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Efficacy of the Electrocardiographic P-Wave Indices (PWIs) in Predicting Atrial High-Rate Episodes (AHREs) With Cardiac Implantable Electronic Devices (CIEDs)

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Abstract

Atrial fibrillation (AF) is a common arrhythmia that increases the risk of stroke and mortality. Patients with AF who have cardiac implantable electronic devices (CIEDs) are at risk of developing atrial high-rate episodes (AHREs), which can lead to adverse outcomes. Several electrocardiographic P-wave indices have been studied as potential predictors of AHREs, including P-wave duration (PWD), P-wave dispersion (PWDIS), P-wave peak time (PWPT), and PR interval. This review aimed to assess the efficacy of these P-wave indices in predicting AHREs in patients with AF and CIEDs. The review included studies that found that PWD and PWDIS were significantly associated with AHREs. Additionally, studies have shown that P-wave peak time and PR interval may also predict AHREs. However, limitations such as variability in cut-off values and differences in patient populations and CIED types suggest the need for standardized diagnostic criteria. Overall, P-wave indices may be useful in identifying patients at risk for AHREs, but further research is needed to establish their clinical utility.

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Introduction

Atrial fibrillation (AF) is a common arrhythmia associated with significant morbidity and mortality[1]. The prevalence of AF is increasing worldwide, with an estimated 33 million cases globally in 2010, and projections indicate that this number will double by 2050 [2]. AF is associated with an increased risk of stroke, heart failure, and other cardiovascular events, and its management is a major challenge for clinicians [3]. Cardiac implantable electronic devices (CIEDs), including pacemakers, implantable cardioverter-defibrillators (ICDs), and cardiac resynchronization therapy (CRT) devices, have revolutionized the management of arrhythmias by providing accurate monitoring and timely intervention [4].

One of the challenges in the management of AF is the identification of atrial high-rate episodes (AHRE), which are often asymptomatic and may be missed on routine clinical examination [5]. AHRE refers to episodes of atrial tachycardia or fibrillation that last for more than 5 minutes, with a minimum heart rate of 180 beats per minute [6]. The detection of AHRE is important because it has been associated with an increased risk of stroke, heart failure, and mortality [7].

The electrocardiographic P-wave is the electrical representation of atrial depolarization, and the P-wave indices (PWIs) include P-wave peak time (PWPT), PR interval, maximum P-wave duration (PWDmax), minimum P-wave duration (PWDmin), and P-wave dispersion (PWDIS) [8]. Prolonged P-wave peak time in V1 lead (PWPTV1) has been associated with increased AF incidence [9]. The PWPT refers to the time interval from the onset of the P-wave to its maximum amplitude. PWPT has emerged as a potential marker of atrial electrical remodeling and a predictor of AF recurrence [10]. Several studies have reported an association between longer PWPT and increased risk of AF recurrence in patients with paroxysmal and persistent AF [10][11][12].

Given the potential clinical significance of PWIs as predictors of AF recurrence, there is increasing interest in assessing their utility in predicting AHRE. This review article aims to evaluate the current evidence on the efficacy of PWIs in predicting AHRE in patients with CIEDs. We will discuss the pathophysiological basis of PWIs, the methods of PWI measurement, and the existing evidence on the association between PWIs and AHRE. Additionally, we will explore the potential clinical applications of PWI measurement in the management of AF, including risk stratification and treatment optimization.

Methods

A comprehensive literature search was conducted using electronic databases, including PubMed, Embase, and the Cochrane Library. The search was performed using a combination of keywords and medical subject headings (MeSH), including "P-wave peak time," "atrial high-rate episode," "cardiac implantable electronic devices," "atrial fibrillation," and "arrhythmia." The inclusion criteria for the articles were as follows: (1) studies evaluating the association between PWPT and AHRE in patients with CIEDs, (2) studies published in the English language, and (3) studies published between 2010 and 2023. After screening the articles by titles and abstracts, the full text of potentially relevant articles was reviewed. Data extraction was performed by two independent reviewers, and any discrepancies were resolved by discussion and consensus. The extracted data included study design, sample size, patient characteristics, CIED type, PWPT measurement method, AHRE detection method, follow-up duration, and outcomes. All data from the studies were presented in a narrative fashion.

