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Original Research Article

Prevalence and Factors Associated with Electrocardiographic Abnormalities among Adults Attending Methadone Assisted Therapy in Dodoma, Central Tanzania

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Abstract: ***Background:*** Patients with opioid use disorder are at a higher cardiovascular risk due to the effect of opioids on the cardiovascular system. Cardiac conduction abnormalities, electrical activity impairment, cardiac arrhythmias and ventricular hypertrophy are reported in the opioid population. ***Aim:*** This study aimed to assess the prevalence and factors associated with ECG abnormalities among adults with opioid use disorder attending at Itega addiction center for methadone assisted therapy [MAT]. ***Methods**:* A cross-sectional analytical study was conducted among adult outpatients attending Itega addiction center in Dodoma. A calculated sample size of 321was attained through convenience sampling approach. A standard 12-lead ECG was recorded for each participant and interpreted by two independent cardiologists. Univariate and multivariable logistic regression were computed to determine the factors associated with ECG abnormalities. Under adjusted analysis, a p-value of less than 0.05 was considered significant for factors associated with ECG abnormalities after controlling for all the variables with a minimum p-value of 0.2 at univariate analysis. ***Results:*** The majority 308 [95.95%] of the participants were males, 197 [61.37%] had attained primary educational level and the mean age of the participants was 35.44 ± 6.54 years. The overall prevalence for any ECG abnormalities in this study was 26.47%, Sinus bradycardia 59[18.4%] being the most observed ECG abnormality followed by QTc prolongation 27[8.41%]. A month's increase in the duration on MAT and being a female were significantly associated with lower odds of ECG abnormalities [AOR =0.85, 95% CI =0.74-0.96 p =0.014] and [AOR = 0.05, 95% CI = 0.01-0.59, p = 0.017] respectively. ***Conclusion:*** The high prevalence of ECG abnormalities implies high cardiovascular abnormalities among population with opioid use disorder. Given that majority of the ECG abnormalities are treatable, integrating cardiovascular in the population would be beneficial for this population.

Keywords: Methadone Assisted Therapy [MAT], Electrocardiogram abnormalities, Opioid use disorders.

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INTRODUCTION

Opioid use continues to be major problem of public health important worldwide, as per 2019 report; 53 million people are estimated to use opioids and opioids is responsible for the two thirds of 587,000 drug related death by 2017[1]. At the same time, up to 300,000 people are estimated to use opioids with significant proportion affected by HIV/AIDS and Hepatitis B virus[2]. Heroin is particularly the most abused opioid worldwide, in the United States; 808,000 [0.3%] of people aged 12 years and older used heroine between 2017-2018 while 157,000[0.5%] of the young adult populations age 18-25 years use heroin in the same period[3].

Although, the biological pathway between opioid exposure and cardiovascular disease[CVD], association between opioid drug use and increased risk of cardiovascular event such heart failure [MI] and myocardial infarction[HF] [4]. The presence of

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cardiovascular diseases have been observed as electrocardiographic abnormalities in the population, these include arrhythmias, sinus bradycardia, hypotension, benign atrial-ventricular block and the resulting atrial or ventricular automatic ectopy and tachycardia[5]. Several factors have been associated with ECG abnormalities in opioid use which include the sex, age ,comorbid diseases prior to treatment, duration on methadone treatment, other prescription drugs which interact with methadone and concomitant use of other illicit drugs while on treatment[6].

While there are diverse ECG abnormalities in among patients with opioid use disorders, majority of studies have focused mainly on the QTc prolongation. Furthermore, there are no studies done in Tanzania reporting the burden and predictors of cardiovascular abnormalities in opioid population. This study therefore aims to determine the prevalence and factors associated with the ECG abnormalities among adults with opioid use disorders attending Methadone Assisted Therapy at Itega addiction centre in Dodoma, Tanzania.

METHODS

Study design and setting

A cross-sectional analytical study was carried out at Itega MAT clinic located at Itega addiction centre, a satellite centre of Mirembe mental health hospital [The National Mental Hospital] in Dodoma city, Tanzania with around 500 enrolled clients at the time of study. Itega addiction clinic is located in Itega area, has one psychiatrist, five medical officers, four nurses, one social worker, one occupational therapist, one laboratory scientist and two pharmacists. The clinic is conducted every day from 7.30hrs to 15.30hrs attending up to 300 patients per day with opioid and other drug use disorders. Prior to initiation of treatment, all patients are counselled and screened for drug use, comorbid psychiatric conditions, HIV and Hepatitis B and C. The patients attend daily for the methadone dose, which is given in the form of a solution. The initial starting dose is 30 mg increased gradually according to the patients' symptoms of withdrawal.

