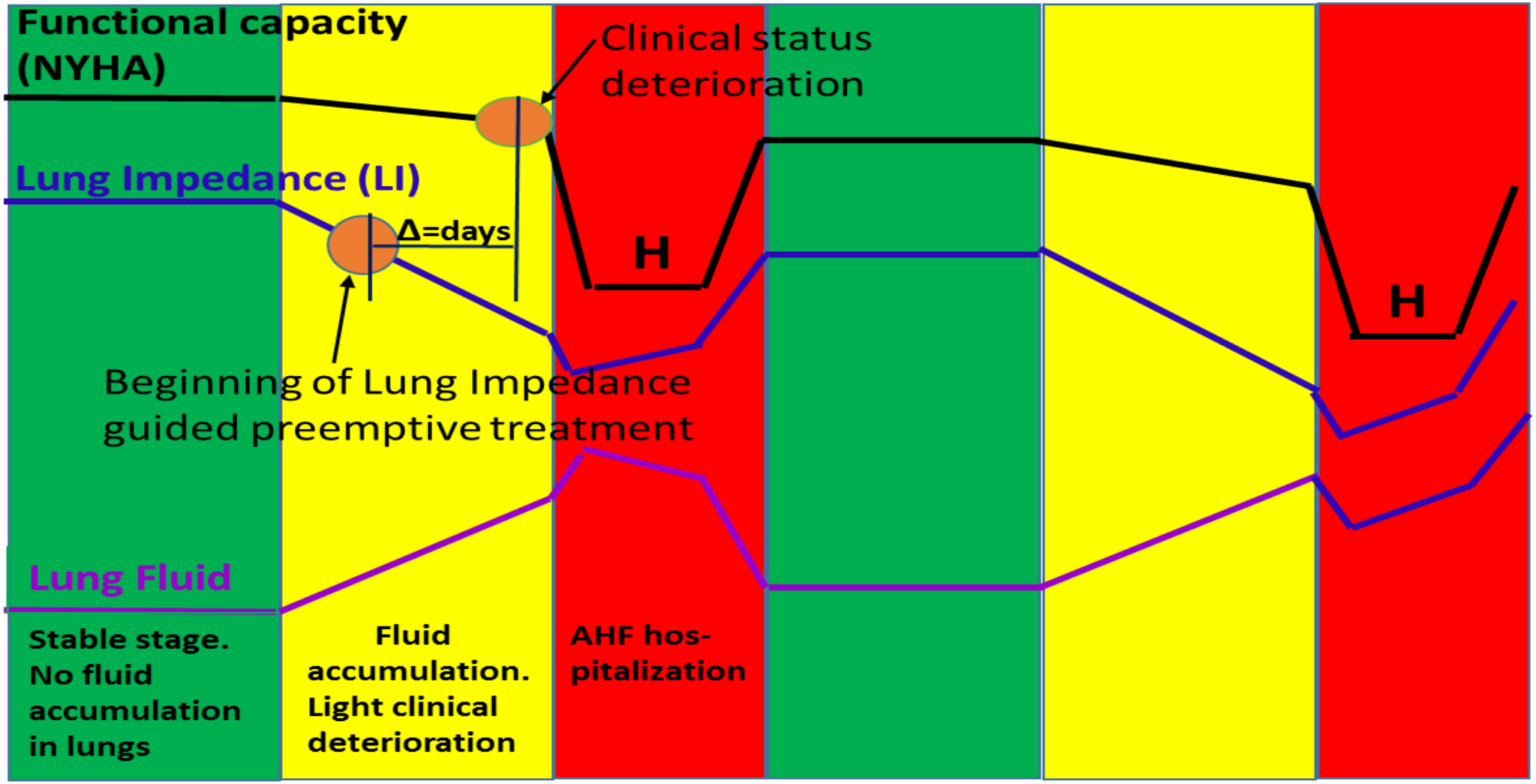
Non-invasive Lung IMPEDANCE-Guided Preemptive Treatment in Chronic Heart Failure Patients: a Randomized Controlled Trial (IMPEDANCE-HF trial)

