The Relationship Between Chronic Kidney Disease And Myocardial Perfusion Imaging

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The prevalence of CKD in the US adult population is **11%** (19.2 million).

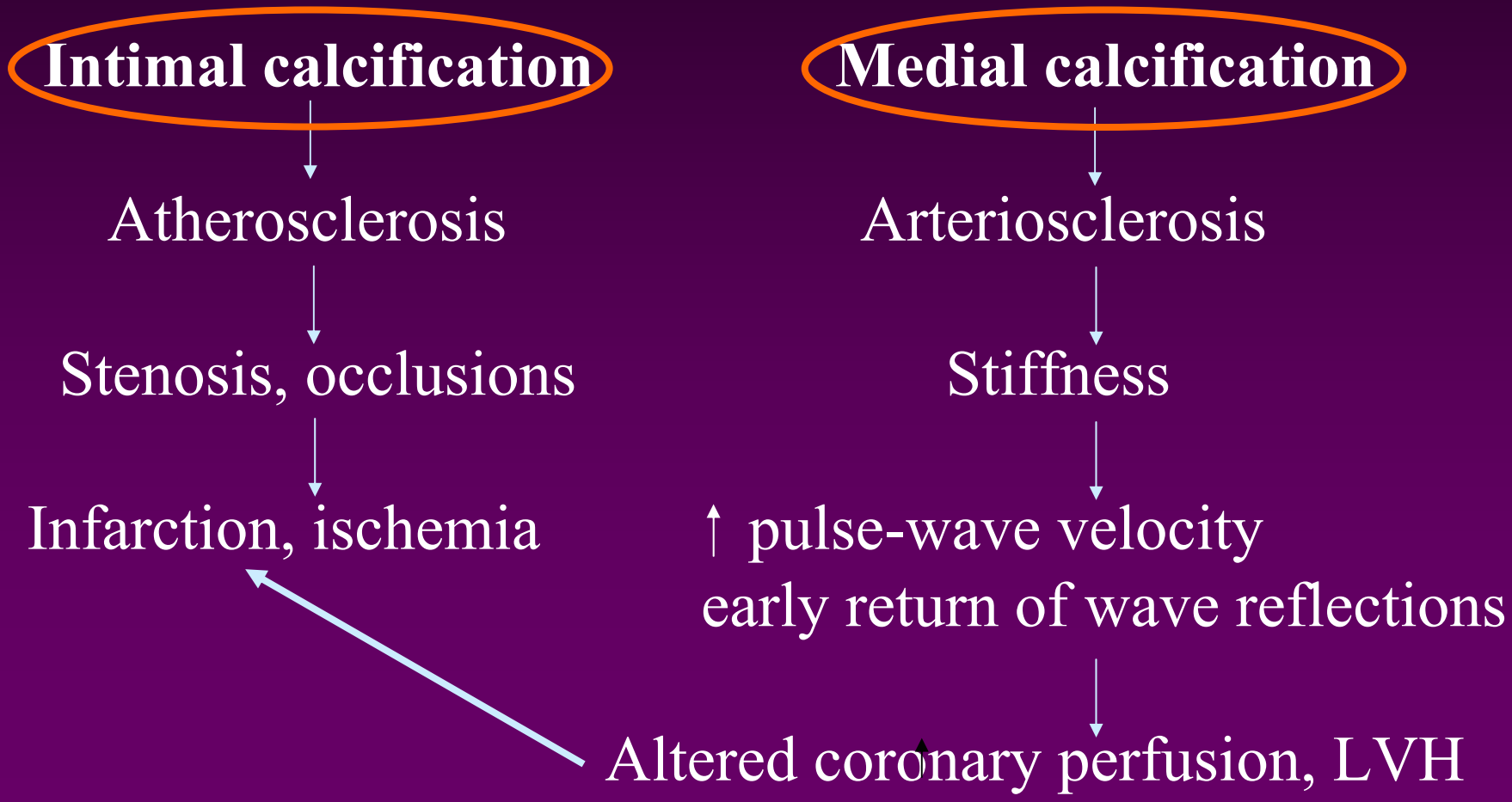
Stage 1	Proteinuria GFR ≥90 ml/min	5.9 million (3.3%)
Stage 2	GFR 60-89 ml/min	5.3 million (3.0%)
Stage 3	GFR 30-59 ml/min	7.6 million (4.3%)
Stage 4	GFR 15-29 ml/min	0.4 million (0.2%)
Stage 5	GFR<15 ml/min	0.3 million (0.2%)

Aside from hypertension and diabetes, age is a key predictor of CKD, and 11% of individuals older than 65 years without hypertension or diabetes had stage 3 or worse

