



## Higher Resting Heart Rate is Associated with Metabolic Syndrome and Lower Ejection Fraction in Patients With Diabetes and Known Coronary Artery Disease in Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) Trial

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### Introduction

- Neuroadrenergic status affects key regulatory mechanisms of cardiovascular as well as metabolic function.
- Both Metabolic Syndrome (Met S) and the presence of a high resting heart rate have been shown to be associated with increased cardiovascular events.
- However, the relation between Met S and resting heart rate is unknown.

### Methods

- We evaluated 2252 patients in Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) trial.
- All patients had Type 2 Diabetes and coronary artery disease (CAD) and were randomized to early revascularization and aggressive medical therapy versus aggressive medical therapy alone for CAD and to insulin-sensitizing versus insulin-providing treatments for diabetes.
- The ATP III definition of Met S was used. Since all patients had Type 2 Diabetes Met S was defined as presence of  $\geq 2$  of the following risk factors (RF)
  1. Waist circumference  
Men  $>102$  cm ; Women  $>88$  cm
  2. Triglycerides  $\geq 150$  mg/dL
  3. HDL cholesterol  
Men  $< 40$  mg/dL; Women  $< 50$  mg/dL
  4. Blood pressure  $\geq 130/\geq 85$  mm Hg
- Linear regression model adjusted for age, sex, use of beta blockers, exercise and LDL levels was used to evaluate the relation of Met S and its RFs to resting heart rate as measured on the 12 lead ECG.
- The relationship between heart rate and ventricular function as measured by left ventricular ejection fraction (LVEF) was also evaluated using linear regression adjusting for age, gender, LDL, beta blockers, exercise, and prior revascularization.

### Results

- In BARI 2D, 90.8% of the participants had the Met S. The mean heart rate was  $68.3 \pm 12.5$  beats per minute. The heart rate was higher ( $p < 0.001$  for trend) with increasing number of risk factors for Met S.

### Results

Baseline Characteristics according to Heart Rate ( N=2293)	Heart Rate < 78 N=1811	Heart Rate $\geq 78$ N=482	P-value
Age in years, mean	62.6	61.4	$<0.05$
Female, %	28.0	35.7	0.001
Male, %	72.0	64.3	
Sedentary, %	21.4	24.1	NS
Current smoker, %	11.7	14.5	0.09
Diabetes duration (years) mean	10.8	11.3	NS
HbA1c, mean	7.67	8.13	0.0001
History of MI, %	31.9	32.1	NS
Hypertension requiring treatment, %	82.5	82.2	NS
Hypercholesterolemia requiring treatment, %	83.3	76.1	$<0.001$
BMI in $\text{kg/m}^2$ , mean	31.5	32.7	$<0.001$

Total for Met S analyses (n=2252)	Heart Rate mean, SD	P-value
Metabolic Syndrome (n= 2045 )	$68.5 \pm 12.6$	
No Metabolic Syndrome (n=207 )	$65.5 \pm 11.8$	$<0.001$
According to number of RFs		
0 or 1 RF (n=207)	$65.5 \pm 11.8$	
2 RFs (n=536)	$67.1 \pm 12.6$	
3 RFs (n=778)	$68.6 \pm 12.6$	
4 RFs (n=731)	$69.6 \pm 12.5$	$<0.001$

Total for LVEF analyses (n=2168)	Heart Rate mean, SD	P-value
LVEF $< 50\%$ (n= 379)	$70.1 \pm 13.6$	
LVEF $\geq 50\%$ (n= 1839 )	$68.0 \pm 12.4$	0.005
According to LVEF Categories		
$< 35\%$ (n=66)	$72.6 \pm 13.3$	
35-49% (n=299)	$69.6 \pm 13.6$	
$\geq 50-60\%$ (n=1158)	$68.1 \pm 12.3$	
$> 60\%$ (n=645)	$67.8 \pm 12.5$	0.008

### Results

- Multiple linear regression analyses demonstrated that as compared to individuals without Met S, the heart rate was significantly higher in participants with Met S (regression coefficient: 3.0,  $p=0.001$ ). Participants with 2 RFs had adjusted regression coefficient of 1.5 ( $p=0.13$ ), presence of 3 RF regression coefficient of 3.0 ( $p=0.002$ ) and participants with all 4 RF had a regression coefficient of 4.1 ( $p < 0.001$ ).
- The heart rate was significantly higher in participants with lower EF ( $p < 0.001$  for trend). Compared to participants with EF of 60% participants with EF  $< 35\%$  had adjusted regression coefficient of 5.5 ( $p < 0.001$ ).

### Conclusion

- In patients with type 2 diabetes and confirmed CAD the presence of Metabolic Syndrome is associated with higher resting heart rate.
- Higher resting rate is associated with ventricular dysfunction.
- Higher heart rate due to sympathetic overactivity is a manifestation of autonomic dysfunction and may be one way by which Met S imparts higher risk for cardiovascular disease.
- Higher resting heart rate in diabetic patients with CAD identifies a subgroup in whom additional secondary preventive strategies may be necessary.

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