Novel measure of electrical dyssynchrony predicts response in cardiac resynchronization therapy: Results from the SMART-AV Trial

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Abstract

Background—Cardiac resynchronization therapy (CRT) reduces mortality and morbidity in selected heart failure (HF) patients. However, not all patients respond to CRT.

Objective—We hypothesized that a novel measure of electrical dyssynchrony, sum absolute QRST integral (SAI), predicts CRT response independent of QRS duration and morphology.

Methods—We retrospectively analyzed baseline 12-lead electrocardiograms (ECGs) of SMART-AV study participants [N=234, mean age 67 y, 70% male, 60% ischemic cardiomyopathy (ICM), mean left ventricular ejection fraction (LVEF) 25%, mean QRS duration 152ms, 77% had left bundle branch block (LBBB)]. Baseline pre-implant ECGs were digitized, transformed into orthogonal XYZ, and analyzed automatically by customized Matlab software. SAI was measured as an averaged arithmetic sum of absolute areas under the QRST curve.

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Patients were followed prospectively 6 months after CRT-D implantation. Patients with a decrease in left ventricular end-systolic volume 15mls after 6 months of CRT were considered responders. Logistic regression model was adjusted for age, gender, BBB morphology, LVEF, type of cardiomyopathy and QRS duration.

Results—Patients with the high mean SAI (3rd tertile) had 2.5 times greater odds of response than those with low mean SAI (1st tertile; OR 2.5, 95% CI 1.3–5.0, p=0.010), and 1.9 times greater than the lower two tertiles combined (OR 1.9, 95%CI 1.1–3.5; P=0.03). Adjustment for renal function (OR 2.33 (95%CI 1.32, 4.11); P=0.003) and LV lead position in RAO/LAO (OR 1.7 (95%CI 0.9, 3.2); P=0.087) did not attenuate association of SAI with outcome.

Conclusion—High SAI QRST independently predicts CRT response in the SMART-AV study.

Keywords

Cardiac resynchronization therapy; heart failure; remodeling; SAI QRST

Introduction

Cardiac resynchronization therapy (CRT) is a powerful electrical treatment for patients with systolic HF and electrical dyssynchrony. However, about a third of CRT recipients do not improve with pacing optimally. Despite the initial promise, assessment of mechanical dyssynchrony did not improve patient selection[1]. It is now accepted that electrical, rather than mechanical, dyssynchrony needs to be present for CRT to be beneficial. Electrical dyssynchrony is traditionally characterized by QRS duration[2–4] and morphology[3, 5]. However, QRS duration is an imperfect predictor of CRT response. A positive correlation between QRS duration and CRT benefit was shown in many, but not all, studies[6]. Marked QRS widening (178 ms) in patients with LBBB was associated with non-responsiveness to CRT[7]. Moreover, similar CRT response was shown in LBBB patients with QRS duration 120–150 ms and above 150 ms[8]. Likewise, there is a discrepancy regarding the definition of a CRT-responding conduction abnormality.

SAI QRST[9, 10] is a simple ECG marker of electrical remodeling and arrhythmia vulnerability, which in post-MI patients showed a correlation with the time passed since MI[11]. Moreover, SAI QRST predicted sustained ventricular arrhythmias with appropriate ICD therapies[9–11] and cardiac death[11] in patients with and without conduction abnormalities. SAI QRST was developed as a simplified measure of action potential heterogeneity in the heart.. In healthy heart, electrical activation behaves as a dipole, with non-dipolar components of activation[12] < 20%, whereas in heart failure multipolarity of activation is increasing[13]. Theoretically multipolarity of electrical activation means electrical dyssynchrony. SAI QRST reflects multipolarity of electrical activation, consistent with electrical dyssynchrony, and global electrical heterogeneity in the heart[14]. We hypothesized that SAI QRST is independently associated with CRT response.

Methods

Study population

The study population was drawn from the SMART AV randomized clinical trial[15]. The SMART AV trial was conducted with the goal to compare three different CRT optimization strategies: AV delay optimization with echocardiography, intracardiac electrogram – based SmartDelay™ algorithm, and a fixed nominal AV delay. The trial was conducted in accordance with the Helsinki Declaration and the ethics or regulatory committee of each participating institution. All study participants gave written informed consent before entering the study.

The SMART AV trial randomized 980 HF patients with NYHA class III–IV despite optimal medical therapy, with LVEF 35% and QRS duration 120 ms. Complete heart block was an exclusion criterion in the SMART AV trial. Baseline resting 12-lead ECGs were collected before CRT device implantation as an image of paper-printed routine clinical ECG. All SMART AV participants with available: (1) paired baseline and 6 month echocardiographic studies, and (2) baseline 12-lead ECG were considered for inclusion in this study. For the present analysis, patients were excluded if the ECG image quality was insufficient (resolution < 200 DPI and a grayscale color depth < 8 bit), to permit ECG digitization.

