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Recommended Citation
Kashou, Anthony H; Evenson, Christopher M; Noseworthy, Peter A; Muralidharan, Thoddi R; DeSimone, Christopher V; Deshmukh, Abhishek J; Asirvatham, Samuel J; and May, Adam M, "Differentiating wide complex tachycardias: A historical perspective." Indian Heart Journal. 73, 1. 7 - 13. (2021). https://digitalcommons.wustl.edu/oa_4/620
Differentiating wide complex tachycardias: A historical perspective

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Abstract
One of the most critical and challenging skills is the distinction of wide complex tachycardias into ventricular tachycardia or supraventricular wide complex tachycardia. Prompt and accurate differentiation of wide complex tachycardias naturally influences short- and long-term management decisions and may directly affect patient outcomes. Currently, there are many useful electrocardiographic criteria and algorithms designed to distinguish ventricular tachycardia and supraventricular wide complex tachycardia accurately; however, no single approach guarantees diagnostic certainty. In this review, we offer an in-depth analysis of available methods to differentiate wide complex tachycardias by retrospectively examining its rich literature base – one that spans several decades.

1. WCT definition and etiologies
Wide complex tachycardia (WCT) is a general term that broadly encompasses ventricular tachycardia (VT) and supraventricular wide complex tachycardia (SWCT). Simply defined, WCTs are rapid heart rhythms (i.e., ≥100 beats per minute) that simultaneously possess a prolonged QRS duration (i.e., ≥120 ms). In general, WCTs include VT, SWCT due to aberrant conduction, SWCT owing to pre-excitation via accessory pathway conduction, SWCTs due to QRS prolongation brought forth by toxic-metabolic derangements (e.g., hyperkalemia), and rapid ventricular pacing. Among these, VT is considered the most common1 – accounting for about 80% of WCTs sampled from patients evaluated in electrophysiology laboratories.2-7 However, the prevalence of various WCT etiologies differs considerably according to the examined sample population. At present, only a few retrospective studies have attempted to wholly examine any WCT that was encountered in actual clinical practice.8-10 As such, the true incidence of VT among WCTs in real-life clinical settings remains largely uncertain.

2. WCT differentiation using 12-lead ECG interpretation
Successful WCT differentiation hinges upon the physician's ability to accurately interpret a 12-lead electrocardiogram (ECG). This difficult task may be accomplished using the ever-expanding arsenal of manually-applied and computer-aided ECG algorithms and criteria.2-4,6,7,11-16 Beginning in the 1960s, a steady stream of novel and thoughtfully designed manual ECG interpretation criteria and algorithms have emerged to help clinicians differentiate WCTs successfully – each proving their diagnostic value in controlled research settings. However, each of these manual WCT differentiation methods possesses shortcomings. When traditional manual WCT differentiation approaches are considered more broadly, the most emblematic limitation is that their diagnostic performance inextricably relies upon clinicians' precise interpretation and execution of the prescribed manual approach – a constraint that is espoused by nearly all WCT differentiation criteria and algorithms. Unfortunately, since it is not feasible to prospectively evaluate the diagnostic performance of conventional algorithms in clinical settings, this limitation has yet to be clearly defined by evidentiary means. Therefore, we can only assume that the diagnostic efficacy of manual ECG interpretation approaches is sufficiently preserved in generalized, real-world clinical practice.

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3. Clinical implications of WCT differentiation

Patients who present with VT deserve a prompt and accurate diagnosis. Without question, VT can be life-threatening, often requiring swift diagnostic and therapeutic interventions. In the case of pulseless VT, its immediate recognition, followed by prompt external defibrillation and anti-arrhythmic drug initiation, can be lifesaving. In addition, attributable precipitant etiologies for VT, such as myocardial ischemia, must be strongly considered, especially since the therapeutic approach may be urgent coronary revascularization. In other circumstances, VT may be triggered or exacerbated by electrolyte imbalances or hemodynamic disturbances, both of which require treatment. In the absence of reversible VT precipitants, more invasive management options may be pursued, including VT ablation.