Michael Shochat, MD, BSc, PhD[a], Avraham Shotan, MD[a], David S Blondheim, MD[a], Mark Kazatsker, MD[a], Iris Dahan, MSIT[a], Aya Asif, MD[a], Yoseph Rozenman, MD[b], Ilia Kleiner, MD[c], Jean Marc Weinstein, MBBS, FRCP[c], Aaron Frimerman, MD[a], Lubov Vasilenko, MD[a], Simcha R Meisel, MD, MSc[a]

[a]Heart Institute, Hillel Yaffe Medical Center, Hadera, Rappaport School of Medicine, Technion, Haifa, Israel; [b]Cardiovascular Institute, Wolfson Medical Center, Holon, Sackler Faculty of Medicine, Tel-Aviv University, Israel, [c]Cardiology Department, Soroka University Medical Center, Beer Sheva, Israel.

I, Michael Shochat, is The Directory of Board RSMM technology Company produced device for congestion monitoring

Hypothesis of the study

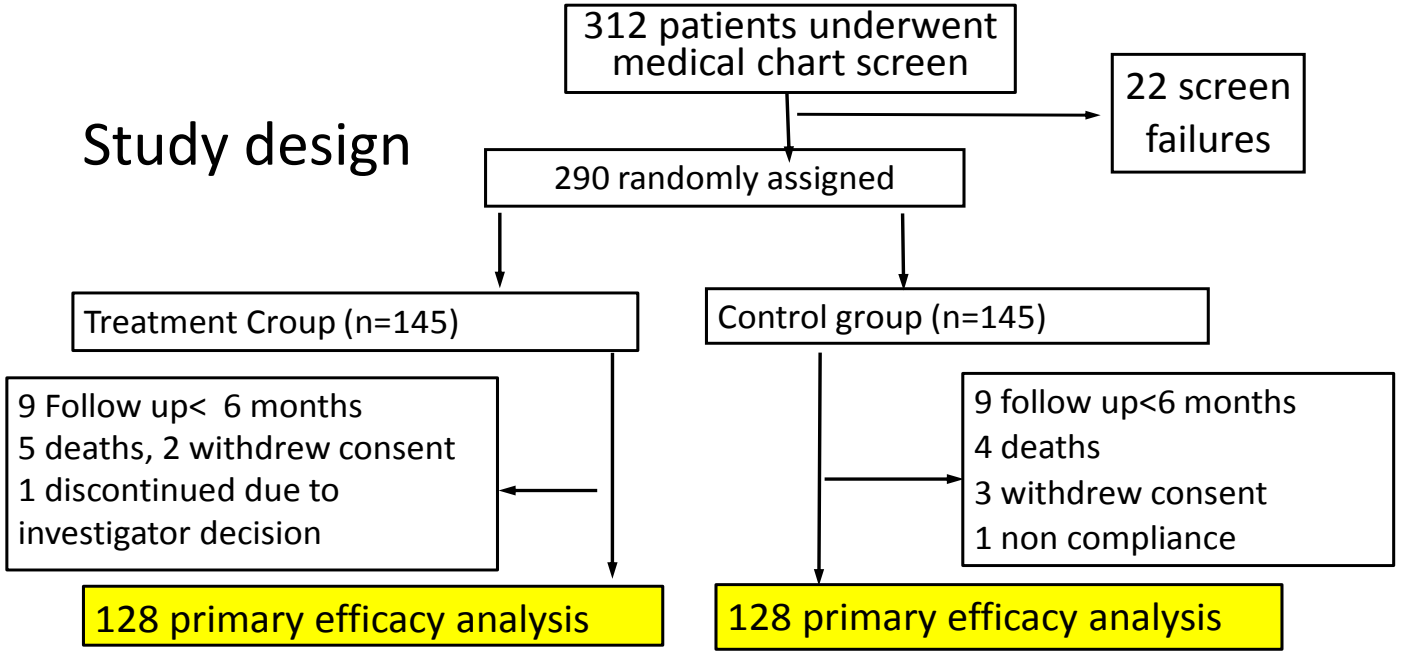


Dynamics Patients Functional Capacity, Lung Fluid accumulation and Lung Impedance during different stages of pulmonary edema development.

