Journal of Electrocardiology 54 (2019) 61–68

Contents lists available at ScienceDirect

Journal of Electrocardiology

journal homepage: www.jecgonline.com

The WCT Formula: A novel algorithm designed to automatically differentiate wide-complex tachycardias

Adam M. May, MD [a,*], Christopher V. DeSimone, MD, PhD [a], Anthony H. Kashou, MD [b], David O. Hodge, MS [c], Grace Lin, MD [a], Suraj Kapa, MD [a], Samuel J. Asirvatham, MD [a], Abhishek J. Deshmukh, MBBS [a], Peter A. Noseworthy, MD [a], Peter A. Brady, MB, ChB, MD [a]

[a] Department of Cardiovascular Diseases, Mayo Clinic, United States of America
[b] Department of Medicine, Mayo Clinic, United States of America
[c] Department of Department of Health Sciences Research, Mayo Clinic, United States of America

ARTICLE INFO

Keywords:
Wide complex tachycardia
Ventricular tachycardia
Supraventricular tachycardia
Computerized electrocardiogram interpretation

ABSTRACT

Background: The accurate differentiation of wide complex tachycardias (WCTs) into ventricular tachycardia (VT) or supraventricular wide complex tachycardia (SWCT) remains problematic despite numerous manually-operated electrocardiogram (ECG) interpretation methods. We sought to create a new WCT differentiation method that could be automatically implemented by computerized ECG interpretation (CEI) software.
Methods: In a two-part study, we developed and validated a logistic regression model (i.e. WCT Formula) that utilizes computerized measurements and computations derived from patients' paired WCT and subsequent baseline ECGs. In Part 1, a derivation cohort of paired WCT and baseline ECGs was examined to identify independent VT predictors to be incorporated into the WCT Formula. In Part 2, a separate validation cohort of paired WCT and baseline ECGs was used to prospectively evaluate the WCT Formula's diagnostic performance.
Results: The derivation cohort was comprised of 317 paired WCT (157 VT, 160 SWCT) and baseline ECGs. A logistic regression model (i.e. WCT Formula) incorporating WCT QRS duration (ms) ($p < 0.001$), frontal percent amplitude change (%) ($p < 0.001$), and horizontal percent amplitude change (%) ($p < 0.001$) yielded effective WCT differentiation (AUC of 0.96). The validation cohort consisted of 284 paired WCT (116 VT, 168 SWCT) and baseline ECGs. The WCT Formula achieved favorable accuracy (91.5%) with strong sensitivity (89.7%) and specificity (92.9%) for VT.
Conclusion: The WCT Formula is an example of how contemporary CEI software could be used to successfully differentiate WCTs. The incorporation of similar automated methods into CEI software may improve clinicians' ability to accurately distinguish VT and SWCT.

Introduction

The successful differentiation of wide complex tachycardias (WCTs) into ventricular tachycardia (VT) or supraventricular wide complex tachycardia (SWCT) has undeniably important therapeutic and prognostic implications. Accurate non-invasive VT or SWCT diagnoses can be the indispensable foundation to appropriate, high-quality and cost-effective patient care; while incorrect WCT diagnoses, followed by inappropriate clinical decisions, may lead to adverse, even fatal, patient outcomes [1,2]. For example, an incorrect SWCT diagnosis for an "actual" VT may expose a patient to harmful medical therapies (e.g. calcium-channel blockers) and/or other unsafe clinical decisions (e.g. dismissal to home). Conversely, an incorrect VT diagnosis for an "actual" SWCT, while not immediately dangerous, could lead to undesirable downstream effects including excessive healthcare utilization (e.g. intensive care unit admission) and/or inappropriate invasive procedures (e.g. automatic implantable cardioverter-defibrillator (AICD) implantation).

Despite the availability of numerous manually-operated electrocardiogram (ECG) criteria and/or algorithms [3–11], the accurate differentiation of VT and SWCT remains a problematic clinical undertaking. At present, clinicians must carefully examine 12-lead ECGs and manually apply specific, sometimes complex, ECG criteria to render correct VT

Abbreviations: WCT, wide complex tachycardia; VT, ventricular tachycardia; SWCT, supraventricular wide complex tachycardia; AICD, automatic implantable cardioverter-defibrillator; ECG, electrocardiogram; CEI, computerized ECG interpretation; PAC, percent amplitude change; MI, myocardial infarction; LVEF, left ventricular ejection fraction; AAD, antiarrhythmic drug; BBB, bundle branch block.

* Corresponding author at: 200 First St. SW, Rochester, MN 55905, United States of America.
E-mail address: may.adam@mayo.edu (A.M. May).

https://doi.org/10.1016/j.jelectrocard.2019.02.008
0022-0736/

or SWCT diagnoses. As a consequence, traditional diagnostic approaches rely heavily on ECG interpreter experience and are particularly vulnerable to their improper application and/or refrained utilization.

Therefore, we sought to create a new WCT differentiation method that could be automatically implemented by computerized ECG interpretation (CEI) software. Through an exclusive examination of computerized measurements derived from paired WCT and baseline ECGs, we constructed a logistic regression model (i.e. WCT Formula) capable of automatic VT probability estimation.

Methods

Study design

In a two-part investigation, we developed and validated a logistic regression model (i.e. WCT Formula) composed of computerized measurements and calculations derived from paired WCT and subsequent baseline ECGs. In Part 1, a derivation cohort of paired WCT and baseline ECGs were examined to identify independent VT predictors to be incorporated into the WCT Formula. In Part 2, the WCT Formula's performance was prospectively evaluated against a separate validation cohort of paired WCT and baseline ECGs. Patient data acquisition and analysis was approved by the Mayo Clinic Institutional Review Board.

Electrocardiogram selection

Paired WCT and baseline ECGs were acquired within clinical settings at the Mayo Clinic Rochester or Mayo Clinic Health System of South Eastern Minnesota between September 2011 and November 2016. Electrocardiograms were standard, 12-lead recordings (paper speed: 25 mm/s, voltage amplification: 10 mm/mV) identified within our institution's centralized MUSE ECG data archives (*GE Healthcare;* Milwaukee, WI).

