Παρουσίαση ερευνητικού έργου

Πανεπιστημιακό Νοσοκομείο Ιωαννίνων
Β' Καρδιολογική Κλινική

Study of peripheral circulation in patients with Heart Failure

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AIMS OF THE STUDY

To investigate in stabilized AHF patients

- Differences in indices of vascular function in relation to
  - the presence of ischemic heart disease (IHD)
  - different HF pathophysiology (HFREF vs HFPEF)
- Whether vascular function may be associated with exercise capacity
- The prognostic role of vascular function indices on major cardiovascular events (MACE) at 6 months after hospitalization for AHF.
- Whether change in functional status at 6 months after optimal medical therapy in patients admitted for an AHF syndrome may be related to changes in central hemodynamics and vascular function

Methods – Study population and Protocol

Study Population

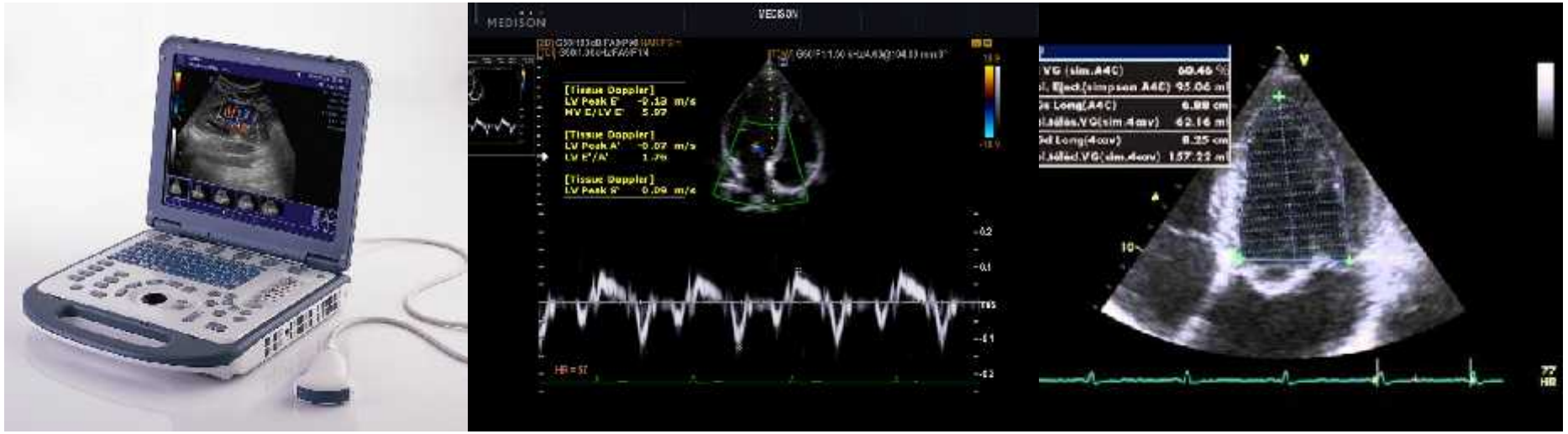
100 consecutive patients hospitalized due to **Acute Heart Failure syndrome,** (new onset or chronic HF decompensation)

- ✓ Patients with recent coronary syndromes, severe chronic diseases, atrial fibrillation **were excluded**.
- ✓ Patients were studied after stabilization **24-48h** prior to discharge
- ✓ Telephone follow-up at 3, 6, 12 months

At 6 months → re-evaluation with detailed clinical assessment, vascular studies and echocardiography → ***60 patients so far***

Methods – Cardiac Ultrasound

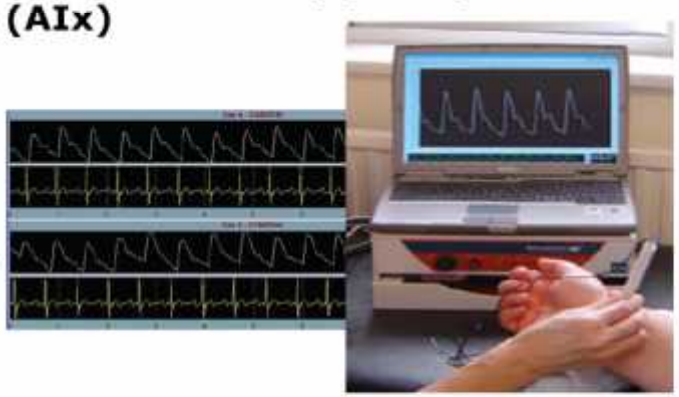
Echocardiography (Vivid-I ultrasound, General Electric)
Conventional and tissue Doppler parameters



