

IL PAZIENTE FRAGILE IN CARDIOLOGIA

TRATTAMENTO DEL PAZIENTE FRAGILE CON
SCOMPENSO CARDIACO

INDICAZIONE ALL'IMPIANTO DI DEVICE

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Torino, 11/5/2019

**DEFIBRILLATORE IMPIANTABILE (ICD)
(+/-)
TERAPIA DI RESINCRONIZZAZIONE CARDIACA (CRT)**

Cardiac contractility modulation (CCM)

Elevato numero di “morti improvvise” (milder symptomatics)
Molte hanno origine “elettrica”: aritmie ventricolari / bradi-asistolie
La terapia medica ottimizzata ha un ruolo “preventivo” limitato
Scarso ruolo preventivo dei farmaci antiaritmici

ESC GUIDELINES 2016



-> DEFIBRILLATORE IMPIANTABILE (ICD)

PREV. SECONDARIA

MORTE IMPROVVISA- 50%
MORTALITA' GLOBALE - 28%

PREV. PRIMARIA

MORTE IMPROVVISA - 60%
MORTALITA' GLOBALE – 23/31%
NNT 50 (/anno)

ESC GUIDELINES 2015

Recommendations for implantable cardioverter-defibrillator in patients with heart failure

Recommendations	Class ^a	Level ^b	Ref ^c
Secondary prevention An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients who have recovered from a ventricular arrhythmia causing haemodynamic instability, and who are expected to survive for >1 year with good functional status.	I	A	223–226
Primary prevention An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients with symptomatic HF (NYHA Class II–III), and an LVEF ≤35% despite ≥3 months of OMT, provided they are expected to survive substantially longer than one year with good functional status, and they have: <ul style="list-style-type: none"> • IHD (unless they have had an MI in the prior 40 days – see below). • DCM. 	I	A	149, 156, 227
	I	B	156, 157, 227
ICD implantation is not recommended within 40 days of an MI as implantation at this time does not improve prognosis.	III	A	158, 228
ICD therapy is not recommended in patients in NYHA Class IV with severe symptoms refractory to pharmacological therapy unless they are candidates for CRT, a ventricular assist device, or cardiac transplantation.	III	C	229–233
Patients should be carefully evaluated by an experienced cardiologist before generator replacement, because management goals and the patient's needs and clinical status may have changed.	IIa	B	234–238
A wearable ICD may be considered for patients with HF who are at risk of sudden cardiac death for a limited period or as a bridge to an implanted device.	IIb	C	239–241

CAD = coronary artery disease; CRT = cardiac resynchronization therapy; DCM = dilated cardiomyopathy; HF = heart failure; ICD = implantable cardioverter-defibrillator; IHD = ischaemic heart disease; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NYHA = New York Heart Association, OMT = optimal medical therapy.

^aClass of recommendation.

^bLevel of evidence.

^cReference(s) supporting recommendations.

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ESC GUIDELINES 2016

L'EFFICACIA SULLA PREVENZIONE DELLA MORTE IMPROVVISA DELL'ICD PUO' ESSERE PARZIALMENTE O COMPLETAMENTE NEUTRALIZZATA DALL'INCREMENTO DELLA MORTALITA' DA INSUFFICIENZA CARDIACA

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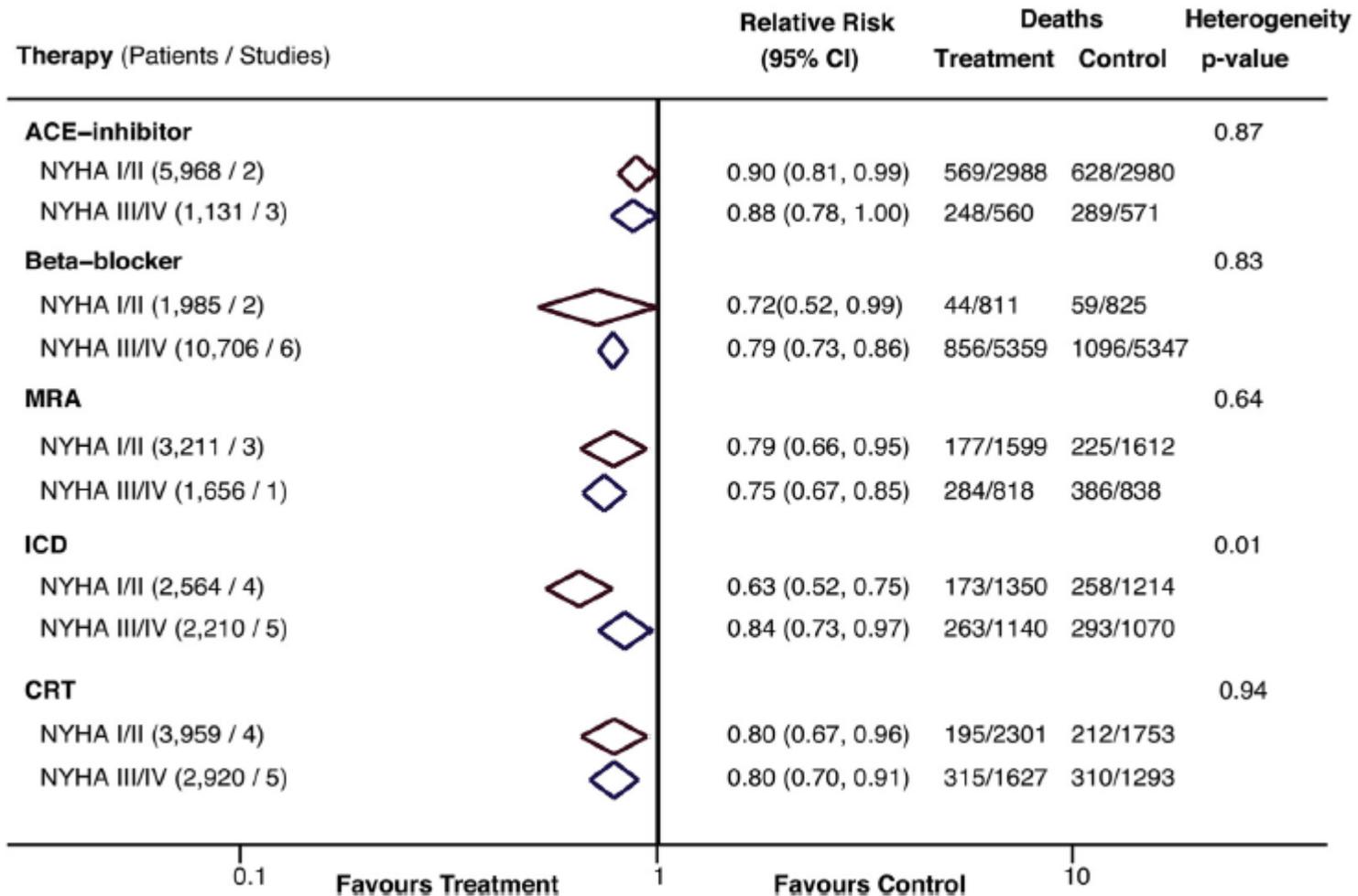
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^bLevel of evidence.

