

## ***Ecocardiografia con contrasto ...perchè no?***

***Nicola Gaibazzi***

***Parma***

*Durante ecostress  
ma già prima di iniziare la fase di stress l'utilizzo di contrasto può essere informativo in modo  
incrementale rispetto all'ecocardiografia standard*

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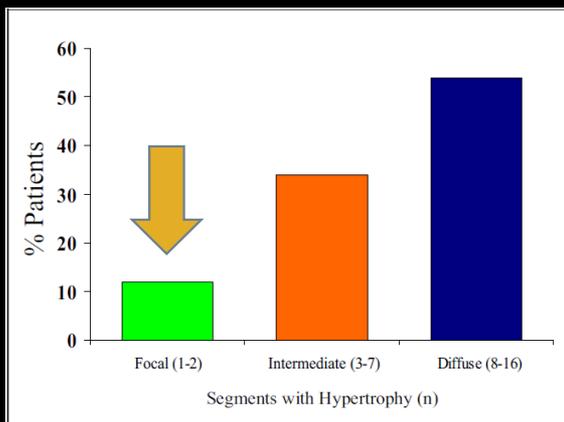
Vol. 54, No. 3, 2009  
ISSN 0735-1097/09/\$36.00  
doi:10.1016/j.jacc.2009.05.006

**FOCUS ISSUE: HYPERTROPHIC CARDIOMYOPATHY**

**Clinical Research**

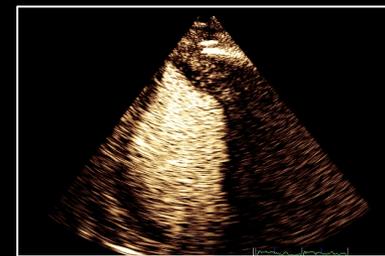
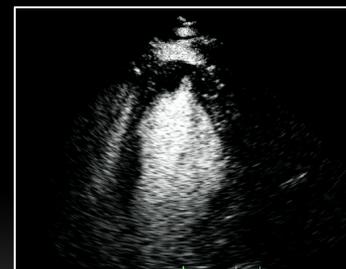
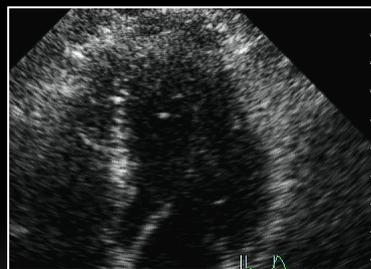
## Hypertrophic Cardiomyopathy Phenotype Revisited After 50 Years With Cardiovascular Magnetic Resonance

Martin S. Maron, MD,\* Barry J. Maron, MD,† Caitlin Harrigan, BA,\* Jacki Buros, BA,‡  
C. Michael Gibson, MD, MS,‡§ Iacopo Olivotto, MD,|| Leah Biller, BA,† John R. Lesser, MD,†  
James E. Udelson, MD,\* Warren J. Manning, MD,‡§ Evan Appelbaum, MD‡§  
*Boston, Massachusetts; Minneapolis, Minnesota; and Florence, Italy*

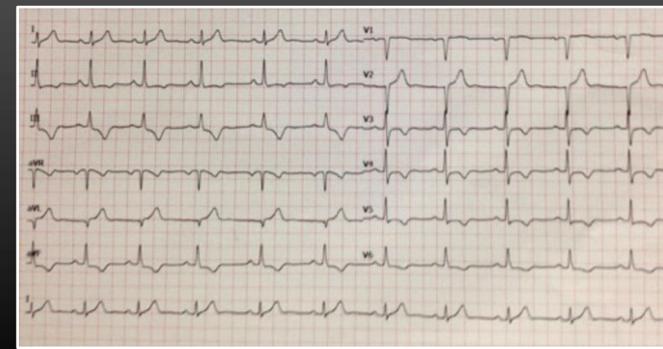


**Figure 2** Prevalence of Hypertrophied Segments

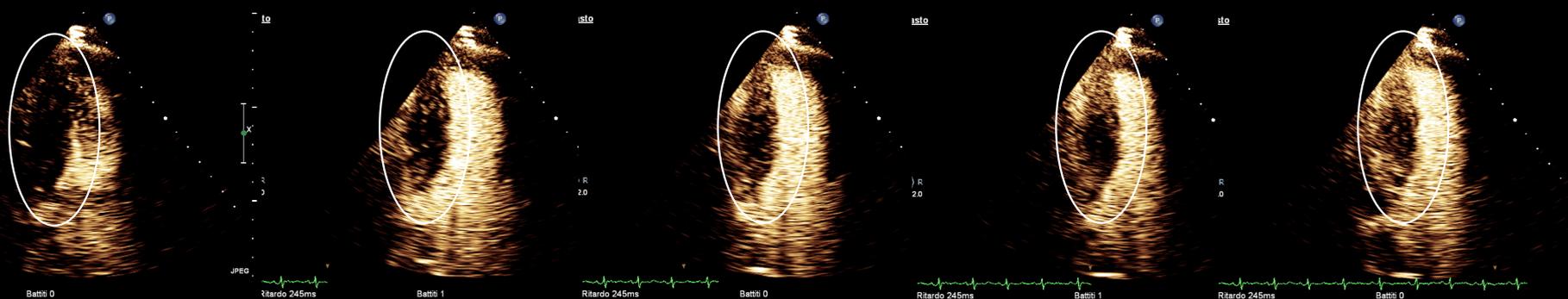
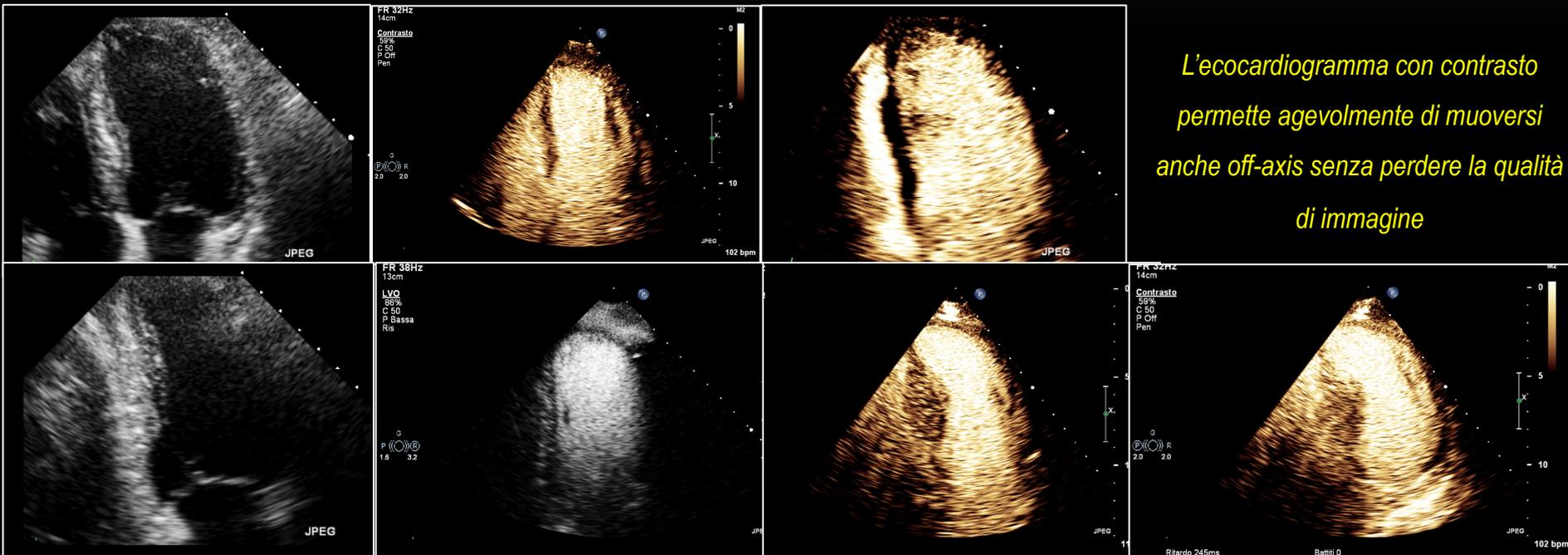
Prevalence of focal (1 to 2 hypertrophied segments), intermediate (3 to 7 segments), and diffuse left ventricular hypertrophy (8 to 16 segments) within the cohort of 333 patients with hypertrophic cardiomyopathy.

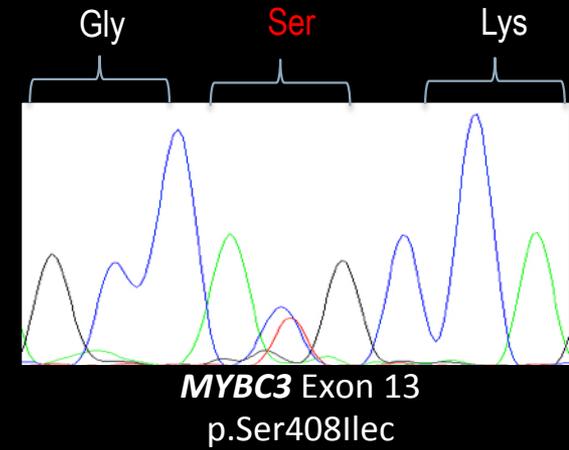
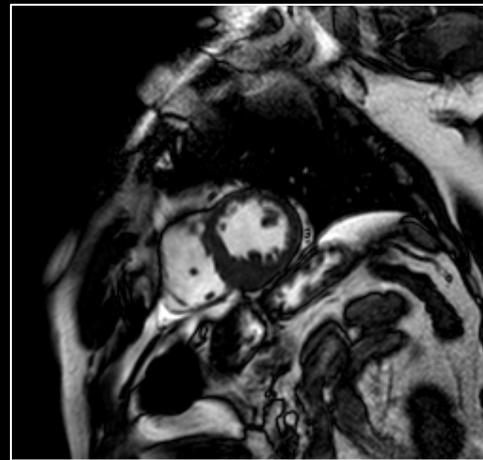
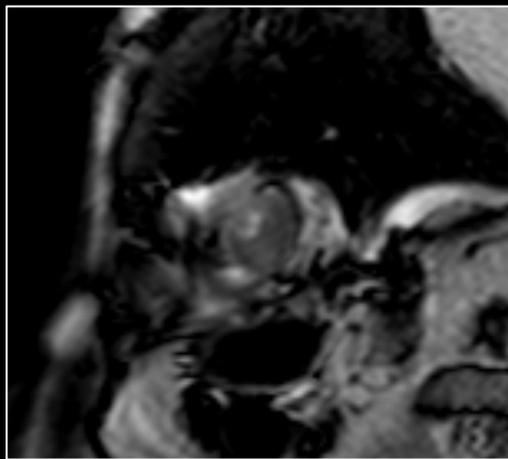
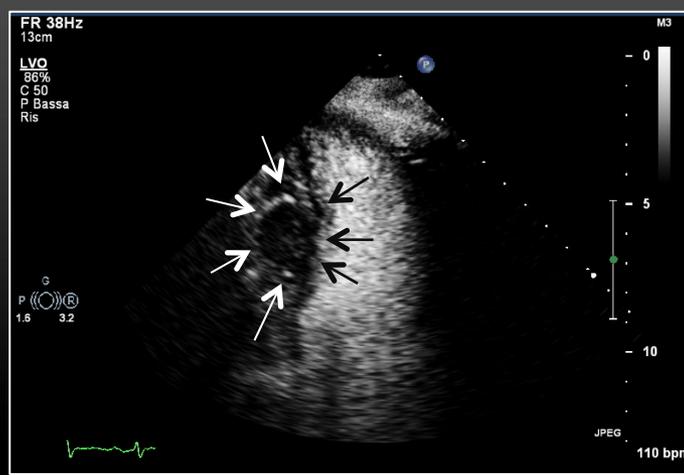
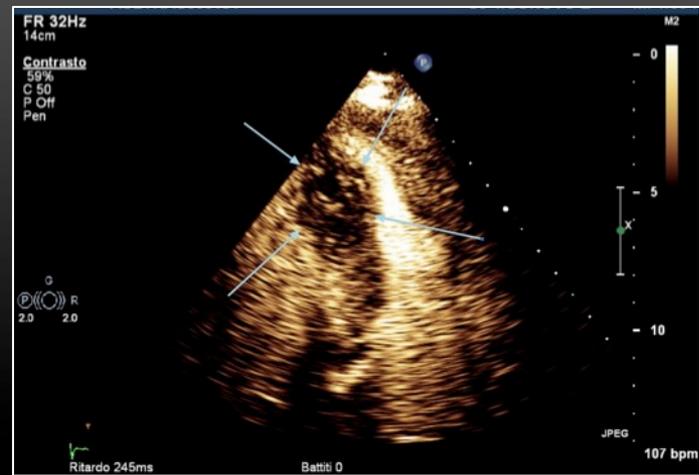


52enne che si presenta ad ecostress perché all'ultimo controllo annuale ECG (sportivo) si rileva una T invertita non presente nel 2013.



