# The interplay of heart rate variability and ventricular repolarization parameters in the obese state: a review

Akash Tomar[a], Himani Ahluwalia[b], S Ramkumar[c], Sanghamitra Pattnaik[d], Debarshi Nandi[e] and Prashant Raturi[f]

**The impact of obesity on heart rate variability (HRV) and ventricular repolarization, both vital indicators of cardiovascular health, is the focus of this review. Obesity, measured by BMI, waist circumference, and waist-to-hip ratio, significantly increases cardiovascular disease (CVD) risk due to structural and autonomic heart changes. Findings show that obese individuals exhibit prolonged QT and Tpeak-to-Tend (Tpe) intervals, suggesting delayed ventricular recovery and greater arrhythmia risk. Additionally, obesity-induced autonomic imbalance favors sympathetic activity over parasympathetic, reducing HRV and raising arrhythmogenic potential. Elevated QT and Tpe intervals reflect extended cardiac recovery phases, which contribute to poor cardiac outcomes. The Tpe interval could serve as an early marker of cardiac dysfunction in obese populations, highlighting the importance of early intervention to reduce CVD risk and enhance treatment strategies for obesity-related cardiovascular changes.**
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[a]Department of Physiology, Kasturba Medical College, Manipal Academy of Higher Education, Manipal, Karnataka, [b]Department of Physiology, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, [c]Department of Physiology, Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Dehradun, Uttarakhand, [d]Department of Physiology, Army College of Medical Sciences, [e]Department of Physiology, Lady Hardinge Medical College and Associated Hospitals and [f]Department of Cardiology, G B Pant Institute of Postgraduate Medical Education and Research, New Delhi, India

Correspondence to Akash Tomar, MD, Department of Physiology, Kasturba Medical College, Manipal Academy of Higher Education, Karnataka, Manipal, 576104, India
E-mail: akash.tomar@manipal.edu

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## Introduction

### Obesity

Obesity is defined by the WHO as abnormal or excessive fat that accumulates and presents a risk to health. In 2016, 39% of the world's adult population (39% in men and 40% in women) were overweight, while 13% of the world's adult population (11% in men and 15% in women) were reported as obese [1]. Obesity in a normal population has been classified by BMI. Obesity can also be measured by other factors such as total body fat percentage, waist circumference (WC), hip circumference, waist-to-hip ratio (WHR), and skinfold thickness [2]. In some studies, the association of abdominal obesity with various metabolic risk factors appears to be stronger than generalized adiposity [3,4]. Obesity is found to be a major risk factor for the development of type 2 diabetes, asthma, hypertension, stroke, coronary artery disease, cancer, liver and gallbladder diseases, sleep apnea, osteoarthritis, and gynecological complications [5–8].

### Obesity and risk of cardiovascular diseases

Obesity is among the leading causes of elevated cardiovascular disease (CVD) mortality and morbidity in adults and children [9–11]. It is a fast-growing problem and is independently associated with many adverse health effects and an increased risk of premature death [5]. Cardiovascular mortality and morbidity have been shown to be elevated in individuals who have, particularly, a central deposition of adipose tissue, that is, abdominal obesity [5,12]. It has been associated with elevated blood pressure, thus leading to hypertension, which in turn, leads to many other morbidities such as stroke, myocardial infarction, heart failure, and arterial aneurysms [13]. Obesity is also associated with dyslipidemia, diabetes, insulin resistance, and elevated levels of fibrinogen and C-reactive protein, all of which increase the risk of CVD events [14].

The adverse effects of obesity on cardiovascular function and structure are well documented [6,15]. There are alterations in the structure of cardiac tissue such as left atrial enlargement and remodeling, and ventricular hypertrophy. These changes may ultimately result in obesity-induced left ventricular diastolic and systolic dysfunction and right and left ventricular heart failure. Several hemodynamic changes, such as increased total blood volume, stroke volume, cardiac output, and an increase in pulmonary and left atrial pressure, are seen in an obese state [16,17]. So it is true to state that the

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cardiovascular system faces the challenge of increased workload in obesity [6].