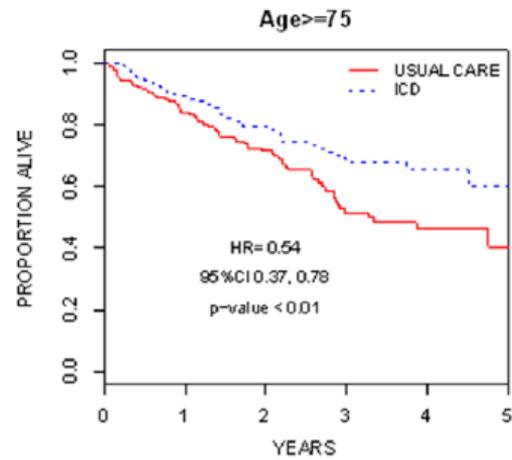
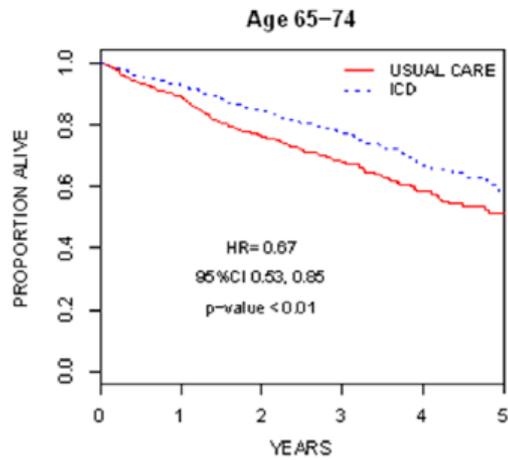
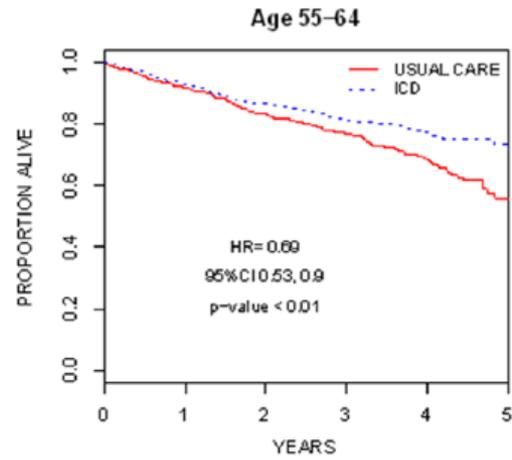
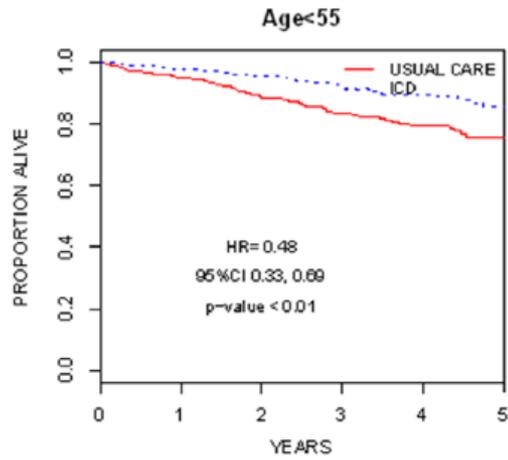
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ESC GUIDELINES 2016

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X CLASSE NYHA



X ETA'

Cardiovasc Qual Outcomes. 2015;8:179-186.