L'ecocardiogramma con contrasto permette agevolmente di muoversi anche off-axis senza perdere la qualità di immagine





*CONTRAST-FACILITATED COLOR DOPPLER RILEVA CON MAGGIOR FACILITÀ:*

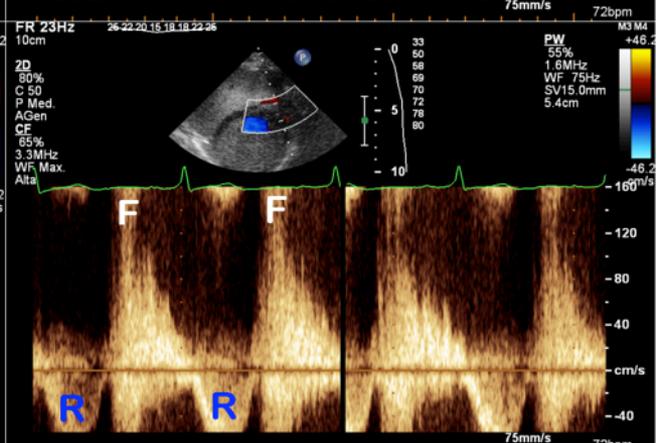
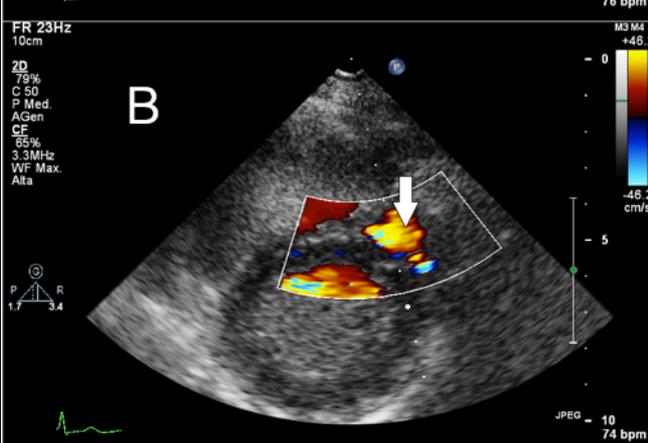
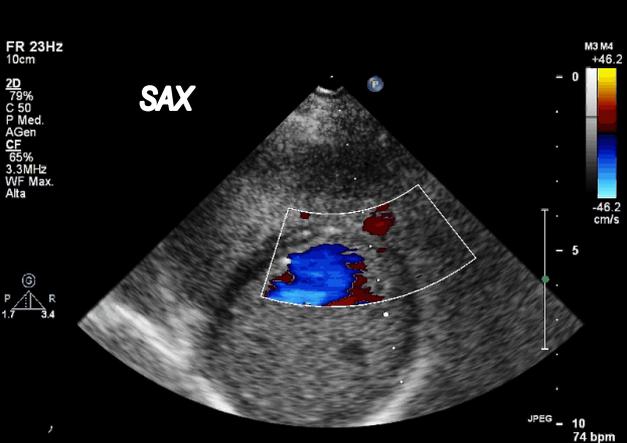
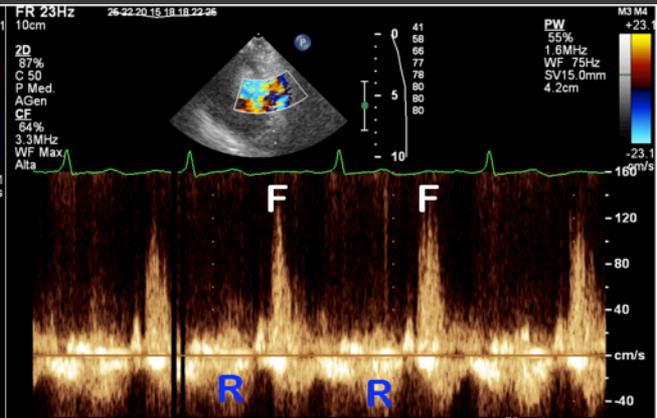
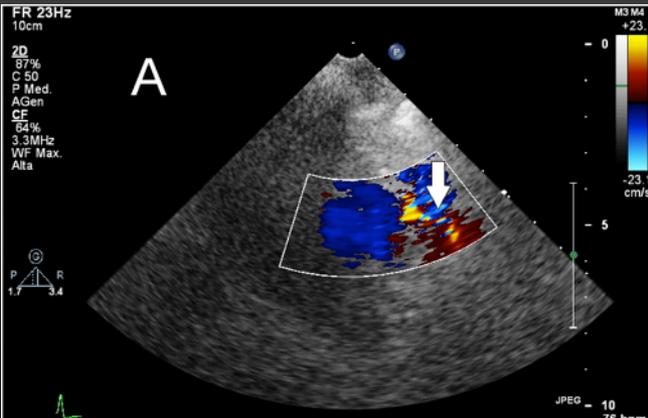
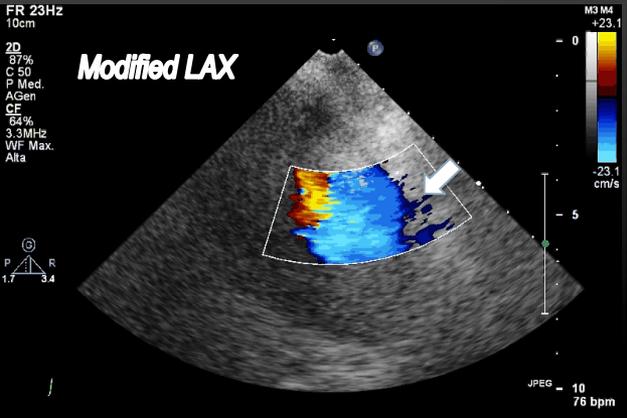
*PONTI MIOCARDICI, IL DECORSO INTRAMIOCARDICO E TORTUOSITÀ SEVERE*

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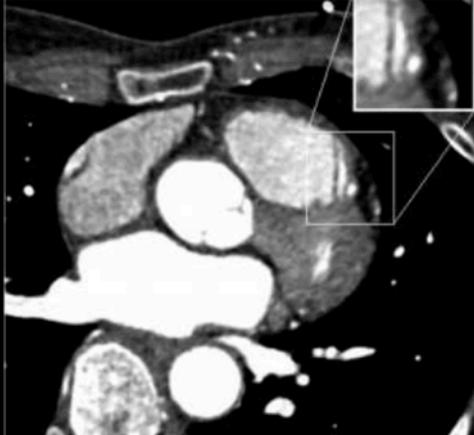
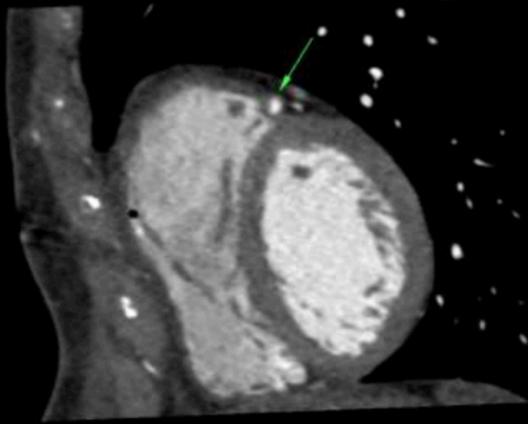
*...VARIANTI CONGENITE ASSOCIATE ALLE X-SYNDROMES ?*

Rest

# Dolore toracico durante esercizio



Rest contrast-echo mostra "fingertip" e reverse systolic flow



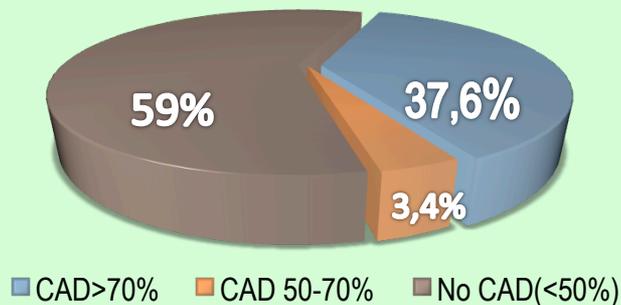
## Stresseco per ottimizzare l'indicazione ad Angiografia Coronarica

Oggi almeno 1 su 3 Pazienti che vanno a coronarografia per sospetta CAD non ha poi CAD ostruttiva!

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

### Low Diagnostic Yield of Elective Coronary Angiography



#### CONCLUSIONS

In this study, slightly more than one third of patients without known disease who underwent elective cardiac catheterization had obstructive coronary artery disease. Better strategies for risk stratification are needed to inform decisions and to increase the diagnostic yield of cardiac catheterization in routine clinical practice.

Table 2. Predictors of Obstructive Coronary Artery Disease.

Variable	Wald Chi-Square Statistic	Adjusted Odds Ratio (95% CI)
Age, per 5-yr increase	6146.2	1.29 (1.28–1.30)
Body-mass index, per 5-unit increase*	550.3	0.92 (0.91–0.92)
Male sex	8632.9	2.70 (2.64–2.76)
White race†	50.2	1.21 (1.15–1.28)
Diabetes‡		
Insulin-dependent	1932.3	2.14 (2.07–2.21)
Non-insulin-dependent	1187.8	1.45 (1.42–1.48)
Dyslipidemia	972.8	1.62 (1.57–1.67)
Use of tobacco		
Current	790.4	1.50 (1.45–1.54)
Former	34.3	1.09 (1.06–1.12)
Hypertension	561.4	1.29 (1.26–1.32)
Peripheral vascular disease	449.5	1.54 (1.48–1.61)
Cerebrovascular disease	197.8	1.26 (1.21–1.30)
Ejection fraction, per 5% increase	374.7	1.08 (1.07–1.09)
Congestive heart failure	83.1	0.80 (0.76–0.84)
Glomerular filtration rate, per 5-unit increase§	31.3	1.01 (1.00–1.01)
Renal failure¶		
Requiring dialysis	26.9	1.30 (1.18–1.43)
Not requiring dialysis	14.1	1.45 (1.07–1.23)
Chronic lung disease	298.6	0.78 (0.76–0.80)
Presence of symptoms		
Typical	353.6	1.91 (1.78–2.05)
Atypical	84.2	0.76 (0.71–0.80)
Noninvasive testing**		
Positive result	48.9	1.28 (1.19–1.37)
Equivocal result	25.3	0.79 (0.71–0.86)
Negative result	19.4	0.82 (0.74–0.89)

Low diagnostic yield of elective coronary angiography.

Patel MR, Peterson ED, Dai D, Brennan JM, Redberg RF, Anderson HV, Brindis RG, Douglas PS.

N Engl J Med. 2010 Mar 11;362(10):886-95.

## Coronary Artery Disease

### Detection of Significant Coronary Artery Disease by Noninvasive Anatomical and Functional Imaging

Danilo Neglia, MD, PhD; Daniele Rovai, MD; Chiara Caselli, PhD; Mikko Pietila, MD; Anna Teresinska, PhD; Santiago Aguadé-Bruix, MD; Maria Nazarena Pizzi, MD; Giancarlo Todiere, MD; Alessia Gimelli, MD; Stephen Schroeder, MD; Tanja Drosch, MD; Rosa Poddighe, MD, PhD; Giancarlo Casolo, MD, PhD; Constantinos Anagnostopoulos, MD; Francesca Pugliese, MD, PhD; Francois Rouzet, MD; Dominique Le Guludec, MD, PhD; Francesco Cappelli, MD, PhD; Serafina Valente, MD; Gian Franco Gensini, MD; Camilla Zawaideh, MD; Selene Capitanio, MD; Gianmario Sambuceti, MD; Fabio Marsico, MD; Pasquale Perrone Filardi, MD; Covadonga Fernández-Golfín, MD; Luis M Rincón, MD; Frank P. Graner, MSc; Michiel A. de Graaf, MSc; Michael Fiechter, MD; Julia Stehli, MD; Oliver Gaemperli, MD; Eliana Reyes, MD, PhD; Sandy Nkomo, BSc; Maija Mäki, MD, PhD; Valentina Lorenzoni, MSc; Giuseppe Turchetti, PhD; Clara Carpeggiani, MD; Martina Marinelli, PhD; Stefano Puzzuoli, BSc; Maurizio Mangione, PhD; Paolo Marcheschi, PhD; Fabio Mariani, MSc; Daniela Giannessi, MSc; Stephan Nekolla, PhD; Massimo Lombardi, MD; Rosa Sicari, MD; Arthur J.H.A. Scholte, MD, PhD; José L. Zamorano, MD; Philipp A. Kaufmann, MD; S. Richard Underwood, MD\*; Juhani Knuuti, MD\*; The EVINCI Study Investigators

Questi sono i dati di accuratezza reali dell'ecostress con sola analisi della cinetica nel 2015!

Oggi:

- 1) Pazienti meno selezionati con minor prevalenza di CAD
- 2) I dati di accuratezza vanno corretti per il referral bias, di cui tradizionalmente non si teneva invece conto

Table 4. Sensitivity and Specificity of Imaging Techniques for the Detection of Significant Coronary Stenoses at ICA Using Local Analysis, Without and With Correction for Verification Bias

	Technique						
	CCTA (N=475)	MPI (N=389)	WMI (N=346)	SPECT (N=293)	PET (N=96)	ECHO (N=261)	CMR (N=85)
Sensitivity, % (95% CI)	91 (86-95)	74*† (66-82)	49‡ (38-59)	73 (64-81)	81 (62-95)	45 (33-57)	57 (39-75)
Sensitivity after correction for verification bias, % (95% CI)	82 (74-91)	59†‡ (50-69)	36‡ (27-45)	53 (43-63)	74 (53-95)	32 (22-43)	46 (27-64)
P value	0.008	0.001	0.011	<0.001	0.622	0.028	0.256
Specificity, % (95% CI)	92 (89-95)	73†‡ (68-78)	92 (88-95)	67 (60-74)	89 (81-96)	90 (86-94)	97 (91-100)
Specificity after correction for verification bias, % (95% CI)	92 (89-95)	70†‡ (63-76)	90 (86-94)	59 (50-68)	89 (82-96)	88 (84-94)	96 (90-100)
P value	0.920	0.232	0.524	0.023	0.891	0.572	1

CCTA indicates computed coronary tomography angiography; CI, confidence interval; CMR, cardiac magnetic resonance; ICA, invasive coronary angiography; MPI, myocardial perfusion imaging; PET, positron emission tomography; SPECT, single photon computed emission tomography; and WMI, wall motion imaging. P value from binomial probability test for comparison between corrected and uncorrected values.

