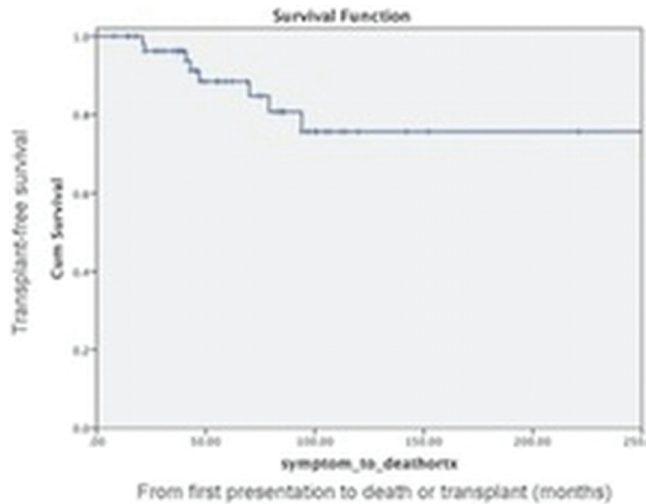


dysfunction (EF < 40%) for patients with initially normal LV function after the initial presentation were 77.6 months and 71.0 months, respectively.

18 patients (17%) either died (n=6) or had cardiac transplant (n=12). Figure shows Kaplan-Maier curves for survival free of death or transplantation. General prognostic signs of heart failure, low LV function, high pro-BNP and LBBB, were associated with adverse outcome in CS.



Conclusions: CS is progressive cardiomyopathy that leads to LV dysfunction despite normal LV function at the time of initial presentation. The rate of death or cardiac transplant is 17%.

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First nationwide study of sudden cardiac death due to arrhythmogenic right ventricular cardiomyopathy in the young; fifty percent have symptoms prior to death

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Purpose: The aim of this nationwide study was to investigate symptoms prior to death in all persons ≤ 35 years who died suddenly from arrhythmogenic right ventricular cardiomyopathy (ARVC) in Denmark between 2000-2006.

Methods: We included all deaths (6,629) in persons 1-35 years in Denmark between 2000-2006. Thereby we identified 314 autopsied sudden cardiac deaths (SCD) from which 16 died due to ARVC. Using the National Patient Registry, which is a database containing ICD-10 codes and dates of admission and discharge from hospitals of all Danish citizens, we could identify the time, place and diagnosis given at any admission to a hospital, as well as the patient's general practitioner (GP). Hospitals and GP's were contacted by letter to retrieve all medical files. A control group of 74 persons in the same age group, who died in accidents in the same time interval were used.

Results: In total eight of the 16 ARVC cases had antecedent cardiac symptoms (syncope, palpitations, angina, dyspnoea and fatigue) prior to death, and seven of them sought medical attention. The symptoms in the case group were significantly higher than in the control group. (1/74 - $p < 0.001$, Fisher exact test). Four of the patients experienced prodromal symptoms (angina, dyspnoea, syncope), two of which also had antecedent symptoms, making a total of 10 patients (63%) experiencing cardiac symptoms before death. None of the SCD cases were diagnosed with ARVC pre-mortem. One was diagnosed with myocarditis and three were diagnosed with asthma. From the seven patients who sought medical attention due to symptoms, six had an ECG performed of which two showed changes characteristic of ARVC, and three had further cardiac examination than an ECG. In total six of the patients died during strenuous physical activity and four of them were athletes, making these four deaths sports related sudden cardiac deaths. Five died during everyday activities.

Conclusion: This is the first nationwide study to report antecedent and prodromal symptoms in young SCD by ARVC victims. Half of the cases had antecedent cardiac symptoms prior to death. This was significantly higher than in the control group. All but one of the symptomatic cases sought medical attention, but none were diagnosed before death. A high percentage of the patients were athletes and an even higher percentage died during strenuous physical activity. We recommend a high degree of attention towards conducting sufficiently thorough cardiac investigation in young patients with cardiac symptoms.