Wide complex tachycardias were defined as ECGs satisfying WCT criteria (QRS duration ≥ 120 ms; heart rate ≥ 100 bpm) plus a formal ECG laboratory interpretation of [1] "ventricular tachycardia," [2] "supraventricular tachycardia," or [3] "wide complex tachycardia." Baseline ECGs were defined as the most proximate, subsequent ECG not fulfilling WCT criteria.

Polymorphic VTs and SWCTs with varying atrioventricular conduction (e.g. atrial fibrillation) were not evaluated. Only WCTs with a paired subsequent, baseline ECG and definite clinical diagnosis established by the patient's overseeing physician were analyzed. Abbreviated WCTs (e.g. three beat run of non-sustained VT) occurring within a dominant baseline ECG rhythm were not evaluated. Electrocardiogram pairs demonstrating irrevocably faulty computerized ECG measurements due to pacing stimuli or ECG artifact were excluded.

Derivation and validation cohorts

The derivation cohort consisted of 317 paired WCT (157 VT, 160 SWCT) and baseline ECGs from 213 patients presenting to the Mayo Clinic Rochester (September 2011–March 2015). The validation cohort was comprised of 284 paired WCT (116 VT, 168 SWCT) and baseline ECGs from 206 patients presenting to the Mayo Clinic Rochester and/or Mayo Clinic Health System of South Eastern Minnesota – including 40 additional patient care locations: community hospitals, emergency departments, and outpatient clinics (April 2015–November 2016).

Fig. 1 shows a flow diagram of validation cohort selection. One-hundred sixteen out of 400 consecutive WCTs were excluded. Seventy abbreviated WCTs occurring within a dominant baseline ECG rhythm were excluded. Twenty-nine WCTs did not have a subsequent baseline ECG. Nine narrow-complex tachycardias exhibited inappropriately prolonged QRS duration measurements. Five ECG pairs were disqualified due to faulty QRS amplitude measurements of pacing stimuli ($n = 4$) or ventricular assist device artifact ($n = 1$). Two WCTs were recorded using unconventional ECG lead placements (i.e. right-sided chest leads). One WCT did not have a definite clinical diagnosis.

ECG laboratory diagnosis

Formal ECG interpretation was provided by a rotating consortium of expert electrocardiographers supervising the Mayo Clinic's ECG Laboratory – 7 heart rhythm cardiologists and 14 non-heart rhythm cardiologists. The ECG interpretation strategy(s) utilized to differentiate WCTs was determined by the supervising interpreter. Supervising interpreters had access to patients' electronic medical record and archived ECGs. Interpretive diagnoses of WCTs were semi-qualitatively re-categorized according to diagnostic certainty: [1] definite VT, [2] probable VT, [3] definite SWCT, [4] probable SWCT and [5] undifferentiated.

Clinical diagnoses

Clinical diagnoses (VT or SWCT) were established by the patient's overseeing physician. Physicians responsible for clinical diagnoses were categorized according to their level of expertise: [1] heart rhythm cardiologist, [2] non-heart rhythm cardiologist and [3] non-cardiologist. The "most expert" overseeing physician (heart rhythm cardiologist > non-heart rhythm cardiologist > non-cardiologist) determined the patient's final clinical diagnosis.

Patient characteristics

Clinical data including age, gender, coronary artery disease, prior myocardial infarction (MI), prior cardiac surgery, congenital heart disease, cardiomyopathy (ischemic or non-ischemic), most proximate valuation of left ventricular ejection fraction (LVEF) (≥50%, 49–31%, ≤30%), prior pacemaker or AICD implantation, and ongoing Vaughan-Williams Class I and III antiarrhythmic drug (AAD) use were recorded from electronic medical record.

Automated ECG measurements

Computerized ECG measurements including QRS duration (ms), corrected QT interval duration (ms), and frontal plane QRS axis (°) (i.e. R axis on ECG printout) were provided by *GE Healthcare's* MUSE ECG interpretation software. QRS complex waveform measurements were derived from the

dominant QRS complex "template" within individual ECG leads. The amplitude (μV) of QRS waveforms above (*r*/*R* and *r*′/*R*′) and below (*q*/*QS*, *s*/*S*, and *s*′/*S*′) the isoelectric baseline were accessed from *GE Healthcare's* MUSE "measurement matrix" data archives. Only amplitude measurements representative of QRS complex waveforms were analyzed.

ECG Calculations

QRS duration change

The absolute difference in QRS duration (ms) measurements between paired WCT and baseline ECGs was calculated.

QRS axis change

The absolute change in frontal plane QRS axis (°) between paired WCT and baseline ECGs was calculated. The magnitude of QRS axis change ranged from 0° (i.e. no axis shift) to 180° (i.e. complete axis shift to the straight angle opposite).

Frontal and horizontal percent amplitude change

Frontal and horizontal percent amplitude change (PAC) is a measure of percent (%) QRS amplitude change between paired WCT and baseline ECGs. Both PAC calculations utilize computerized QRS waveform (*q*/*QS*, *r*/*R*, *s*/*S*, *r*′/*R*′, *s*′/*S*′) amplitude (μV) measurements from select ECG leads within their corresponding frontal (aVR, aVL, aVF) or horizontal (V1, V4, V6) ECG plane (Supplementary Fig. S1).

