Risk Factors and Outcomes Associated with the Development of Ischemic Events in Patients who Receive Cardiac Resynchronization Therapy

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NO DISCLOSURE

Background

- *The Multicenter Automatic Defibrillator Implantation Trial – Cardiac Resynchronization Therapy (MADIT – CRT), 2009 , NEJM* - significant 34% reduction in death or non-fatal heart failure

- The clinical and echocardiographic benefit of cardiac resynchronization therapy in the MADIT-CRT population was *less pronounced among patients with ischemic cardiomyopathy (ICM)*

Background

- The presence of ischemic heart disease may limit therapeutic response to CRT

  - extensive myocardial scarring
  - occurrence of recurrent ischemic events following device implantation

Background

- There are limited data regarding:
  - risk factors for the development of ischemic events (IE) among patients with ICM who receive CRT-D
  - the effect of IE on the clinical benefit of the device

Aims

- The present study was designed to:

1) identify risk factors for IE in patients with ICM who receive device therapy

2) evaluate whether treatment with CRT-D in ICM patients reduces the risk for the development of IE

3) assess the effect of the development of IE following CRT-D implantation on the subsequent risk of HF or death

Methods

- MADIT – CRT – 1820 patients , among them **1045 with ICM**

- **Ischemic Event (IE)** during follow-up was defined as hospitalization for acute coronary syndromes and/or coronary interventions (either PCI or CABG) after enrollment in the trial.

Methods

- Outcome measures:

1) the occurrence of a first IE during follow-up or the composite endpoint of a first IE or death

2) effect of time-dependent ischemic events among CRT-D recipients on the subsequent occurrence of HF or death

