ST elevation. Clinical, laboratory, ECG echocardiographic and angiographic data were obtained at admission time and after 6 months follow up. Rs 2274273 and LGALS-3 mRNA expression were detected by real time PCR.
Results: T allele according to dominant model was significantly associated with LV enlargement (diameter and volume) (p=0.037, p=0.034), global radial strain (p=0.003) and LV spherical index (p=0.032). LGALS-3 mRNA expression was significantly higher in: patients with maladaptive remodeling (p=0.045), apical LV dilatation and remodeling (0.046) and in patients who developed HF after six month follow up (p=0.021).
Conclusions: Our exploratory results suggested that rs 2274273 T allele and LGALS-3 mRNA could bear the risk for more severe post MI LVR and HF development. Further replication and validation in a larger group of patients is inevitable.

P5297 | BEDSIDE
Plasma volume and its relation with glomerular filtration rate in patients admitted with acute decompensated heart failure

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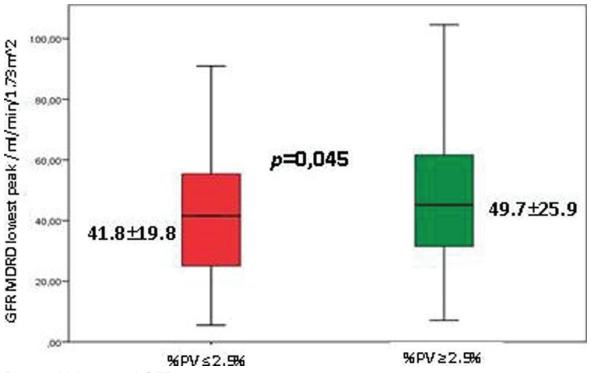
Background: Excessive depletion of vascular volume after diuretic therapy for acute decompensated heart failure (ADHF) is common and may lead not only to activation of the renin-angiotensin-aldosterone system but also to acute kidney injury. Our aim is to evaluate the relation between the degree of contraction of vascular volume, using the percentage of alteration in the plasma volume and the glomerular filtration rate (GFR), after the use of diuretics, in patients admitted with ADHF.
Methods: Retrospective study of 258 patients (74.2±17.3 years, 45.7% male) admitted in the emergency department between January and June 2016, for ADHF, defined by the presence of ≥2 signs or symptons of heart failure. All the patients were treated with diuretic therapy. We evaluate the diference between admission and discharge values of hemoglobin (ΔHb), hematocrit (ΔHtc), sodium (ΔNa), and the GFR evaluted by the Modification of Diet in Renal Disease (MDRD). The relative change in plasma volume (%PV) from admission until discharge was estimated by: {([Hb admission/Hb discharge]x [(100-Htc discharge)/(100-Htc admission)])-1}x100.
Results: Of the 258 patients admitted with ADHF, we excluded 11.6% (n=30) for missing laboratory values or description of blood loss/need of blood transfusion during hospital stay. After diuretic therapy (average of maximum dose of furosemide administered 69.3±17.3mg), the incidence of increase in the %PV was 61% (n=139) and in the decrease was 39% (n=89). We further divide the patients in two groups according to the average %PV (2.5%): group 1 with preserved volume [%VP >2.5% (from >2.5% to 44%, n=101], and the group 2 with diminished volume [%VP <2.5% (from -13.8% to <1.5%, n=127]. There were no statistically significant difference regarding ΔNa (average of 0.73±3.52mEq for group 1 vs. 1.52±4.56mEq for group 2, p=0.396). Patients in the group 2 showed greater positive variations of ΔHb (group 1 average of -1.34±0.78 g/dl vs. group 2 0.57±1.01g/dl p≤0.001) and in ΔHtc (group 1 average of -4.66±2.69% vs. group 2 2.21±3.23%, p≤0.001). We also conclude that patients in the group 2, with volume contraction, where those who, during hospital stay, had the lowest peak GFR (average of 49.7±25.9 ml/min/1.73m^2 for group 1 vs 41.8±19.8ml/min/1.73m^2 for group 2, p=0.045).



Plasma Volume and GFR

Conclusions: The present study establish a relation between the percentage of alteration in the plasma volume and the lowest peak value of GFR (acute kidney injury), in patients with ADFH, treated with diuretic therapy. Besides that, the values of hemoglobin and hematocrit seems to be the most useful laboratory values to evalute congestion vs contraction of volume. The sequential evaluation of the percentage of variation in the PV could be a useful tool to avoid the overuse of diuretic therapy in these patients and prevent the ocorrence of acute kidney injury during hospital admission.