Methods – Vascular parameters 1

Carotid- femoral Pulse Wave Velocity (PWV)
Augmentation index (AIx)
Central pressures

Sphygmocor System, version 7.01
Atcor Medical, Sidney

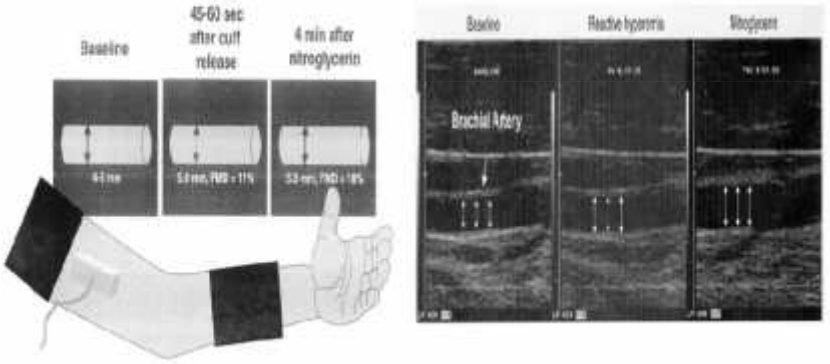


Large and Small artery compliance

HDI CR-2000, Hypertension Diagnostics

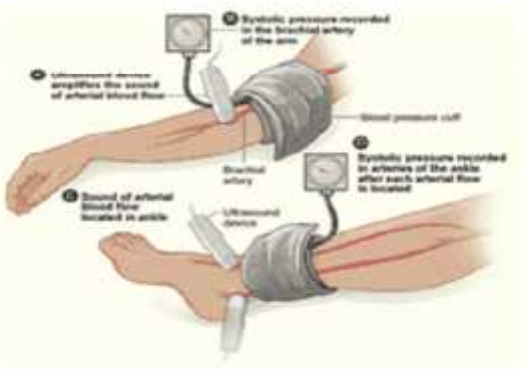
Methods – Vascular parameters 2

Flow-Mediated Dilation (FMD)



Vivid-I ultrasound, General Electric

Ankle-brachial index (ABI)



Methods – 6 minute walking test

A valid indicator of functional capacity in patients with HF providing an assessment of the patient’ s ability to perform submaximal activities of daily living

BASELINE POPULATION CHARACTERISTICS

Age, years	71±11
Male gender, n (%)	72 (79)
Current smoker, n (%)	25 (28)
Hypertension, n (%)	78 (86)
Diabetes, n (%)	36 (40)
Dyslipidemia, n (%)	57 (63)
CAD, n (%)	61 (67)
Anemia, n (%)	35 (39)
COPD, n (%)	15 (17)
Ischemic HF, n (%)	50 (55)
HFPEF, n (%) (LVEF>40%)	28 (31)
NYHA III-IV, n (%)	69 (76)
Hospitalization duration , days	8 (3,38)
BMI, kg/m²	27.3±4.5
HDL, mg/dl	40±10
LDL, mg/dl	100±33
Hemoglobin, g/dl	13.3±2.0
Glucose, mg/dl	136 (65,393)
Ure, mg/dl	63±28
eGFR EPI ml/min/1.73 m²	57.9±16.7
6MWT, m	256±155

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Vascular measurements	
Systolic BP, mmHg	123±20
Diastolic BP, mmHg	72±10
Pulse pressure, mmHg	51±17
Carotid-femoral PWV, m/s	11.4±3.5
AIx, %	22.7±9.0
Central SBP, mmHg	112±19
Central DBP, mmHg	72±11
Central PP, mmHg	40±17
FMD, %	3.24±1.17
C1 (large artery compliance)	13.2±6.6
C2 (small artery compliance)	4.0±2.5

Echocardiography	
LVEDD, mm	57±10
LAVI, ml/m²	48±10
E/A	1.13 (0.21, 5.22)
E/E'	14.5±6.3
TV Sv, cm/sec	11.7±3.6
LVOT VTI, cm	17.7±5.5
LVEF, %	37±15
LVSVI, ml/m²	33±10
PASP, mmHg	36±17
IVC, mm	15±6