In contrast to VT, patients with SWCT generally demonstrate a more benign clinical course. By definition, SWCTs encompass a wide-ranging variety of etiologies, including sinus tachycardia, atrial tachycardia, multifocal atrial tachycardia, atrial fibrillation and flutter, atrioventricular (AV) reentrant tachycardia, and AV nodal reentrant tachycardia. In some circumstances, SWCT rhythms may cause hemodynamic instability. However, among hemodynamically stable patients, diagnostic and therapeutic interventions can be undertaken and tachyarrhythmias may be properly addressed through judicious non-pharmacological (e.g., Valsalva) or pharmacological interventions (e.g., beta-blockers or amiodarone). Rarely, invasive ablative options are needed in the acute setting but may be an option for non-pharmacologic and definitive treatment.

The hazard of inappropriately treating VT as SWCT, and vice versa, should not be underestimated. The dreaded misdiagnosis of an actual VT as an SWCT can unintentionally expose patients to an actual VT as an SWCT can unintentionally expose patients to an actual VT as an SWCT can unintentionally expose patients to an actual VT as an SWCT can unintentionally expose patients to an actual VT as an SWCT can unintentionally expose patients to an actual VT as an SWCT can unintentionally expose patients to an actual VT as an SWCT can unintentionally expose patients to an actual VT as an SWCT can unintentionally expose patients to an actual VT as an SWCT can unintentionally expose patients to an actual VT as an SWCT can unintentionally expose patients to an actual VT as an SWCT can unintentionally expose patients to an actual VT as an SWCT can unintentionally expose patients to an actual VT as an SWCT can unintentionally expose patients to an actual VT as an SWCT can unintentionally expose patients to an actual VT as an SWCT can unintentionally expose patients to an actual VT as an SWCT can 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of the evaluated VTs but was absent in all SWCTs. Thus, the authors confirmed AV dissociation to be a highly specific characteristic of VT—a diagnostic criterion that continues to be one of the most trusted electrocardiographic criteria to secure VT diagnoses.

4.4. 1988, Kindwall and Josephson: Morphological criteria—left bundle morphology

In order to complement the works of Swanick et al and Wellens et al from the decade prior, Kindwall and Josephson introduced a multicomponent differentiation approach to address WCTs having a LBBB pattern. In their work, they proposed four separate ECG criteria intended to distinguish VT from SWCT with LBBB aberrancy, including the presence of (i) an R wave with a duration of >30 ms in lead V1 or V2, (ii) any Q wave in lead V6, (iii) the onset of the QRS to the nadir of the S wave duration of >60 ms in lead V1 or V2, and (iv) notching of the down-stroke of the S wave in lead V1 or V2. When used collectively, the authors reported that the four criteria were 100% sensitive and 89% specific for VT. Though subsequent study has demonstrated limitations for the proposed criteria, they continue to function as an essential piece of what is collectively referred to as the “morphological criteria” for WCTs with a LBBB pattern.

4.5. 1988, Akhtar: Criteria supportive of VT

In 1988, Akhtar et al sought to identify electrocardiographic parameters useful in differentiating VT and SWCT. In their work, they evaluated a wide variety of ECG criteria from 150 patients with WCTs (122 VT and 28 SWCT) in order to distinguish those that enable successful WCT differentiation. The presence of four criteria were identified as being supportive of a VT diagnosis: (i) AV dissociation, (ii) positive QRS concordance, (iii) “northwest” QRS axis (i.e., QRS axis between −90° and −180°), (iv) coexisting left bundle branch block (LBBB) and right axis deviation, (v) QRS duration ≥ 140 ms for WCTs with a RBBB pattern and QRS duration ≥ 160 ms for WCTs with a LBBB pattern, and (vi) dissimilar QRS morphology during tachycardia compared to baseline preexcising bundle branch block. Like previous authors and colleagues, they did not organize these individual criteria into a serviceable diagnostic algorithm. Nonetheless, their work helped (i) establish novel criteria to differentiate WCTs effectively (e.g., northwest QRS axis) and (ii) reconfirm previously described criteria to distinguish VT from SWCT.

4.6. 1991, Brugada: The original multistep algorithm

In 1991, one of the most well-known and often utilized methods to differentiate WCTs was introduced by Brugada and colleagues. At the time of its introduction, the Brugada algorithm was the first multistep algorithm designed to differentiate VT from SWCT. The authors hoped that through its simple and straightforward application, the Brugada algorithm would help clinicians accurately and wholly commit to VT or SWCT diagnoses.

