

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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FOCUS ISSUE: HYPERTROPHIC CARDIOMYOPATHY

Clinical Research

Hypertrophic Cardiomyopathy Phenotype Revisited After 50 Years With Cardiovascular Magnetic Resonance

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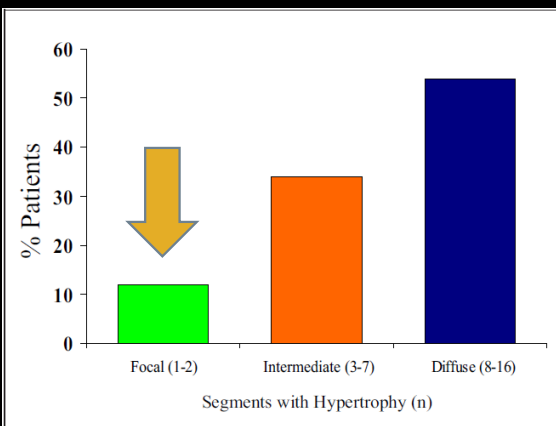
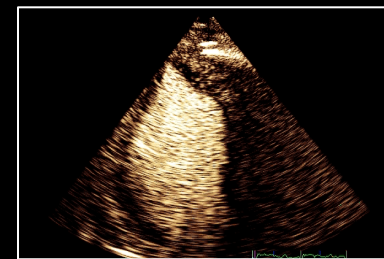
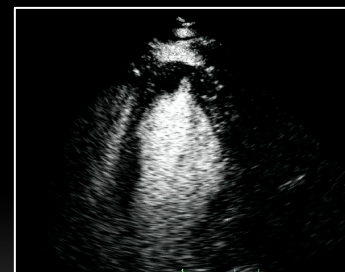
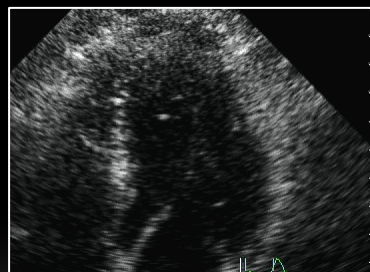
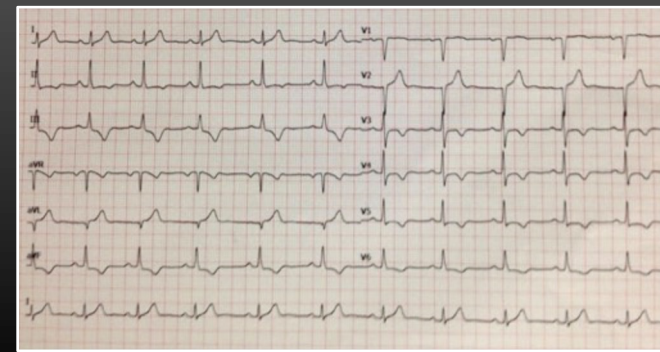


Figure 2 Prevalence of Hypertrophied Segments

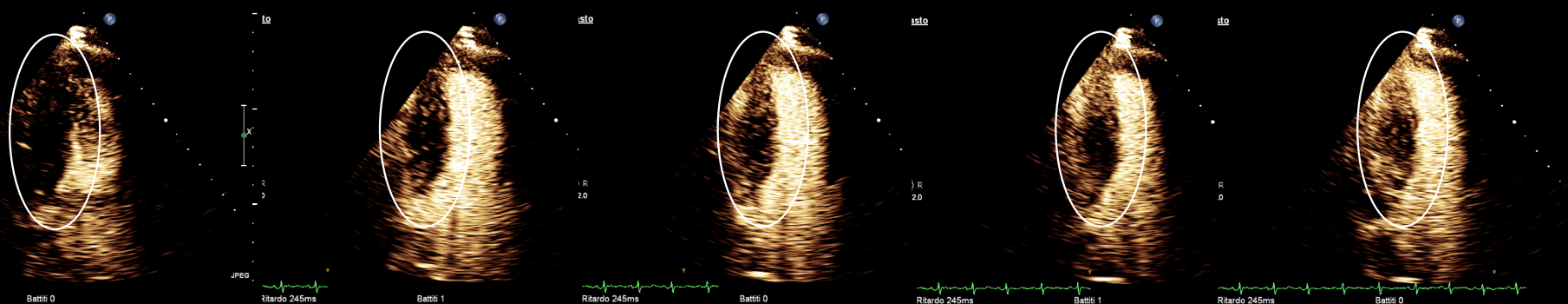
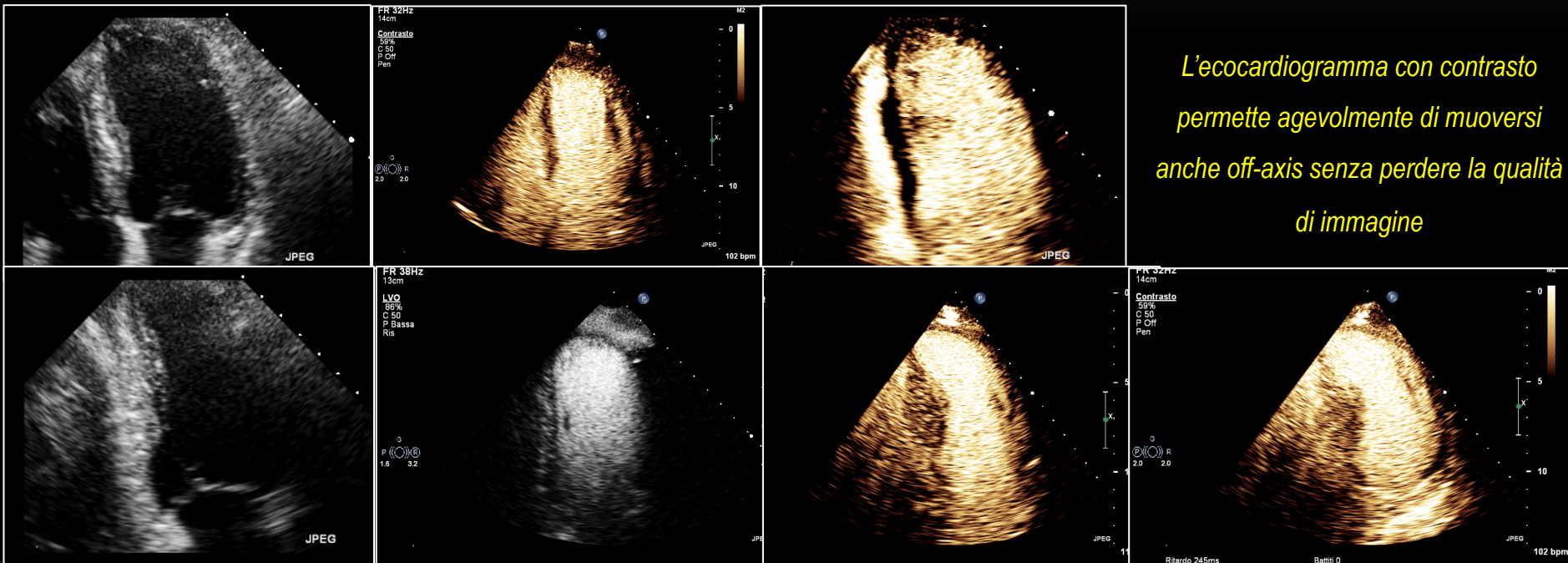
Prevalence of focal (1 to 2 hypertrophied segments), intermediate (3 to 7 segments), and diffuse left ventricular hypertrophy (8 to 16 segments) within the cohort of 333 patients with hypertrophic cardiomyopathy.

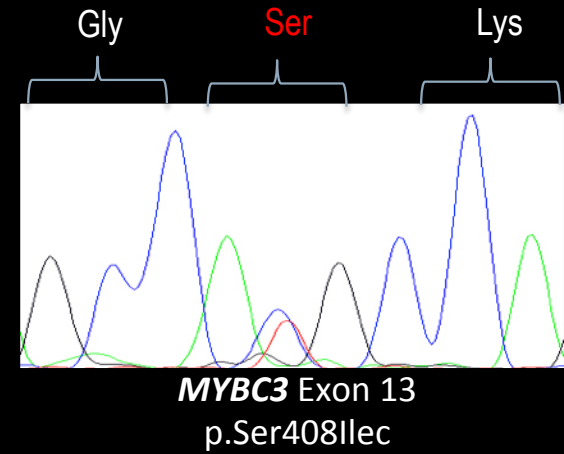
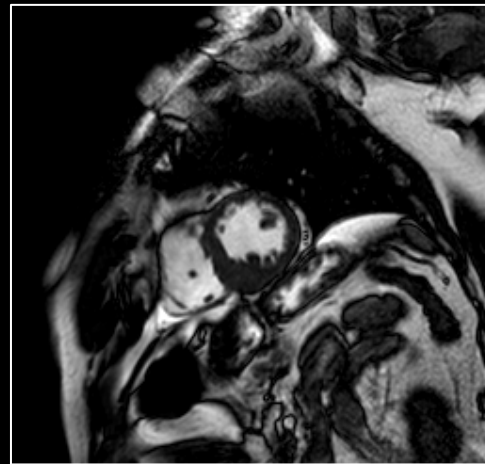
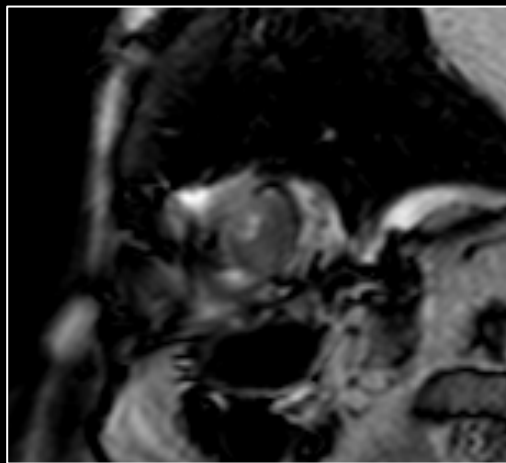
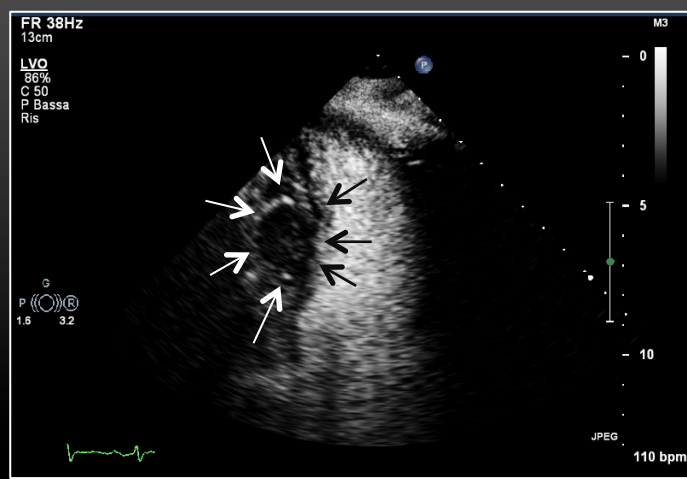
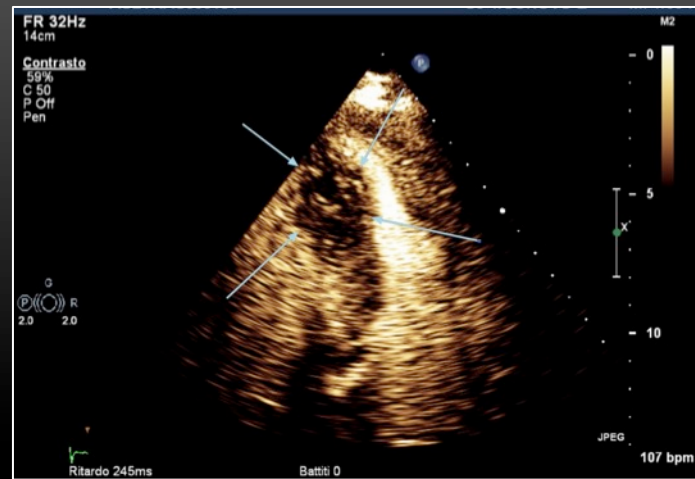


52enne che si presenta ad ecostress perché all'ultimo controllo annuale ECG (sportivo) si rileva una T invertita non presente nel 2013.



