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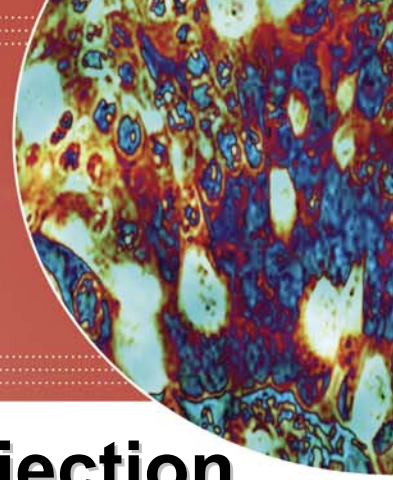

Improvement of stress Left Ventricular Ejection Fraction (LVEF) rather than rest LVEF after Bone Marrow Cells (BMC) transplantation in Heart Failure (HF) patients.

TELCECORI HF

TELCECORI HEART FAILURE
Pilot case-control study

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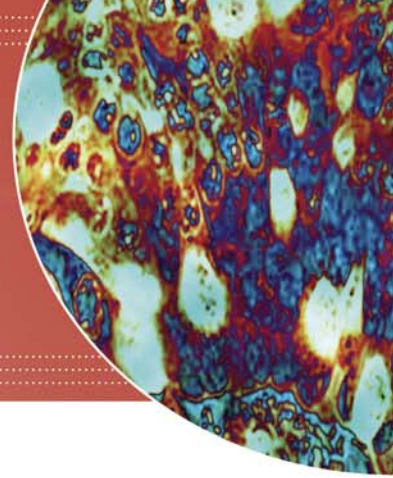

Conflict of Interest Statement

Within the past 12 months, I or my spouse/partner have had a financial interest /arrangement or affiliation with the organization(s) listed below.

Physician Name	Company/Relationship
Jorge Tuma M.D.	Rejuvacell / Scientific Advisor

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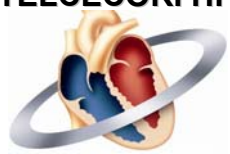

Background

- Pilot studies suggest that transcoronary transplantation of progenitor cells may improve LVEF in HF patients with promising results.

- The Standart Method to evaluate the successful stem cell treatment in different trials was LVEF at REST. Echo-MRI-Angiography-Spect.

- The Best Method to evaluate the response of LVEF after cell transplantation infused into coronary veins in patients with HF is unknown.

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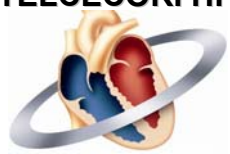

Endpoints of the study

- **Primary Endpoints**: Assess Safety of Autologous BMC by Retrograde Injection into the Coronary Veins in patients with severe left ventricular dysfunction.

- **Secondary Endpoints**: Assess Efficacy of Autologous BMC injections in terms of symptoms, functional class (NYHA) and rest - stress LVEF (SPECT) at baseline and 12 months follow up.

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Inclusion and Exclusion Criteria

INCLUSION

- Chronic CAD with ischemic cardiomyopathy.
- LVEF ≤ 35%.
- Ineligibility for percutaneous, surgical and cardiac resynchronization.
- Signed informed consent.

EXCLUSION

- NYHA IV.
- Cardiogenic shock.
- Severe co-morbidity.

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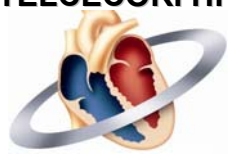

Methods
Baseline Evaluation

- BMC and Control group:
- History and physical examination
- Laboratory evaluation: CBC, blood chemistry, CRP, CPK-MB ,Troponin
- Exercise stress test with bicycle protocol
- Spect at rest and stress LVEF

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Baseline characteristics of patients BMC and Control Group