Remodeling response to CRT

LV volumetric changes were measured as the mechanical response to CRT. LV systolic function and LV volumes were assessed by 2-dimensional echocardiography before and 6 months after CRT[15]. LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), and LVEF were measured. Consistent with the pre-defined SMART AV study design, patients with a decrease in LVESV 15mls after 6 months of CRT were prospectively defined as primary endpoint responders. In addition, relative changes in LVESV were assessed retrospectively, as a secondary outcome. Patients with a decrease in LVESV 15% following 6 months of CRT were defined as secondary outcome responders.

ECG digitization

Routine clinical 12-lead ECGs were collected before CRT device implantation as images of ECG paper printouts. ECG printout images were digitized using the ECGScan 2.0 (AMPS LLC, Italy) if image resolution was 200 DPI and a grayscale color depth was 8 bit. ECGScan produced high resolution (500 Hz) digital ECG output in XML standard file as required by the Food and Drug Administration.

ECG analysis: sum absolute QRST integral

ECG analysis was performed by investigators (JP and LGT) blinded to the study outcome and patients clinical characteristics. Customized Matlab (MathWorks, Inc, Natick, MA) software was used. The digitized 12-lead ECG signal was transformed into orthogonal XYZ ECG by using inverse Dower transformation matrix. The absolute value of the area under the entire QRST waveform was calculated for each orthogonal lead (X, Y, and Z), and

averaged per beat. Absolute QRST integral values on X, Y, and Z leads were then added together to obtain averaged SAI QRST[9–11, 16] (Figure 1).

Statistical analysis

SAS 9.3 (SAS Institute, Inc, Cary, NC) was used for data analysis. Continuous variables were reported as mean ±standard deviation (SD), unless otherwise specified. SAI QRST variable was categorized into tertiles. One-way ANOVA was used to compare continuous variables among tertiles of SAI QRST. The Fisher's exact test was used to compare categorical variables. Multivariate logistic regression analysis was performed to determine association of SAI QRST with CRT response, after adjustment for covariates: age, gender, type of cardiomyopathy (ischemic vs. non-ischemic), LVEF, QRS duration and BBB morphology (LBBB vs. non-LBBB). Renal function and sodium value at baseline, as well as LV lead position in right anterior oblique (RAO) and left anterior oblique (LAO) views were also considered for inclusion in the multivariate model, but ultimately excluded to improve model fit. Another reason to exclude LV lead position in the final model was its different nature: LV lead position represents a procedural characteristic, while all other variables in the final model represent baseline patient characteristics. The remodeling response to CRT served as an outcome in this analysis: absolute reduction in LVESV ≥ 15mls served as a primary outcome; relative reduction in LVESV ≥ 15% served as a secondary outcome. Relationship of SAI QRST to CRT response was tested in clinically important subgroups: patients with LBBB vs. non-LBBB; elderly (≥ 65y) vs. younger (<65 y) participants; males vs. females; QRS duration ≥ 150 ms vs. < 150ms; patients with ischemic vs. non-ischemic cardiomyopathy, apical / basal vs. mid RAO LV lead position, and anterior / anterolateral / anteroseptal vs. posterior/posterolateral LAO LV lead position. We also tested interaction of SAI QRST tertiles with covariates expressed as the binary variables described above. A *P*-value of <0.05 was considered significant.

Results

Study population characteristics and SAI QRST

This study population was composed of 234 SMART AV study participants with successfully digitized ECGs and available paired echocardiography data at baseline and 6 months CRT. Mean age was 67±10 years, N=163 (70%) were male. More than half (N=140, 60%) of the cohort have had ischemic cardiomyopathy with mean LVEF 25±7%, and N=179 (77%) had LBBB. Mean QRS duration was 152±20 ms. Clinical characteristics of study participants are shown in Table 1.

On average, 2.7±0.9 beats were included in analysis. Distribution of SAI QRST was skewed. Mean SAI was 64.5±79.4 mV*ms. Median SAI was 48.0 (interquartile range 18.1–81.5) mV*ms. Representative examples of 12-lead ECGs in study participants with SAI in the 1st, 2nd, and the 3rd tertile are shown in Figure 2.

In univariate analysis (Table 1) demographic characteristics (age, sex, race), body composition (body mass index), type of cardiomyopathy, type of conduction abnormality, and major comorbidities (diabetes) did not affect SAI. However, severity of HF was clearly

associated with SAI. Baseline LVESV gradually and significantly increased from the lowest to the highest SAI QRST tertile, whereas LVEF trended towards steady decreasing. There were significantly more patients with advanced NYHA class III–IV amongst participants with SAI QRST in the two upper tertiles. QRS duration progressively widened with increasing SAI QRST from the lowest to middle, and from middle to the highest tertile (Table 1).