By design, the Brugada algorithm makes use of four highly specific ECG criteria, each organized in a stepwise fashion, to distinguish VT and SWCT. Algorithm users are prompted to address a sequential series of inquiries to determine whether an ECG parameter consistent with VT is present or absent. The algorithm’s prompted questions are presented in a hierarchical order:

Step 1 Is there absence of RS complexes in the precordial leads?
Step 2 Is the RS interval ≥ 100 ms in any precordial lead?
Step 3 Is AV dissociation present?
Step 4 Is the morphology criteria for VT present in leads V1-2 and V6?

If the ECG interpreter secures an affirmative response at any step in the algorithm, WCT differentiation is complete and a VT diagnosis is secured. On the other hand, if the interpreter navigates through the entire algorithm, and yields a negative response at each step, then the final diagnosis is SWCT by default.

In their original study, the authors found that the Brugada algorithm yielded strong accuracy (98%) with high diagnostic sensitivity (99%) and specificity (97%) for VT. Remarkably, of the 554 WCTs used to validate the proposed algorithm, only 5 VTs and 6 SWCTs were misclassified. Individually, the first step yielded weak sensitivity (21%) but perfect specificity (100%). After the second step, cumulative sensitivity improved (66%), and overall specificity remained strong (98%). After the third step, cumulative sensitivity further increased (82%) without a meaningful sacrifice in overall diagnostic specificity (98%). Finally, after completing all four steps, the collective sensitivity (99%) and specificity (97%) were especially strong.

However, following the Brugada algorithm’s introduction, subsequent appraisals have yet to independently reproduce the diagnostic performance ascribed by the original authors. In general, attempts to validate diagnostic performance have shown that the Brugada algorithm typically misclassifies 15–30% of
evaluated WCTs. Additionally, multiple independent studies have reported that the Brugada algorithm yields strong sensitivity (~90%) but rather modest specificity (~60%) for VT. Nevertheless, the Brugada algorithm is generally regarded as an effective diagnostic tool to differentiate WCTs, and it remains one of the most widely recognized and frequently adopted WCT differentiation strategies.

4.7. 1994, Griffith: VT as default diagnosis

In 1994, Griffith et al proposed a new framework to distinguish VT and SWCT.17 In their work, the authors devised a reversed approach to differentiate WCTs (i.e., Griffith algorithm), wherein VT, instead of SWCT, was regarded as the default diagnosis. Provided that VT is ordinarily associated with more significant morbidity and mortality compared to SWCT, the authors thoughtfully reasoned that VT ought to be the diagnosis that is less easily missed. Therefore, they constructed an approach where SWCT could only be diagnosed through the confirmation of highly specific criteria for SWCT. In other words, SWCT diagnoses may be established when the standard criteria of typical LBBB pattern (i.e., rS or QS complex in leads V1 and V2, r wave onset to S wave, etc) are met, whereas SWCT diagnoses may be reached once negative answers are obtained for any algorithm step. Thus, if classical LBBB or RBBB features are absent, then VT is the diagnosis by default.

In their study,17 the application of this reverse approach yielded an overall sensitivity and specificity for VT of 91% and 76%, respectively. Thus, while prioritizing diagnostic sensitivity for VT, an attendant reduction of specificity was observed. Similar concessions are readily appreciated in subsequent validation studies that independently evaluated the Griffith algorithm's diagnostic performance.27,28 Within the seminal report brought forth by Jastrzebski et al,28 the Griffith algorithm demonstrated strong sensitivity (94%) but weak specificity (40%) for VT, which was significantly less than the diagnostic specificity achieved by the Brugada, Bayesian, and lead II R-wave peak time (RWPT) algorithms.

4.8. 2000, Lau: Bayesian algorithm

In 2000, Lau et al29 put forth a novel WCT differentiation method to differentiate VT and SWCT using likelihood ratios (LRs). In this method (i.e., Bayesian algorithm), a predetermined pre-test odds of VT is transformed into a post-test odds of VT through the calculation odds or posterior odds of VT. In this iteration, algorithm users were prompted to sequentially address the following questions:

Step 1 Is AV dissociation present?  
Step 2 Is the width of an initial r or q wave <40 ms in V1 and V2?  
Step 3 Are classical aberrant morphological patterns consistent with bundle branch or fascicular block present?  
Step 4 Is the ratio of the voltage excursion during the initial [Vi] and terminal [Vt] 40 ms of the QRS complex (i.e., Vi/Vt) < 1 in any lead?

