

The Role of Ventricular Electrical Delay to Predict Left Ventricular Remodeling With Cardiac Resynchronization Therapy

Results from the SMART-AV Trial

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Presenter Disclosure Information

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Introduction

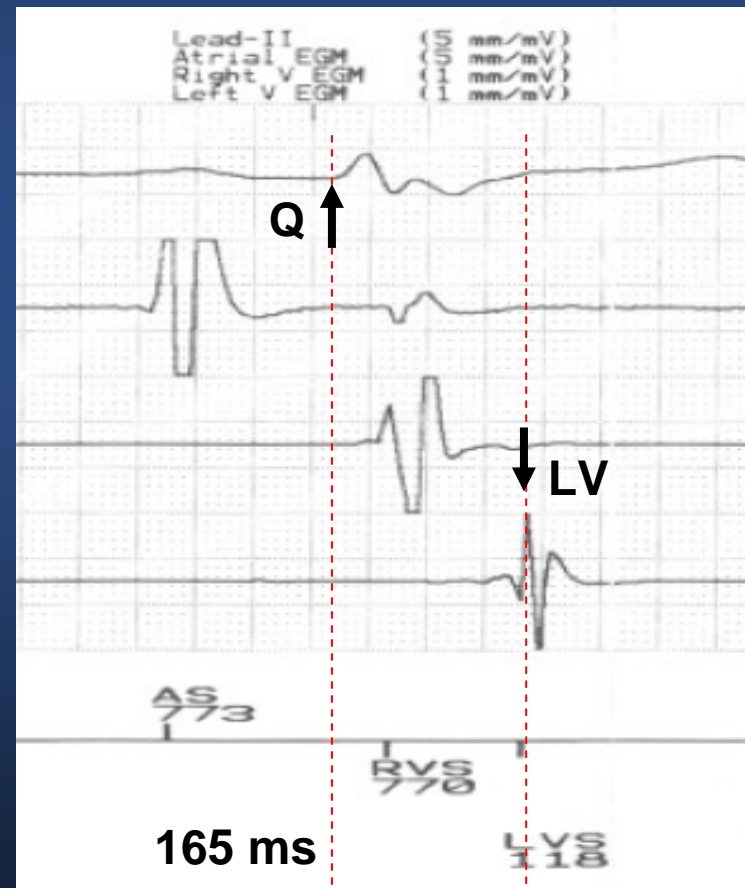
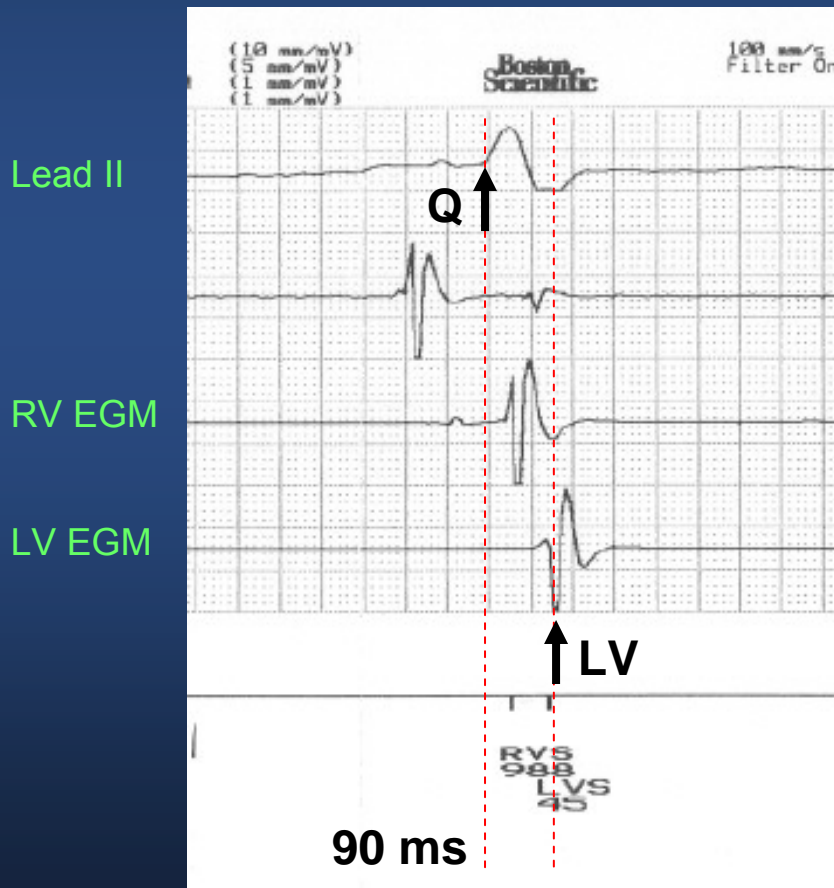
- Prospective, randomized trials have demonstrated that cardiac resynchronization therapy (CRT) improves quality of life, exercise capacity, LV systolic function and decreases hospitalizations for heart failure (HF)
- Subgroup analyses have identified QRS duration and QRS morphology as independent predictors of CRT outcomes
- This has reinforced the concept that electrical delay or electrical dyssynchrony is an important factor for predicting benefit from CRT
- Identifying such predictors is important as most studies show that about one third of subjects are “non responders”