CHARACTERISTIC	BMC (N = 10)	CONTROL GROUP (N=6)	p-value
Age – yr Mean	65 ±14.3	64 ±10	NS
Male sex - N (%)	9 (90%)	6 (100%)	NS
Systemic Hypertension - N (%)	7 (70%)	6 (100%)	NS
Hyperlipidemia – N (%)	6 (60%)	5 (83.3%)	NS
Diabetes Mellitus - N (%)	4 (40%)	2 (33.3%)	NS
Previous myocardial infarction	10 (100%)	6 (100%)	NS
Previous percutaneous coronary interventional	5 (50%)	4 (66.6%)	NS
Previous coronary artery bypass surgery	7 (70%)	4 (66.6%)	NS
NYHA III (%)	10 (100%)	6 (100%)	NS
Ejection Fraction – Mean	28.47 ±7.03	25.95 ±8.3	NS

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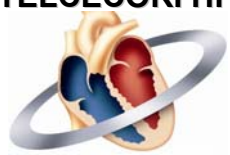

Bone Marrow Aspiration and Isolation of Mononuclear Cells

- Bone marrow 350 ml was aspirated from the posterior iliac crest 4 hours prior to cell injection. Using local anesthesia.
- Procedure were isolated by density gradient on Hess hydroxy-ethyl starch.
- The $CD34^{+}$ and mononuclear cell suspension were implanted retrogradely by coronarography of the coronary veins previous occlusion of the balloon over the wire for 8 to 10 minutes, in a median volume of 50 ml nearly 4 hours after extraction and preparation.

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Infusion of stem cells through the coronary venous system (Technique)

The coronary sinus is cannulated and an angioplasty balloon is advanced into the great cardiac vein. The balloon is positioned in the selected cardiac vein, depending on the territory to be treated. After balloon inflation, with consequent flow interruption in the coronary venous system, the cell infusate is delivered under low pressure Through the lumen of the balloon catheter. This delivery mode supposedly provides a broad and uniform distribution of cells.

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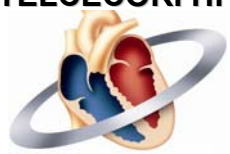

Material and Methods

- After the injection, patients stayed hospitalized for 12 hours, and they underwent cardiac monitoring (telemetry) and serial enzyme control.
- In the follow up period, they underwent Spect at rest and stress LVEF at one year after the procedure.

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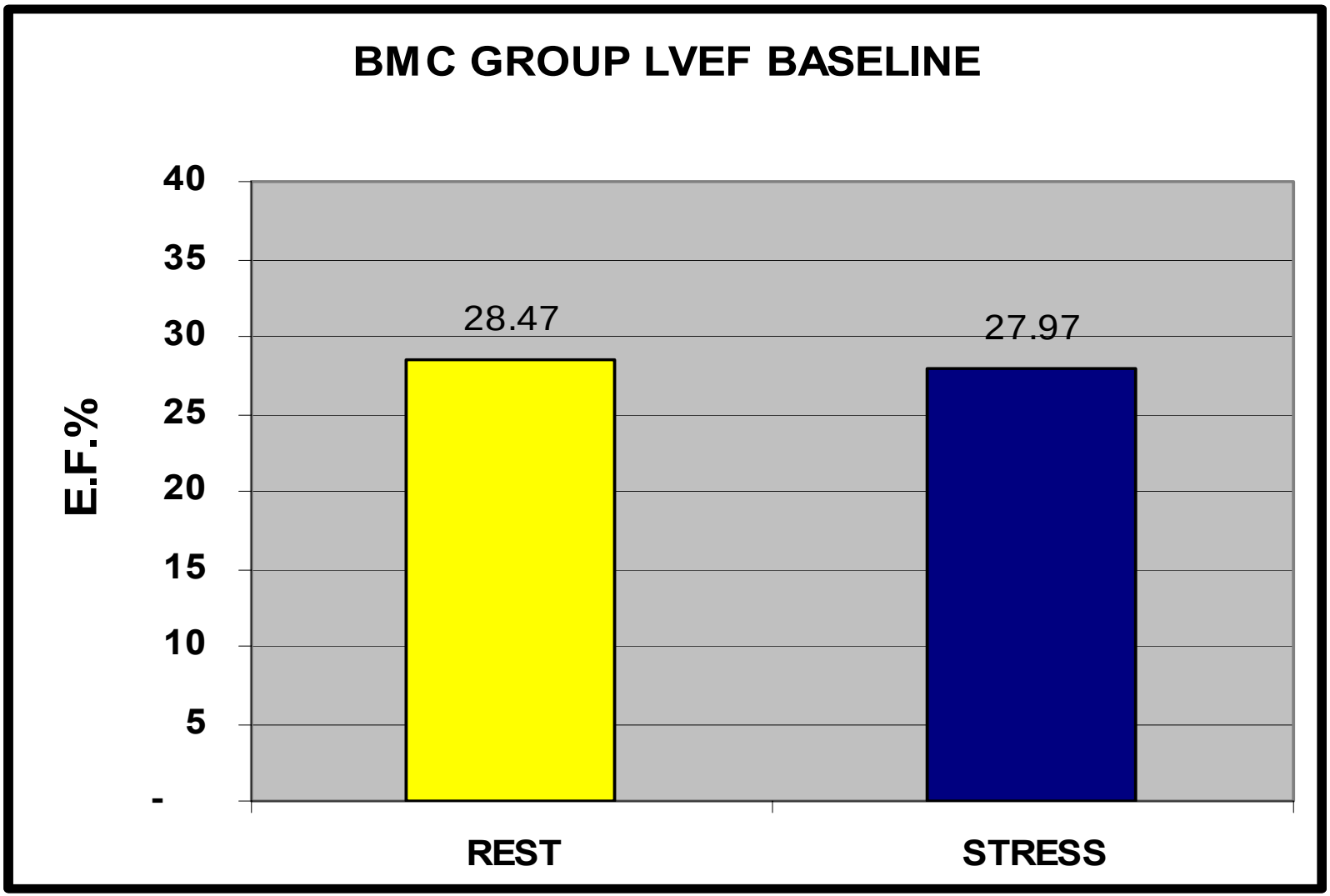
SPECT results
Median basal LVEF