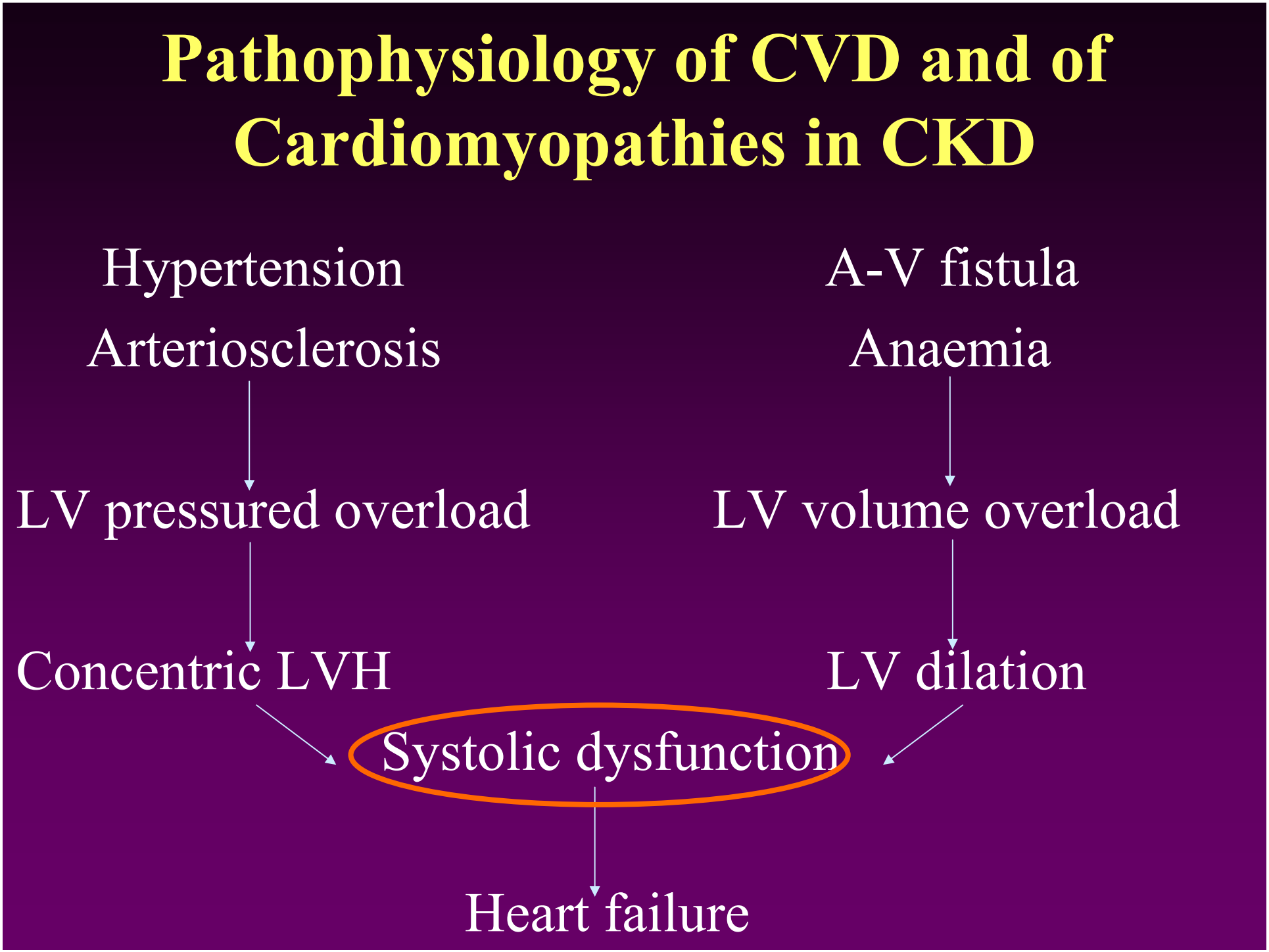
Am J Kidney Dis 41:1-12

Pathophysiology of CVD and of Cardiomyopathies in CKD

Arterial calcification



Pathophysiology of CVD and of Cardiomyopathies in CKD

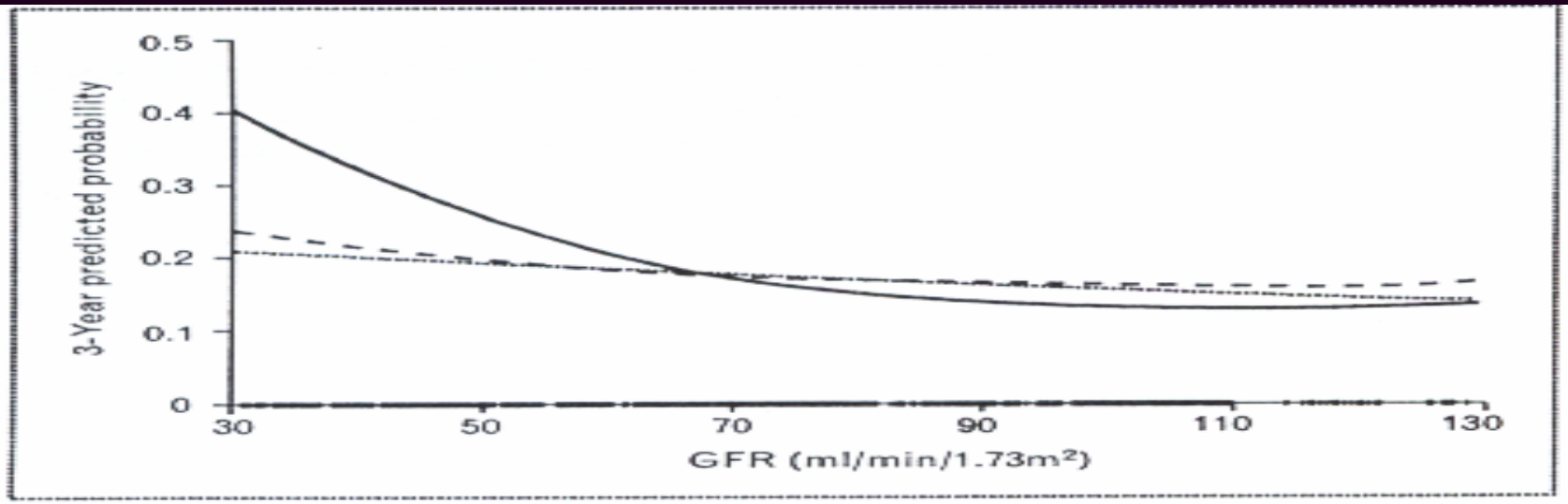


Coronary calcification (CAC) is associated with coronary plaque burden in the gral population.

	Non-diabetic non-CKD	Non-diabetic CKD	Diabetic non-CKD	Diabetic CKD
High CAC (>400)	1.4%	3.5%	4.7%	55.7%

Dallas Heart Study J Am Soc Nephrol 2005;16:507-513

CV Events and GFR



GFR, Glomerular filtration rate. ———— Unadjusted (GFR linear); - - - - - - - - adjusted (GFR linear); — — — — adjusted (GFR with cubic splines). Reprinted with permission from Manjunath *et al.* [20].

CV events occur more frequent than renal events in CKD.
50% of CKD pts die of CV cause.
CV mortality rate 15 to 30 times higher than the age-adjusted CV mortality rate in the general population.

Noninvasive Cardiac Risk Stratification of Diabetic and Nondiabetic Uremic Renal Allograft Candidates Using Dipyridamole–Thallium-201 Imaging and Radionuclide Ventriculography

Kenneth A. Brown, MD, Jeffrey Rimmer, MD, and Carl Haisch, MD

0041-1337/90/4901-0100$02.00/0
TRANSPLANTATION

Vol. 49, 100–103, No. 1, January 1990
Printed in U.S.A.

INEFFECTIVENESS OF DIPYRIDAMOLE SPECT THALLIUM IMAGING AS A SCREENING TECHNIQUE FOR CORONARY ARTERY DISEASE IN PATIENTS WITH END-STAGE RENAL FAILURE[1]

THOMAS H. MARWICK,[2] DONALD R. STEINMULLER, DONALD A. UNDERWOOD, ROBERT E. HOBBS, RAYMUNDO T. GO, CLAUDIA SWIFT, AND WILLIAM E. BRAUN

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- Cardiovascular events increased as the glomerular filtration rate (GFR) declined.

Go AS, et al. N Engl J Med (2004) 351, pp. 1296-305.

- Early diagnosis of CAD by myocardial perfusion imaging (MPI), might have an important impact on long-term outcomes.

Prognostic Value of Stress Tl^{-201} Myocardial Perfusion SPECT Imaging in Patients With Decreased Glomerular Filtration Rate

Shay Livschitz, MD; Knobler H, MD; Zurnitski T, MD; Vered S, MA*, Oettinger M, MD; Rosa Levy, MS; David Faraggi, PHD*; Abraham Caspi, MD.

Kaplan Medical Center, Rehovot;
Haifa University, Haifa*, Israel.

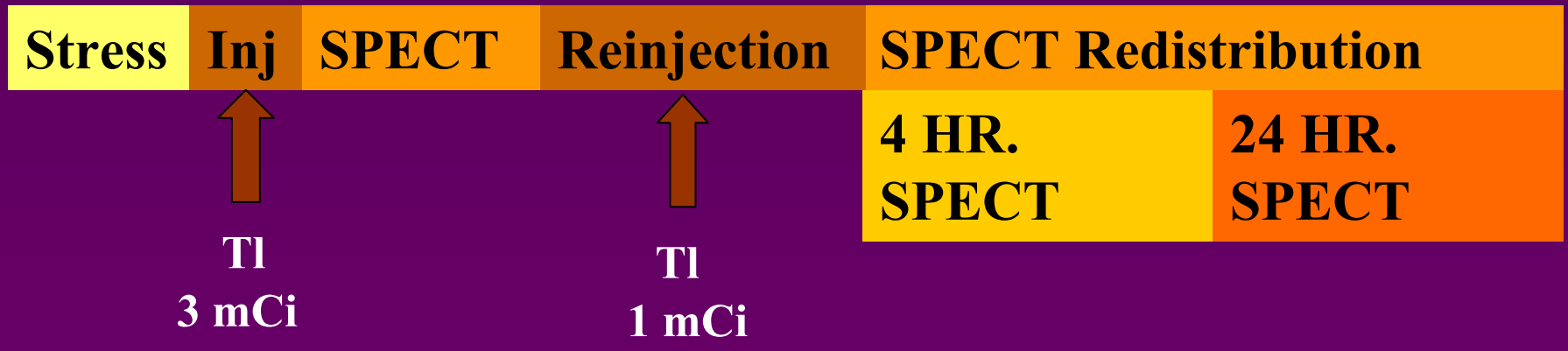
Material and Methods

Patient Selection

137 pts with an estimated GFR of less than 60 ml/min (mean eGFR was 26.3±16.4 ml/min).

Cockroft-Gault formula: 140-age (years) X weight (kg)/ 72 X serum creatinine concentration (mg/dl) X 0.85 if female

Stress-rest Tl^{-201} SPECT myocardial perfusion study:

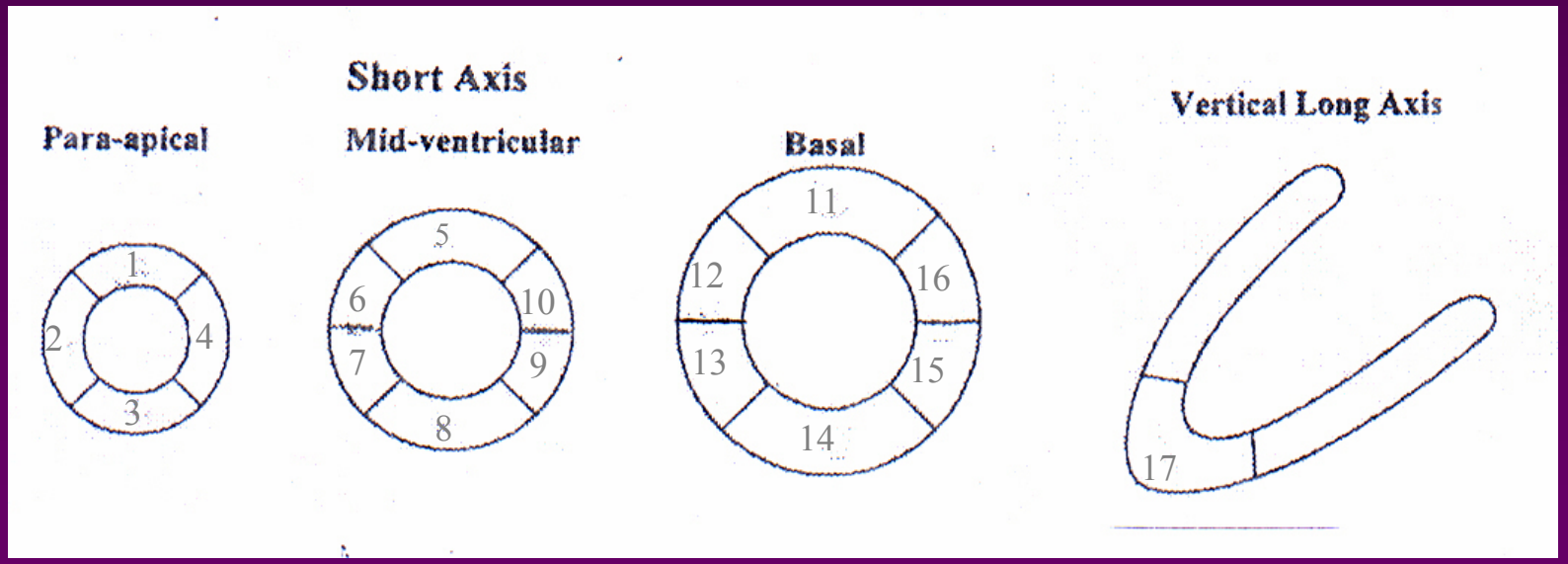


Myocardial Perfusion Analysis

Semiquantitative Visual Analysis:

- 17 segments, 5 scale scoring system: 0= normal, 4= no uptake.