\*P<0.001 MPI vs CCTA.

†P<0.001 MPI vs WMI.

‡P<0.001 MPI or WMI vs CCTA.

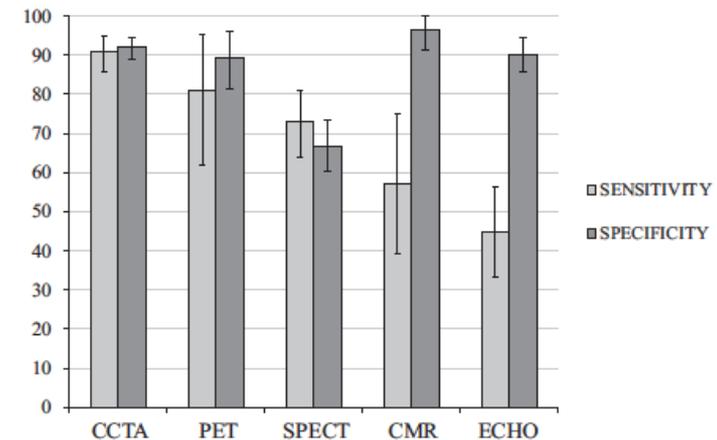


Figure 3. Sensitivity and specificity of noninvasive imaging techniques.

CCTA indicates coronary computed tomography angiography; CMR, cardiac magnetic resonance; ECHO, echocardiography; PET, positron emission tomography; and SPECT, single-photon computed emission tomography.

Clinical Implications of Referral Bias in the Diagnostic Performance of Exercise Testing for Coronary Artery Disease

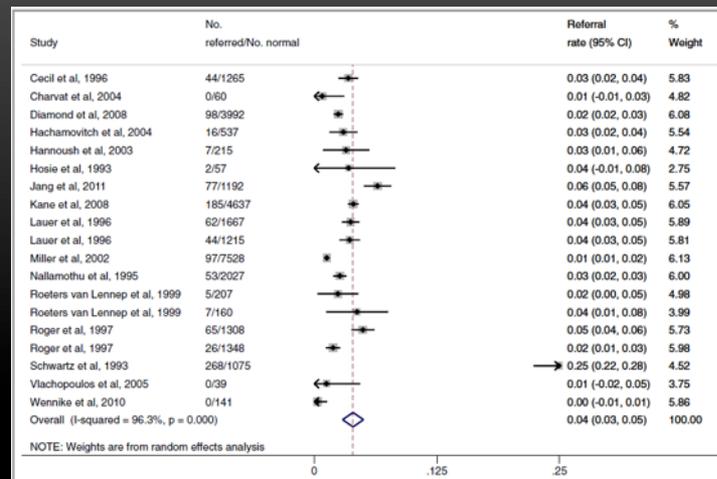
Joseph A. Ladapo, Saul Blecker, Michael R. Elashoff, Jerome J. Federspiel, Dorice L. Vieira, Gaurav Sharma, Mark Monane, Steven Rosenberg, Charles E. Phelps and Pamela S. Douglas

J Am Heart Assoc. 2013;2:e000505; originally published December 13, 2013;

doi: 10.1161/JAHA.113.000505

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Online ISSN: 2047-9980



**Conclusions**—Exercise echocardiography and myocardial perfusion imaging are considerably less sensitive and more specific for coronary artery disease after adjustment for referral. Given these findings, future work should assess the comparative ability of these and other tests to rule-in versus rule-out coronary artery disease. (*J Am Heart Assoc.* 2013;2:e000505 doi: 10.1161/JAHA.113.000505)

Table 2. Diagnostic Effectiveness of Exercise ECHO and MPI With and Without Adjustment for Referral

	ECHO		MPI	
	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Sensitivity, % (95% CI)	Specificity, % (95% CI)
Unadjusted*	84 (80 to 89)	77 (69 to 86)	85 (81 to 88)	69 (61 to 78)
Adjusted†	34 (27 to 41)	99 (99 to 100)	38 (31 to 44)	99 (99 to 100)

ECHO indicates echocardiography; MPI, myocardial perfusion imaging.

\*Diagnostic effectiveness based in random-effects meta-analysis of sensitivity and specificity reported in 15 studies of exercise ECHO and 30 studies of exercise MPI (45 studies in total).

†Adjusted for referral rates to cardiac catheterization after abnormal or normal exercise test result.

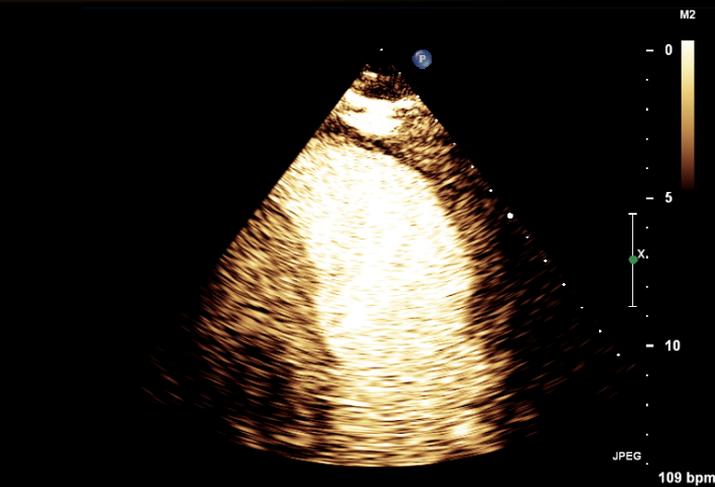
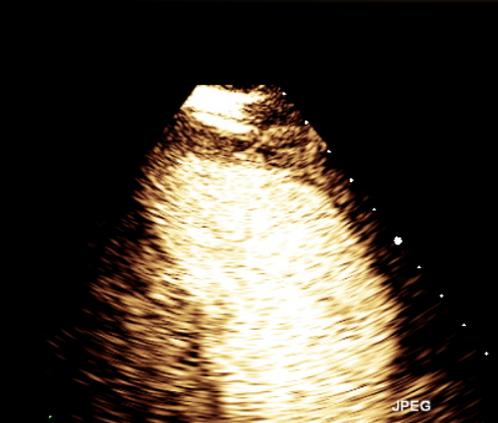
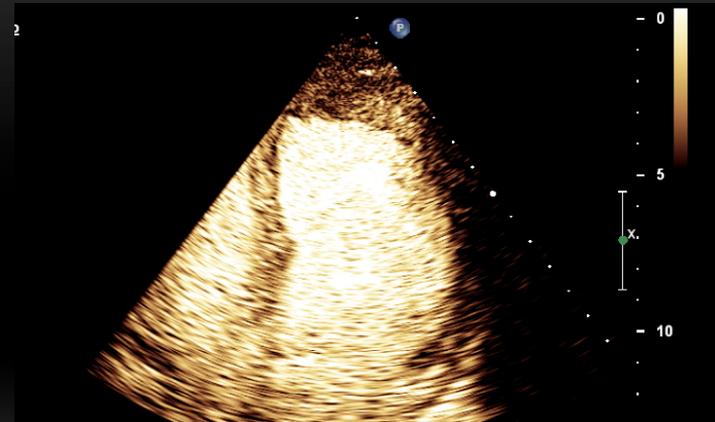
**Tutti i tests provocativi (non solo stresseco) hanno un problema di sensibilità e quindi molti falsi negativi, una volta che si considerino pz anche con sintomi non tipici da sforzo e il referral bias..**  
**Nella pratica abbiamo bisogno di incrementare la sensibilità, anche se questo costasse una lieve riduzione di specificità, che è invece già elevatissima**

Il tipico caso che dimostra quanto **bene** lo stress eco funzioni semplicemente analizzando la cinetica

Rest

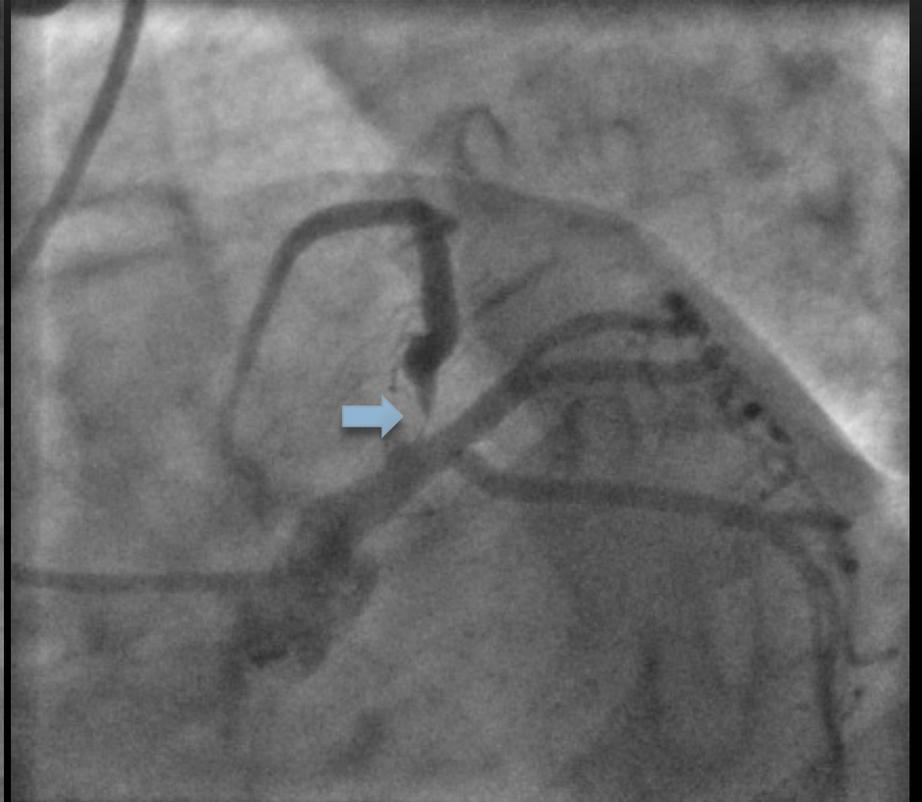
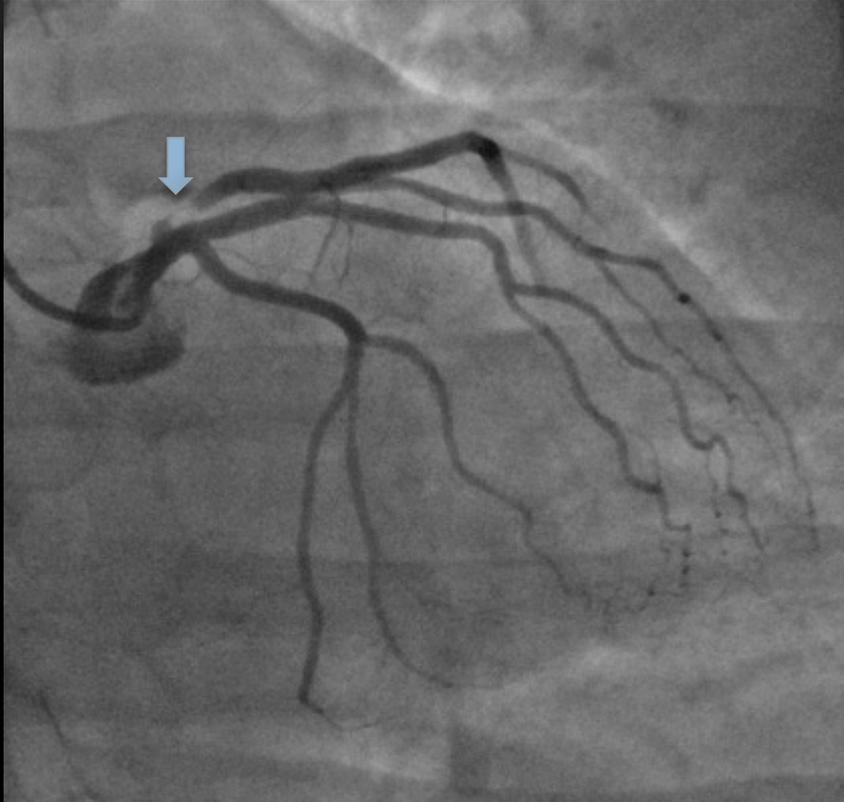


Stress



Nessun dubbio! Estese e severe alterazioni della cinetica (come sempre accade associate a chiaro difetto di perfusione) nel territorio della LAD

*LAD Proximale subocclusa*



# L'analisi della perfusione miocardica aumenta la sensibilità per CAD ostruttiva qualsiasi sia la modalità di stress-imaging, quando aggiunta all'analisi della cinetica

## Lo stress-eco con contrasto è una metodica ideale per analizzare sia cinetica che perfusione

### Incremental Value of Perfusion over Wall-Motion Abnormalities with the Use of Dobutamine–Atropine Stress Myocardial Contrast Echocardiography and Magnetic Resonance Imaging for Detecting Coronary Artery Disease

Sandra Nivea dos Reis Saraiva Falcão, M.D.,\* Carlos Eduardo Rochitte, M.D.,\* Wilson Mathias Junior, M.D.,\* Luiz Quaglia, M.D.,\* Pedro Alves Lemos, M.D.,\* João César Nunes Sbrano, M.D.,\* José Antonio Franchini Ramires, M.D.,\* Roberto Kalil Filho, M.D.\* and Jeane Mike Tsutsui, M.D.†

