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**CARRIERA ACCADEMICA:** 2004-2006: Professore associato confermato; 2006 (dal 01/06): Professore straordinario; 2009 (dal 01/06): Professore Ordinario.

**INSEGNAMENTI.** Laurea Magistrale: Cardiologia, Semeiotica medica (Elettrocardiografia); Laurea breve in Fisioterapia: Cardiologia.

**CURRICULUM** Laureato in Medicina e Chirurgia nell'A gosto 1972 (lode) all'Università di Bologna, si è specializzato in Malattie dell'Apparato Cardiovascolare presso l'Università di Padova nel Luglio 1975. Fellow di ricerca presso il Brompton Hospital (Londra) nel periodo 1975/1976 e presso la Johns Hopkins University (Baltimore) nel periodo 1985/1987, è stato assistente ed aiuto ospedaliero dal 1976 al Novembre 1999 presso la Divisione di Cardiologia dell'Ospedale Maggiore dell'Azienda Ospedaliera di Verona. Professore Associato di Cardiologia dell'Università di Verona dal Novembre 1999 al Dicembre 2004, è stato, nello stesso periodo Responsabile del Servizio di Cardiologia dell'Ospedale Policlinico dell'Azienda Ospedaliera di Verona. Professore Ordinario di Cardiologia all'Università del Piemonte Orientale "A.A vogadro", è Direttore della Cattedra, della Cardiologia Clinica e del Dipartimento Cardiovascolare dell'Azienda Ospedaliero-Universitaria "Maggiore della Carità" di Novara dal Dicembre 2004. Il principale argomento di ricerca sviluppato in questi anni è stato il fenomeno del rimodellamento ventricolare postinfarto e lo studio della funzione diastolica. È stato Consigliere della Società Italiana di Cardiologia (1999-2002, 2007-2009), Chairman del Working Group on Myocardial Function della Società Europea di Cardiologia (2001-2002) e Coordinatore del Gruppo di Ecocardiografia della Società Italiana di Cardiologia (2003-2005). Dal Gennaio 2009 a tutt'oggi ricopre il ruolo di Presidente della Società Italiana di Cardiologia.

**CAMPIONI DI INDAGINE NELLA RICERCA.** Meccanismi della disfunzione ventricolare sisto-diastolica; fisiopatologia della disfunzione adiacente all'area ischemica; meccanica ventricolare nell'ischemia acuta e cronica; rimodellamento ventricolare postinfarto e teoria del vaso pervio; doppler-emodinamica, con particolare riferimento a: funzione atriale e riempimento ventricolare sinistro .

## **TEMI CORRENTI DI RICERCA.**

*Myocardial contrast echocardiography after myocardial infarction: relation between residual myocardial perfusion, contractile reserve and long term remodeling.* Background: Previous studies have shown the potential role played by intracoronary myocardial contrast echocardiography (MCE) in predicting long-term remodeling and function after myocardial infarction (MI). Scanty data, however, are available on the role of intravenous MCE in this regard.

Purpose of the study: to assess the role of residual myocardial blood volume (MBV) in the asynergic region in modulating ventricular volume changes over time post-MI.

Methods: 32 consecutive patients with an anterior MI were studied using low-dose (10-15 µgr/kg/min) dobutamine echo (Dob) and intravenous triggered MCE (Levovist infusion 400 mg/ml over 2') >6 days after the acute event. In all patients the left anterior descending artery was identified as the infarct-related vessel (residual stenosis after stenting 39±33%). Videointensity plots were generated from the apical approach using a 12 segment model, with the results fitted to an exponential function. Quantitative estimation of the positive and plateauing value of the curve was then assessed for each ventricular segment, assuming that higher peak intensity reflects greater MBV, and averaged for the asynergic region. Ventricular volumes were assessed according to biplane Simpson's method at baseline, during Dob and after 254±190 days.