Problem: Patients with chronic heart failure (CHF) frequently require re-hospitalization due to exacerbation of heart failure (HF).

Aim: The present study was undertaken to prove the hypothesis that LI-guided treatment based on noninvasive assessment of pulmonary congestion may improve long-term outcome in ambulatory outpatient CHF patients.

Study design



Methods

Inclusion criteria:

1. CHF patients with HF hospitalizations within last year. NYHA II-IV.
2. Left Ventricle Ejection Fraction < 35%
3. Glomerular Filtrating Rate > 25 mL/min per 1.73 m^2

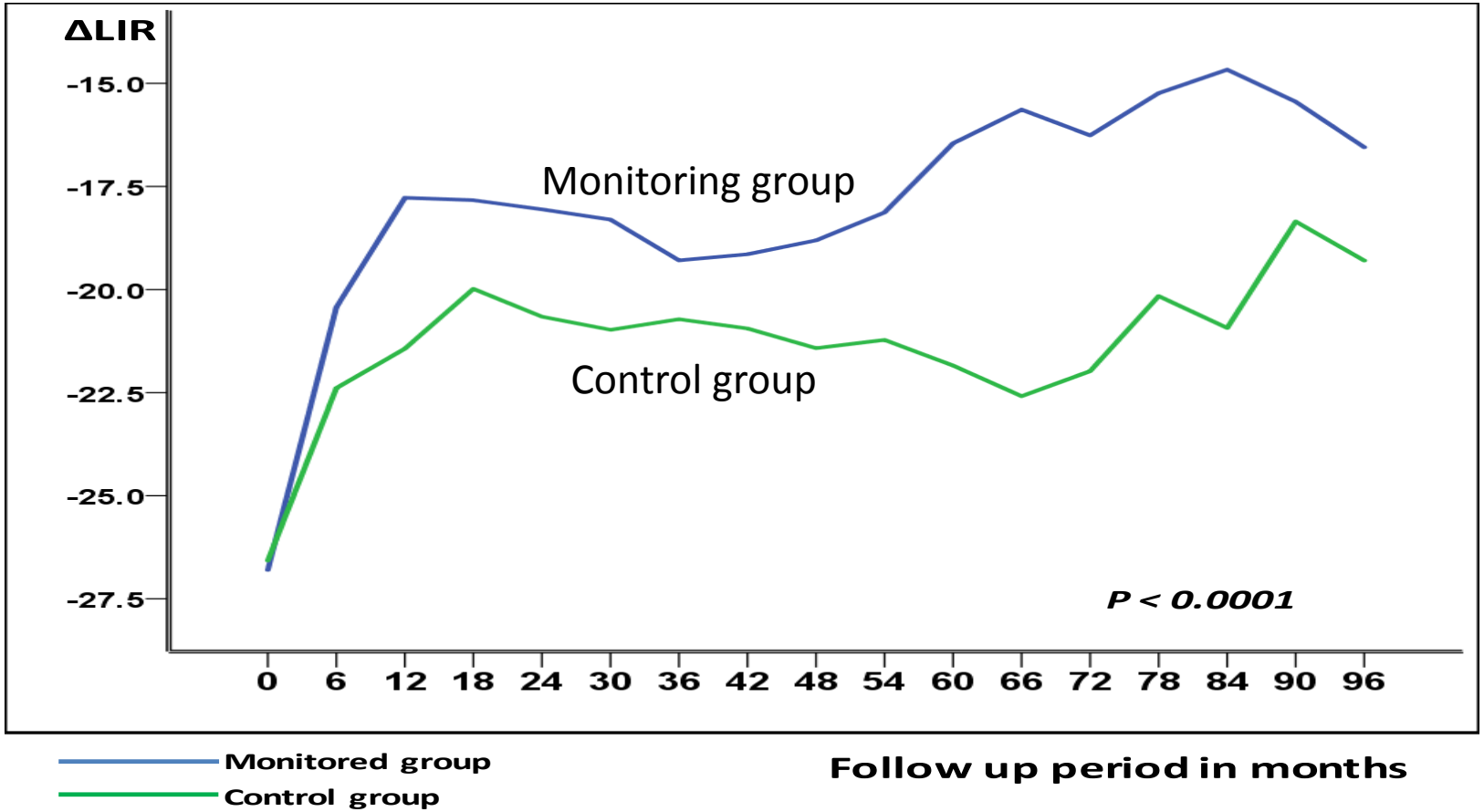
Patients were randomized (1:1) in a single blind design in 2 centers, and treated in out-patient clinics with monthly visits. Patients of monitored group were treated by clinical assessment and Lung Impedance and control group according to clinical assessment only.