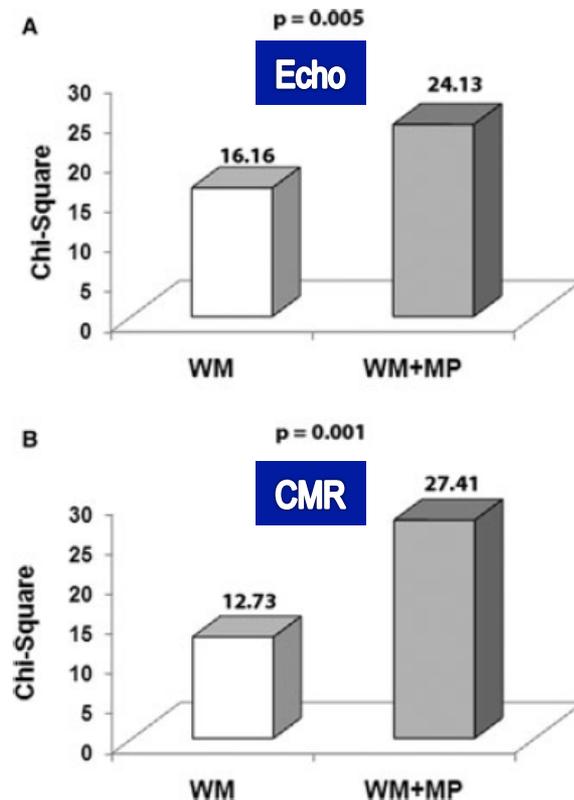
\*Heart Institute (InCor), University of São Paulo Medical School, São Paulo, Brazil; and †Fleury Group, Heart Institute (InCor), University of São Paulo Medical School, São Paulo, Brazil

**TABLE III**

Diagnostic Parameters of RTMCE and CMR for Detecting Patients with Coronary Artery Disease

	RTMCE (n = 42)		CMR (n = 42)	
	WM	WM+MP	WM	WM+MP
Sensitivity	72 (54–90)	88 (75–100)	80 (64–96)	92 (81–100)
Specificity	88 (73–100)	88 (72–100)	82 (64–100)	82 (64–100)
PPV	90 (77–100)	91 (80–100)	87 (73–100)	88 (76–100)
NPV	68 (49–88)	83 (66–97)	74 (54–93)	88 (71–100)
Accuracy	79 (66–91)	88 (75–96)	80 (69–92)	88 (78–98)

Data are percentage with respective 95% confidence interval. RTMCE = real time myocardial contrast echocardiography; CMR = cardiovascular magnetic resonance; MP = myocardial perfusion; NPV = negative predictive value; PPV = positive predictive value; WM = wall motion.



**Figure 1.** Incremental value of combined wall motion (WM) and myocardial perfusion (MP) (expressed on y-axis as chi-square values with incremental degrees of freedom) over WM alone by real time myocardial contrast echocardiography (A) and cardiovascular magnetic resonance (B).

# Come risolvere la problematica della bassa sensibilità per CAD?

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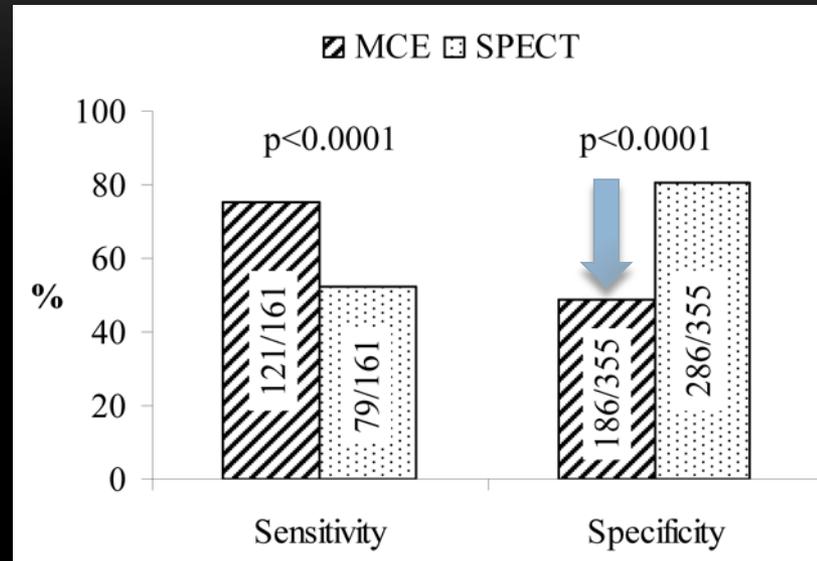
**Cardiac Imaging**

### Comparison of Sulfur Hexafluoride Microbubble (SonoVue)-Enhanced Myocardial Contrast Echocardiography With Gated Single-Photon Emission Computed Tomography for Detection of Significant Coronary Artery Disease

A Large European Multicenter Study

Roxy Senior, MD,\* Antonella Moreo, MD,† Nicola Gaibazzi, MD,‡ Luciano Agati, MD,§  
Klaus Tiemann, MD,|| Bharati Shivalkar, MD,¶ Stephan von Bardeleben, MD,#  
Leonarda Galiuto, MD,\*\* Hervé Lardoux, MD,†† Giuseppe Trocino, MD,‡‡ Ignasi Carrió, MD,§§  
Dominique Le Guludec, MD,|||| Gianmario Sambucetti, MD,¶¶ Harald Becher, MD,##  
Paolo Colonna, MD,\*\*\* Folkert ten Cate, MD,††† Ezio Bramucci, MD,‡‡‡ Ariel Cohen, MD, PhD,§§§  
Gianpaolo Bezante, MD,||||| Costantina Aggeli, MD,¶¶¶ Jaroslaw D. Kasprzak, MD###

London, Harrow, United Kingdom; Milan, Parma, Rome, Monza, Genoa, Bari, and Pavia, Italy;  
Münster and Mainz, Germany; Edegem, Belgium; Corbeil-Essonnes and Paris, France; Barcelona, Spain;  
Edmonton, Alberta, Canada; Rotterdam, the Netherlands; Athens, Greece; and Łódź, Poland



STUDIO DI PARAGONE CON SPECT:

DIPIRIDAMOLO USATO A BASSA DOSE (0.56 MG/KG), INSUFFICIENTE PER UNA ANALISI DI CINETICA

**STANDALONE PERFUSION STRESSECHO IS NOT THE SOLUTION ACCORDING TO THESE DATA**

# COME APPARE LA PERFUSIONE DOPO STRESSOR? ALCUNI ESEMPLI..

1.5-2 secondi dopo flash distruttivo il miocardio si riperfonde completamente se non c'è stenosi >50%

Myocardial Blood Flow

=

MB Volume

×

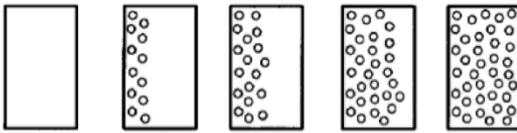
MB Velocity

**Circulation**

American Heart Association  
Learn and Live™

Quantification of Myocardial Blood Flow With Ultrasound-Induced Destruction of Microbubbles Administered as a Constant Venous Infusion  
Kevin Wei, Ananda R. Jayaweera, Sorosh Firoozin, Andrei I. Linka, Danny M. Sliwa and Sanjay Kaul  
Circulation 1998;97:473-483

A. B. C. D. E.



← E →

$d_1$

$d_2$

$d_3$

$d_4$

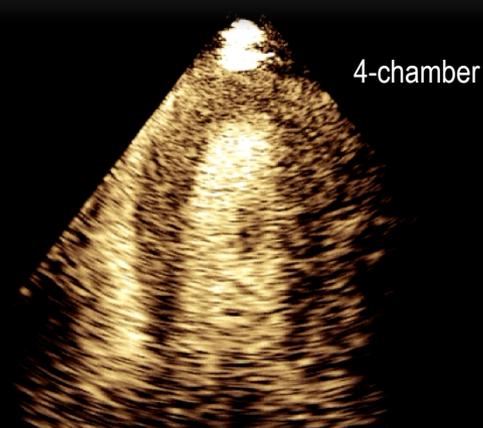
time → 0

$t_1$

$t_2$

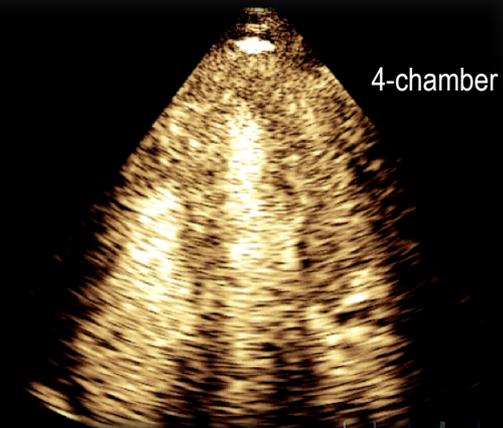
$t_3$

$t_4$



4-chamber

Endsystolic triggering:  
1 endsystolic image per cycle



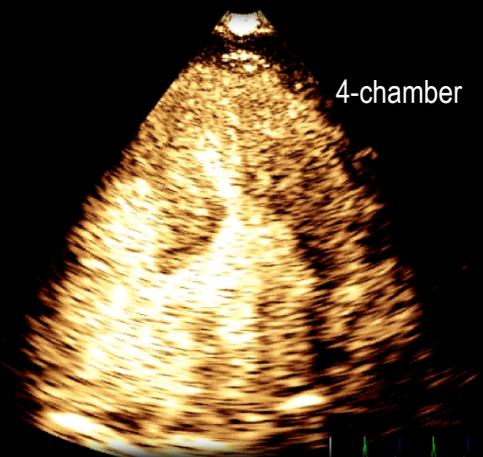
4-chamber

Endsystolic triggering:  
1 endsystolic image per cycle



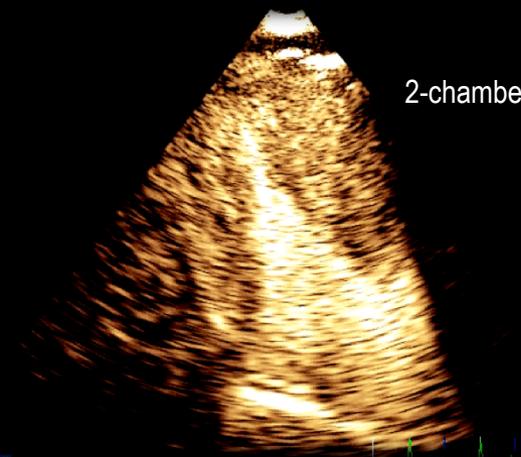
4-chamber

Real-time imaging:



4-chamber

Endsystolic triggering:  
1 endsystolic image per cycle

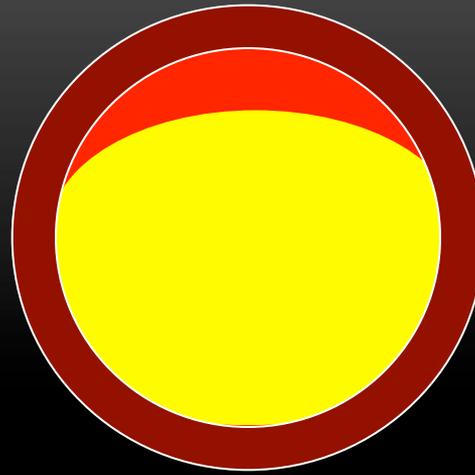


2-chamber

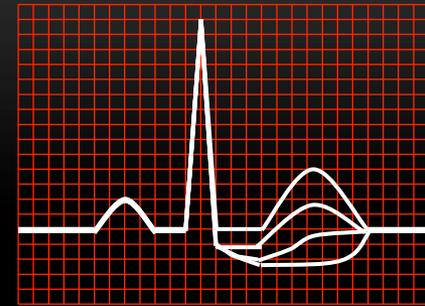
Endsystolic triggering:  
1 endsystolic image per cycle

Abbiamo bisogno della **perfusione**?

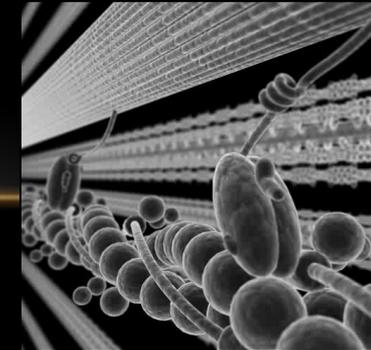
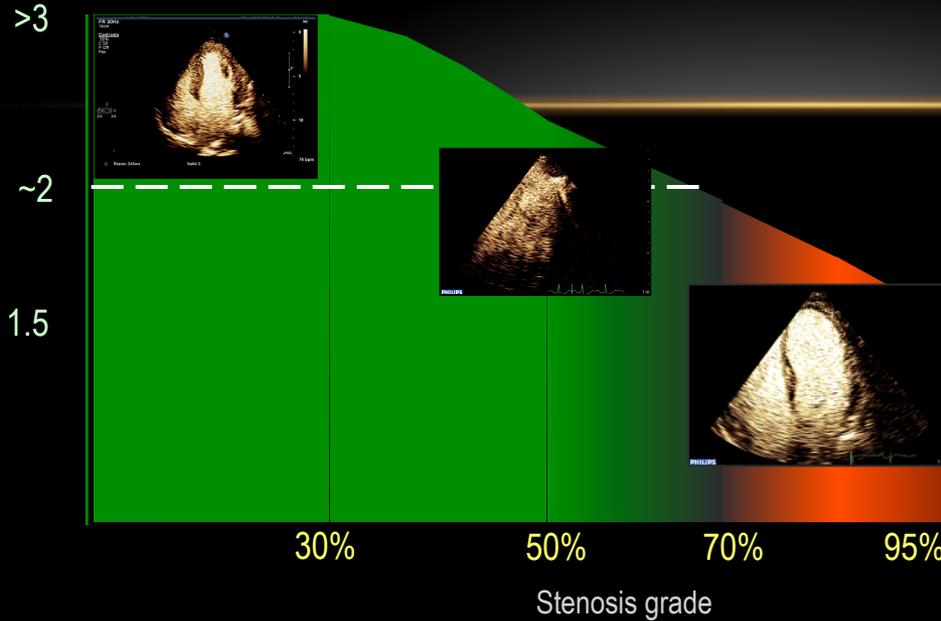
Gould revisited



