Identificazione precoce di cardiotossicità con biomarkers

Come gestire le informazioni da Troponina e BNP

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Cardiotossicità

Perché??

- Impiego di fattori di crescita ematologici, antiemetici, altre terapie di supporto che diminuiscono l'impatto della tossicità dei chemioterapici
- Nuovi farmaci: "target therapy". Trastuzumab, che ha manifestato una tossicità cardiaca inattesa
- Sviluppo di farmaci che agiscono sui microvasi del tumore, hanno effetto anti-angiogenetico
- Sempre più diffuse le chemioterapie adiuvanti: aumentano la sopravvivenza, ma anche il "pool" di pazienti potenzialmente suscettibili allo sviluppo di cardiotossicità tardiva (I bambini guariti da patologia neoplastica hanno un aumento di 8 vv nella mortalità di origine cardiaca)

"In breast cancer alone current estimates predict that More than 2 million survivors are at risk for cardiotoxicity"

Cardiotossicità: tipi

Acuta (più rara)

- immediatamente dopo CT
- variazioni ECG (poco significative)
- aritmie (poco significative)
- miopericardite (rarissima e talora fatale)

Cronica (più frequente)

- dose-dipendente
- insorgenza tardiva
- CMP dilatativa ipo-cinetica
- prognosi infausta

Cardiotossicità: meccanismi

Catena respiratoria mitocondriale

Vie non enzimatiche con incorporazione ferro

Generazione radicali liberi

Aumento

Nel tempo la funzione del Ventricolo sinistro viene alterata, Come conseguenza della diminuzione Dello spessore della parete E per la depressa capacità contrattile

AC

acc

Ri

dai mitocondri

solo!)

contrattilità

Alterata produzione ATP intracellulare

Alterata produzione Ca^{2+}-ATPase reticolo sarcoplasmico

Farmaci CT ed effetto cardiotossico

Drug	Cardiotoxic effect	Incidence	Reference
Doxorubicin	LV dysfunction/CHF	Dose-dependent, overall incidence ~2.2%, cumulative dose >550 mg/m^2 ~7%	2
Trastuzumab	LV dysfunction/CHF	In ~28% when used in combination with anthracycline and cyclophosphamide, ~4% as monotherapy	3
Cyclophosphamide	LV dysfunction/CHF	In ~19% when part of high-dose chemotherapy regime	4
Arsenic	QT/QTc prolongation, torsades de pointes	Varying reports between 40% and 100% (QT prolongation)	5
5-HT$_3$ receptor antagonists	QT/QTc prolongation	Common, clinical significance uncertain	6
Taxanes	Sinus bradycardia, and AV conduction disturbance	In ~29% of patients and ~3% of patients, respectively	7
Fluoropyrimidines	ACS	Varies from 1.2% to 18%	8
Aromatase inhibitors	Hypercholesterolemia?, increased coronary events?	Overall cardiovascular events ~4.1% (non-significant increase)	9
Cisplatin-based chemotherapy for testicular cancer	HT, hypercholesterolemia, and ACS	In ~39%, ~79%, and ~6% of long-term survivors, respectively	10
Bevacizumab	HT	~11% of patients	11

5-HT = serotonin; **ACS** = acute coronary syndromes; **AV** = atrioventricular; **CHF** = congestive heart failure; **HT** = hypertension; **LV** = left ventricular; **?** indicates potential.

Youssef Am J Cardiovasc Drugs 2005

The best treatment of anthracycline-induced cardiomyopathy is prevention of the disorder in the first instance. This may be achieved by careful monitoring of cardiac function/status via a number of non-invasive investigations with the aim of suspending or altering the treatment when early damage is detected and before clinical signs and symptoms develop. An ideal monitoring test would have high sensitivity and specificity to prevent unnecessary treatment alteration, which may compromise anti-tumor effect.

Youssef Am J Cardiovasc Drugs 2005

Monitoraggio

- ECG: poco utile
- ECHO:
  - LVEF
  - ECHO sotto stress
  - Valutazione dei parametri di funzionalità diastolica
  - Raccomandata nel follow-up di pazienti trattati con AC (classe I, ACC/AHA)
  - Vantaggi: costo contenuto, relativamente facile e disponibile
  - Svantaggi: poco riproducibile, operatore dipendente, non predittiva
- Angiografia con radionuclidi: poco utile e non predittiva di cardiotossicità
- **Marcatori sierici: troponina, peptidi natriuretici**

Il ruolo della Troponina

Available online at www.sciencedirect.com
ScienceDirect
Toxicology 245 (2008) 206–218
TOXICOLOGY
www.elsevier.com/locate/toxicol

Review

Cardiac troponin is the most effective translational safety biomarker for myocardial injury in cardiotoxicity

Peter James O'Brien*

- High cardiac specificity
- High sensitivity
- Wide diagnostic window

- Minimally invasive
- Less expensive than ECHO and MUGA
- No irradiation of the patients
- Easily repeated
- No interobserver variability

Left Ventricular Dysfunction Predicted by Early Troponin I Release After High-Dose Chemotherapy