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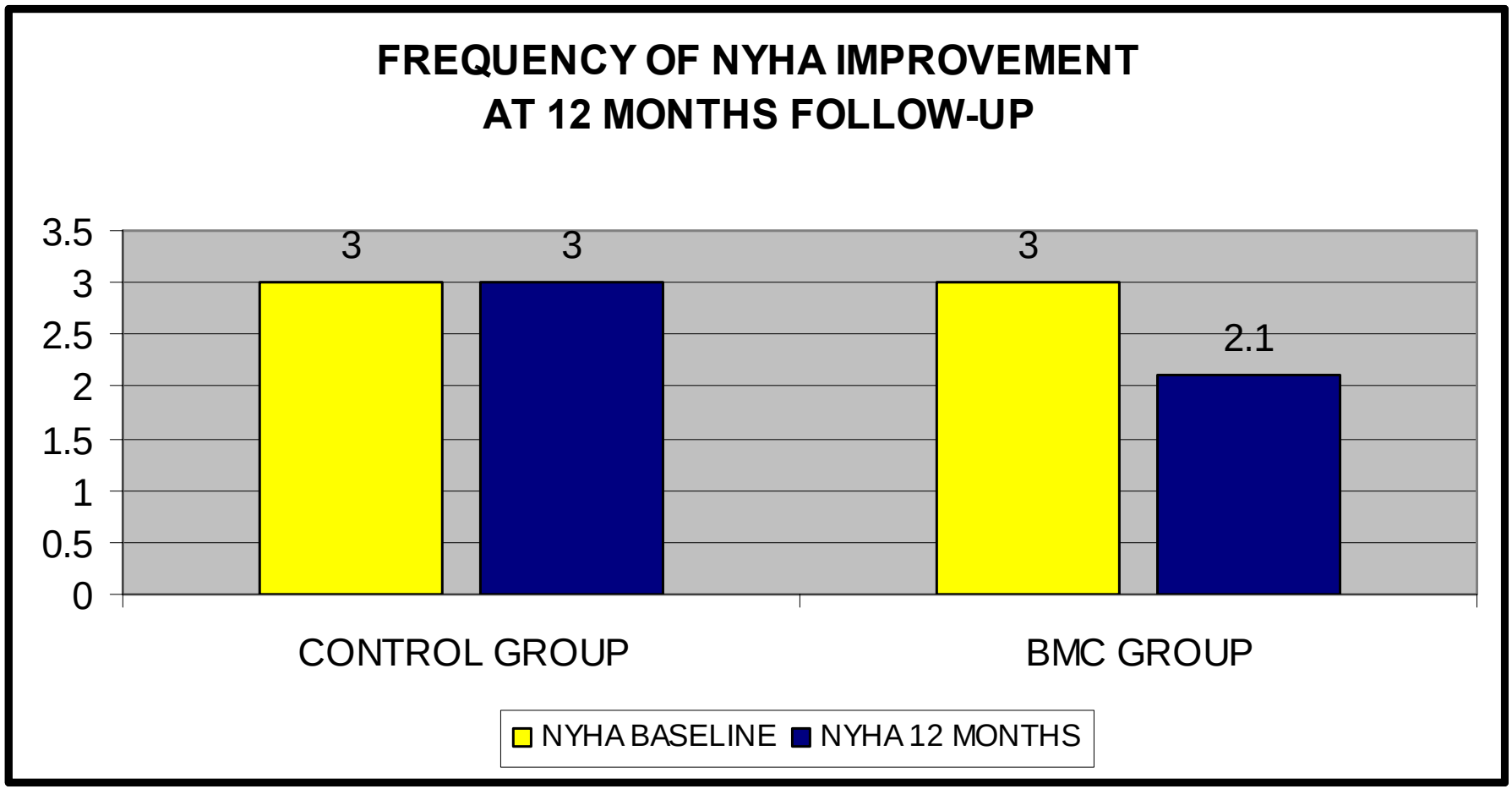
Improvement of NYHA Control Group vs. BMC Group