TABLE 1 Comorbidities Included in the Analysis

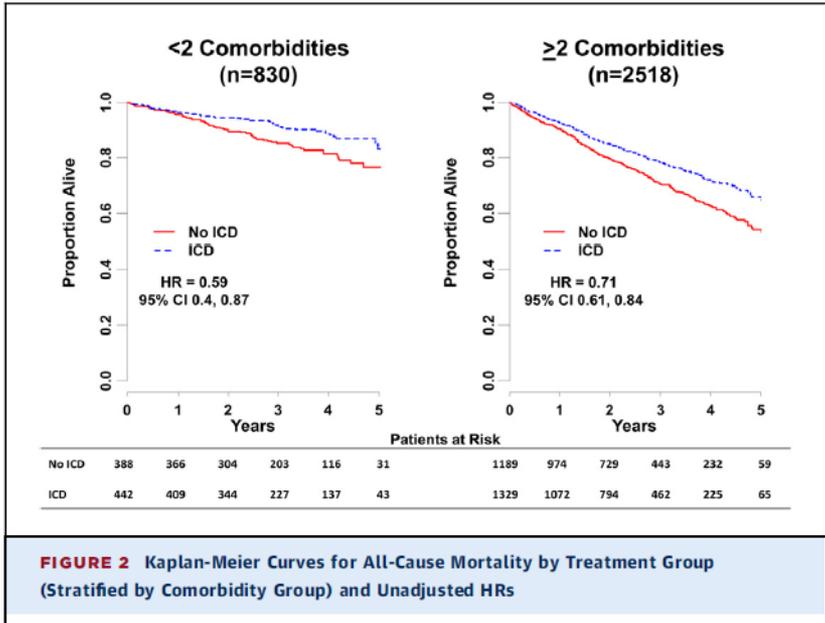
	<2 Comorbidities (n = 830)		≥2 Comorbidities (n = 2,518)	
	Control (n = 388)	ICD (n = 442)	Control (n = 1,189)	ICD (n = 1,329)
Smoking	221 (58)	211 (48)	1,047 (89)	1,165 (88)
Ischemic heart disease	55 (14)	77 (17)	877 (74)	1,041 (79)
Chronic kidney disease	15 (6)	17 (6)	484 (46)	524 (43)
Diabetes	20 (5)	33 (8)	462 (39)	476 (36)
Pulmonary disease	2 (1)	12 (3)	180 (26)	183 (28)
Atrial fibrillation	6 (2)	8 (2)	97 (14)	103 (16)
Peripheral vascular disease	0 (0)	0 (0)	20 (10)	18 (10)

Values are n (%).
ICD = implantable cardioverter-defibrillator.

TABLE 2 Unadjusted and Adjusted Survival Differences Between ICD and Control Groups at 5 Years by Number of Comorbidities

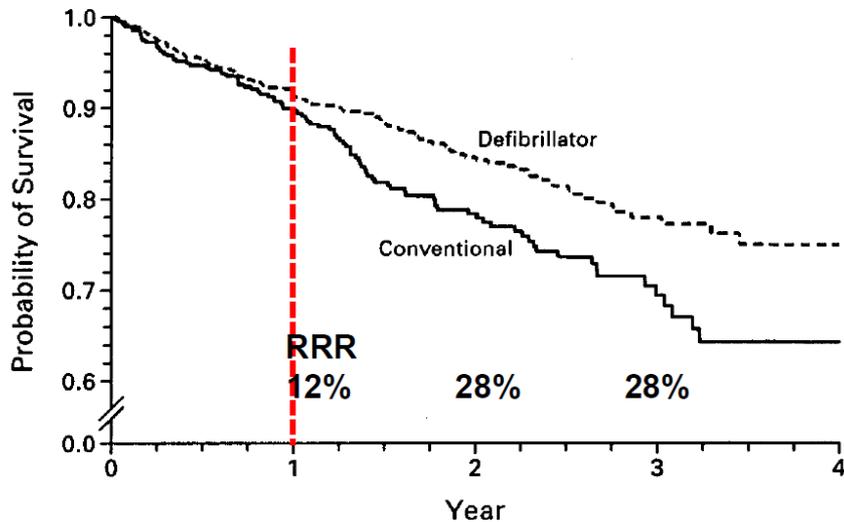
No. of Comorbidities	Unadjusted		Adjusted	
	Median Survival Difference (ICD - Control)	95% CI	Median Survival Difference (ICD - Control)	95% CI
0	0.11	(0.05 to 0.17)	0.13	(0.06 to 0.19)
1	0.12	(0.07 to 0.18)	0.13	(0.07 to 0.19)
2	0.13	(0.08 to 0.18)	0.13	(0.08 to 0.18)
3	0.11	(0.06 to 0.16)	0.11	(0.06 to 0.15)
4	0.06	(-0.01 to 0.14)	0.06	(0.00 to 0.14)
5	0.00	(-0.13 to 0.12)	0.00	(-0.10 to 0.12)
6	-0.06	(-0.19 to 0.07)	-0.05	(-0.18 to 0.09)

No patient had all 7 comorbidities. Posterior probability of interaction between treatment and comorbidity, $p < 0.01$ (unadjusted and adjusted).
CI = confidence interval; ICD = implantable cardioverter-defibrillator.



X COMORBIDITA'

PERCHE ASPETTATIVA DI VITA > 1 ANNO?