In the following year, the authors offered an abridged approach known as the simplified aVR algorithm.3 For this algorithm, important differences included (i) the absence of the AV dissociation criterion, (ii) the omission of the complex QRS morphology criteria, and (iii) restricting ECG examination to only lead aVR. In this iteration, algorithm users were prompted to sequentially evaluate the following questions using only lead aVR:

Step 1 Is an initial R wave present?  
Step 2 Is the width of an initial r or q wave >40 ms?  
Step 3 Is there notching on the initial downstroke of a predominately negative QRS complex?  
Step 4 Is the ventricular activation-velocity ratio $\leq 1$ (i.e., Vi/Vt ≤ 1)?

In their original reports,3,7 the Vereckei and simplified aVR algorithms yielded excellent VT and SWCT predictions (91% and 92% accuracy, respectively) and achieved marginally superior diagnostic performance compared to the Brugada algorithm. Although the original Vereckei algorithm has yet to be independently validated, subsequent appraisals of the simplified aVR algorithm have not reproduced the diagnostic performances described by the original authors.4,5,6,7,8,9,10,11 For example, as reported by Kaiser et al,7 the simplified aVR algorithm attained strong sensitivity (89%) but poor specificity (29%) for VT; interestingly, this performance was similar to what they observed for the Brugada algorithm (sensitivity 90%, specificity 36%).

Both the Vereckei and simplified aVR algorithms introduced two innovative electrophysiological concepts: (i) a dominant R wave in lead aVR is consistent with VT, and (ii) the examination of the relative differences in ventricular activation velocity between the initial and terminal components of the QRS complex can help differentiate VT and SWCT. The authors reasoned that the presence of an initial dominant R wave to be incompatible with SWCT since the initial septal and later main ventricular activation wavefronts...
produced by SWCTs ordinarily proceed away from lead aVR. Concerning relative differences in ventricular activation velocity, the authors pointed out that SWCT due to LBBB or RBBB aberrancy will usually display rapid initial QRS deflections arising from rapidly depolarized myocardial segments stimulated by preserved components of His-Purkinje network, thereby producing an r or q wave duration <40 ms and V1/Vt > 1. In contrast, since VT depolarization wavefronts commonly propagate and spread from a site of origin outside the His-Purkinje network, and thereby must utilize slower cardiomyocyte-to-cardiomyocyte conduction, they frequently generate more “slurred” initial deflections of the QRS complex (e.g., V1/Vt ≤ 1).

4.10. 2010, Pava: R-wave peak time

In 2010, Pava and colleagues⁴ proposed a straightforward stand-alone criterion for differentiating WCTs known as the lead II RWPT (R-wave peak time). As defined by the authors, the RWPT denotes the time elapsed between the QRS complex onset and peak or nadir of the first positive or negative deflection, respectively. According to the criterion, if lead II RWPT >50 ms, VT is diagnosed. Alternatively, if RWPT <50 ms in lead II, SWCT is diagnosed.

Similar to other WCT differentiation criteria,²⁻⁴¹⁹¹⁴ the lead II RWPT attempts to leverage commonly observed differences in ventricular activation velocity between VT and SWCT. In other words, it facilitates the identification of VTs that spread from a site of origin remote from specialized conduction tissue. In this circumstance, VTs must first utilize slower cardiomyocyte-to-cardiomyocyte conduction to activate the ventricular myocardium, which in turn yields more prolonged upstroke of the QRS complex (i.e., RWPT > 50 ms) than what is ordinarily observed for SWCT.

In its original report,⁴ the overall diagnostic performance of the lead II RWPT criterion was exceptional (area under the curve [AUC] 0.97) and yielded strong sensitivity (93%) and specificity (99%) for VT. However, similar to independent appraisals of other WCT differentiation methods, subsequent validation studies have yet to reproduce comparable results.⁵⁻⁸,¹¹ The independent appraisal by Jastrzebski and colleagues⁹ demonstrated that the lead II RWPT was less sensitive (60%) but more specific (83%) for VT than other conventional algorithms, including the Brugada, Griffith, Bayesian, and simplified aVR algorithms.

4.11. 2016, Jastrzebski: The VT score

In 2016, Jastrzebski and colleagues⁴ devised a novel points-based algorithm (i.e., the VT score) designed to “rule-in” VT. As discussed in their reports,²⁻⁴ the algorithm creators reasoned that VT could not be assuredly ruled out by way of traditional 12-lead ECG interpretation methods because some VTs are morphologically indistinguishable from SWCT. Additionally, the authors astutely articulated the increasingly common problem of VT over-diagnosis, which may inadvertently lead to inappropriate and unnecessary medical interventions (e.g., ICD implantation) for patients who otherwise would not be subjected to them. For these reasons, the authors were inspired to construct a points-based method that would offer confirmatory or near-definite VT diagnoses.