Ischemic vs Non-Ischemic HF

	IHD-HF	Non IHD-HF	P value
SBP, mmHg	124±21	126±21	0.701
DBP, mmHg	70±11	73±11	0.297
PP, mmHg	54±18	54±18	0.961
HR, bpm	66±9	66±11	0.947
AIx75, %	23.7±8.0	22.0±10.6	0.504
CSBP, mmHg	112±19	115±20	0.546
CDBP, mmHg	70±11	74±10	0.174
CPP, mmHg	43±17	43±18	0.968
FMD, %	3.24±1.18	3.43±1.22	0.494
C1, ml/mmHg	13.0±6.3	12.5±6.2	0.733
C2, ml/mmHg	3.4 (1.4, 12.2)	2.8 (1.7, 11.3)	0.338
C1 normal, n (%)	27 (63)	22 (74)	0.527
C2 normal, n (%)	16 (37)	12 (41)	0.665
6MWT, m	245±153	269±161	0.543

	IHD-HF	Non IHD-HF	P
LVEDD, mm	56.8±9.8	57.6±11.1	0.753
EF, %	34.6±13.2	41.4±18.2	0.094
LVOT VTI, cm	18.2±7.6	19.6±5.2	0.410
E/'E	14.9±7.1	15.6±7.2	0.702
PASP, mmHg	40±19	34±18	0.217
E/A	1.32 (0.21, 21.00)	0.89 (0.44, 4.80)	0.356

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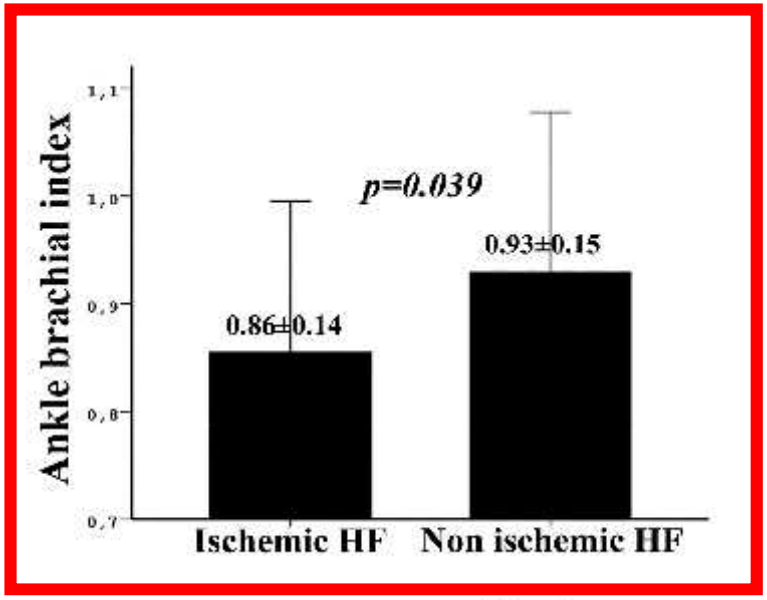
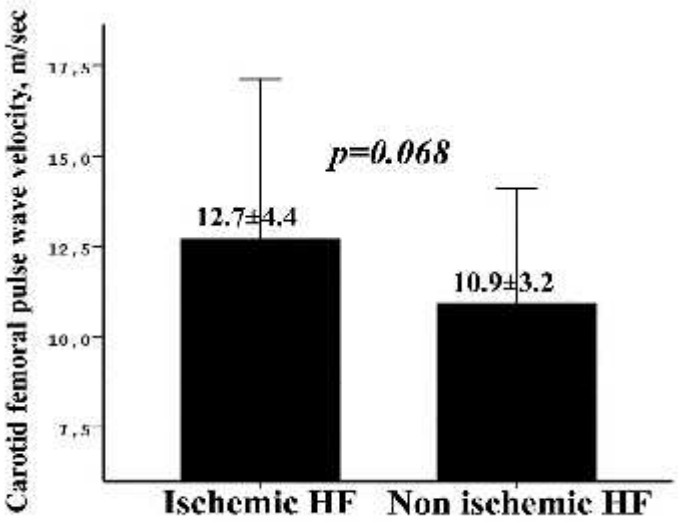
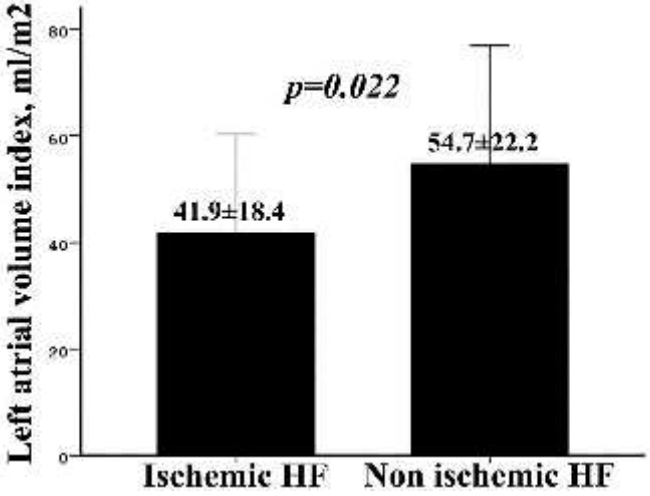
Ischemic vs Non-Ischemic HF