5 scale scoring system: 0= normal, 1=mild, 2=moderate, 3=severe reduced 4= no uptake.



Material and Methods

MPI visual analysis:

- **Normal MPI** = 42 (31%)
- **Abnormal MPI** = 95 (69%)
  - Ischemic pattern = 49 (51%)
  - MI pattern = 14 (15%)
  - Combined pattern = 32 (34%)

Material and Methods

Follow-up : (18 months)

- **Hard events:** Cardiac death or
  Myocardial infarction (n= 22)
- **Soft events:** Coronary revascularization or
  Unstable angina (n= 25)

Patient Classification

- **Event group** = 47 (34%.)
- **Non-event group** = 90 (66%)

Results: Clinical Data

	Event Group n= 47	Non-event Group n= 90	P value
Age, mean ± SD	70.5 ± 9.3	65.8 ± 9.4	0.006
Gender, male*	37 (79)	63 (70)	NS
Hx of CAD ,*	33 (70)	35 (39)	0.0005
Hyperlipidemia,*	22(47)	36 (40)	NS
DM,*	22 (47)	39 (43)	NS
HTN,*	41 (87)	67 (74)	NS
PVD,*	13 (28)	15 (17)	NS
Smoking,*	5 (11)	10 (11)	NS

* Expressed in number of pts. and percentage (%).

Results: Stress ECG and Myocardial Perfusion Imaging

	Event Group n= 47	Non-event Group n= 90	P value
Normal Stress ECG ,*	38 (81)	88 (98)	0.0016
Ischemic Stress ECG,*	4 (9)	0	
Non-diag. Stress ECG,*	5 (10)	2 (2)	
LV TID*	10 (21)	11(12)	0.04
LV enlargement*	10 (21)	17 (19)	
Normal lung uptake	14 (41)	42 (61)	0.07
Severe lung uptake	5 (15)	3 (4)	

* Expressed as number of pts. and percentage (%)

Results: Stress-Rest Tl ^{201} Myocardial Perfusion Imaging

	Event Group n= 47	Non-event Group n= 90	P value
Normal MPI ,*	2 (4)	40 (44)	
Abnormal MPI,*	45 (96)	50 (56)	
Ischemic-MPI pattern	22 (47)	27 (30)	<0.0001
MI-MPI pattern	6 (13)	8 (9)	
Combined-MPI pattern	17 (36)	15 (17)	

* Expressed in number of pts. and percentage (%).

Positive predictive value = 47.4%

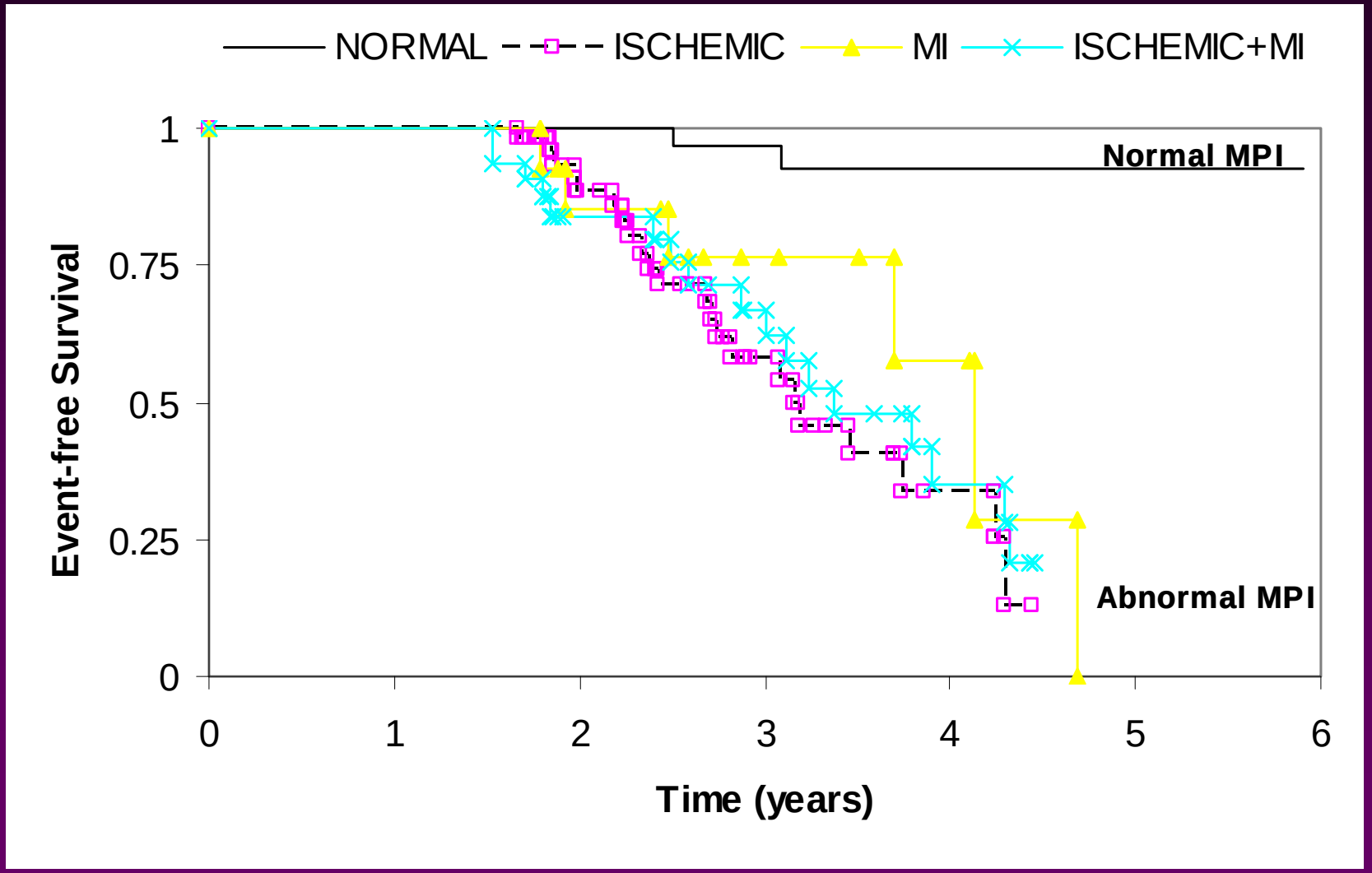
Negative predictive value = 95.2%

Myocardial Perfusion Imaging

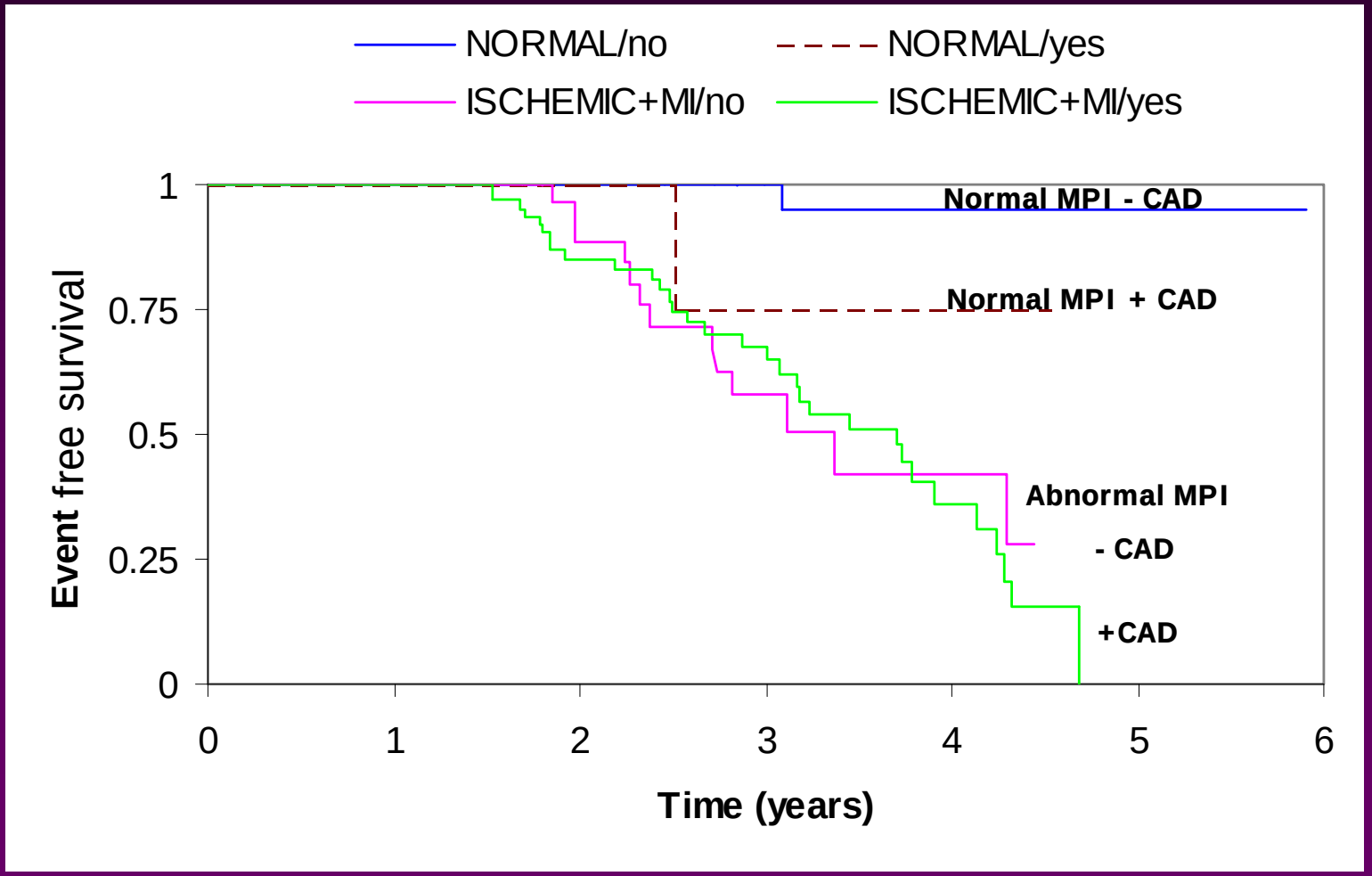
	Soft Event n= 25	Non-event n= 90	P value
Normal MPI ,*	2 (8)	40 (44)	0.0028
Ischemic-MPI pattern	11 (44)	27 (30)	
MI-MPI pattern	5 (20)	8 (9)	
Combined-MPI pattern	7 (28)	15 (17)	