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Mixed phenotypes: implications in family screening of inherited cardiomyopathies

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Introduction and purpose: Mixed phenotypes are relatively common in family screening of cardiac diseases, though rarely mentioned in clinical literature. We aim to present the prevalence of mixed forms in a dedicated inherited cardiac disease unit.

Methods: 4890 individuals from 827 families consecutively evaluated from Feb-03 to Jul-12 were included in the study. Index cases were referred after diagnosis of hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), isolated left ventricular non-compaction (ILVNC), arrhythmogenic right ventricular cardiomyopathy (ARVC), as well as channelopathies such as Brugada Syndrome (BS), Long QT Syndrome (LQTS) and familial conduction disease. Families with neuromuscular conditions were also included. Individuals were grouped according to preponderant phenotype in their families, regardless of their own diagnosis. In cases of ILVNC, families were reclassified if diagnostic criteria of another condition were met in two or more individuals. We excluded probands whose families were not evaluated.

Results: Number of evaluated families/ evaluated individuals /and prevalence of diagnoses for most prevalent conditions were as follows: HCM 405/ 2324/ 40%; DCM 115/ 854/ 42%; RAVD 42/ 242/ 31%; ILVNC 39/ 179/ 39%; BS 121/ 626/ 22%; LQTS 34/ 192/ 37%. Globally, 1847 individuals (38%) in 423 families presented diagnostic criteria for at least one inherited cardiac disease; 242 individuals presented mixed phenotypes (5% of evaluated, 13% of affected). Prevalence of mixed phenotypes was 1.8% for HCM; 14.3% for DCM (91%: LVNC criteria); 6.2% for ARVC; 10.6% for ILVNC. Cardiomyopathy traits were also present in channelopathies: e.g. DCM criteria were present in 0.5% of BS and 1.6% of LQTS. Atrial or ventricular septal defects were more frequent in ILVNC (7.3% vs 0.6%; $p < 0.001$), while prevalence in other conditions was similar to that expected in general population.

369 individuals in 29% of evaluated families presented diagnostic or dubious findings for conditions other than expected in their families. Even probands presented in 8.0% cases different phenotypes than preponderant in their families.

Conclusion: Overlapping between phenotypes of different inherited cardiac conditions is relatively common. Mixture of phenotypes can appear in a same individual, or may present as varying diagnoses in different individuals from a same family. While some of these cases might be related to coexistence of different mutations, there is evidence that a same mutation can manifest as different phenotypes.

STATE OF THE ART – RENAL DENERVATION THERAPY: HOPE AND HYPE

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The blood pressure lowering effects of renal denervation in a real world population of patients with uncontrolled hypertension: early outcomes from the Global SYMPLICITY registry

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Purpose: The Global SYMPLICITY Registry was designed to assess the safety and effectiveness of low energy radiofrequency ablation of renal artery nerves using the Symplicity™ renal denervation system to lower blood pressure in a real world population of hypertensive patients. The registry will provide additional data regarding the effects of renal denervation on comorbid conditions that are postulated to be similarly influenced by increased sympathetic tone.

Methods: The Global SYMPLICITY Registry is a prospective, open-label, multi-centre study enrolling patients at up to 200 sites worldwide. Adult patients with uncontrolled hypertension who are considered appropriate candidates for renal denervation by their physician are treated with the Symplicity™ catheter according to the approved Instructions for Use. Office-based and ambulatory blood pressure measurements, changes in antihypertensive medications and measures of renal function, vascular complications and other protocol-defined safety events and other tests specific to the patient's clinical condition(s) are collected.

Results: There are currently 752 patients enrolled with approximately half being enrolled in Germany. Based on preliminary data from 588 treated patients the mean age of patients is 60.0 \pm 12.8 years, 62% are males, and 36.2% have at least one comorbidity (42.0% have diabetes mellitus, 8.5% have heart failure, 11.9% have a history of atrial fibrillation, 29.5% have chronic kidney disease, and

14.5% have sleep apnea). At baseline, those being treated for hypertension were taking an average of 4.2 ± 1.3 anti-hypertensive medications and had an office systolic BP of 163.8 ± 22.7 mm Hg. Change in office and ambulatory blood pressure at 3 and 6 month follow-up in approximately 200 real world patients treated with the Symplicity catheter will be available for presentation at ESC. Peri-procedural and short-term safety will also be reported.