Sample size

A sample size of 316 was calculated using the Kish and Leslie formula, $N = Z^2 [P [1-P]/d^2]$, where: N = sample size, Z=Score for 95% Confidence interval which is 1.96, P=Prevalence of ECG abnormalities in methadone assisted clinic previous study by [7], p=29%, d=Marginal error set at 5%. With 5% contingency, 16 participants were added to make a final sample size of 332.

Sampling Techniques

Non-probability sampling [consecutive sampling] was applied whereby all clients attending at Itega MAT clinic who met the inclusion criteria were recruited in the study. The participants were enrolled consecutively whereby the first contact with the participants was at the waiting lounge before going to the clinician for daily care after routine registration. At this point, they were introduced about the study including overall procedures about the study and asked to participate after receiving their routine daily care. Study procedures were applied consecutively from one client to next without skipping until the sample size was reached.

Inclusion and Exclusion Criteria

The study included all patients above 18 years attending at Itega MAT clinic with the capacity to provide informed consent and must be on steady methadone dose for at least seven days. We excluded those in the active phase of psychiatric illness such as psychotic symptoms and could not comprehend instructions for the assessment process. Also excluded were the patients with signs of intoxication [Slurred speech, difficulty maintaining their balance, Slowed reaction, and aggressiveness. Those with a known history of severe cardiovascular condition since childhood or known congenital heart disease or on treatment for cardiovascular conditions before opioid use were also excluded.

Study variables

Outcome variables

The outcome variable was defined as having one or more electrographic abnormalities which included the following; QTc prolongation in milliseconds [ms], sinus bradycardia, sinus tachycardia, left atrial enlargement, right atrial enlargement, left ventricular hypertrophy. At first, it was dichotomized [Yes=presence of ECG abnormality /No= absence of ECG abnormality]. The specific criteria for each ECG abnormality were referred from the Standard definition of terms summarized in the table 1, below.

Table 1: Summary of the standard definition for each ECG abnormality

ECG Abnormality	Definition
Atrial fibrillation [A fib-]	is a common heart rhythm disorder that presents with a Rapid heart rate of 400 to 600 beats per minute, Coarse fibrillatory waves, irregular QRS, absence of P waves[8]
Atrial flutter [Afl]-	occurs when re-entrant circuit is present, causing a repeated loop of electrical activity to depolarize the atrium at a heart rate between 250 to 350 beats per minute presenting with saw tooth pattern P waves [8]
Sinus arrhythmia	Variation of the P-P interval, from one beat to the next, of at least 0.12 seconds, or 120 milliseconds [8]
Multifocal atrial rhythm	Presents with a rate>100B/M, P wave, Variable PR interval, normal QRS[9].

