FRAGMENTED QRS ON THE 12 LEAD ECG: A MARKER OF SUDDEN CARDIAC DEATH

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Background

- Heart disease is the major cause of Death in the US, contributing to >600,000 deaths/year
- SCD contributed to 50% of those deaths, and of those half of them occur in patients with no known heart disease
- Survival after:
  - Out of hospital cardiac arrest is 5.6%
  - Inpatient cardiac arrest: 25.5%

Background

- Severely reduced EF, wide QRS duration, and EF<30 with NSVT are predictor of SCD.
- In most patients predictors of SCD are unknown.
- The number of patients needed to treat to prevent SCD is undesirably high.
- For that, screening the general population for risk stratification of SCD currently cannot be performed.
- Therefore the search for good predictors of SCD is warranted.

Background

- The 12-lead ECG represents both the depolarization and repolarization phases of the heart.
- Major repolarization abnormalities are markers of SCD with low predictive value and include: J point elevation, QT prolongation, T wave alternans, and ST-T wave abnormalities
- Could a depolarization abnormality be a marker of SCD?
- Is fQRS be a marker of SCD?

Background on fQRS

- It is a notching in QRS complex that is not secondary to BBB.
- In one study with 10,904 middle aged patients in Finland,
  - Incidence was reported as 19.7% in the general population.
  - fQRS in lateral leads in patients with CAD was associated with ↑ mortality
- It predicts mortality in patients with acute coronary syndrome and in patients with cardiomyopathy.
- Predictor of arrhythmic events in patients with ischemic and nonischemic cardiomyopathy
- Meta-analysis has shown that fQRS predicts SCD even in patients with EF>35%

Das et al, *Heart Rhythm*. 2010;7:74-80.
Ozcan et al, *Electrocardiol*. 2014;19:351-7.
Terho et al, *Am J Cardiol*. 2014;114:141-7.
Das et al, *Am J Cardiol*. 2009;104:1631-7.
Rosengarten et al, *Europace*. 2015;17:969-77

Background on fQRS

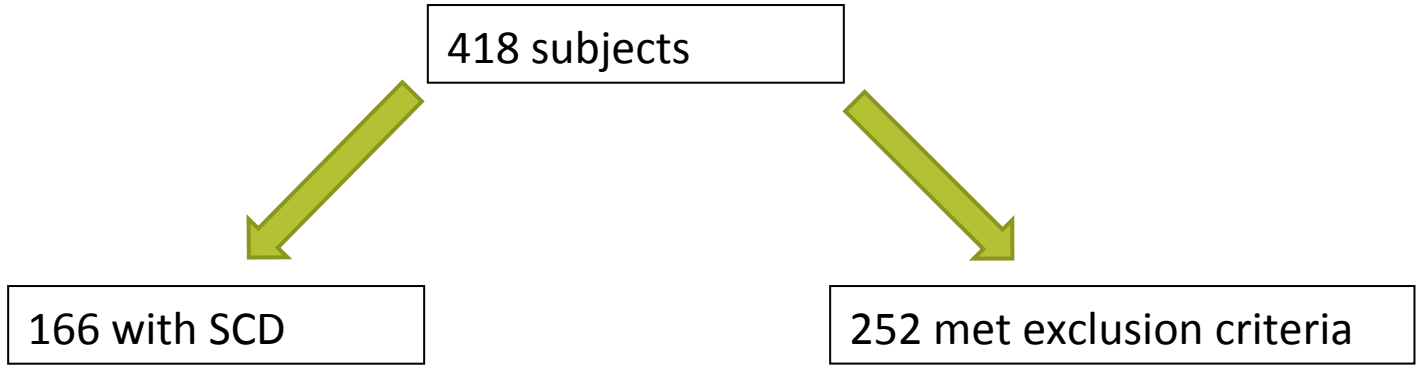
- It has been confirmed on autopsy that fQRS complexes represent “islands” of viable myocardial tissue within myocardial scar.
- These “islands” of myocardium have slow impulse conduction as a result of the partially depolarized and depressed action potential upstroke velocities, which are likely responsible for the inhomogeneous activation of the ventricles.

Background on fQRS

- Therefore, different morphologies of fQRS are caused by shifting of the QRS vector during depolarization in and around the areas of scarred or ischemic myocardium and depend on their extent and location in the ventricle

Methods

- Identified all patients discharged with CA (2000-2014) at Methodist.



1. Lack of at least one interpretable ECG at any point in time in the EMR.
2. Age <18 at the time of cardiac arrest.
3. Cardiac arrest from a non-cardiac cause or no history of cardiac arrest.