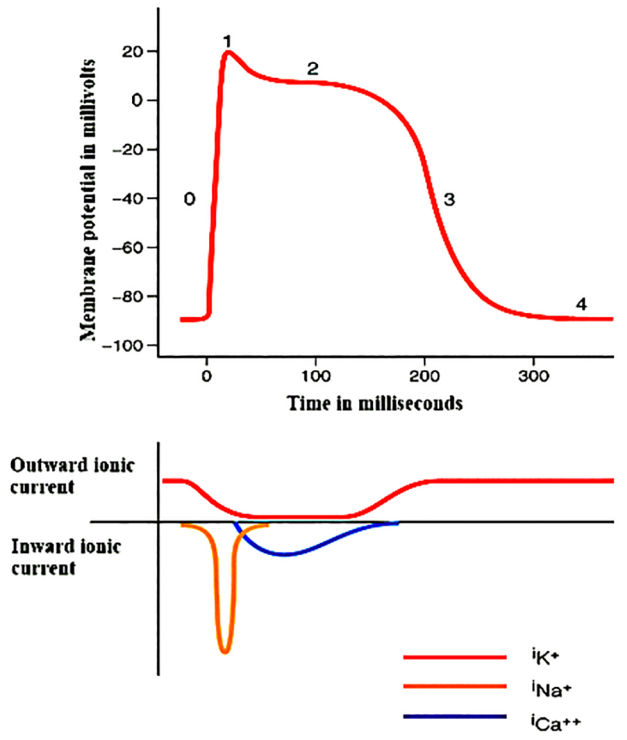
### The difference of three layers of myocardium in their cardiac action potential

During the cardiac cycle, depolarization is triggered by the inward movement of positive ions (mainly sodium and calcium), while repolarization results from the outward flow of potassium ions. The stability of electrical activity, particularly the plateau phase, is supported by redundancy and voltage-gated ion channel regulation [18,19]. Potassium channels play a key role in this, known as 'repolarization reserve'.

The cardiac action potential is divided into five distinct phases, with different currents active in each phase as shown in Fig. 1.

The ventricular myocardium is made of three layers: epicardial, mid-myocardial (M), and endocardial, each with different repolarization characteristics as shown in Fig. 2. M cells, similar to Purkinje fibers, show prolonged action potential duration (APD) and early afterdepolarizations [20]. The endocardial layer has longer action potentials than the epicardium [21–23]. Transmural dispersion of repolarization, the difference in APD across myocardial layers, is linked to re-entrant arrhythmias [20]. The Tpeak-to-Tend (Tpe) interval, Tpe/QT ratio, and Tpe/QTc ratio are emerging markers for ventricular repolarization, specifically measuring M cell repolarization [20]. Unlike the QT interval, which includes both depolarization and repolarization, the Tpe interval focuses on repolarization and is less influenced by heart rate due to the intrinsic properties of myocytes.

**Fig. 1**




Cardiac action potential showing different phases and ionic currents during these phases (created in Microsoft Paint).

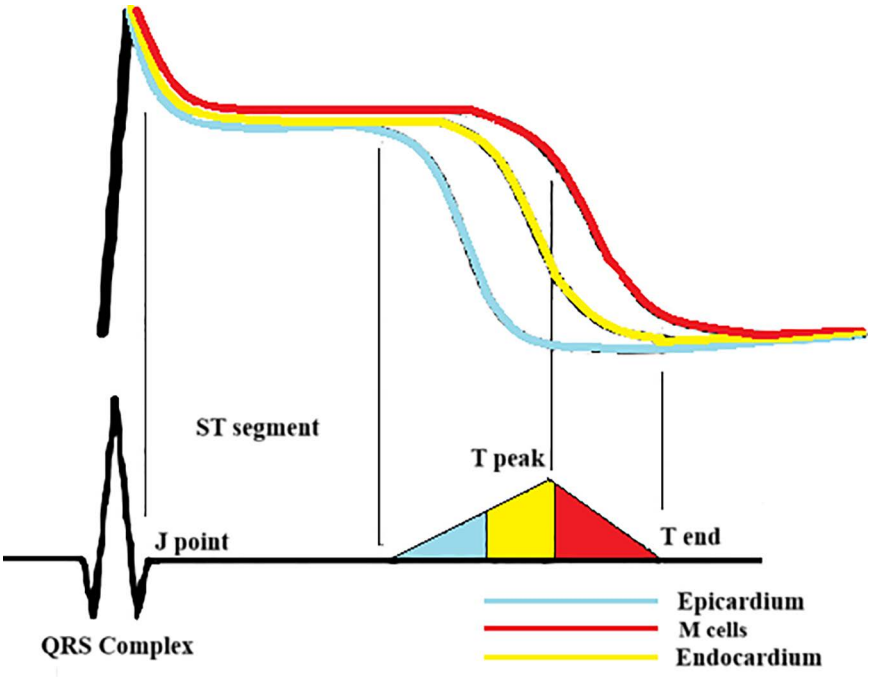
### Obesity and its relationship with ventricular repolarization