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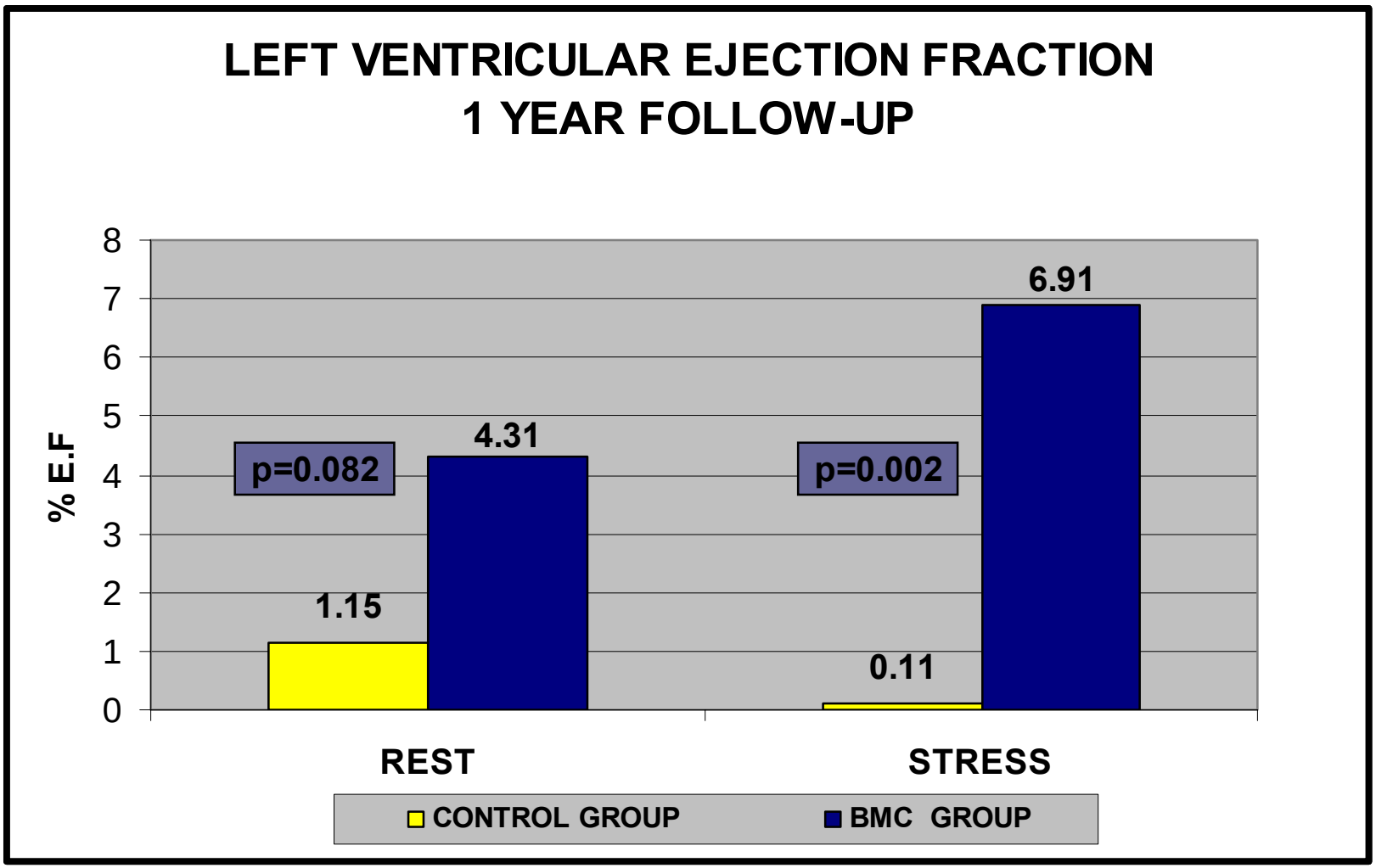
Improvement of LVEF Control Group vs. BMC Group