Methods

- 12-lead EKGs were extracted from the charts:
  - prior to cardiac arrest if applicable
  - within 48 hours after cardiac arrest
  - outpatient f/u
- We had 1-3 EKGs per patient

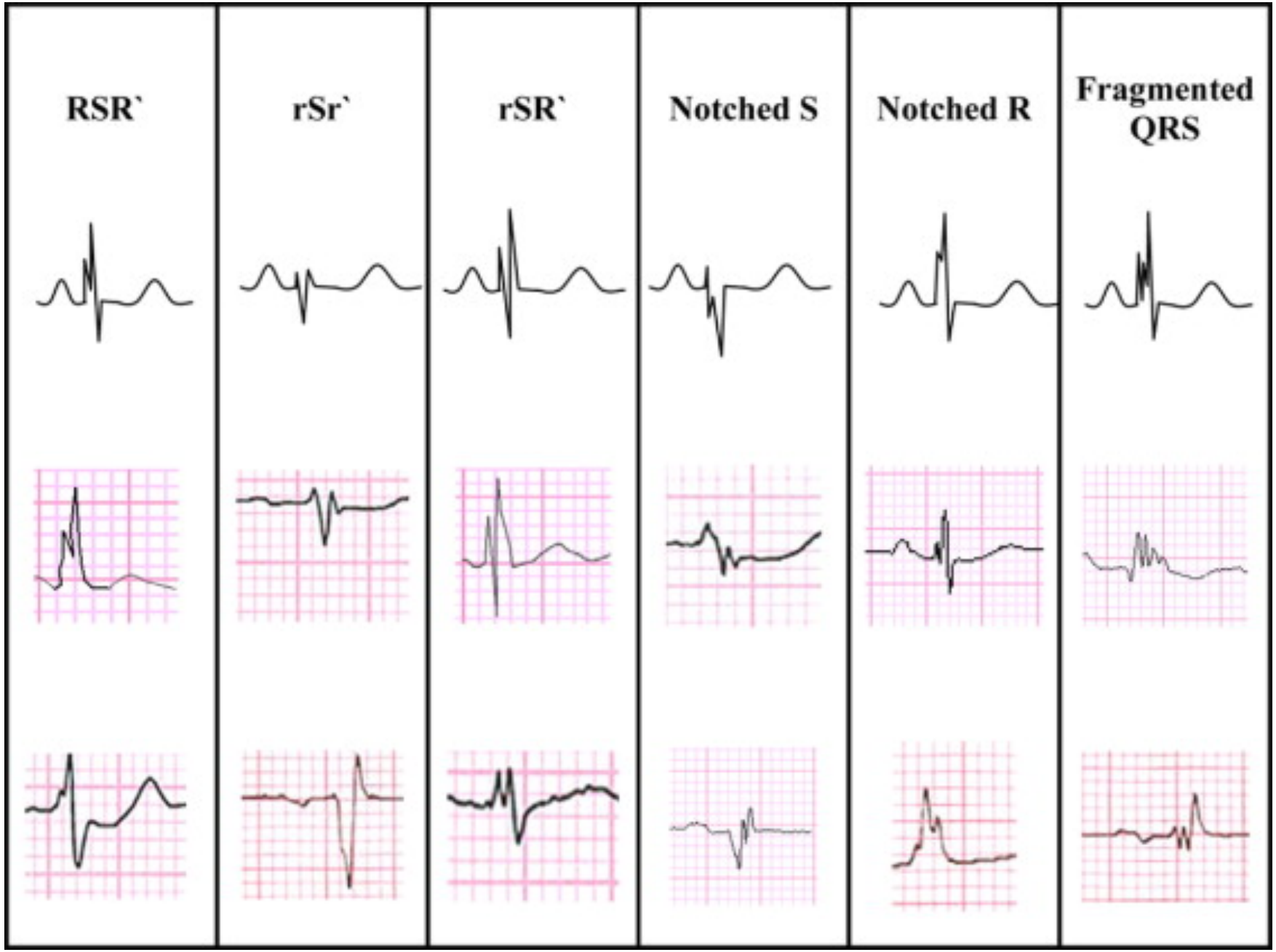
Methods

- All identifiers were removed from the EKGs (CA and healthy controls) prior to review by two blinded-readers.
- The presence or absence of fQRS was documented as well as the major lead territories involved