Obesity leads to structural heart changes such as left atrial enlargement, ventricular hypertrophy, and remodeling, which affect heart function and electrical activity [16,17]. These changes include prolonged PR and QT intervals, reduced QRS amplitude, and altered ventricular repolarization, seen on an ECG as the T wave. New parameters, such as the Tpe and JT intervals, are better indicators of ventricular repolarization [24–26].

Ventricular repolarization is influenced by factors such as age, gender, and BMI [20,27,28]. Obesity is linked to prolonged QT intervals, a risk factor for conditions such as long QT syndrome and arrhythmias. Increased BMI causes various ECG changes: increased P wave duration and dispersion [29,30], prolongation of the PR interval [29,31], low QRS voltage in the limb leads [31,32], leftward shift of heart axis [31–33], various markers of left ventricular hypertrophy [34,35], and prolongation of corrected QT interval and the QT interval duration [32]. Moreover, alterations in the Tpe interval have been found in overweight and obese young adults [36]. These changes result from factors such as increased chest wall fat, pericardial fat, and sympathetic nervous system (SNS) activity [37]. As there is a relationship between free fatty acids, cardiac sympathetic nervous activity, and repolarization abnormalities, the QT interval duration and QTc interval duration have been reported to be increased in obesity and appear to be influenced by autonomic tone. This autonomic dysfunction, with a sympathovagal imbalance, is a potential mechanism underlying QT prolongation in obese subjects [38].

Research shows a positive correlation between obesity and ventricular repolarization markers (QT and Tpe intervals) [36,39,40]. Many studies have also shown a positive relation between obesity and ventricular repolarization variables, as overweight and obese individuals have prolonged QT interval, Tpe interval, and higher Tpe/QT ratio [36,39,40]. Kumar *et al.* [39] documented longer values of QTc interval in the obese group compared with controls. Sharma *et al.* [40] also showed longer QTc interval values in Indian males recently. Hussain and Farooque [36] have also shown that ventricular repolarization parameters (Tpe interval along with QT and QTc interval) are related to BMI, WHR, and body surface area.

**Fig. 2**




Different layers of myocardium have different repolarization phases (created in Microsoft Paint).

Vardar *et al.* [41] found that there is no relation between BMI and QT interval in normal healthy male individuals; however, they only took normal-weight and overweight populations in their study and did not mention about the obese population. Another study by Nomura *et al.* [42] also stated that obesity does not have any role in the prolongation of the QT interval; however, they studied these in coronary artery disease patients only.

QT interval prolongation is significant in life-threatening arrhythmias, with obesity-related autonomic dysfunction contributing to these electrical disturbances [18,21,22,43–45]. Perturbations of ventricular depolarization and repolarization (due to ischemia, bundle branch block, pre-excitation, extrasystolic beats, drugs, or genetic abnormalities of cardiac ion channels) can alter the T wave configurations and prolong QT interval duration, favoring arrhythmogenesis [43,44].

### Obesity as a factor for deranged autonomic function

Obesity is often linked to autonomic dysfunction, increasing sympathetic activity and reducing parasympathetic (vagal) tone, which impairs cardiac rhythm control. WHR, indicating visceral fat, is strongly connected to higher sympathetic and lower parasympathetic activity [46] and these changes directly affect the ventricular myocardium and cardiac repolarization duration [47]. The autonomic nervous system (ANS) governs many body functions, including metabolism [48–50]. In obese individuals, ANS alterations can promote further weight gain, creating a feedback loop where obesity worsens ANS activity. While WHR is a strong predictor of cardiac autonomic imbalance, BMI has a weaker association with heart rate variability (HRV), a marker of cardiac autonomic function. Some studies have also suggested that decreased sympathetic activity in obesity disrupts homeostasis, contributing to excess energy storage [51]. Small increases in WHR can raise the risk of cardiovascular issues due to these autonomic changes [46]. Therefore, early testing for altered ANS function could help prevent complications [50].