P5298 | BEDSIDE
Novel ECG-based measure of ventricular dyssynchrony and its evaluation in MADIT-CRT patients with left bundle branch block

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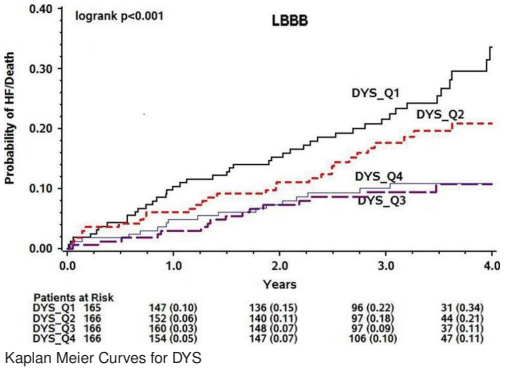
Background: Improving the selection of HF patients with left bundle branch block (LBBB) who benefit from cardiac resynchronization therapy (CRT) remains one of the challenges of modern medicine.
Objectives: We developed a novel ECG method for the measurement of electrical ventricular dyssynchrony (DYS) and evaluated, in MADIT-CRT patients, its association with heart failure progress (HF) or death, and 12-month changes (%) in left ventricular end systolic volume (LVESV).
Methods: Ten-minute resting supine high-resolution 12-lead ECG was recorded before CRT in 663 LBBB patients enrolled in a MADIT-CRT trial. The signal-averaged QRS amplitude envelopes were computed for leads V1 to V6 and 3 frequency bandwidths: 150–250, 250–350 and 150–350 Hz. The dyssynchrony was measured as the mean delay between V1 and V6 for peak maximums and centers of masses. We report its median value (DYS) that reflects the overall electrical depolarization activation delay (in ms) between the mid-septum and left ventricular lateral wall. Higher DYS corresponds to higher dyssynchrony.
Results: 109 LBBB patients met the MADIT-CRT primary endpoint – HF or death (18f, 66±12 yrs) and 554 did not (186f, 64±11 yrs). Kaplan-Meier survival curves are presented below using four quartiles of the DYS parameter value. In addition, we found a modest but statistically significant negative association between LVESV percent change at 12 month from implantation and baseline DYS values (R2=5%, p<0.001). Patients with a DYS below the median value had twice the risk of heart failure or death (HR=1.9, CI: 1.2–3.0, p=0.008). Cox multivariate proportional hazards regression models were adjusted for multiple clinical factors including baseline QRS duration, creatinine level, Worst NYHA class 3 months prior to enrollment and left atrial volume adjusted for body surface area.



Kaplan Meier Curves for DYS

Conclusions: The proposed computerized ECG-based technology provides insights into the baseline and post-implantation level of electrical dyssynchrony that may help selecting the LBBB patients who will benefit from CRT.
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P5299 | BENCH
Endothelin-1 receptor antagonist and adrenomedullin improve functional recovery after myocardial infarction

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Background: Endothelin 1 (ET-1) is markedly increased in myocardium during ischemia, and provides a bulk of metabolic, structural and functional disorders. Adrenomedullin (AM) is a vascular wall peptide able for a versatile control of the cardiovascular continuum.
Aim: The in vitro evaluation of the cardiac functional effects of ET-1 receptor antagonist or human recombinant AM administration in rats after myocardial infarction (MI).
Materials and methods: MI has been reproduced classically by ligation of the left coronary artery. BQ-123, a selective antagonist of ET-1 receptor type A was i/p administered immediately after MI during 7 days (0,3 mg/kg, daily). AM also during 7 days after MI was i/p continuously infused (2,0 μg/h) by using an implanted minipump. Both sham-operated rats and rats with MI but without medication received respectively saline solution. The functional indices of working isolated heart perfused by Neely-Morgan method were assessed after 2 and 5 weeks after the last medication.
Results: First and foremost is to note that both remedies significantly reduced rat mortality: 15% (BQ-123) and 18% (AM) vs 34% (MI). At the term of 2 weeks ET-1 receptor antagonist showed a better capacity to improve functional recov-