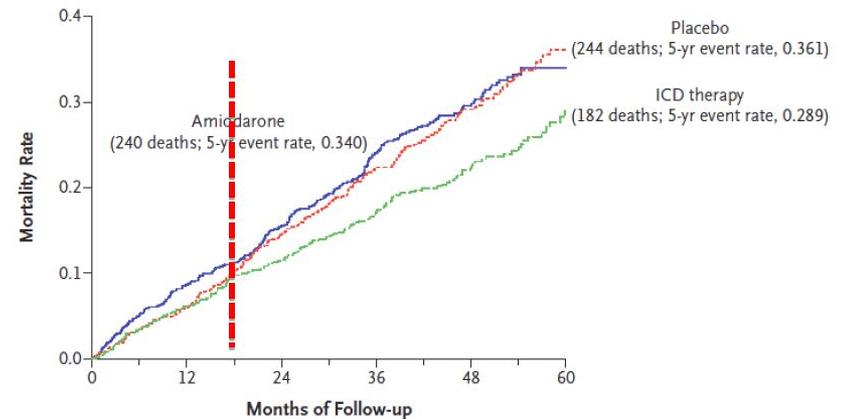


MADIT II Trila: Timing of Survival Benefit

Moss et al, NEJM 2002

SCD-HeFT

	Hazard Ratio (97.5% CI)	P Value
Amiodarone vs. placebo	1.06 (0.86–1.30)	0.53
ICD therapy vs. placebo	0.77 (0.62–0.96)	0.007



No. at Risk	0	12	24	36	48	60
Amiodarone	845	772	715	484	280	97
Placebo	847	797	724	505	304	89
ICD therapy	829	778	733	501	304	103

NEJM 2005; 352:225

Meccanismo della desincronia cardiaca nello scompenso

Prolungamento dell'intervallo A-V:

- favorisce l'insufficienza mitralica diastolica
- compromissione riempimento ventricolare -> ↓ della contrattilità ventricolare

Ritardi di conduzione inter e intraventricolari:

- contrazione desincronizzata di regioni del vsx -> ripercussioni sulla gittata
- insufficienza mitralca funzionale
- rimodellamento sfavorevole del vsx

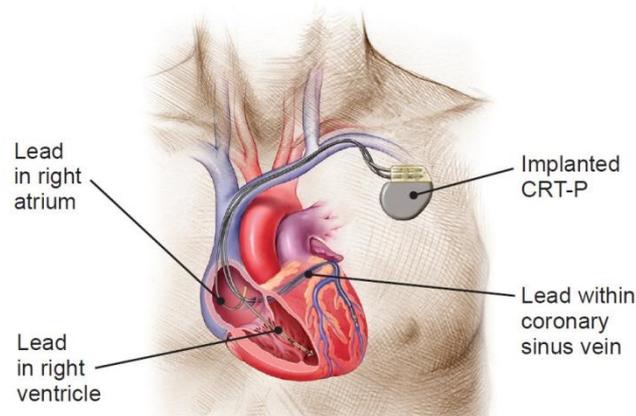
ESC GUIDELINES 2013

-> TERAPIA DI RESINCRONIZ. CARDIACA (CRT)

COMPANION

MADIT CRT

CARE-HF



**_In pazienti ben selezionati:
SINTOMI -MORTALITA' GLOBALE
-22%
OSPEDALIZZAZIONE – 35%**

Recommendations for cardiac resynchronization therapy implantation in patients with heart failure

Recommendations	Class ^a	Level ^b	Ref ^c
CRT is recommended for symptomatic patients with HF in sinus rhythm with a QRS duration ≥ 150 msec and LBBB QRS morphology and with LVEF $\leq 35\%$ despite OMT in order to improve symptoms and reduce morbidity and mortality.	I	A	261–272
CRT should be considered for symptomatic patients with HF in sinus rhythm with a QRS duration ≥ 150 msec and non-LBBB QRS morphology and with LVEF $\leq 35\%$ despite OMT in order to improve symptoms and reduce morbidity and mortality.	IIa	B	261–272
CRT is recommended for symptomatic patients with HF in sinus rhythm with a QRS duration of 130–149 msec and LBBB QRS morphology and with LVEF $\leq 35\%$ despite OMT in order to improve symptoms and reduce morbidity and mortality.	I	B	266, 273
CRT may be considered for symptomatic patients with HF in sinus rhythm with a QRS duration of 130–149 msec and non-LBBB QRS morphology and with LVEF $\leq 35\%$ despite OMT in order to improve symptoms and reduce morbidity and mortality.	IIb	B	266, 273
CRT rather than RV pacing is recommended for patients with HFrEF regardless of NYHA class who have an indication for ventricular pacing and high degree AV block in order to reduce morbidity. This includes patients with AF (see Section 10.1).	I	A	274–277
CRT should be considered for patients with LVEF $\leq 35\%$ in NYHA Class III–IV ^d despite OMT in order to improve symptoms and reduce morbidity and mortality, if they are in AF and have a QRS duration ≥ 130 msec provided a strategy to ensure bi-ventricular capture is in place or the patient is expected to return to sinus rhythm.	IIa	B	275, 278–281
Patients with HFrEF who have received a conventional pacemaker or an ICD and subsequently develop worsening HF despite OMT and who have a high proportion of RV pacing may be considered for upgrade to CRT. This does not apply to patients with stable HF.	IIb	B	282
CRT is contra-indicated in patients with a QRS duration < 130 msec.	III	A	266, 283–285

“...CRT improves cardiac performance in appropriately selected patients and improves symptoms and well-being and reduces morbidity and mortality....”

ESC GUIDELINES 2016

QUANTI SONO???