Results

- 1045 MADIT-CRT patients with ICM

100 (9.5%) had an IE

95% were associated with an ACS

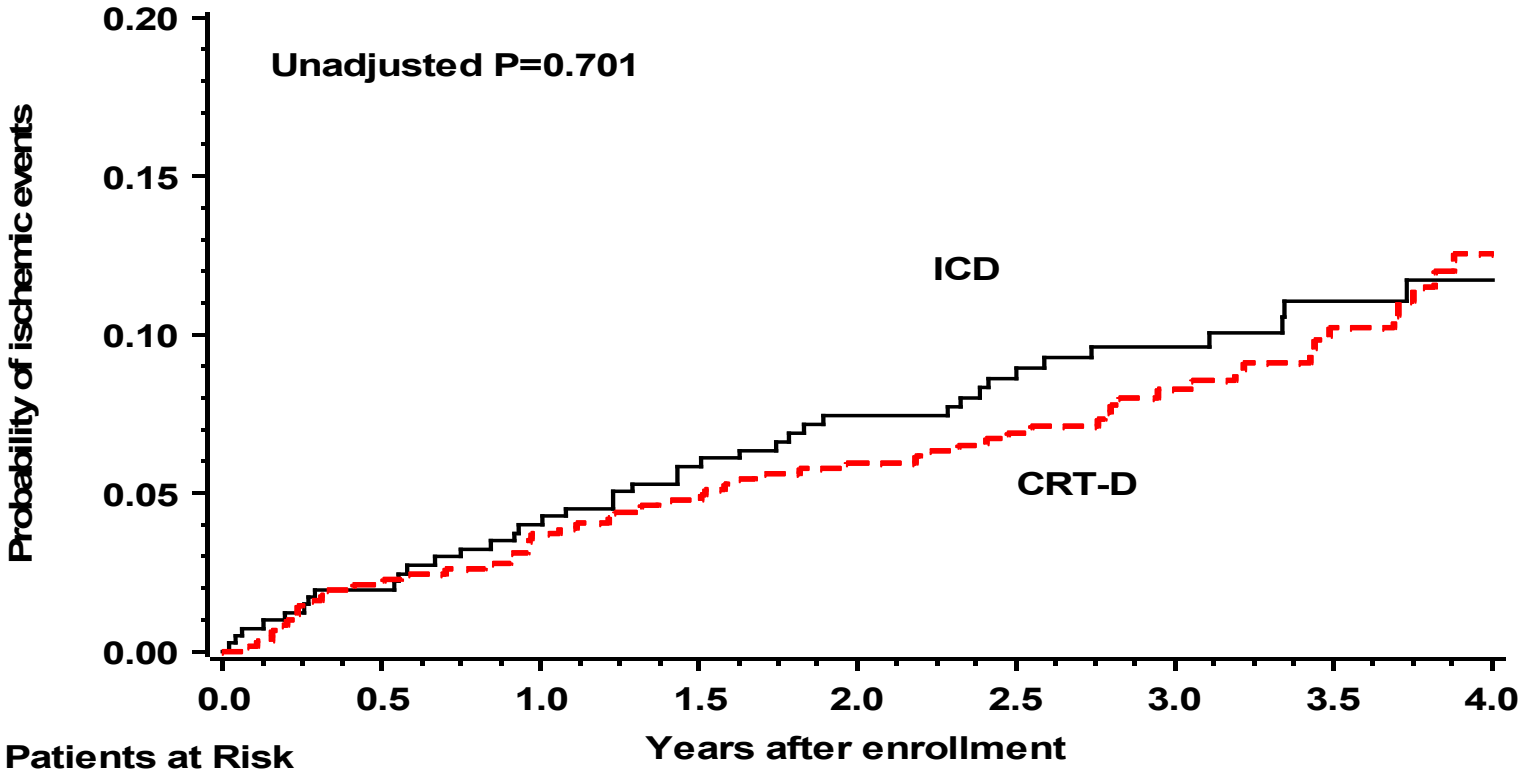
13% with a revascularization procedure

(7% CABG and 6% PCI)

Baseline Characteristics

Characteristics	Ischemic Events (n=100)	No ischemic events (n=945)	P-Value
Randomized to CRT-D	59%	60%	0.80
Age ≥ 65	65%	63%	0.73
HR ≥ 80bpm	11%	12%	0.74
BUN > 25mg/dl	19%	29%	0.04
SBP≥140mmHg	28%	18%	0.02
LBBB	47%	59%	0.03
Diabetes	43%	34%	0.08
Any hospitalization in the year before enrollment	67%	53%	0.006
Prior non-CABG revascularization	71%	45%	<0.001

Cumulative Probability of Ischemic Events by Device-Type



Patients at Risk

ICD	416	361 (0.05)	274 (0.09)	112 (0.12)
CRT-D	629	566 (0.04)	436 (0.07)	162 (0.13)

Predictors for the Occurrence of Ischemic Events and Ischemic Events or Death during Follow-up Among Study Patients

Variable	*ENDPOINT: ISCHEMIC EVENTS*		*ENDPOINT: ISCHEMIC EVENTS OR DEATH*	
	HR	**P- Value**	**HR**	**P- Value**
CRT-D vs. ICD	***0.87***	***0.51***	***0.90***	***0.45***
LBBB	0.62	0.02	0.76	0.04
CABG	1.88	0.003	1.42	0.01
Prior PCI	3.21	<0.001	1.67	<0.001
SBP ≥140 mmHg	1.67	0.02	1.47	0.06