Objective

- To investigate the relationship between the intrinsic electrical delay at the LV stimulation site and clinical endpoints due to CRT in a prospectively designed substudy of the SMART-AV Trial
 - Electrical delay was defined by the time interval from the first QRS deflection on a surface ECG to local intrinsic activation at the LV stimulation site (“Q-LV”)

QLV Interval Measurement

The QLV interval was measured in sinus rhythm and in the absence of ventricular pacing as the interval from the onset of QRS from the surface ECG to the first large positive or negative peak of the LV EGM during a cardiac cycle



Description of SMART-AV Trial

SMART-AV Inclusion

- NYHA class III or IV
- $EF < 0.35$
- $QRS \geq 120ms$
- Expected to be in sinus rhythm at the time of implant
- Receiving optimal pharmacologic therapy
- Randomized: N = 980

Primary Endpoint:

- LVESV at 6 months

Secondary Endpoints:

- 6 min walk, EF, NYHA Class, LVEDV, LVEF, QOL (MLWHF)

SMART-AV Exclusion

- Complete heart block or unable to tolerate pacing at VVI-40-RV for up to 14 days
- Previously received CRT

Substudy Patient Characteristics

N =	426
Age, years	66 ± 11
Gender (%Male)	66%
Ischemic heart disease	59%
LV ejection fraction (%)	26 ± 7
NYHA functional class	
I	0%
II	3%
III	94%
IV	3%
Cardiac medications	
ACE/ARB	84%
Beta-blocker	92%
Diuretic	82%
ECG characteristics	
QRS duration (ms)	151 ± 19
LBBB (%)	75%