### Heart rate variability as a measure of cardiac autonomic function

HRV is the measurement of the interval between consecutive heartbeats that is analyzed, rather than the heart rate itself. HRV mirrors the regularity of heartbeats: more regularity means lower HRV, and vice versa [52]. HRV is a useful tool for assessing autonomic function, reflecting parasympathetic and sympathetic activity [52]. The clinical relevance of HRV was first appreciated in 1965 when Hon and Lee [53] noted that fetal distress was preceded by alterations in interbeat intervals before any appreciable change occurred in heart rate. More interest in HRV began in the 1970s with studies on diabetic neuropathy and postinfarction mortality. Ewing *et al.* [54] devised several simple bedside tests of short-term RR differences to detect autonomic neuropathy in diabetic patients. The association of higher risk of postinfarction mortality

with reduced HRV was first shown by Wolf *et al*. [55] in 1977. By the 1980s, power spectral analysis became a key method for evaluating autonomic control. HRV gained further recognition for predicting mortality after myocardial infarction [56] and remains a valuable tool for risk stratification in cardiology [52]. A table explaining the different HRV parameters is given in Supplementary Table 2, Supplemental digital content 1, *http://links.lww.com/CAEN/A66*.

Reduced HRV is associated with CVDs and predicts poor outcomes in these conditions [57]. Understanding HRV's complexities led to the formation of standards by the European Society of Cardiology and the North American Society of Pacing and Electrophysiology [52]. Although HRV is less direct than measures such as plasma catecholamine or baroreflex sensitivity, it is widely accepted as a quantifier of ANS activity [58,59]. Lombardi and Stein [60] reviewed the relationship between HRV and 'sympathovagal' balance, while Zuern *et al*. [61] and Huikuri and Stein [62] evaluated HRV and HRT as tools for risk assessment in patients recovering from myocardial infarction. Nonlinear indices of HRV, which reflect heart rate dynamics, have been shown to have greater prognostic value for cardiovascular events compared with traditional HRV indices [63,64]. Understanding HRV's strengths and limitations allows its application in diagnosing clinical conditions and developing effective therapies for diseases that affect HRV.

### Cardiac action potential affected by autonomic nervous system

The ANS plays a crucial role in maintaining cardiovascular homeostasis. Research investigating the effects of gender and daily fluctuations on the ANS and cardiac repolarization markers has provided new insights into autonomic physiology [65]. Studies have shown that vagal tone decreases and sympathetic tone increases with age [66].

Experimentally it has been seen that intravenous catecholamine administration reduces the dispersion of repolarization across the heart's ventricles. Autonomic nerve discharges, as in physiological conditions, lead to localized neurotransmitter release, which shortens the refractory period and increases repolarization dispersion [67]. Thus, autonomic changes directly affect the ventricular myocardium, impacting the duration of cardiac repolarization as well [47].

### Lacunae in existing knowledge

Different studies propose the effects of obesity on many cardiac functions, but there is a paucity of research on the assessment of the Tpe interval as a marker of transmural dispersion of ventricular repolarization and its quality to measure and detect early changes in cardiac pathology. HRV as a measure of cardiac autonomic function and its effect on ventricular repolarization parameters (in terms of the parameter of Tpe interval) in obesity needs to be investigated more. This review proposes to investigate the interplay between obesity and altered autonomic functions, which may influence cardiac repolarization parameters.

## Methods

We conducted a literature search for papers published up to October 2024 on the effect of ventricular parameters and HRV in obese state, using three medical databases: PubMed, Embase, and Scopus with the search strategy including the terms: 'heart rate variability', 'ventricular repolarisation' and 'Obesity'. Qualitative and quantitative data were extracted through the interpretation of each article in cycles to avoid missing on data of potential value.