Daniela Cardinale, MD, Maria Teresa Sandri, MD,† Alessandro Martinoni, MD, Alessio Tricca, LabTech,† Maurizio Civelli, MD, Giuseppina Lamantia, MD, Saverio Cinieri, MD,* Giovanni Martinelli, MD,* Carlo M. Cipolla, MD, Cesare Fiorentini, MD

Milan, Italy

- 204 pts
- High-dose chemotherapy
- TnI 0,12,24,48,72 h after CT
- N. 65 (32%) TnI +
- N. 139 (68%) TnI -

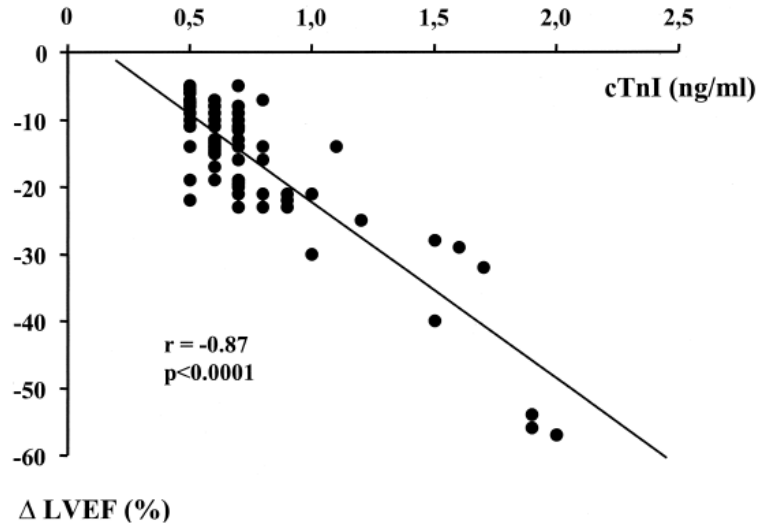

Figure 4. Scatterplot of left ventricular ejection fraction (LVEF) changes against troponin I value in cTnI+ patients. cTnI = cardiac troponin I.

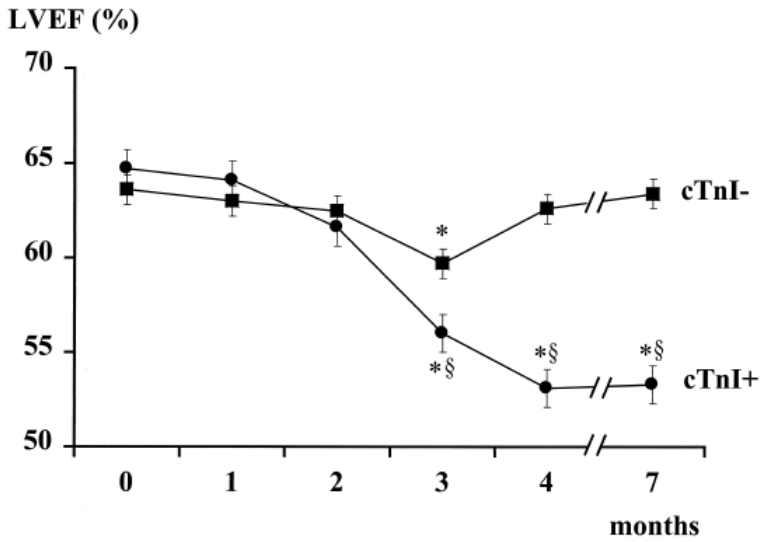

Figure 2. Left ventricular ejection fraction (LVEF) at baseline and during the seven months of follow-up of troponin I positive (cTnI+; **solid circle**) and negative (cTnI−; **solid square**) patients. *$p < 0.001$ vs. baseline (month 0); §$p < 0.001$ vs. cTnI− group. Data are shown as mean ± 95% confidence interval.

J Am Coll Cardiol 2000

Prognostic Value of Troponin I in Cardiac Risk Stratification of Cancer Patients Undergoing High-Dose Chemotherapy

Daniela Cardinale, MD; Maria T. Sandri, MD; Alessandro Colombo, MD; Nicola Colombo, MD; Marina Boeri, MD; Giuseppina Lamantia, MD; Maurizio Civelli, MD; Fedro Peccatori, MD; Giovanni Martinelli, MD; Cesare Fiorentini, MD; Carlo M. Cipolla, MD

- 703 patients, with poor prognosis malignancy, treated with HDC
- Follow-up 42 months
- MACE incidence

- TnI determined:
  - before and soon after
  - 1 month after HDC:
  - TnI -/- = n. 495 (70%)
  - TnI +/- = n. 145 (21%)
  - TnI +/+ = n. 63 (9%)