Main text

Overview of P-wave indices

P-waves are the first electrical impulses of the heart's cardiac cycle, and they reflect the electrical activity of the atria[13]. The PWIs are a set of electrocardiogram (ECG) parameters used to assess the P-wave characteristics, such as duration, morphology, and timing. Here's a detailed overview of the PWIs, including PWPT, PR interval, maximum PWDmax, minimum PWDmin, and PWDIS. **Figure 1** summarizes the PWIs in an illustration.

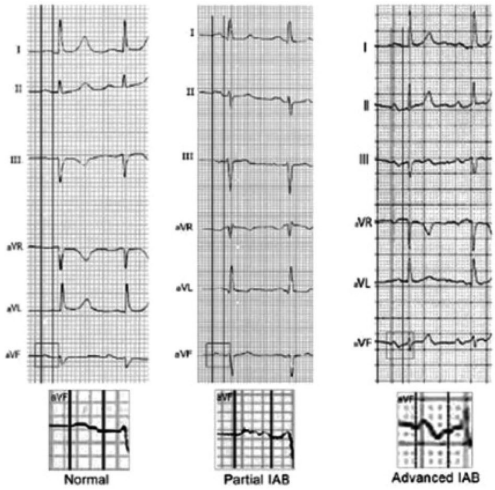
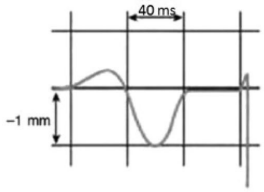
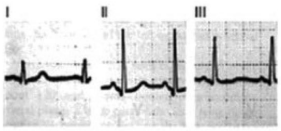
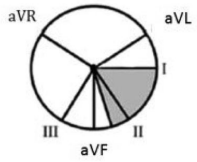
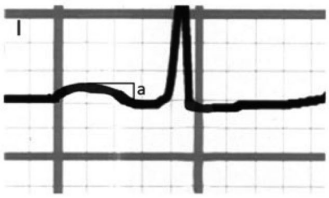
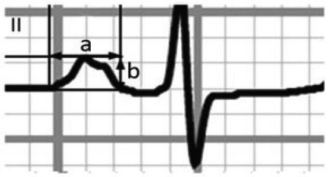
A **Normal** Partial and Advanced Interatrial block	
B PtfV1	Abnormal P terminal force in V1 40 ms x -1mm 
C P axis	 Normal P wave axis (0° to +75°) 
D P voltage	It is considered abnormal if P-wave voltage is ≤0.1mV in lead I. a= voltage. 
E P area	It is considered abnormal if in lead II, half duration of P (a) x voltage of P ≥ 4ms x mV (b). a= duration b= voltage 
F P dispersion	It is the difference between P wave maximum and minimum duration in the 12 leads ECG.

Figure 1. Summary of P-wave indices on a 12-lead surface ECG

Definitions

P-wave peak time (PWPT)

PWPT is the time interval from the onset of the P-wave to its maximum amplitude. It reflects the atrial depolarization time and is measured in milliseconds (ms). The normal range for PWPT is between 80 and 120 ms [13]. An increased PWPT is often seen in patients with atrial fibrillation, atrial flutter, and other atrial arrhythmias [14].

PR interval

The PR interval is the time interval from the onset of the P-wave to the onset of the QRS complex. It reflects the conduction time from the atria to the ventricles through the atrioventricular (AV) node. It is measured in milliseconds (ms) and is normally between 120 and 200 ms [13]. An increased PR interval is seen in conditions that slow AV node conduction, such as AV block [15].

Maximum P-wave duration (PWDmax)

PWDmax is the duration of the longest P-wave in any of the ECG leads. It reflects the maximum atrial depolarization time and is measured in milliseconds (ms). The normal range for PWDmax is less than 120 ms [13]. An increased PWDmax is seen in conditions that affect atrial conduction, such as atrial fibrillation, atrial flutter, and other atrial arrhythmias [16].

Minimum P-wave duration (PWDmin)

PWDmin is the duration of the shortest P-wave in any of the ECG leads. It reflects the minimum atrial depolarization time and is measured in milliseconds (ms). The normal range for PWDmin is less than 40 ms [13]. An increased PWDmin is seen in conditions that affect atrial conduction, such as atrial fibrillation, atrial flutter, and other atrial arrhythmias [16].