## Results

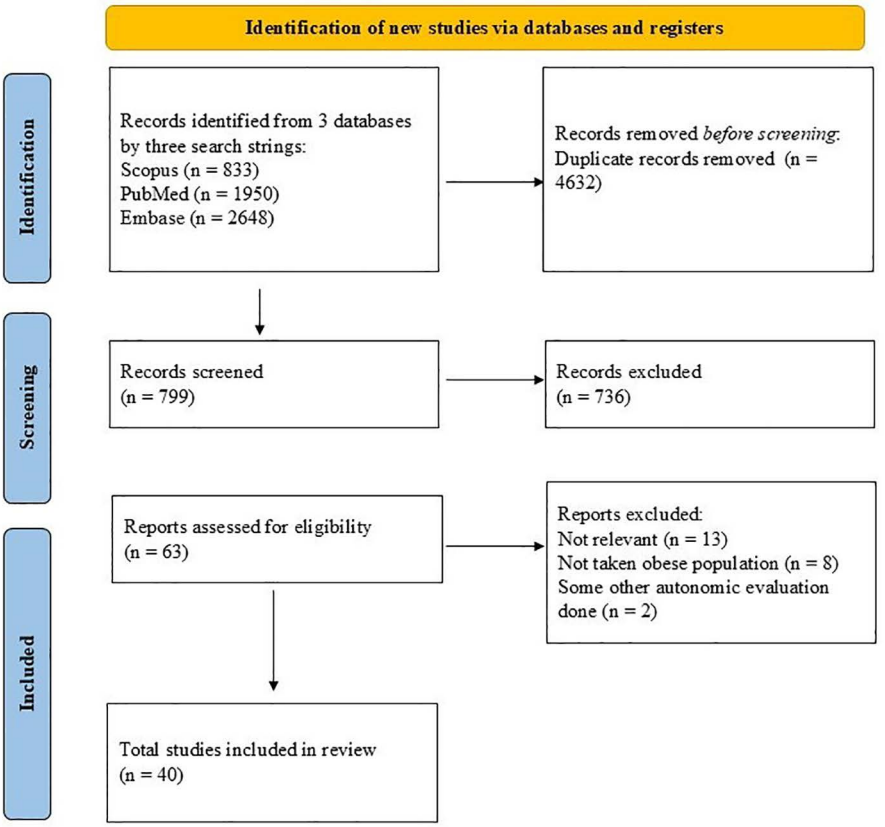
A total of 40 studies were then identified by excluding various studies. Studies published till October 2024, written in English and pertaining to our study parameters were taken into consideration. A consort diagram of the studies included and excluded in this review is shown in Fig. 3. A table on the number of studies that were found after using the search strings mentioned in the methods section is given in Supplementary Table 1, Supplemental digital content 2, *http://links.lww.com/CAEN/A67*.

## Discussion

Obesity has been known to be a common cause of cardiovascular morbidity and mortality. In recent times, obesity has been on the rise in developing nations [69], thus affecting populations as an important risk factor for cardiovascular morbidities and sudden cardiac death (SCD) [15]. Obesity causes changes in the anatomic features of all organs in the body, including the heart. The cardiac changes include myocardial hypertrophy, fibrosis, focal myocardial disarray, and increased volume of epicardial fat [35]. All these changes have been associated with cardiovascular morbidity and mortality. It also affects the functioning of all body systems, of which autonomic and cardiovascular systems are no exceptions.

Most of the time, individuals with a higher BMI also have higher WHR and WC. Increased BMI, WHR, and WC have already been stated as risk factors for cardiovascular morbidity in a number of studies [6,8,11,35,40,70]. Ahmad *et al*. [70] documented a strong positive correlation of WHR and WC with BMI in rural Malaysians (WC: $r = 0.78$, WHR: $r = 0.24$) with a $P$ value <0.001. In another study conducted by Shirasawa *et al*. [71], wherein 117 163 Japanese young adults were analyzed for central adiposity, positive correlations of WC and WHR with BMI and the risk of cardiovascular morbidity were also documented.

**Fig. 3**




Consort diagram of studies included in this review [68].

Many studies have shown higher values of blood pressure in the obese [72]. Deshmukh *et al.* [73] documented positive correlations of SBP and DBP with BMI, WC, and WHR. Higher levels of blood pressure in an obese state have already been established as one of the many risk factors for the development of arteriosclerosis, atherosclerosis, coronary artery disease, and stroke [74].

The findings in studies done by Al-Qurashi *et al.* [75] and Yar [76] documented a higher heart rate in the obese Saudi population. Zhang *et al.* [77] documented higher values of heart rate in overweight individuals and also showed the risk of the development of diabetes in the follow-up of subjects with a higher value of BMI, WHR, and WC when compared to a normal-weight population. A positive linear correlation between resting heart rate (RHR) and BMI has also been recorded in the study done by Al-Qurashi *et al.* [75]. Another study conducted by Zhang *et al.* [78] suggests that an elevated heart rate is a warning sign of an increased risk of cardiovascular dysfunction and a risk factor for cardiac morbidity.