	Hard Event n= 22	Non-event n= 90	P value
Normal MPI ,*	0	40 (44)	0.0012
Ischemic-MPI pattern	11 (50)	27 (30)	
MI-MPI pattern	1 (5)	8 (9)	
Combined-MPI pattern	10 (45)	15 (17)	

Kaplan-Meier Curves of Cardiac Event-free Survival in Stress-Rest Tl 201 SPECT MPI



Survival Curve of Tl ^{201} SPECT MPI for Total Cardiac Events and Previous History of CAD



Predictive Value of Myocardial Perfusion Single-Photon Emission Computed Tomography and the Impact of Renal Function on Cardiac Death

Abdul Hakeem, MD; Sabha Bhatti, MD; Kathryn Sullivan Dillie, MD, PhD; Jeffrey R. Cook, MD; Zainab Samad, MD; Michelle D. Roth-Cline, PhD; Su Min Chang, MD

Circulation **2008**;118:2540-2549

Objective

To determine the incremental prognostic value of MPI SPECT in the risk stratification of pts with varying degrees of renal dysfunction.

To study the impact of renal dysfunction on CV outcomes .

To determine whether renal dysfunction combined with SSS provides additional prognostic information superior to either marker alone.

Methods

Patient population

1652 consecutive pts referred for SPECT-MPI at the Memorial Veterans Hospital between 6-02 and 7-05.

Exclusions criteria:

acute renal failure

revascularization within 60 days of MPI

Chronic Kidney Disease: eGFR <60 mL .min. 1.73 m^2 (32% of pts)

Stress Protocols and Imaging Analysis

- Rest/stress Mibi SPECT MPI.
- Stress: symptom-limited treadmill test 32%
  adenosine 68%

- Standard 20-segment model
- SSS groups: normal <4
  mild 4 to 8
  moderate to severe >8
- Ischemia: SSS≥4 and SDS ≥2
- Scar: SSS≥4 and SDS<2

Patient Follow up and End Points

- Follow up for an average of 2.15±0.8 years
- Primary end point: cardiac death (CD)=114
- Secondary end point: all cause mortality (ACM)=217

  nonfatal MI (NFMI)= 73

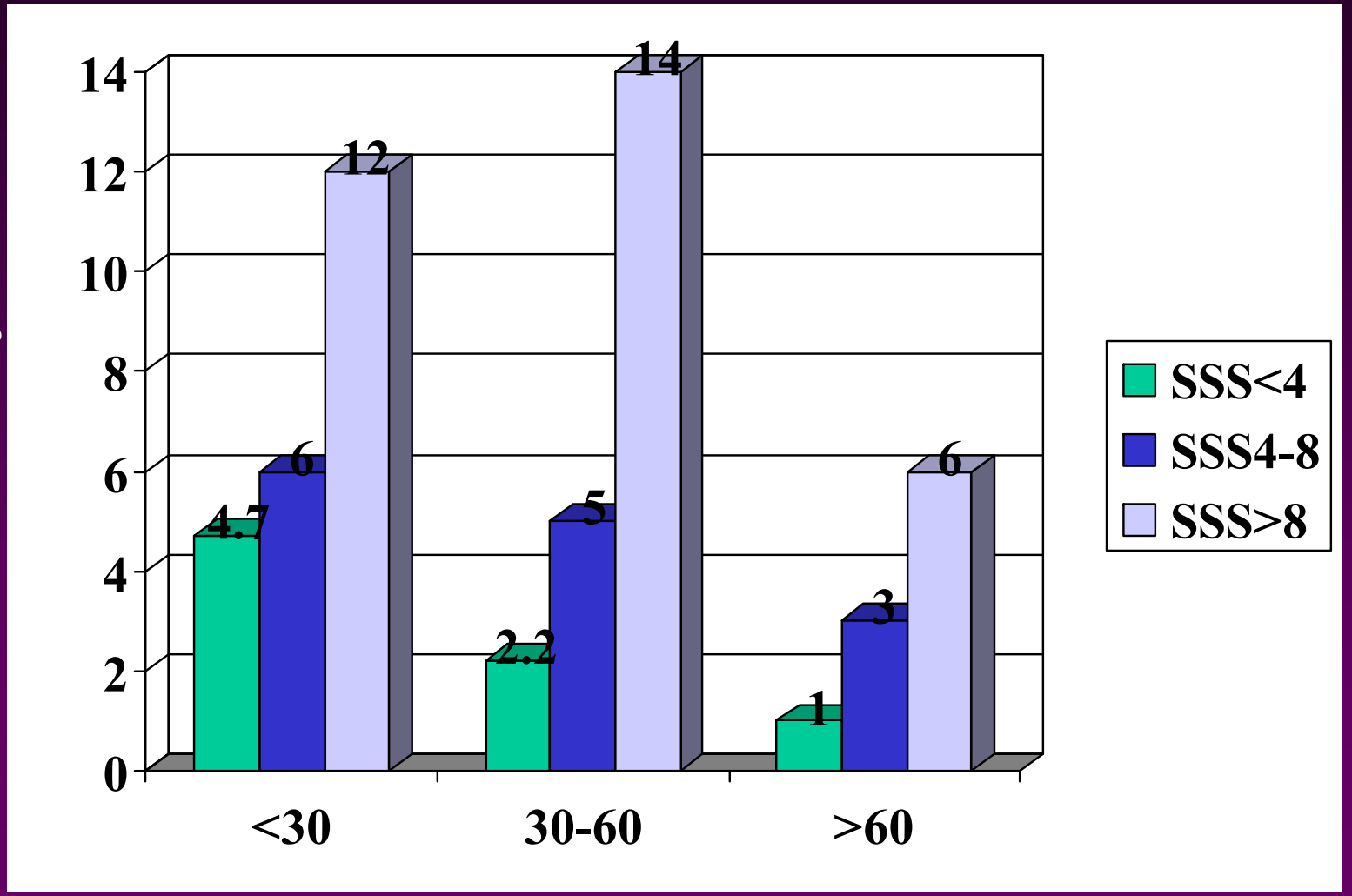
Unadjusted Events Rates

	eGFR >60mL NMPI	eGFR <60mL NMPI		eGFR >60mL AMPI	eGFR <60mL AMPI	
	Annual Rate	Annual Rate	*p*	Annual Rate	Annual Rate	*p*
CD	0.8%	2.7%	0.001	4%	9.5%	<0.0001
ACM	4%	6.2%	0.048	6.5%	12.5%	<0.0001