WCT Formula

The WCT Formula delivers VT probability estimates (0.000%–99.999%) using computerized ECG measurements and mathematical computations derived from paired WCT and baseline ECGs. The logistic regression structure of the WCT Formula is outlined below:

$$\mathbf{X}_{\beta} = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 = \mathrm{Ln}\left(\frac{P}{1-P}\right)$$

$$\mathbf{X}_{\beta} = -14.4289 + (0.0623)(\text{WCT QRS duration}) + (0.0279)(\text{Frontal PAC}) + (0.0391)(\text{Horizontal PAC}) = \mathrm{Ln}\left(\tfrac{P}{1-P}\right)$$

$$\mathbf{P} = \left(\frac{e^{-14.4289+(0.0623)(\text{WCT duration})+(0.0279)(\text{Frontal PAC})+(0.0391)(\text{Horizontal PAC})}}{1+e^{-14.4289+(0.0623)(\text{WCT duration})+(0.0279)(\text{Frontal PAC})+(0.0391)(\text{Horizontal PAC})}}\right)$$

The WCT Formula's explanatory variables include three VT predictors (X_x): WCT QRS duration (ms), frontal PAC (%) and horizontal PAC (%). Each VT predictor (X_x) is assigned a beta coefficient (β_x) according to its influence on the binary outcome (VT or SWCT). The "constant" term (B_0) is the y-intercept of the least squares regression line. The weighted sum predictor (X_β) and VT probability (P) are derived from integrated VT predictor (X_x) values.

Statistical evaluation

Categorical variables were compared using Chi-square tests. Wilcoxon rank-sum tests were used to compare continuous variables. A logistic regression model (i.e. WCT Formula) was assembled using independent VT predictors. A receiver operator characteristic curve was used to summarize the WCT Formula's diagnostic performance for the derivation cohort. Paired ECGs of the validation cohort were assigned estimated VT probabilities (0.000%–99.999%) by the WCT Formula. The diagnostic performance of various VT probability partitions was appraised according to their agreement with the overseeing physician's clinical diagnosis. Kappa (κ) statistics were used to assess agreement between the WCT Formula's 50% VT probability partition (VT ≥ 50%; SWCT < 50%), clinical diagnosis, and ECG laboratory interpretation. Agreement was characterized as "almost perfect" (κ = 0.81–1.00), "substantial" (κ = 0.61–0.80), "moderate" (κ = 0.41–0.60), "fair" (κ = 0.20–0.40), "slight" (κ = 0.00–0.20), and "poor" (κ < 0.00) [12]. McNemar's test was used to evaluate for lack of agreement among diagnostic standards. Statistical analyses were completed using SAS version 9.4 (*SAS Institute*, Cary, North Carolina).

Results

Part I: WCT Formula derivation

Derivation cohort

Clinical diagnosis and ECG laboratory interpretation data is summarized in Supplementary Table S1. The majority (86.1%) of clinical diagnoses were established by heart rhythm or non-heart rhythm cardiologists. Most (91.8%) WCTs were assigned definitive or probable interpretive diagnoses by the ECG laboratory. Just over half of WCTs (51.4%) were derived from patients who underwent an electrophysiology procedure and/or possessed an implantable device.

Patient characteristics are summarized in Supplementary Table S2. The VT group included more ECG pairs from patients with coronary artery disease, prior MI, prior cardiac surgery, ongoing AAD use, ischemic cardiomyopathy, non-ischemic cardiomyopathy, and implanted AICD. Baseline ECGs with ventricular pacing were more common in the VT group, whereas preexisting BBB was more prevalent in the SWCT group. No SWCTs demonstrated atrioventricular pre-excitation.

ECG measurements and calculations

Paired ECGs in the VT group expressed greater baseline ECG QRS duration, WCT QRS duration, QRS duration change, QRS axis change, frontal PAC and horizontal PAC than the SWCT group (Table 1). Furthermore, the VT group demonstrated greater WCT QRS duration, QRS axis change, frontal PAC and horizontal PAC among each baseline ECG subgroup: QRS duration < 120 ms, QRS duration ≥ 120 ms, and ventricular pacing (Table 2).

Logistic regression model

The WCT Formula's logistic regression model, composed of WCT QRS duration ($p < 0.001$), frontal PAC ($p < 0.001$) and horizontal PAC ($p < 0.001$), demonstrated favorable WCT differentiation (AUC 0.96) for the derivation cohort (Fig. 2). The median and proportional distribution of WCT Formula constituents are illustrated in Fig. 3.

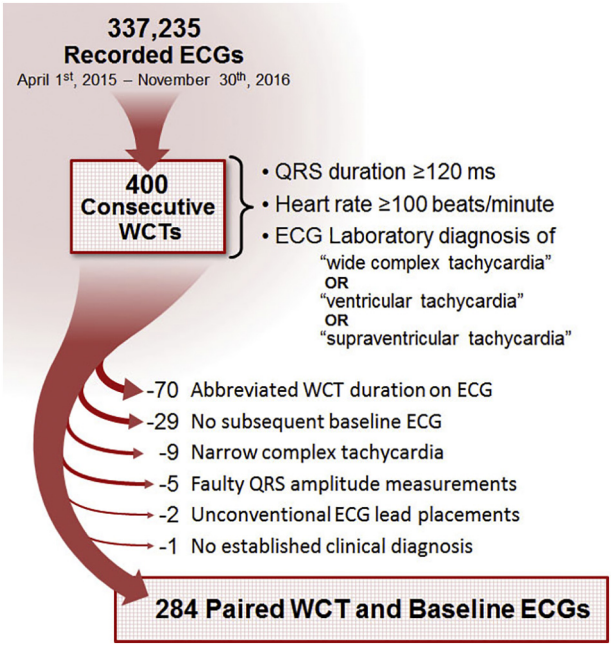

Fig. 1. Validation cohort selection. Flow diagram depicting validation cohort selection.

Part II: WCT Formula validation

Validation cohort

Clinical diagnosis and ECG laboratory interpretation data is summarized in Supplementary Table S3. When compared with the derivation cohort, the validation cohort included more WCTs with definitive or probable interpretive diagnoses coded by the ECG laboratory (validation cohort: 98.2% vs. derivation cohort: 91.8%) (Supplementary Table S4).

Patient characteristics are summarized in Supplementary Table S5. Apart from having varying proportions of ECG pairs from patients with severely reduced LVEF (<30%) (derivation cohort: 37.9% vs. validation cohort: 22.5%) and baseline ventricular pacing (derivation cohort: 24.9% vs. validation cohort: 17.6%), no differences were observed between the validation and derivation cohorts (Supplementary Table S6).