The VT score is comprised of seven well-established and easy-to-apply WCT differentiation criteria, each possessing high specificity for VT diagnoses: (i) an initial R wave in lead V1, (ii) an initial r wave interval > 40 ms in lead V1 or V2, (iii) a notched S wave in lead V1, (iv) an initial R wave in lead aVR, (v) RWPT > 50 ms in lead II, (vi) the absence of an RS complex in leads V1–V6, and (vii) the presence AV dissociation. To apply the algorithm, interpreters must inspect the recorded ECG for each of the aforementioned WCT differentiation criteria, each worth a specific point value, in order to accrue a final score (i.e., VT score) representative of overall VT likelihood. According to its points-based structure, each criterion yields one point, except for AV dissociation, which earns two points.

As detailed in the original report,⁴ WCTs accruing ≥1 points demonstrated increased VT probability (positive predictive value [PPV] 83%), while scores ≥ 3 (PPV 99.6%) and ≥4 (PPV 100%) secured virtually conclusive VT diagnoses. Intriguingly, more than half (57%) of evaluated VTs could be diagnosed with near-certainty (i.e., VT score ≥ 3). At present, the VT score’s diagnostic performance has yet to be independently validated.

4.12. 2019, Pachón: Point-based scoring algorithm

In 2019, Pachón and colleagues²³ introduced a point-based scoring algorithm designed to identify near-definite VT or SWCT diagnoses. In their report, the authors selected a variety of well-established and novel ECG criteria — each demonstrating exceptionally strong positive predictive values (i.e., PPV > 95%) for VT or SWCT diagnoses — to be organized into a novel point-based scoring method. According to the scoring algorithm, if a criterion specific for VT was present, +1 point was allotted. Alternatively, if a criterion specific for SWCT was present, −1 point was allocated. Once all criteria are evaluated, the total accrued points are used to determine the final diagnosis: a negative score strongly favors SWCT, a positive score strongly favors VT, and a score of zero is considered indeterminate.

To apply the scoring algorithm, the presence or absence of seven specific criteria (and their point values) must be considered: (i) tachycardia QRS morphology identical to the QRS morphology on baseline ECG (−1 point), (ii) AV dissociation (+1 point), (iii) QS complex or initial q wave in lead V6 in cases of tachycardia with LBBB morphology (+1 point), (iv) sudden normalization and morphology changes in patients with atrial fibrillation on baseline ECG (−1 point), (v) wide QRS complex tachycardia with complete or high-grade AV block (+1 point), (vi) contralateral bundle branch block (BBB) morphology in patients with organic BBB (+1 point), and (vii) abnormal Q wave on baseline ECG (+1 point).

As described in their report,²³ near-definite VT (i.e., PPV of 98% for a score ≥ 1 and PPV of 100% for a score ≥ 2) or SWCT (i.e., PPV of 98% for a score = −1) diagnoses were established for a large proportion (52%) of evaluated WCTs. However, the advantage gained by determining near-certain VT and SWCT diagnoses was naturally counterbalanced by permitting a substantial proportion (48%) of evaluated WCTs to remain in diagnostic uncertainty. At present, the diagnostic performance of this new points-based algorithm has yet to be independently validated.

4.13. 2019, Chen: Limb lead algorithm

In 2019, Chen and colleagues⁶ devised a three-step WCT differentiation algorithm that focuses solely on basic QRS morphological characteristics in the limb leads (i.e., leads I, II, III, aVL, aVF, and aVR). Their algorithm, the so-called limb lead algorithm, establishes VT diagnoses if at least one of the following was present:

Step 1 A monophasic R wave in lead aVR.
Step 2 A predominantly negative QRS in leads I, II, and III, or.
Step 3 An opposing QRS complex in the limb leads (i.e., concordant monophasic QRS in all three inferior leads and concordant monophasic QRS complexes in two or three of the remaining limb leads that have an opposite polarity to that of the inferior leads).
In this algorithm, the authors leveraged the orientation of the mean electrical vector (i.e., QRS axis) to discriminate VT from SWCT. Ordinarily, VT, and not SWCT, may exhibit a “northwest” or predominately rightward superior QRS axis (Steps 1 and 2). Furthermore, the authors utilized the notion that monomorphic and diametrically opposed QRS complexes in the limb leads is commonly present among varieties of VT but typically absent among SWCT due to abberancy.

