REVIEW ARTICLE

QRS-T Angle: A Review

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For proper distribution of preventative resources, a more robust method of cardiac risk stratification should be encouraged in addition to merely reduced ejection fraction. To this end, the QRS-T angle, an electrocardiogram-derived measure of the difference in mean vectors of depolarization and repolarization, has been found associated with sudden cardiac death and other mortal and morbid outcomes in multiple observational studies over the past decade. The use of both frontal and spatial QRS-T angle in the prediction of future cardiac events including sudden cardiac death, all-cause mortality, and further cardiac morbidity is reviewed here.

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In this era of device cardiology, appropriate risk stratification equals proper distribution of resources, such that those with the highest risk have the clearest indication for various technologies. One prominent example is risk of sudden cardiac death (SCD) and use of implantable cardiac defibrillators (ICDs). Tools are available to assist in this process of risk stratification. The electrocardiogram (ECG) has proven to be high yield in stratifying patients to a greater or lesser degree of risk for a variety of cardiac morbidity and general mortality as it remains inexpensive, noninvasive, quick to perform, and quick to result. Vectorcardiography (VCG)—though an aged method of ECG analysis—has reemerged with the advent of digital electrocardiography. VCG visualizes movement of the heart vector through cardiac cycle as loops. The QRS loop reflects depolarization, whereas the T loop reflects repolarization. By VCG, one can measure a spatial angle between depolarization and repolarization, specifically a spatial angle between the spatial QRS vector and spatial T vector, namely spatial QRS-T angle. An abnormally wide QRS-T angle has emerged as a prominent variable in stratifying cardiac risk.

HISTORY AND MECHANISM

VCG emerged as a field of electrocardiography in the 1920s when Hubert Mann coined the concept of "loops" to express potential vectors during the cardiac cycle.[1] Einthoven had also indicated that a vector quantity could define electric forces from the heart recorded on the surface of the body a decade prior.[2] Multiple lead systems for measuring the VCG then developed, but the Frank system—emerging in the 1950s—became the most commonly used.[3] The QRS-T angle, a value obtained through VCG analysis, has been studied extensively since 1934, when Wilson et al. developed a concept of "ventricular gradient," which is a vectorial sum of a spatial QRS-T angle.[4] He postulated that spatial ventricular gradient (1) expresses the heterogeneity of the action potential morphology, (2) is largely independent of the ventricular activation sequence, and (3) characterizes a "primary T-wave," or primary

heterogeneity of repolarization, which was confirmed by later experimental and theoretical studies.[5–7] Unlike spatial ventricular gradient, spatial QRS-T angle characterizes a "secondary T-wave," i.e., secondary repolarization heterogeneity, whereby repolarization abnormalities secondary to depolarization abnormalities—i.e., changes in ventricular conduction—are highlighted including premature ventricular contraction, ventricular pacing, and bundle branch block, in the absence of primary action potential morphology heterogeneity. In this way QRS-T angle complements the ventricular gradient, where both might be used to adequately assess a patient with either a primary, secondary, or mixed (e.g., left ventricular hypertrophy [LVH]) repolarization abnormality. Given that the mechanistic assertions above are based on somewhat antiquated primary research, there is a need for modern studies into the mechanisms of both ventricular gradient and QRS-T angle.

METHODS OF MEASUREMENT

The spatial QRS-T angle can be derived from manipulations of the VCG. Briefly, the VCG is either constructed using the orthogonal Frank leads or transformed from a digital 12-lead ECG. Spatial QRS-T angle could be directly measured as spatial "peak" QRS-T (SP QRS-T) angle, or calculated as a spatial "mean" QRS-T (SM QRS-T) angle. We briefly review differences between these two approaches below. For additional details we refer reader to the manuscript by Cortez and Schlegel.[8]

SP QRS-T Angle

SP QRS-T angle measures QRS-T angle at the moment of maximum magnitude of the spatial QRS vector and T vectors within a three-dimensional QRS loop and T loop, respectively. As an example, details of the measurement of SP QRS-T angle, as performed in Tereshchenko laboratory, were described by Sur et al.[9] First, the origin point is detected as halfway between the two points in one cardiac cycle that are closest in space but separated in time on a vectorcardiographic loop. Then, the peak of the spatial QRS and T vectors are detected as the furthest points from the origin point in the QRS-loop and T-loop, respectively (Fig. 1). The SP QRS-T angle is calculated using the definition of the normalized inner product of spatial peak QRS and T vectors.