ery. In indicated series (BQ-123, AM, MI, and control) the main left ventricle parameters followed as: systolic pressure (SP, mm Hg) – 94,5±8,5 ($p<0,05$ vs MI); 88,7±7,6; 77,2±7,5 and 136,3±7,4; end-diastolic pressure (EDP, mm Hg) - 14,5±0,7 ($p<0,05$ vs MI); 15,8±0,7 ($p<0,05$ vs MI); 19,2±1,4 and 10,2±0,6; izovolumetric +dP/dTmax - 8088±520 ($p<0,05$ vs MI); 7330±480 ($p<0,05$ vs MI); 6715±440 and 9677±475 and cardiac output (CO, ml/min) – 31,4±2,4 ($p<0,05$ vs MI); 28,3±2,5 ($p<0,05$ vs MI); 23,5±2,3 and 40,7±2,8. After 5 weeks functional benefit was more conspicuous, and importantly is that it appeared similar for both medications. Thus, CO increased comparatively to MI by 39–40%, PS elevated by 27–28%, and EDP has fallen averagely by 1/3. Of particular note both remedies ensured after 5 weeks a positive inotropic effect of isolated heart on ET-1 action in concentration of 10–6 M manifested by SP elevation by 6,7% (in control – 11,7%) followed respectively by CO increase almost of 10,6%. In MI series ET-1 action was associated with decrease of both SP by 9,62% and CO by 8,5%.

Conclusion: A 7 days administration of ET-1 receptor antagonist (BQ-123) or adrenomedullin ameliorates heart function recovery after MI: (i) earlier benefit (2nd week) belongs to BQ-123, (ii) but at 5th week effects appear similarly.

P5300 | BEDSIDE
Prognostic implications of baseline and change from baseline values of plasma biomarkers that reflect extracellular matrix regulatory mechanisms and collagen synthesis in patients with heart failure

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Introduction: Myocardial fibrosis is an important pathophysiologic mechanism underlying the development of heart failure (HF). Plasma biomarkers that reflect mechanisms of extracellular matrix (ECM) homeostasis, collagen synthesis and profibrotic state have prognostic value in HF patients.

Purpose: Examine association between rate of primary composite outcome (CV death or HF hospitalization) and biomarkers of ECM homeostasis and collagen synthesis in PARADIGM-HF.

Methods: Biomarkers available at both baseline and 8 months after randomization in ≈ 1700 patients: aldosterone, sST2, TIMP-1, MMP-2, MMP-9, Gal-3, PINP, PIIINP. Baseline biomarker values and changes from baseline to 8 months were related to primary outcome.

Results: Baseline values of sST-2, TIMP-1, and PIIINP were associated with primary outcome rate (Table). Change from baseline to 8 months in sST-2 and TIMP-1 was associated with primary outcome or CV death rate.

Conclusions: Baseline and change from baseline values of biomarkers associated with profibrotic signaling have important prognostic value.

P5301 | BEDSIDE
Comprehensive assessment of left ventricular myocardial deformation in takotsubo syndrome using cardiovascular magnetic resonance myocardial feature tracking

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Background: Takotsubo syndrome (TTS) is characterized by transient left ventricular (LV) dysfunction due to a distinctive pattern of contraction abnormalities with apical, midventricular or basal ballooning.

Objectives: The present study sought to comprehensively assess LV deformation in TTS using cardiovascular magnetic resonance myocardial feature tracking (CMR-FT), a less operator dependent and more accurate technique compared to visual analysis.

Methods: A total of 141 TTS patients presenting to 2 centers underwent CMR imaging during the acute phase (median 2 days after admission). Follow-up CMR data after a median of 3.5 months were available in a subgroup of 21 patients. CMR-FT to determine LV peak circumferential (CS), radial (RS) and longitudinal strain (LS) was performed in a core laboratory.

Results: Median LV peak CS, RS and LS during acute TTS were -19%, 19% and -12%, respectively. All strain parameters showed a strong correlation with LV ejection fraction ($p<0.01$ for all). The apical ballooning type was associated with significantly lower LV peak CS ($p<0.01$) and LS ($p<0.01$) compared to midventricular or basal ballooning. A segmental analysis at basal, midventricular and apical levels resulted in a reliable discrimination of different ballooning patterns using peak CS and LS values. RS was less suited for the differentiation of ballooning types. All strain parameters improved significantly in the subgroup of patients with follow-up CMR data ($p\leq0.01$ for all). Compared to surviving patients, TTS patients with fatal events during long-term follow-up showed significantly lower LV peak LS during the acute phase (p=0.04). This association was not observed regarding CS and RS.

Conclusions: CMR-FT enables the quantitative assessment of transient, regional contraction abnormalities as well as global LV performance and dysfunction in TTS with subsequent improved diagnostic and prognostic potential.