Association of SAI QRST with primary outcome mechanical response on CRT

Among the 234 patients included in the analysis, 108 (46%) were observed to be primary CRT responders. Patients with the high mean SAI (3rd tertile) had 2.5 times greater odds of response to CRT than those with low mean SAI (1st tertile), and 2.0 times greater than the lower two tertiles combined (Figure 3; CRT response of 35%, 44%, and 59% for 1st, 2nd and 3rd tertiles, respectively), in spite of more frequent unfavorable apical LV lead placement (Table 1). A trend towards the interaction between SAI and BBB morphology was observed (P=0.17). The effect size was larger in the non-LBBB patients (N=54). Non-LBBB patients with the SAI in the highest 3rd tertile had nearly 6 times greater odds of response than those with SAI in the lower two tertiles combined.

In adjusted logistic regression analyses no statistically significant interactions of SAI with clinically important baseline characteristics were observed (Figure 4). Importantly, there was a significant association of SAI QRST with CRT response in the following subgroups: patients with non-LBBB, females and patients at least 65 years old. Additionally, there was a trend towards stronger association of SAI with CRT response in patients with ischemic cardiomyopathy and QRS duration < 150 ms.

Further adjustment of minimally (by demographics) adjusted logistic regression model (Table 2) by cardiomyopathy type, LVEF, renal function, sodium level, did not affect strength of association between SAI and primary outcome. Addition in the model QRS duration and BBB morphology only slightly attenuated odds ratio. IIn the final adjusted model (Table 3) SAI remained significant predictor of primary outcome after adjustment by major known predictors of CRT response: gender, BBB morphology, QRS duration, LVEF, age and cardiomyopathy type.

Association of SAI QRST with secondary outcome mechanical response on CRT

A total of 109 of the 234 patients (46%) were observed to be secondary responders, in which response was defined by a relative reduction in LVESV by at least 15%. Agreement between the primary and secondary definitions of response was high (Kappa coefficient = 0.89). Despite the high agreement between the two outcomes of response, the effect size of association of SAI QRST with the secondary outcome was smaller, as compared to the association of SAI with primary outcome (Figure 5). Accordingly, statistical power of the study was insufficient to demonstrate statistical significance of the association. Importantly, no differences in direction and trends in the association of SAI with primary and secondary outcomes were observed.

Discussion

The main finding of the study is that simple ECG metric SAI QRST, easily obtainable from automated analysis of 12-lead ECG, is independently (beyond QRS duration, BBB morphology, LVEF, cardiomyopathy type, gender, age) associated with CRT response in the SMART-AV randomized clinical trial. The observed association of baseline high SAI QRST with CRT response suggests that SAI QRST estimates electrical dyssynchrony. After validation of our finding in another prospective study, measurement of SAI QRST could become an important component of the "electrical dyssynchrony score" for selection of CRT candidates, especially in the "gray area" subgroups: HF patients with non-LBBB conduction defect, QRS duration 120–149 ms, and ischemic cardiomyopathy.

After more than 10 years of CRT application, the recent ACCF/AHA/HRS device guideline update[17] narrowed the recommendations for CRT based on electrical dyssynchrony measures: QRS duration and morphology. These appropriately implemented guideline changes were based on a strong evidence of CRT benefit in LBBB[5, 18] patients with QRS 150ms[3, 6, 19]: more than 8,000 patients in NYHA class I-IV HF were evaluated in landmark randomized controlled trials[18, 20, 21]. It was shown that electrical, but not mechanical[22], dyssynchrony should guide electrical CRT therapy. However, currently used measures of electrical dyssynchrony (QRS duration and morphology) have limitations.

QRS duration is an imperfect measure of electrical dyssynchrony[8, 23]. QRS duration characterizes only duration of depolarization, but does not describe the electrical substrate, amenable for cardiac resynchronization. On one hand, a non-negligible percentage of patients with QRS 150 ms do not respond[23]. A marked QRS widening (178 ms) as a sign of HF severity was related to less CRT benefit[7], raising the question that QRS duration is not capable of distinguishing electrical dyssynchrony from severe mechanical dyssynchrony due to LV and frequently accompanied RV dilatation[24, 25], hypertrophy, and scar, which is not responsive to resynchronization. On the other hand, a high percentage of patients with QRS 120–149 ms does respond, and could even demonstrate super-response,[3, 8] on CRT.

QRS morphology is an imperfect measure of electrical dyssynchrony[26], as well. In addition to LBBB patients[5], non-LBBB patients with 15% decrease in LVESV index significantly improved long-term survival with CRT[26]. Detailed anatomy of the His-Purkinje system is extremely complex and highly individualized. At the same time, QRS morphology does carry important information. Josephson and Wellens[25] recently highlighted known ECG features that could help to separate electrical dyssynchrony due to LBBB from the non-amenable to CRT mechanical dyssynchrony due to RV dilatation[27]. These features include a marked discrepancy in QRS voltages in the extremity and precordial leads[28]. SAI QRST, by calculating summed area under QRST curve, takes into account amplitudes of orthogonal XYZ leads. Reynolds et al[24] showed that ECG signs of RV dilation in LBBB may help identify HF patients unlikely to benefit from CRT. SAI QRST, by calculating summed area under QRST curve, incorporates all QRST morphology features, which are not taken into account by classical definition of ventricular conduction abnormalities.