$$SP\ QRS\text{-}T\ angle = \arccos \frac{QRSp^*Tp}{|QRSp|^*|Tp|}. \tag{1}$$

SM QRS-T angle

Alternatively, spatial QRS-T angle could be measured as an SM QRS-T angle. SM QRS-T angle uses the mean value of the spatial QRS vector over time during the QRS loop, and the mean value of the spatial T vector over time during the T loop, accordingly.[9] In case of symmetrical loop "peak" and "mean" vectors are equal to each other.

$$SM\ QRS\text{-}T\ angle = \arccos \frac{QRSm^*Tm}{|QRSm|^*|Tm|}. \tag{2}$$

The same equation could be expressed in several other ways:

$$SM\ QRST\ angle = \arccos$$
$$\times \frac{QRSx \times Tx + QRSy \times Ty + QRSz \times Tz}{\sqrt{QRSx^2 + QRSy^2 + QRSz^2} \times \sqrt{Tx^2 + TY^2 + Tz^2}} \tag{3}$$

$$SM\ QRS\text{-}T\ angle = \arccos$$
$$\times \left(\frac{\left(\left[\int_{Qbeg}^{J-p} Vx\right] \times \left[\int_{J-p}^{Tend} Vx\right]\right) + \left(\left[\int_{Qbeg}^{J-p} Vy\right] \times \left[\int_{J-p}^{Tend} Vy\right]\right) + \left(\left[\int_{Qbeg}^{J-p} Vz\right] \left[\int_{J-p}^{Tend} Vz\right]\right)}{\sqrt{\left(\int_{Qbeg}^{J-p}|Vx|\right)^2 + \left(\int_{Qbeg}^{J-p}|Vy|\right)^2 + \left(\int_{Qbeg}^{J-p}|Vz|\right)^2} \times \sqrt{\left(\int_{J-p}^{Tend}|Vx|\right)^2 + \left(\int_{J-p}^{Tend}|Vy|\right)^2 + \left(\int_{J-p}^{Tend}|Vz|\right)^2}} \right). \tag{4}$$
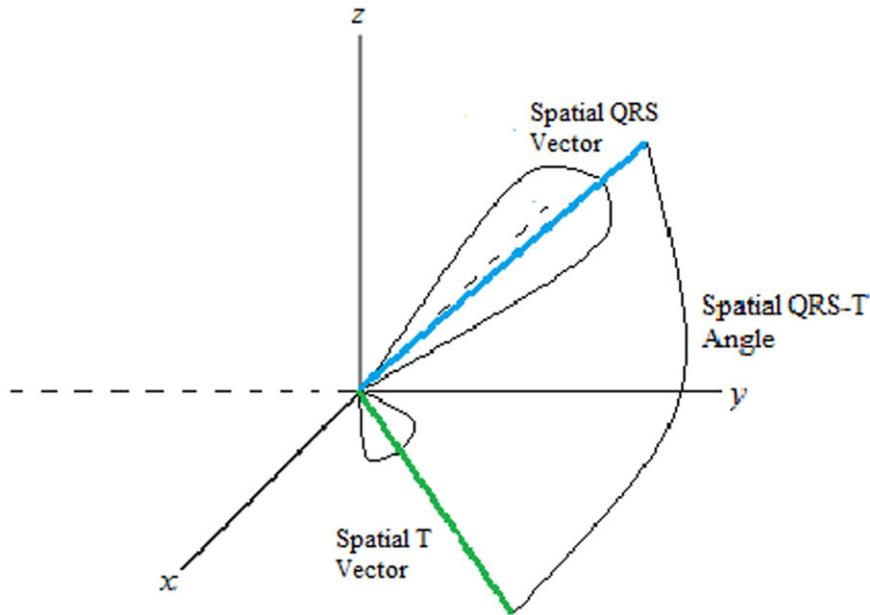
Figure 1. Schematic presentation of a spatial QRS-T angle.