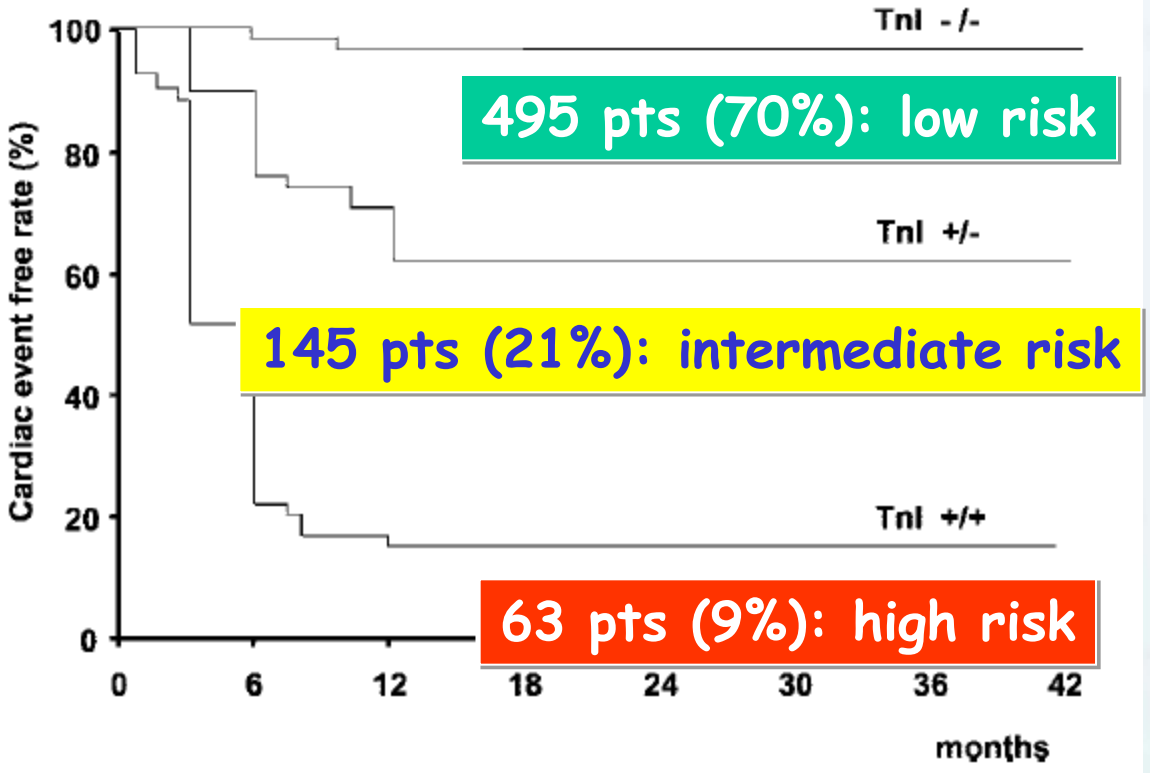

Figure 3. Cumulative cardiac events rate in 3 study groups. $P<0.001$ for $TnI^{+/+}$ vs $TnI^{-/-}$ and $TnI^{+/-}$, and for $TnI^{+/-}$ vs $TnI^{-/-}$.

Circulation 2004

Prognostic Value of Troponin I in Cardiac Risk Stratification of Cancer Patients Undergoing High-Dose Chemotherapy

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TABLE 3. Cardiac Events in the Study Groups

	Total (n=703)	TnI$^{-/-}$ (n=495)	TnI$^{+/-}$ (n=145)	TnI$^{+/+}$ (n=63)
Sudden death	3 (0.4)	0 (0)	0 (0)	3 (5)
Cardiac death	2 (0.3)	0 (0)	0 (0)	2 (3)
Acute pulmonary edema	3 (0.4)	0 (0)	1 (0.7)	2 (3)
Heart failure	47 (7)	1 (0.2)	18 (12)	28 (44)
Asymptomatic left ventricular dysfunction	37 (5)	2 (0.4)	24 (17)	11 (17)
Life-threatening arrhythmias	17 (2)	2 (0.4)	10 (7)	5 (8)
Conduction disturbances requiring pacemaker implantation	2 (0.3)	0 (0)	0 (0)	2 (3)
Cumulative events	111 (16)	5 (1)	53 (37)*	53(84)*†

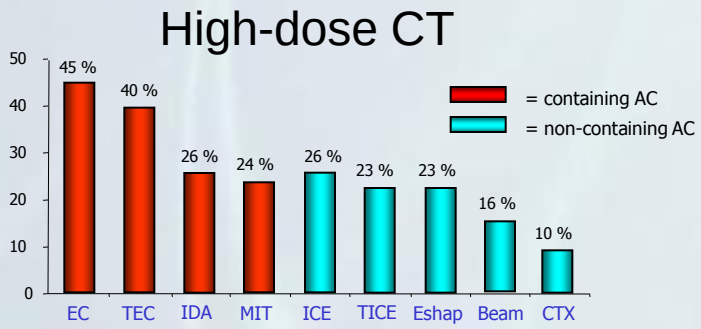
Values are given as n (%).

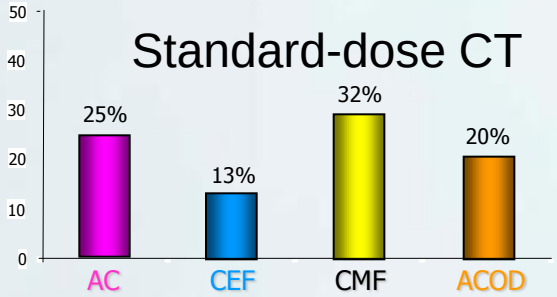
*$P<0.001$ vs TnI$^{-/-}$ group; †$P<0.001$ vs TnI$^{+/-}$ group.