WCT Formula: diagnostic performance

The WCT Formula's VT probability assignments yielded effective VT and SWCT differentiation (Table 3, Fig. 4). Most (76.7%) VTs were categorized as having high VT probability (≥90.0%) with a compatible positive predictive value (97.8%). Similarly, most (70.8%) SWCTs were categorized as having low VT probability (<10.0%) with a compatible negative predictive value (97.5%). A 50% VT probability partition yielded the highest overall accuracy (91.5%) with strong sensitivity (89.7%) and specificity (92.9%) for VT. Overall accuracy did not differ among patients with (90.9%) or without (91.8%) an electrophysiology procedure ($p = 0.79$).

Table 1
Electrocardiographic variables.[a]

	SWCT (n = 160)	VT (n = 157)	p value
Baseline QRS duration (ms)	135.9 (28.1)	147.5 (44.0)	0.03
Baseline QTc duration (ms)	483.2 (43.4)	500.4 (63.2)	0.07
WCT QRS duration (ms)	144.4 (18.1)	177.1 (32.4)	<0.001
QRS duration change (ms)	18.1 (22.4)	45.1 (34.3)	<0.001
QRS axis change (°)	24.9 (32.6)	82.2 (56.7)	<0.001
Frontal PAC (%)	34.9 (28.2)	124.2 (87.1)	<0.001
Horizontal PAC (%)	44.8 (25.2)	115.3 (62.9)	<0.001

[a] Standard deviation is in parentheses. PAC = percent amplitude change; SWCT = supraventricular tachycardia; VT = ventricular tachycardia.

Twelve out of 116 (10.3%) "clinical VTs" were categorized as SWCT using the WCT Formula's 50% VT probability partition – 6 expressed a QRS duration <140 ms; 9 demonstrated a frontal plane QRS axis shift < 40°; 4 exhibited an unchanged QRS configuration at lead V1; 2 exhibited an unchanged QRS configuration at lead V6 (Supplementary Table S7).

Twelve out of 168 (7.1%) "clinical SWCTs" were categorized as VT using the WCT Formula's 50% VT probability partition – 7 expressed a QRS duration ≥ 160 ms; 9 demonstrated a frontal plane QRS axis shift ≥ 40°; 5 exhibited QRS morphology changes at lead V1; 12 exhibited QRS morphology differences at lead V6 (Supplementary Table S8).

WCT Formula: diagnostic agreement

Supplementary Fig. S2 summarizes the distribution of shared and non-shared WCT diagnoses between the WCT Formula's 50% VT probability partition, clinical diagnosis and ECG laboratory interpretation. The WCT Formula's VT diagnoses yielded substantial to almost perfect agreement with ECG laboratory interpretation ($\kappa = 0.78$, CI 0.71–0.85) and clinical diagnosis ($\kappa = 0.83$, CI 0.77–0.90). The WCT Formula's SWCT diagnoses demonstrated substantial to almost perfect agreement with ECG laboratory interpretation ($\kappa = 0.72$, CI 0.65–0.80) and clinical diagnosis ($\kappa = 0.83$, CI 0.77–0.90). The WCT Formula and ECG laboratory did not differ in their degree of agreement with clinical diagnosis ($p = 0.72$).

Discussion

We present a novel WCT differentiation method that can be automatically implemented by CEI software. Through an exclusive examination of computerized measurements derived from paired WCT and baseline ECGs, we unified well-established and customized VT predictors into a logistic regression equation (i.e. WCT Formula) capable of automatic VT probability prediction.

WCT Formula: prospective evaluation

In a prospective evaluation, the WCT Formula correctly differentiated the vast majority of WCTs. In doing so, the WCT Formula produced a VT probability continuum that accurately segregates most (~75%) WCTs as having high (≥90%) or low (<10%) VT probability. Furthermore, the WCT Formula independently achieved favorable diagnostic agreement with our institution's physicians and ECG laboratory. Remarkably, despite the ECG laboratory's presumably persuasive influence on patients' final clinical diagnosis, the WCT Formula agreed with patients' clinical diagnosis just as well as the ECG laboratory.

WCT Formula: explanation and rationale

Computerized ECG measurements

By design, the WCT Formula operates solely on computerized ECG measurements derived from contemporary CEI software. This approach permits the formation of automated VT prediction models that may be incorporated in CEI software.

Logistic regression model

The WCT Formula delivers VT probability estimations (0.000% - 99.999%) from independent VT predictors concomitantly "weighed" according to their influence on the binary outcome (VT vs. SWCT). Given each VT predictor's direct relationship with VT likelihood, the WCT Formula estimates higher VT probability for ECG pairs with greater WCT QRS duration, frontal PAC and/or horizontal PAC (Supplementary Fig. S3). In an opposite manner, the WCT Formula estimates lower VT probability for ECG pairs with smaller WCT QRS duration, frontal PAC and/or horizontal PAC (Supplementary Fig. S4).

Table 2
Electrocardiographic variables among baseline ECG sub-groups.[a]

Electrocardiographic measurements	Baseline QRS duration <120 ms VT (n = 54) SWCT (n = 42)			Baseline QRS duration ≥ 120 ms VT = (n = 103) SWCT (n = 118)			Baseline ventricular pacing VT (n = 69) SWCT (n = 10)		
	VT	SWCT	p value	VT	SWCT	p value	VT	SWCT	p value
WCT QRS duration (ms)	171.1 (33.1)	143.1 (19.9)	< 0.001	180.2 (31.8)	144.9 (17.5)	< 0.001	187.2 (26.4)	157.2 (17.7)	< 0.001
QRS duration change (ms)	71.5 (32.4)	41.5 (21.1)	< 0.001	31.3 (26.3)	11.2 (16.8)	< 0.001	37.5 (30.7)	23.0 (45.0)	0.19
QRS axis change (°)	93.7 (50.5)	45.1 (47.6)	< 0.001	76.2 (59.1)	17.8 (21.2)	< 0.001	90.2 (58.2)	26.6 (26.7)	< 0.001
Frontal PAC (%)	116.2 (59.0)	47.0 (25.1)	< 0.001	128.4 (98.7)	30.6 (29.4)	< 0.001	135.8 (94.6)	61.9 (75.6)	0.004
Horizontal PAC (%)	128.8 (72.6)	57.9 (26.7)	< 0.001	108.2 (56.3)	40.1 (23.0)	< 0.001	123.6 (66.4)	49.2 (25.4)	< 0.001

[a] Standard deviation is in parentheses. PAC = percent amplitude change; SWCT = supraventricular wide complex tachycardia; VT = ventricular tachycardia; WCT = wide complex tachycardia.