Spatial "Simple" QRS-T Angle

For those investigators who do not have readily available recorded or transformed XYZ leads, Rautaharju et al.[10] developed simplified approach to compute spatial QRS-T angle, which uses leads aVF, V_2, V_5, and V_6. This approach includes several steps. First, "net" values of QRS complex amplitudes are calculated in each of aVF, V_2, V_5, and V_6 leads as $QRS_{net} = R_{amp} - |S/QS_{amp}|$. "Net" values of the T wave are calculated by measuring positive and negative T wave amplitudes, accordingly: $T_{net} = (+)T_{amp} - |(-)T_{amp}|$. Then, spatial magnitudes of QRS and T are calculated according to equations: $QRS_{sm} = [(QRS_{net}V_6)^2 + (QRS_{net}aVF)^2 + (QRS_{net}V_2)^2]^{1/2}$ and $T_{sm} = [(T_{net}V_5)^2 + (T_{net}aVF)^2 + (T_{net}V_2)^2]^{1/2}$. Finally, simple spatial QRS-T angle (SS QRS-T angle) is calculated as following:

Planar Frontal QRS-T Angle

Projection of three-dimensional spatial QRS and T vectors onto the frontal plane produces frontal QRS_f and T_f vectors, respectively. The angle between the frontal QRS_f and T_f vectors is designated the frontal QRS-T angle (Figure 2). Frontal QRS-T angle can be easily calculated from a standard 12-lead ECG as the absolute value of the difference between the frontal plane QRS axis and T axis. If such a difference exceeds 180 degrees, then frontal QRS-T angle is calculated as 360° minus the absolute value of the difference between the frontal plane QRS axis and T axis.

Frontal versus Spatial QRS-T Angle

Multiple observational studies have included in their analyses both frontal and spatial methods

$$\text{SS QRS-Tangle} = \arccos\left(\frac{(QRSnetV_6 \times TnetV_5) + (QRSnetaVF \times TnetaVF) + (QRSnetV_2 \times TnetV_2)}{QRSsm \times Tsm}\right)$$
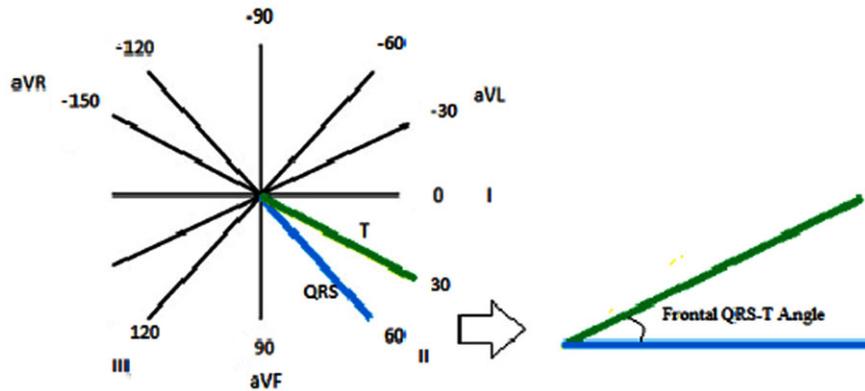
Figure 2. Measurement of a planar frontal QRS-T angle.

of computing QRS-T angle,[11–14] often directly comparing their diagnostic and prognostic utility. Cross-study comparison has proven challenging as each study often defines its own normal angles, not to mention significant population variance between studies. A 2011 observational study by Brown et al.[11] compared the operating characteristics of spatial and frontal QRS-T angle as a diagnostic tool for predicting underlying hypertrophic cardiomyopathy, left ventricular systolic dysfunction, and coronary heart disease (CHD). Digital ECGs of 580 total subjects were analyzed (370 with disease and 210 without). Not unexpectedly, spatial QRS-T angle was found to predict underlying cardiac disease more consistently than frontal angles, suggesting improved diagnostic utility.