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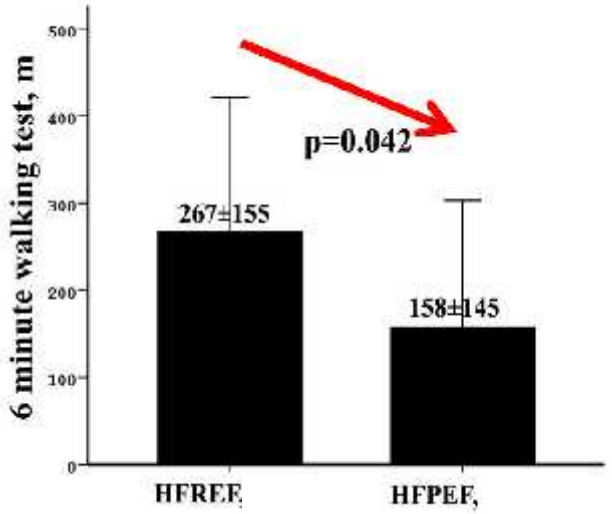
HFREF vs HFPEF

	HFPEF	HFREF	P value
DBP, mmHg	76±13	71±11	0.085
HR, bpm	66±8	66±10	0.861
PWV, m/sec	12.9±3.5	11.7±4.1	0.371
AIx75, %	23.8±10.0	22.8±8.9	0.709
CDBP, mmHg	75±11	71±10	0.218
ABI	0.90±0.06	0.88±0.16	0.460
FMD, %	3.31±0.88	3.30±1.26	0.970
C1, mmHg	9.9±6.1	13.3±6.1	0.079
C2, mmHg	3.2 (1.7, 8.2)	3.4 (1.4, 12.2)	0.699

	HFPEF	HFREF	P value
LVDD, mm	46±7	60±9	**<0.001**
EF	63±9	32±10	**<0.001**
LVOT VTI, cm	22.8±6.1	17.8±6.3	**0.013**
LAVI, ml/m^2	51±18	46±21	0.494
E/'E	16±3	15±8	0.420
PASP, mmHg	36±17	37±19	0.782
E/A	0.8 (0.6, 2.7)	1.4 (0.2, 21.0)	0.476