Obesity affects and alters hemodynamic and autonomic functions in the body [50]. It produces an increment in total blood volume and cardiac output, which is partly caused by the increased metabolic demand induced by excess body weight [7]. Thus, at any given level of activity, the cardiac workload is greater for obese subjects [16,79]. Additionally, in the obese population, fat continuously accumulates in arterial vessels, blocking the blood flow of large arteries and increasing peripheral arterial resistance [7]. Obese subjects, however, have an overall higher cardiac output due to modulation in left ventricular muscle mass and lower total peripheral resistance, which can be explained by the fact that, in adipose tissue vascular beds, the resistance of blood flow decreases [80]. All these factors lead to an increase in heart rate, which can directly increase myocardial oxygen consumption and induce the breaking up of elastic fibers within the arterial wall along with other wear and tear in cardiovascular tissue. An increased RHR in obese and overweight individuals could also be due to decreased parasympathetic and increased sympathetic activity in obesity [81]. HRV values, when correlated with obesity indices, indicate that obesity causes sympathovagal imbalance with a dominant sympathetic drive and decreased parasympathetic action on the heart. Thus, the effect of obesity

on the cardiovascular system can be due to mechanical challenges posed by higher weight and alterations in the autonomic state of these individuals.

### Obesity and electrocardiographic parameters

Longer PR intervals have already been established in obese populations, as shown by previous studies [31–33]. Mshui *et al.* [82] found a longer QTc interval in the obese group (445 ± 32 ms) compared with the normal-weight group (388 ± 29 ms), with a *P* value of <0.0001. A study on the Indian population, conducted by Hussain and Farooque [36], comparing QTc intervals with BMI, found significantly higher values of QTc intervals in overweight (390.17 ± 18.98 ms) and obese (413.56 ± 31.35 ms) subjects compared with normal-weight (374.83 ± 18.18 ms) subjects (*P* value <0.01). This has also been recorded in previous studies by Park *et al.* [28] on obese women and by Hussain and Farooque [36], who documented a positive correlation between normal-weight and obese populations. A previous study by Arslan *et al.* [83] in young men documented a statistically significant positive correlation of QTc interval with WC ($r = 0.357$, $P < 0.001$). A study conducted by Hussain and Farooque [36] also previously documented a positive correlation of WHR with QTc ($r = 0.54$, $P < 0.05$). These studies signify that central obesity parameters such as WC and WHR affect the duration of the QTc interval, which is a parameter for measuring ventricular depolarization and repolarization in the cardiac cycle.

Inanir *et al.* [84] found a significantly shorter Tpe interval in the normal-weight control group (68.6 ± 8.1 ms) compared with the obese group (79.2 ± 9.7 ms), with a *P* value of < 0.001. The study by Inanir *et al.* [84] also found that the values of Tpe were higher in the obese compared with normal-weight subjects, and a statistically significant positive correlation was also found between BMI and the Tpe interval ($r = 0.458$, $P = 0.011$) in subjects of all three groups. Another study conducted by Hussain and Farooque [36] in the Indian population showed shorter durations of the Tpe interval in the normal-weight (86.47 ± 13.32 ms) and overweight (87.04 ± 17.01 ms) groups, with longer values in the obese group (90.27 ± 11.77 ms). They also observed a statistically significant positive correlation of Tpe with BMI ($r = 0.21$, $P < 0.05$) and WHR ($r = 0.25$, $P < 0.05$). A recent study by Dykiert *et al.* [85] also found a relationship between Tpe interval and QT dispersion in the obese state. This finding signifies that in the obese state, as the values of these indices increase, the Tpe/QT ratio also increases. It has already been documented in studies that longer Tpe interval values are directly related to increased chances of cardiac morbidity (arrhythmia) [26,86] and a study by Panikkath *et al.* [87] stated that the risk of cardiac mortality (SCD) increases with longer durations of the Tpe interval.