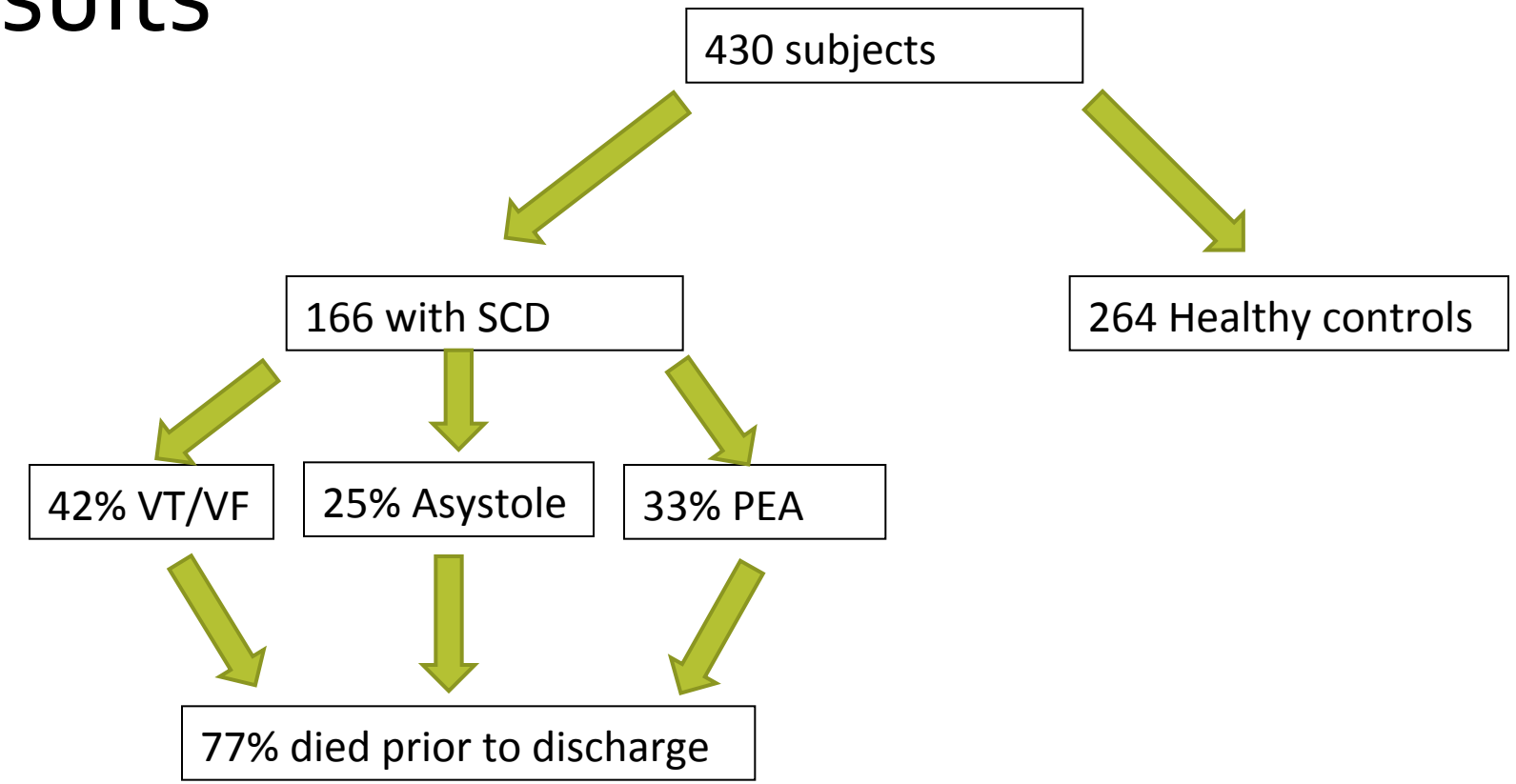
Methods

- fQRS was defined as:
  - Presence of various RSR′ patterns with (QRS<120) w/wo Q wave
  - This includes >1 R′
  - Notching of the R wave or S wave
  - AND present in 2 contiguous leads.
  - Exclude incomplete RBBB, RBBB, LBBB.
    - Exclude if RSR′ in V1 or V2 with QRS>100
    - Exclude if RSR′ in V5, V6, or Lead I with QRS>120

fQRS



Results


430 subjects
166 with SCD
264 Healthy controls
42% VT/VF
25% Asystole
33% PEA
77% died prior to discharge