P5302 | BENCH
SCN10A/NaV1.8 channels play a critical role in cellular electrophysiology and arrhythmogenesis of the failing human heart

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In heart failure (HF), persistent current through Na channel (INaL) is enhanced and may lead to arrhythmias. However, the role of neuronal sodium channel NaV1.8 in HF is unknown. Here, we investigated the regulation and electrophysiological contribution of NaV1.8 in the human failing heart. Co-immunocytochemistry showed that NaV1.8 expressed at both T-tubules and intercalated disk and overlapped with Ca/Calmodulin Kinase II (CaMKII) in human and mouse ventricular myocytes. Western blot revealed significant upregulation of NaV1.8 in human HF (n=8), whereas the predominant cardiac isoform NaV1.5 is downregulated compared to non-failing (NF, n=10) myocardium ($P<0.05$). Co-immunoprecipitation showed a significant interaction between NaV1.8 and CaMKII in HF and NF (n=3 vs. 3). Whole-cell patch clamp showed a potent reduction in both INaL integral and action potential duration (APD) after inhibition with novel Nav1.8 specific blockers either A-803467 (30 nmol/L) or PF-01247324 (1 μmol/L) in ventricular human failing myocytes. Importantly, the incidence of arrhythmias per time presented in the form of delayed afterdepolarizations and spontaneous action potentials were significantly suppressed after addition of PF-01247324 in isoproterenol (ISO, 30 nmol/L) treated ventricular cardiomyocytes isolated from patients with HF. Furthermore, using confocal microscopy (Fluo4 AM), we studied the diastolic Ca spark frequency (CaSpF). In HF, both A-803467 and PF-01247324 resulted in significant decrease of CaSpF (~43%). Additionally, we measured INaL, APD and CaSpF in mouse ventricular cardiomyocytes lacking Nav1.8 (SCN10A–/–) vs. wild-type (WT). In WT, the addition of ISO resulted in increase of INaL (control:-54.88±3.96 vs. ISO: -78.47±3.85 A*ms*F-1, n=10 vs. 19, $P<0.01$) and CaSpF (control: 0.2±0.1 vs. ISO: 0.7±0.1 μm^{-1} s^{-1}, n=87 vs. 65; $P<0.0001$). Importantly, in SCN10A–/– ISO-dependent increase in INaL was completely abolished, while CaSpF was reduced compare with WT ($P<0.05$).

Abstract P5300 – Table 1

Marker	Visit	Median [IQ range]	Baseline levels vs outcomes HR (95% CI), p-value log-transformed, per SD		8-month changes vs subsequesnt outcomes HR 99% CI), p-value log-transformed per log2	
			Primary outcome*	CV Death*	Primary outcome**	CV Death**
Aldo (pmol/L)	Base	275 [173, 464]	1.21 (0.86–1.07)	1.00 (0.86–1.16)	0.91 (0.78–1.07)	0.91 (0.74–1.11)
	M8	243 [154, 394]	p=0.45	p=0.99	p=0.26	p=0.34
sST2 (ng/mL)	Base	32.2 [25.4, 41.5]	1.21 (1.11–1.33)	1.25 (1.10–1.42)	1.69 (1.29–2.272)	1.22 (0.84–1.75)
	M8	31.0 [24.7, 39.3]	p<0.001	p<0.001	p<0.001	p=0.29
TIMP-1 (ng/mL)	Base	125 [106, 152]	1.26 (1.12–1.43)	1.61 (1.34–1.94)	1.13 (0.79–1.60)	1.93 (1.21–3.08)
	M8	123 [102, 152]	p<0.001	p<0.001	p=0.51	p=0.006
MMP-2	Base	135 [117, 158]	1.08 (0.97–1.20)	1.05 (0.89–1.24)	1.04 (0.76–1.43)	1.11 (0.74–1.67)
	M8	133 [114, 153]	p=0.16	p=0.54	p=0.80	p=0.63
MMP-9	Base	64.1 [38.2, 126.2]	1.01 (0.91–1.13)	0.98 (0.83–1.15)	1.00 (0.89–1.13)	0.98 (0.83–1.16)
	M8	59.3 [35.7, 109.2]	p=0.81	p=0.77	p=0.97	p=0.80
Gal-3	Base	17.1 [13.9, 21.2]	1.07 (0.97–1.19)	1.08 (0.94–1.24)	1.39 (0.98–1.98)	1.38 (0.89–2.15)
	M8	17.9 [14.4, 22.3]	p=0.16	p=0.26	p=0.06	p=0.16
PINP	Base	36.0 [27.0, 48.0]	1.01 (0.90–1.14)	1.08 (0.91–1.28)	1.08 (0.84–1.40)	1.21 (0.87–1.68)
	M8	34.5 [25.5, 46.5]	p=0.86	p=0.40	p=0.53	p=0.26
PIIINP	Base	4.7 [3.6, 5.9]	1.18 (1.04–1.33)	1.30 (1.09–1.56)	1.25 (0.95–1.65)	1.23 (0.87–1.73)
	M8	4.5 [3.6, 5.8]	p=0.010	p=0.004	p=0.10	p=0.25

*Adjusted for treatment + baseline covariates. **Adjusted for treatment + baseline covariates + all baseline biomarkers.