Results: Baseline volumes appeared to be directly related to the extent of the asynergic region ( $p<.01$ ) but showed no relation with the normalized videointensity (NVI) in that area. Overall diastolic ventricular volumes did not change at follow-up (from  $69\pm16$  to  $69\pm20$  ml/sqm, NS), although wall

motion score index (WMSI from 1.7±0.3 to 1.6±0.3, p=.001), ejection fraction (EF from 45±9 to 52±8 %, p=.004) and the ratio of end-systolic pressure/volume (ESP/V) (from 3.4±1.4 to 4.7±2.1 mmHg/ml/sqm, p<.001) significantly improved with Dob. Videointensity in the asynergic region, normalized to the remote myocardium (NVI), however, exhibited a significant interaction with the change in diastolic volume between baseline and follow-up (p=.044), with patients with the highest NVI exhibiting reverse remodeling (n=11, from 69±16 to 65±16 ml/sqm) over time as compared with the remaining population (n=21, from 68±16 to 73±21 ml/sqm). This was not true when parameters derived from Dob (change in WMSI, EF and ESP/V) were used. A multivariate analysis, including variables known to affect post-MI ventricular dilation ranked NVI second (p=.066), after baseline stroke volume (p=.005), in predicting changes in diastolic volumes over time.

Conclusions: Unlike predischarge inotropic stimulation, residual MBV in the dysfunctioning muscle, as assessed quantitatively by intravenous MCE early after the acute event, has the potential to modulate chronic ventricular remodeling in patients who suffered an anterior MI.

**Cardiac Dyssynchrony Quantitated by Time-to-Peak or Temporal Uniformity of Strain at Longitudinal, Circumferential, and Radial Level: Implications for Resynchronization Therapy.** Background: The standard deviation of time to peak strain (TPS-SD) has been proposed as an index of left ventricular (LV) dyssynchrony in patients to be resynchronized. However, TPS-SD is sensitive to noise, and the influence of outliers on TPS-SD is also relevant. Alternatively, dyssynchrony can be indexed by temporal uniformity of strain (TUS), whereby a time plot of regional strains, arranged for LV location, is subjected to Fourier analysis. If segments shorten simultaneously (synchronously), the plot appears as a straight line, with power only in the zero-order Fourier term, whereas regionally clustered dyssynchrony generates an undulating plot with higher power in the first-order term. TUS index reflects zero-order relative to first-order plus zero-order power.

Methods: In this study, TUS and TPS-SD were computed in 68 patients (QRS duration ≥ 120 ms; ejection fraction # 0.35) in whom longitudinal, circumferential, and radial strains were measured using speckletracking two-dimensional echocardiography before and 3 to 6 months after cardiac resynchronization therapy(CRT), together with LV volumes.

Results: Following CRT, LV volume decreased (diastolic, -10.620%) and ejection fraction improved from 0.23 +/- 0.07 to 0.30 +/- 0.10 ( $P < .001$  for both). Circumferential strain was ameliorated as well ( $P = .054$ ). Twoway analysis of variance revealed TUS improvement after CRT ( $P = .043$ ), with a trend for CRT to contrast asynchrony at the circumferential (+0.06 6 0.25) and longitudinal (+0.05 6 0.18) levels compared with the radial level (-0.002 6 0.18) (interaction  $P = .06$ ). This was not true for TPS-SD. Multivariate analysis revealed that only TUS, assessed before CRT circumferentially, predicted ejection fraction improvement after CRT. Other asynchrony variables failed in the model.

Conclusion: Dyssynchrony indexed by circumferential TUS yields greater CRT benefits than that indexed by TPS-SD, supporting the idea of targeting TUS-measured dyssynchrony as a more informative quantitative measurement in CRT patients.

#### **PUBBLICAZIONI PIÙ RECENTI.**

1: De Luca G, Santagostino M, Secco GG, Cassetti E, Giuliani L, Franchi E, Coppo L, Iorio S, Venegoni L, Rondano E, Dell'era G, Rizzo C, Pergolini P, Monaco F, Bellomo G, Marino P. Mean platelet volume and the extent of coronary artery disease: Results from a large prospective study. *Atherosclerosis*. 2009 Feb 20. [Epub ahead of print] PubMed PMID: 19426979.