Frontal and horizontal PAC calculations

The means by which VT may propagate within and depolarize the ventricular myocardium is virtually unlimited. As a consequence, VTs may express an immeasurable variety of QRS complexes that are electrocardiographically distinct from their respective baseline ECG. In contrast, the manner SWCTs depolarize the ventricular myocardium is ordinarily confined to the same His-Purkinje network or implantable device system utilized by the baseline heart rhythm; in rarer instances, SWCTs may be due to ventricular pre-excitation using separate atrioventricular accessory pathways. As a result, many SWCTs, especially those with preexisting aberrancy or ventricular pacing, demonstrate similar QRS configurations as the baseline ECG. On the contrary, SWCTs arising from "functional" aberration exhibit recognizably different QRS complex configurations. However, since most functional SWCTs demonstrate antegrade impulse propagation and ventricular depolarization confined in the His-Purkinje network, they are destined to express a relatively constrained variety of electrocardiographically distinct QRS complexes.

Provided that QRS morphology changes are naturally linked to changes in QRS waveform amplitude, we hypothesized the extent of QRS amplitude change between paired WCT and baseline ECGs would help distinguish VT and SWCT. Since QRS amplitude changes signal attendant changes in the mean electrical vector of ventricular depolarization, we also hypothesized the extent of change in the mean electrical vector is primarily influenced by the underlying WCT rhythm (Fig. 5).

The frontal and horizontal PAC calculations were designed to quantify mean electrical vector changes between paired WCT and baseline ECGs. Both calculations determine the percent (%) change in QRS amplitude that occurs at specific ECG lead combinations within the frontal (aVR, aVL, aVF) or horizontal (V1, V4, V6) ECG plane. In order to broadly detect and quantify changes in the axis and/or voltage intensity of the mean electrical vector, each PAC calculation utilizes ECG leads that are in effect separated by approximately 120°. In the case of V4, its mathematical inverse equivalent, "inverse V4," is separated equidistant from V1 and V6 by approximately 120°.

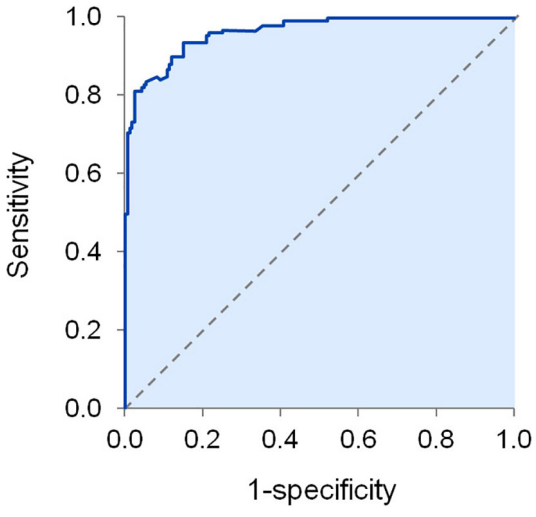

Fig. 2. Diagnostic performance. Receiver operating characteristic curve for the WCT Formula (AUC of 0.96).

Given that VT expresses a more expansive means to depolarize the ventricular myocardium, we expected it would commonly demonstrate larger changes to the mean electrical vector within the frontal and horizontal ECG planes. Therefore, we similarly anticipated VT would ordinarily yield greater frontal and horizontal PACs than SWCT.

Our findings are in agreement with the multivariate analysis reported by Griffith and colleagues [13]. In their study, large frontal plane QRS axis shifts (≥40°) from the baseline sinus rhythm ECG were found to be the 3rd strongest independent VT predictor (after MI history and lead aVF QRS configuration) among 15 clinical and 11 electrocardiographic variables. In a similar manner, each PAC calculation detects sizable changes in the mean electrical axis of ventricular depolarization. Yet, more advantageously, both PAC calculations quantify changes not only in the mean electrical axis but also the voltage intensity and/or QRS morphologic configuration produced by ventricular depolarization.

Our findings are also supported by observations described by Dongas et al. in 1985 [14]. In their study, WCTs with unchanged QRS morphologies (at leads V1, II and III) compared to the preexisting BBB in sinus rhythm were almost invariably SWCT, while WCTs with observably different QRS morphologies were likely VT. Since variations to QRS morphology are closely linked with changes in QRS amplitude, we unsurprisingly found SWCT generated smaller frontal and horizontal PACs than VT among patients with baseline ECG QRS prolongation (QRS duration ≥ 120 ms). Intriguingly, we observed SWCT produces smaller frontal and horizontal PACs than VT among patients without baseline ECG QRS prolongation (QRS duration < 120 ms). That is to say, our findings suggest functional SWCTs, morphologically distinct from their baseline ECG, similarly generate smaller PACs than VT.

WCT Formula: strengths

Automated application

The WCT Formula does not rely upon ECG interpreters' ability to recall and manually apply conventional WCT differentiation criteria. Rather, the WCT Formula is designed to automatically deliver estimations of VT probability irrespective of the ECG reader's interpretation abilities. Successful application merely requires automated ECG measurements derived from the WCT and baseline heart rhythm – which may be recorded before or after the WCT event.