Conclusion: Renal denervation can significantly lower blood pressure in patients with treatment-resistant hypertension. This large real world registry will provide a large body of safety and efficacy data to further guide appropriate use of RDN in diverse patient populations.

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Renal artery denervation via catheter-based delivery of low-power radiofrequency energy provides safe and durable blood pressure reduction: complete 3 year results from SYMPLICITY HTN-1

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Purpose: Ablation of nerves within the renal arteries using low power radiofrequency energy has been shown to significantly reduce blood pressure (BP) in patients with severe hypertension unresponsive to standard pharmacologic treatments. Concerns regarding the long-term safety and effectiveness of this novel therapy requires careful follow-up of patients who have undergone the renal denervation (RDN) procedure.

Methods: Symplicity HTN-1, an open-label cohort study, enrolled 153 patients with treatment-resistant hypertension (systolic BP ≥ 160 mm Hg despite the use of ≥ 3 antihypertensive drugs including a diuretic). There were 144 patients consented for 2 year follow-up and 129 patients consented for 3 year follow-up. Changes in office-based BP and HR, distribution of BP measurements, medication usage and safety were monitored through 3 years follow-up. Using a response criterion of ≥ 10 mm Hg reduction in systolic BP (SBP) the proportion of patients with a late (after 1 month) BP response was determined.

Results: Follow-up is currently complete for 105 patients to 2 years and 34 patients to 3 years. Mean age at baseline was 57 ± 11 years; 39% of patients were female; 31% had type 2 diabetes mellitus; eGFR was 83 ± 20 mL/min and BP was $175/98 \pm 17/15$ mmHg. Mean SBP change post-RDN was -28.9 mmHg (95% CI $-33.5, -24.4$) at 2 years and -31.3 mmHg (95% CI $-36.5, -26.1$) at 3 years ($P < 0.01$ for both). At 3 years 41.2% of patients had a SBP < 140 mm Hg and the proportion of patients with SBP > 180 mm Hg dropped from 30% to 5.9%. Among the patients with < 10 mm Hg drop in SBP at 1 month, 64%, 71%, and 83% had responded at 1, 2 and 3 years follow-up respectively. There was one progression of a pre-existing renal artery stenosis and 1 new moderate stenosis requiring no treatment reported at 18 months, 2 cases of hypotension and transient renal failure (1 each at 18 and 24 months) and 3 deaths (3 days, 6 mo and 18 mo post-RDN) considered unrelated to the RDN procedure. Overall no net changes in medication usage are observed.

Conclusions: BP reductions following RDN in patients with treatment-resistant hypertension persist through 2 and 3 years follow-up. A proportion of patients appear to be late responders to RDN treatment which is not explained by medication changes. Safety and efficacy data on the full completed 3 year cohort of patients will be presented.

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Renal denervation by endocardial ablation system

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Background: Transcatheter renal denervation (TRD) obviously may be done with endocardial ablation systems which allow exactly the same mode/parameters of energy delivery while small 5-7F endocardial catheters may be easily manipulated in renal artery. However, in contrast with novel renal ablation devices still at the development stage, endocardial ablation systems are mature equipment with proven success, predictable behavior and lower price.

Greater length/diameter of endocardial ablation electrode provide greater contact area meaning proportionally lower current density and thereby risk of overheating, i.e. more safe ablation.

Objective: To assess the safety and efficacy of TRD done by endocardial ablation system.

Methods: We performed bilateral TRD using endocardial ablation catheter 5F, 4 mm in 52 patients (aged 53.7 ± 9.6 years, 27 male) with true drug-resistant hypertension. Sequentially 4-8 point RF ablations separated radially and axially in renal artery and segmental branches were done in temperature-control mode with target $T=60$ C. All patients were instructed to continue existed pharmacotherapy. Efficacy was evaluated by the changes in office and ambulatory BP at 6 and 12 months after TRD. Safety endpoints included adverse events, changes in renal blood flow (ultrasound doppler flowmetry) and renal function (proteinuria, serum creatinine) at 1 week, 6 and 12 months after TRD (NCT01499810 at ClinicalTrials.gov).