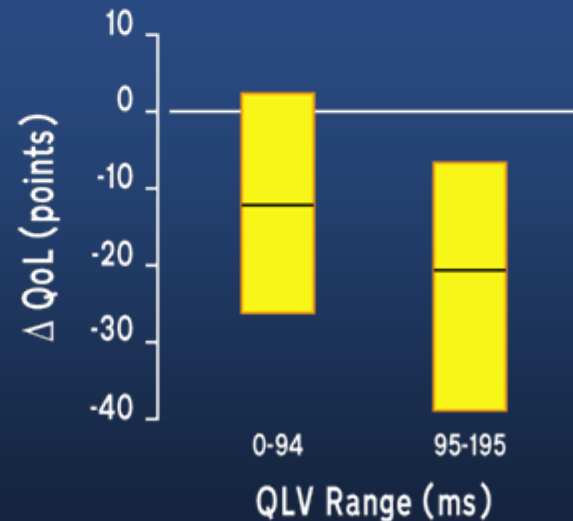
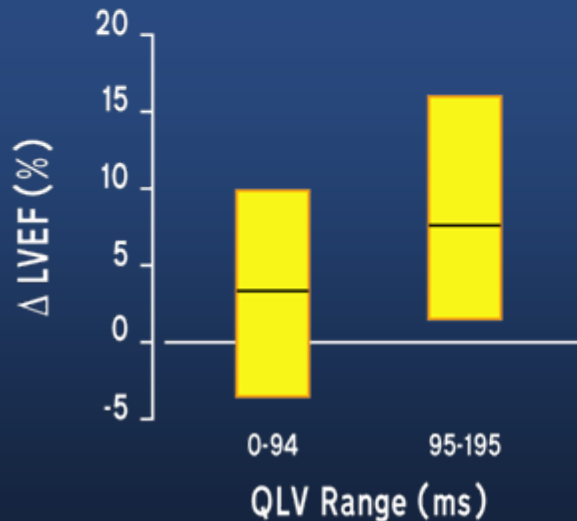
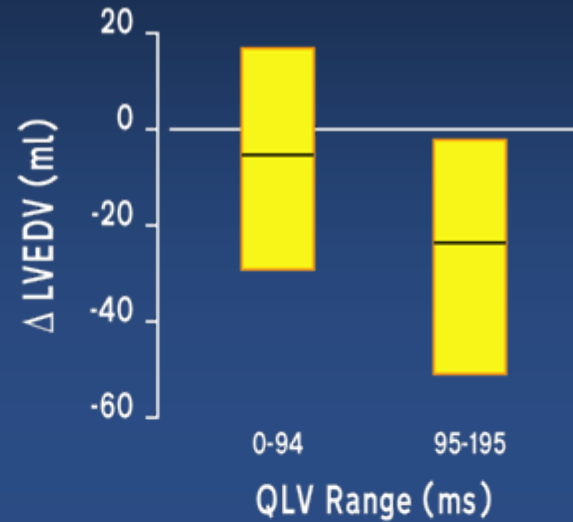
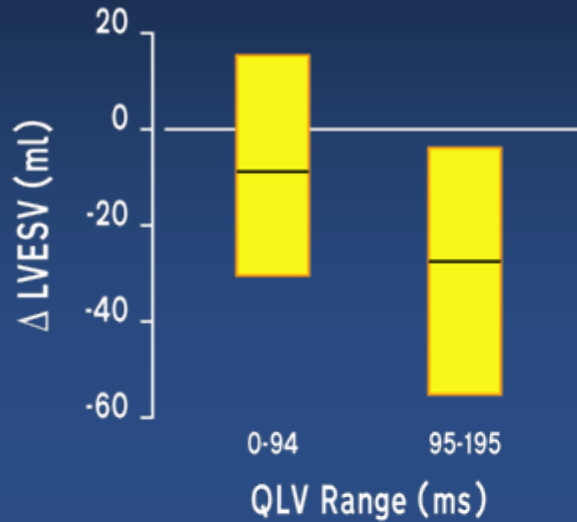
All values were similar to the larger full cohort (n=980) enrolled in the SMART-AV trial, except a slightly shorter mean QRS duration in the substudy cohort

QRS: 151±19 vs. 154±21 ms (p<0.05)