Lung Impedance (LI) was measured by non-invasive device on each visit. Baseline (normal) Lung Impedance (BLI) was calculated for each patient. **ΔLIR = [(LI/BLI – 1)*100]. ΔLIR-** reflecting the degree of decreasing LI from baseline (normal) level. In other words **ΔLIR -** reflects the degree of pulmonary congestion on current visit in comparison with normal condition.

From previous investigations has shown that all HF hospitalizations occurred when ΔLIR was in interval -24% to -50%. Therefore, pre-specified interval for anti-congestive intervention in the monitored group was chosen when ΔLIR decrease was more than -18%.

Groups well matched according clinical and laboratory criteria. Minimal follow up 1 year and average follow up 48 months.

Results



Mean follow up period is 48 months

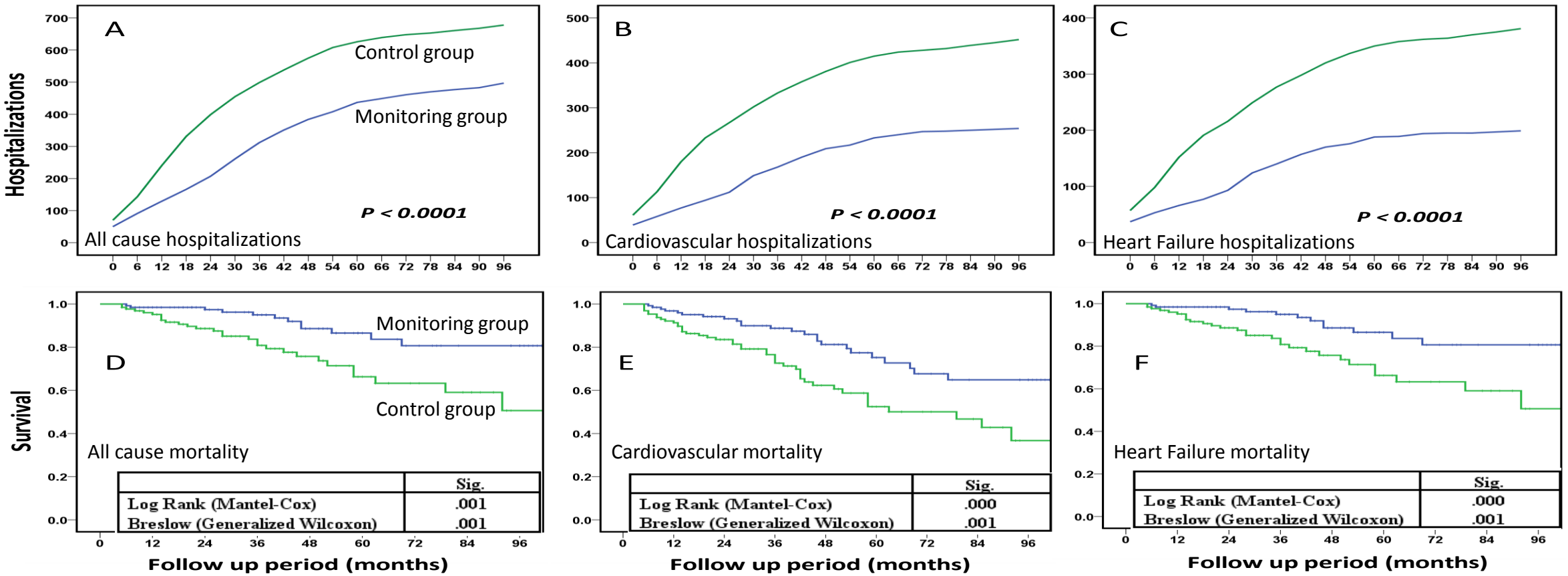
Difference in pulmonary congestion between groups during follow up period

ΔLIR - Lung Impedance Ratio. ΔLIR = [(current LI/BLI)-1], LI – Lung Impedance measured at current visit, BLI –baseline lung impedance.

