessed in a randomized trial. **Methods:** REVIVED-BCIS2 was a prospective, multi-centre randomized controlled trial of percutaneous coronary intervention (PCI) versus optimal medical therapy (OMT) alone for patients with severe left ventricular dysfunction, extensive coronary disease and viable myocardium. The primary outcome of this prespecified analysis is a composite of all-cause death and aborted sudden death (defined as appropriate implantable cardioverter defibrillator (ICD) therapy or resuscitated cardiac arrest). Secondary outcomes included cardiovascular death or aborted sudden death; aborted sudden death or sustained ventricular arrhythmias and the number of appropriate ICD therapies. **Results:** Seven hundred patients were enrolled across 40 centers in the United Kingdom between 2013 and 2020. 347 patients were assigned to the PCI group and 353 to the OMT group. Median follow up duration was 41 [27-60] months. The median left ventricular ejection fraction was 28%. Overall, 53.1% had an ICD and/or cardiac resynchronization therapy device inserted before randomization or during follow up. All-cause death or aborted sudden death occurred in 144 (41.6%) patients in the PCI group and 142 (40.2%) patients within the OMT group (hazard ratio 1.03 (0.82 to 1.30, p=0.80). There were no between-group differences in the occurrence of any of the secondary outcomes. **Conclusions:** PCI did not reduce all-cause mortality or aborted sudden death in patients with ischemic left ventricular dysfunction and should not be undertaken solely to reduce potentially fatal ventricular arrhythmias. Implantation of an ICD, in eligible patients, should not be deferred until revascularization is performed. **Trial registration:** ClinicalTrials.gov number, NCT01920048.

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**19609**

### Natriuretic Response With Acetazolamide in Acute Heart Failure With Volume Overload: Analysis From the ADVOR Trial

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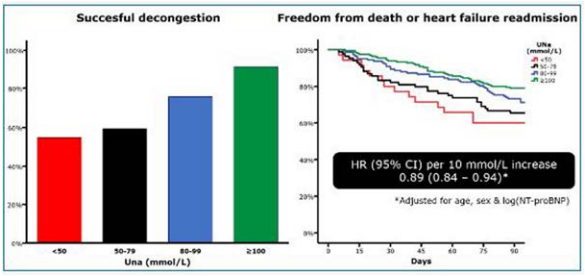
**Background:** The ADVOR trial showed a better chance of successful decongestion and shorter length of stay with acetazolamide (ACZ) on top of standardized intravenous loop diuretic therapy among patients with acute decompensated heart failure (HF) and unequivocal clinical signs of fluid overload. Main results of the ADVOR trial will be released during the European Society of Cardiology meeting on August 27, 2022. The effect of ACZ on natriuresis and its impact on clinical outcomes has not been studied well. **Objective:** This analysis of the ADVOR trial investigates the effect of ACZ on natriuresis and its association with successful decongestion and clinical outcomes. **Methods:** All ADVOR participants with 2 available urine collections (≥500 mL) from randomization until the next morning and during the next 24 h were included. Urine sodium concentration (UNa) was measured over the whole period. The effect of ACZ on UNa and total natriuresis was assessed. Finally, the association between the natriuretic response and the primary trial end point of successful decongestion, as well as the pre-specified secondary end point of death or HF readmission, was evaluated. **Results:** Out of the 519 ADVOR participants, 460 had urinary collections (ACZ: 231 vs. placebo: 229). UNa was 92±25 mmol/L and total natriuresis 437±308 mmol in the overall population. UNa was 12 mmol/L (95% CI, 8-16 mmol/L) and total natriuresis 106 mmol (95% CI, 50-162 mmol) higher in the ACZ compared to placebo arm. Higher UNa was associated with a higher probability of successful decongestion [OR (95% CI) per 10 mmol/L = 1.21 (1.12-1.32); p<0.001; Figure on the left]. Adjusting for UNa resulted in an effect of ACZ on successful decongestion that was no longer significant (p=0.211). During 3 months of follow-up, 59 patients died (12.8%) and 85 (18.5%) were readmitted for HF. After adjustment for age, sex, estimated glomerular filtration rate at baseline, and NT-proBNP, higher UNa was associated with a significantly reduced risk of death or HF readmission [HR (95% CI) per 10 mmol/L = 0.91 (0.85-0.97); p=0.003; Figure on the right]. Total urine output was associated with a higher probability of successful decongestion [OR (95% CI) per 1 L = 1.21 (1.08-1.35); p=0.001], but not with clinical outcome [HR (95% CI) per 1 L = 0.92 (0.82-1.03); p=0.167]. **Conclusions:** ACZ increases the chance of successful decongestion in acute decompensated HF, which is mediated by its effect on natriuresis. Natriuretic response was a powerful predictor of event-free survival, which supports its use as an attractive surrogate outcome in future acute decompensated HF trials.