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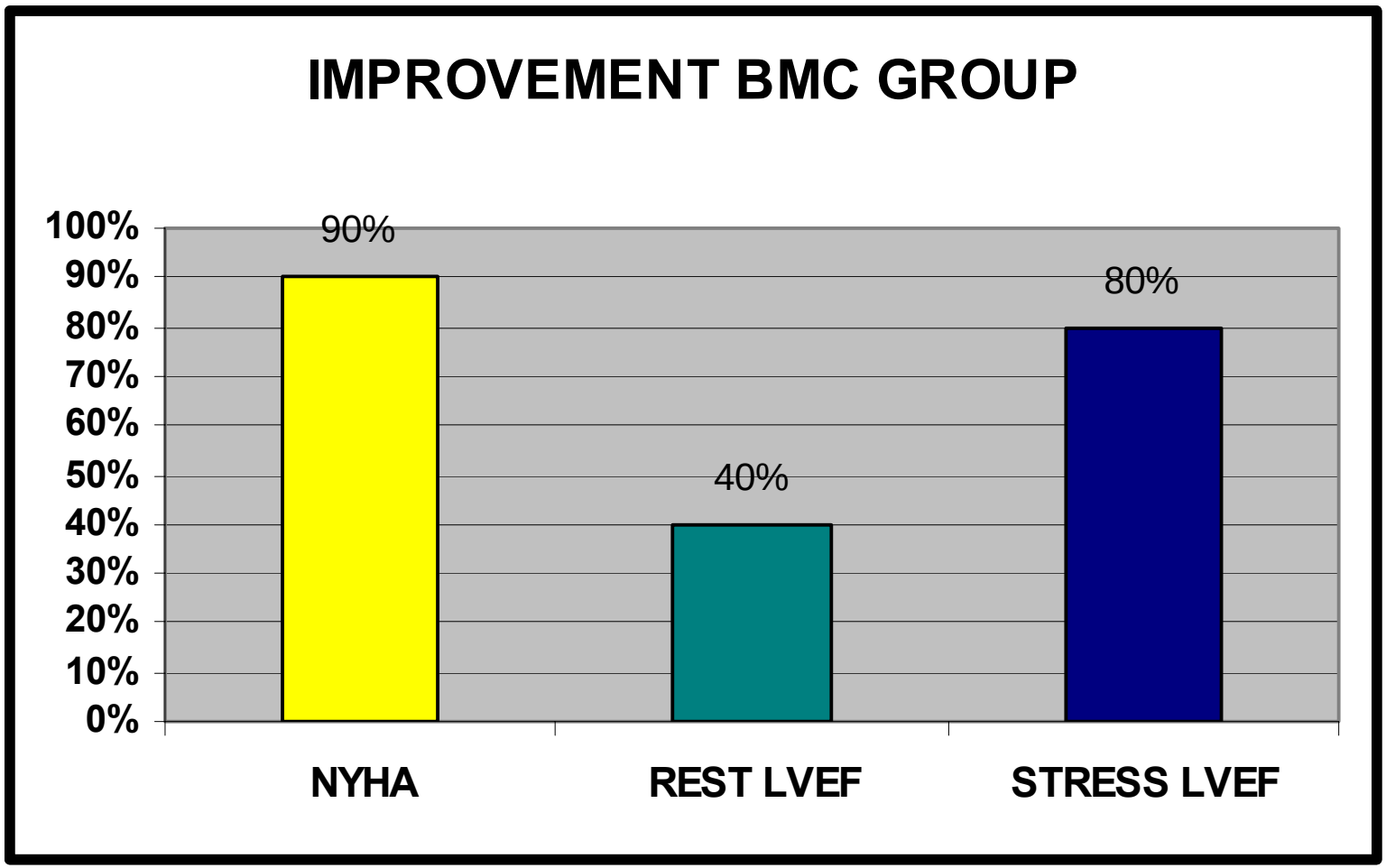
NYHA and Rest - Stress LVEF