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





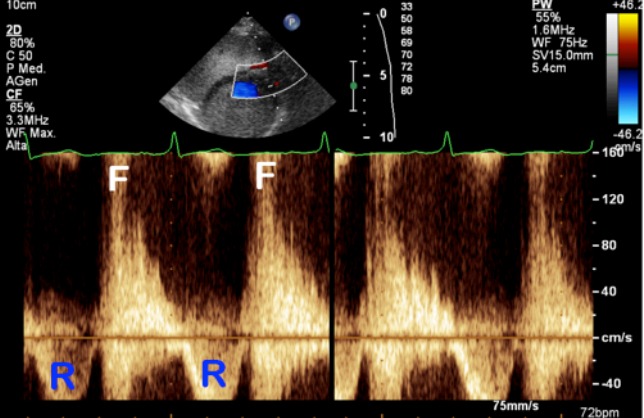
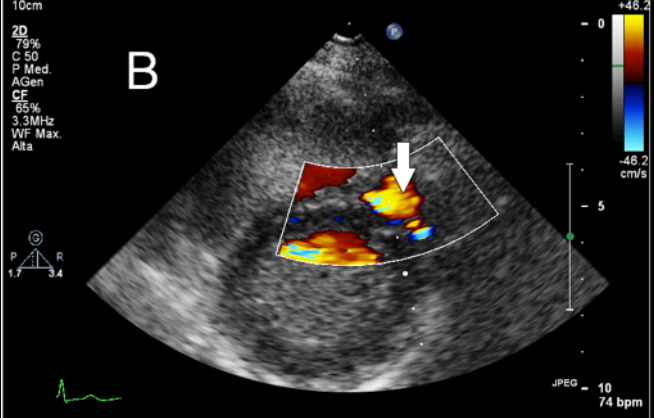
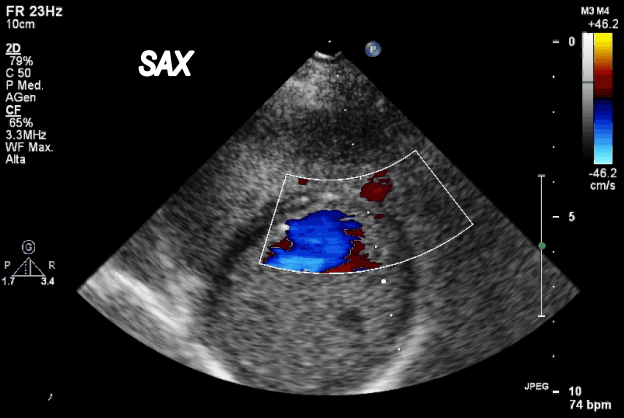
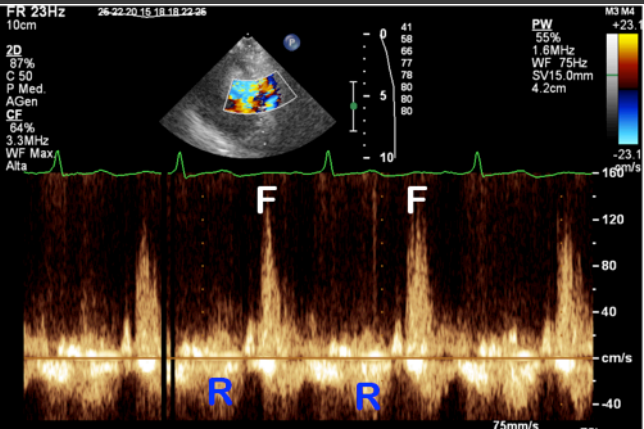
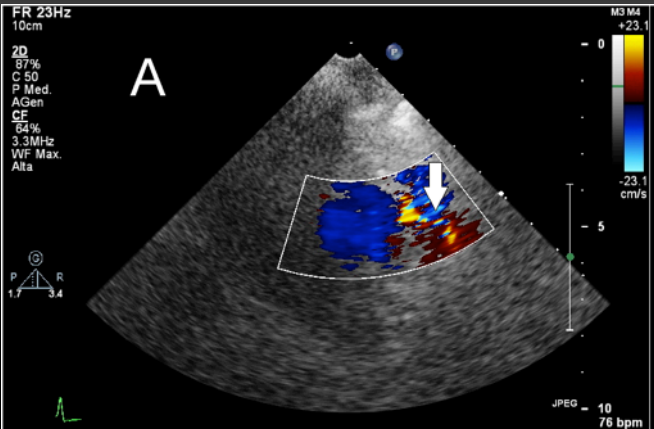
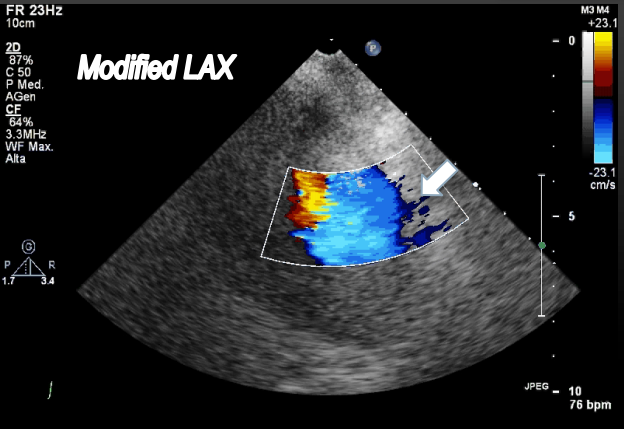
CONTRAST-FACILITATED COLOR DOPPLER RILEVA CON MAGGIOR FACILITÀ:

PONTI MIOCARDICI, IL DECORSO INTRAMIOCARDICO E TORTUOSITÀ SEVERE

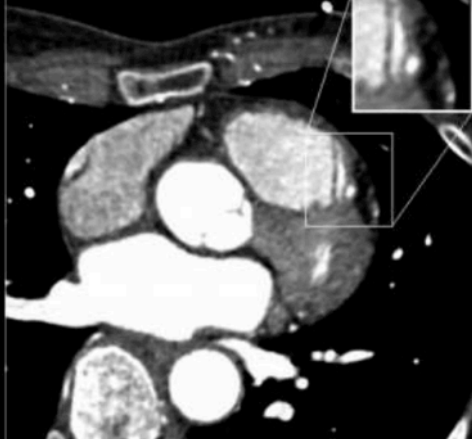
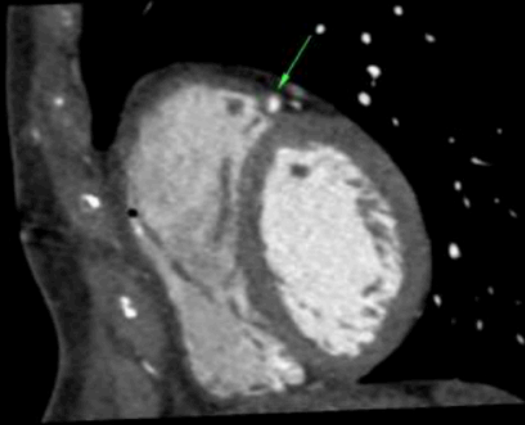
...VARIANTI CONGENITE ASSOCIATE ALLE X-SYNDROMES ?

Rest

Dolore toracico durante esercizio



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



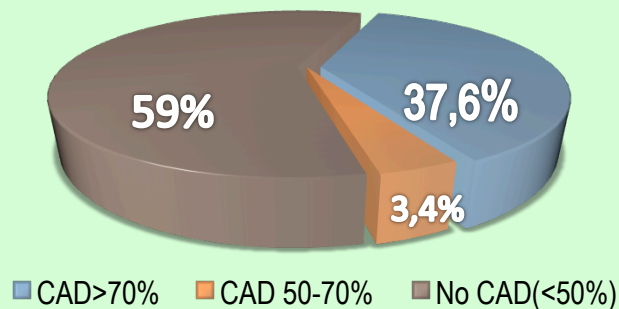
Stresseco per ottimizzare l'indicazione ad Angiografia Coronarica

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.

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.

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)

Coronary Artery Disease

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

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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.

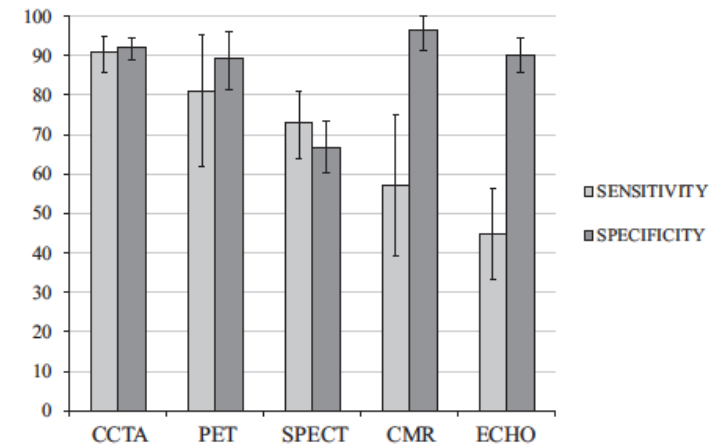


Figure 3. Sensitivity and specificity of noninvasive imaging techniques.

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

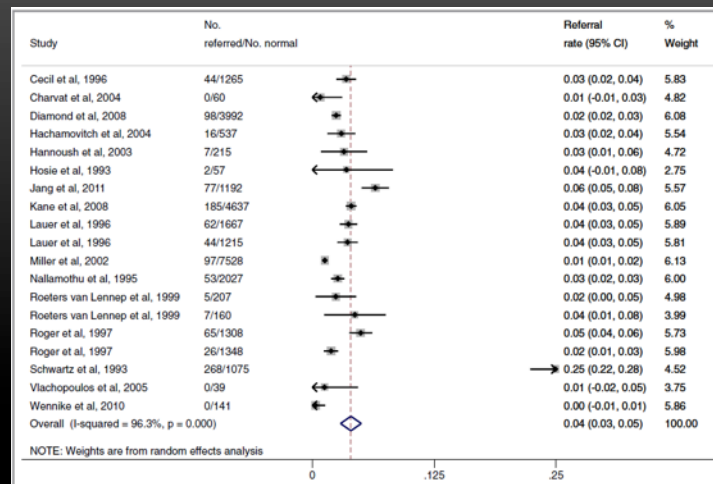
Joseph A. Ladapo, Saul Blecker, Michael R. Elashoff, Jerome J. Federspiel, Dorice L. Vieira, Gaurav Sharma, Mark Monane, Steven Rosenberg, Charles E. Phelps and Pamela S. Douglas

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

doi: 10.1161/JAHA.113.000505

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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.