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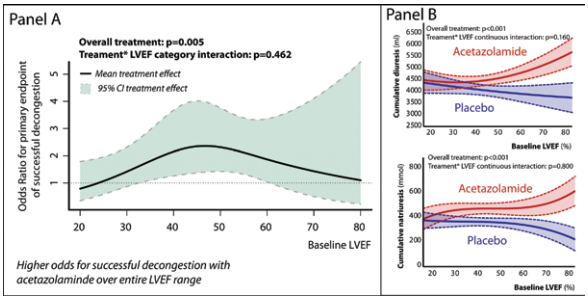
**19679**

## Decongestion With Acetazolamide in Acute Decompensated Heart Failure Across the Spectrum of Left Ventricular Ejection Fraction: *A Pre-Specified Analysis From the ADVOR Trial*

Pieter Martens[1], Jeroen Dauw[2], Frederik Verbrugge[3], Evelyne Meekers[2], Kevin Damman[4], FRANK RUSCHITZKA[5], Wai Hong W Tang[6], Matthias Dupont[7], Wilfried Mullens[8]; [1]Cardiovascular medicine, Cleveland Clinic, Cleveland, OH, [2]Cardiology, Ziekenhuis Oost Limburg, Genk, Belgium, [3]cardiology, Univ Hosp Brussels, Jette, Belgium, [4]Cardiovascular medicine, Univ of Groningen, groningen, Netherlands, [5]Cardiology, Univ Hosp Zurich, Zurich, Switzerland, [6]Cardiovascular medicine, CLEVELAND CLINIC, Cleveland, OH, [7]Cardiology, ZOL Genk, Genk, Belgium, [8]Cardiology, ziekenhuis oost limburg genk, Genk, Belgium

**Background:** Acetazolamide inhibits proximal tubular sodium reabsorption and improved decongestion in the Acetazolamide in Decompensated heart failure with Volume OveRload (ADVOR) trial. It remains unclear whether the decongestive effects of acetazolamide differ across the spectrum of left ventricular ejection fraction (LVEF). **Methods:** This is a pre-specified analysis of the randomized, double-blind, placebo-controlled ADVOR trial that enrolled 519 patients with acute heart failure, clinical signs of volume overload, NTproBNP >1,000 ng/L or BNP >250 ng/ml, to receive intravenous acetazolamide (500 mg once daily) or placebo on top of standardized intravenous loop diuretics (twice oral maintenance dose). Randomization was stratified according to LVEF (≤40% or >40%). The primary endpoint was successful decongestion, defined as the absence of signs of volume overload within three days from randomization without the need for mandatory escalation of decongestive therapy because of poor urine output. **Results:** Median LVEF was 45% (25-75th percentile: 30-55%) and 43% had a LVEF ≤40%. Patients with lower LVEF were younger, more likely to be male, with a higher prevalence of ischemic heart disease, a higher NTproBNP, less atrial fibrillation, and lower estimated glomerular filtration rate. In interaction analysis approaching LVEF as the randomization strata (≤/>40%), or as HFrEF, HFmrEF and HFpEF and on a continuous scale (panel A), no interaction on the overall beneficial treatment effect of acetazolamide on the primary endpoint of complete decongestion (OR=1.77, 95% CI=[1.18-2.63], p=0.005, all p-values for interaction >0.401) was found. Acetazolamide resulted in improved diuretic response measured by higher cumulative diuresis and natriuresis (panel B) and shortened length of stay without treatment effect modification by baseline LVEF (all p-values for interaction >0.160). **Conclusions:** Acetazolamide when added to high dose loop diuretics in patients with AHF improves the rate of complete decongestion, improves diuretic response and shortens length of stay, irrespective of LVEF.

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**19558**

## Empagliflozin and Cardiac Remodeling in People Without Diabetes: Primary Results of EMPA-HEART 2 CardioLink-7 Randomized Placebo-Controlled Trial

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**Introduction:** SGLT2 inhibitors broadly reduced heart failure events in clinical trials but their potential direct cardiac benefits remain unclear. Furthermore, it is unknown if these drugs afford cardiac benefits in the absence of diabetes and prevalent heart failure. Thus, we conducted a randomized trial of empagliflozin vs. placebo on cardiac remodeling (assessed by cardiac magnetic resonance imaging [cMRI]) in people with neither T2D nor heart failure (ClinicalTrials.gov Identifier: NCT04461041). **Methods:** Between April 14, 2021 and January 31, 2022, we screened individuals ≥18 and ≤85 years old without diabetes but with ≥1 of the major criteria (LV mass indexed to baseline body surface area [BSA] {LVMi} of ≥96 g/m$^2$ for women and ≥116 g/m$^2$ for men [by echocardiogram]; or LVMi ≥81 g/m$^2$ for women and ≥85 g/m$^2$ for men [by cMRI]; LV hypertrophy [by ECG]; structural heart disease [interventricular septal thickness or posterior wall thickness ≥11 mm]; persistent hypertension [≥140/90 mmHg] despite being on ≥3 antihypertensive medications) or ≥2 of the minor criteria (history of an MI ≥3 months ago, eGFR ≥30 and ≤60 mL/min/1.73m$^2$, BMI ≥27 kg/m$^2$). A total of 169 were randomized to empagliflozin (10 mg/day) or placebo for 6 months. The primary outcome was the cMRI-assessed 6-month change in LVMi from baseline. Other measures included 6-month changes in LVEDV (indexed to BSA), LVESV (indexed to BSA), LVEF, LV wall stress, LV diastolic and