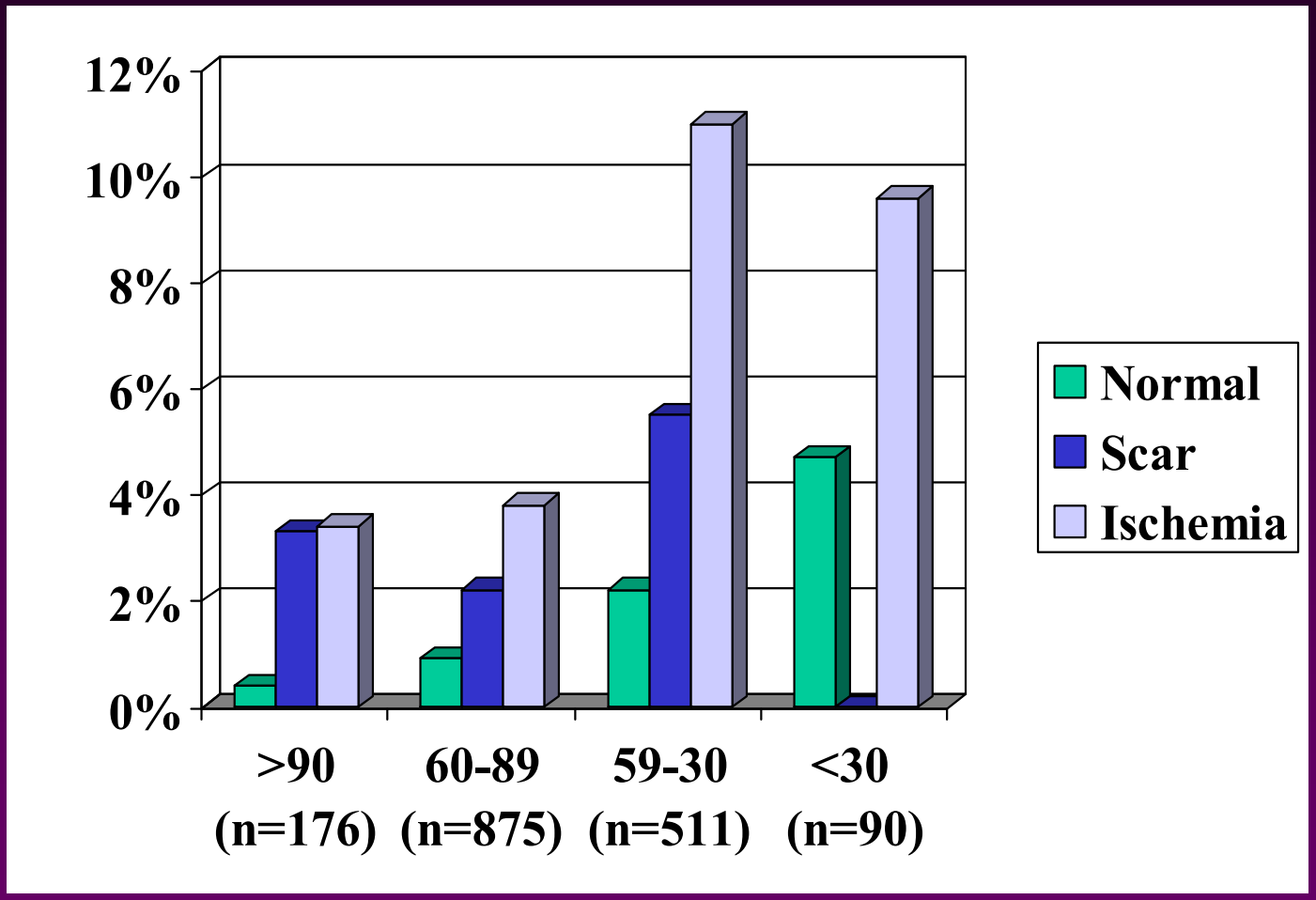
Patient Characteristics by Scan Defect and Kidney Function

Patient Characteristics	No Defect (n=988)			Defect (n=664)		
	eGFR >60 mL · min^{-1} · 1.73 m^{-2} (n=684)	eGFR <60 mL · min^{-1} · 1.73 m^{-2} (n=304)	*P*	eGFR >60 mL · min^{-1} · 1.73 m^{-2} (n=364)	eGFR <60 mL · min^{-1} · 1.73 m^{-2} (n=300)	*P*
Age, y	62±10	69±10	<0.0001	64±9	70±9	<0.0001
Males	98% (668)	93% (284)	0.001	99% (361)	98% (296)	0.71
Revascularization	22% (153)	21% (65)	0.73	48% (175)	46% (137)	0.54
Smoker	30% (204)	19% (57)	0.0003	30% (109)	22% (67)	0.027
Diabetes	29% (196)	45% (136)	<0.0001	37% (134)	46% (138)	0.017
Hypertension	73% (497)	81% (247)	0.0039	74% (270)	79% (238)	0.12
Hyperlipidemia	71% (486)	66% (200)	0.13	81% (292)	74% (221)	0.046
Known CAD	29% (198)	28% (84)	0.67	61% (221)	60% (181)	0.92
History of MI	11% (78)	12% (35)	0.96	32% (116)	29% (88)	0.48
LVEF ≤40%	4% (27)	9% (26)	0.003	33% (118)	40% (121)	0.034
BMI						
>25 kg/m^2	84% (572)	86% (260)	0.45	79% (288)	85% (254)	0.066
>30 kg/m^2	50% (344)	49% (149)	0.71	48% (175)	52% (155)	0.36
Medications						
ACEI/ARB	58% (363)	58% (179)	0.92	61% (229)	61% (198)	0.85
β-Blocker	64% (399)	62% (191)	0.55	65% (245)	64% (206)	0.81
CCB	20% (124)	26% (81)	0.029	22% (84)	24% (77)	0.59
Nitrates	21% (131)	16% (51)	0.099	21% (81)	18% (59)	0.29
Statin	68% (424)	71% (222)	0.26	70% (267)	65% (210)	0.22
Angina	34% (233)	23.5% (71)	0.0007	32% (116)	28.4% (85)	0.35
Shortness of breath	14% (93)	13% (39)	0.84	14% (50)	12% (36)	0.56
Ejection fraction			0.0028			0.0049
>50%	92% (615)	86.5% (250)		47.5% (169)	37% (103)	
35% to 50%	7% (48)	11% (32)		34.5% (123)	34% (96)	
<35%	0.8% (5)	2.5% (7)		18% (64)	26% (74)	

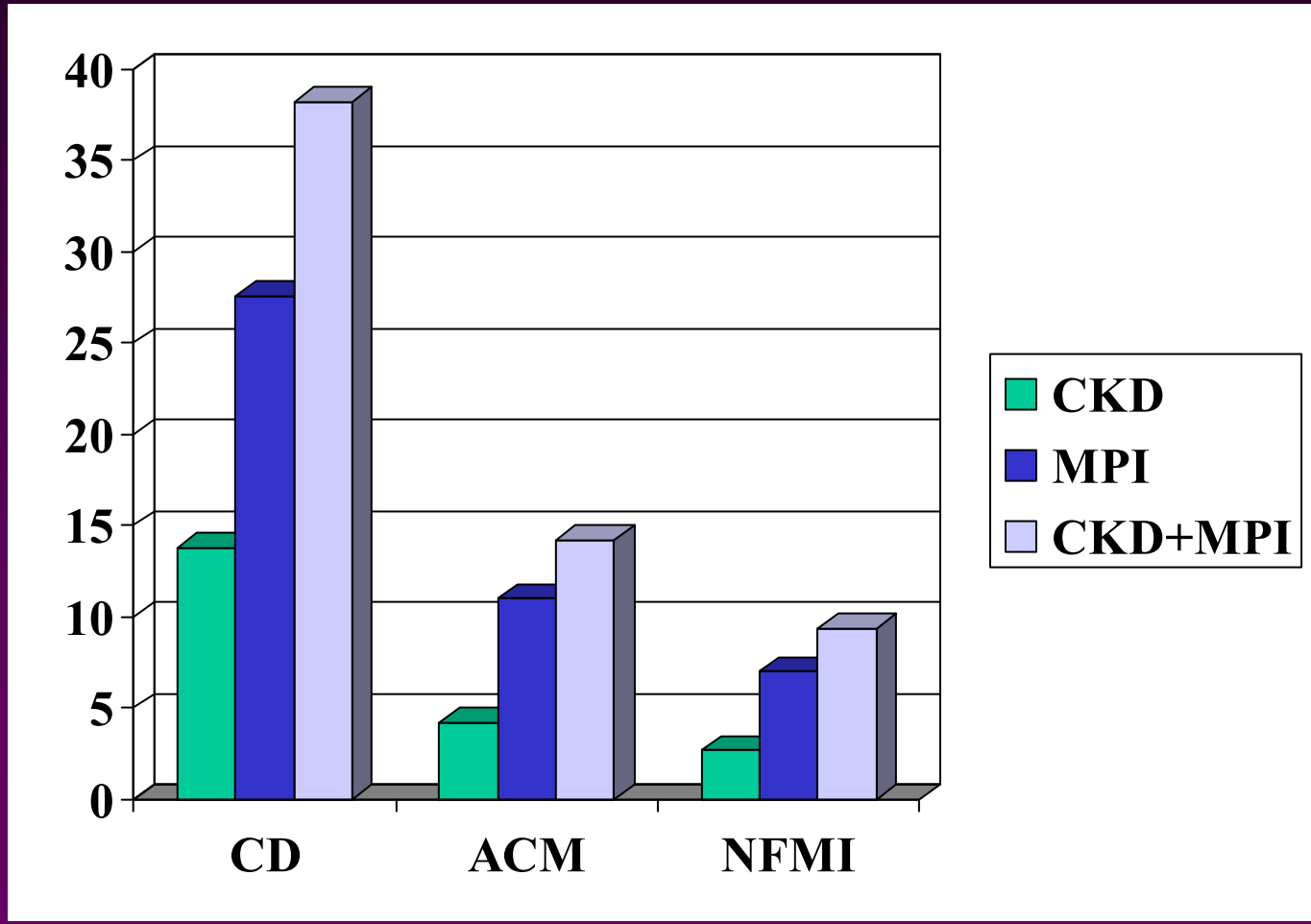
Perfusion Defects and Cardiac Death



Ischemia, Scar and Outcomes



Change in Model χ^2 with Addition of CKD and MPI to Cox Proportional Hazards Models



Incremental Prognostic Value of Myocardial Perfusion Imaging in Patients Referred to Stress Single-Photon Emission Computed Tomography With Renal Dysfunction

Mouaz H. Al-Mallah, MD, MSc; Rory Hachamovitch, MD, MSc;
Sharmila Dorbala, MBBS; Marcelo F. Di Carli, MD

Circ Cardiovasc Imaging.2009;429-436

Objective

To determine the incremental prognostic value of MPI SPECT in predicting mortality,

in a large prospective cohort of pts,

across the entire spectrum of renal function

Methods

Patient population

7348 consecutive pts referred for SPECT-MPI at the Brigham and Women's Hospital between 3-02 and 10-06.