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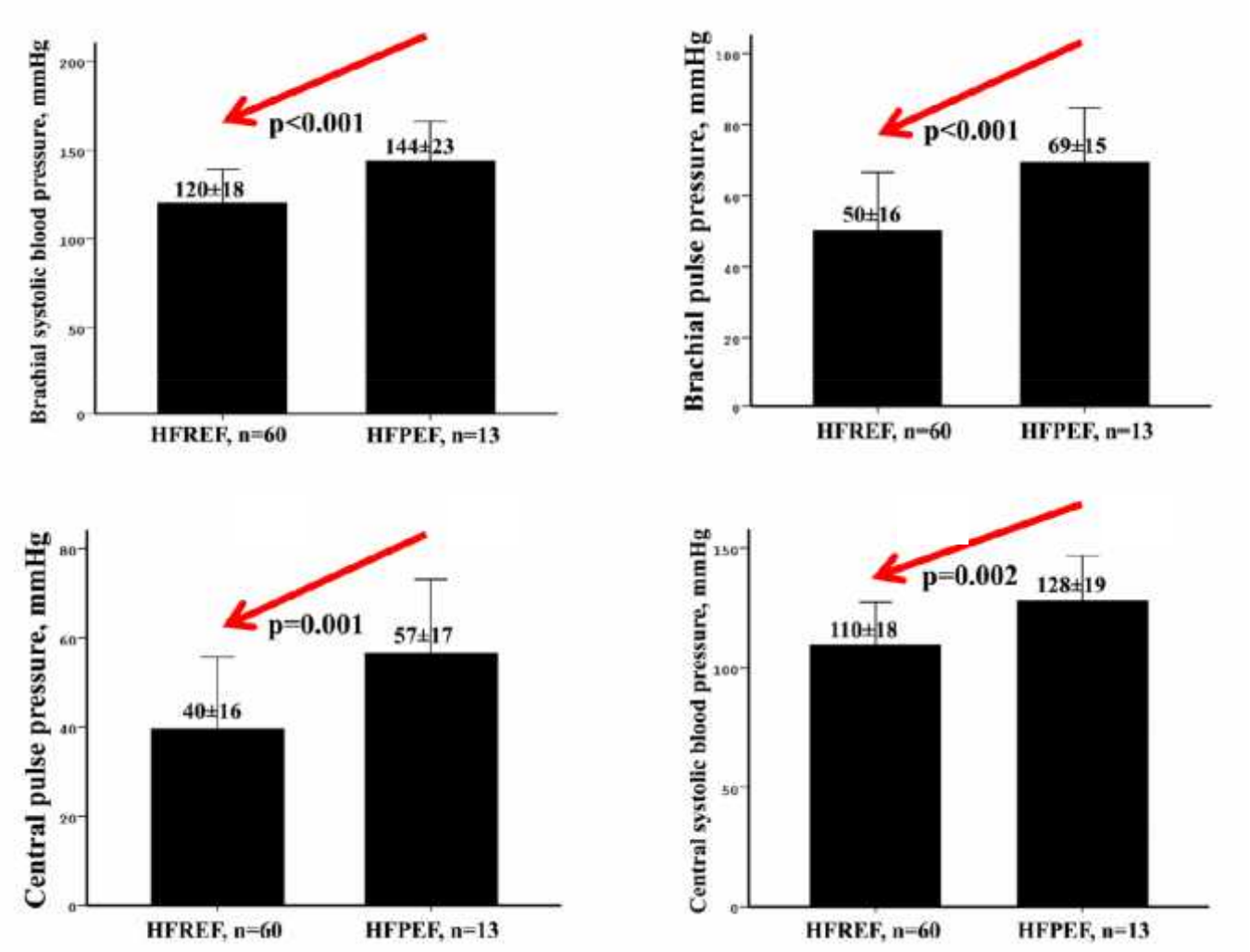
HFREF vs HFPEF



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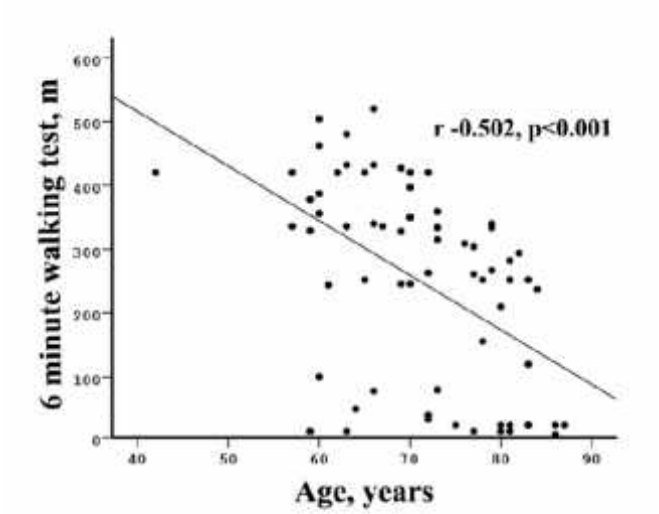
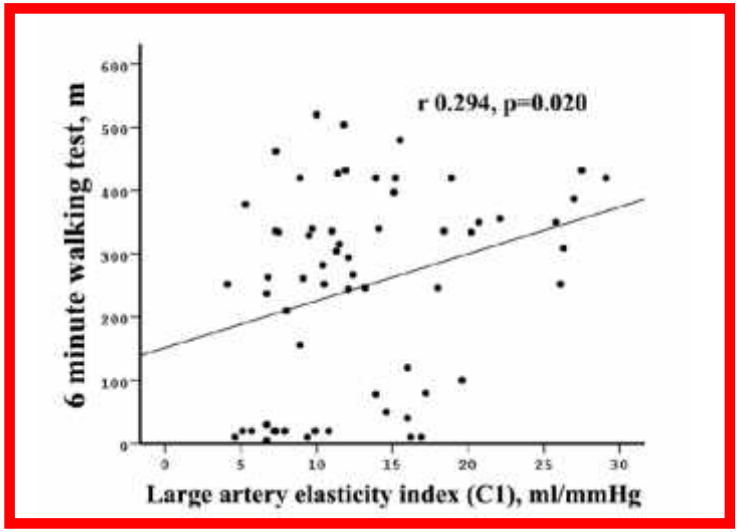
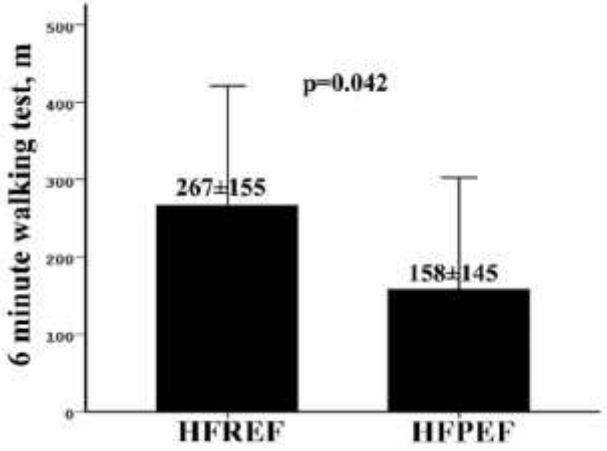
Predictors of 6MWT