P-wave dispersion (PWDIS)

PWDIS is the difference between PWDmax and PWDmin. It reflects the heterogeneity of atrial conduction and is measured in milliseconds (ms). The normal range for PWDIS is less than 40 ms [13]. An increased PWDIS is seen in conditions that affect atrial conduction, such as atrial fibrillation, atrial flutter, and other atrial arrhythmias [17]. PWDIS is considered to be a risk factor for the development of atrial fibrillation and stroke [18].

Advanced inter-atrial block

Advanced Inter-Atrial Block (aIAB) is a cardiac conduction disorder that affects the electrical activity of the atria[19]. It is characterized by a prolonged P-wave duration, biphasic P-wave morphology in leads III and aVF, and biphasic or notched P-wave morphology in lead II [19]. This indicates that there is an inter-atrial conduction block in Bachmann's bundle, which is a specialized bundle of fibers that facilitates electrical conduction between the right and left atria [20]. aIAB is associated with an increased risk of developing atrial fibrillation, which is a common cardiac arrhythmia that can lead to serious complications such as stroke and heart failure [21]. Therefore, the detection and management of aIAB is important in the prevention of these complications. Treatment options for aIAB may include medication to control heart rate and rhythm, as

well as lifestyle modifications such as exercise and weight management [19].

Significance of P-wave indices in arrhythmias

PWIs are an important aspect of the ECG that can provide valuable insights into the underlying mechanisms of cardiac arrhythmias. The P-wave represents the electrical activity of the atria, and its morphology and timing can be used to diagnose and monitor a wide range of arrhythmias, including atrial fibrillation, atrial flutter, and other atrial tachyarrhythmias [13].

PWPT is an important P-wave index that reflects the time it takes for the atria to depolarize[14]. An increased PWPT is often seen in patients with atrial fibrillation, atrial flutter, and other atrial arrhythmias [14]. This is because these conditions result in abnormal atrial depolarization patterns, which can prolong the PWPT [22]. An increased PWPT can also be a sign of conduction delays or blockages in the AV node, which can result in abnormal electrical activity in the ventricles [23]. Therefore, PWPT can be used as a marker of atrial electrical dysfunction and as an indicator of the severity of atrial arrhythmias.

The PR interval is another important P-wave index that reflects the time it takes for the electrical impulse to travel from the atria to the ventricles through the AV node [15]. Prolongation of the PR interval is often seen in conditions that slow AV node conduction, such as AV block, and can result in abnormal electrical activity in the ventricles [24]. This can lead to symptoms such as fatigue, lightheadedness, and fainting. In addition, prolonged PR intervals can be a sign of underlying heart disease or other medical conditions [25]. Therefore, the PR interval can be used to diagnose and monitor the progression of cardiac conduction abnormalities.

PWDmax and minimum PWDmin are important PWIs that reflect the maximum and minimum atrial depolarization times, respectively [16]. An increased PWDmax and PWDmin are often seen in conditions that affect atrial conduction, such as atrial fibrillation, atrial flutter, and other atrial arrhythmias [26]. These conditions can cause abnormal atrial depolarization patterns, which can result in prolonged or shortened PWDs [27]. Therefore, PWDmax and PWDmin can be used as markers of atrial electrical dysfunction and as indicators of the severity of atrial arrhythmias.

PWDIS is another important P-wave index that reflects the heterogeneity of atrial conduction[18]. PWDIS is calculated as the difference between PWDmax and PWDmin and reflects the degree of variation in atrial depolarization times across different parts of the atria [13]. An increased PWDIS is often seen in patients with atrial fibrillation, atrial flutter, and other atrial arrhythmias and can be a risk factor for the development of these conditions [28]. This is because PWDIS can lead to the formation of reentrant circuits, which can sustain and perpetuate atrial fibrillation.

The significance of PWIs in arrhythmias lies in their ability to provide valuable information about the underlying mechanisms of these conditions [29]. By assessing PWIs, clinicians can diagnose and monitor the progression of arrhythmias and tailor treatment strategies to individual patients.

Clinical correlates

There are several clinical correlates associated with PWIs that can help clinicians to identify and manage these conditions. **Table 1** shows a summary of P-wave indices in reference cohorts[28][30][31][32][33][34][35][36].