ECGi evaluates 3-dimensional activation of LV and RV, and therefore, could potentially characterize specific details of electrical dyssynchrony in individual patients. A small pilot ECGi study predicted clinical CRT response better than QRS duration or morphology[29]. However, ECGi is an expensive and time-consuming technology. In contrast, SAI QRST could be easily calculated from routinely available 12-lead ECG, while providing 3-dimensional data regarding activation and recovery.

SAI QRST is a composite ECG marker that measures summed area under the QRST curve in 3-dimensions (X, Y, and Z), and therefore, accounts for both QRS duration and QRS morphology. SAI QRST is better suited to capture complexity of electrical dyssynchrony in HF than either QRS duration, or QRS morphology alone. In this study, SAI QRST was strongly associated with baseline LVESV and NYHA HF class. Even after adjustment for QRS duration, BBB morphology, LVEF, cardiomyopathy type, gender, and age, SAI QRST predicted primary CRT response. No test for interaction reached statistical significance in this study, likely due to insufficient statistical power for the subgroups analysis. However, observed trends suggest that SAI QRST could become an important asset for selection of CRT candidates amongst HF patients with non-LBBB conduction defect, QRS duration 120–149 ms, and ischemic cardiomyopathy. Future prospective studies are needed to test this hypothesis.

Recently van Deursen et al[30] in a smaller study showed that, similar to SAI QRST, ECG parameter QRS_{AREA}, which is a sum of the areas under the QRS on three orthogonal XYZ ECG leads (i.e. SAI QRS), was significantly larger in CRT responders, as compared to non-responders. In univariable analysis, QRS_{AREA} predicted CRT response better than QRS duration and conventionally defined LBBB morphology and was comparable with the proposed refined definition of LBBB[31]. The findings of van Deursen et al[30] are consistent with results of our study. Notably, unlike QRS_{AREA}, SAI QRST considers the entire cardiac cycle, including the repolarization phase. Including the repolarization potentially allows detection of cardiac memory due to old BBB, and provides insight in into "new or intermittent" vs. "old or chronic" ventricular conduction abnormality[32]. Furthermore, calculation of SAI QRST (rather than SAI QRS) simplifies the ECG metric and makes it more robust and potentially more reproducible.

Consistently with the results of this study, in MADIT II[11] and PROSE-ICD[9, 10] SAI QRST was associated with HF severity (LVEF[9, 11], LV diastolic diameter[9]) and HF outcomes[11]. Risk of HF hospitalizations and death was higher in MADIT II participants with SAI QRST in the highest quartile. Notably, SAI QRST correlated with the time after MI[11] and many clinical characteristics, which suggested that SAI QRST is a measure of electrical remodeling. Consistently with clinical findings, Kozmann et al[14] *in silico* showed that SAI QRST is a measure of non-dipolarity of activation and heterogeneity of action potential morphology distribution. Combining together SAI QRST, QRS duration, and QRS morphology into an "electrical dyssynchrony score" could conceivably improve selection of CRT candidates. More electrical dyssynchrony predicts more remodeling and more remodeling is associated with fewer hospitalizations and less ventricular arrhythmia. Future prospective studies are needed to test this hypothesis.

Limitations

Several limitations of this study must be considered. This study is a post-hoc analysis of a large multicenter randomized controlled trial. Moreover, only a subgroup of study participants, but not the entire SMART AV study population was analyzed. Therefore, before implementation in clinical practice all results should be validated in a prospective study. Definition of a primary outcome CRT response was based on absolute LVESV value reduction, whereas a standard measure of CRT response (relative reduction in LVESV 15%) served as a secondary outcome. Additionally, we analyzed digitized ECGs, rather than digitally recorded ECGs, as in all our previous studies of SAI QRST[9–11, 16], and therefore SAI thresholds are directly not comparable. Future studies are needed to compare SAI QRST measured on digitally recorded ECG vs. digitized ECG. It is clearly preferable to use digitally recorded ECGs for any automated analysis. However, this study showed that automated analysis of digitized ECG can provide meaningful results, which opens an important avenue for post-hoc analyses of numerous previously conducted studies that collected ECG printouts, but did not save digital ECG. Retrospective post-hoc analyses of conducted clinical studies are encouraged by NIH as a wise use of resources. Finally, limited statistical power did not allow conclusive analyses of subgroups. Future studies are needed to compare predictive value of SAI QRST in patients with QRS duration 120–149 ms, non-LBBB patients, and ischemic cardiomyopathy patients.