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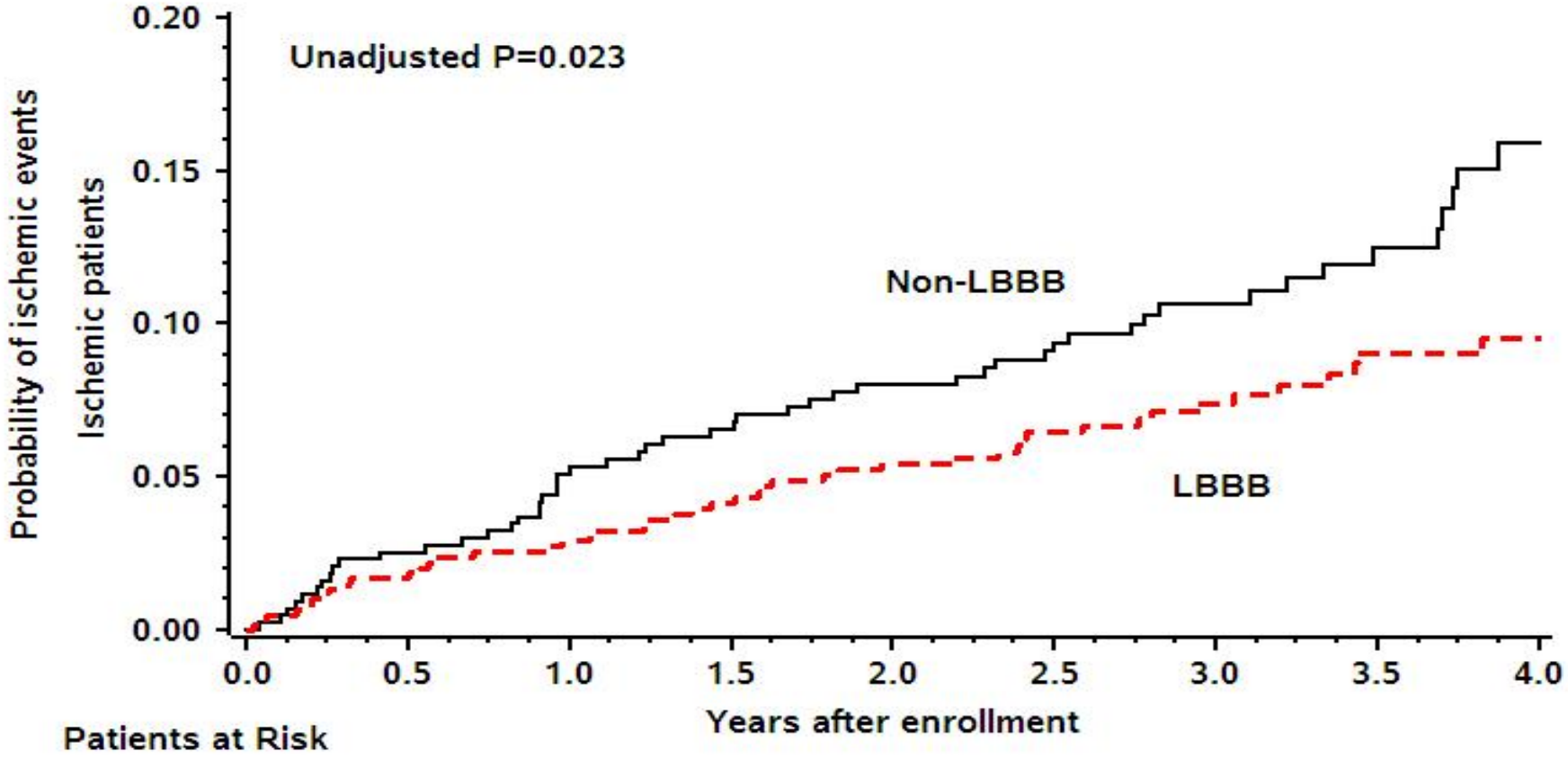
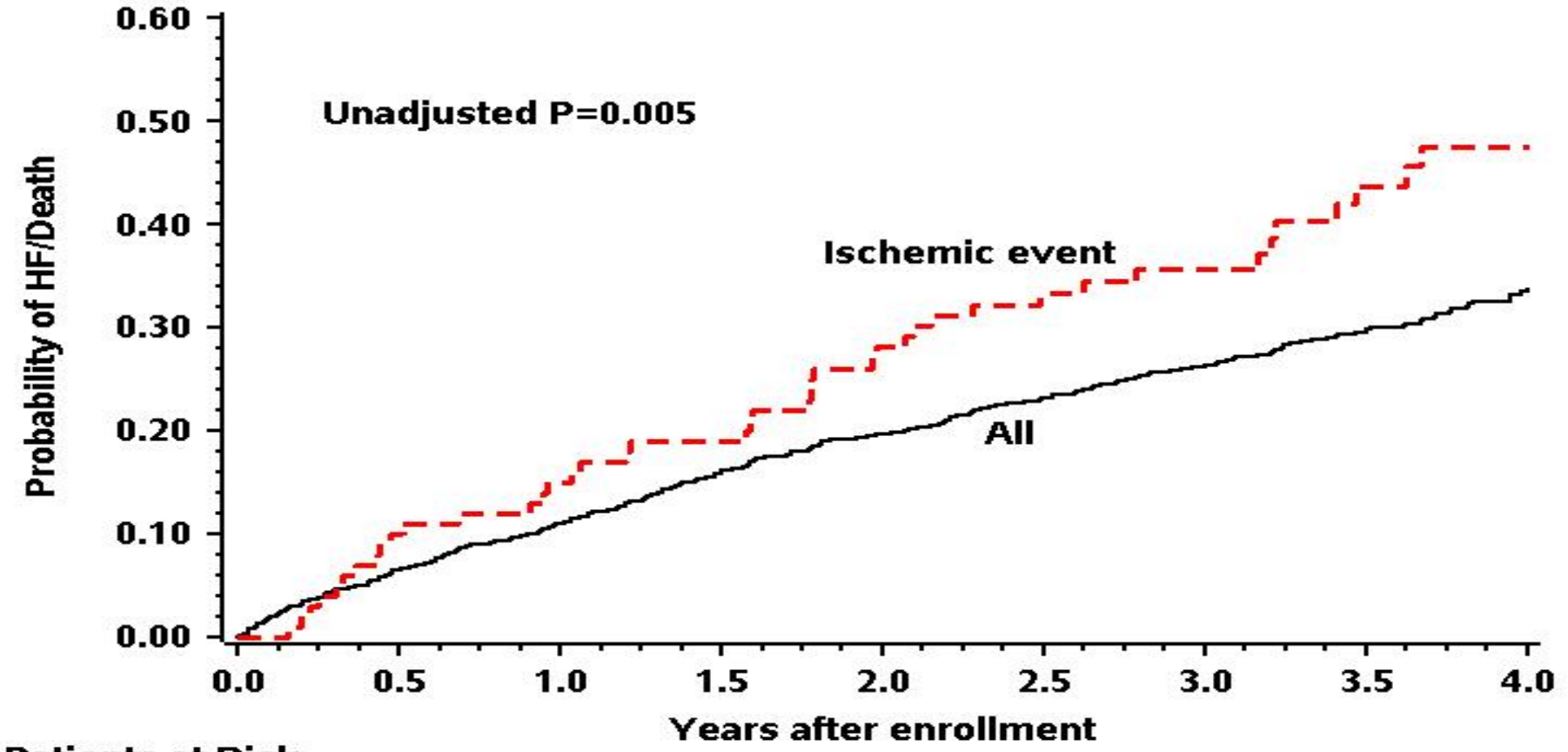
Cumulative Probability of Ischemic Events by QRS Morphology at Enrollment