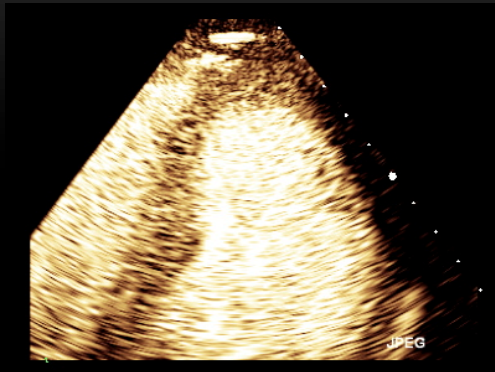
*Diagnostic effectiveness based in random-effects meta-analysis of sensitivity and specificity reported in 15 studies of exercise ECHO and 30 studies of exercise MPI (45 studies in total).

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

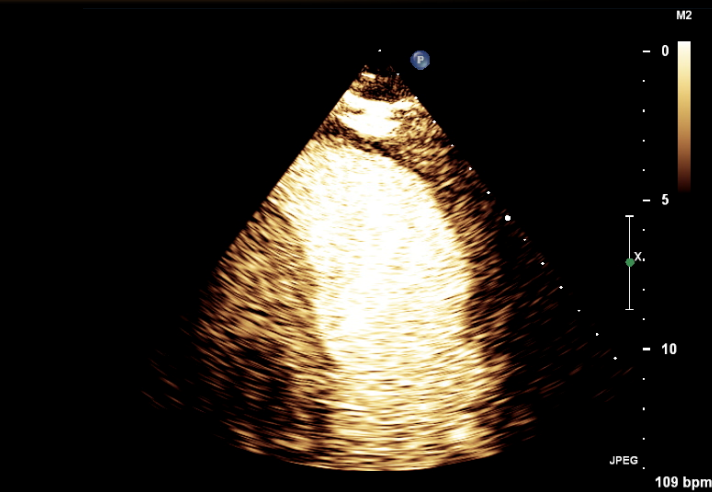
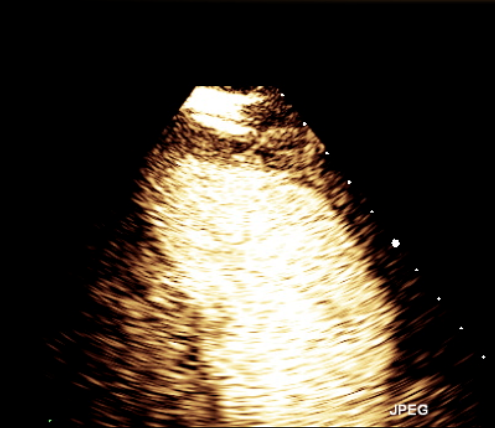
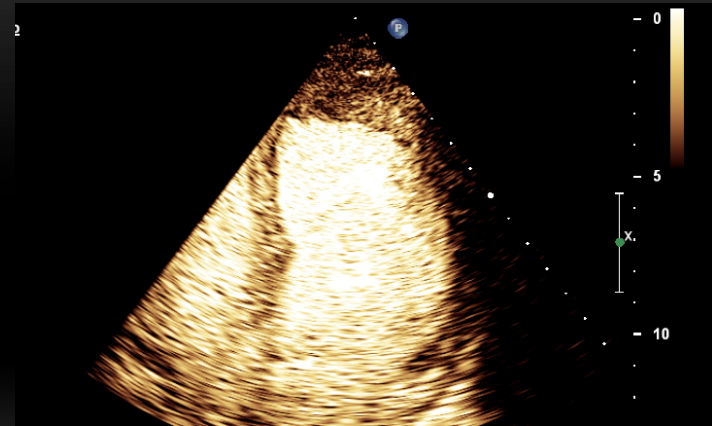
Tutti i tests provocativi (non solo stresseco) hanno un problema di sensibilità e quindi molti falsi negativi, una volta che si considerino pz anche con sintomi non tipici da sforzo e il referral bias..
Nella pratica abbiamo bisogno di incrementare la sensibilità, anche se questo costasse una lieve riduzione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

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

Rest

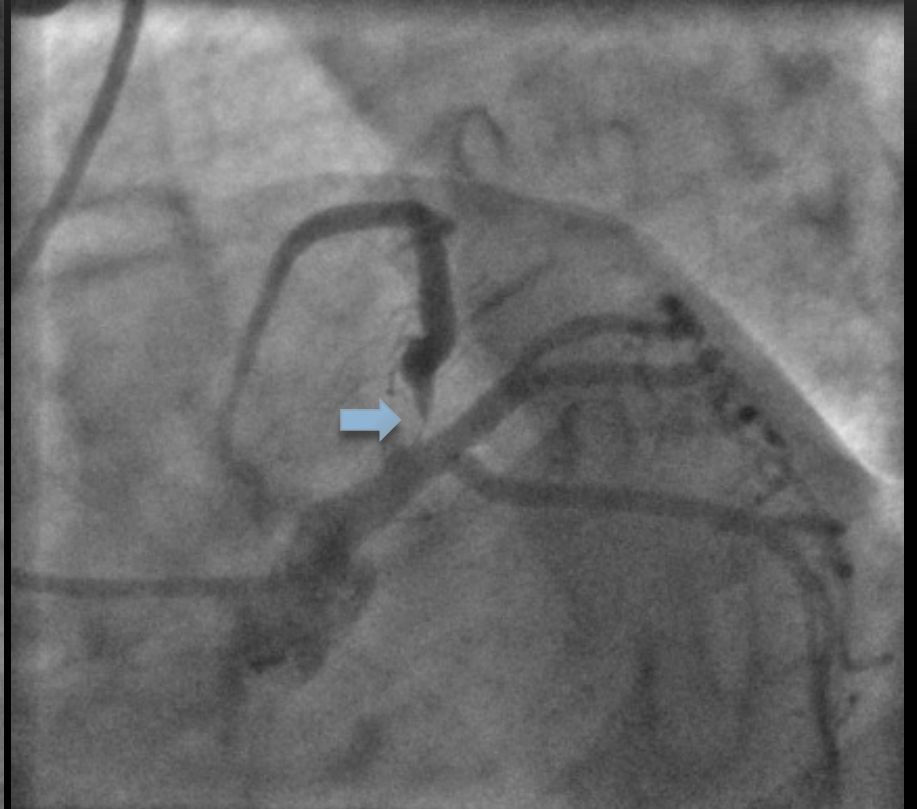
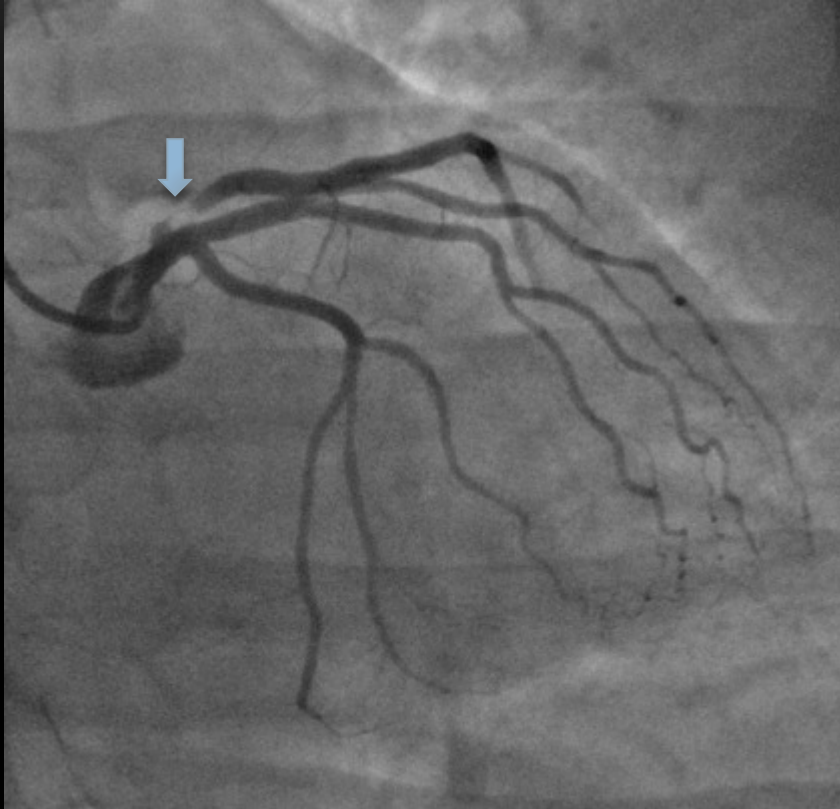


Stress



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.†

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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.

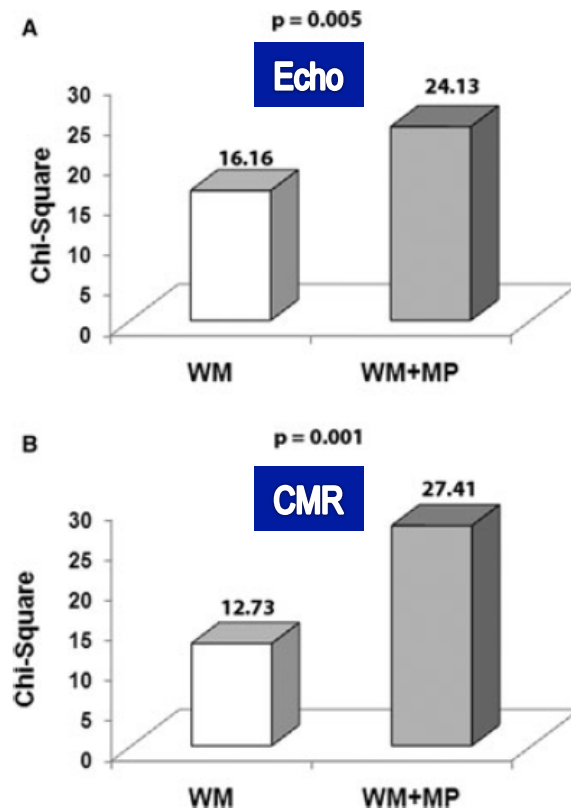


Figure 1. Incremental value of combined wall motion (WM) and myocardial perfusion (MP) (expressed on y-axis as chi-square values with incremental degrees of freedom) over WM alone by real time myocardial contrast echocardiography (A) and cardiovascular magnetic resonance (B).

Come risolvere la problematica della bassa sensibilità per CAD?