VT probability estimation

At present, the preferred diagnostic strategy of manual WCT differentiation methods is to assign absolute VT or SWCT diagnoses according to the presence (or absence) of select differentiation criteria [6,7,9,10]. While this approach is meant to help clinicians commit to correct VT

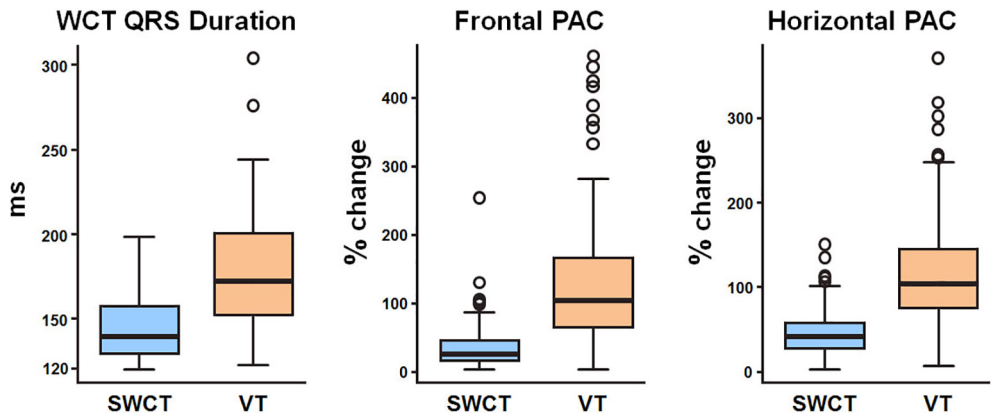

Fig. 3. WCT Formula constituents. Box-plots demonstrating the median and proportional distribution of WCT QRS duration (ms), frontal PAC (%) and horizontal PAC (%).

Table 3
WCT Formula VT probability partitions.[a]

VT probability partition	Accuracy (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Positive LR	Negative LR
99%	78.5	49.1 (40.0–58.2)	98.8 (97.2–100.0)	96.6 (92.2–100.0)	73.8 (68.0–79.5)	41.28 (10.28–165.72)	0.51 (0.43–0.62)
90%	88.9	76.7 (69.0–84.4)	98.8 (97.2–100.0)	97.8 (94.8–100.0)	86.0 (81.2–90.9)	64.44 (16.19–256.50)	0.24 (0.17–0.33)
75%	90.1	81.9 (74.9–88.9)	95.8 (92.8–98.9)	93.1 (88.2–98.0)	88.5 (83.8–93.1)	19.66 (9.47–40.80)	0.19 (0.13–0.28)
50%	91.5	89.7 (84.1–95.2)	92.9 (89.0–96.8)	89.7 (84.1–94.2)	92.9 (89.0–96.8)	12.55 (7.25–21.73)	0.11 (0.07–0.19)
25%	89.1	94.8 (90.8–98.9)	85.1 (79.7–90.5)	81.5 (74.9–88.0)	96.0 (92.8–98.1)	6.37 (4.43–9.17)	0.06 (0.03–0.13)
10%	81.7	97.4 (94.5–100.0)	70.8 (64.0–77.7)	69.8 (62.7–76.8)	97.5 (94.9–100)	3.34 (2.63–4.24)	0.04 (0.01–0.11)
1%	50.4	100.0 (96.9–100.0)	16.1 (10.5–21.6)	44.1 (39.1–51.2)	100 (87.2–100.0)	1.19 (1.12–1.27)	0.00

[a] Numbers in parentheses are 95% confidence intervals. LR = Likelihood Ratio; NPV = Negative Predictive Value; PPV = Positive Predictive Value; VT = ventricular tachycardia.

or SWCT diagnoses, it tends to leave them unaware of the likelihood that their diagnoses are actually accurate. In contrast, the WCT Formula simultaneously "weighs" multiple coexistent WCT predictors to deliver an unambiguous estimation of VT likelihood.

WCT Formula: weaknesses

According to the WCT Formula's structure, "actual" VTs may be erroneously classified as SWCT if they demonstrate narrow QRS durations (e.g. fascicular VT) and/or very similar mean electrical vectors compared to the baseline ECG (e.g. bundle branch re-entry). Correspondingly, we observed erroneous SWCT predictions for clinical VTs demonstrating narrower QRS durations and/or similar QRS configurations compared to the baseline ECG (Supplementary Table S7, Supplementary Fig. S5). On the other hand, the WCT Formula may erroneously classify "actual" SWCTs as VT if they express wider QRS durations (e.g. QRS prolongation due to AAD drug use) and/or pronounced changes to the mean electrical vector (e.g. new left BBB aberrancy). Accordingly, we observed erroneous VT predictions for clinical SWCTs exhibiting wider QRS durations and/or dissimilar QRS configurations compared to the baseline ECG (Supplementary Table S8, Supplementary Fig. S6).

The WCT Formula's application would be expectedly vulnerable to inaccurate computerized QRS duration and/or amplitude measurements. Although our study demonstrates that modern-day CEI software can successfully accommodate the WCT Formula, a small proportion of ECG pairs required exclusion due to faulty computerized measurements. Therefore, further refinements in QRS complex and ECG artifact (e.g. pacing stimuli) identification are still needed to promote the WCT Formula's application.

Successful WCT Formula application requires contemporary CEI software to simultaneously evaluate paired WCT and baseline ECGs. In circumstances where WCT patients present without a previously recorded and archived ECG to be utilized by the WCT Formula, acquisition of patients' subsequent baseline ECG, following WCT event resolution, would be necessary for successful WCT Formula application. In such cases, clinicians will need to temporarily rely on conventional WCT differentiation methods to guide their decision-making.

Study limitations

Our study utilized clinically encountered WCTs formally diagnosed by our institution's ECG laboratory and physicians. Though a substantial proportion of WCTs were derived from patients who did not undergo an electrophysiology procedure, the WCT Formula's overall accuracy did not differ among patients with or without an accompanying electrophysiology procedure.