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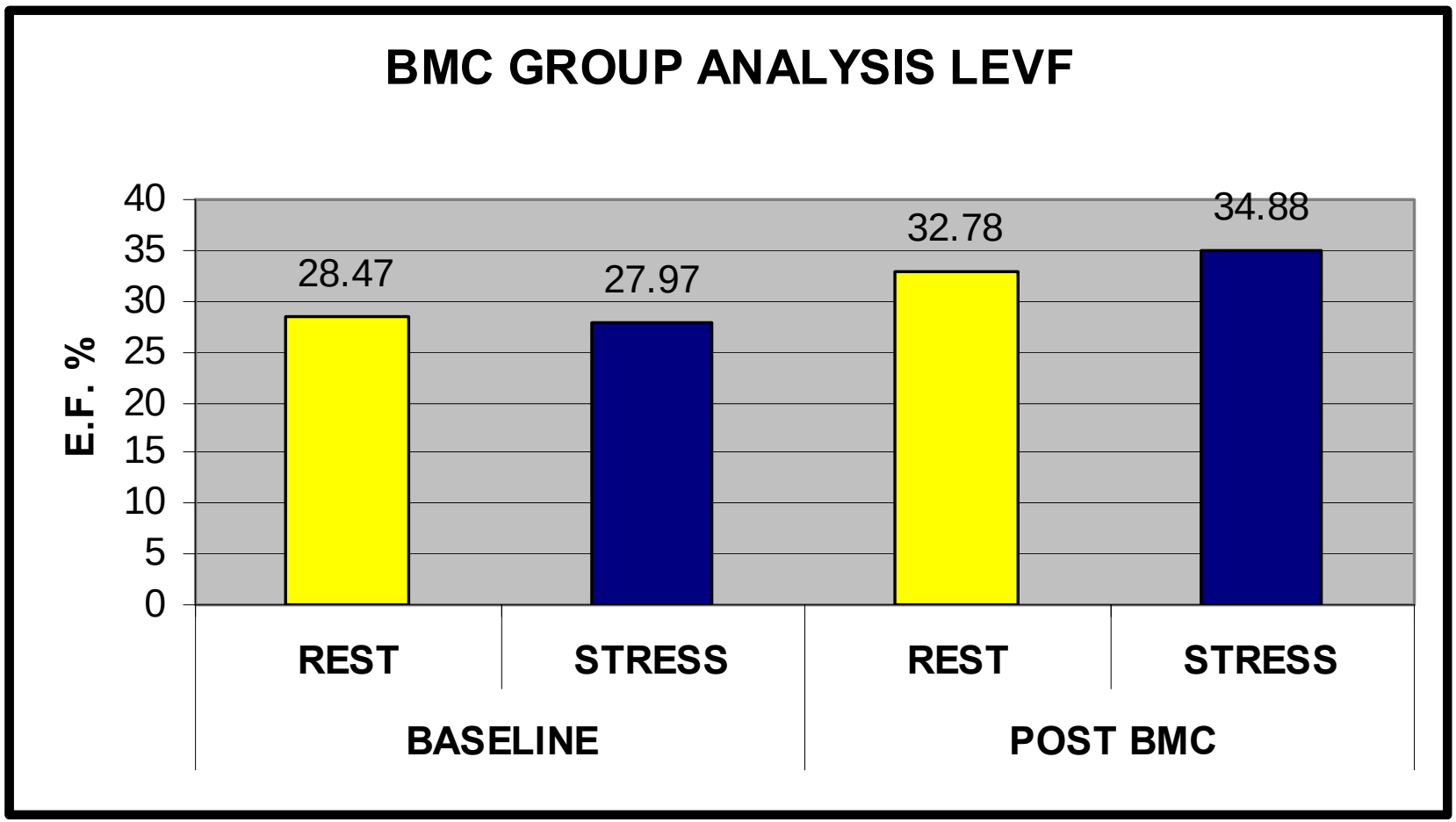
Basal and 1 year follow-up