	Healthy controls (HC)	SCD	SCD vs. HC
Characteristic	N =264	N =166	P-value
Male gender	148 (56.1%)	103 (62.0%)	n/a
Age at Cardiac Arrest*	61.3 ± 16.1	65.2 ± 15.4	0.0115
fQRS in ≥2 contiguous ECG leads	59 (22.3%)	95 (57.2%)	<.0001
> 1 Lead Territory in Those with fQRS	1 (1.7%)	16 (16.8%)	0.0035
Q wave in ≥2 contiguous ECG leads	4 (1.5%)	14 (8.4%)	0.0005
fQRS and/or Q wave ≥2 contiguous ECG leads	62 (23.5%)	100 (60.2%)	<.0001
Number of ECGs			<0.0001**
1	209 (79.2%)	84 (50.6%)	
2	53 (20.1%)	77 (46.4%)	
3	2 (0.8%)	5 (3.0%)	
QRS > 150 in any ECG	5 (1.9%)	36 (21.7%)	<.0001
History of Hypertension	128 (48.5%)	120 (72.3%)	<.0001
History of Hyperlipidemia	63 (23.9%)	79 (47.6%)	<.0001
History of Myocardial infarction	0 (0.0%)	65 (39.2%)	<.0001
History of Cardiomyopathy	0 (0.0%)	69 (41.6%)	<.0001
History of Atrial Arrhythmias	15 (5.7%)	35 (21.1%)	<.0001
History of Pulmonary Disease	24 (9.1%)	42 (25.3%)	<.0001
Family history of CAD	37 (14.0%)	25 (15.1%)	n/a
Family history of SCD	3 (1.1%)	1 (0.6%)	n/a
Beta blocker therapy	45 (17.0%)	77 (46.4%)	<.0001
QT prolonging drugs	27 (10.2%)	59 (35.5%)	<.0001
Antiarrhythmic therapy	6 (2.3%)	13 (7.8%)	0.0063

Variable	SCD vs. HC		
	Odds Ratio	95% CI	P-Value
fQRS in any ECG	3.58	2.15-5.96	<.0001
Q wave in any ECG	5.07	1.43-17.93	0.0118
Male gender vs female	1.15	0.69-1.92	0.5821
Age at Cardiac Arrest *	1.00	0.98-1.01	0.7719
QRS > 150 in any ECG	11.85	4.16-33.77	<.0001
Number of ECGs			0.2221
3 vs. 1	1.49	0.20-11.10	0.6955
2 vs. 1	1.65	0.94-2.91	0.0843
History of Hypertension	1.66	0.93-2.98	0.0864
History of Hyperlipidemia	1.29	0.74-2.25	0.3649
History of Myocardial infarction**	N/A	N/A	N/A
History of Cardiomyopathy**	N/A	N/A	N/A
History of Atrial Arrhythmias	1.91	0.80-4.54	0.1454
History of Pulmonary Disease	2.66	1.34-5.27	0.0051
Beta blocker use	1.70	0.95-3.05	0.0750
QT prolonging drug use	3.08	1.61-5.88	0.0007
Antiarrhythmic therapy	0.90	0.25-3.24	0.8773

Discussion

- Patients who experienced SCD had a:
  - Significantly higher prevalence of fQRS (57.2%) compared to healthy controls (22.3%)
  - This translated to an OR of 3.58
  - Higher incidence of fQRS in multiple major lead territories (16.8% vs. 1.7%, p =0.0035)
- Prior studies showed that patients with fQRS to have a higher risk of death (RR 1.71, 95% CI 1.02–2.85) and ventricular arrhythmia (RR 2.20, 95% CI 1.05–4.62).

Discussion

- Hospitalized patients with fQRS have a significantly higher risk for ventricular tachycardia/ventricular fibrillation (20.3%) vs. patients without fQRS (7.6%)
- MADIT II sub-study showed that the presence of fQRS (especially identified in inferior leads) was predictive of SCD, SCD or appropriate ICD shock, and all-cause mortality in patients with ischemic cardiomyopathy.

Discussion

Compared to the Finnish study:

- Similar rate of fQRS in a generally healthy population
- Significantly increased rate of fQRS in multiple major lead territories among patients who suffered SCD

Limitations

- Retrospective study.
- Many patients die before a 12-lead ECG is recorded.
- fQRS on a 12-lead ECG requires an optimal low-pass filter setting (100 or 150 Hz) and fragmentation may be missed with a low pass filter setting of 60 Hz or less

Conclusion

- The use of multiple known ECG markers of abnormal repolarization and depolarization may provide a high predictive value for SCD and be a vital screening tool with incremental value to established risk markers such as reduced LVEF.
- This could be established in a prospective study, which is also difficult to design as SCD occurs in the majority of the patients without prior warning.