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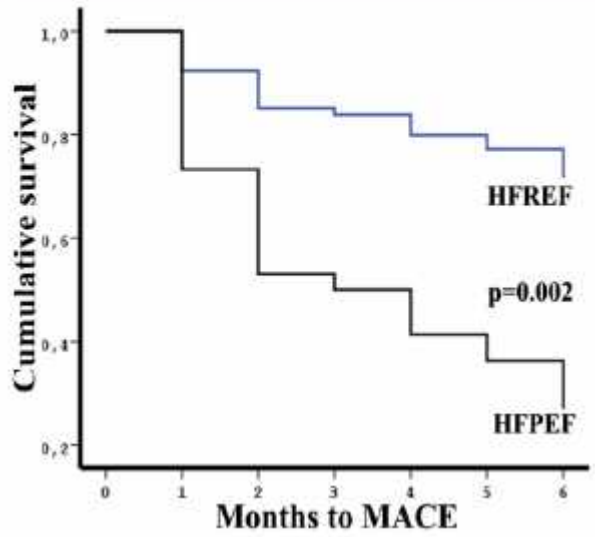
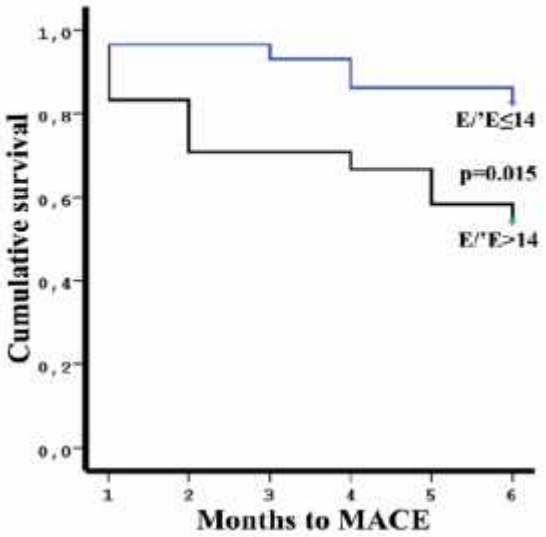
FOLLOW-UP ANALYSIS
MACE at 6 months

37% MACE

- ✓ Rehospitalization for AHF
- ✓ Non fatal MI and stroke
- ✓ Death

	Univariate analysis			Multivariate analysis		
	HR	95% CI	p	HR	95%CI	p
LVEF/SD	2.10	1.37 – 3.22	0.001	-	-	-
HFPEF	3.93	1.69 – 9.15	0.002	4.68	1.97 – 11.10	<0.001
HDL/SD	0.56	0.35 – 0.89	0.014	0.51	0.31 – 0.85	0.010
E/'E >14	3.61	1.55 – 8.65	0.015	3.22	1.11 – 9.36	0.042
SBP/SD	1.63	1.08 – 2.46	0.021	-	-	-