Exclusions criteria:

- prior heart transplantation
- cardiomyopathy
- advanced valvular disease
- recent MI

Stress and Imaging Protocols

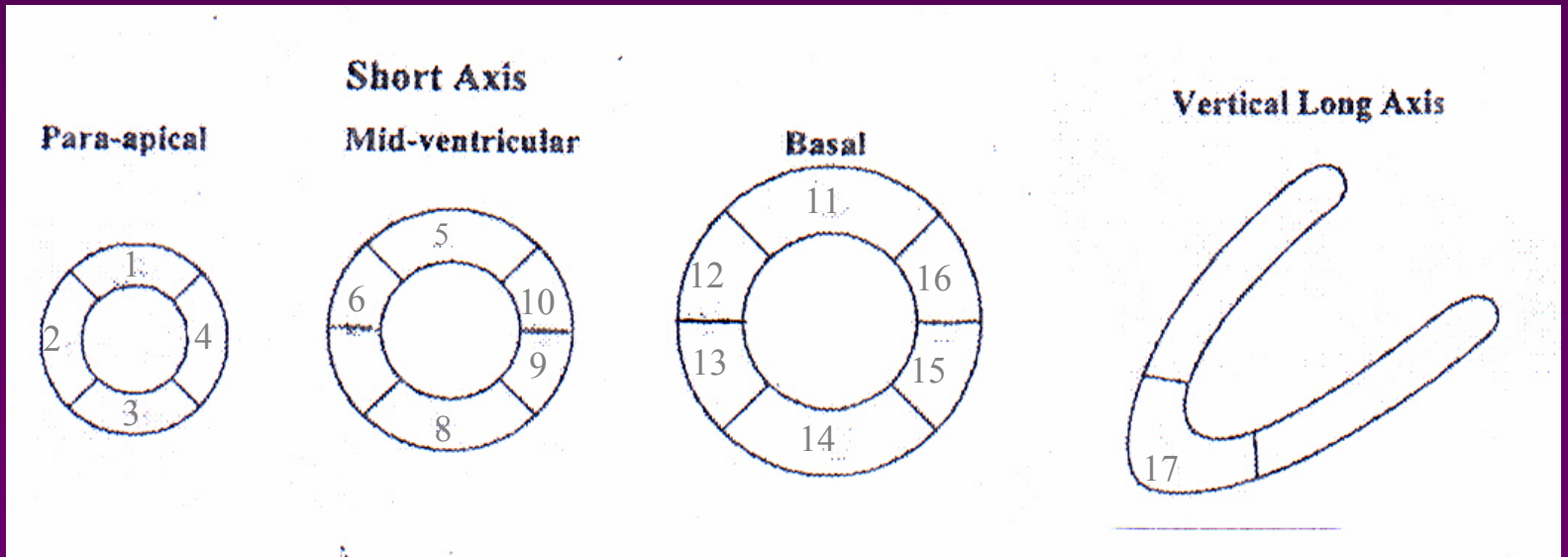
Rest/stress Mibi SPECT MPI

Stress: symptom-limited treadmill test 59.3%

- adenosine 35.1%
- dobutamine 5.6%

Image Analysis

- Standard 17-segment model
- Ischemia: mild, SDS 1-3
  moderate, SDS 4-7
  severe, SDS >7
- High risk scans as myocardium at risk >20% (SSS/68)



Quantification of Renal Function

- Creatinine measured within 180 days
- **Estimated GFR groups:**

  <30 mL/min per 1.73 m^2 + dialysis pts

  30-59 mL/min per 1.73 m^2

  60-89 mL/min per 1.73 m^2

  ≥90 mL/min per 1.73 m^2

Results: Baseline Characteristics

	All Patients	GFR ≥90 mL/min/1.73 m²	GFR 60–89 mL/min/1.73 m²	GFR 30–59 mL/min/1.73 m²	GFR <30 mL/min/1.73 m²	*P* Value
n	7348	3260	2888	935	265	
Age, y	63 (54, 73)	59 (51, 67)	68 (58, 75)	74 (66, 81)	65 (52, 75)	<0.001
Age ≥65 y	3500 (47.6)	1027 (31.5)	1618 (56)	725 (77.5)	130 (49.1)	<0.001
BMI, kg/m²	28 (25, 32)	28 (25, 32)	28 (25, 32)	28 (24, 32)	27 (24, 31)	.033
Women	3648 (50.1)	1596 (49)	1456 (50.4)	507 (54.2)	125 (47.2)	0.028
Blacks	1225 (16.7)	663 (20.3)	345 (11.9)	128 (13.7)	89 (33.6)	<0.001
Hypertension	5220 (71.0)	2100 (64.4)	2068 (71.6)	814 (87.1)	238 (89.8)	<0.001
Dyslipidemia	4443 (60.5)	1865 (56.9)	1830 (63.4)	613 (65.6)	144 (54.3)	<0.001
Diabetes	1913 (26)	753 (23.1)	669 (23.2)	350 (37.4)	141 (53.2)	<0.001
Family history of premature CAD	2605 (35.5)	1243 (38.1)	1032 (39.6)	277 (29.6)	53 (20)	<0.001
Smoking	1244 (16.9)	709 (21.7)	378 (13.1)	121 (12.7)	36 (13.6)	<0.001
Prior CAD	2350 (32)	865 (26.5)	969 (33.6)	414 (44.3)	102 (38.5)	<0.001
Prior MI	1251 (17)	487 (14.9)	487 (16.9)	209 (22.4)	68 (25.7)	<0.001
Prior PCI	1353 (18.4)	525 (16.1)	576 (19.9)	208 (22.2)	44 (16.6)	<0.001
Prior CABG	831 (11.3)	251 (7.7)	344 (11.9)	194 (20.7)	42 (15.8)	<0.001

Data are presented as n (%) or median (interquartile range). BMI indicates body mass index; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft.