Acknowledgments

Abbreviations

CRT	Cardiac resynchronization therapy
HF	heart failure
LBBB	left bundle branch block
MI	myocardial infarction
SAI QRST	Sum absolute QRST integral
ICD	implantable cardioverter defibrillator
AV	atrioventricular
NYHA	New York Heart Association
LVEF	left ventricular ejection fraction
RV	right ventricular
ECGi	Electrocardiographic imaging

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Clinical Perspectives

In this study we showed that ECG measure of electrical dyssynchrony, SAI QRST, is independently (after adjustment for QRS duration, BBB morphology, LVEF, cardiomyopathy type, gender, age) associated with CRT response in the SMART-AV randomized clinical trial. This finding suggests that development of the "electrical dyssynchrony score" (which would combine several markers of electrical dyssynchrony: QRS duration, QRS morphology, and SAI QRST) is feasible, and may improve selection of approriate CRT candidates in the future, especially in the "gray area" subgroups: HF patients with non-LBBB conduction defect, QRS duration 120–149 ms, and ischemic cardiomyopathy. However, validation of our findings in another prospective study needs to be done first, before implementation in clinical practice. The observed trend towards stronger association of SAI with both non-LBBB conduction defect, and anterior/anteroseptal/anterolateral LV lead position, suggests that anterior /anteroseptal / anterolateral LV lead placement may be recommended for patients with non-LBBB conduction defect (e.g. anterior fascicular block) and SAI in the highest 3rd tertile. This hypothesis should be tested in the future randomized clinical trial.
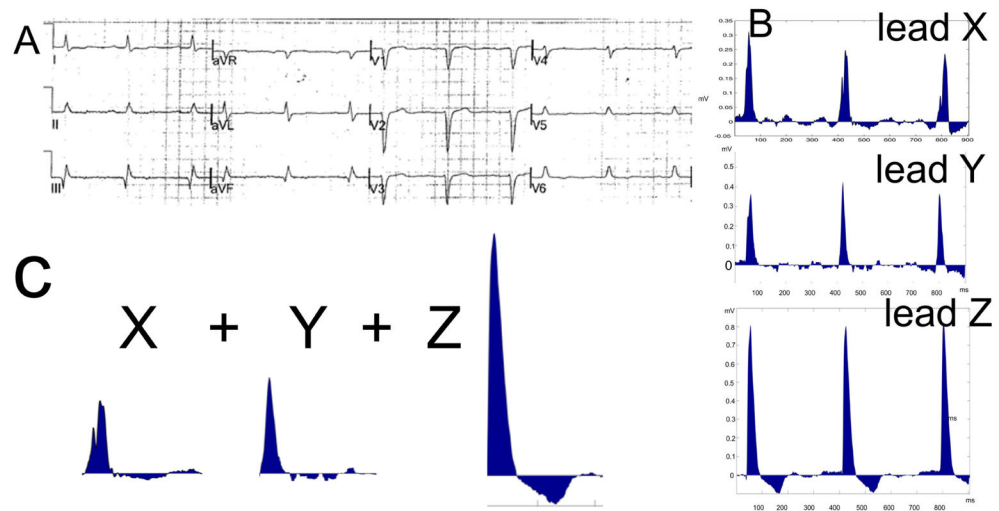
Figure 1.
Schematic presentation of the method. **A.** 12-lead ECG. **B.** Digtized transformed XYZ ECG. **C.** Averaged area under QRST curve on X, Y, and Z leads is summed to obtain SAI.