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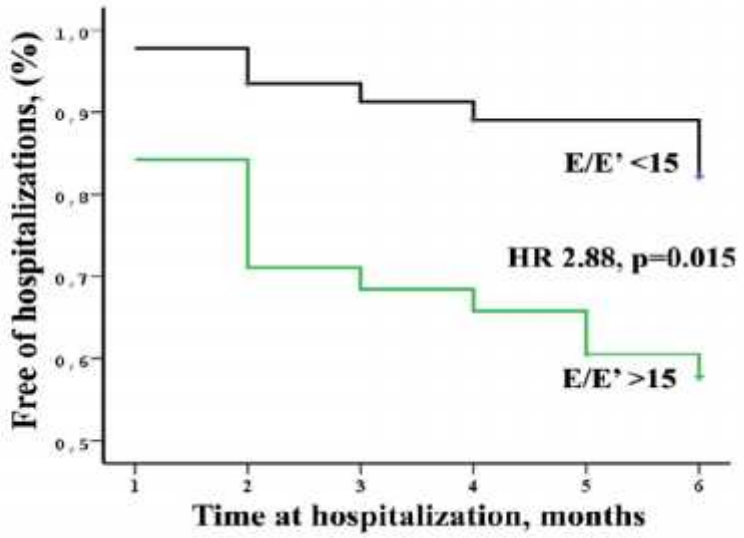
FOLLOW-UP ANALYSIS – HF REHOSPITALIZATIONS

During the 6-month follow-up, (25%) patients were admitted to the hospital for a new AHF syndrome

Independent predictors of 6-month readmission in multivariate analysis:

- Higher LVEF (p=0.006)
- E/E' > 15 (p=0.004)

PREDICTORS OF REHOSPITALIZATION			
	Univariate analysis		
	HR	95% CI	p
LVEF %	1.04	1.01-1.07	0.013
E/'E >15	2.88	1.23-6.75	0.015
Brachial DBP	1.04	1.00-1.08	0.033
Ischemic HF	0.40	0.17-0.94	0.036
Central DBP	1.04	1.00-1.08	0.041
HDL	0.96	0.92-1.00	0.058
BMI	1.09	0.99-1.19	0.072



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FOLLOW-UP ANALYSIS - MORTALITY

13% Mortality

Cox regression analysis						
	Univariate analysis			**Multivariate analysis**		
	HR	**95% CI**	**p**	**HR**	**95% CI**	**P**
PWV/SD	2.0	1.3, 3.1	**0.003**	3.6	1.4, 9.5	**0.01**
NYHA IV	6.2	1.5, 25.9	**0.013**	11.4	1.4, 92.9	**0.023**
****Hospital days/SD***	1.6	1.1, 2.3	**0.029**	3.2	1.1, 9.5	**0.033**
FMD/SD	0.4	0.1, 0.9	**0.037**	-	-	-
Age/SD	2.4	0.9, 6.0	**0.055**	-	-	-

****Logarithm transformed***

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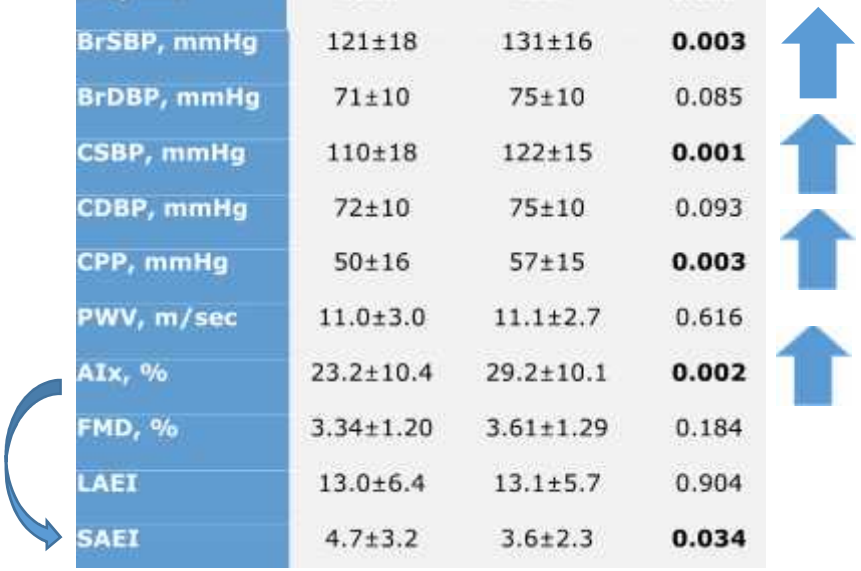
CHANGES AT FOLLOW-UP