The WCT Formula was derived and evaluated using paired WCT and subsequent baseline ECGs separated by varying, sometimes lengthy,

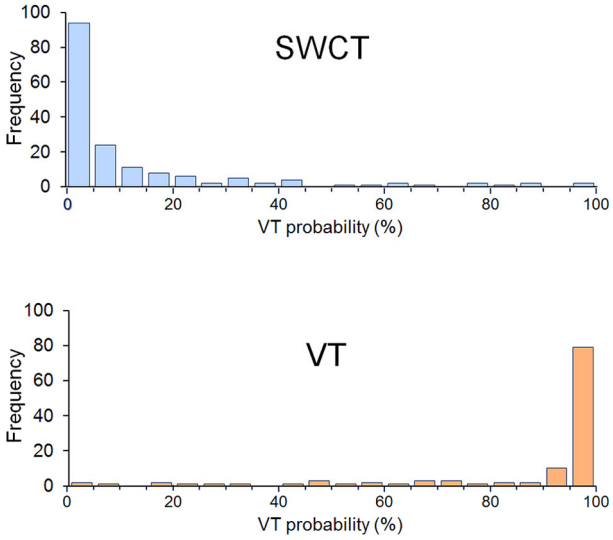

Fig. 4. VT and SWCT differentiation. Histograms demonstrating the distribution of VT and SWCT according to the WCT Formula's VT probability estimates.

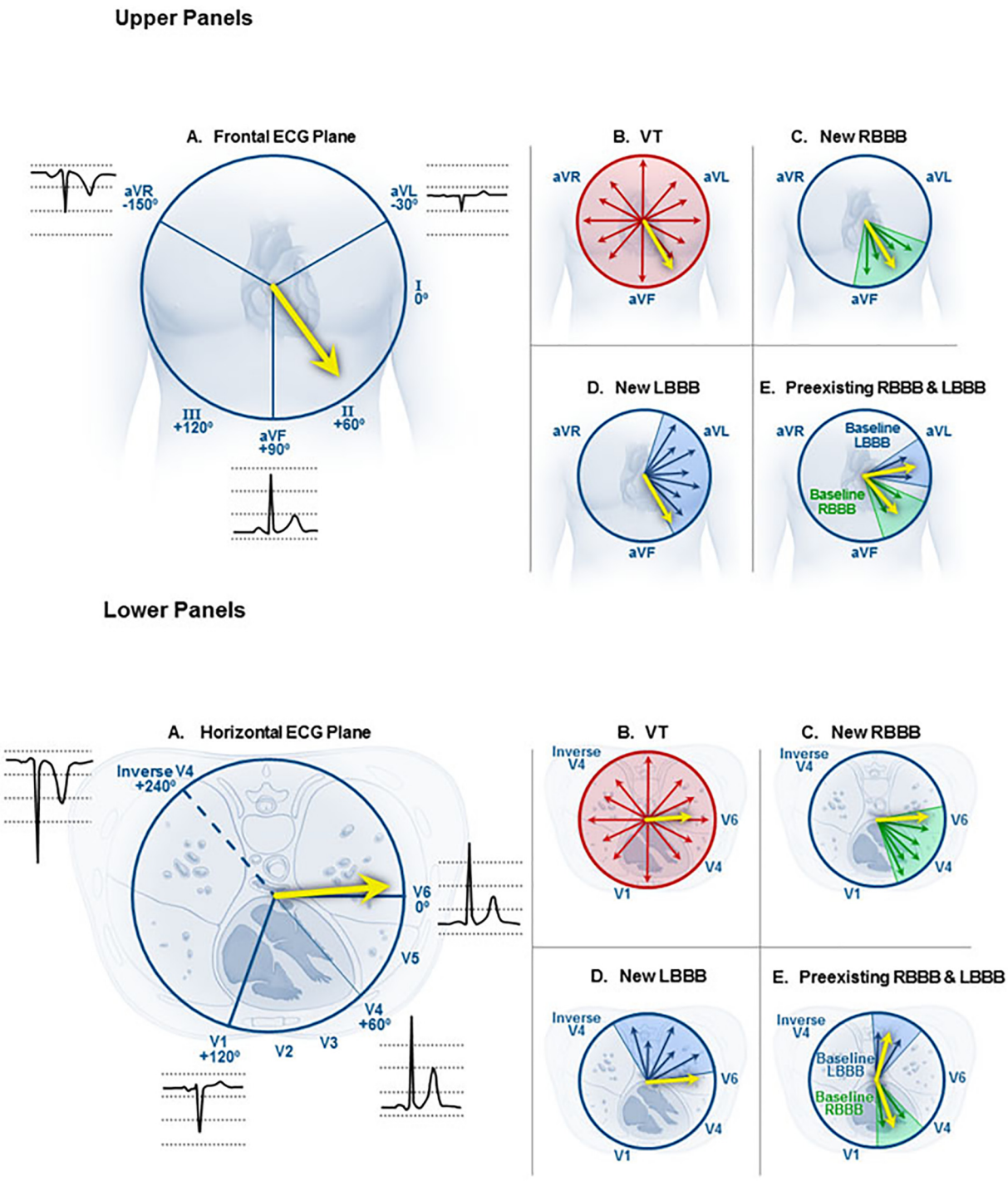

Fig. 5. Mean electrical vector changes upon WCT initiation. Summary of mean electrical vector changes that occur within the frontal (upper panels) and horizontal (lower panels) ECG planes after WCT initiation. Heavy yellow arrows represent the mean electrical vector of the baseline ECG. Color-shaded regions represent the expected range of mean electrical vectors after WCT onset. Panel A shows the prototypical mean electrical vector for a normal baseline ECG. VT (Panel B) demonstrates an expansive range of possible mean electrical vectors. SWCTs due to functional RBBB (Panel C) or LBBB (Panel D) exhibit a constrained range of potential mean electrical vectors. SWCTs due to preexisting BBB (Panel E) demonstrate minimal mean electrical vector changes.

time intervals. Deviations in ECG electrode placement and/or major changes to the patient's baseline ECG (e.g. new ventricular pacing) were able to negatively influence the WCT Formula's performance. Moreover, it is conceivable unexpected differences in model performance would be recognized when using baseline ECGs acquired before the WCT event. Thus, additional research is necessary to determine the WCT Formula's efficacy using baseline ECGs recorded [1] without variations in ECG electrode placement, and [2] before WCT events.

