



# The Association of Brachial Artery Flow-Mediated Dilatation and Long-Term Cardiovascular Events in Subjects without Heart Disease

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האיגוד הישראלי לכירורגית לב וחזה  
THE ISRAEL SOCIETY OF CARDIOTHORACIC SURGERY

האיגוד הקרדיולוגי בישראל  
ISRAEL HEART SOCIETY



The 60<sup>th</sup> International Conference of the Israel Heart Society  
in association with the Israel Society of Cardiothoracic Surgery

22-23 April 2013, ICC International Convention Center, Jerusalem

**Disclosure Information:  
No relationships exist related  
to this presentation by all authors.**

# Aim of the Study

To find out the long-term association of peripheral vascular endothelial function and clinical outcome in healthy subjects with no apparent heart disease.

# Study Population

- We prospectively assessed flow-mediated dilation (FMD) in 618 consecutive healthy subjects without known coronary artery disease (CAD) who were examined in our endothelial function laboratory:
  - 387 (63%) men, 231 (37%) women
  - Mean age  $54 \pm 11$  years (range: 17-81)

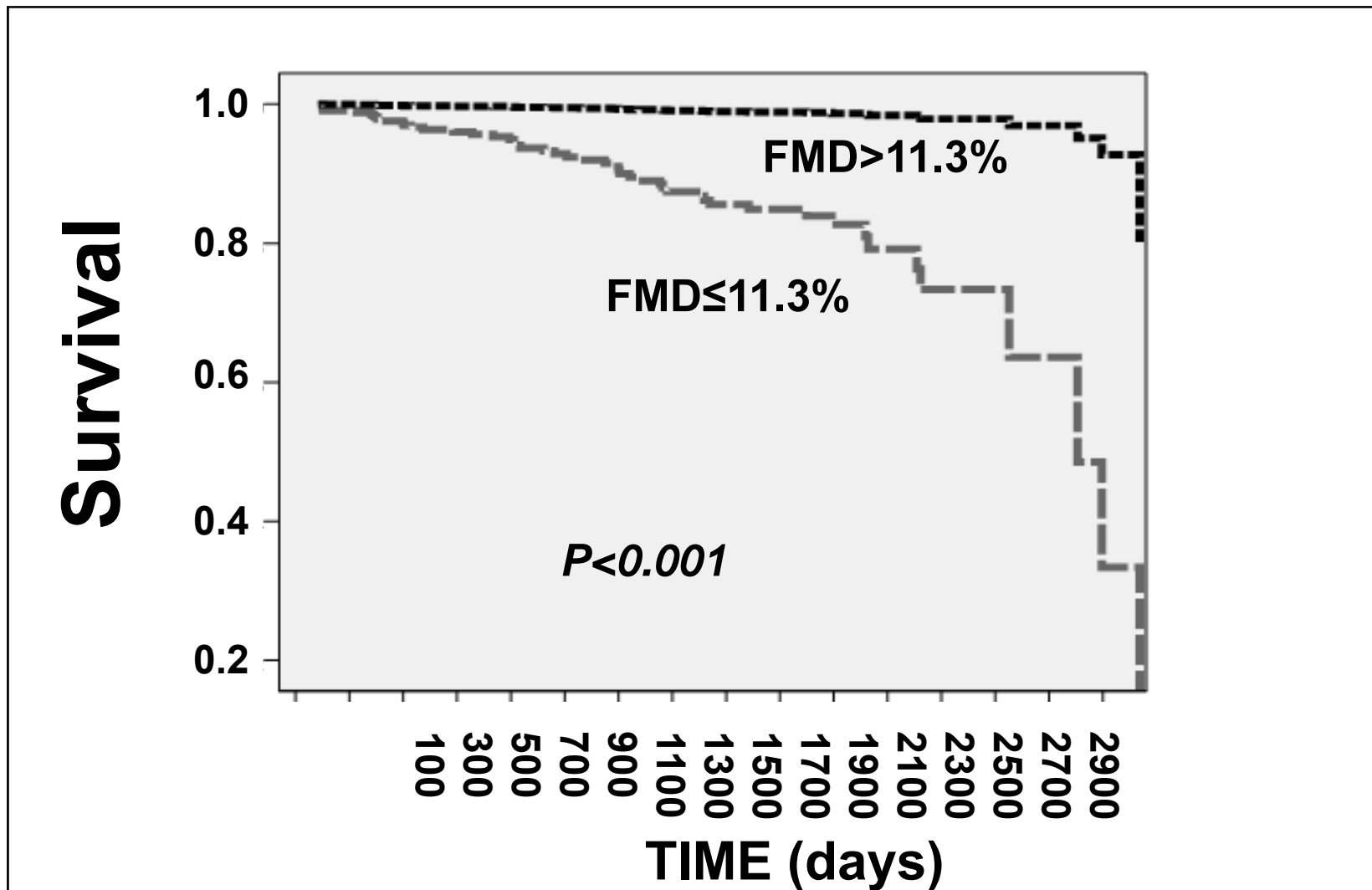
# Long-Term Follow Up

All patients were followed by telephone contact after a mean of  $4.6 \pm 1.8$  years for combined adverse cardiovascular endpoints, including all-cause mortality, non-fatal myocardial infarction, hospitalization for heart failure or angina pectoris, stroke, coronary artery bypass grafting and percutaneous coronary interventions.