Results: No acute damage of renal arteries from RF ablation was detected by

intraoperative angiography. There were 7 minor periprocedural events typical for endovascular procedures and non-related to RF ablation. At the time of this analysis 39 and 25 patients completed respectively 6 and 12 months follow-up. No significant changes in renal blood flow or renal function were detected at 6 or 12 months after TRD.

Office BP dropped significantly by -27.5 ($p < 0.001$)/ -13.9 ($p < 0.001$) (mmHg, systolic/diastolic) at 6 months and then further decreased by -32.6 ($p < 0.001$)/ -15.5 ($p < 0.001$) at 12 months after TRD. The lowering of mean 24-h BP was quite modest at 6 months -11.5 ($p < 0.001$)/ -6.8 ($p < 0.001$) however also continued to decrease and reached powerful level of -15.4 ($p < 0.001$)/ -10.4 ($p < 0.001$) at 12 months follow-up.

Conclusions: TRD done by endocardial ablation system is safe in patients with resistant hypertension and causes significant long-term lowering of BP which tends to increase over time.

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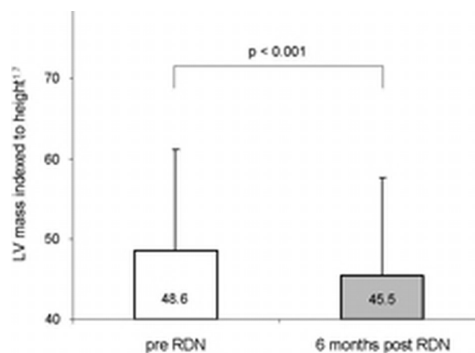
Results from a multicenter CMR-study in patients with resistant hypertension - pre and post renal denervation

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Purpose: The present study aimed to investigate the effect of renal denervation (RDN) on left ventricular mass and function, evaluated by cardiac magnetic resonance (CMR), in patients with resistant hypertension.

Methods: CMR was performed in 45 patients at baseline and 6 months after RD in a multicenter setting. In addition, twelve patients with resistant hypertension served as controls.

Results: Patients were middle aged (63 ± 11 years vs. 70 ± 8 years in the control group), had poorly controlled BP and were heavily medicated. The resting SBP/DBP among the RDN-group decreased significantly from $167.5 \pm 24.2/90.1 \pm 14.7$ mmHg at baseline to $149.1 \pm 21.1/82.6 \pm 15.3$ mmHg ($p < 0.001$) at 6 months whereas there were no changes in the control group during follow-up. LV mass indexed to height^{1.7} decreased by 7% from 48.6 ± 12.6 g/m^{1.7} at baseline to 45.5 ± 12.2 g/m^{1.7} 6 months ($p < 0.001$) after RDN (figure). In the control-group LV mass remained unchanged (44.8 ± 11.9 g/m^{1.7} at baseline vs. 44.1 ± 10.7 g/m^{1.7} at 6 months; $p=0.431$). Among the subgroup of subjects with reduced myocardial contractility at baseline circumferential myocardial strain decreased from -14.2% to -17.5% after RDN ($p=0.003$), indicating an improvement of 23%. There were no changes in circumferential strain in the control group (-16.3% at baseline vs. -16.8% at follow-up, $p=0.694$).



Impact of renal denervation on LV mass

Conclusions: RDN significantly reduced LV-mass and improved myocardial contractility (circumferential strain) in patients with resistant hypertension, as diagnosed by CMR. This might have important prognostic implications in patients with resistant hypertension.

STATE OF THE ART – IMAGING TO PREDICT FUTURE ISCHAEMIC EVENTS

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Prognostic implications of non-culprit plaques in acute coronary syndrome: non-invasive assessment with coronary CT angiography

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Purpose: Coronary CTA is a reliable non-invasive risk stratification tool for pa-