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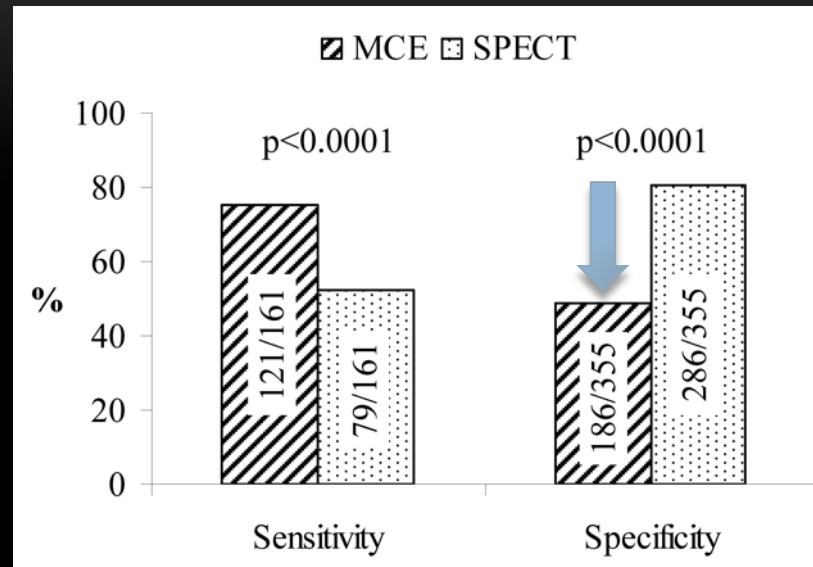
Cardiac Imaging

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

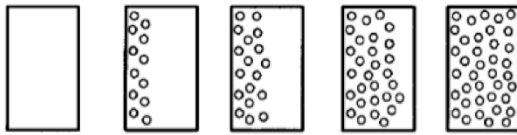
×

MB Velocity

Circulation American Heart Association
 JOURNAL OF THE AMERICAN HEART ASSOCIATION Learn and Live™

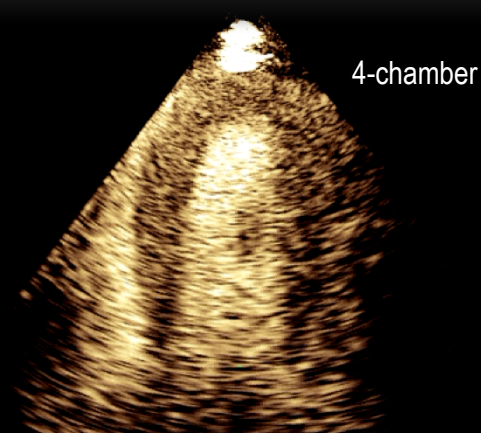
Quantification of Myocardial Blood Flow With Ultrasound-Induced Destruction of Microbubbles Administered as a Constant Venous Infusion
 Kevin Wei, Ananda R. Jayaweera, Sorosh Farooqi, Andrei I. Laska, Danny M. Sliwa and Sanjay Kaul
 Circulation 1998;97:473-483

A. B. C. D. E.



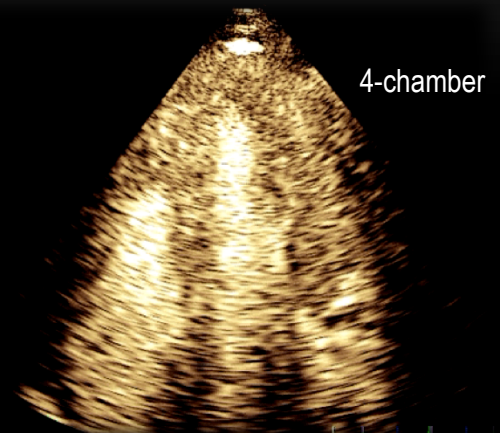
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time → 0



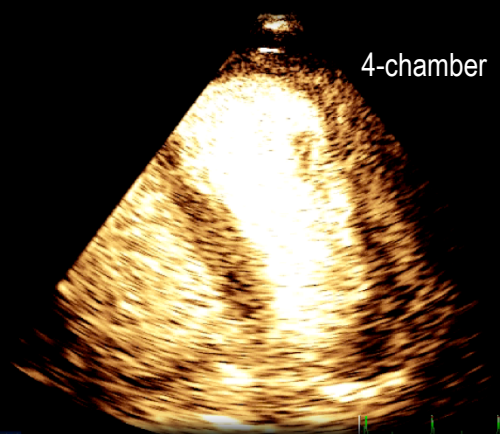
4-chamber

Endsystolic triggering:
1 endsystolic image per cycle



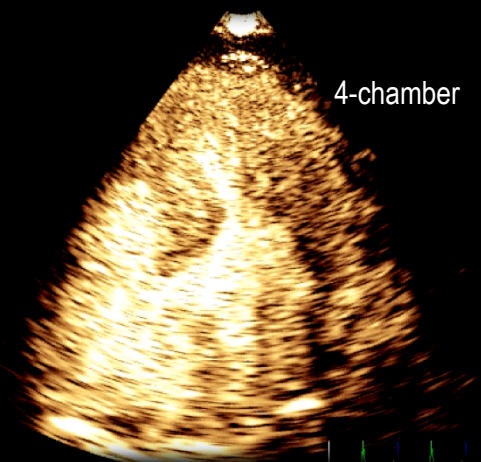
4-chamber

Endsystolic triggering:
1 endsystolic image per cycle



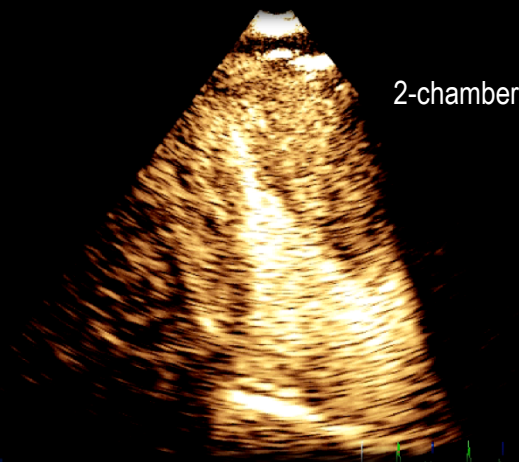
4-chamber

Real-time imaging:



4-chamber

Endsystolic triggering:
1 endsystolic image per cycle

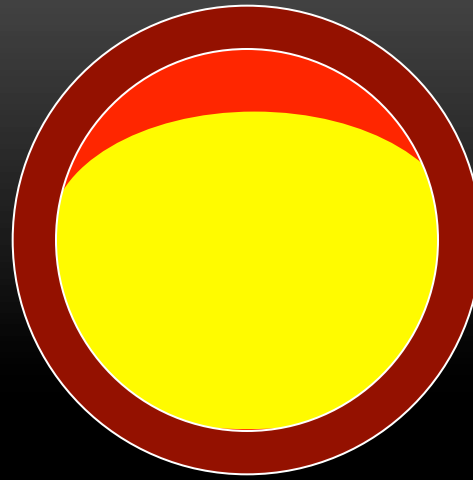


2-chamber

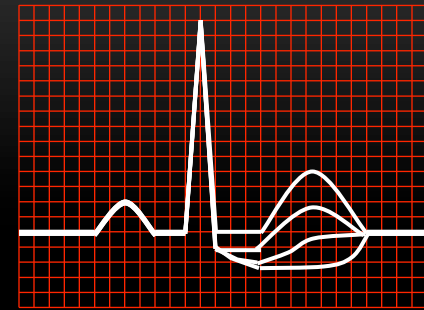
Endsystolic triggering:
1 endsystolic image per cycle

Abbiamo bisogno della **perfusione**?

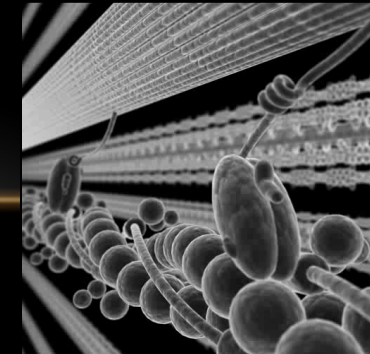
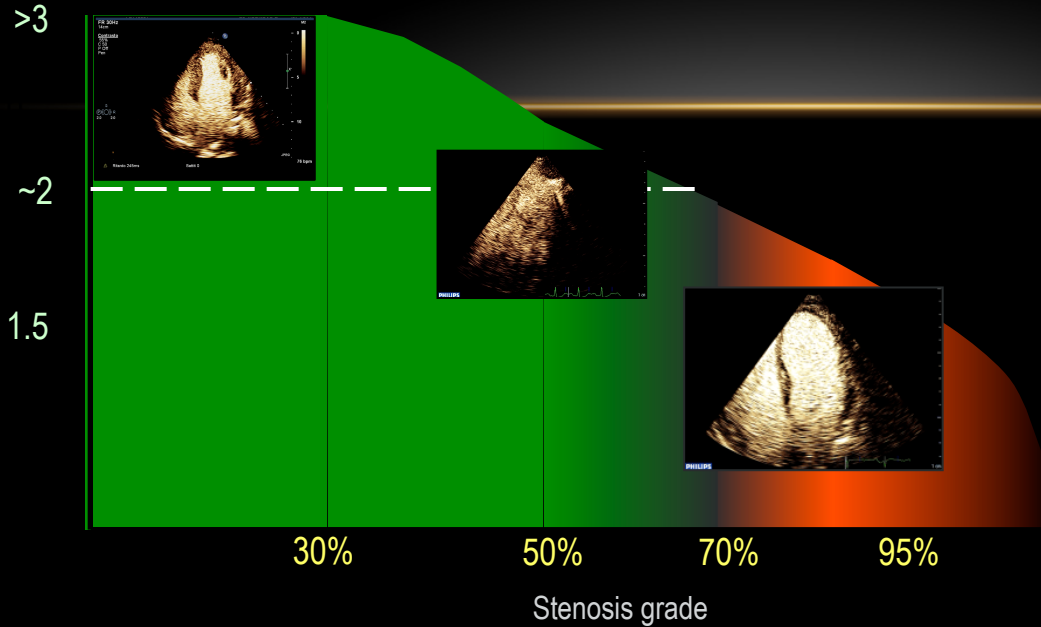
Gould revisited



ECG



CFR



WM

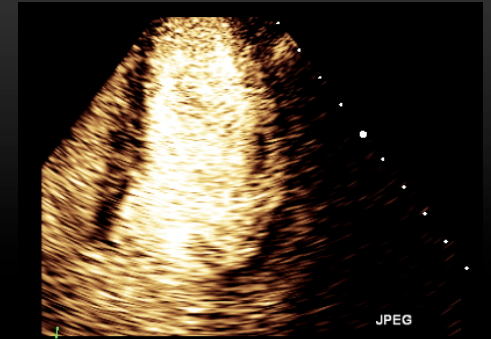
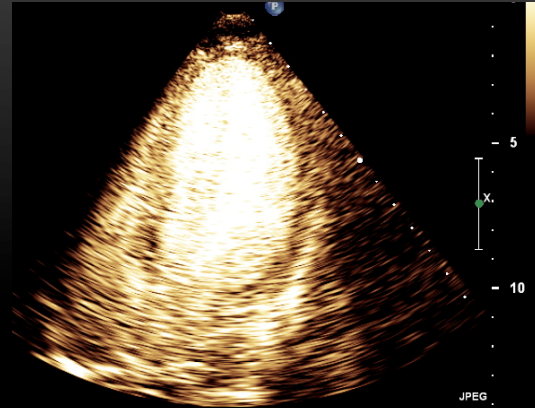
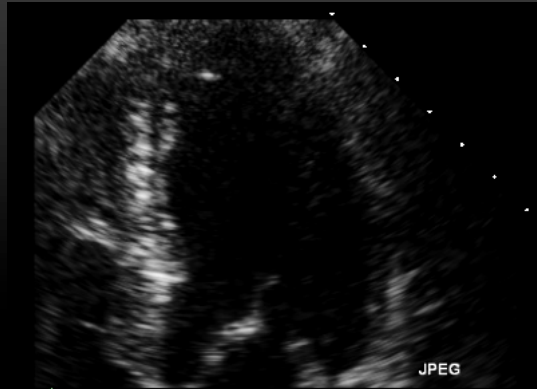
Comportamento dei markers di ischemia per gradi crescenti di stenosi. Le alterazioni di perfusione diventano evidenti prima di quelle di cinetica, dopo stressor