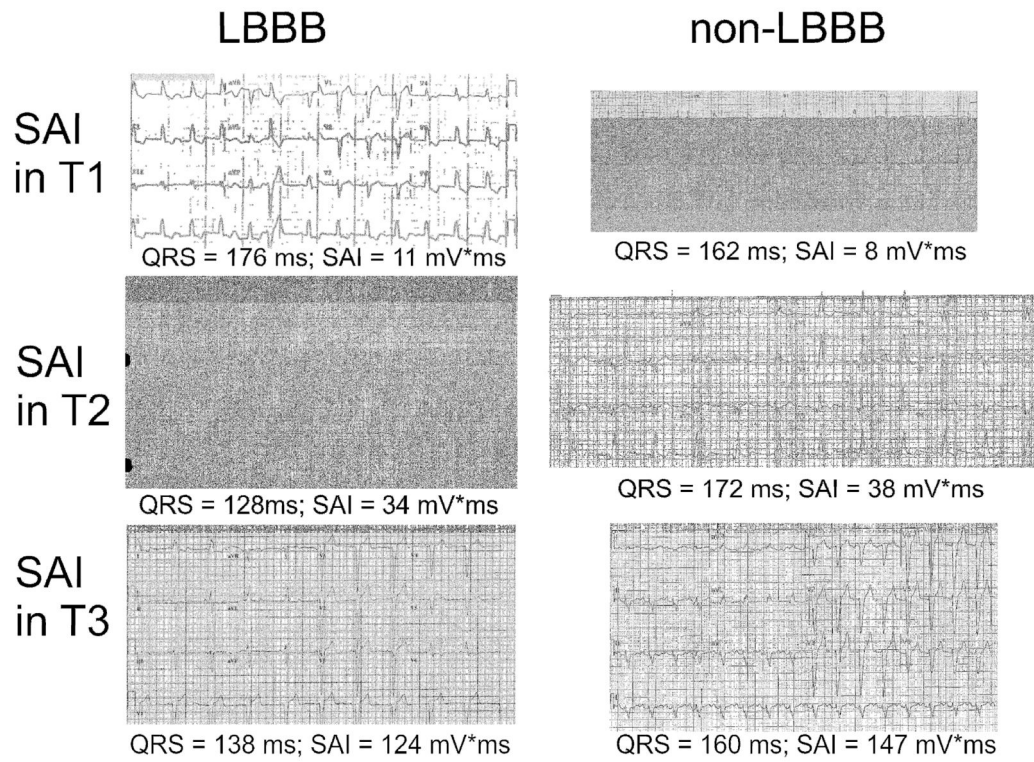
Figure 2.
Representative examples of 12-lead ECGs in participants with LBBB and non-LBBB QRS morphology and SAI in the 1st, 2nd, and the 3rd tertile (T1-T2-T3).
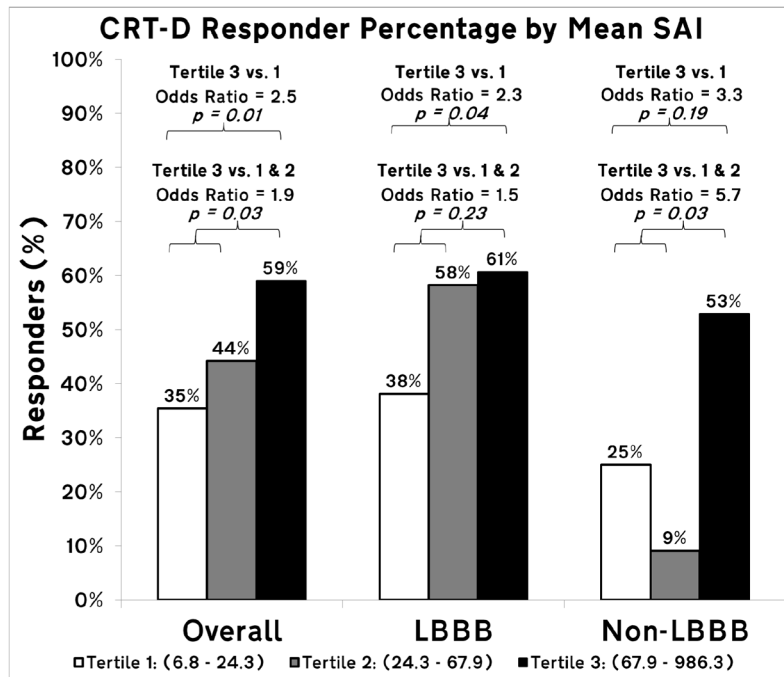
Figure 3.
Bar graph of primary CRT responder percentage by mean SAI QRST tertiles for all study participants, and for bundle branch block (BBB) morphology subgroups (LBBB and non-LBBB). Reported odds ratios are adjusted by age, gender, type of cardiomyopathy, LVEF, QRS duration and BBB morphology.
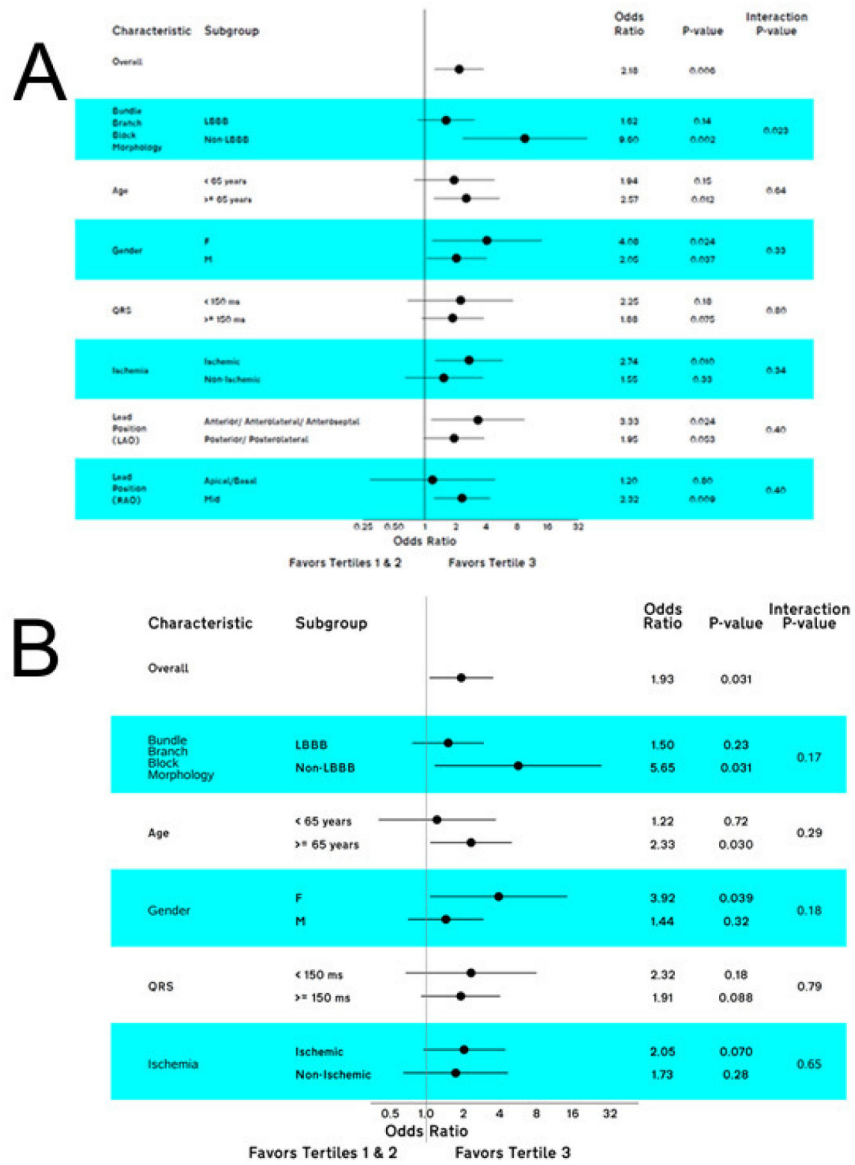
Figure 4.
A. Unadjusted and B. adjusted primary CRT response, associated with SAI QRST tertiles in clinically relevant subgroups.
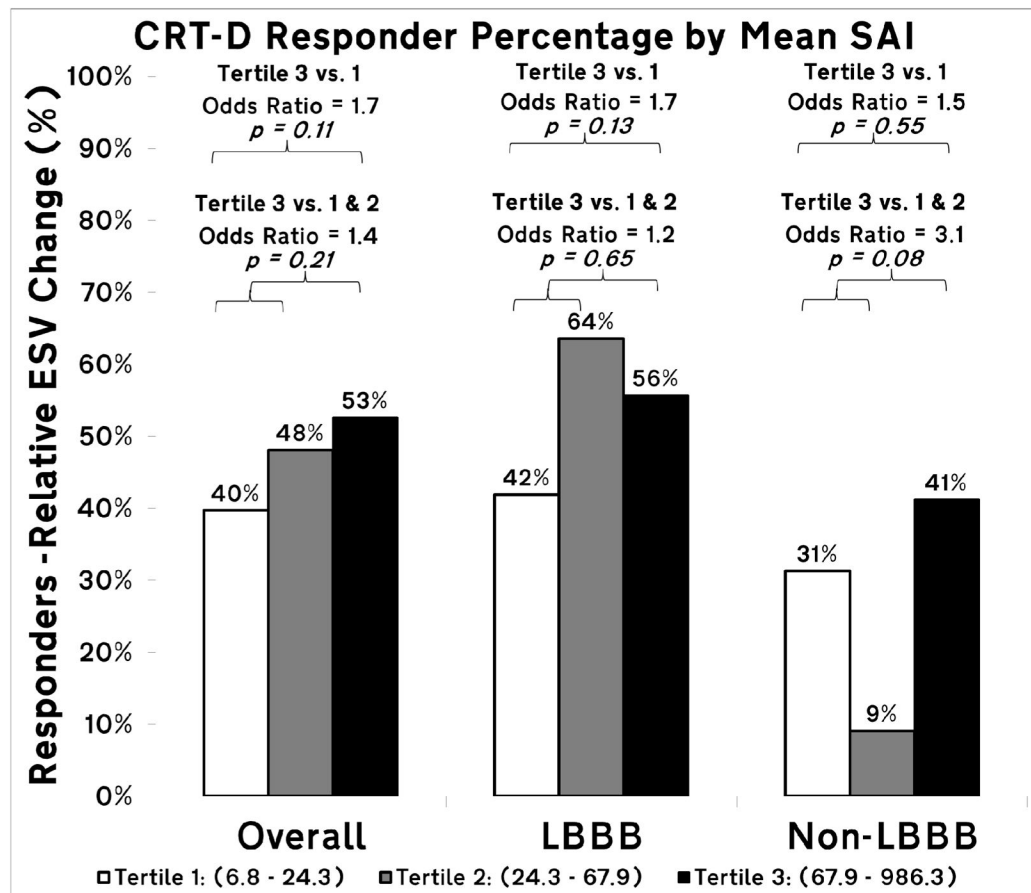
Figure 5.
Bar graph of secondary CRT responder percentage by mean SAI QRST tertiles for all study participants, and for bundle branch block (BBB) morphology subgroups (LBBB and non-LBBB). Unadjusted odds ratios are reported.