Values expressed as mean ± SD

Results: CRT Response By Median QLV

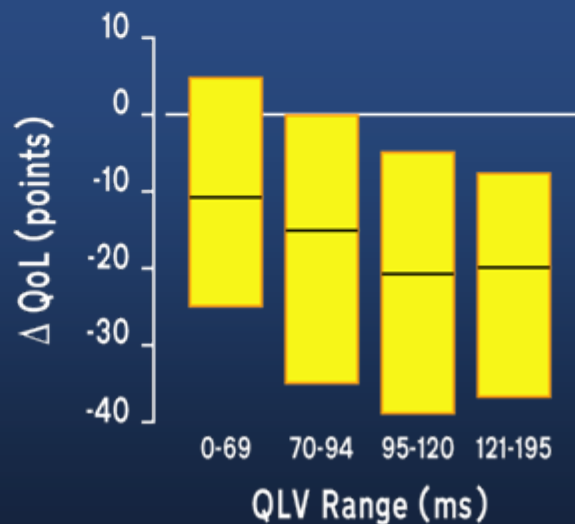
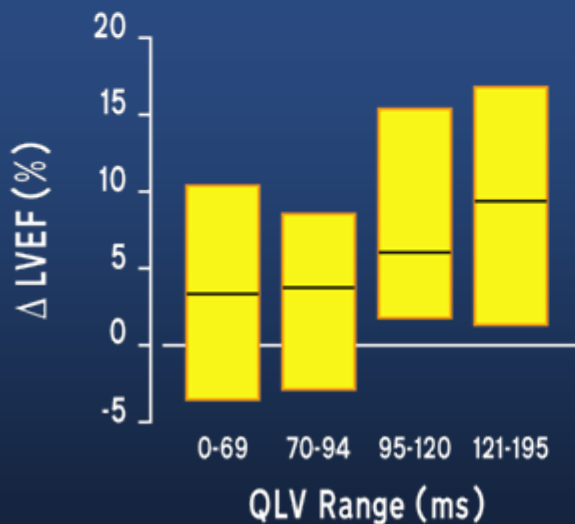
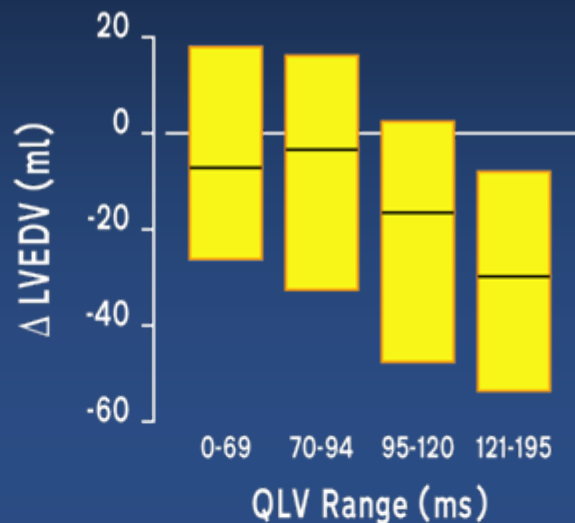
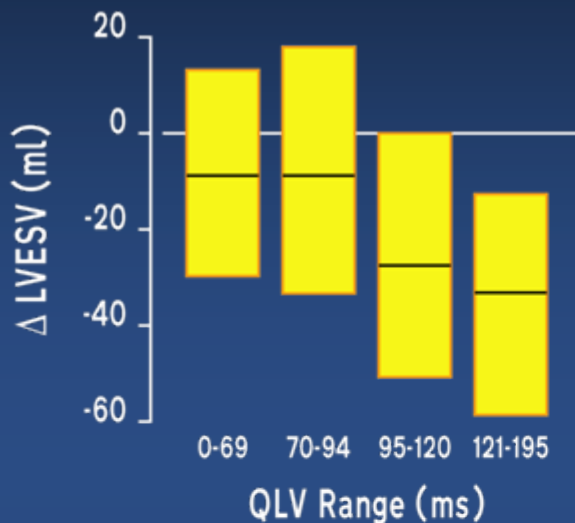
Implant to 6 Months



Data presented as median ± inter-quartile range

All $p < 0.001$
Wilcoxon test

Results: CRT Response By QLV Quartiles



Data presented as median ± inter-quartile range

All $p < 0.001$
Kruskal-Wallis test

Results: Chronic Response Rates by QLV Quartile

QLV	LVESV Response Rate (>15% reduction)	QOL Response Rate (>10 point reduction)
All Patients	50%	60%
0-70 ms	39%	50%
70-95 ms	40%	55%
95-120 ms	58%	65%
120-195 ms	68%	72%
Pearson Chi-sq	<.001	.004

Results: Functional Secondary Outcomes

	QLV Quartiles				Total:	Overall p-value	Q4 vs. Q1 p-value
	Q1: 0 - 70 ms	Q2: 70 - 95 ms	Q3: 95 - 120 ms	Q4: 120 - 195 ms			
Patients w/ HF events	12.1%	7.1%	6.4%	6.3%	8.2%	0.37	0.17
Δ Six minute walk distance	52 ± 118	68 ± 91	50 ± 104	70 ± 93	59 ± 103	0.36	0.13
NYHA Class							
Improved	89 (73.0%)	79 (80.6%)	76 (71.0%)	77 (83.7%)	321 (76.6%)	0.04	0.04
No Change	33 (27.1%)	16 (16.3%)	30 (28.0%)	14 (15.2%)	93 (22.2%)		
Worsened	0 (0%)	3 (3.1%)	1 (.9%)	1 (1.1%)	5 (1.2%)		