Circulation 2004

TnI positivity in different schedules

IEO experience





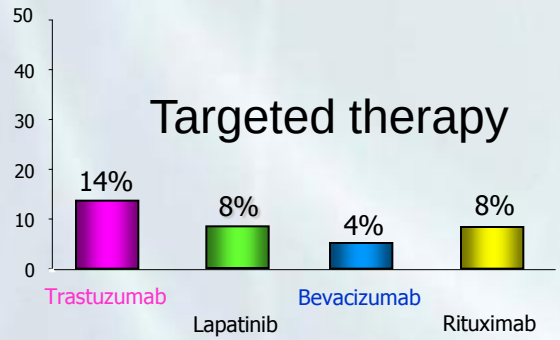


TABLE I. Troponins in the Assessment of Anthracycline Cardiotoxicity in Humans

Study	Patients no.	Malignant disease	Anthracycline	Dose (mg/m^2)	Schedule	Biomarker	Cut-off value	Troponin measurement	Echocardiography	Results
Fink [22]	Children (n = 22)	Various	Various	60–460 (mean 180)	Various	cTnT	0.14 μg/L	6, 12, 24, 28 and 72 hr later	Before treatment + 3 weeks after	No rise in cTnT
Kismet [23]	All ages (n = 24)	Solid tumors	DXR	400–840 (median 480)	n.a.	cTnT	0.01 ng/ml	Concomitant with imaging	Following last DXR (>1 month, median interval 12 months)	No statistically significant rise in cTnT
Mathew [24]	Children (n = 15)	Various	Various	11–375	Various	cTnI	Laboratory-specific	Baseline, then serially after each 25–50 mg/m^2 cum. dose	Before each (>300 mg/m^2) every other (<300 mg/m^2) course	No changes in TnI levels despite mild decline in systolic heart function
Soker [25]	Children (n = 31)	Hematologic (ALL 87%)	Various	30–600 (mean 227)	Various	cTnI	0.5 ng/ml	At least 1 month after anthracycline doses	Concomitant with cTnI	No changes in cTnI levels
Lipschultz [27]	Children (n = 15)	ALL	DXR	45–222 (median 60)	n.a.	cTnT	0.03 ng/ml	Baseline, 1–3 days after each cycle	Late after cTnT (0.67 years)	Positive correlation between cTnT and LV end-diastolic dimension/wall thickness
Missov [33]	Adults (n = 55)	Hematologic	n.a.	240–300	Every 3–4 weeks	cTnI	Against controls	Baseline, 7–10 days following intermediate cumulative dose	Concomitant with cTnI (radionuclide angiography)	Elevated cTnI in anthracycline versus baseline (2×), versus controls (4×) despite preserved LVEF
Auner [32]	Adults (n = 78)	Hematologic	Various	26–135 (per cycle)	Cycles of 3–5 weeks	cTnT	0,03 ng/ml	Every 48 hr	Baseline, 3 months after end	Peak 21st day/duration 3.5 days cTnT + predicted lower LVEF than cTnT-status
Kilickap [31]	Adults (n = 41)	Various	Various	50–480 (mean 228)	n.a.	cTnT	0.01 ng/ml	Baseline, 3–5th day after first dose, after treatment	Baseline, after end of treatment	Elevated cTnT in early treatment predictive of diastolic dysfunction
Kremer [20]	Children (n = 38)	Various	Various	Mean 255	n.a.	cTnT	0.01 ng/ml	After 4–6, 24 hr	Baseline, during, after therapy	Early cTnT increase not high sensitive (33%) for predicting LV dysfunction
Cardinale [28]	Adults (n = 204)	Various	HDC	Various	Various	cTnI	0.5 ng/ml	After 0, 12, 24, 36 and 72 hr of every cycle	1, 2, 3, 4 and 7 months after HDC	Elevated cTnI strong predictive of low LVEF
Sandri [34]	Adults (n = 179)	Various	HDC	45–600	3–4 cycles	cTnI	0.08 μg/ml	Before, 0, 12, 24, 36 and 72 hr after each cycle	LVEF after 1, 2, 3, 4, 7 and 12 months after end	Elevated cTnI predictive of low LVEF
Cardinale [35]	Adults (n = 211)	Breast cancer	HDC/radiation	Various	3 cycles	cTnI	0.5 ng/ml	Before, 0, 12, 24, 36 and 72 hr after each cycle	LVEF after 1, 2, 3, 4, 7 and 12 months after end	Elevated cTnI predictive of low LVEF
Cardinale [29]	Adults (n = 703)	Various	HDC/radiation	90–600	1–4 cycles	cTnI	0.08 ng/ml	Before, 0, 12, 24, 36 and 72 hr after each cycle/ 1 month after treatment	LVEF before, 1, 3, 6 and 12 months after end and every 6 months thereafter	Elevated cTnI (especially persisting 1 month later) predictive of low LVEF
Speechia [30]	Adults (n = 79)	AML/ALL	Various	21–450	Various	cTnI	0.15 ng/ml	Baseline, 2 days after 3 days, 6th, 9th dose (induction consolidation) and 3, 6, 12 and 18 months after	Concomitant with cTnI	Elevated cTnI diagnostic of low LVEF, troponin + patients had normal LVEF at late follow up
Lipshultz [26]	Children (n = 206)	ALL	DXR	300	10 doses	cTnT	0.01 ng/ml	158 patients: before, daily after induction doses, 7 days after a dose, at completion	Before, during, after DXR therapy	Increased cTnT in DXR treated pts compared to DXR + DZX pts, no differences in echo indexes

DXR: doxorubicin; HDC: high dose chemotherapy; LVEF: left ventricular ejection fraction; n.a: non-available.