In the EuroHeart Failure survey, 36% of those who had LV function assessed had an LVEF \leq 35% and, of these, 41% had a QRS duration \geq 120 ms; 34% had LBBB and 17% had QRS \geq 150 ms.

EuroHeart Failure survey
Eur J Heart Fail 2007;9:491–501

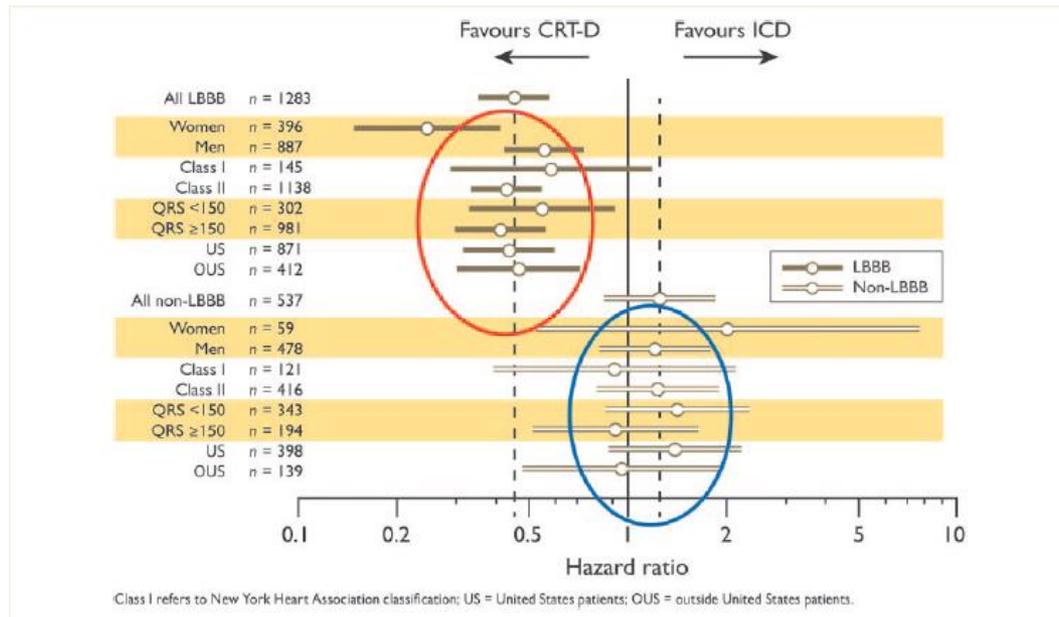
In the Italian Network on CHF (IN-CHF) registry, 1391 patients (25%) had complete LBBB

Italian Network on CHF (IN-CHF)
registry Am Heart J 2002;143:398–05

The annual incidence of LBBB is about 10% in ambulatory patients with left ventricular systolic dysfunction (LVSD) and chronic HF

Eur J Heart Fail 2008;10:696–702.

IL 5–10% DEI PAZIENTI CON SCOMPENSO AVREBBERO INDICAZIONE ALL'IMPIANTO DI CRT
DI QUESTI 1/3 VENGONO IMPIANTATI



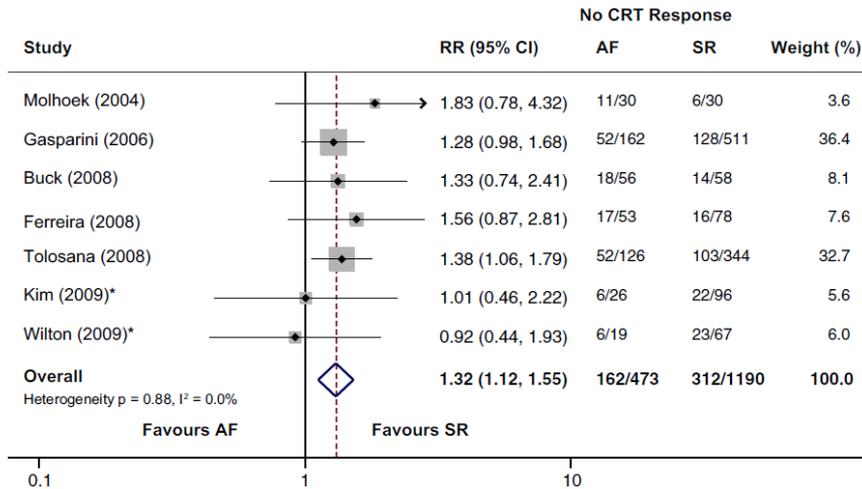
CARDIOPATIA ISCHEMICA

BBsx (LBBB) predice risposta a CRT in tutti i sottogruppi analizzati vs BBdx / IVCD* (non LBBB)

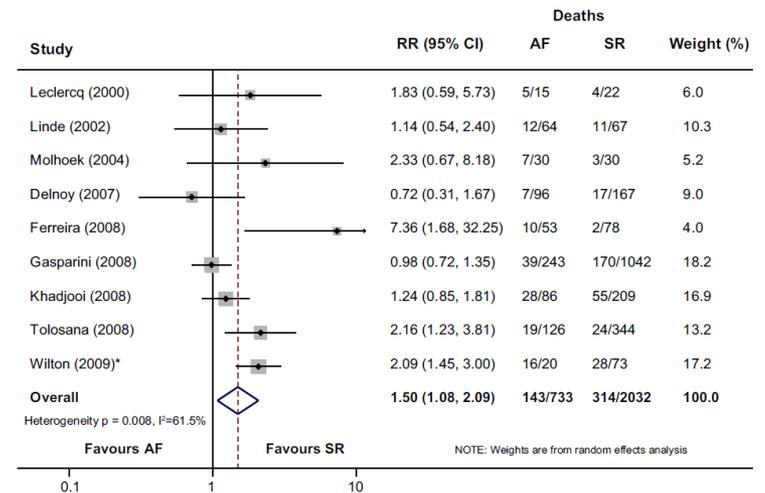
Non LBBB = prevalentemente ischemici

Pattern ischemico: rallentamento diffuso di conduzione da danno endocardico con minor dissincronia