Prolonged QT and Tpe intervals in obese individuals suggest that there is altered cardiac electrophysiology, as evidenced by an increased duration of both ventricular depolarization and repolarization. Since the Tpe/QT ratio is also higher in the obese, it, however, may imply that the duration of repolarization of the M cells of the myocardium contributes more to the total duration of the QT interval in the obese [88]. The prolongation of the Tpe interval may be attributed to the structural effects of obesity on the heart, which profoundly impacts the M cells of the myocardium. A multitude of factors in obesity may contribute to these structural changes, as obesity is associated with systemic inflammation, generalized enlargement of fat depots, and uncontrolled release of fatty acids into the circulation [89]. These features support the occurrence of cardiac adiposity, with an increase in intramyocardial triglyceride content and an enlargement of the volume of fat surrounding the heart and vessels. Triglyceride accumulation is associated with left ventricular hypertrophy and dysfunction, which may lead to longer ventricular repolarization parameters in overweight or obese individuals [27]. These increased values may lead to various cardiac morbidities (arrhythmias) and predisposition to SCD. There are also increased chances of long QT syndrome, which is itself an independent risk factor for cardiac mortality [43]. As previously mentioned, the Tpe interval measures the repolarization of the mid-myocardial layer (M cells) of the myocardium. It can be asserted that longer Tpe values may relate to abnormalities in this layer of the heart due to obesity. This indicates that obesity may play a role in local myocardial changes occurring in the heart of an individual.

Thus, a prolonged Tpe interval also implies that the myocardium spends more time repolarizing, making it more susceptible to arrhythmogenic stimuli, as it is during this phase that the heart is in a state of relative refractory period.

### Obesity and autonomic function as assessed by heart rate variability

Earlier reports by Laederach-Hofmann [90] indicate that mid-frequency bands (a mix of sympathetic and parasympathetic tone) are negatively correlated with BMI and WHR, especially at rest, with WHR showing stronger significance. The high-frequency (HF) band, representing parasympathetic tone, is negatively correlated with BMI as well. Increased body weight reduces both sympathetic and parasympathetic activity, with a relatively higher reduction in parasympathetic activity, contributing to higher sympathetic drive.

Rajalakshmi *et al.* [91] demonstrated decreased HRV, higher sympathetic, and lower parasympathetic nerve activity in obese participants, with BMI being a major determinant of time-domain and frequency-domain indices. The study by Bray [49] indicated that reduced sympathetic activity and increased vagal activity cause increased insulin secretion and changes in hepatic

metabolism, which facilitate nutrient storage and reduce mobilization, thereby disturbing energy homeostasis and leading to obesity. Studies on populations show that obese patients are more prone to ventricular arrhythmia and that obesity is a strong predictor of SCD in men [92]. Poliakova *et al.* [93] studied 97 men with no endocrinological or cardiovascular abnormalities and related the obesity indices with the HRV of the subjects. They found BMI to be negatively significantly associated with standard deviation of average RR interval (SDARR). They also identified a statistically significant negative correlation in the root mean square of standard deviation of all RR intervals (RMSSD) and the percentage of RR intervals more than 50 ms from the previous interval (pRR50) with WC as well. SDARR represents both SNS and parasympathetic nervous system (PNS) activity in humans and is highly correlated with very low-frequency (VLF) and low-frequency (LF) band power, as well as total power in the measurement of short-term HRV [94]. Thus, a negative correlation of these parameters with obesity indices indicates decreased activity of both PNS and SNS. A previous study by Kleiger *et al.* [95] indicates that higher SDRR values decrease the risk of mortality in acute myocardial infarction patients (5.3 times) when compared to those with lesser values of SDARR. A negative correlation between WHR and RMSSD has been previously documented by studies done by Kim *et al.* [96] and Yi *et al.* [97], both of which found a strong negative correlation between the two. RMSSD was negatively associated with WC, a finding that aligns with previous studies by Windham *et al.* [98] and Farah *et al.* [99]. As RMSSD is an index for parasympathetic function reflecting vagal influence on the heart, lower values of RMSSD indicate decreased PNS activity in obese individuals. WHR and pRR50 were significantly negatively correlated, and pRR50 and WC were negatively correlated, as documented in studies by Farah *et al.* [99] and Yi *et al.* [97]. The pRR50 is an index for measuring HF parameters in the heart and is closely correlated with PNS activity. It is also correlated with RMSSD and HF power, which provide insight into PNS activity. This is considered a more reliable index than short-term SDRR measurements for brief samples of 5 minutes [100]. Thus, the findings described in the above studies indicate a decreased parasympathetic tone in an obese state. The observations of reduced indices of parasympathetic activity, that is, RMSSD and pRR50 in the time domain, and HF in the frequency domain imply that obese individuals have significantly reduced parasympathetic activity compared with normal-weight and overweight individuals. A higher LF/HF ratio, despite significantly lower LF and LF power%, also suggests derangement of both sympathetic and parasympathetic limbs of the ANS in an obese state, with more pronounced parasympathetic derangement [101]. The VLF band is known to be an index for long-term regulatory effects in the body and is ideally measured in 24-hour recordings; in short-term HRV analysis, it may not be as reliable as parameters such as RMSSD and pRR50 [94].