Germanakis I et al, Pediatr Blood Cancer 2008

hs cTn and cardiotoxicity

Early Detection and Prediction of Cardiotoxicity in Chemotherapy-Treated Patients

Heloisa Sawaya, MD, PhD[a], Igal A. Sebag, MD[d], Juan Carlos Plana, MD[f], James L. Januzzi, MD[a], Bonnie Ky, MD[g], Victor Cohen, MD[e], Sucheta Gosavi, MD[a], Joseph R. Carver, MD[g], Susan E. Wiegers, MD[g], Randolph P. Martin, MD[h], Michael H. Picard, MD[a], Robert E. Gerszten, MD[a], Elkan F. Halpern, PhD[c], Jonathan Passeri, MD[a], Irene Kuter, MD[b], and Marielle Scherrer-Crosbie, MD, PhD[a,*]

- 43 breast cancer patients, scheduled to receive AC and trastuzumab
- hs cTnI and ECHO before CT, at 3 and 6 months

Decreases in longitudinal strains and radial strains and elevated hsTnI at 3 months were PREDICTIVE of patients who developed cardiotox at six months

Table 3
Univariate analysis of predictors of ca

Variable	No (n = 34)	Yes (n = 9)	p Value (Prediction of Cardiotoxicity)	Odds Ratio	95% Confidence Interval
Change in the LVEF at 3 months (%)	1.2 ± 9	5.6 ± 8	0.9	5.5	0.45–100
Change in longitudinal strain at 3 months (%)	3 ± 10	15 ± 8	0.01	500	6.7–110,000
Change in radial strain at 3 months (%)	2 ± 23	22 ± 22	0.02	250	4–40,000
Change in NT-proBNP at 3 months (%)	46 ± 240	56 ± 190	0.91	1	0.65–1.4
Elevation hsTnI at 3 months	6 (18%)	6 (67%)	0.006	9	1.8–50

Multivariate analysis

Table 4
Sensitivity, specificity, and positive and negative value of the predictors of cardiotoxicity

Predictor	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
10% decrease in longitudinal strain	7/9 (78%)	27/34 (79%)	7/14 (50%)	27/29 (93%)
Elevated hsTnI at 3 months	6/9 (67%)	28/34 (82%)	6/12 (50%)	28/31 (90%)
10% decrease in longitudinal strain and elevated hsTnI at 3 months	5/9 (55%)	33/34 (97%)	5/6 (83%)	33/37 (89%)
10% decrease in longitudinal strain or elevated hsTnI at 3 months	8/9 (89%)	22/34 (65%)	8/20 (40%)	22/23 (97%)

Troponina - Conclusioni

- La Troponina è un marcatore precoce che predice lo sviluppo di una disfunzione clinica del VS
- Il grado di incremento è correlato alla severità della disfunzione
- Permette la selezione dei pazienti da monitorare più strettamente e per i quali instaurare strategie terapeutiche di prevenzione (alto valore predittivo negativo)
- Dovrebbe essere utilizzata nell'ambito della definizione della cardiotossicità

Il ruolo dei peptidi natriuretici

N-Terminal Pro-B-Type Natriuretic Peptide after High-Dose Chemotherapy: A Marker Predictive of Cardiac Dysfunction?

Maria T. Sandri,[1*] Michela Salvatici,[1] Daniela Cardinale,[2] Laura Zorzino,[1] Rita Passerini,[1] Paola Lentati,[1] Maria Leon,[3] Maurizio Civelli,[2] Giovanni Martinelli,[4] and Carlo M. Cipolla[2]