ECG



CFR



WM

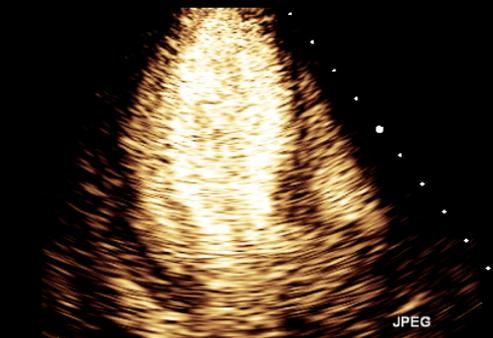
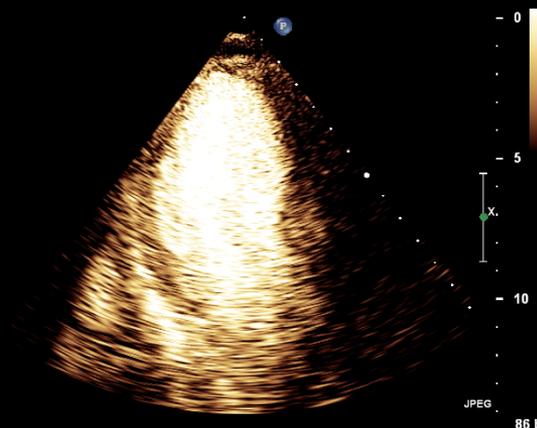
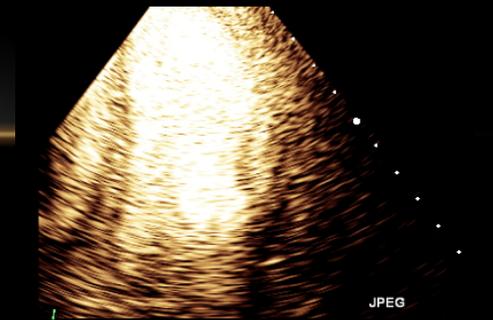
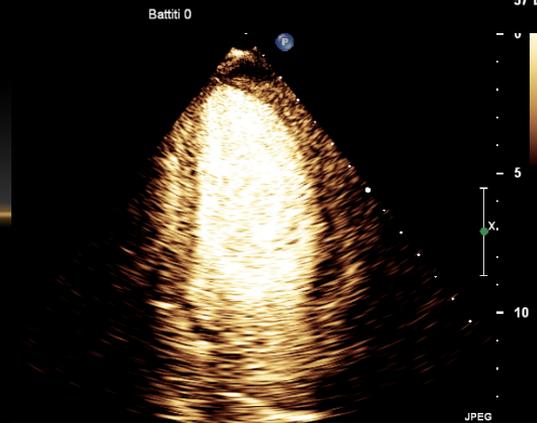
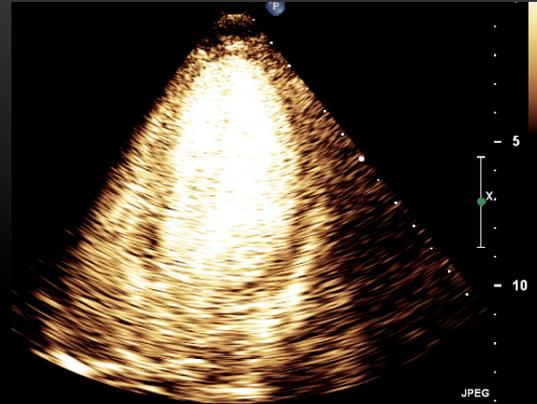
**Comportamento dei markers di ischemia per gradi crescenti di stenosi. Le alterazioni di perfusione diventano evidenti prima di quelle di cinetica, dopo stressor**

# Il tipico caso che mostra quanto male lo stressecho funzioni usando solo la cinetica **Cinetica**

Rest no contrasto

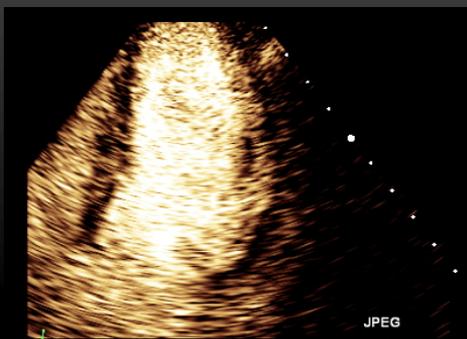
Rest contrasto

Stress contrasto



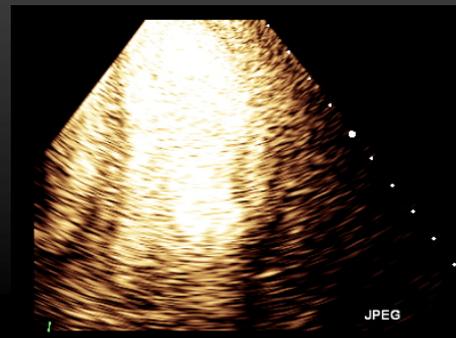
# Il tipico caso che mostra quanto male lo stress echo funzioni usando solo la cinetica

FR 32Hz  
14cm  
**Contrasto**  
59%  
C 50  
P Off  
Pen



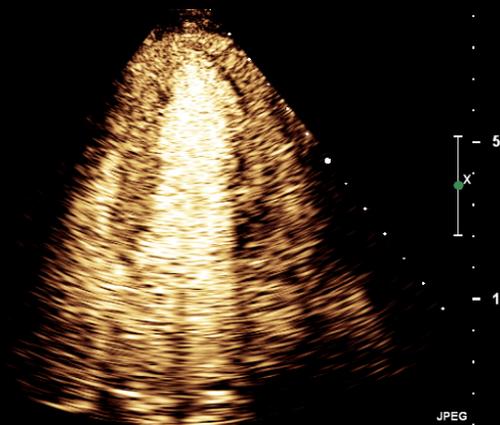
Cinetica

FR 32Hz  
14cm  
**Contrasto**  
59%  
C 50  
P Off  
Pen

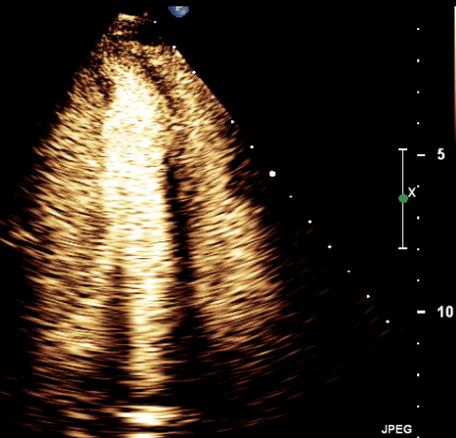


Perfusione

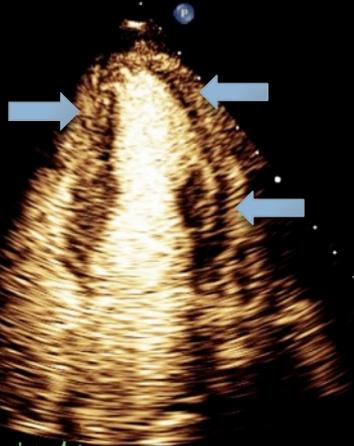
G  
P R  
2.0 2.0



G  
P R  
2.0 2.0



FR 32Hz  
14cm  
**Contrasto**  
59%  
C 50  
P Off  
Pen



101 bpr  
M2  
FR 32Hz  
14cm  
**Contrasto**  
59%  
C 50  
P Off  
Pen



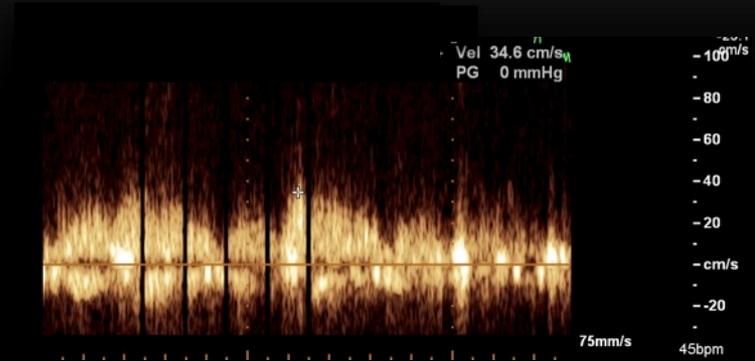
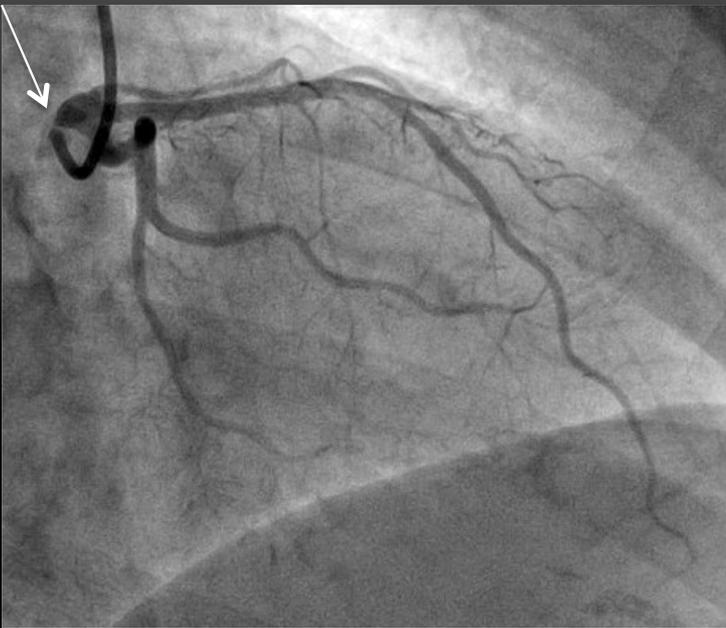
Ritardo 245ms  
Battiti 1

102 bpm

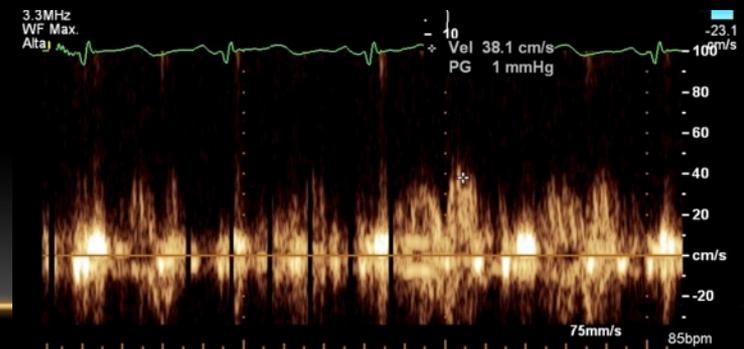
Ritardo 245ms  
Battiti 0

103 bpm

**Si pensa generalmente che le stenosi molto severe non vengano  
"mancate" dallo stressseco standard con sola analisi della cinetica, ma  
invece succede e con conseguenze potenzialmente disastrose**



*Doppler CFR-LAD molto ridotta=1.1  
CFR è molto utile se è il territorio della LAD quello affetto*



## Contrast-Enhanced Transthoracic Second Harmonic Echo Doppler With Adenosine

A Noninvasive, Rapid and Effective Method for Coronary Flow Reserve Assessment

Carlo Caiati, MD, Norma Zedda, MD, Cristiana Montaldo, MD, Roberta Montisci, MD, Sabino Illiceto, MD, FACC

Cagliari, Italy

# 1999!

## Detection of Coronary Artery Disease by Combined Assessment of Wall Motion, Myocardial Perfusion and Coronary Flow Reserve: A Multiparametric Contrast Stress-Echocardiography Study

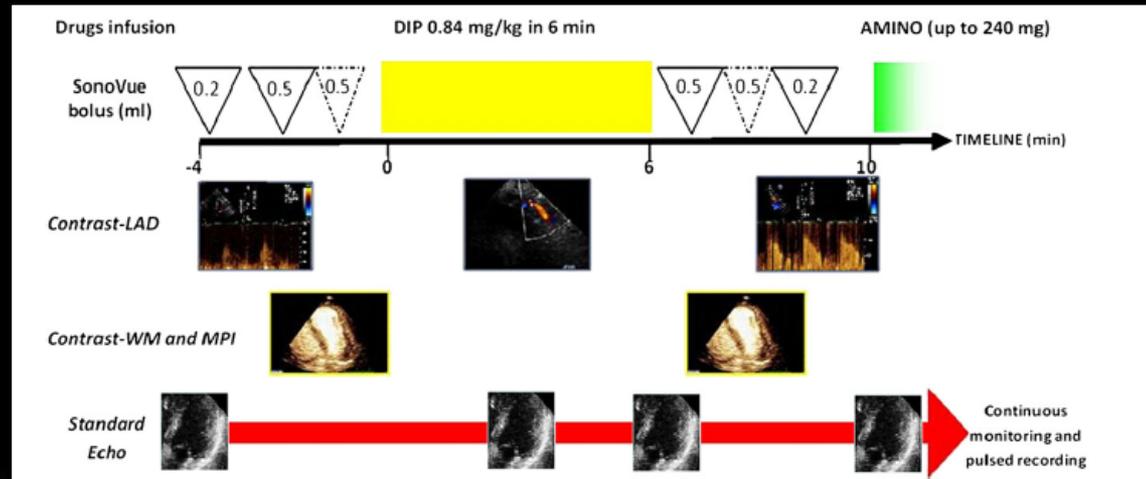
Nicola Gaibazzi, MD, PhD, Fausto Rigo, MD, and Claudio Reverberi, MD, Parma and Mestre-Venice, Italy