2: Bertola B, Rondano E, Sulis M, Sarasso G, Piccinino C, Marti G, Devecchi P, Magnani A, Francalacci G, Marino PN. Cardiac Dyssynchrony Quantitated by Time-to-Peak or Temporal Uniformity of Strain at Longitudinal, Circumferential and Radial Level: Implications for Resynchronization Therapy. *J Am Soc Echocardiogr*. 2009 May 5. [Epub ahead of print] PubMed PMID: 19423288.

3: De Luca G, Ucci G, Cassetti E, Marino P. Benefits from small molecule administration as compared with abciximab among patients with ST-segment elevation myocardial infarction treated with primary angioplasty: a meta-analysis. *J Am Coll Cardiol*. 2009 May 5;53(18):1668-73. PubMed PMID: 19406342.

4: Ribichini F, Tomai F, De Luca G, Bocuzzi G, Presbitero P, Pesarini G, Ferrero V, Ghini AS, Pastori F, De Luca L, Zavalloni D, Soregaroli D, Garbo R, Franchi E, Marino P, Minelli M, Vassanelli C. A multicenter, randomized study to test immunosuppressive therapy with oral prednisone for the prevention of restenosis after percutaneous coronary interventions: cortisone plus BMS or DES versus BMS alone to eliminate restenosis (CEREA-DES) - study design and rationale. *J Cardiovasc Med (Hagerstown)*. 2009 Feb;10(2):192-9. PubMed PMID: 19377384.

5: Bortnik M, Leverone M, Teodori G, Marcolongo M, Occhetta E, Marino P. Ventricular fibrillation in acute mitral valve insufficiency caused by chordae tendineae rupture: report of a surgically corrected case. *J Cardiovasc Med (Hagerstown)*. 2009 Mar;10(3):261-3. PubMed PMID: 19283885.

6: Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA, Waggoner AD, Flachskampf FA, Pellikka PA, Evangelisa A. Recommendations for the valuation of left ventricular

diastolic function by echocardiography. Eur J echocardiogr. 2009 Mar;10(2):165-93. PubMed PMID: 19270053.

7: Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA, Waggoner AD, Flachskampf FA, Pellikka PA, Evangelista A. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. J Am Soc Echocardiogr. 2009 Feb;22(2):107-33. Review. PubMed PMID: 19187853.

8: Menon V, Pearte CA, Buller CE, Steg PG, Forman SA, White HD, Marino PN, Katritsis DG, Caramori P, Lasevitch R, Loboz-Grudzien K, Zurakowski A, Lamas GA, Hochman JS. Lack of benefit from percutaneous intervention of persistently occluded infarct arteries after the acute phase of myocardial infarction is time independent: insights from Occluded Artery Trial. Eur Heart J. 2009 Jan;30(2):183-1. Epub 2008 Nov 21. PubMed PMID: 19028780; PubMed Central PMCID: PMC2639108.

9: De Luca G, Biondi-Zoccai G, Marino P. Transferring patients with ST-segment elevation myocardial infarction for mechanical reperfusion: a meta-regression analysis of randomized trials. Ann Emerg Med. 2008 Dec;52(6):665-76. Review. PubMed PMID: 19027496.

10: De Luca G, Marino P. Antithrombotic therapies in primary angioplasty: rationale, results and future directions. Drugs. 2008;68(16):2325-44. doi:10.2165/0003495-200868160-00005. Review. PubMed PMID: 18973396.

11: De Luca G, Cassetti E, Marino PN, Melandri G, Di Mario C. [The CARESS-in-AMI trial]. G Ital Cardiol (Rome). 2008 Sep;9(9):585-92. Italian. PubMed PMID:18783079.

12: Dini FL, Buralli S, Gallina S, Galderisi M, Mele D, Mondillo S, Agricola E, Di Bello V, Sciomer S, Ansalone G, Di Salvo G, Montisci R, Nistri S, Rosa GM, Marino PN; Gruppo di Studio di Ecocardiografia della Società Italiana di Cardiologia. [Principles of cardiovascular dynamics in the perspective of echocardiography]. G Ital Cardiol (Rome). 2008 Aug;9(8):536-44. Review. Italian. PubMed PMID: 18780550.