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

Rest no contrasto

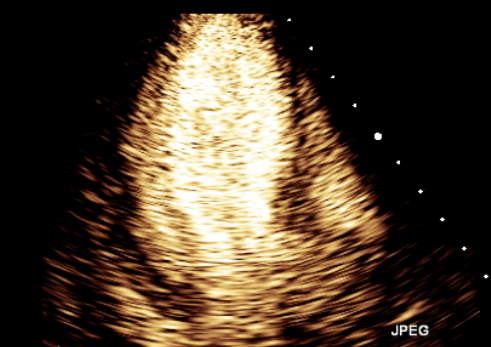
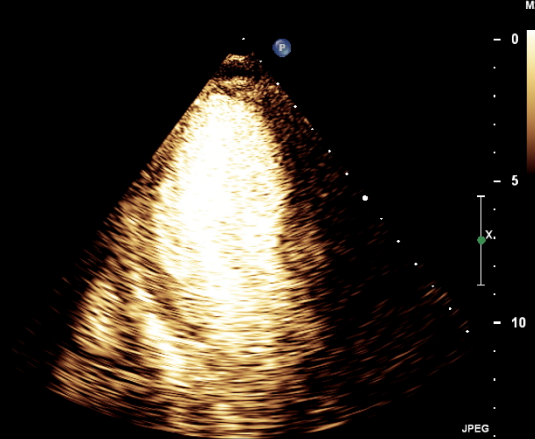
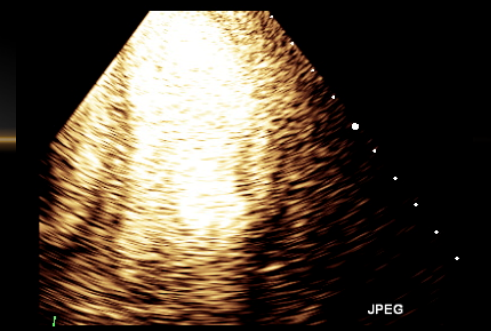
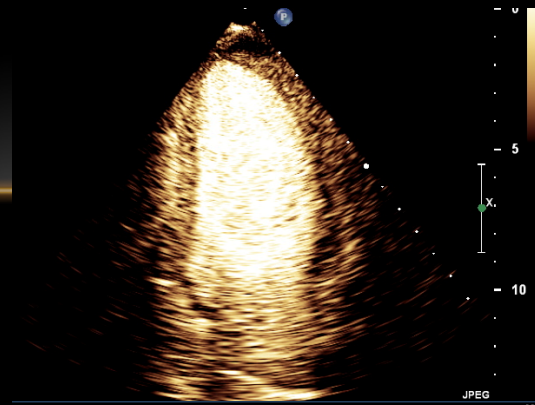
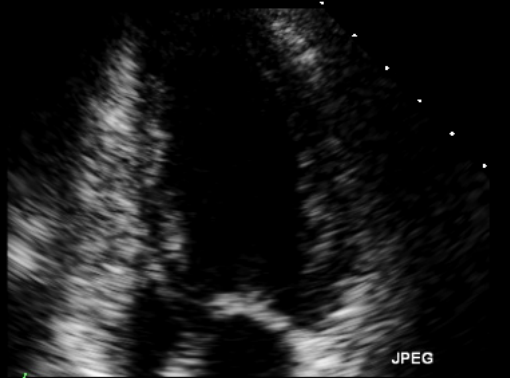
Rest contrasto

Stress contrasto



Battiti 0

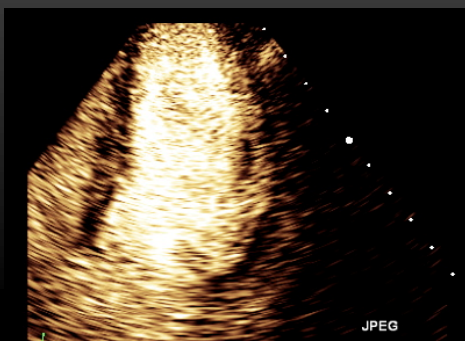
57 b



86 bpm

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

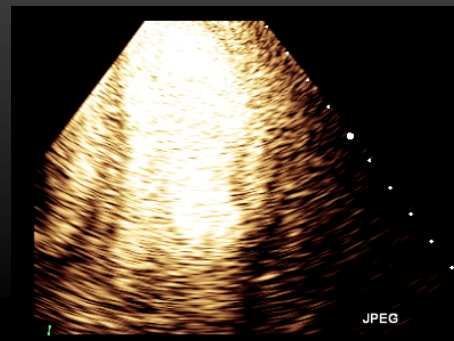
FR 32Hz
14cm
Contrasto
59%
C 50
P Off
Pen



JPEG

Cinetica

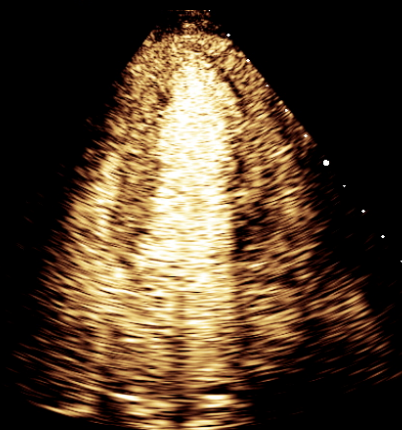
M2 FR 32Hz
14cm
Contrasto
59%
C 50
P Off
Pen



JPEG

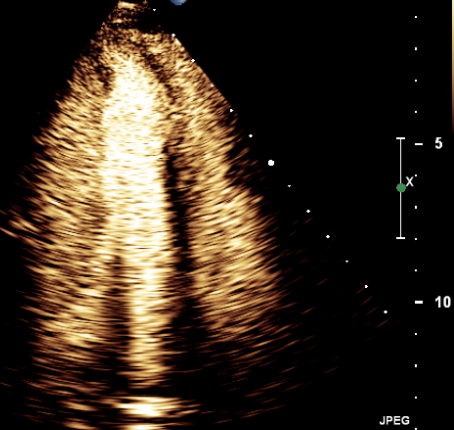
Perfusione

G
P R
2.0 2.0



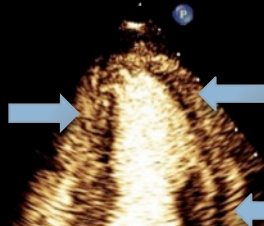
JPEG

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



JPEG

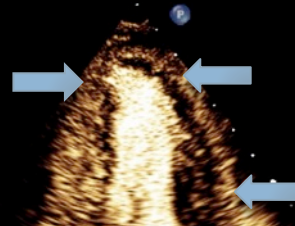
FR 32Hz
14cm
Contrasto
59%
C 50
P Off
Pen



JPEG

102 bpm

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



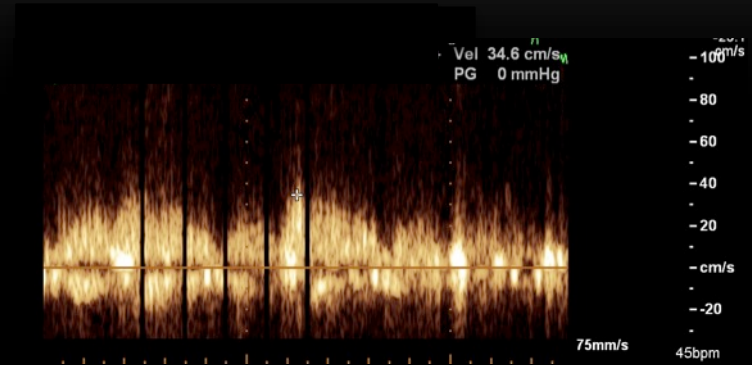
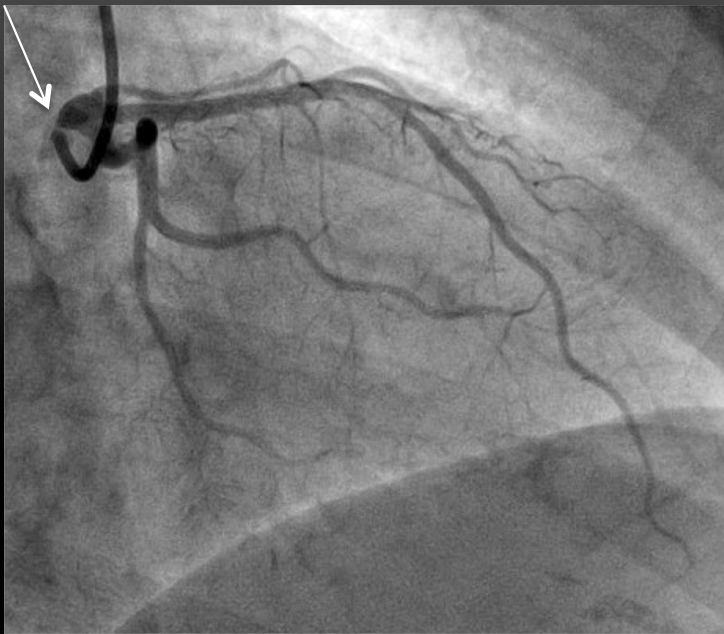
JPEG

103 bpm

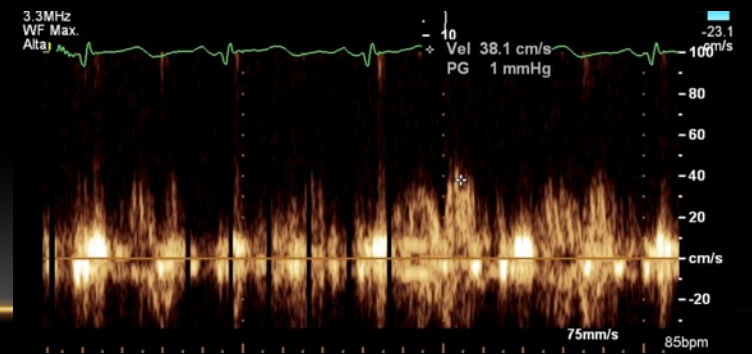
Ritardo 245ms
Battiti 1

Ritardo 245ms
Battiti 0

**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

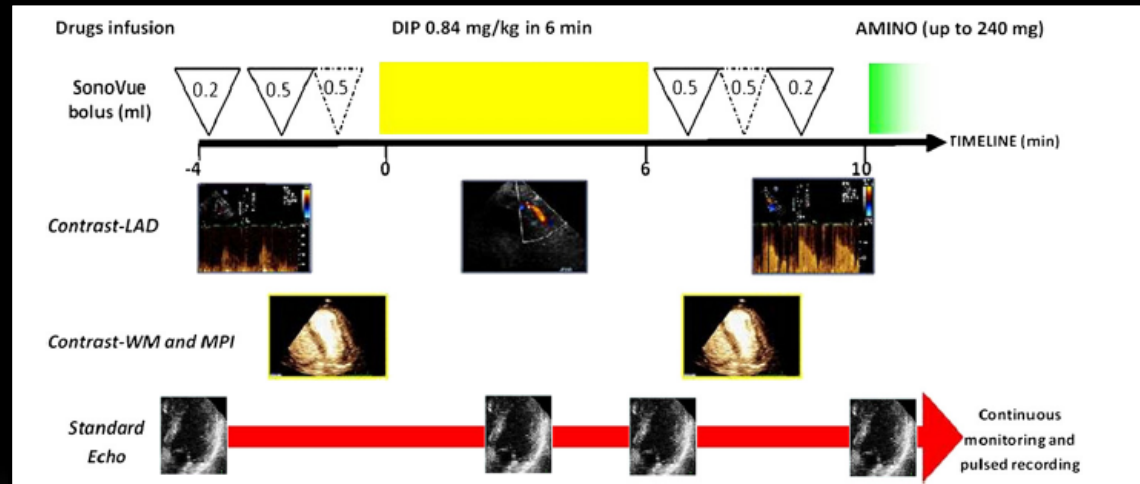
Nicola Gaibazzi, MD, PhD, Fausto Rigo, MD, and Claudio Reverberi, MD, Parma and Mestre-Venice, Italy