Table 1. Summary of P-wave indices in reference cohorts

Author [ref]	Study design	Clinical context	P-wave duration	P-wave dispersion
Dagli [30]	Cross-sectional	Hypertension	64 ± 10.2	30.3 ± 6.6
Andrikopoulos [31]	Cross-sectional	Paroxysmal atrial fibrillation	101.4 ± 10.1	29.8 ± 8.7
Gialafos [32]	Cohort	Young men	96.0 ± 11.0	38.0 ± 10.0
Yigit [33]	Cross-sectional	Exercise on P-wave indices	94.0 ± 2.3	52.1 ± 2.0
Ariyarajah [34]	Cross-sectional	Ambulatory patients	40-170	N/A
Gunduz [35]	Cross-sectional	Diastolic dysfunction	104 ± 9	43 ± 9
Aytemir [28]	Cross-sectional	Paroxysmal atrial fibrillation	101.0 ± 11.0	27.0 ± 10.0
Dilaveris [36]	Cross-sectional	Paroxysmal atrial fibrillation	101.0 ± 10.0	28.0 ± 7.0

One of the most significant clinical correlates associated with PWIs is the risk of developing atrial fibrillation[29]. Prolonged PWD and increased PWDIS have been identified as risk factors for the development of AF and can help clinicians to identify patients who are at higher risk for this condition [16][17][18]. In addition, the presence of other cardiac risk factors such as hypertension, diabetes, and heart failure can also increase the risk of developing AF in patients with abnormal PWIs [30]. Another clinical correlate associated with PWIs is the presence of other cardiac conditions such as heart block and atrial flutter. Prolonged PR intervals and biphasic P-wave morphology can be indicative of heart block, while rapid and irregular P-wave morphology can be indicative of atrial flutter [15]. These conditions can lead to serious complications such as heart failure and stroke, and early diagnosis and management are essential to prevent these outcomes. Finally, PWIs can also be used to assess the response to treatment in patients with cardiac arrhythmias. For example, a decrease in P-wave duration and dispersion following treatment for atrial fibrillation can be indicative of successful treatment and may help to guide further management [37].

One of the most important PWIs in the context of ischemic stroke is PWD[38]. Increased PWD has been associated with an increased risk of developing ischemic stroke, as it reflects the heterogeneity of atrial conduction that can lead to atrial fibrillation and thromboembolism [39]. Several studies have investigated the relationship between PWD and ischemic stroke (**Table 2**) [40][41][42]. One of the most important PWIs in the context of sudden cardiac death (SCD) is PWD[43]. Increased PWD has been associated with an increased risk of developing SCD, as it reflects the heterogeneity of atrial conduction that can lead to ventricular arrhythmias and SCD [44]. Several studies have investigated the relationship between PWD and SCD. In a study of 424 patients with coronary artery disease, PWD was significantly higher in patients who experienced SCD compared to those who did not [43]. Furthermore, PWD was an independent predictor of SCD, with higher PWD associated with a higher risk of SCD. Another important P-wave index in the context of SCD is the PTFV1 [45]. Other PWIs that have been investigated in the context of SCD include PWPT and maximum PWDmax[29].

PWPT is a measure of the time from the onset of the P-wave to its maximum amplitude. Increased PWPT has been associated with an increased risk of SCD in patients with cardiovascular disease. Similarly, PWDmax, which is a measure of the duration of the P-wave, has been associated with an increased risk of SCD [29].

Table 2. Studies demonstrating the association of P-wave indices with ischemic stroke without atrial fibrillation

Author [ref]	P-wave indices used	Outcome	Atrial fibrillation
O'Neal [40]	P-wave axis, aIAB	Incident ischemic stroke	Adjusted
Maheshwari [41]	P-wave axis, P-wave duration, P-wave terminal force in lead V1	Incident ischemic stroke	Included
Kamel [42]	P-wave terminal force in lead V1	Iscident ischemic stroke subtypes	Adjusted

Atrial high-rate episodes in cardiac implantable electronic devices

Atrial high-rate episodes (AHREs) are defined as episodes of atrial arrhythmia with a rate exceeding a certain threshold (usually > 180 beats per minute) that are detected by CIEDs, such as pacemakers, ICDs, and CRT devices [46]. The detection of AHREs is important because they are associated with an increased risk of stroke and other adverse outcomes [47].