A previous study by Rajalakshmi *et al.* [91] showed that HF power ($ms^2$) was negatively correlated with BMI ($r = -0.40$), WC ($r = -0.37$), and WHR ($r = -0.37$), and there was also a negative correlation of high frequency normalized units (HFnu) with BMI ($r = 0.32$) and WC ($r = 0.28$). The HF band reflects parasympathetic activity and is referred to as the respiratory band because it corresponds to HRV related to the respiratory cycle. Total vagal blockage virtually eliminates HF oscillations [102]. The modulation of vagal tone helps maintain the dynamic autonomic regulation important for cardiovascular health. Deficient vagal inhibition is implicated in increased morbidity [103]. Therefore, findings show that as obesity increases, there is a decrease in parameters measured in the HF band, such as HF power, HF power%, and HFnu. This shows that obese subjects have reduced parasympathetic activity compared with normal-weight and overweight subjects.

High LF band reflects increased sympathetic activity [104]. Some earlier studies on sympathetic nerve activity in obese individuals have produced conflicting results; a few studies have shown a decrease [105,106], while many others have shown an increase in sympathetic activity in obesity [107–113]. Newer studies, however, have been more toward increased sympathetic activity in the obese state [114].

### The interplay

These findings suggest that the QTc interval is affected by autonomic activity in the heart. The Tpe interval, on the other hand, is unaffected by the autonomic modulation occurring in the heart, which is also known to be less influenced by ANS modulations. All these findings indicate a significant impact of the obese state on cardiac electrophysiology, which could be a consequence of hemodynamic, structural, and autonomic changes observed in obesity. Adipose tissue is metabolically active, releasing proinflammatory and arrhythmogenic adipocytokines that influence ventricular APD by modulating ionic channel activity. These adipocytokines, together with autonomic neuropathy, contribute to arrhythmogenic risk. Neuropathy typically affects the longest nerve fibers first, with early signs seen as vagus nerve denervation, leading to reduced HRV. As autonomic changes progress, local neurotransmitter release shortens the refractory period, directly affecting the ventricular myocardium and thereby altering cardiac repolarization duration. This complex interaction between adipose-driven inflammation and autonomic neuropathy highlights their combined influence on cardiac electrical stability. To the best of our knowledge, this is one of the first reviews of

**Fig. 4**


Interplay of autonomic functions and ventricular repolarization in the obese state (created in Microsoft PowerPoint).

its kind to examine autonomic functions as measured by HRV and ventricular repolarization parameters. These findings have been described in Fig. 4.

Variations in measuring HRV and ventricular repolarization markers across studies could influence comparability. Most of the studies included in the review are cross-sectional in nature, limiting the ability to infer causation or long-term effects of obesity. While associations are documented, the underlying molecular mechanisms linking obesity, HRV, and ventricular repolarization remain insufficiently explored.

## Conclusion

This review highlights the significant impact of obesity on HRV and ventricular repolarization, which are critical markers of cardiovascular health. Obesity-induced structural and functional changes, including prolonged QT and Tpe intervals, suggest delayed cardiac recovery and increased arrhythmogenic risk. The autonomic imbalance favoring sympathetic over parasympathetic activity exacerbates these risks. The Tpe interval emerges as a potential early marker for cardiac dysfunction in obese individuals, emphasizing the need for early intervention strategies to mitigate CVD risks. These findings underscore the importance of integrating measures to address obesity in cardiovascular health management, fostering better treatment outcomes.

## Acknowledgements

### Conflicts of interest

There are no conflicts of interest.

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