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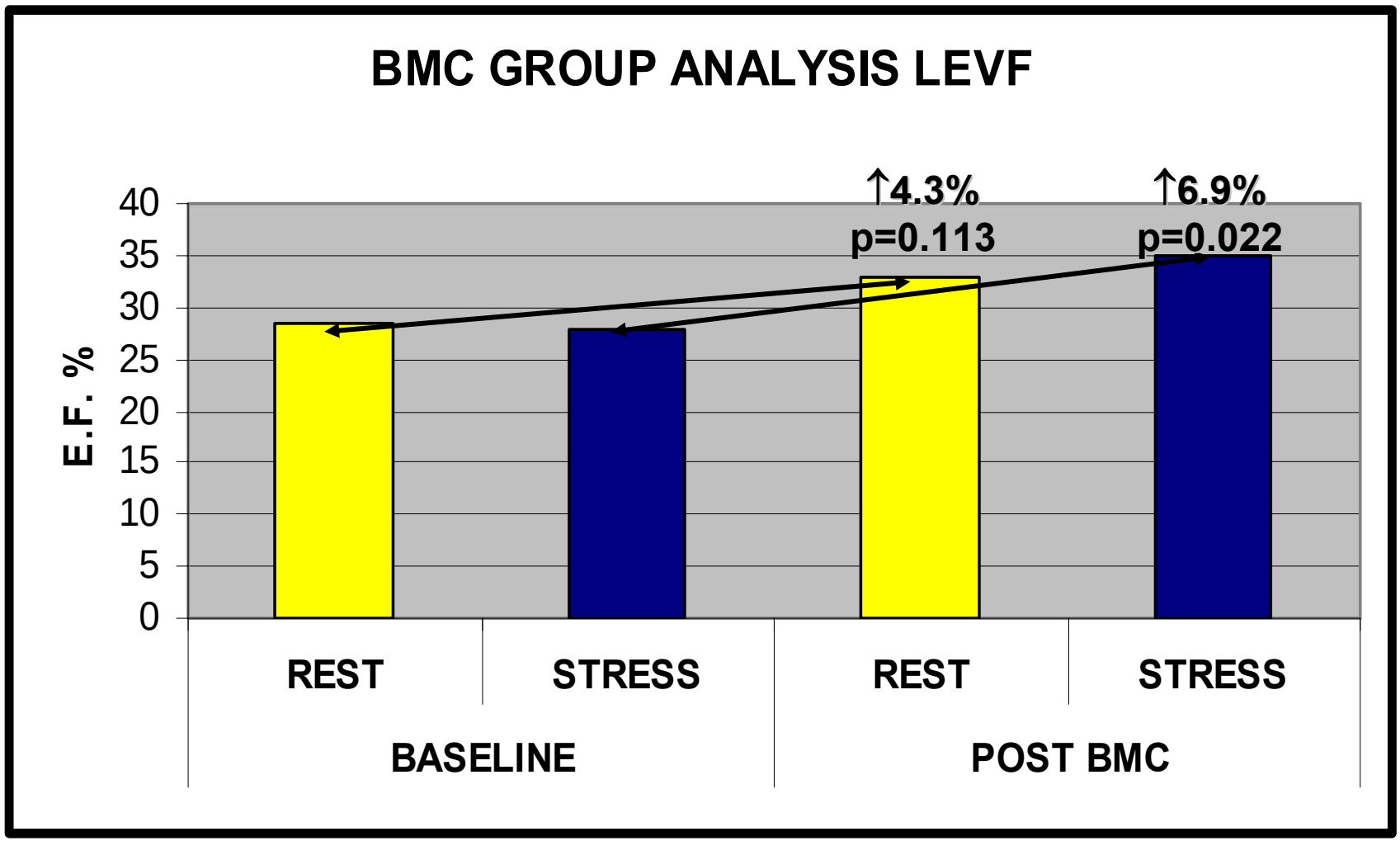