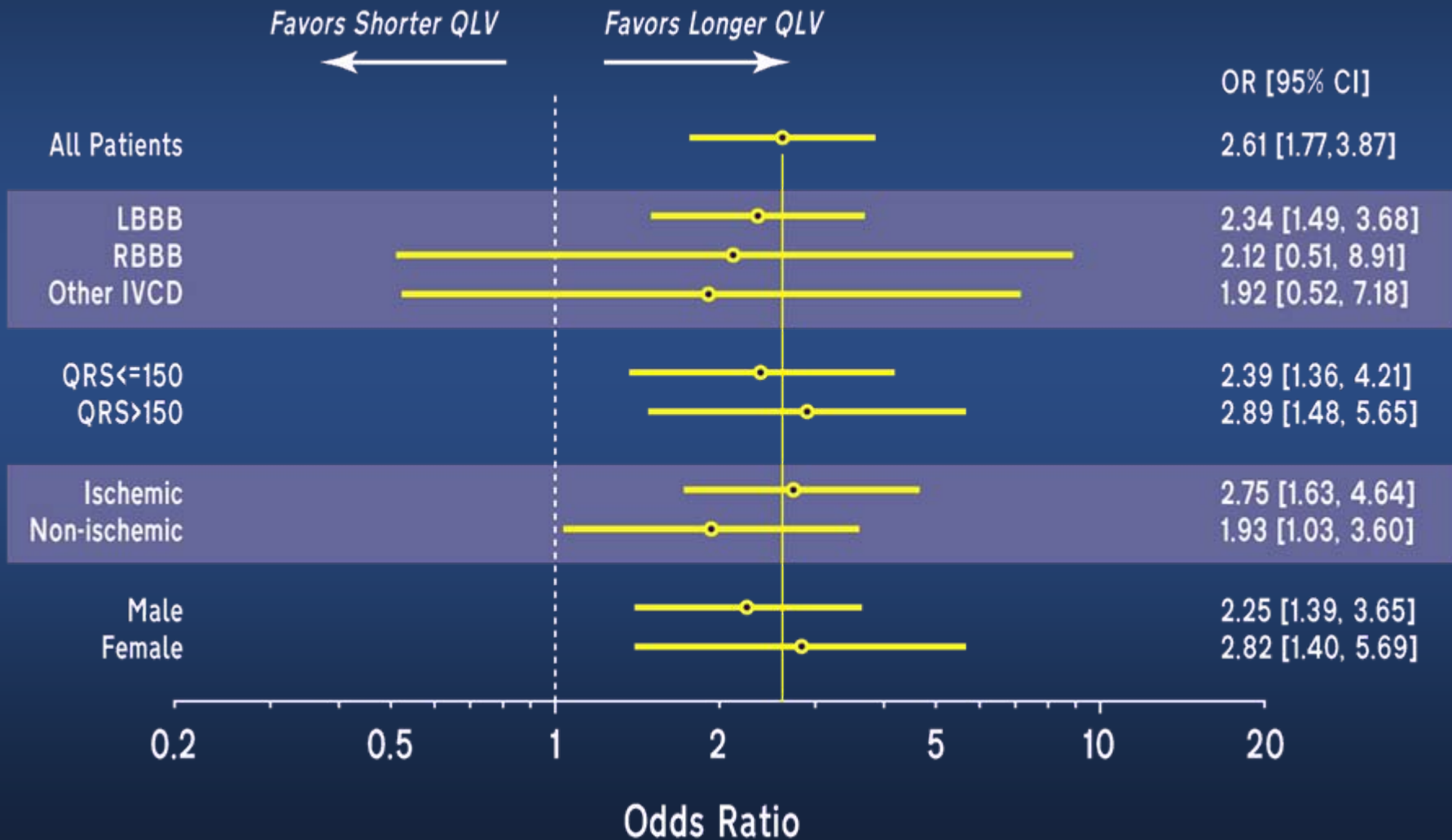
Odds Ratio of CRT Response

Multivariate Logistic Regression

	Odds Ratio (95% CI), p-value	
Covariate	LVESV response	QOL response
QLV: 2 nd quartile vs. 1 st quartile	1.10 (.62 - 1.95), .74	1.30 (.75 - 2.26), .35
QLV: 3rd quartile vs. 1st quartile	1.86 (1.04 - 3.31), .04	1.86 (1.05 - 3.31), .03
QLV: 4th quartile vs. 1st quartile	3.21 (1.58 - 6.50), .001	2.73 (1.35 - 5.54), .005
Age (per 1 year increase)	1.00 (.98 - 1.02), .80	.99 (.97 - 1.01), .21
LVEF (per 1% increase)	.98 (.94 - 1.01), .19	1.00 (.96 - 1.03), .83
Ischemic vs. non-Ischemic	.58 (.37 - .91), .02	1.05 (.67 - 1.64), .85
QRS (>150 ms vs. ≤ 150 ms)	.86 (.53 - 1.40), .54	.88 (.55 - 1.43), .61
LBBB vs. non-LBBB	1.20 (.72 - 2.01), .48	1.17 (.71 - 1.93), .53
Male vs. Female	.53 (.33 - .85), .01	.56 (.34 - .91), .02
NYHA class IV vs. I-III	1.67 (.44 - 6.29), .45	3.41 (.69 - 16.92), .13
LVESV (per 1ml increase)	1.00 (.99 - 1.01), .98	1.00 (.99 - 1.00), .68