ECG Abnormality	Definition
Premature Ventricular Contraction [PVC]	Presence of sinus tachycardia, atrial tachycardia, atrial fibrillation, AVNRT complexes, atrial flutter, multifocal atrial tachycardia, accelerated junctional tachycardia[9].
Premature Supraventricular contraction [PSVC contraction]	Presence of sinus tachycardia, atrial tachycardia, atrial fibrillation, AVNRT complexes, atrial flutter, multifocal atrial tachycardia, accelerated junctional tachycardia[9].
Left atrial enlargement [LAE]	P wave in lead II is greater than ≥120ms [10].
Bi-atrial enlargement [BAE]	P wave in lead II is greater than 120ms and higher than ≥2.5mm[10].
Left Ventricular hypertrophy [LVH]	Sokolow-LyonSV-I+RV-5or RV-6=≥35 mm [whether male or female][10].
Left Ventricular hypertrophy with strain	SV-I+RV-5or RV-6=≥35 mm [whether male or female] with T waves changes[10].
Right Ventricular hypertrophy [RVH]	R/S ratio of greater than 1 in lead V1 in the absence of other causes or if the R wave in lead V1 is greater than 7 millimetres, tall P duration≤0.120seconds[10].
QRS duration	0.80-0.120seconds[10].
PR interval	0.12-0.20seconds [10].
QTc prolongation	Normal 350ms-440ms.Prolonged >440ms[11]
Q waves	>3mm in depth or 40ms duration any lead except III, aVR [10].
ST segment elevation	>1mm in limb leads and >2mm in the chest leads[12]
ST segment depression	>0.5 mm below PR isoelectric-line between J-Junction and beginning of T in V4,V5,V6,1,aVL.>1mm in any lead [10].
Peaked T waves	T waves taller than 5mm in limb leads and taller than 10mm in chest leads[8]
AV-block 1	PR interval greater than 0.20 seconds[10].
AV-block 2:1	PR interval progressively longer until one P wave is blocked and QRS is dropped[10].
Complete AV-block 2	PR interval varies greatly, waves normal /may be superimposed on QRS or T waves[10].
Left anterior hemi block	Left axis deviation and slightly prolonged QRS[12]
Left posterior hemi block	Left axis deviation and slightly prolonged QRS[12]
Complete right bundle branch block	Lead V1-RSR',V6-widened slurred S wave[9]
Complete left bundle branch block	T wave inversion in lateral leads [1, V2 and V5-V6]. Lead 6- M pattern[10].

Independent variables

This included sociodemographic factors such as age [in years], sex, marital status, education, and employment status. Clinical factors included Hypertensive Heart Diseases [HTN], Diabetes Mellitus [DM], Anxiety and Depressive disorders, Hepatitis B and C viruses and Body Mass Index [BMI]. The substance use-related factors included smoking of cannabis and cigarette, alcoholism, use of diazepam and cocaine within the past week and concurrent substance use before methadone use. Opioid related factors included the duration on opioid, the duration on methadone treatment, and the current methadone dose in milligrams.

Measurement of study variables

Electrocardiographic Abnormalities

A standard 12-lead ECG [BPL 9108], [SN H911180104201N000] machine manufactured by BPL medical technology in India was used. The participants had to wear a loose-fitting garment with buttons on the front and women were asked to remove or loosen their brassiere. The participants lied in a supine position, electrode patches and leads were applied as per the protocol. Upper limbs are placed between the elbow and shoulders.

Lower limbs leads were placed a few inches above the ankle. Precordial leads were placed, V1 in the fourth intercostal space at the right border of the sternum. V2 is placed at the fourth intercostal space at the left border of the sternum. V3 placed midway between V2 and V4. V4 placed in the mid-clavicular line in the fifth intercostal space. V5 is placed in the anterior axillary line on the same horizontal level as V4 and V5. The participants were instructed to remain still while the ECG was obtained. Before recording the display was checked for error messages and paper speed of 25mm per second and amplitude of 10mm/Mv was used. The intervals [QT, QRS, and PR] were manually measured by hands using EKG calipers and rulers. PR interval, QRS duration, QT interval, QRS axis, Q, R, S, T waves voltage, and ST-segment were measured in each lead. P waves voltage was measured in lead V1 alone. Right atrial enlargement was defined as P wave voltage > 0.25 mV. Left atrial enlargement was defined as a biphasic P wave in V1. Left ventricular hypertrophy was calculated using Sokolow-Lyon voltage [sum of amplitude of the s waves in lead V1 and R waves in lead V 5 or V 6>3.5mV]. Sinus bradycardia was considered when heart rate <60 B/M, sinus tachycardia was considered when heart rate is >100 B/M.[8],[15].

The beginning of the QT interval was measured from the first deflection from the isoelectric line after the p wave. The end of the QT interval was defined at the point where the steepest tangent at the descending part of the T wave crosses the isoelectric line. The longest QT

interval measured in lead II, V2, or V5 from each ECG was used in further analysis of data. QTc interval was calculated using Bazzet's formula. Bazzett's formula [QTc interval] = [QT interval] /√ [RR interval],[16][17]. QTc interval >450ms for males and >470 for females was considered prolonged in this study [18 ,19,20].