13: Sciomer S, Galderisi M, Magrí D, Goffredo C, Ansalone G, Dini FL, Di Salvo G, Gallina S, Mele D, Montisci R, Nistri S, Mondillo S, Di Bello V, Marino PN; Gruppo di Studio di Ecocardiografia della Società Italiana di Cardiologia. [The non-invasive catheterization laboratory]. G Ital Cardiol (Rome). 2008 Aug;9(8):526-35. Review. Italian. PubMed PMID: 18780549.

14: De Luca G, Dudek D, Sardella G, Marino P, Chevalier B, Zijlstra F. Adjunctive manual thrombectomy improves myocardial perfusion and mortality in patients undergoing primary percutaneous coronary intervention for ST-elevation myocardial infarction: a meta-analysis of randomized trials. Eur Heart J. 2008 Dec;29(24):3002-10. Epub 2008 Sep 5. Review. PubMed PMID: 18775918.

15: Bortnik M, Occhetta E, Ruggeri C, Marino P. Transient trifascicular block complicating myocardial contusion after blunt chest trauma: a case report. J Cardiovasc Med (Hagerstown). 2008 Sep;9(9):937-40. PubMed PMID: 18695435.

16: De Luca G, Marino P. Advances in antithrombotic therapy as adjunct to reperfusion therapies for ST-segment elevation myocardial infarction. Thromb Haemost. 2008 Aug;100(2):184-95. Review. PubMed PMID: 18690336.

- 17: Bortnik M, Occhetta E, Marino P. Orthostatic hypotension as an unusual clinical manifestation of pheochromocytoma: a case report. *J Cardiovasc Med (Hagerstown)*. 2008 Aug;9(8):839-41. PubMed PMID: 18607252.
- 18: Nistri S, Galderisi M, Faggiano P, Antonini-Canterin F, Ansalone G, Dini FL, Di Salvo G, Gallina S, Mele D, Montisci R, Sciomer S, Di Bello V, Mondillo S, Marino PN; Working Group on Echocardiography of the Italian Society of Cardiology. Practical echocardiography in aortic valve stenosis. *J Cardiovasc Med (Hagerstown)*. 2008 Jul;9(7):653-65. Review. PubMed PMID: 18545063.
- 19: De Luca G, Cassetti E, Marino P. Impact of duration of clopidogrel prescription on outcome of DES as compared to BMS in primary angioplasty: a meta-regression analysis of randomized trials. *J Thromb Thrombolysis*. 2009 May;27(4):365-78. Epub 2008 May 23. PubMed PMID: 18498003.
- 20: De Luca G, Gibson CM, Bellandi F, Murphy S, Maioli M, Noc M, Zeymer U, Dudek D, Arntz HR, Zorman S, Gabriel HM, Emre A, Cutlip D, Biondi-Zocca G, Rakowski T, Gyongyosi M, Marino P, Huber K, van't Hof AW. Early glycoprotein IIb-IIIa inhibitors in primary angioplasty (EGYPT) cooperation: an individual patient data meta-analysis. *Heart*. 2008 Dec;94(12):1548-58. Epub 2008 May 12. Review. PubMed PMID: 18474534; PubMed Central PMCID: PMC2582788.
- 21: Agricola E, Galderisi M, Mele D, Ansalone G, Dini FL, Di Salvo G, Gallina S, Montisci R, Sciomer S, Di Bello V, Mondillo S, Marino PN; Echocardiographic Study Group of the Italian Society of Cardiology. Mechanical dyssynchrony and functional mitral regurgitation: pathophysiology and clinical implications. *J Cardiovasc Med (Hagerstown)*. 2008 May;9(5):461-9. Review. PubMed PMID: 18403997.
- 22: De Luca G, Stone GW, Suryapranata H, Laarman GJ, Menichelli M, Kaiser C, Valgimigli M, Di Lorenzo E, Dirksen MT, Spaulding C, Pittl U, Violini R, Percoco G, Marino P. Efficacy and safety of drug-eluting stents in ST-segment elevation myocardial infarction: a meta-analysis of randomized trials. *Int J Cardiol*. 2009 Apr 3;133(2):213-22. Epub 2008 Apr 3. PubMed PMID: 18394731.
- 23: De Luca G, Suryapranata H, Marino P. Reperfusion strategies in acute ST-elevation myocardial infarction: an overview of current status. *Prog Cardiovasc Dis*. 2008 Mar-Apr;50(5):352-82. Review. PubMed PMID: 18313480.
- 24: Coser A, Franchi E, Marini M, Cemin R, Benini A, Beltrame F, Marini A, Pascotto M, Rognoni A, Ambrosio G, Marino PN. Intravenous contrast echocardiography after myocardial infarction: relationship among residual myocardial perfusion, contractile reserve and long-term remodelling. *J Cardiovasc Med (Hagerstown)*. 2007 Dec;8(12):1012-9. PubMed PMID: 18163012.
- 25: Di Bello V, Galderisi M, de Gregorio C, Ansalone G, Dini FL, Di Salvo G, Gallina S, Mele D, Sciomer S, Montisci R, Mondillo S, Marino PN; Working Group of Echocardiography of the Italian Society of Cardiology (SIC), Italy. New echocardiographic technologies in the clinical management of hypertensive heart disease. *J Cardiovasc Med (Hagerstown)*. 2007 Dec;8(12):997-1006. Review. PubMed PMID: 18163010.
- 26: De Luca G, Marino P. Adjunctive benefits from low-molecular-weight heparins as compared to unfractionated heparin among patients with ST-segment elevation myocardial infarction treated