AHREs can be detected by CIEDs using various sensing modalities, including atrial electrograms, atrial rate histograms, and atrial tachycardia detection algorithms [48]. The duration and frequency of AHREs can vary widely, from brief, self-terminating episodes to sustained, persistent arrhythmias. The underlying mechanisms of AHREs are also diverse and can include atrial fibrillation, atrial flutter, atrial tachycardia, and other atrial arrhythmias [46].

The incidence of AHREs detected by CIEDs is high, with estimates ranging from 10% to 40% depending on the patient population and device type [49]. AHREs are particularly common in patients with heart failure, hypertension, and diabetes, as well as in older patients and those with structural heart disease [50].

Detection of atrial high-rate episodes

The detection of AHREs by CIEDs can also have important implications for clinical management[48]. In patients with a history of stroke or transient ischemic attack, the detection of AHREs can prompt the initiation of anticoagulation therapy to reduce the risk of future stroke. Similarly, in patients with heart failure, the detection of AHREs can be a marker of disease progression and may prompt the initiation of additional therapies such as beta-blockers or angiotensin receptor blockers [51].

Atrial electrograms (AEG) are the gold standard for detecting AHREs, as they allow for the direct visualization of atrial activity [52]. The AEG is a recording of the electrical activity in the atria, which is captured by the CIED's lead and stored in the device's memory. AHREs can be identified on atrial electrograms as rapid, irregular atrial activity that exceeds a predefined threshold [52]. An AEG is a recording of the electrical activity of the atria of the heart. It is obtained by placing one or more electrodes in the atria, typically through a catheter inserted into a vein and threaded into the heart under

fluoroscopic guidance. The AEG provides valuable information about the atrial rhythm, conduction, and morphology and is used in the diagnosis and management of a variety of cardiac arrhythmias, including atrial fibrillation, atrial flutter, and atrial tachycardia. The AEG waveform consists of several components, including the P-wave, which represents atrial depolarization, and the T-wave, which represents atrial repolarization. The morphology and duration of the P-wave can provide important information about the underlying atrial rhythm and conduction. For example, a prolonged P-wave duration or abnormal P-wave morphology may indicate the presence of atrial conduction abnormalities, such as inter-atrial block or left atrial enlargement. The AEG can also be used to identify and characterize specific types of atrial arrhythmias. For example, atrial fibrillation is characterized by a rapid and irregular atrial rhythm with no discernible P-waves on the AEG, while atrial flutter is characterized by a regular sawtooth pattern of atrial activity with a fixed atrial rate and variable ventricular response. In addition to its diagnostic value, the AEG can also be used to guide the treatment of atrial arrhythmias. For example, during catheter ablation procedures for atrial fibrillation or other arrhythmias, the AEG can be used to guide the placement of ablation lesions in the atria. The AEG can also be used to monitor the success of ablation procedures by assessing the presence or absence of atrial arrhythmias following the procedure.

Atrial rate histograms are another commonly used modality for detecting AHREs[53]. These histograms display the distribution of atrial rates over time and can be generated by the CIED's programming software. AHREs can be identified on atrial rate histograms as spikes in the distribution of atrial rates above a predefined threshold [53]. Atrial tachycardia detection algorithms are automated algorithms that are programmed into CIEDs to detect various types of atrial arrhythmias, including AHREs [48][54]. These algorithms use a combination of rate and rhythm criteria to identify AHREs, which can then be stored in the device's memory for later review. The frequency of AHREs can be programmed by the clinician to a specific threshold, typically above 180 beats per minute, which is a common threshold for identifying significant AHREs that may require further clinical management.

Management of atrial high-rate episodes

The management of AHREs detected by CIEDs can be challenging, and there needs to be a consensus on the optimal approach [55]. In general, the management of AHREs should be tailored to the individual patient based on their clinical history, comorbidities, and other risk factors.

For patients with a high burden of AHREs, the initiation of anticoagulation therapy may be appropriate to reduce the risk of stroke [56]. The choice of anticoagulant should be guided by the patient's clinical history and comorbidities, as well as their risk of bleeding. Direct oral anticoagulants (DOACs) such as apixaban, dabigatran, edoxaban, and rivaroxaban are effective in reducing the risk of stroke in patients with atrial fibrillation [57]. They may be appropriate for some patients with AHREs.