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Characteristics of patients BMC Group 1 year Follow-up

Patient Number	Age	NYHA		End Diastolic Volume (ml)		End Systolic Volume (ml)		Left Ventricular Ejection Fraction (%)		
		Baseline	1 year	Baseline	1 year	Baseline	1 year	Baseline	1 year	STRESS Improvement
1	68	3	2	160	157	126	110	21.3	29.9	**8.7**
2	68	3	2	213	204	180	145	15.5	28.9	**13.4**
3	41	3	2	306	346	248	256	19.0	26.0	**7.1**
4	55	3	2	247	191	162	117	34.4	38.7	**4.3**
5	81	3	3	94	92	64	62	31.9	32.6	**0.7**
6	67	3	2	125	125	83	77	33.6	38.4	**4.8**
7	80	3	2	178	171	120	104	32.6	39.2	**6.6**
8	69	3	2	224	265	157	152	29.9	42.6	**12.7**
9	81	3	2	207	205	145	125	30.0	39.0	**9.1**
10	48	3	2	174	180	119	120	31.6	33.3	**1.7**
Mean ± SD	65.9 ±13.68	3 ±0.0	2.1 ±0.32	192.8 ±60.87	193.6 ±71.21	140.4 ±51.77	126.8 ±53.0	27.97 ±6.78	34.88 ±5.47	**6.91 ±4.23**

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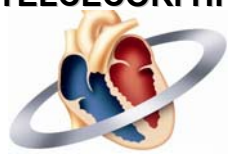

Results

- There were no complications in the procedure.
- There were no enzyme elevations and also no arrhythmias were detected.
- NYHA Class Improvement in 90% in the BMC.
- Rest LVEF Increased 4.3% in the BMC 4 of 10.
- Stress LVEF Increased 6.9% in the BMC 8 of 10.
- After one year follow-up the rest LVEF did not find statistical difference, but stress LVEF did.

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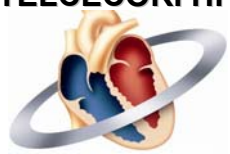
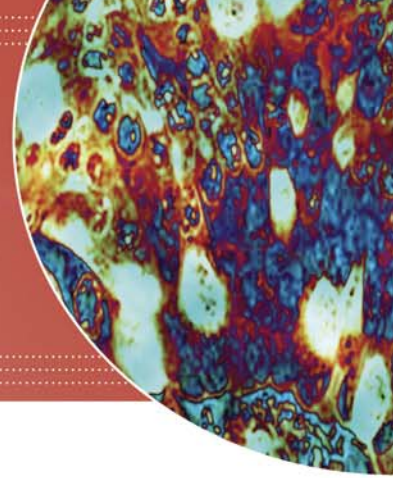


Conclusions

1. Infusion of progenitor cell into the coronary vein is safe and feasible in patients with left ventricular dysfunction.

2. BMC led to significant improvement in symptoms, functional capacity and the stress LVEF may improve even in patients without improved resting LVEF and also the stress LVEF was accompanied by improved functional status.

3. Our study showed that Assessment of resting function may not be the ideal end point to evaluate successful cell infusion. And may underestimate the benefit of cell therapy.



THANK YOU

Jorge Tuma M.D.

Lima – Perú