T A B L E Effect of Lung Impedance guided treatment on efficacy endpoints

	Monitored Group (n=128) 511 years follow up	Control Group (n=128) 411 years follow up	Hazard ratio (95% CI)	p Value	NNT
Primary efficacy endpoints					
Acute heart failure hospitalizations up to 12 months	67* (0.52)†	158* (1.23)†	0.51 0.38-0.68	<0.0001	1.4
Acute heart failure hospitalizations during entire follow up	211* (0.41)†	386* (0.94)†	0.63 0.53-0.75	<0.0001	1.9
Secondary efficacy endpoints					
All hospitalizations during entire follow up (number, events per patient per year)	528* (1.03)†	691* (1.68)†	0.66 0.59-0.74	<0.0001	1.6
Cardiac hospitalization during entire follow up	274* (0.54)†	464* (1.13)†	0.62 0.53-0.72	<0.0001	1.8
Non-cardiac hospitalization during entire follow up	254* (0.50)†	227* (0.55)†	0.96 0.80-1.15	=0.63	
All-cause mortality during entire follow up	42* (0.08)†	59* (0.14)†	0.52 0.35-0.78	=0.002	7.5
Cardiac mortality during entire follow up	26* (0.05)†	47* (0.11)†	0.41 0.25-0.67	<0.0001	6.1
Heart Failure mortality during entire follow up	13* (0.03)†	31* (0.08)†	0.35 0.15-0.58	=0.0001	7.1
Non-cardiac mortality during entire follow up	16* (0.03)†	12* (0.03)†	0.96 0.45-2.04	=0.92	

Randomized Impedance HF trial. 256 CHF out hospital patients (1:1). Mean = 48 months Follow Up. Monitoring group was treated according Lung Impedance and Control group according clinical assessment



A - All cause hospitalizations **B – Cardiovascular hospitalizations** **C – Heart Failure hospitalizations** **Monitored group**
D - All cause mortality **E – Cardiovascular mortality** **F – Heart Failure mortality** **Control group**

Cumulative rate of hospitalizations and survival analyses during follow up period

T A B L E Drug modifications during entire follow up			
Medications	Monitored Group	Control Group	p
Beta Blockers (average cumulative dose during Follow Up period)	0.74*	0.74*	NS
ACE inh/ARB (average cumulative dose during Follow Up period)	0.79*	0.83*	NS
	Rate of changes in medical therapy		
Total	3166 (6.2)†	1244 (3.0)†	<0.05
Diuretics	1530 (48%) ‡	515 (42%) ‡	<0.05
Beta Blockers	792 (25%) ‡	303 (24%) ‡	<0.05
ACE inh /ARB	410 (13%) ‡	142 (11%) ‡	<0.05
Nitrates	166 (5%) ‡	78 (6%) ‡	<0.05
MRA	154 (5%) ‡	144 (12%) ‡	NS
Digoxin	114 (4%) ‡	62 (5%) ‡	<0.05

*Medication dose as a percent of maximal guideline-recommended was calculated as average for entire follow up period. †Rate of medicine modifications/patient-year. ‡Absolute number of drug modifications and percent modifications from total. ACEI = Angiotensin converting enzyme inhibitor; ARB = Angiotensin Receptor Blocker; MRA = Mineralocorticoid receptor antagonist.

Conclusions

The IMPEDANCE-HF is the first trial demonstrating that non-invasive LI-guided pre-emptive therapy of worsening pulmonary congestion in CHF patients with reduced LVEF:

1. Prevents AHF, cardiovascular, and all cause hospitalizations
2. Reduces all-cause, cardiovascular and HF mortality
3. LI monitoring should be considered in patients with CHF with reduced LV function to improve outcomes.