Despite not being intentionally excluded, no SWCTs exhibiting atrioventricular pre-excitation were analyzed. Additional research is needed to evaluate the WCT Formula's capacity to distinguish VT from pre-excited SWCTs.

The WCT Formula's diagnostic performance was not directly evaluated against other WCT differentiation methods [6–11]. Although the WCT Formula compares favorably to independent appraisals of manually-applied WCT differentiation methods [15–19], “head to

head" evaluations are needed to make an acceptable comparison of diagnostic performance. Thus, further research is necessary to determine whether the WCT Formula has diagnostic superiority over conventional interpretation methods.

Conclusions

The WCT Formula is an example of how modern-day CEI software could be used to automatically distinguish VT and SWCT. This novel WCT differentiation approach has the natural advantage of automatically delivering estimations of VT probability irrespective of clinicians' ECG interpretation skills. The incorporation of similar automated methods into CEI software may improve clinicians' ability to accurately distinguish VT and SWCT.

Funding

This work was supported by the Department of Cardiovascular Diseases, Mayo Clinic.

Acknowledgements

The authors thank Mr. Kevin M. Youel and Mr. Bryce W. Bergene of Mayo Clinic's Media Support Service for their exceptional contribution to this present article's figure designs.

Author contributions

Conception/design: AMM; analysis and interpretation: AMM, CVD; manuscript drafting and revision: all authors; final approval: all authors.

Conflict of interest statement

Authors, Adam May and Peter Brady, are obliged to disclose that they are "would be" beneficiaries of intellectual property that currently has "patent pending" status. The technology in question relates directly to this manuscript's content. This technology was developed without industry funding or influence, and was disclosed to Mayo Clinic Ventures who possesses the intellectual property rights. Attempts to market this invention to industry stakeholders has not yet taken place.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jelectrocard.2019.02.008.

References

[1] Stewart RB, Bardy GH, Greene HL. Wide complex tachycardia - misdiagnosis and outcome after emergent therapy. Ann Intern Med 1986;104:766–71.
[2] Buxton AE, Marchlinski FE, Doherty JU, Flores B, Josephson ME. Hazards of intravenous verapamil for sustained ventricular tachycardia. Am J Cardiol 1987;59:1107–10.
[3] Wellens HJ, Bar FW, Lie KI. The value of the electrocardiogram in the differential diagnosis of a tachycardia with a widened QRS complex. Am J Med 1978;64:27–33.
[4] Akhtar M, Shenasa M, Jazayeri M, Caceres J, Tchou PJ. Wide QRS complex tachycardia. Reappraisal of a common clinical problem. Ann Intern Med 1988;109:905–12.
[5] Kindwall KE, Brown J, Josephson ME. Electrocardiographic criteria for ventricular tachycardia in wide complex left bundle branch block morphology tachycardias. Am J Cardiol 1988;61:1279–83.
[6] Brugada P, Brugada J, Mont L, Smeets J, Andries EW. A new approach to the differential diagnosis of a regular tachycardia with a wide QRS complex. Circulation 1991;83:1649–59.
[7] Griffith MJ, Garratt CJ, Mounsey P, Camm AJ. Ventricular tachycardia as default diagnosis in broad complex tachycardia. Lancet 1994;343:386–8.
[8] Lau EW, Pathamanathan RK, Ng GA, Cooper J, Skehan JD, Griffith MJ. The Bayesian approach improves the electrocardiographic diagnosis of broad complex tachycardia. Pacing Clin Electrophysiol 2000;23:1519–26.
[9] Vereckei A, Duray G, Szenasi G, Altemose GT, Miller JM. New algorithm using only lead aVR for differential diagnosis of wide QRS complex tachycardia. Heart Rhythm 2008;5:89–98.
[10] Pava LF, Perafan P, Badiel M, et al. R-wave peak time at DII: a new criterion for differentiating between wide complex QRS tachycardias. Heart Rhythm 2010;7:922–6.
[11] Jastrzebski M, Sasaki K, Kukla P, Fijorek K, Stec S, Czarnecka D. The ventricular tachycardia score: a novel approach to electrocardiographic diagnosis of ventricular tachycardia. Europace 2016;18:578–84.
[12] Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977;33:159–74.
[13] Griffith MJ, de Belder MA, Linker NJ, Ward DE, Camm AJ. Multivariate analysis to simplify the differential diagnosis of broad complex tachycardia. Br Heart J 1991;66:166–74.
[14] Dongas J, Lehmann MH, Mahmud R, Denker S, Soni J, Akhtar M. Value of preexisting bundle branch block in the electrocardiographic differentiation of supraventricular from ventricular origin of wide QRS tachycardia. Am J Cardiol 1985;55:717–21.
[15] Isenhour JL, Craig S, Gibbs M, Littmann L, Rose G, Risch R. Wide-complex tachycardia: continued evaluation of diagnostic criteria. Acad Emerg Med 2000;7:769–73.
[16] Lau EW, Ng GA. Comparison of the performance of three diagnostic algorithms for regular broad complex tachycardia in practical application. Pacing Clin Electrophysiol 2002;25:822–7.
[17] Jastrzebski M, Kukla P, Czarnecka D, Kawecka-Jaszcz K. Comparison of five electrocardiographic methods for differentiation of wide QRS-complex tachycardias. Europace 2012;14:1165–71.
[18] Kaiser E, Darrieux FC, Barbosa SA, et al. Differential diagnosis of wide QRS tachycardias: comparison of two electrocardiographic algorithms. Europace 2015;17:1422–7.
[19] May AM, Brenes-Salazar JA, DeSimone CV, et al. Electrocardiogram algorithms used to differentiate wide complex tachycardias demonstrate diagnostic limitations when applied by non-cardiologists. J Electrocardiol 2018;51:1103–9.