For patients with a low burden of AHREs, the initiation of anticoagulation therapy may not be necessary. Instead, the focus should be on optimizing the management of underlying cardiovascular risk factors such as hypertension, diabetes, and hyperlipidemia [58]. In some cases, initiating antiarrhythmic therapy such as beta-blockers or calcium channel blockers may also be appropriate to reduce the frequency and duration of AHREs.

For patients with persistent or symptomatic AHREs, more aggressive interventions such as catheter ablation may be considered [59]. Catheter ablation is a minimally invasive procedure in which a catheter is inserted into the heart and used to destroy small areas of tissue responsible for generating abnormal electrical signals [60]. Ablation is effective in reducing the frequency and duration of AHREs in some patients, particularly those with atrial fibrillation.

Another approach to managing AHREs is the use of remote monitoring systems that allow for the continuous monitoring of patients with CIEDs [61]. These systems can detect AHREs in real time and alert healthcare providers, allowing for prompt intervention when necessary. Remote monitoring is effective in detecting AHREs and reducing the time to appropriate clinical management, particularly in patients with high-risk features such as heart failure or prior stroke.

P-wave indices for predicting atrial high-rate episodes

Multiple studies have investigated the efficacy of these P-wave indices in predicting AHREs in various patient populations (**Table 1**). While these studies suggest that P-wave indices may have utility in predicting AHREs, there are some limitations to their use. First, the accuracy of P-wave indices in predicting AHREs may vary depending on the patient population and the type of CIED being used. Additionally, the cut-off values for P-wave indices that predict AHREs may differ across studies, making it challenging to establish standardized diagnostic criteria. Finally, while P-wave indices may be useful in identifying patients at risk for AHREs, they may not be useful in predicting the specific type or duration of arrhythmia.

Future directions

The study assessing the efficacy of P-wave peak time in predicting AHREs in patients with CIEDs is an important step in the development of more accurate predictive tools for detecting cardiac arrhythmias. Moving forward, there are several future directions that could be pursued to improve the accuracy and clinical utility of this approach. One possible direction is to incorporate additional electrocardiographic features into the predictive model. For example, a study of patients with heart failure found that combining P-wave duration and PR interval improved the predictive accuracy for AHREs compared to using either measure alone. By incorporating multiple electrocardiographic features, a more comprehensive predictive model could be developed that is better able to capture the complex mechanisms underlying arrhythmia development. Another possible direction is to integrate other types of patient data into the predictive model, such as clinical and demographic factors, as well as imaging and laboratory data. For example, a recent study found that combining electrocardiographic data with measurements of left atrial volume and function improved the ability to predict the development of atrial fibrillation. By integrating multiple types of patient data, a more personalized approach to arrhythmia prediction could be developed that takes into account the unique characteristics of each patient. A third possible direction is to develop more advanced machine-learning algorithms for predicting AHREs. Machine learning algorithms can analyze large datasets and identify patterns and correlations that might not be apparent to human researchers. By leveraging these advanced algorithms, more accurate and clinically relevant predictive models could be developed that can be applied to a wide range of patient populations. Finally, future research could focus on using P-wave indices to guide

clinical decision-making. For example, patients with high-risk P-wave indices could be monitored more closely for the development of arrhythmias or could be considered for prophylactic treatments to prevent arrhythmia development. By using P-wave indices to guide clinical decision-making, patient outcomes could be improved, and healthcare resources could be used more efficiently.

Conclusion

In conclusion, the assessment of PWIs has shown promising results in predicting the occurrence of AHREs in patients with CIEDs and atrial fibrillation. While further studies are necessary to establish standardized cut-off values and diagnostic criteria, the current evidence supports the use of P-wave peak time as a potential tool for identifying patients at risk for AHREs. Early detection of these episodes can help clinicians implement appropriate treatment and preventive measures, ultimately improving patient outcomes. The use of PWIs in predicting AHREs has the potential to become an important aspect of clinical practice and should continue to be investigated in future research.

Statements and Declarations

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Authors contribution:

- Concept JM AM
- Methodology MSQK MA YS
- Validation MA YS AM
- Lit search YS MA
- First draft MB SK YS AB SAS
- Final draft AB SAS YS MA

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