Table 1

Demographic and clinical charactristics of SMART-AV participants with SAI QRST tertiles.

Baseline Characteristic	All Patients N=234	Tertile 1 (6.8–24.3) N=79	Tertile 2 (24.3–67.8) N=77	Tertile 3 (67.9–986.3) N=78	ANOVA P-value
Age(years), Mean±SD	67 ± 10	67 ± 10	66 ± 10	66 ± 11	0.83
Female, N(%)	71 (30.3%)	27 (34.2%)	23 (29.9%)	21 (26.9%)	0.62
White, N(%)	181 (79.7%)	65 (82.3%)	61 (81.3%)	55 (75.3%)	0.55
BMI (kg/m^2), Mean±SD	30.2 ± 6.3	29.9 ± 6.5	30.3 ± 6.5	30.3 ± 5.9	0.92
NYHA Class I, N(%)	1 (0.4%)	1 (1.3%)	0 (0.0%)	0 (0.0%)	
NYHA Class II, N(%)	9 (3.9%)	7 (9.0%)	1 (1.3%)	1 (1.3%)	0.055
NYHA Class III, N(%)	215 (92.3%)	69 (88.5%)	72 (93.5%)	74 (94.9%)	
NYHA Class IV, N(%)	8 (3.4%)	1 (1.3%)	4 (5.2%)	3 (3.8%)	
LBBB, N(%)	179 (76.5%)	63 (79.7%)	55 (71.4%)	61 (78.2%)	0.43
Ischemic cardiomyopathy, N(%)	140 (59.8%)	47 (59.5%)	51 (66.2%)	42 (53.8%)	0.30
LVEF(%), Mean±SD	24.7 ± 6.9	25.8 ± 6.5	24.9 ± 6.9	23.5 ± 7.2	0.12
LVESV(ml), Mean±SD	126 ± 66	109 ± 51	115 ± 55	154 ± 80	< 0.001
QRS(ms), Mean±SD	152 ± 20	147 ± 21	150 ± 20	160 ± 15	< 0.001
Diabetes, N(%)	95 (40.6%)	36 (45.6%)	28 (36.4%)	31 (39.7%)	0.50
Lead Position (LAO)					
Anterior/ Anterolateral/ Anteroseptal, N (%)	66 (29.1%)	26 (33.3%)	16 (21.3%)	24 (32.4%)	0.19
Posterior/ Posterolateral, N (%)	161 (70.9%)	52 (66.7%)	59 (78.7%)	50 (67.6%)	
Lead Position (RAO)					
Apical, N (%)	25 (11.0%)	5 (6.4%)	8 (10.7%)	12 (16.2%)	0.061
Basal, N (%)	9 (4.0%)	2 (2.6%)	1 (1.3%)	6 (8.1%)	
Mid, N (%)	193 (85.0%)	71 (91.0%)	66 (88.0%)	56 (75.7%)	

Table 2

Association of SAI QRST with CRT response.

Predictor=SAI QRST tertiles	Odds Ratio (95%CI) (Tertile 3 vs. Tertiles 1 & 2)	P	AIC[*]
Model 1 (unadjusted)	2.18 (1.25, 3.79)	0.011	319.26
Model 2 (adjusted by age, sex)	2.33 (1.32, 4.11)	0.005	315.02
Model 3 (model 2 + by cardiomyopathy type)	2.21 (1.25, 3.93)	0.007	311.17
Model 4 (model 2 + LVEF)	2.23 (1.26, 3.95)	0.006	314.57
Model 5 (model 2 + BBB morphology, QRS)	2.00 (1.10, 3.62)	0.023	307.23
Model 6 (model 2 + renal function)	2.33 (1.32, 4.11)	0.003	316.92
Model 7 (model 2 + sodium)	2.26 (1.28, 4.00)	0.005	312.98
Model 8 (model 2+ LVEF, CM type, QRS, BBB morph, renal function, Na)	1.86 (1.02, 3.41)	0.044	307.01
Model 9 (model 2+ LVEF, CM type, QRS, BBB morph, LV lead position (RAO and LAO))	1.71 (0.92, 3.17)	0.087	306.44
FINAL MODEL, (model 2+ LVEF, CM type, QRS, BBB morph)	1.87 (1.03, 3.42)	0.041	306.06

[*]
Smaller AIC indicates better model fit

Table 3

Full final logistic regression model predicting primary CRT response.

Predictor	Comparison	Odds ratio (95%CI)	P
SAI QRST tertiles	T3 vs. T1/T2	1.87 (1.03, 3.42)	0.041
Gender	M vs. F	0.52 (0.27, 0.99)	0.048
Ischemic cardiomyopathy	Ischemic vs. Non-Ischemic	0.60 (0.32, 1.10)	0.100
Age	Per 5 years	1.02 (0.89, 1.18)	0.74
BBB morphology	LBBB vs Non-LBBB	2.29 (1.11, 4.71)	0.025
QRS duration	Per 10 ms	1.16 (1.00, 1.34)	0.049
LVEF	Per 1%	0.97 (0.93, 1.01)	0.16