LBBB: massima dissincronia di attivazione per prevalente disturbo elettrico



Rischio non risposta a CRT in Fa vs in RS



Rischio di morte in pazienti dopo CRT in Fa vs in RS

FIBRILLAZIONE ATRIALE (Fa)

La prevalenza di fa aumenta con la gravità dello scompenso (20 -> 50% ma è causa o conseguenza??)

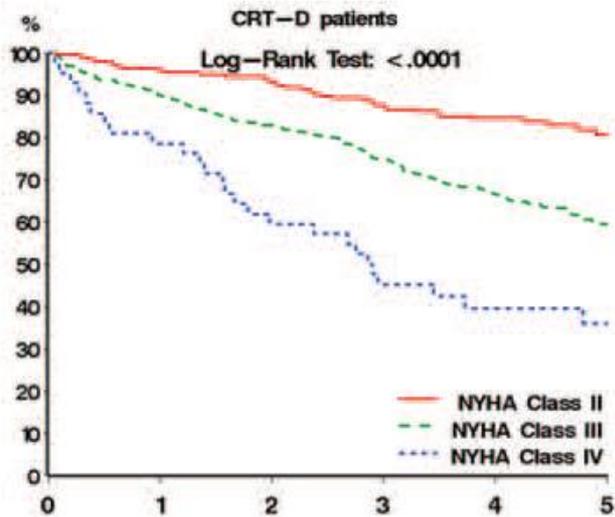
Oltre il 20% dei pazienti che ricevono CRT sono fibrillanti

I pazienti in Fa nei trials in genere sono più anziani più gravi e hanno maggior comorbidità

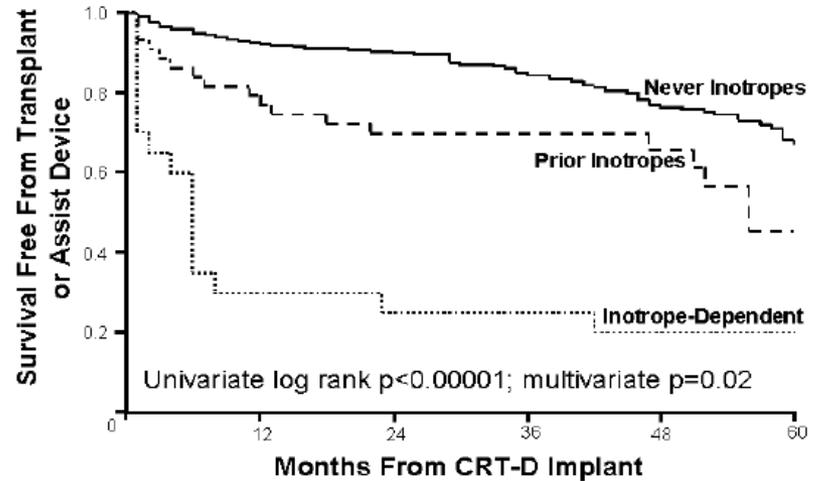
Il ritmo rapido ed irregolare in fa condiziona bassa percentuale di cattura biventricolare.

La CRT nei pazienti in Fa ha una minor probabilità di successo; in pazienti hanno maggior mortalità.

AV ablation??



	Years					
	0	1	2	3	4	5
Patients at Risk						
NYHA Class IV	42	33	25	19	13	10
NYHA Class III	471	424	390	352	248	157
NYHA Class II	196	188	183	172	122	70
Event %						
NYHA Class IV	100	78.6	59.5	45.2	39.6	36
NYHA Class III	99.8	90	82.8	74.7	66.6	59.5
NYHA Class II	100	95.9	93.4	87.8	84.5	80.7



Adelstein et al. Heart Rhythm 2011

European Journal of Heart Failure
(2016) 18, 693–702

Classe NYHA – GRAVITA' SCOMPENSO

- Il beneficio della CRT-D si riduce con l'aumentare della classe clinica:
- **HR** di decesso / trapianto: NYHA III VS NYHA II: 2.41
NYHA IV vs NYHA II: 5.2
- La necessità di uso di inotropi influenza ampiamente la risposta alla CRT