400 pazienti che eseguono coronarografia clinicamente indicata in 2 centri

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

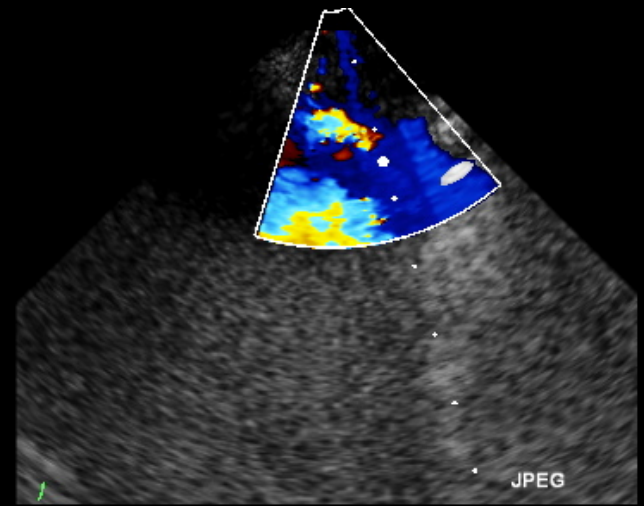
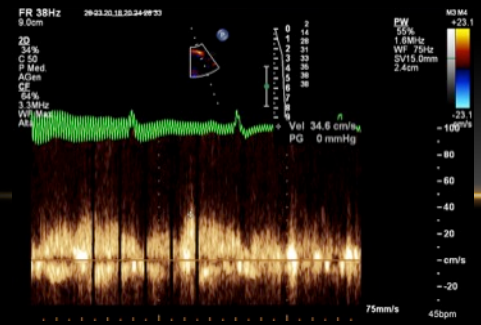
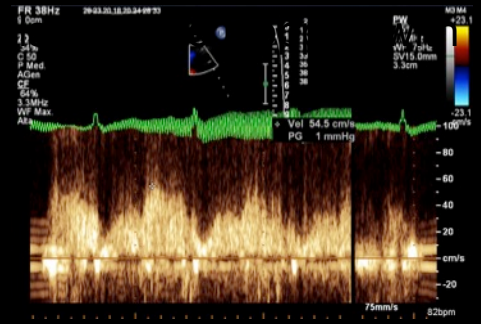
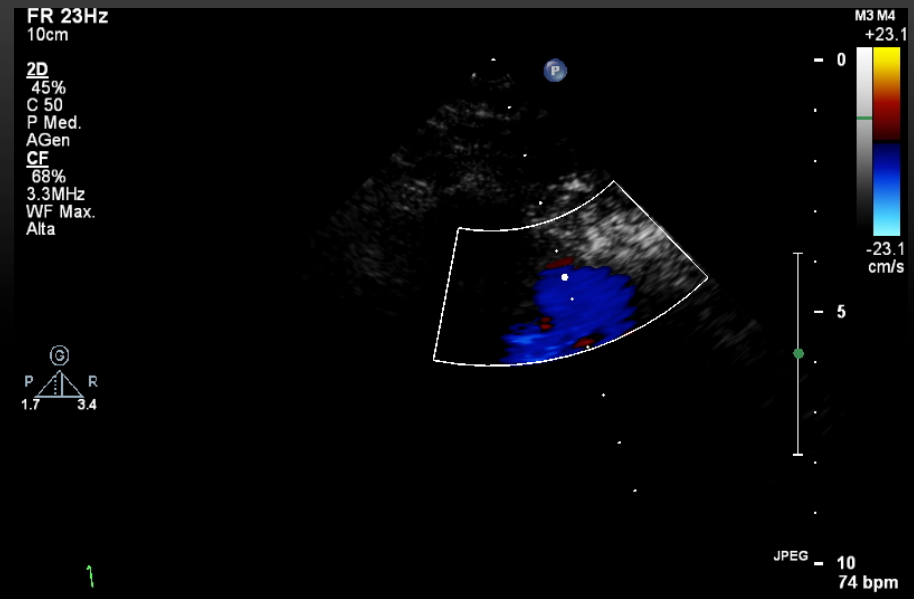
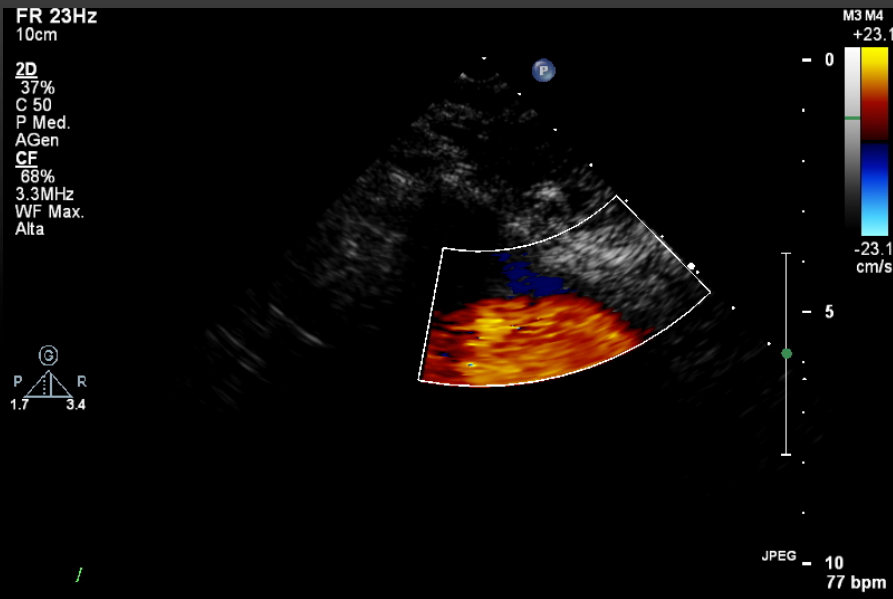
Characteristic	Value
Age (years)	66 ± 11 (29–91)
Men/women	263/137
Risk factors and history	
Hypertension	288 (72%)
Hypercholesterolemia	256 (64%)
Smoking	92 (23%)
Diabetes mellitus	112 (28%)
Family history of CAD	84 (21%)
Ejection fraction	55 ± 7
Reduced ejection fraction (<50%)	128 (32%)
Prior CAD*	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



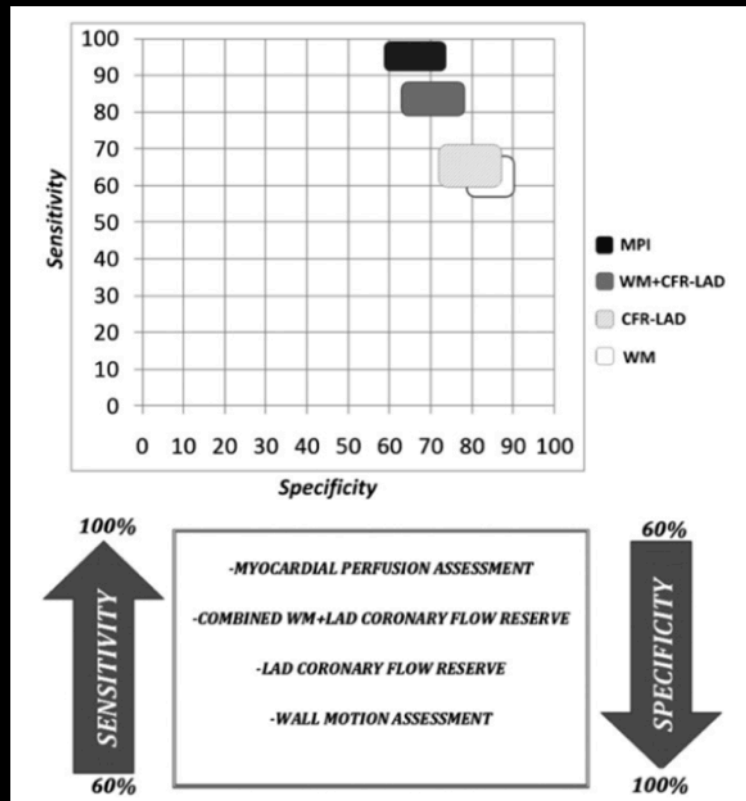
Detection of Coronary Artery Disease by Combined Assessment of Wall Motion, Myocardial Perfusion and Coronary Flow Reserve: A Multiparametric Contrast Stress-Echocardiography Study