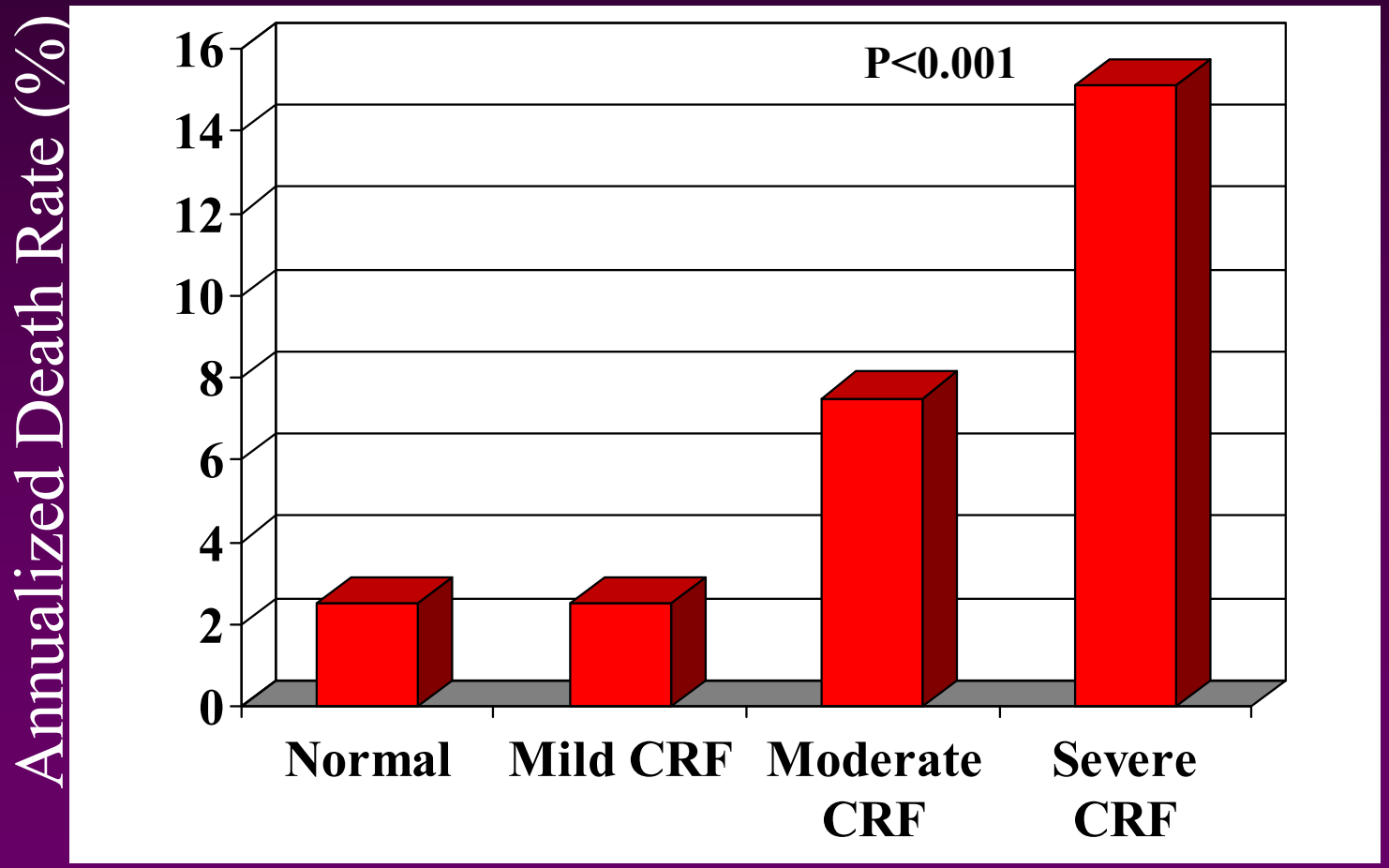
Results: Stress Testing and Imaging

	All Patients	GFR >90 mL/min/1.73 m^2	GFR 60–89 mL/min/1.73 m^2	GFR 30–59 mL/min/1.73 m^2	GFR <30 mL/min/1.73 m^2	*P* Value
n	7348	3260	2888	935	265	
Reason for the test						
Chest pain	3882 (52.8%)	1865 (57.2%)	1501 (52.0%)	426 (45.6%)	90 (34.0%)	<0.001
Dyspnea	2103 (28.6%)	843 (25.8%)	851 (29.5%)	339 (36.3%)	70 (26.4%)	<0.001
Normal baseline ECG	1413 (19.2%)	715 (21.9%)	549 (19%)	119 (12.7%)	30 (11.3%)	<0.001
Exercise stress test	4356 (59.3%)	2179 (66.8%)	1777 (61.5%)	347 (37.1%)	53 (20%)	<0.001
Peak HR >85%	2634 (35.8%)	1223 (56.2%)	1006 (56.6%)	143 (41.2%)	17 (32.1%)	<0.001
Ischemic ECG response	653 (8.7%)	209 (6.4%)	275 (9.5%)	136 (14.6%)	33 (12.5%)	<0.001
LVEF	62 (54, 70)	62 (55, 70)	63 (54, 71)	62 (52, 71)	53 (41, 64)	<0.001
Abnormal MPI	2256 (30.7%)	817 (25.1%)	929 (32.2%)	398 (42.7%)	121 (45.8%)	<0.001
High-risk MPI	572 (7.8%)	182 (5.6%)	234 (8.1%)	115 (12.3%)	41 (15.5%)	<0.001
Intermediate-high Duke treadmill score	1705 (39.2%)	732 (33.6%)	747 (42%)	193 (55.6%)	33 (62.3%)	<0.001
SSS	6 (4, 11)	6 (4, 10)	6 (4, 11)	8 (5, 14)	8 (5, 12)	0.003
SDS	2 (2, 3)	2 (2, 2)	2 (1, 3)	2 (1, 3)	2 (1, 3)	0.697

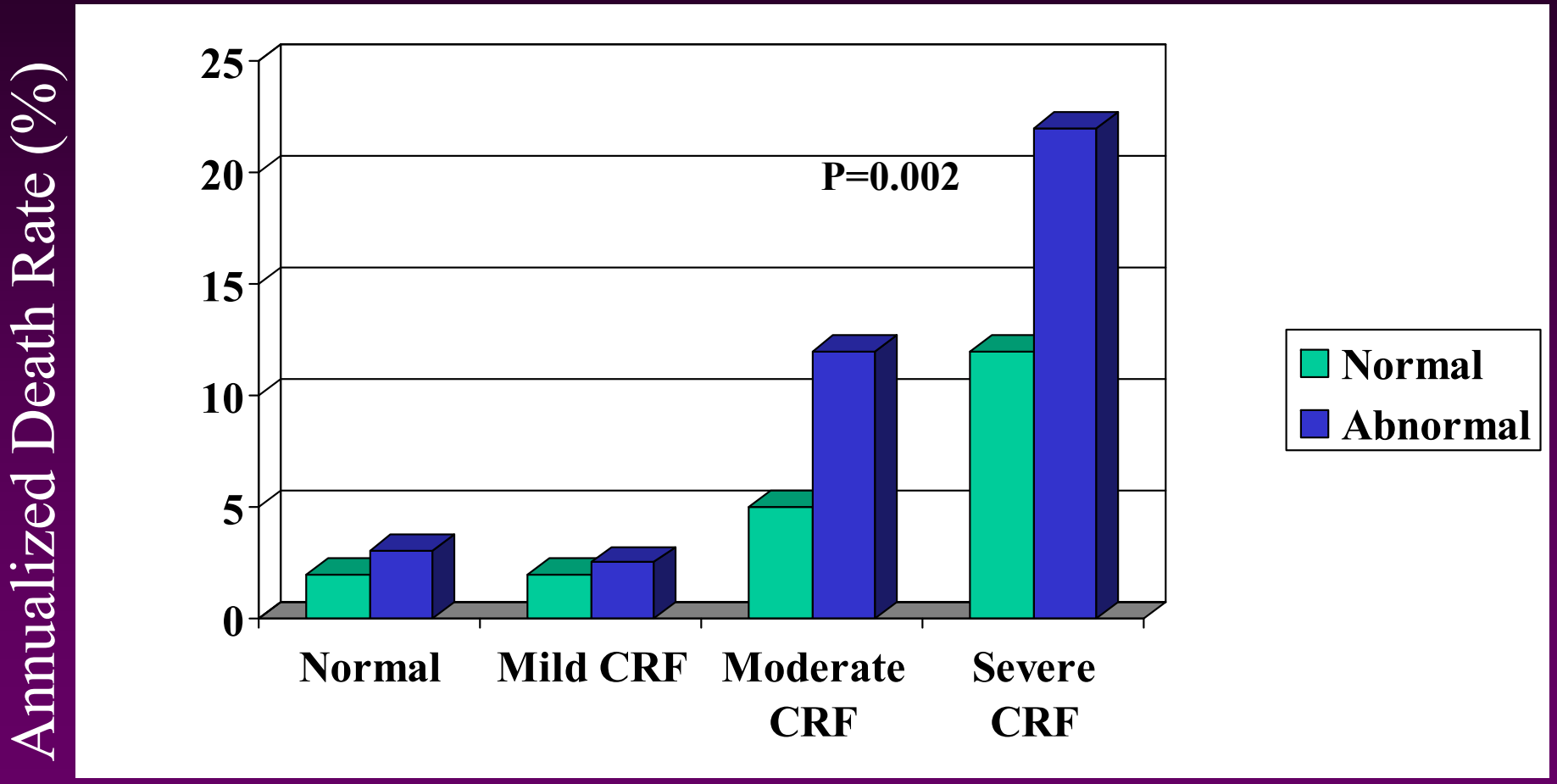
Data are presented as n (%) or median (interquartile range). HR indicates heart rate.

Annualized Rate of Death Across the Spectrum of Renal Function

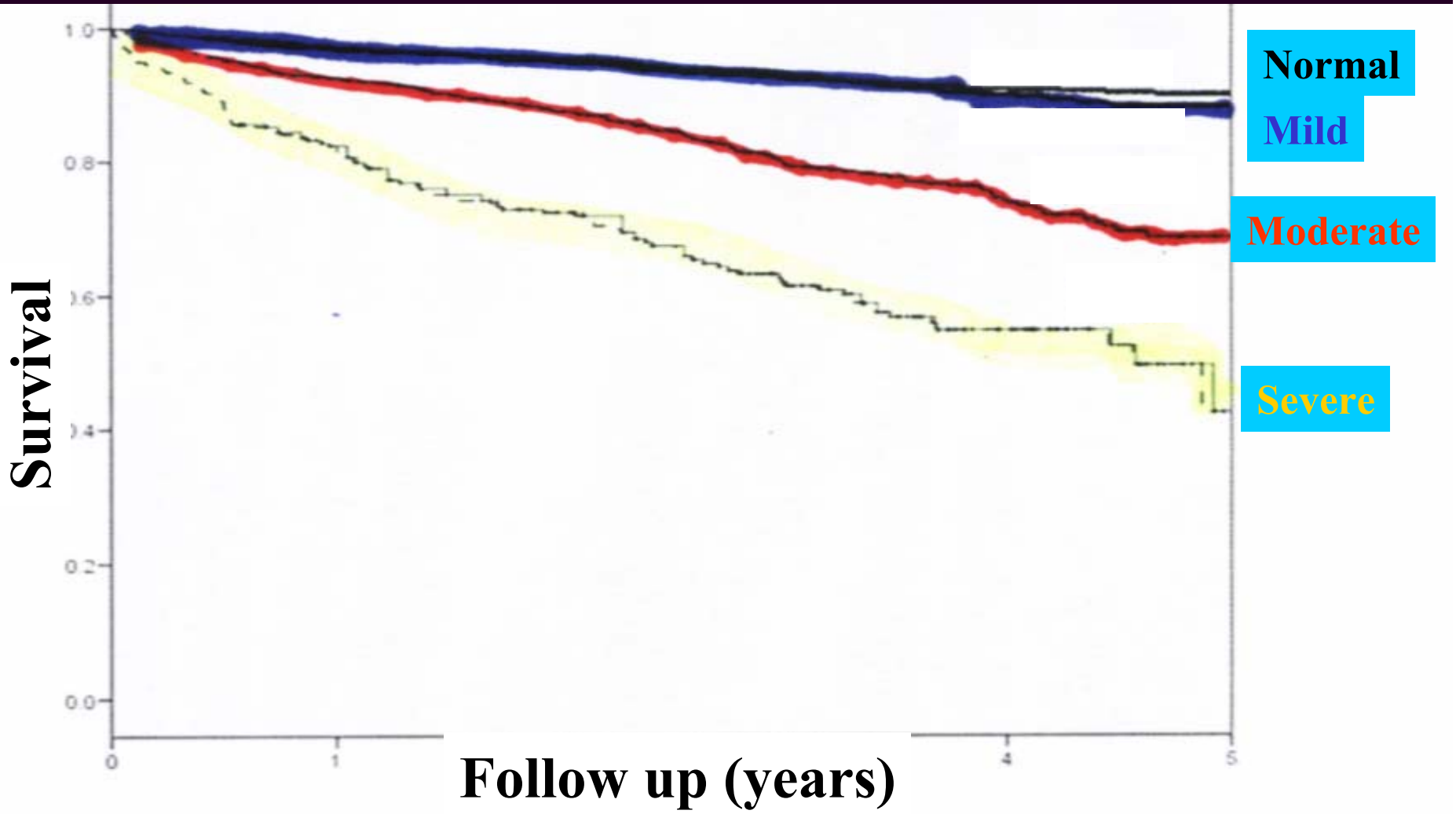
Follow-up period 2,6 years
693 (9,4%) died of all causes