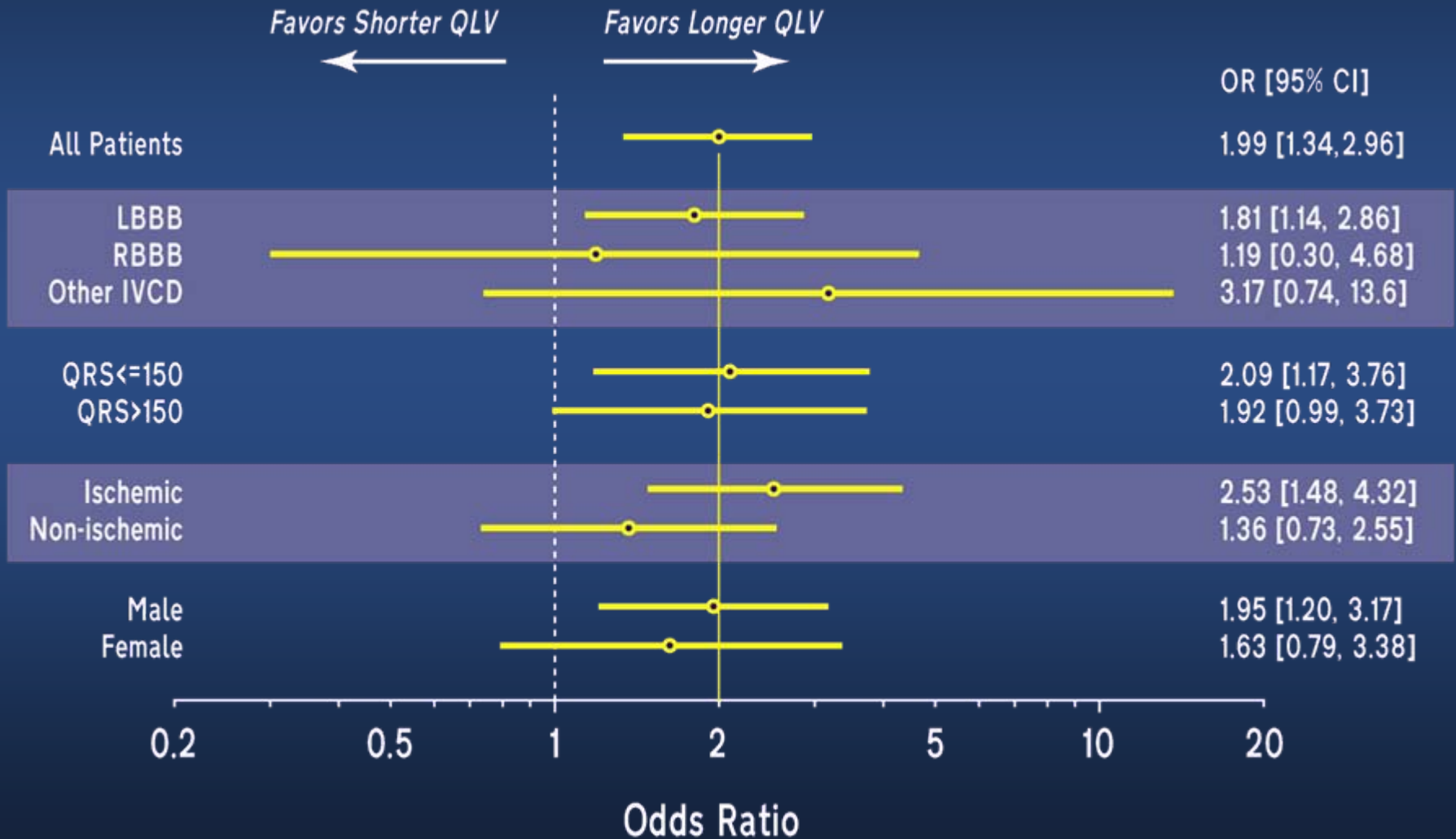
LVESV Response by Sub-group

Univariate Logistic Regression Results



QOL Response by Sub-group

Univariate Logistic Regression Results



Summary

In the SMART-AV Trial Substudy:

- When stratified by QLV duration quartiles, CRT response rates at 6 months increased:
 - Reverse remodeling (>15% reduction of LV end systolic volume) response increased from 39% to 68%
 - QOL (>10 points reduction) response increased from 50% to 72%.
- Patients in the highest quartile of QLV had a ~3x fold increase in their odds of a ESV and QOL response after correcting for QRS duration, BBB type and clinical characteristics

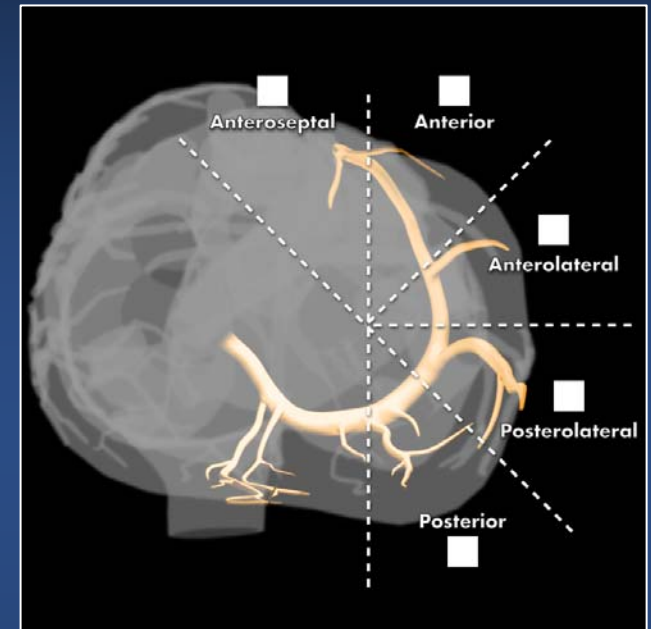
Conclusions

- Electrical dyssynchrony, as measured by QLV, was a strong and independent predictor of outcomes with CRT
- The best outcomes were observed with a QLV > 95 ms, so this cutoff should be considered when selecting LV lead position at the time of CRT implantation
- Further study is warranted to assess the value of using QLV rather than anatomic location to guide lead positioning to improve response rates with CRT

Backup

Relationship between Electrical Intervals and Anatomical Locations

- The location of the LV lead was not controlled in this study
 - Most leads were placed in the anterolateral or posterolateral veins, as reported by the implanting physicians
- 46 of 426 (11%) had apical leads
- 13 of 426 (3%) had anterior or septal leads
- These small numbers preclude any meaningful analysis of the impact of lead location on QLV or response rate
- However, even in similar vein locations, there was marked variation in QLV
 - Mid-anterolateral (n=89): QLV range = 10 – 195 ms
 - Mid-posterolateral (n=230): QLV range = 15 – 195 ms



Odds Ratio of CRT Response

Multivariate Logistic Regression

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4 th quartile vs. 1 st quartile	3.21 (1.58 - 6.50), .001	2.73 (1.35 - 5.54), .005

* Adjusted for baseline EF, LVESV, Etiology of HF, LBBB, Gender, NYHA, QRS and age

Odds Ratio of CRT Response

Multivariate Logistic Regression

(after adjustment for QLV)

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