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



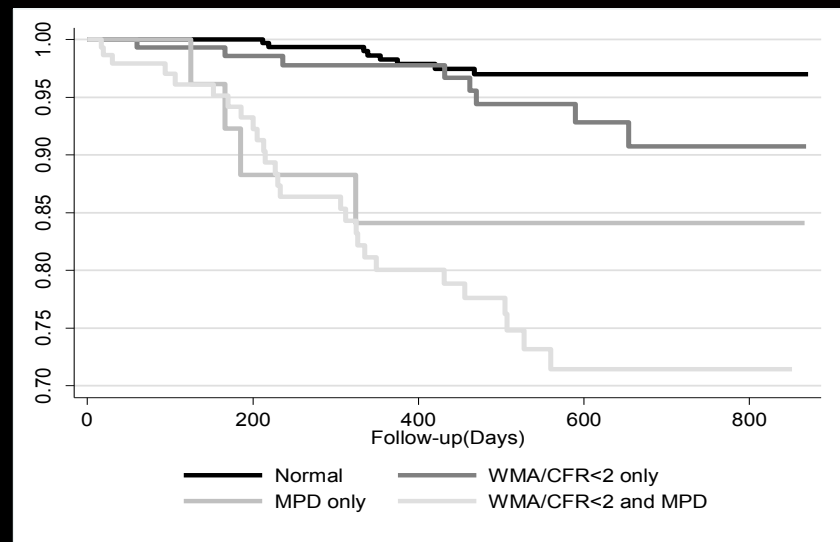
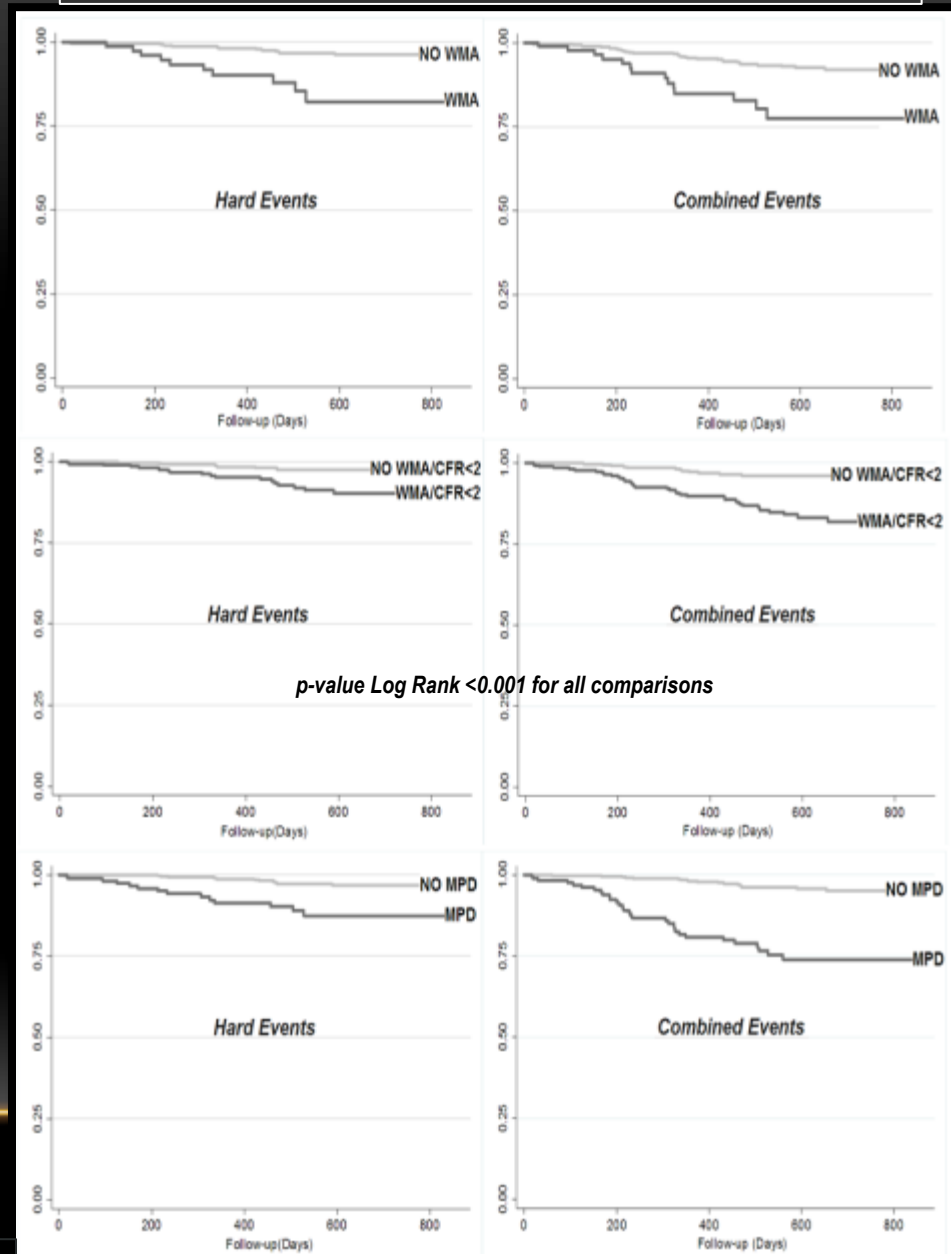
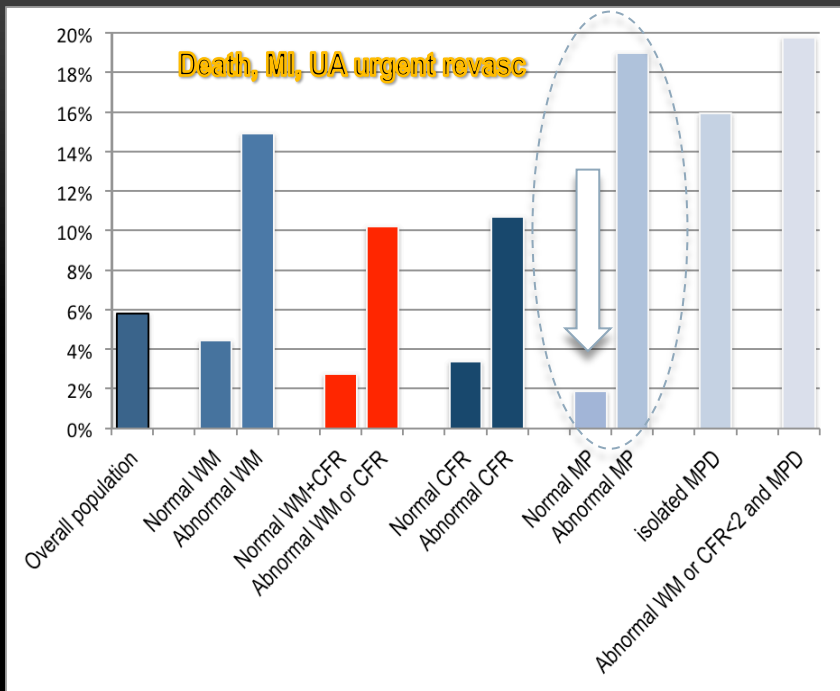
Anche l'aggiunta della misurazione della CFR-LAD facilitata da contrasto aumenta significativamente la sensibilità, abbassando relativamente la specificità

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

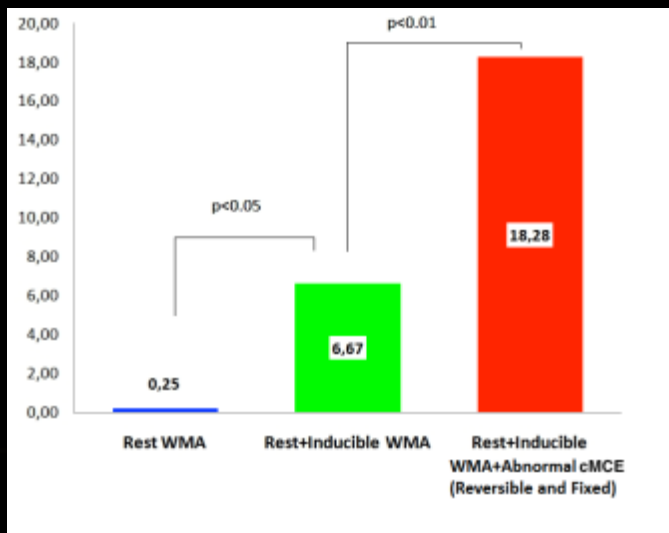
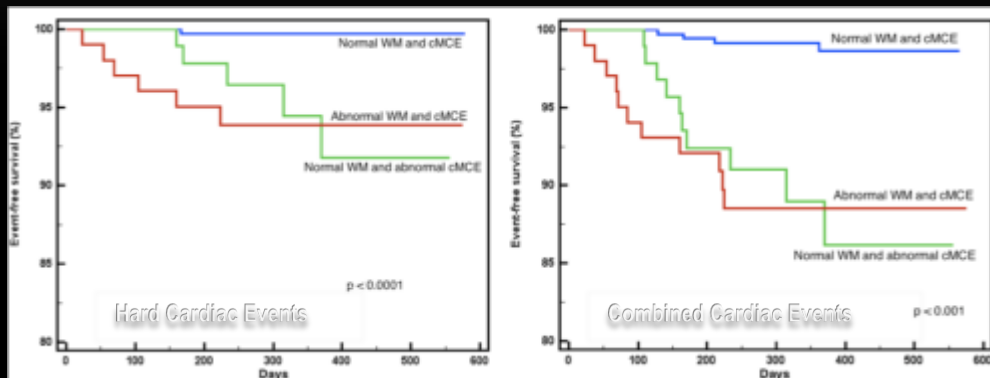
Comparative Prediction of Cardiac Events by Wall Motion, Wall Motion plus Coronary Flow Reserve or Myocardial Perfusion Analysis: A Prospective Multicenter Study of Contrast Stress Echocardiography



..e la Prognosi?

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

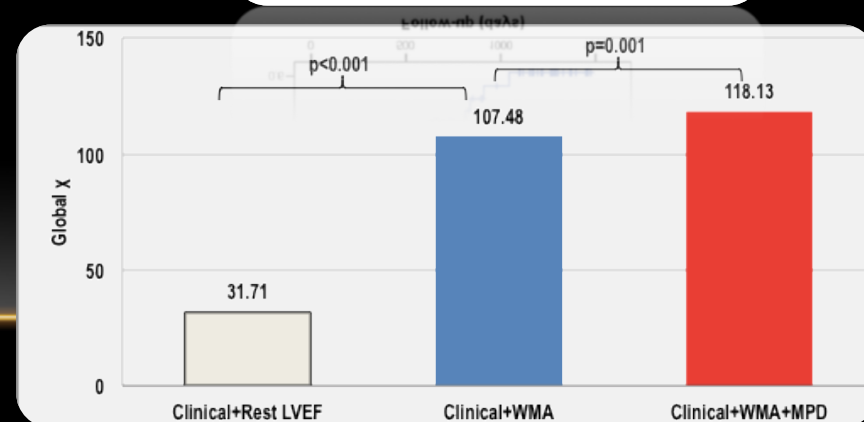
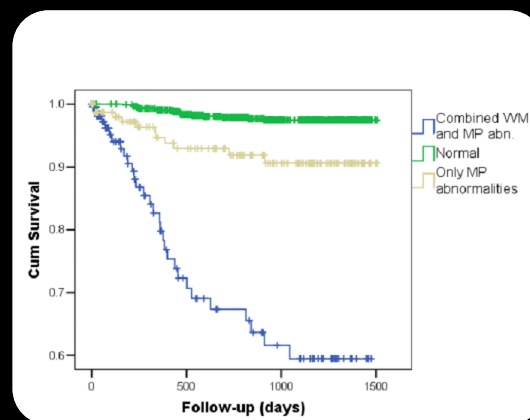
Contrast Stress-Echocardiography Predicts Hard Cardiac Events in Patients with Suspected Acute Coronary Syndrome but non-diagnostic Electrocardiogram and Normal 12-hour Troponin.



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

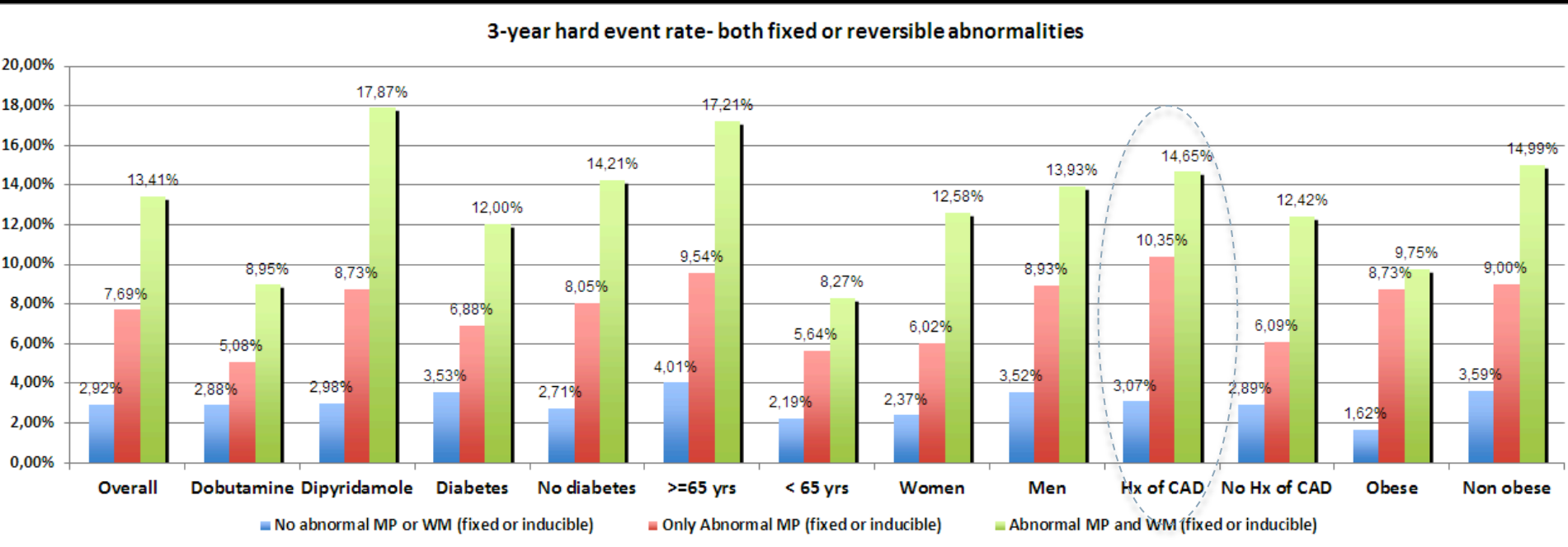
Circulation. 2012;126:1217-1224; originally published online August 7, 2012;
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The online version of this article, along with updated information and services, is located on the World Wide Web at:
<http://circ.ahajournals.org/content/126/10/1217>




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

Impact of cardiac magnetic resonance imaging on human lymphocyte DNA integrity

**Michael Fiechter^{1,2†}, Julia Stehli^{1†}, Tobias A. Fuchs[†], Svetlana Dougoud¹,
 Oliver Gaemperli¹, and Philipp A. Kaufmann^{1,2*}**

¹Department of Radiology, Cardiac Imaging, University Hospital Zurich, Ramistrasse 100, NLK C 42, Zurich CH-8091, Switzerland; and ²Zurich 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.