400 pazienti che eseguono coronarografia clinicamente indicata in 2 centri

**Table 1** Demographics and coronary angiographic and stress echocardiographic results (n = 400)

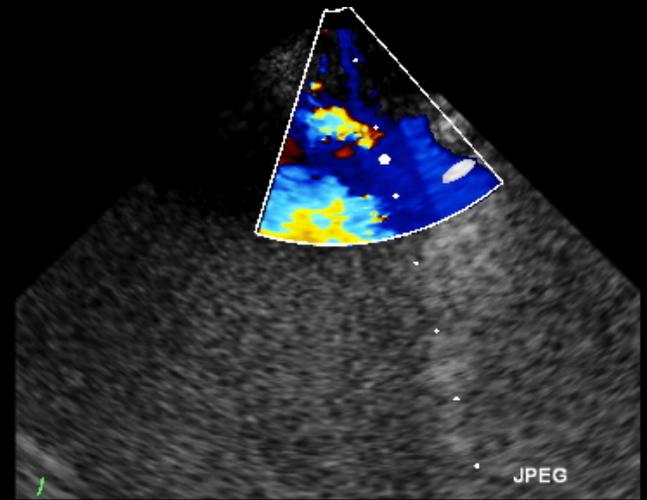
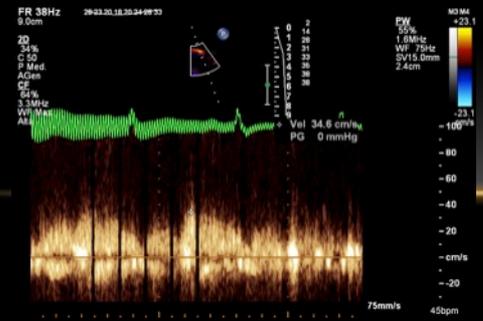
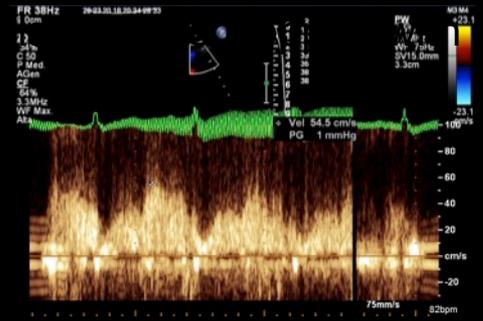
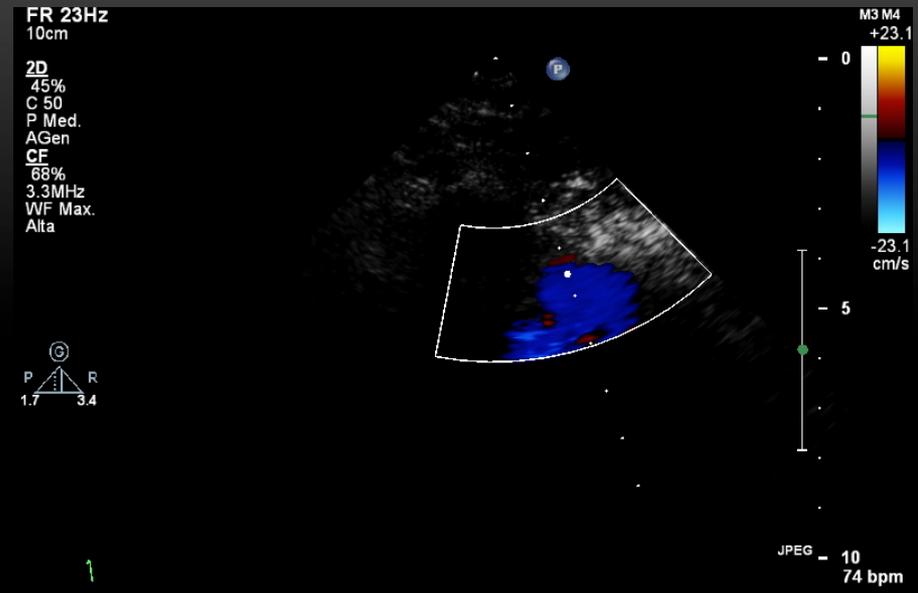
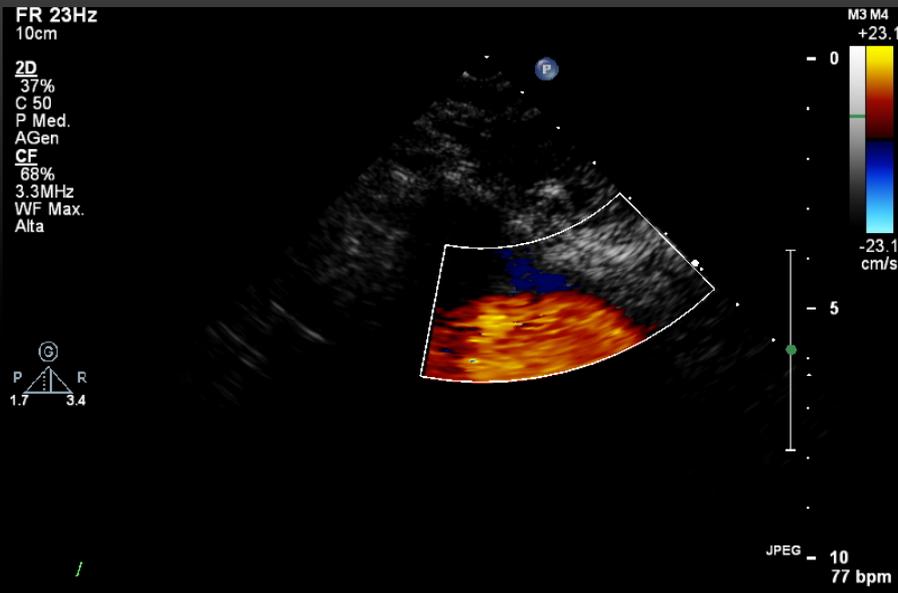
Characteristic	Value
Age (years)	66 ± 11 (29–91)
Men/women	263/137
Risk factors and history	
Hypertension	288 (72%)
Hypercholesterolemia	256 (64%)
Smoking	92 (23%)
Diabetes mellitus	112 (28%)
Family history of CAD	84 (21%)
Ejection fraction	55 ± 7
Reduced ejection fraction (<50%)	128 (32%)
Prior CAD*	132 (33%)
Previous myocardial infarction	91 (23%)
Previous revascularization	104 (26%)
Coronary angiographic results	
Patients with CAD > 50%	268 (67%)
One-vessel disease	134 (34%)
Two-vessel disease	82 (21%)
Three-vessel disease	52 (13%)
LAD disease (>50%)	202 (47%)
Stress echocardiographic results	
Patients with reversible WM abnormalities	188 (47%)
Patients with CFR-LAD < 1.9	200 (50%)
Patients with reversible WM abnormalities or CFR-LAD < 1.9	264 (66%)
Patients with reversible MPI abnormalities	302 (76%)

Data are expressed as mean ± SD (range) or as number (percentage).



# Rest no contrasto, no visible LAD flow

# Rest contrasto (piccolo bolo), flusso LAD visibile



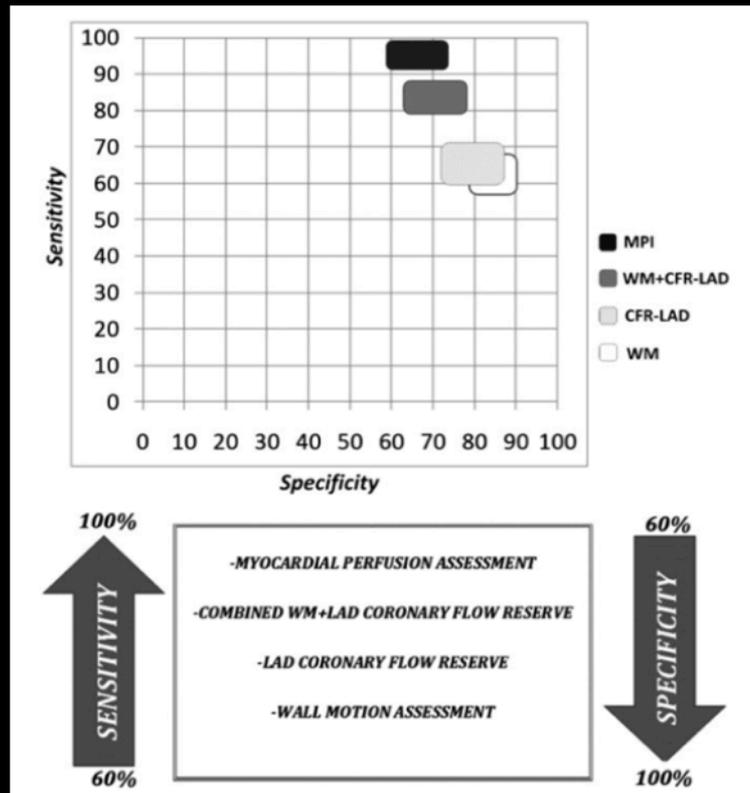
# Detection of Coronary Artery Disease by Combined Assessment of Wall Motion, Myocardial Perfusion and Coronary Flow Reserve: A Multiparametric Contrast Stress-Echocardiography Study

Nicola Gaibazzi, MD, PhD, Fausto Rigo, MD, and Claudio Reverberi, MD, *Parma and Mestre-Venice, Italy*

La maggiore accuratezza della Perfusione miocardica+Cinetica contro sola Cinetica per la diagnosi di CAD è sostanzialmente dovuta all'aumento di sensibilità, con diminuzione di specificità relativamente minore

400 pz, tutti con indicazione clinica a coronarografia

Dipiridamolo 0.84mg/kg/6min



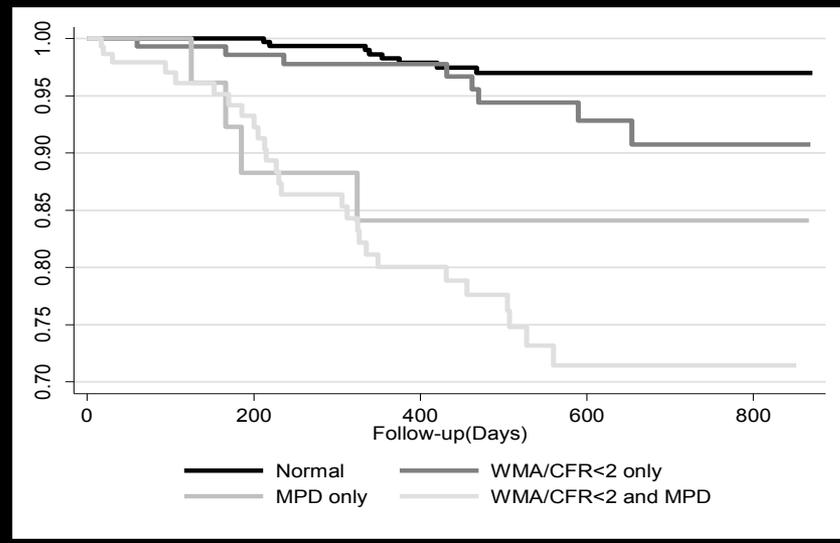
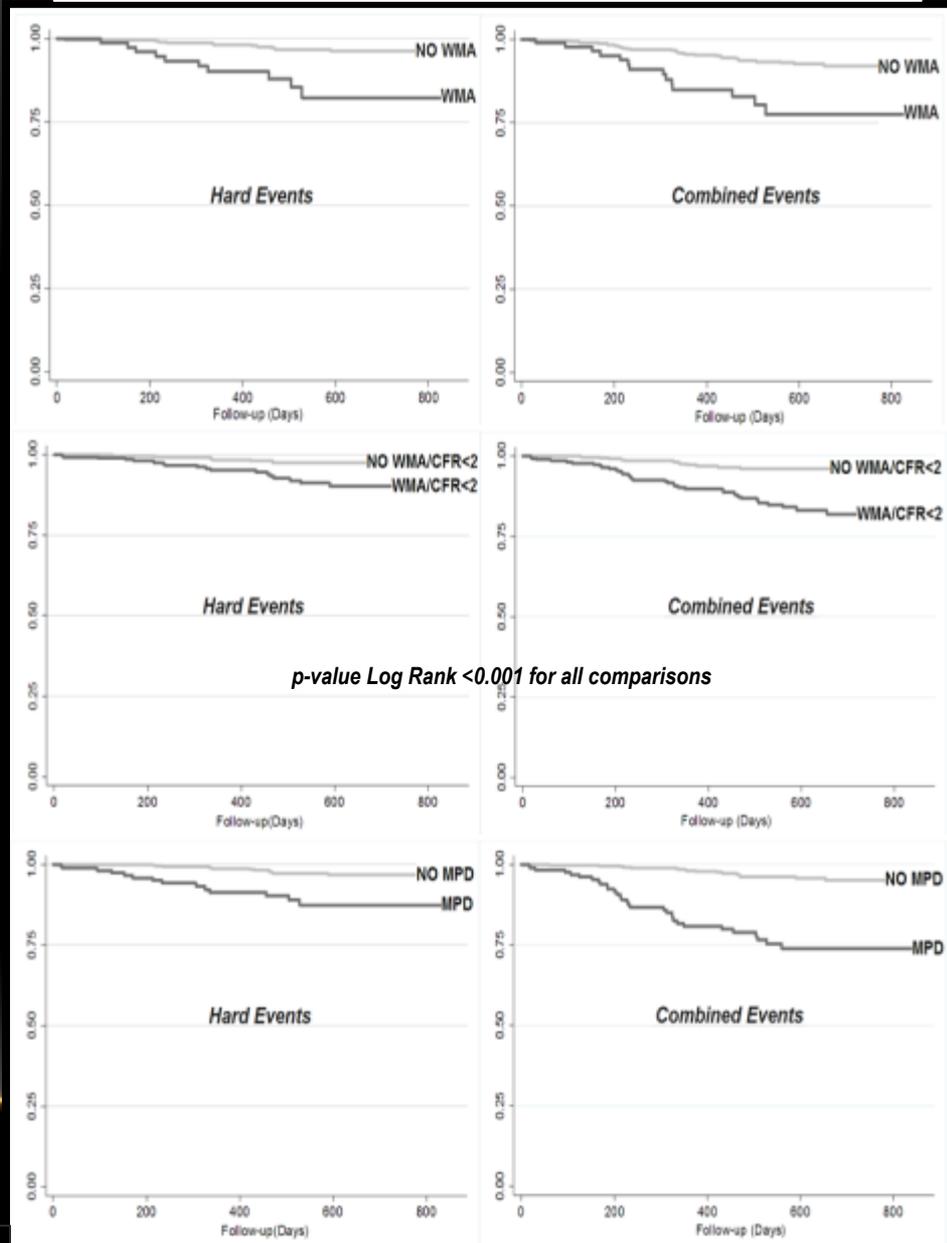
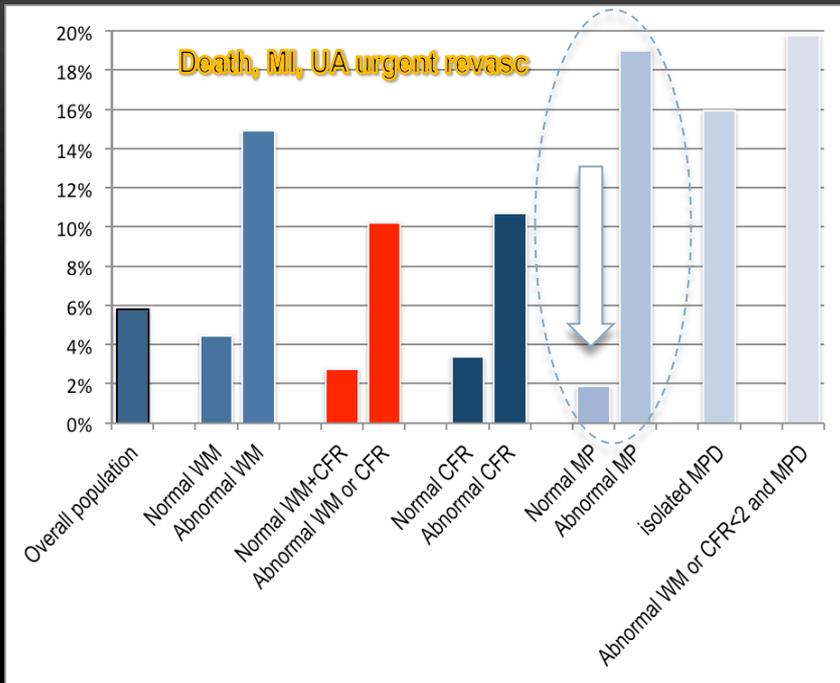
Anche l'aggiunta della misurazione della CFR-LAD facilitata da contrasto aumenta significativamente la sensibilità, abbassando relativamente la specificità