As these measures have been lauded more for their prognostic utility than diagnostic, there have been more studies to compare value in this regard. A 2009 study of patients with ICDs for ischemic cardiomyopathy concluded that both frontal and spatial methods held prognostic utility, though spatial angle seemed to hold stronger predictive value for ventricular tachyarrhythmias—a reasonable surrogate for SCD—than frontal angle.[14] The Atherosclerosis Risk in Communities (ARIC) study of cardiovascular disease (CVD)-free participants indicated a statistically significant increased risk of mortality and incident CHD in men and women with abnormal spatial and frontal QRS-T angles.[12] When correcting for other clinical variables, however, the only value to retain statistical significance for these outcomes in this study was spatial QRS-T angle in women, suggesting less utility for frontal QRS-T angle in lower risk populations. A 2012 study of 7052 patients free of CVD indicated significant predictive capacity for total and cardiac mortality with widened spatial QRS-T angle. The frontal angle was only predictive in the male population—a result discordant with the aforementioned ARIC study, which only retained significance in the female population. Unfortunately, these two studies did not use equivalent normal ranges for the values of frontal angle, a common difficulty encountered in study comparison on this topic.[13]

QRS-T Angle in Healthy Individuals

The QRS-T angle, whether it is measured by spatial or frontal methods, varies by gender and age. Generally, women have a smaller angle at baseline than men, and in both sexes, the angle widens with age. Normal frontal angles are generally smaller than normal spatial angles.

Data describing the normal ranges of spatial QRS-T angle, from either the Frank lead system or new digital ECG transformation methods, are varied. An earlier study in 1964 using the Frank lead system to calculate the spatial QRS-T angle on 510 healthy men who were on average 40 years of age arrived at an upper limit of normal around 105° for men.[15] Other studies since that time have mainly used the inverse Dower method, arriving at values ranging (by population) from 75°[12, 16] to 130°.[17] The largest study to report normality for men was an ARIC cohort of 5434 men aged around 54 years with an upper limit of normal of 110°.[16] The upper limit defined for women in this study was 90°. For women, most studies have been more recent, the largest being a cohort of postmenopausal women in the Women's Health Initiative (WHI), with an upper limit of normal of 73°.[18] Unfortunately there are no studies to

stratify spatial QRS-T normality by age. Most argue that this range should be stratified by age, gender, and method of digital ECG transformation, as some methods systematically overestimate derived vectors from the digital ECG.[8] Of note, typically Dower-related reconstructions have ranged higher than other approximations of the Frank lead system, including the Frank lead system itself, such that if a set of normal ranges were defined with the Dower method, then there is a false negative risk if a patient's VCG were to be analyzed using different methods without this systematic error. As reported by Cortez and Schlegel, the Dower-related reconstruction typically yields a spatial QRS-T angle from 66° to 81°, whereas those derived from Kors' regression-related reconstructions have typically ranged from 44° to 65°, with values obtained from the true Frank leads being 35°–51°.[8]

Among studies included below, the upper limits of normal for the frontal angle have ranged (Tables 1–3). Historically, upper limits of normal have been between 45° and 60°.[19] A 2012 cohort of older patients deemed free of CVD at the start of the study described the gender-specific upper limits of normal as 39° for women and 81° for men.[13]

Association with SCD

Beginning with initial observational study by Kors et al. into the use of the spatial QRS-T angle as an indicator of cardiac death,[20] a variety of studies have looked at this question in various populations from low risk[21] to high risk,[14,20] and all have discovered a concerning association with both cardiac mortality and SCD. See Table 1 for cross-study comparisons.

The initial study from 2003[20] describing these associations in the Rotterdam population, a group of 6134 patients from the general population, discovered a statistically significant hazard ratio of 5.6 for SCD in patients with an abnormal spatial QRS-T angle, which remained significant when controlling for clinical and other ECG risk factors. Of note, QRS-T angle carried the highest ratio among other traditional ECG indicators of poor prognosis, including ST depression, T wave inversion, left ventricular hypertrophy by ECG criteria, abnormal T wave axis, and prolonged QTc.

A study conducted on 277 dialysis patients in 2013[22] also showed significantly increased risk in patients with an abnormally wide QRS-T angle, with a hazard ratio of 4.5 that remained significant on multivariate analysis. This is to say that the spatial QRS-T angle carries with it a higher predictive value among groups traditionally considered to be at higher risk of cardiovascular morbidity and mortality.