Factors Independently Associated with the Occurrence of Heart Failure or Death among CRT-D Patients

Variable	Hazard Ratio	P-Value
Development of an ischemic event*	***2.13***	***0.01***
LVEF < 25%	1.47	0.004
Creatinine (per 0.1 mg increment)	1.44	<0.001
Diabetes mellitus	1.65	<0.001
LVESV Index	1.00	0.001
Age > 65 years	1.64	<0.001
Current Smoking	1.40	0.04
Hospitalization for any cause during previous year	1.60	<0.001
Diastolic blood pressure > 80mmHg	1.42	0.02

Cumulative Probability of Heart Failure or Death during Follow-up Following the Development of an Ischemic Event in CRT-D Patients



Conclusions

- The development of ischemic events in patients enrolled in MADIT- CRT was associated with ***specific risk factors, including the presence of LBBB***

- Treatment with ***CRT-D does not appear to reduce the risk for IE*** as compared with ICD-only therapy

- The development of ***IE*** following CRT-D implantation is independently associated with ***>2 fold increase in the risk for subsequent HF and death***

Clinical Implications

- ***The protective effects of CRT against the development of fatal or nonfatal heart failure events are attenuated following the occurrence of IE***

- Our findings suggest that careful follow-up, with appropriate intervention is warranted following the development of IE in patients with ischemic CMP who receive CRT

Thank you