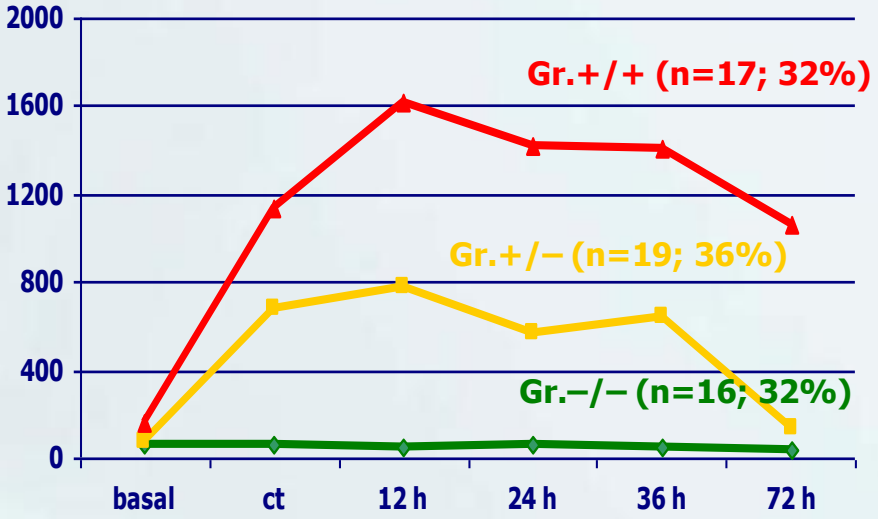
- RETROSPECTIVE STUDY

- 52 PATIENTS AFFECTED with AGGRESSIVE MALIGNANCIES

- TREATED with HDC

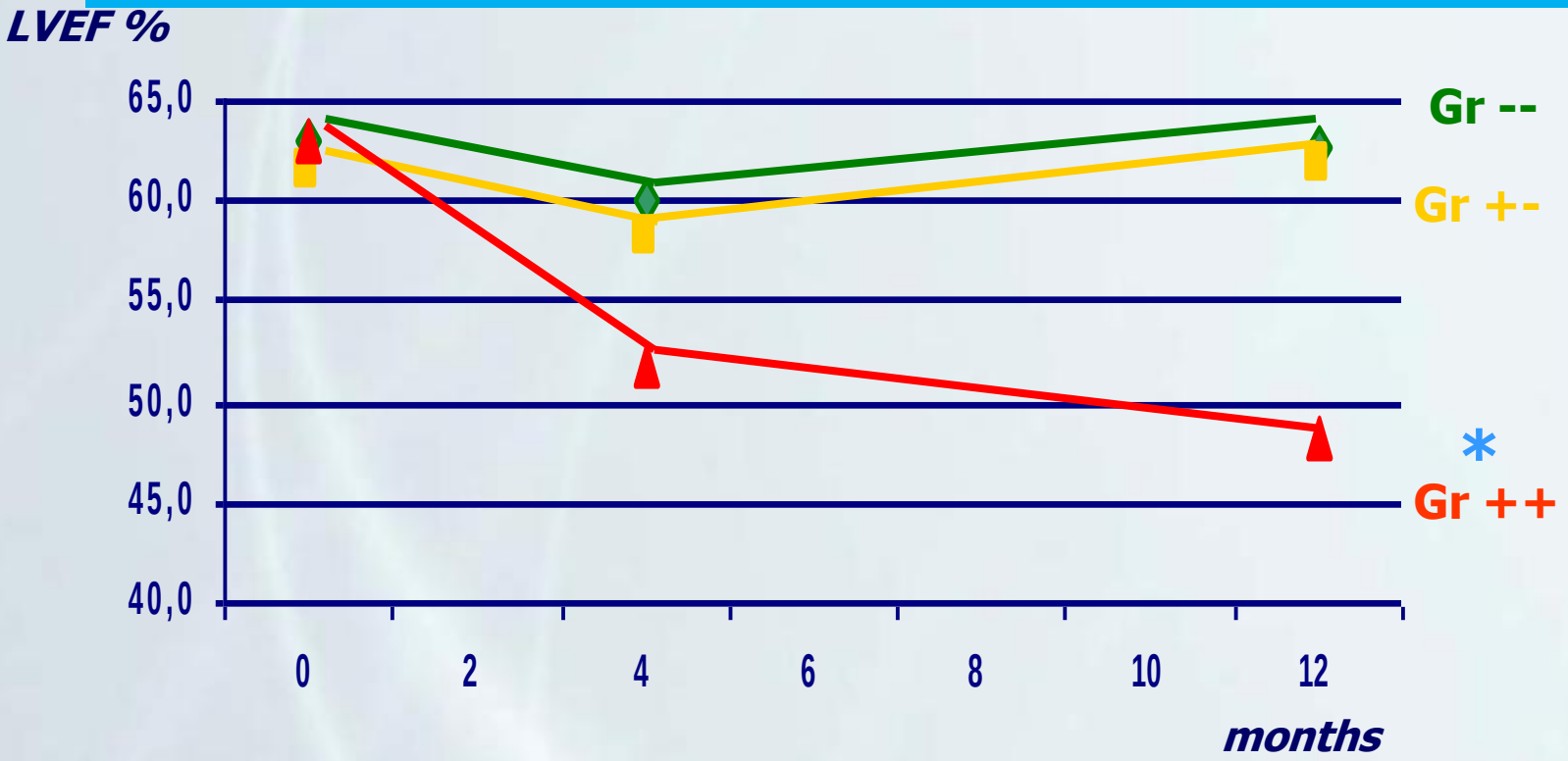
- NT-proBNP VALUES DETERMINED BEFORE, AT THE END, AND 12, 24, 36, 72 h AFTER each HDC ADMINISTRATION

- CARDIAC MONITORING by MEANS of ECHO for at least 1 year



Clinical Chemistry 51:8
1405–1410 (2005)

LVEF and NT-proBNP



* *P<0.001*

Persistent NT-proBNP increase predicts clinical cardiac dysfunction induced by HDC