MADIT II Risk Score

Very High Risk: 5% of study cohort
2-y mortality 50%

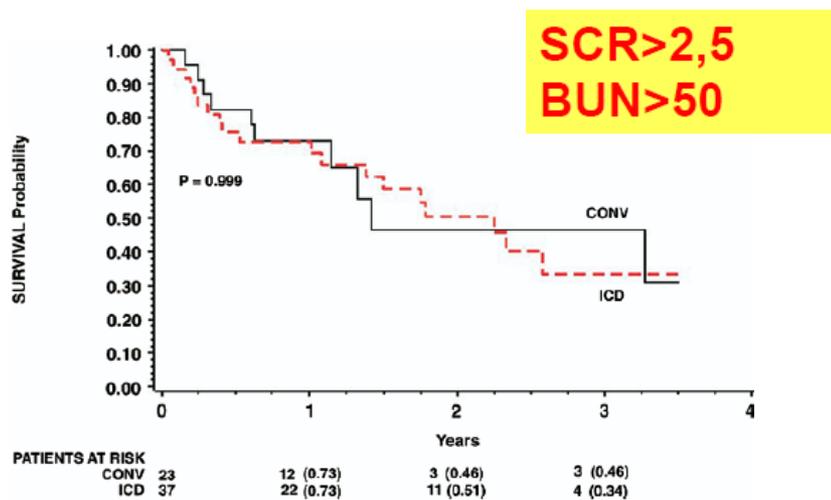


Figure 1 Probability of Survival in VHR Patients

Kaplan-Meier estimates of the probability of survival, by treatment group, in very high-risk (VHR) patients. CONV = conventional therapy group; ICD = implantable cardioverter-defibrillator.

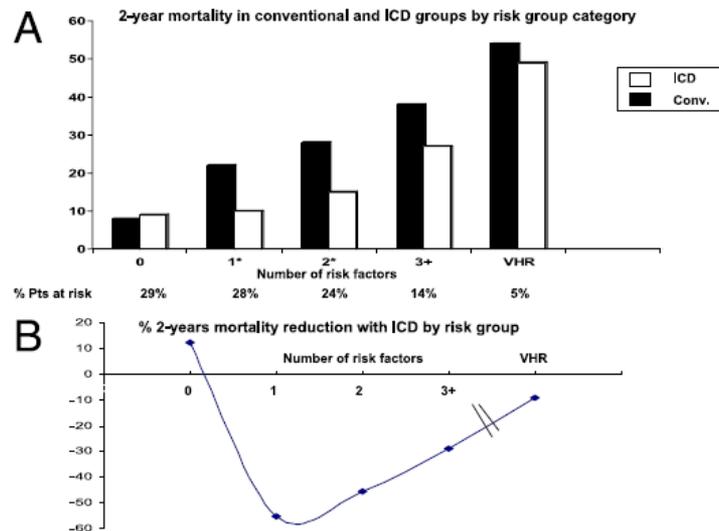


Figure 4 U-Shaped Curve for ICD Efficacy

(A) Two-year Kaplan-Meier mortality rates in the ICD and conventional therapy groups; and (B) the corresponding 2-year mortality rate reduction with ICD by risk score and in VHR patients. *p < 0.05 for the comparison between conventional therapy and ICD groups. Abbreviations: ICD, implantable cardioverter-defibrillator; VHR, very high risk.

Non-VHR
NYHA > II
Età > 70
BUN > 26 < 50
QRS > 0,120
FA

Pts MADIT Risk Score 1-2: riduzione della mortalità con ICD vs conventional therapy > 60%

Charlson Comorbidity Index (CCI)

TABLE I. Charlson Comorbidity Index*

Score	Condition
1	Myocardial infarction (history, not ECG changes only)
	Congestive heart failure
	Peripheral vascular disease (includes aortic aneurysm ≥ 6 cm)
	Cerebrovascular disease: CVA with mild or no residua or TIA
	Dementia
	Chronic pulmonary disease
	Connective tissue disease
	Peptic ulcer disease
	Mild liver disease (without portal hypertension, includes chronic hepatitis)
	Diabetes without end-organ damage (excludes diet-controlled alone)
2	Hemiplegia
	Moderate or several renal disease
	Diabetes with end-organ damage (retinopathy, neuropathy, nephropathy, or brittle diabetes)
	Tumour without metastases (exclude if >5 years from diagnosis)
	Leukaemia (acute or chronic)
3	Lymphoma
	Moderate or severe liver disease
6	Metastatic solid tumour
	AIDS (not just HIV-positive)

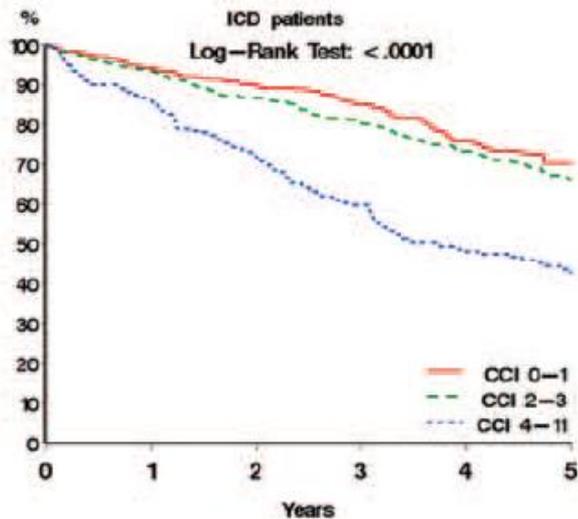
Abbreviations: AIDS = acquired immunodeficiency syndrome; CVA = cerebrovascular accident; ECG = electrocardiogram; HIV = human immunodeficiency virus; TIA = transient ischaemic attack