Frontal QRS-T angle has been less rigorously studied as a predictive indicator of SCD. The largest study to ask this question involved the Finnish CHD cohort of 10,957 middle-aged patients from the general population.[23] A widened frontal QRS-T angle (>100°) in this low-risk group yielded a three-times increased risk of SCD. A similar study in a somewhat lower risk, but older group of 7052 patients from the National Health and Nutrition Examination Survey III cohort deemed free of CVD at the start of the study yielded less impressive, but still significant hazard ratios, indicating a doubling of risk for cardiovascular death (including suspected SCD and other cardiovascular-related causes).[13] Though patients were initially screened to lower risk of baseline CVD, the average age was a decade greater than the Finnish cohort above, and one would expect this would drive hazard ratios up, but with the composite endpoint of CVD death as opposed to SCD, there may be some deaths included which QRS-T angle did not predict, diluting its predictive power.

Association with Documented Ventricular Arrhythmias

Widened QRS-T angle has been shown to predict ventricular arrhythmias. Borleffs et al. conducted this study[14] in a higher risk population of 412 patients who all had ICDs implanted with an endpoint of first appropriate ICD therapy. The significance of an abnormal spatial QRS-T angle was strong, as might be expected, with an adjusted hazard ratio of 7.3 that was also statistically significant.

Association with Cardiovascular Mortality

As one might expect, widened QRS-T angle has been shown to be predictive of cardiovascular mortality as well (Table 2). This end-point acts as a grab bag for multiple adverse events leading to death and is defined differently dependent on the study, with some overlap with SCD, but there was a large study of 38,283 postmenopausal

Table 1. Summary of Observational Studies Relating Wide QRS-T Angle to Sudden Cardiac Death (SCD)

Study	Population Size	Average Age	Population Type	Follow-up Period	Frontal vs. Spatial	Endpoint and Risk
de Bie et al.[22]	277	56 years	Dialysis patients	2.1 years	Spatial (men >130°, women >116°)	SCD: HR 2.99
Pavri et al.[25]	455	58 years	All patients with nonischemic cardiomyopathy.	2.5 years	Frontal (>90°)	Composite (death, appropriate ICD or resuscitated arrest): HR 1.64
Aro et al.[23]	10,957	44 years	General population	30 years	Frontal (>100°)	SCD: HR 2.26

ICD, implantable cardiac defibrillator; HR, hazard ratio.

Table 2. Summary of Observational Studies Relating Wide QRS-T Angle to Cardiovascular Mortality

Study	Population Size	Average Age	Risk	Follow-up Period	Frontal vs. Spatial	Endpoint and Risk
Kors et al.[20]	6134	69 years	General population.	6.7 years	Spatial (>135°)	Cardiac mortality: HR 3.7
Yamazaki et al.[26]	46,573	57 years	VA ECGs obtained for any reason,	6 years	Spatial (>100°)	Cardiac mortality: HR 3.6
Rautaharju et al.[24]	38,283	62 years	Postmenopausal women.	6.2 years	Spatial (>96°)	CHD mortality: HR 2.1
Kentta et al.[21]	1297	56 years	Patients undergoing exercise stress test for CHF follow-up.	4 years	Total cosine R-to-T	Cardiac mortality: HR 5.6
Aro et al.[23]	10,957	44 years	General population	30 years	Frontal (>100°)	Cardiac mortality: NS
Whang et al.[13]	7052	56 years	Patients free of CVD	14 years	Frontal (men >95°, women >43°) & spatial (men >135°, women >120°)	CV mortality: spatial, men: 2.08 spatial, women: 2.05 frontal, men: elevated* frontal, women: NS
Lipton et al.[27]	2347	61 years	Patients undergoing stress ECHO for CHD evaluation.	7 years	Spatial (>135°)	Cardiac death: HR 1.9

CHD, coronary heart disease.

women, which indicated a hazard ratio of 2.12 for death from myocardial infarction in women who had baseline CVD.[24] A similar pattern for worsened cardiovascular mortality with widened spatial QRS-T angle is observed in lower-risk populations, as well as men. A study on 7052 men and women thought free of CVD at the onset of study indicated a significantly increased risk of

Table 3. Summary of Observational Studies Relating Wide QRS-T Angle to Total Mortality