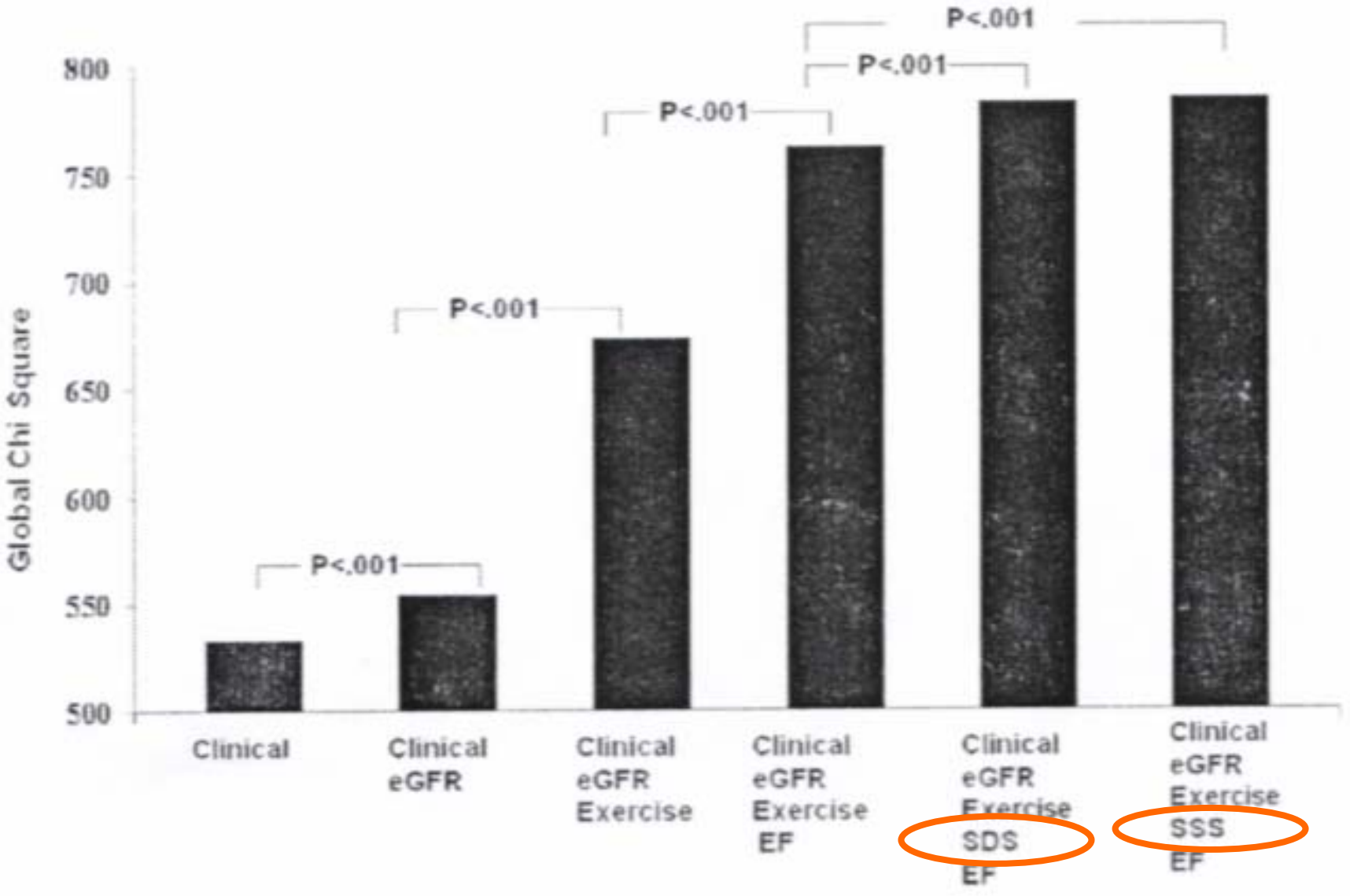
Annualized Rate of Death By SPECT-MPI



Kaplan-Meier Survival Curves In Renal Function Groups



Incremental Prognostic Value of SPECT-MPI



Conclusions

- Interaction exist between renal function and perfusion defects in patients with moderate and severe renal disease

Al-Mallah, Hachamovitch et al. *Circ Cardiovasc Imaging*.2009

- MPI has a powerful prognostic value in predicting cardiac outcomes in patients with varying degrees of renal function.

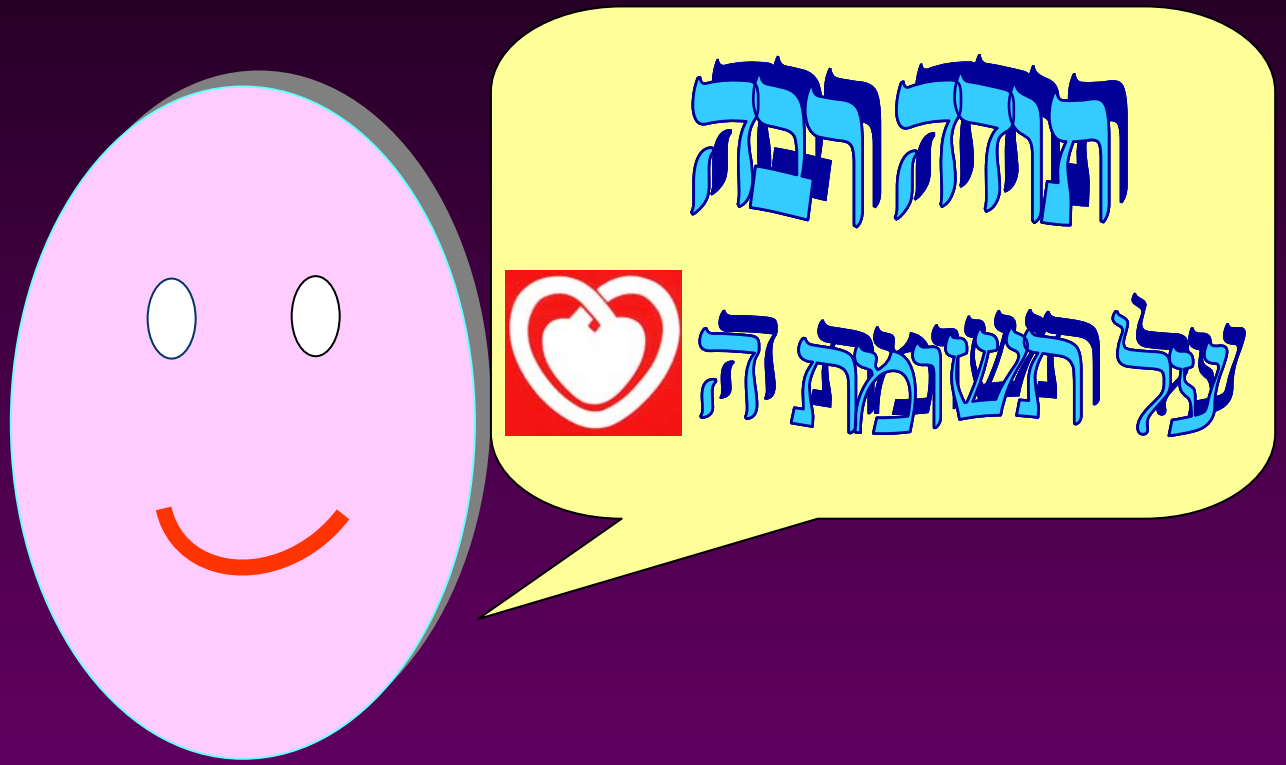
Hakeem, Bhatti, et al. *Circulation*.2008

- Stress Tl-201 SPECT MPI significantly improves the risk stratification in this high risk population.

Livschitz, Knobel et al. ICNIC 8

Implications

- All patients undergoing MPI should have eGFR assessed as part of their evaluation.
- All patients patients with moderate and severe renal dysfunction should undergo a MPI study.
- eGFR should be integrated into clinical risk-prediction models of morbidity and mortality.
- Repeat stress MPI should be performed in pts with CKD, especially those with normal MPI (“warranty period”?)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