- with thrombolysis. A meta-analysis of the randomized trials. Am Heart J. 2007 Dec;154(6):1085.e1-6. Epub 2007 Oct 26. PubMed PMID: 18035079.
- 27: Occhetta E, Bortnik M, Dell'era G, Zardo F, Dametto E, Sassone B, Gabrieli L, Marino P. Evaluation of pacemaker dependence in patients on ablate and pace therapy for atrial fibrillation. Europace. 2007 Dec;9(12):1119-23. Epub 2007 Oct 24. PubMed PMID: 17959682.
- 28: Grossini E, Molinari C, Mary DA, Marino P, Vacca G. The effect of urocortin II administration on the coronary circulation and cardiac function in the anaesthetized pig is nitric-oxide-dependent. Eur J Pharmacol. 2008 Jan 14;578(2-3):242-8. Epub 2007 Oct 2. PubMed PMID: 17936748.
- 29: Rognoni A, Bertola B, Leverone M, Marino P. Subacute thrombosis of the abdominal aorta secondary to a free-floating thrombus in the left ventricle. J Cardiovasc Med (Hagerstown). 2007 Oct;8(10):870-2. PubMed PMID: 17885533.
- 30: De Luca G, Suryapranata H, Marino P. Primary angioplasty vs. thrombolysis. Indian Heart J. 2007 Jul-Aug;59(4):302-10. Review. PubMed PMID: 19126934.
- 31: De Luca G, Suryapranata H, Stone GW, Antonucci D, Biondi-Zoccali G, Kastrati A, Chiariello M, Marino P. Coronary stenting versus balloon angioplasty for acute myocardial infarction: a meta-regression analysis of randomized trials. Int J Cardiol. 2008 May 7;126(1):37-44. Epub 2007 Jun 4. PubMed PMID: 17544528.
- 32: Occhetta E, Bortnik M, Marino P. Permanent parahisian pacing. Indian Pacing Electrophysiol J. 2007 Apr 1;7(2):110-25. PubMed PMID: 17538702; PubMed Central PMCID: PMC1877829.
- 33: Di Salvo G, Galderisi M, Rea A, Ansalone G, Dini FL, Gallina S, Mele D, Montisci R, Sciomer S, Mondillo S, Di Bello V, Marino PN; Gruppo di Lavoro di Ecocardiografia; Società Italiana di Cardiologia. [Evaluation of atrial function by echocardiography]. G Ital Cardiol (Rome). 2007 Apr;8(4):225-35. Review. Italian. PubMed PMID: 17506294.
- 34: Ferrero V, Ribichini F, Rognoni A, Marino P, Brunelleschi S, Vassanelli C. Comparison of efficacy and safety of lower-dose to higher-dose oral prednisone after percutaneous coronary interventions (the IMPRESS-LD study). Am J Cardiol. 2007 Apr 15;99(8):1082-6. Epub 2007 Mar 6. PubMed PMID: 17437731.
- 35: Paulus WJ, Tschöpe C, Sanderson JE, Rusconi C, Flachskampf FA, Rademakers E, Marino P, Smiseth OA, De Keulenaer G, Leite-Moreira AF, Borbely A, Edes I, Handoko ML, Heymans S, Pezzali N, Pieske B, Dickstein K, Fraser AG, Brutsaert DL. How to diagnose diastolic heart failure: a consensus statement on the diagnosis of heart failure with normal left ventricular ejection fraction by the Heart Failure and Echocardiography Associations of the European Society of Cardiology. Eur Heart J. 2007 Oct;28(20):2539-50. Epub 2007 Apr 11. PubMed PMID: 17428822.
- 36: Galderisi M, Nistri S, Ansalone G, Dini FL, Di Salvo G, Gallina S, Mele D, Montisci R, Sciomer S, Mondillo S, Di Bello V, Marino PN; Gruppo di Studio di Ecocardiografia della Società Italiana di Cardiologia. [Pulsed tissue Doppler illustrated to a resident in cardiology]. G Ital Cardiol (Rome). 2007 Feb;8(2):92-101. Review. Italian. PubMed PMID: 17402353.
- 37: Ribichini F, Ferrero V, Rognoni A, Marino P, Brunelleschi S, Vassanelli C. Percutaneous treatment of coronary bifurcations: lesion preparation before provisional bare metal stenting and