In their report, the overall accuracy of the limb leads algorithm was strong (88%), comparable to that achieved by the Brugada (85%) and Vereczei aVR (88%) algorithms but superior to that of lead II RWPT criterion (70%). In addition, the limb leads algorithm demonstrated quite favorable sensitivity (87%) and specificity (91%) for VT. At present, the diagnostic performance of this rather recent work has yet to be independently validated.


Recent work has challenged the limitations accepted by conventional manually-applied ECG interpretation methods. Through the use of well-established and mathematically-formulated independent VT predictors, May and colleagues developed a logistic regression model (i.e., WCT Formula) capable of providing clinicians with an impartial estimation of VT likelihood (i.e., 0.00%–99.99% VT probability). In this model, quantifiable VT predictors (e.g., WCT QRS duration and frontal/horizontal percent QRS amplitude change between paired WCT and baseline ECGs) yielded effective WCT differentiation (AUC 0.96; overall accuracy 92%; sensitivity 90%; specificity 93%). The working group further expanded on this work in Kashou et al., introducing WCT Formula II – a model that again capitalized on the principle of WCT and baseline ECG comparison, specifically changes in frontal and horizontal percent-time voltage areas. WCT Formula II implementation achieved strong diagnostic performance (AUC 0.96) with favorable overall accuracy (88%) as well as sensitivity (85%) and specificity (90%) for VT.

Comparable to WCT Formula I and II, May and colleagues introduced a novel diagnostic model (i.e., VT Prediction Model) that integrates readily accessible ECG determinates (i.e., WCT QRS duration, QRS axis change, and T wave axis change) to achieve effective WCT differentiation. The VT Prediction Model utilizes logistic regression modeling to convert universal computerized ECG measurements (i.e., QRS duration, QRS axis, and T axis) derived from paired WCT and baseline ECGs into impartial estimation of VT probability (0.000%–99.999%). This model may be readily used by online calculators or mobile device applications to help clinicians establish an impartial estimation of VT likelihood for undifferentiated WCTs.

These novel computerized approaches demonstrate the tremendous potential for accurate and automatic WCT differentiation. Furthermore, they represent an important step in the direction towards the integration of computational models that deliver consistent, easy-to-interpret, and impartial diagnostic data – independent of interpreter competency level. Although automated models that deliver estimated VT probabilities are not expected to replace the need for an expert ECG overread, they may function as a serviceable starting point estimate that could be further integrated with standard WCT differentiation methods (e.g., Brugada algorithm) or other relevant diagnostic factors (e.g., underlying structural heart disease or history of myocardial infarction).

5. Future directions

Clinicians, especially those at the front lines of patient care, are commonly thrust into the unexpected and challenging clinical dilemma: “Is this rapid wide complex rhythm VT or SWCT?” As previously mentioned, faulty diagnoses can lead to inappropriate, and sometimes harmful, short-term interventions, diagnostic workup, and long-term management strategies. Given the high stakes and continued challenges, numerous criteria, diagnostic algorithms, and scoring systems have been introduced over the last half-century. While all methods and criteria have demonstrated their own diagnostic strengths, and contributed to an expanding body of work, each possesses diagnostic disadvantages and practical limitations.

As the practice of medicine continues to progress forward, we will continue to encounter this diagnostic dilemma. However, with the birth of artificial intelligence-augmented ECG (AI-ECG) technologies, along with a logarithmic increase in computational power, automated computerized processes to solve this diagnostic problem will continue to emerge. Furthermore, the growing use of mobile and wearable devices, alongside the ability to collect and transfer digitized data offers a new realm of clinical applications to implement novel solutions. Although the ability of AI-ECG algorithms to successfully differentiate WCTs is seemingly not far away, major barriers will need to be overcome before AI-ECG solutions are incorporated in real-world clinical practice. Until then, the development, refinement, and integration of automated WCT differentiation methods that may be readily incorporated into existing computerized software systems appears to be the best means to immediately tackle this classic and long-standing clinical dilemma.

Author contributions

AHK, AMM: Conception, drafting and review of manuscript.
CME: Drafting and review of manuscript.
PAN, SJ A: Mentorship and review of manuscript.
TRM, CVD, AJD: Review of manuscript.

Conflicts of interest

All authors have none to declare.

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