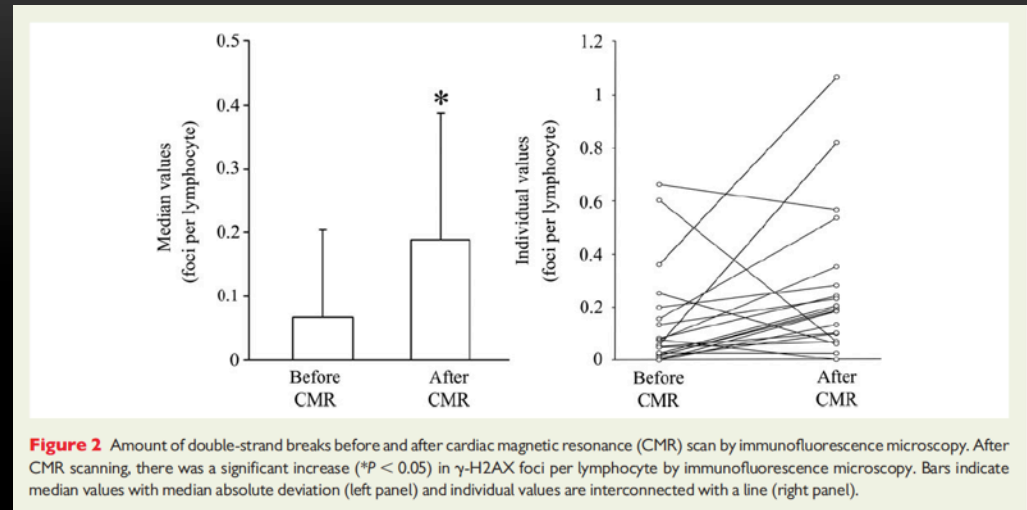

 European Heart Journal (2013) 34, 2337–2339
 doi:10.1093/eurheartj/ehs214

EDITORIAL

Is cardiac magnetic resonance imaging causing DNA damage?

Juhani Knuuti^{1*}, Antti Saraste^{1,2}, Marko Kallio³, and Heikki Minn⁴

¹Turku PET Centre, Turku University Hospital and University of Turku, Kinamyllykatu 4–8, 20520 Turku, Finland; ²Heart Center, Turku University Hospital, Turku, Finland; ³VTT Biotechnology for Health and Wellbeing, Turku, Finland; and ⁴Department 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 ^a	Time of measurement	DSB foci/lymphocyte	Time of measurement	
[¹⁸ F]FDG injection (5 mSv)	0.11	30 min post-injection	0.16	30 min post-PET/CT	May et al. (2012) ¹⁵
CTA (~2 mSv)	0.04	30 min post scan	–		Kuefner et al. (2010) ¹³
CTA (~8 mSv)	0.24	30 min post-scan	0.092 and 0.014	2 and 5 h post-scan	Grudzenski et al. (2009) ¹⁴
CTA (~17 mSv)	0.39	30 min post-scan	–		Kuefner et al. (2010) ¹³
Invasive angiography	0.13 ^b	15 min post-procedure	–		Kuefner et al. (2009) ¹²
1.5T CMR	0.12	At the end of the scan	–		Fiechter et al. (2013) ¹¹

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

^aBaseline level of DSBs is ~0.06–0.08 DSB foci/lymphocyte.

^bMedian 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 ^{a,*}, Nicola Marziliano ^{a,b}, Thomas R. Porter ^c, Gianmarco Negri ^a, Maria Antonietta Demola ^a, Claudio Reverberi ^a, Diego Ardissino ^a

^a Cardiology Department, Parma University Hospital, Parma, Italy

^b Health Sciences Department, University of Campobasso, Campobasso Italy

^c 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

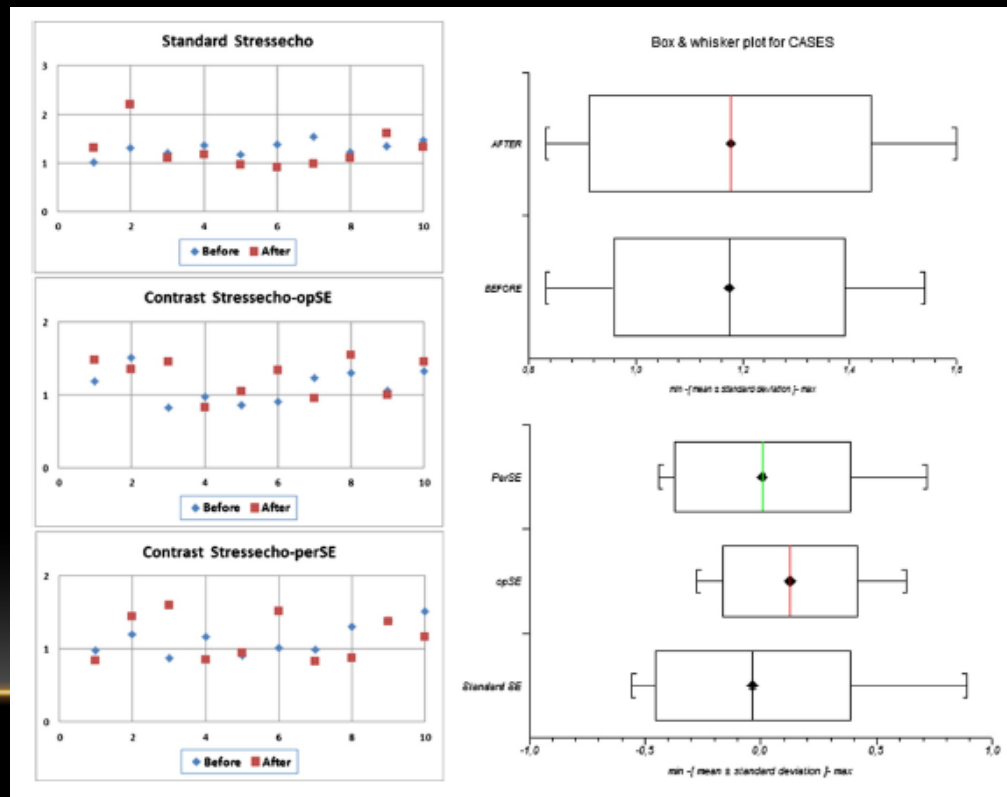
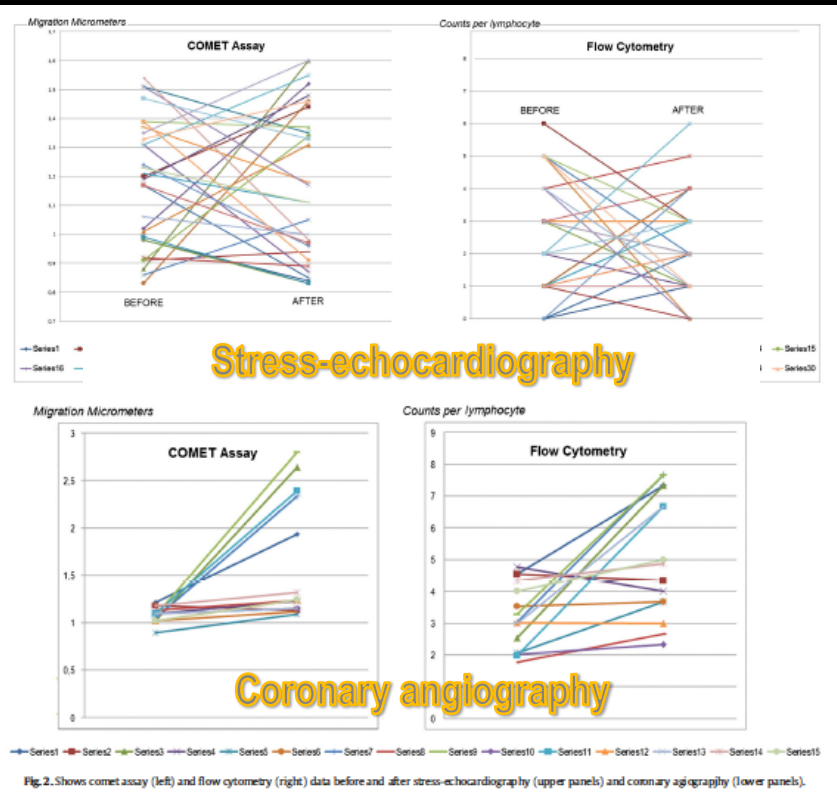


Fig. 2. Shows comet assay (left) and flow cytometry (right) data before and after stress-echocardiography (upper panels) and coronary angiography (lower panels).

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*

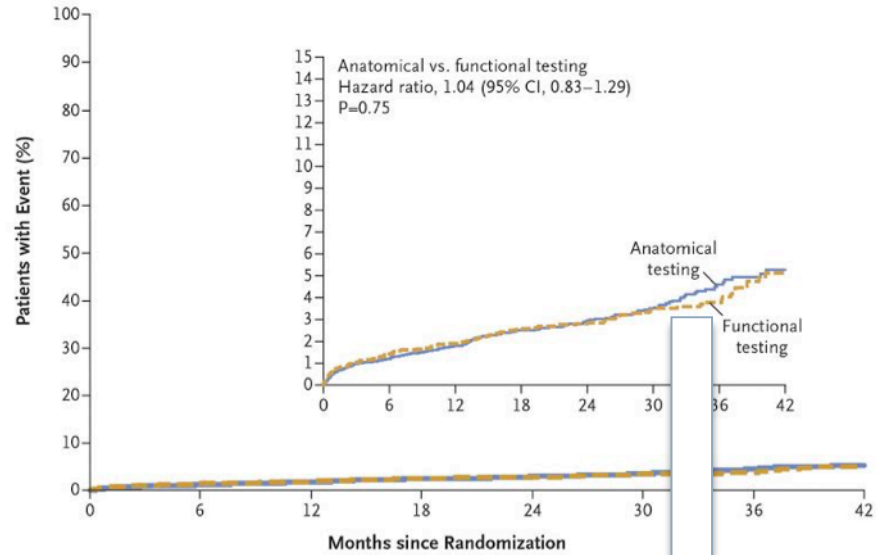


Table 2. End Points According to Study Group.*

End Point	CTA Strategy (N=4996)	Functional-Testing Strategy (N=5007)	Adjusted Hazard Ratio (95% CI)	P Value
Clinical end point — no. of patients				
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
Test-related end point				
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