Data from the literature

Studies on NPs as markers of CT-induced cardiotoxicity, including more than 20 patients

Reference	Population studied	Adult child	Patients (% NP+)	NP evaluated	Cut-off	Time of sampling: Pre-CT	CT	Follow-up	Conclusions
[illegible][31]	[illegible]	[illegible]	[illegible]	BNP	[illegible]	X	X		Concentrations increased after treatment BNP not predictive
[illegible][32]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Concentrations increased in patients with diastolic dysfunction Concentrations increased after treatment but not associated with ventricular dysfunction
Nousiainen et al[35]	Non–Hodgkin lymphoma	A	28 (?)	BNP	Not defined	X		X	BNP associated with diastolic dysfunction
Poutanen et al[36]	Pediatric cancers	C	39 (38%)	BNP	Not defined			X	No clinical usefulness
Daugaard et al[37]	Advanced neoplasia	A	107 (?)	BNP	Not defined	X	X	X	Not useful to replace estimation of LVEF
[illegible][38]	[illegible]	[illegible]	[illegible]	[illegible]	Dependent on sex and age	X	X		Persistent increase associated with development of cardiac dysfunction
[illegible][39]	[illegible]	[illegible]	[illegible]	[illegible]	BNP levels of the healthy control 4.09 ± 2.26 pg/mL			X	Association of higher NT-proBNP levels with diastolic abnormalities
Nakamae et al[40]	Non–Hodgkin lymphoma	A	40 (50%)	ANP, BNP	Not defined	X	X		Early increase in ANP and BNP levels after CT
Pichon et al[41]	Breast cancer	A	79 (49%)	BNP	51.3 ng/L	X	X	X	To predict development of CHF sensitivity 83.3% (CI, 52%-97%) and, specificity 90.2% (CI, 86%-94%)
[illegible][42]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	X	Concentrations increased in patients with ventricular dysfunction BNP associated with EF and SF decreases
[illegible][43]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	X	BNP elevated in patients with late cardiac dysfunction
[illegible][44]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Increased BNP level reflect acute cardiac toxicity during CT but is not associated with evidence of cardiac dysfunction
Zver et al[46]	Multiple myeloma	A	23 (?)	TnI, ET-1, BNP	25 μg/L	X	X	X	BNP and ET-1 levels are sensitive indicator of myocardial injury
Knobloch et al[47]	Breast Cancer	A	48 (29%)	NT-proBNP	125 pg/ml	X	X		NT-proBNP marker of acute toxicity
Horacek et al[48]	Acute leukemia	A	26 (61.5%)	NT-proBNP, TnT,	Male 100 ng/L, female 150 ng/L	X	X	X	NT-proBNP concentrations correlate with systolic and diastolic dysfunctions
[illegible][49]	[illegible]	[illegible]	[illegible]	[illegible]	Dependent on sex and age	X	X	X	NT-proBNP do not predict cardiac dysfunction
[illegible][50]	[illegible]	[illegible]	[illegible]	[illegible]	Not defined	X	X		NT-proBNP is a sensitive marker for the early detection of the course-to-course effects of CT
Mavinkurve-Groothuis et al[51]	Various malignancies	C/A	122 (13%)	NT-proBNP, TnT	Male 10 pmol/L, female 18 pmol/L, children: age-dependent			X	NT-proBNP levels are significantly related to an increase in LVDd
Cil et al[52]	Breast cancer	A	33 (30.3%)	NT-proBNP	5-110 pg/mL	X	X		Association of higher NT-proBNP levels with reduced LVEF

Circa 1000 pazienti (30% bambini)