Study	Population Size	Average Age	Risk	Follow-up Period	Frontal vs. Spatial	Endpoint and Risk
Kors et al.[20]	6134	69 years	General population	6.7 years	Spatial (>135°)	Total mortality: HR 1.8
de Torbal et al.[28]	2641	69 years	Patients evaluated for chest pain	6.3 years	Spatial (>135°)	Total Mortality: HR 1.5
Rautaharju et al. cohort[18]	38.283	62 years	Postmenopausal women	6.2 years	Spatial (>96°)	Total mortality: HR 2.98
Pavri et al.[25]	455	58 years	All patients with nonischemic cardiomyopathy	2.5 years	Frontal (>90°)	Total mortality: NS
Borleffs et al.[14]	412	63 years	Patients with ICD in place	2 years	Spatial (>100°) and frontal (>90°)	Total mortality: spatial: NS frontal: HR 2.3
Zhang et al.[12]	13973	54 years	General population	14.3 years	Spatial (>123 men, >110 women) and frontal (>73 men, >67 women)	Total mortality, men: planar-2.3 spatial-2.16 total mortality, women: planar- 2.57 spatial- 3.08
Lipton et al.[27]	2347	61 years	Patients undergoing stress ECHO for CHD evaluation.	7 years	spatial (>135°)	Total mortality: HR 1.5
Rubulis et al.[29]	187	58 years	Patients with CHD scheduled for first angioplasty.	8 years	Spatial (>101°)	Non-CV death: NS
Lown et al.[30]	1843	60 years	Patients with acute coronary syndrome.	2 years	Frontal (>105°)	Total mortality: HR 1.9
Aro et al.[23]	10.957	44 years	General population	30 years	Frontal (>100°)	Total mortality: HR 1.57
Whang et al.[13]	7052	56 years	Patients free of CVD	14 years	Frontal (men >95°, women >43°) and spatial (men >135°, women >120°)	Total mortality, men: spatial HR 1.78, frontal HR 1.47, total mortality, women: spatial HR 1.46, frontal NS
de Bie et al.[22] 2013	277	56 years	Dialysis patients	2.1 years	Spatial (men >130°, women >116°)	Total mortality: HR 2.33
Gotsman et al.[31]	5038	75 years	Patients with CHF (bother preserved and reduced EF)	1.5 years	Frontal (men >130°, women >125°)	Total mortality, men: HR 1.53 total mortality, women: HR 1.35

CHF = chronic heart failure; EF = ejection fraction, CVD = cardiovascular disease.

cardiac death at 14 years with an abnormally wide spatial QRS-T angle (men >135°, woman >120°), with hazard ratios of 2.05 and 2.08 for men and women, respectively.[13]

Though frontal angle has been shown to be predictive of total mortality, evidence to indicate predictive power for cardiac mortality is not as strong. In a study of 7052 men and women considered free of CVD prior to the study, an abnormally wide frontal QRS-T angle (men >95°, women >43°) indicated increased risk for cardiac death in men, but did not retain significance on multivariate analysis in women. Further yet, a younger, general population study of 10,957 patients did not show a significantly increased risk of nonarrhythmic cardiac death with an abnormally wide frontal QRS-T angle (>100°, not stratified by gender).[23]

Association with All-Cause Mortality

Multiple studies (Table 3) have tracked total mortality as it relates to an abnormally wide spatial QRS-T angle, with all studies positive. The largest study to show a positive association was performed in 38,283 postmenopausal women participating in the WHI cohort.[18] Those with baseline CVD and a wide QRS-T angle had a nearly three-times increased risk of all-cause mortality compared to those with a normal QRS-T angle. This relationship was more modest, yet still significant, in those without baseline CVD with hazar ration of 1.28 for those with a wide spatial QRS-T angle.

Frontal QRS-T angle has been shown in multiple large, varied populations to be predictive of all-cause mortality. The largest study to look at this question seems to be the Finnish CHD cohort.[23] In this study of the general population, a widened (>100°) frontal QRS-T angle yielded a hazard ratio of 1.8 for total mortality that remained statistically significant in multivariate analysis. However, another smaller study of 455 patients in the DEFINITE trial[20] including patients nonischemic cardiomyopathy did not retain significance in multivariate analysis. Again, to emphasize study variance, this study defined abnormal as >90°, and did not stratify by gender.

Summary and Future Direction

Over the past decade, substantial evidence has accumulated for the use of QRS-T angle measure in predicting adverse cardiac outcomes. There is suggestion of a stronger relationship in women. In the future, use of this measure in combination with other ECG risk markers of SCD is needed for development of ECG risk score of SCD, with subsequent evaluation of the ECG SCD risk score in prospective studies to guide preventive interventions.

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