subsequent immunosuppression with oral prednisone. The IMPRESS-Y study. J Interv Cardiol. 2007 Apr;20(2):114-21. PubMed PMID: 17391219.

38: Devecchi P, Plebani L, Occhetta E, Bortnik M, Francalacci G, Magnani A, Marino P. [Electrical storms in patients with implantable cardioverter-defibrillator: incidence and clinical management]. G Ital Cardiol (Rome). 2006 Oct;7(10):695-701. Italian. PubMed PMID: 17171993.

39: Mondillo S, Galderisi M, Ballo P, Marino PN; Study Group of Echocardiography of the Italian Society of Cardiology. Left ventricular systolic longitudinal function: comparison among simple M-mode, pulsed, and M-mode color tissue Doppler of mitral annulus in healthy individuals. J Am Soc Echocardiogr. 2006 Sep;19(9):1085-91. PubMed PMID: 16950462.

40: Occhetta E, Bortnik M, Magnani A, Francalacci G, Marino P. Inappropriate implantable cardioverter-defibrillator discharges unrelated to supraventricular tachyarrhythmias. Europace. 2006 Oct;8(10):863-9. Epub 2006 Aug 17. PubMed PMID: 16916859.

41: Bonapace S, Rossi A, Ciccoira M, Golia G, Zanolla L, Franceschini L, Conte L, Marino P., Zardini P, Vassanelli C. Aortic stiffness correlates with an increased extracellular matrix turnover in patients with dilated cardiomyopathy. Am Heart J. 2006 Jul;152(1):93.e1-6. PubMed PMID: 16824836.

#### Capitoli di libro:

Macciò S, Marino P. Role of the left atrium. Diastolic Heart Failure, a cura di Smiseth OA e Tendera M. Springer-Verlag editore, 2008, pag 53-70.

**Orario di Ricevimento**

(Mercoledì 12.30-13.00- Clinica Cardiologica –  
previo appuntamento telefonico (0321-3733597)