**L'analisi della cinetica necessita di essere integrata almeno da un altro parametro tra CFR-LAD e Perfusione per raggiungere una sensibilità clinicamente accettabile per la diagnosi di CAD**

Quando entrambi sono tecnicamente fattibili, naturalmente la perfusione ha il vantaggio di comprendere tutti e 3 i territori coronarici, pur essendo più complessa e "demanding"

# Prognosi

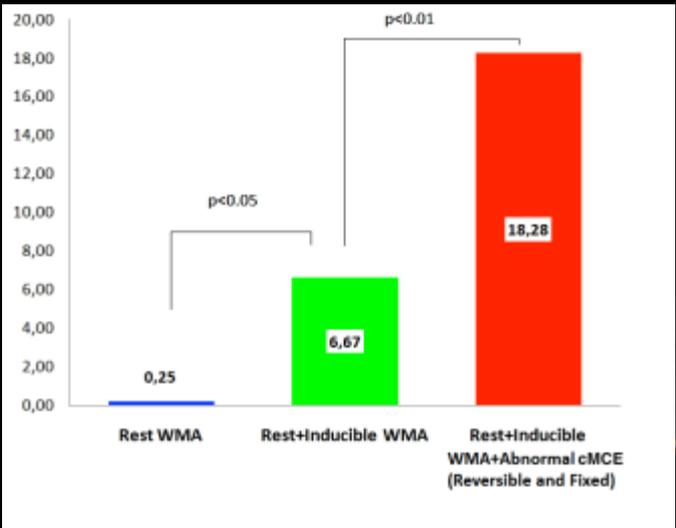
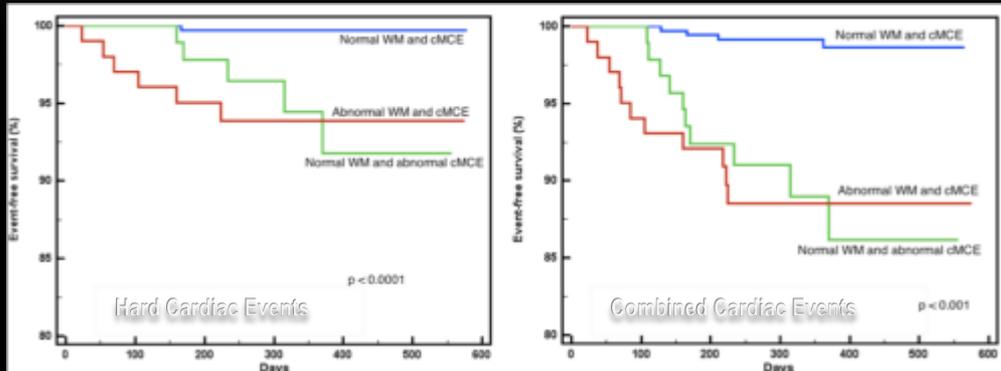
## Comparative Prediction of Cardiac Events by Wall Motion, Wall Motion plus Coronary Flow Reserve or Myocardial Perfusion Analysis: A Prospective Multicenter Study of Contrast Stress Echocardiography



# ..e la Prognosi?

## VALORE INCREMENTALE DELL'ANALISI DELLA PERFUSIONE RISPETTO ALLA SOLA CINETICA PER LA STRATIFICAZIONE DEGLI EVENTI CARDIACI

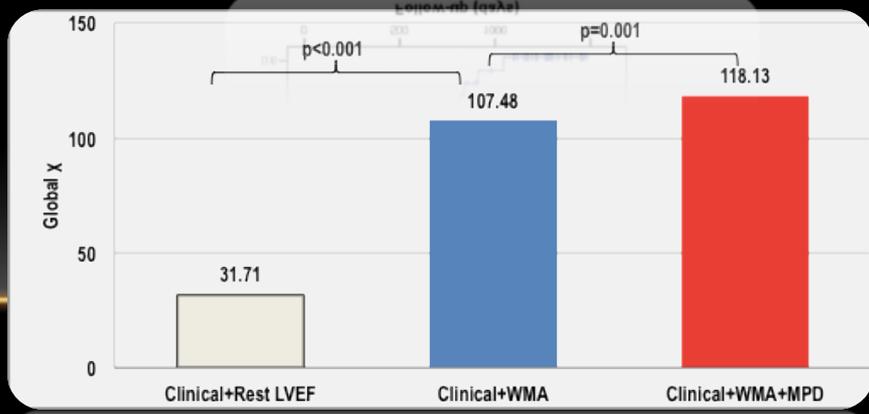
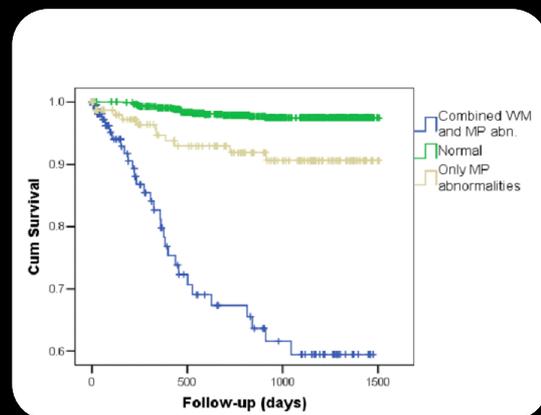
**Contrast Stress-Echocardiography Predicts Hard Cardiac Events in Patients with Suspected Acute Coronary Syndrome but non-diagnostic Electrocardiogram and Normal 12-hour Troponin.**



**Prognostic Value of High-Dose Dipyridamole Stress Myocardial Contrast Perfusion Echocardiography**  
Nicola Gaibazzi, Claudio Reverberi, Valentina Lorenzoni, Sabrina Molinaro and Thomas R. Porter

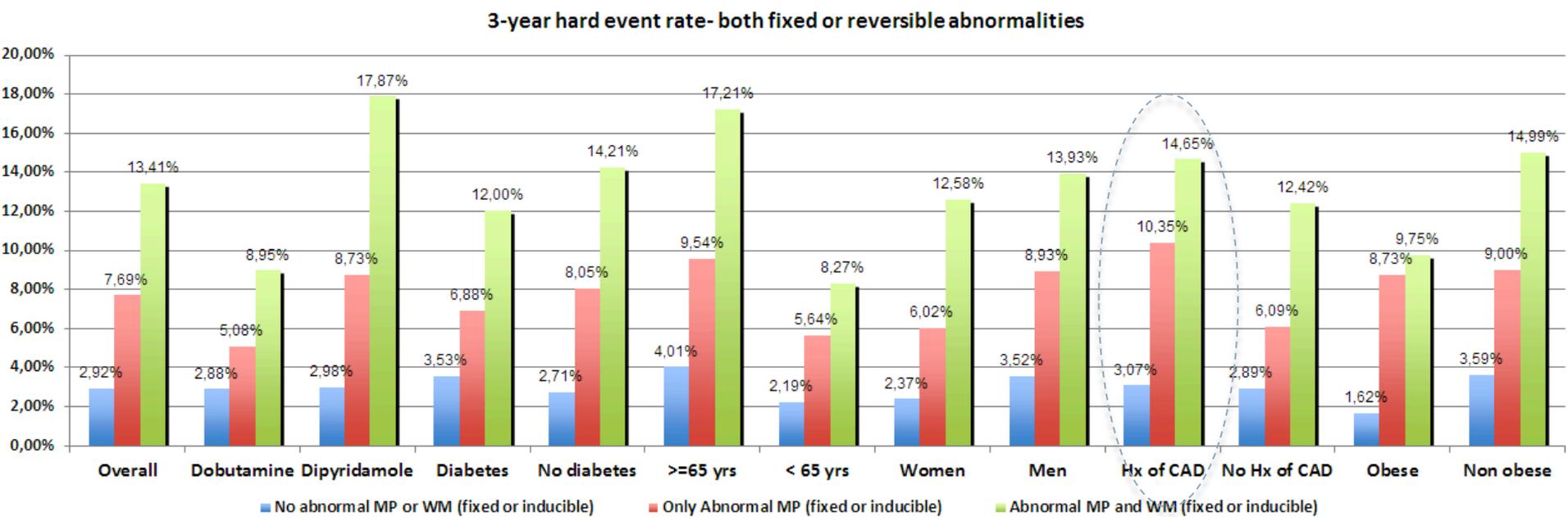
*Circulation*. 2012;126:1217-1224; originally published online August 7, 2012;  
doi: 10.1161/CIRCULATIONAHA.112.110031  
*Circulation* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231  
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The online version of this article, along with updated information and services, is located on the World Wide Web at:  
<http://circ.ahajournals.org/content/126/10/1217>



# ASSESSING MYOCARDIAL PERFUSION WITH REAL TIME STRESS CONTRAST ECHOCARDIOGRAPHY TO RECLASSIFY RISK WITHIN THE GENERAL POPULATION AND VALORE TRASVERSALE DELLA PERFUSIONE NEI SOTTOGRUPPI DI PAZIENTI

Thomas Porter, Claudio Reverberi, Juefei Wu, Feng Xie, Valentina Lorenzoni, Sabrina Molinaro, Nicola Gaibazzi



>3200 patients, submitted

# Safety durante contrast stress-echo: uno step oltre la classica definizione di adverse events:


 European Heart Journal (2013) 34, 2340–2345  
 doi:10.1093/eurheartj/ehs184

**FASTTRACK CLINICAL**

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## Impact of cardiac magnetic resonance imaging on human lymphocyte DNA integrity

**Michael Fiechter<sup>1,2†</sup>, Julia Stehli<sup>1†</sup>, Tobias A. Fuchs<sup>†</sup>, Svetlana Dougoud<sup>1</sup>,  
 Oliver Gaemperli<sup>1</sup>, and Philipp A. Kaufmann<sup>1,2\*</sup>**

<sup>1</sup>Department of Radiology, Cardiac Imaging, University Hospital Zurich, Ramistrasse 100, NLK C 42, Zurich CH-8091, Switzerland; and <sup>2</sup>Zurich Center for Integrative Human Physiology (ZIH), University of Zurich, Zurich, Switzerland  
 Received 1 March 2013; revised 23 April 2013; accepted 8 May 2013; online publish-ahead-of-print 21 June 2013  
 Guest edited by Jeroen Bax, Professor of Cardiology, Leiden University Medical Centre, Leiden, Netherlands.