# Cardiovascular Events During Follow Up

Event	FMD $\leq$ 11.3% N=309	FMD $>$ 11.3% N=309	P
Mortality	6 (1.9%)	1 (0.3%)	0.512
Non fatal MI	5 (1.6%)	1 (0.3%)	0.196
CVA	4 (1.2%)	1 (0.3%)	0.065
CHF	1 (0.3%)	0 (0.0%)	0.323
Angina pectoris	19 (6.1%)	0 (0.0%)	0.206
CABG	3 (0.9%)	1 (0.3%)	0.130
PCI	9 (2.9%)	0 (0.0%)	0.153
<b>All events</b>	<b>47 (15.2%)</b>	<b>4 (1.2%)</b>	<b>0.0001</b>

# Long-Term Outcome



**N=618**

A Kaplan-Meier survival curve showing survival until first composite adverse cardiovascular endpoint (all-cause mortality, non-fatal MI, CHF or angina pectoris hospitalization, CVA, CABG and PCI) in subjects with flow-mediated dilation (FMD) > and ≤ median value of 11.3%, after controlling for traditional risk factors (age, sex, lipoproteins, diabetes, hypertension, BMI).

# Multivariate Analysis of CAD Risk Factors and Long-Term Outcome

Risk factors for CAD	OR	95% C.I.		P
		Lower	Upper	
Age	1.00	0.994	1.014	0.404
Male gender	0.37	0.164	0.854	0.020
Body mass index	0.95	0.887	1.021	0.166
Hypertension	0.84	0.339	2.097	0.713
Hyperlipidemia	0.74	0.305	1.804	0.509
Smoking	1.83	0.630	5.339	0.266
Diabetes mellitus	1.70	0.491	5.939	0.400
Family history	0.24	0.778	1.783	0.176
<b>Median FMD=11.3%</b>	<b>2.93</b>	<b>1.285</b>	<b>6.688</b>	<b>0.003</b>





# Conclusion



**Brachial artery median FMD independently predicts long-term adverse cardiovascular events in healthy subjects, in addition to those derived from traditional risk factor assessment.**

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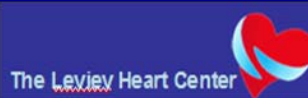
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The Clinical Research Unit



Leviev Heart Center, Sheba Medical Center



# CAD Risk Factors and Medications

Parameter	FMD≤11.3% N=309	FMD>11.3% N=309	P
<b>Males</b>	<b>198 (64%)</b>	<b>188 (61%)</b>	<b>0.454</b>
<b>Hypertension</b>	<b>108 (35%)</b>	<b>83 (27%)</b>	<b>.0045</b>
Hyperlipidemia	130 (42%)	142 (46%)	0.373
Current smokers	43 (14%)	43 (14%)	0.907
Type 2 diabetes	31 (10%)	34 (11%)	0.690
<b>Family history</b>	<b>105 (34%)</b>	<b>121 (39%)</b>	<b>.0241</b>
Aspirin	77 (25%)	65 (21%)	0.124
<b>Statin</b>	<b>80 (26%)</b>	<b>77 (25%)</b>	<b>0.854</b>
Long-acting nitrates	9 (3%)	6 (2%)	0.612
<b>Calcium channel blockers</b>	<b>37 (12%)</b>	<b>22 (7%)</b>	<b>0.040</b>
Furosemide (Fusid)	15 (5%)	12 (4%)	0.844
Spirinolactone	2 (0.6%)	3 (0.9%)	0.653
<b>ACE inhibitors</b>	<b>46 (15%)</b>	<b>25 (8%)</b>	<b>0.005</b>
<b>Beta blockers</b>	<b>53 (17%)</b>	<b>43 (14%)</b>	<b>0.435</b>
Multivitamines	15 (5%)	22 (7%)	0.303

# Age, Lipoproteins and Blood Pressure

Parameter	FMD $\leq$ 11.3% N=309	FMD $>$ 11.3 N=309	P
Age (years)	55 $\pm$ 11	54 $\pm$ 11	0.092
Body mass index (kg/m <sup>2</sup> )	30 $\pm$ 5	28 $\pm$ 5	.0627
Fasting blood glucose (mg/dl)	94 $\pm$ 14	98 $\pm$ 15	0.436
Total cholesterol (mg/dl)	207 $\pm$ 42	210 $\pm$ 47	0.552
LDL cholesterol (mg/dl)	126 $\pm$ 32	129 $\pm$ 37	0.579
Triglycerides (mg/dl)	145 $\pm$ 81	151 $\pm$ 75	0.597
HDL cholesterol (mg/dl)	48 $\pm$ 12	51 $\pm$ 14	0.086
Homocysteine ( $\mu$ mol/l)	13 $\pm$ 5	13 $\pm$ 3	0.561
Systolic blood pressure (mmHg)	138 $\pm$ 22	138 $\pm$ 21	0.799
Diastolic blood pressure (mmHg)	81 $\pm$ 10	80 $\pm$ 11	0.419
Heart rate (beats/min)	66 $\pm$ 10	68 $\pm$ 11	0.137
hs-CRP (mg/l)	2.8 $\pm$ 2.1	3.8 $\pm$ 2.1	0.558
Framingham risk score (% risk/10 years)	7.3	7.2	0.786
Baseline brachial artery diameter (mm)	6.0 $\pm$ 0.9	5.2 $\pm$ 0.9	<0.001
%NTG	16.8 $\pm$ 4.3	17.2 $\pm$ 4.0	0.759