BNP, NTproBNP, ANP

Determinati preCT, durante CT, durante follow-up

Risultati non concordi

D. Cardinale, M.T. Sandri / Progress in Cardiovascular Diseases 53 (2010) 121–129

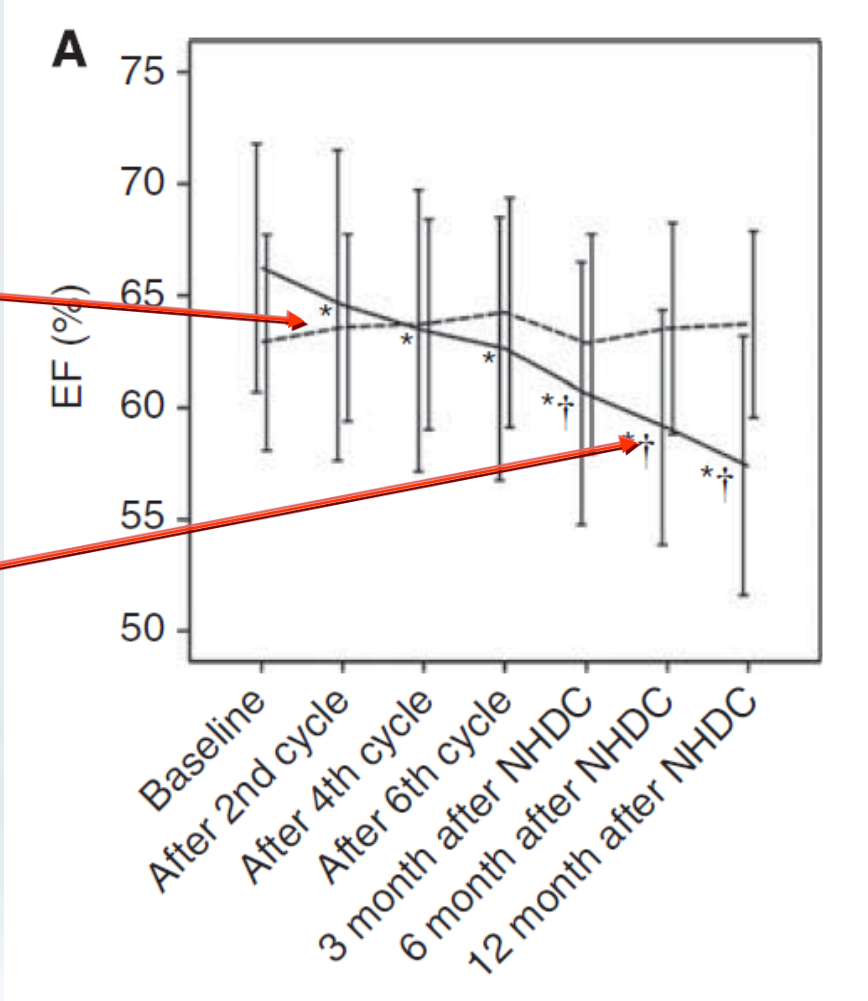
NT-proBNP predictive of cardiotoxicity

- 71 breast cancer pts undergoing non high dose anthracycline CT
- NT-proBNP and TnI evaluated before and 24h after NHCT at each cycle (n=6)
- ECHO performed at baseline, 2, 4, 6 cycle, and then after 3, 6 and 12 months.

Romano S et al, Br J Cancer 2011

NT-proBNP predictive of cardiotoxicity

- 2 patterns:
  - Patients with TRANSIENT NT-proBNP increases (A)
  - Patients with PERSISTENT NT-proBNP increases (B)
- 4 pts developed cardiac events, all in group B



Romano S et al, Br J Cancer 2011

Changes in Cardiac Biomarkers During Doxorubicin Treatment of Pediatric Patients With High-Risk Acute Lymphoblastic Leukemia: Associations With Long-Term Echocardiographic Outcomes

Steven E. Lipshultz, Tracie L. Miller, Rebecca E. Scully, Stuart R. Lipsitz, Nader Rifai, Lewis B. Silverman, Steven D. Colan, Donna S. Neuberg, Suzanne E. Dahlberg, Jacqueline M. Henkel, Barbara L. Asselin, Uma H. Athale, Luis A. Clavell, Caroline Laverdière, Bruno Michon, Marshall A. Schorin, and Stephen E. Sallan

J Clin Oncol 30:1042-1049. © 2012

Our results suggest the utility of assessing cardiac status with biomarkers such as cTnT and NT-proBNP in children receiving doxorubicin for ALL. Serum cTnT levels increased during the first 90 days of therapy, indicating cardiomyocyte damage or death; they were significantly associated with reduced LV mass and LV end-diastolic posterior wall thickness and were marginally associated with a reduced LV thickness-to-dimension ratio 4 years later. Similarly, abnormal NT-proBNP levels during the first 90 days of therapy were associated with an abnormal LV thickness-to-dimension ratio, suggesting pathologic LV remodeling 4 years later. In addition, before, during, and after treatment, a higher percentage of children had increased levels of NT-proBNP (indicating increased LV wall stress) than had abnormal cTnT levels (indicating cardiomyocyte death), suggesting that NT-proBNP may detect cardiac stress before irreversible cardiomyocyte death.

Case 1, pt S.V., breast adjuv.

Date	LVEF	TnI	NT-proBNP
May 2006	59	0.03	
Aug 2006	65	0.04	**626**
Jan 2007	59	**0.11**	31
Mar 2008	63	0.02	94
May 2009	60	0.01	106
Oct 2009	65	0.02	**195**
Nov 2010	70	0.02	**206**
May 2011	65	0.02	**547**
Oct 2011		0.019	**3341**
Nov 2011	**38**		
Feb 2012	**54**	0.01	**1166**

AC x 4 (Jul-Sept)
RT (Aug-Sept)

Follow-up

Start Enalapril 20 mg

Case 2, pt C.A., metastatic

Date	LVEF	TnI	NTproBNP
Dec 2005	62	0.00	164
Mar 2006	60	**0.08**	118
Apr 2006	55	**0.24**	**413**
Jun 2006	**27**		
Sept 2008	**28**	0.00	**735**
Sept 2009	**37**	0.00	**966**
Mar 2010	**30**	0.00	**792**

CEFx6 (Nov 05-Apr 06)

Start Enalapril

07/07 Relapse - Bone

Different CT

Natriuretic Peptides - Conclusions

- No conclusive data (lack of sufficiently powered studies)
- It may be predictive (in few cases with no TnI increase)
- Is elevated when TnI is low, during the follow-up, when the functional damage manifests

Do not ask the listener if absolutely agrees with you, ask him if he proceeds in the same direction

Goethe