 European Heart Journal (2013) 34, 2337–2339  
 doi:10.1093/eurheartj/ehs214

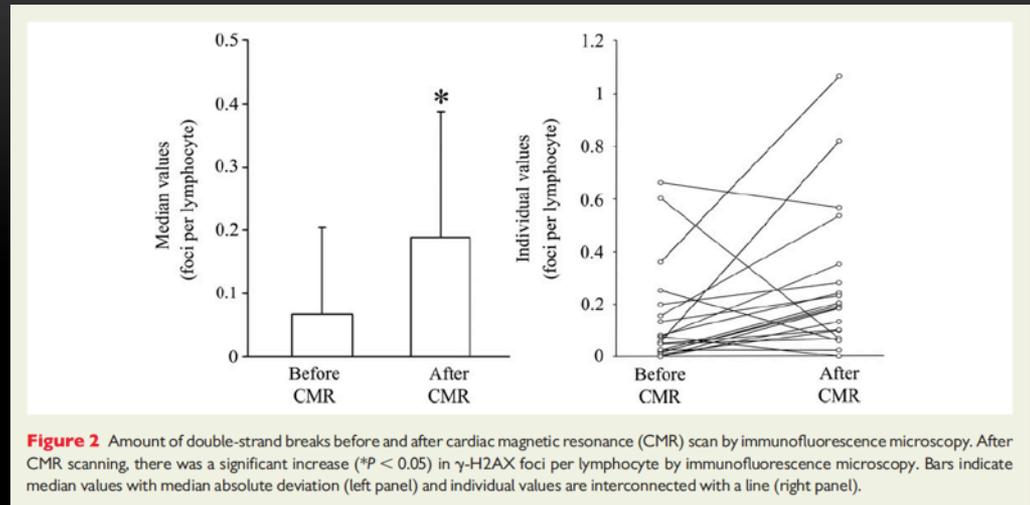
**EDITORIAL**

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## Is cardiac magnetic resonance imaging causing DNA damage?

**Juhani Knuuti<sup>1\*</sup>, Antti Saraste<sup>1,2</sup>, Marko Kallio<sup>3</sup>, and Heikki Minn<sup>4</sup>**

<sup>1</sup>Turku PET Centre, Turku University Hospital and University of Turku, Kinamyllykatu 4–8, 20520 Turku, Finland; <sup>2</sup>Heart Center, Turku University Hospital, Turku, Finland; <sup>3</sup>VTT Biotechnology for Health and Wellbeing, Turku, Finland; and <sup>4</sup>Department of Oncology and Radiotherapy, Turku University Hospital, Turku, Finland  
 Online publish-ahead-of-print 2 July 2013



## Coronarografia, CT-Angio, PET/CT e CMR hanno tutti dimostrato di aumentare DNA-DSBs

**Table 1** Amount of excess DNA double strand breaks per lymphocyte induced by different diagnostic procedures

	Early measurements		Later measurements		Reference
	DSB foci/lymphocyte <sup>a</sup>	Time of measurement	DSB foci/lymphocyte	Time of measurement	
[ <sup>18</sup> F]FDG injection (5 mSv)	0.11	30 min post-injection	0.16	30 min post-PET/CT	May et al. (2012) <sup>15</sup>
CTA (~2 mSv)	0.04	30 min post scan	–		Kuefner et al. (2010) <sup>13</sup>
CTA (~8 mSv)	0.24	30 min post-scan	0.092 and 0.014	2 and 5 h post-scan	Grudzenski et al. (2009) <sup>14</sup>
CTA (~17 mSv)	0.39	30 min post-scan	–		Kuefner et al. (2010) <sup>13</sup>
Invasive angiography	0.13 <sup>b</sup>	15 min post-procedure	–		Kuefner et al. (2009) <sup>12</sup>
1.5T CMR	0.12	At the end of the scan	–		Fiechter et al. (2013) <sup>11</sup>

CMR, cardiac magnetic resonance; CTA, computed tomography angiography; DSB, double-strand break; FDG, fluorodeoxyglucose; PET, positron emission tomography.

<sup>a</sup>Baseline level of DSBs is ~0.06–0.08 DSB foci/lymphocyte.

<sup>b</sup>Median of different non-cardiac diagnostic and interventional procedures.

Letter to the editor

## Assessment of DNA damage associated with standard or contrast diagnostic echocardiography ☆☆☆



Nicola Gaibazzi <sup>a,\*</sup>, Nicola Marziliano <sup>a,b</sup>, Thomas R. Porter <sup>c</sup>, Gianmarco Negri <sup>a</sup>, Maria Antonietta Demola <sup>a</sup>, Claudio Reverberi <sup>a</sup>, Diego Ardissino <sup>a</sup>

<sup>a</sup> Cardiology Department, Parma University Hospital, Parma, Italy

<sup>b</sup> Health Sciences Department, University of Campobasso, Campobasso Italy

<sup>c</sup> Section of Cardiology, Department of Internal Medicine, University of Nebraska Medical Center, Omaha, NE, USA

**Contrast-echo brings echo further regarding its diagnostic yield, but ..is it safe compared with other imaging modalities?**

**30 cases sampled pre and post stressecho vs controls: 10 standard echo, 10 contrast opacification echo, 10 contrast perfusion echo**

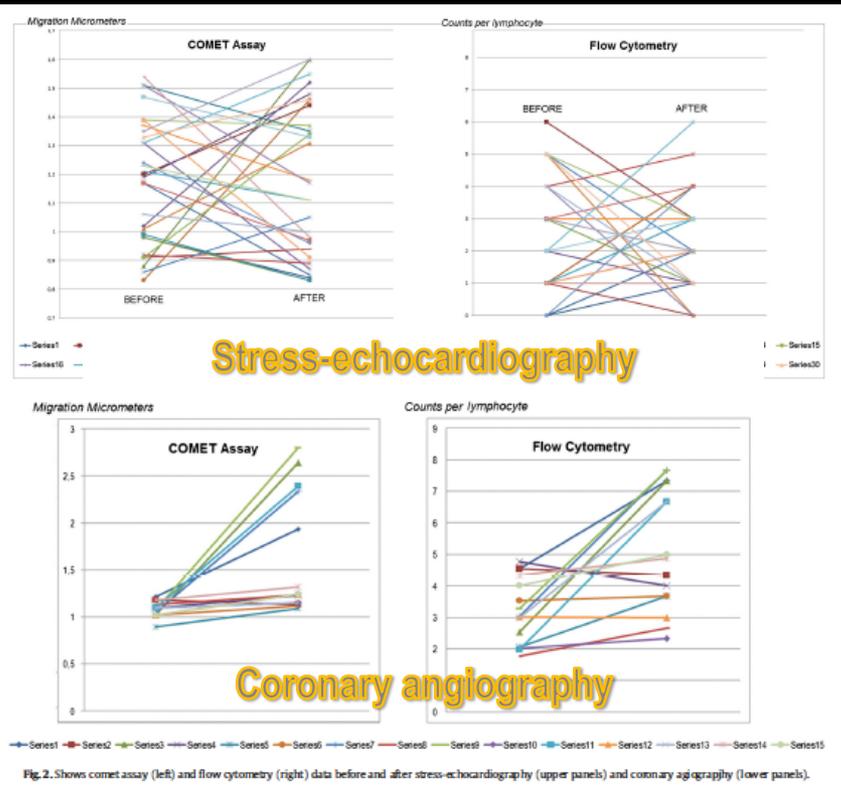
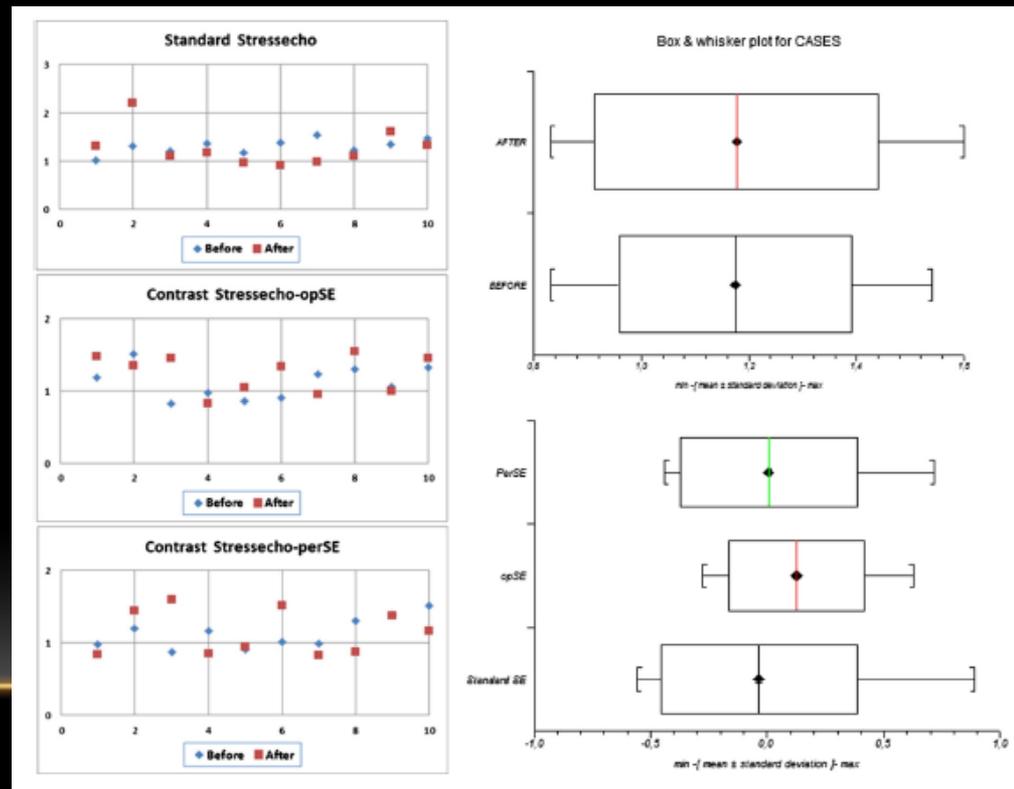


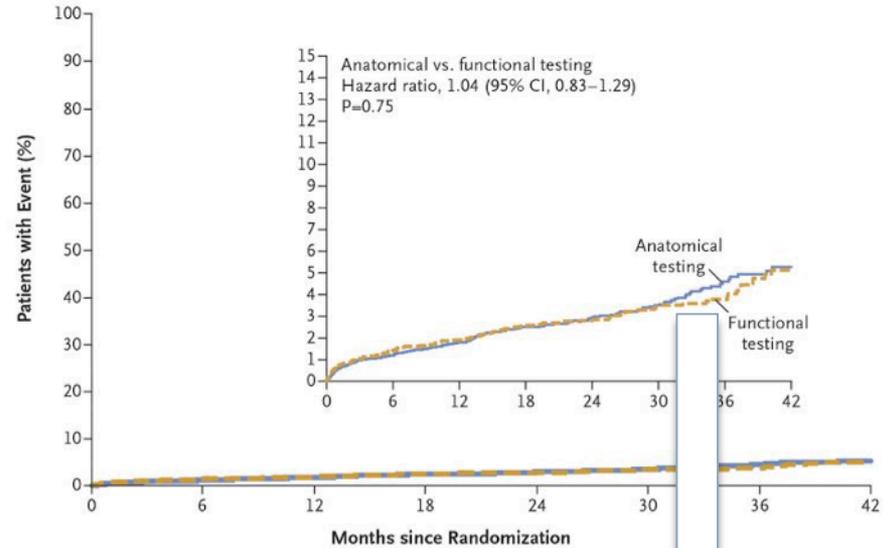
Fig. 2. Shows comet assay (left) and flow cytometry (right) data before and after stress-echocardiography (upper panels) and coronary angiography (lower panels).



ORIGINAL ARTICLE

## Outcomes of Anatomical versus Functional Testing for Coronary Artery Disease

Pamela S. Douglas, M.D., Udo Hoffmann, M.D., M.P.H., Manesh R. Patel, M.D., Daniel B. Mark, M.D., M.P.H., Hussein R. Al-Khalidi, Ph.D., Brendan Cavanaugh, M.D., Jason Cole, M.D., Rowena J. Dolor, M.D., Christopher B. Fordyce, M.D., Megan Huang, Ph.D., Muhammad Akram Khan, M.D., Andrzej S. Kosinski, Ph.D., Mitchell W. Krucoff, M.D., Vinay Malhotra, M.D., Michael H. Picard, M.D., James E. Udelson, M.D., Eric J. Velazquez, M.D., Eric Yow, M.S., Lawton S. Cooper, M.D., M.P.H., and Kerry L. Lee, Ph.D., for the PROMISE Investigators\*



**Table 2. End Points According to Study Group.\***

End Point	CTA Strategy (N=4996)	Functional-Testing Strategy (N=5007)	Adjusted Hazard Ratio (95% CI)	P Value
<b>Clinical end point — no. of patients</b>				
Primary composite end point	164	151	1.04 (0.83–1.29)	0.75
Death from any cause	74	75		
Nonfatal myocardial infarction	30	40		
Hospitalization for unstable angina	61	41		
Major procedural complication	4	5		
Primary end point plus catheterization showing no obstructive CAD	332	353	0.91 (0.78–1.06)	0.22
Death or nonfatal myocardial infarction	104	112	0.88 (0.67–1.15)	0.35
Death, nonfatal myocardial infarction, or hospitalization for unstable angina	162	148	1.04 (0.84–1.31)	0.70
<b>Test-related end point</b>				
Invasive catheterization showing no obstructive CAD — no. (%)	170 (3.4)	213 (4.3)	—	0.02

Contrast-echo farebbe meglio?  
Non lo si può escludere

4692 (93.7%) Underwent functional test as first test  
 3159 (67.3%) Underwent nuclear stress imaging  
 1056 (22.5%) Underwent stress echocardiography  
 477 (10.2%) Underwent exercise ECG  
 315 (6.3%) Did not undergo functional test as first test  
 67 (21.3%) Underwent other test as first test  
 20 (6.3%) Underwent catheterization  
 47 (14.9%) Underwent CTA or CAC scoring  
 246 (78.1%) Did not undergo test  
 2 (0.6%) Underwent test before randomization