	Baseline	Follow-up	P value
NYHA class (%)			
I	0 (0)	4 (9)	
II	12 (27)	26 (58)	
III	23 (51)	14 (31)	
IV	10 (22)	1 (2)	**<0.001**
6 MWT (meters)	273±159	380±130	**<0.001**

	Baseline	Follow-up	P value
β blockers	25 (56)	41 (91)	**<0.001**
Furosemide	21 (47)	35 (78)	**0.003**
MRAs	17 (38)	29 (64)	**0.017**
ACE-I/ARB	25 (56)	34 (76)	0.078
Digoxin	2 (4)	1 (2)	1.000
Thiazides	8 (18)	4 (9)	0.219

	Baseline	Follow-up	P value
LAVI, ml/m²	43±16	45±17	0.603
E/A	1.36±1.22	0.96±0.65	0.091
E/E'	13.1±6.4	11.0±4.2	0.061
LVEF, %	34±13	41±11	<0.001
LVSVI, ml/m²	31.4±9.3	37.3±11.1	0.009
PASP, mmHg	35±17	25±10	<0.001
IVC, mm	15±6	12±4	0.026
BrSBP, mmHg	121±18	131±16	**0.003**
BrDBP, mmHg	71±10	75±10	0.085
CSBP, mmHg	110±18	122±15	**0.001**
CDBP, mmHg	72±10	75±10	0.093
CPP, mmHg	50±16	57±15	**0.003**
PWV, m/sec	11.0±3.0	11.1±2.7	0.616
AIx, %	23.2±10.4	29.2±10.1	**0.002**
FMD, %	3.34±1.20	3.61±1.29	0.184
LAEI	13.0±6.4	13.1±5.7	0.904
SAEI	4.7±3.2	3.6±2.3	**0.034**



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PREDICTORS OF CHANGES IN CLINICAL STATUS

Correlations with improvement in NYHA		
	r	P value
HFREF	-0.376	**0.011**
Ischemic HF	-0.286	0.057
Furosemide	-0.338	**0.023**
B blocker	-0.363	**0.014**
MRA	-0.535	**<0.001**
ΔLVSVI	-0.409	**0.012**

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CONCLUSIONS 1

Ischemic vs Non-Ischemic HF

- *Heart failure process may be associated with vascular changes independent of atherosclerosis*
  - Indices of arterial stiffness/elasticity and endothelial function do not differ depending on the presence of Ischemic Heart Disease
  - Only ABI found to be impaired in association with Ischemic Heart Disease

HFREF vs HFPEF

- HFREF demonstrated lower peripheral and central systolic and pulse pressure compared to HFPEF, without differences in arterial stiffness/compliance
- *Differences in pulse pressure (peripheral or central) between HFREF and HFPEF may reflect differences in stroke volume rather than differences in arterial properties*

CONCLUSIONS 2

Vascular function and exercise intolerance (6MWT distance)

- *Vascular indices of arterial stiffness (reduced compliance) were associated with reduced functional capacity (decreased 6MWT distance)*

Prognostic role of vascular function indices

- *Increased arterial stiffness (PWV) is an independent predictor of mortality at 6 months after a hospitalization for AHF*
- Indices of vascular function were not predictive of MACE or HF rehospitalizations at 6 months follow-up
- The presence of HFPEF and increased LV filling pressures were associated with increased MACE and HF rehospitalizations at 6 months

CONCLUSIONS 3

Changes in vascular indices after optimal medical tx

- *Peripheral and central systolic and pulse pressure and Augmentation Index increased following optimal medical tx indicating probably the increase in LV stroke volume.*
- Improvement in functional status at 6 months was associated with improved LV performance and the use of live-saving therapies, mostly in patients with HF-REF.

ΕΡΕΥΝΗΤΙΚΗ ΟΜΑΔΑ

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- Γιαννίτση Σοφία
- Αντωνίου Σοφία
- Γκίρδης Ιωάννης

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