* For each decade >40 years of age, a score of 1 is added to the above score

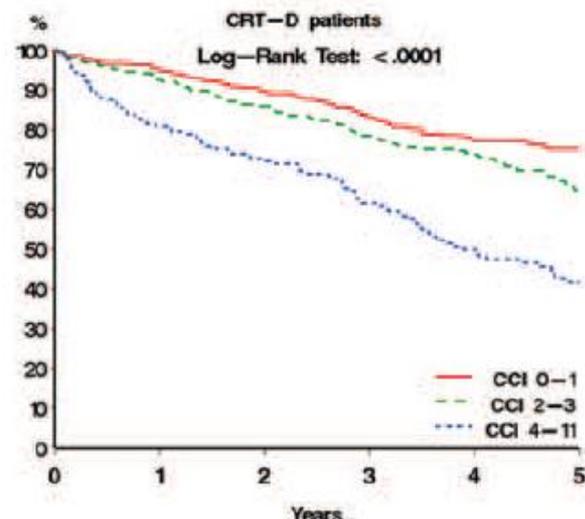
PROBABILITA' DI
SOPRAVVIVENZA A 10 ANNI IN
CASO DI PLURIPATOLOGIA

<https://www.mdcalc.com/charlson-comorbidity-index-cci>

Sopravvivenza in pazienti sottoposti ad impianto di ICD o CRT-D in relazione al CCI



	Patients at Risk					
	0	1	2	3	4	5
CCI 4-11	219	198	158	131	78	52
CCI 2-3	367	343	318	295	201	123
CCI 0-1	305	288	275	260	174	114
	Event %					
	0	1	2	3	4	5
CCI 4-11	100	85.8	72.1	59.8	48.1	42.8
CCI 2-3	100	93.5	86.6	80.4	73.2	66.3
CCI 0-1	100	94.4	89.8	85.2	75.8	70.4

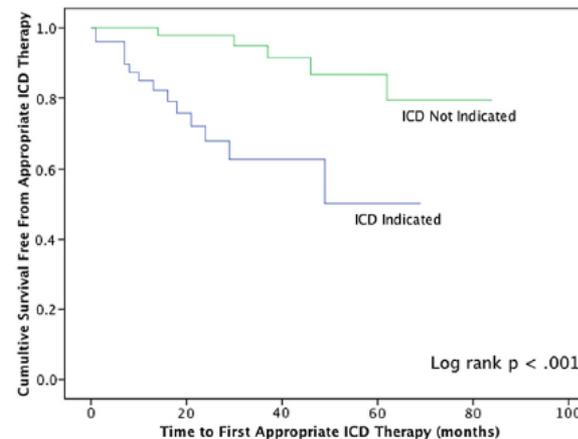
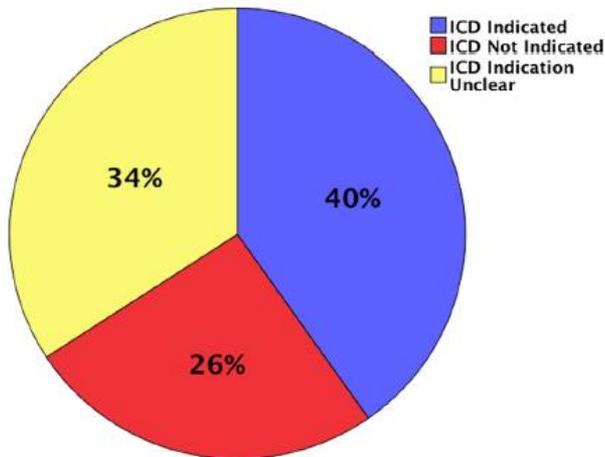


	Patients at Risk					
	0	1	2	3	4	5
CCI 4-11	161	130	117	99	61	39
CCI 2-3	255	236	219	200	144	83
CCI 0-1	293	279	262	244	176	115
	Event %					
	0	1	2	3	4	5
CCI 4-11	100	80.7	72.7	61.5	49.9	41.6
CCI 2-3	100	92.5	85.6	78.4	74.2	64.7
CCI 0-1	99.7	95.2	89.4	83.3	77.3	75.2

Il rischio di decesso correla con il CCI

...e al momento della sostituzione??

- Rispettare le indicazioni delle LG circa la sopravvivenza ad 1 anno
- Età: oltre gli 80 anni a 2 anni da sostituzione: mortalità 38%
- Persistenza delle indicazioni



JACC Vol. 63, No.22, 2014

- Massimalizzare la durata della batteria
- Considerare il downgrading dei dispositivi ICD -> PM (se indicato)
CRTD-> CRTP

...e al fine vita?

EHRA Expert Consensus Statement on the management of cardiovascular implantable electronic devices in patients nearing end of life or requesting withdrawal of therapy



CONSENSUS STATEMENT

In pazienti terminali è più probabile lo sviluppo di situazioni (sepsi ipossiemia disordini elettrolitici..) che aumentino la probabilità di shocks dall'ICD

Gli shocks possono essere dolorosi e psicologicamente stressanti senza riflessi sul prolungamento di una vita qualitativamente accettabile

Se il paziente decede dopo la disattivazione delle terapie la causa del decesso è da ricercare nella patologia sottostante

LA DISATTIVAZIONE DELL'ICD NEL PAZIENTE TERMINALE E' ETICAMENTE ACCETTABILE

CONCLUSIONI

I device per la terapia elettrica dello scompenso sono fortemente supportati dalle linee guida (LG)

Le LG si riferiscono a paziente arruolati nei grossi trials. Poco “real...”
La realtà è il paziente sempre più anziano e pluripatologico

Tra le righe delle linee guida alcuni indicatori di ridotta efficacia dei device ma **non dei chiari cut-off**

Esistono dei **sistemi di score** che possono aiutare nella valutazione complessiva

La decisione definitiva non può che essere collegiale



GRAZIE PER L'ATTENZIONE