Blood Pressure

An electronic blood pressure machine was used in measuring the blood pressure ofall study participants who consented [HEM, Batch 7120, SN 1901006949, Omron Company, Kyoto, Japan]. The participants were instructed not to smoke or take caffeine before taking the measurements. They were seated in a chair with their back supported and arms supported at heart level. Blood pressure was measured after 5 minutes of rest. Measurements were taken from the right arm. A cuff was placed approximately 2-5 cm above the ante-cubital crease. The machine was switched on, and then the start button was pressed to begin inflation of the machine. Blood pressure was recorded from the screen after completion. Two readings were obtained separated by one minute. The average value was recorded in the database.

Body Weight

A digital weighing machine was used for measuring body weight in kilogram [HL - 1, SN 1881041104024, Hesley Company, German]. The scale was placed on a hard surface. Participants removed shoes and were dressed in light clothing. The weight was recorded to the nearest 0.5 kg.

Height

A stadiometer scale was used for measuring height in meters [SECA, batch 217, Birmingham, United Kingdom]. The participants removed their shoes and stood with the back against the stadiometer. The participants were instructed to stand still with their heads at level with a stadiometer. The movable piece of stadiometer was fitted above the head of the participant. The height was recorded to the nearest meter.

Body Mass Index

The body mass index [BMI] was calculated as weight in kg divided by height in meter squares [kg/m^2]. Table 2 presents the categorization of the BMI.

Table 2: BMI classification [WHO, 2006]

Category	BMI range [kg/m^2]
Underweight	<18.5
Normal	18.5-24.9
Overweight	25-29.9
Obese	≥30

Depressive and Anxiety symptoms

After enrollment in the MAT, the participants are screened for anxiety and depression after seven days as a routine.

Depression was screened using the PHQ-9 tool which has been validated in Tanzania with a sensitivity of 78% and specificity of 87%, a cut-off score of 9 with an internal good consistency Cronbach's alpha 0.83 [$\alpha = 0.83$] [13]. The PHQ -9 scores of 5,10,15, and 20 represented mild moderate, moderately severe,and severe depression, respectively. [13] Anxiety was screened using a Swahili version of the GAD 7 tool which has been validated in Kenya with good internal consistency [$\alpha = 0.82$] [14].

Data collection procedure

Data were collected by the principal investigator [PI] and five research assistants including three medical officers and two registered nurses. The research assistants were trained on data collection for four days, whereby it involved familiarization with the data collection form and instruments for measuring variables. A data collection form was used to collect the required data [Appendix II]. The data collection form comprised four sections. Section I: sociodemographic characteristics, section II: Clinical characteristics, section III: behavioral factors, and section IV: ECG findings and abnormalities. Interaction with the participants during data collection was done in a separate room to maintain privacy. It took approximately 30-50 minutes to complete the assessment and interview of each participant.

Pre-testing of data collection tools was done before the commencement of the study, whereby a pilot study was done two weeks before the commencement of the study. This included 20 clients on MAT; the trained research assistants interviewed the participants using the data collection forms and the research instruments were used for measurable variables. This helped in assessing the applicability of the tools and provided an estimate of a time frame for the interviews to make the necessary adjustments. Two research assistants [medical doctors] who had special training on measuring ECG were given the task of placing ECG electrodes with the supervision of the PI. The ECG results were interpreted by two independent cardiologists who were blinded to patient history and clinical presentation and in case of discordant interpretation, a third was to be consulted.

Data management and analysis

Data analysis was done using SPSS version 24, cross-checking for the missing data and other errors were done after running frequency tables and crosstabs. Categorical variables were summarized in proportions

and percentages while and continuous variables were summarized in mean ± standard deviation [SD] or Median and Interquartile range. The prevalence of ECG abnormalities was analysed by using descriptive statistics in which the overall prevalence of ECG abnormalities was determined and presented as a percentage**.** Binary logistic regression was used to determine the factors associated with ECG abnormalities. All variables with statistically significant p-value ≤ 0.2 under univariate logistic regression adjusted for multivariable analysis and a p-value reaching ≤ 0.05 was considered statistically significant after adjusting for confounders**.**

RESULTS

Sociodemographic and Clinical Characteristics of Study Participants

The study included a total of 321 participants with a mean age of 35.44 ± 5.55 years. The majority 308 [95.95%] were males, 197 [61.37%] had attained primary educational level, 249 [77.57%] were single or never married, and being unemployed comprised of 259 [80.69%] of the participants.

Regarding serological results, 52 [16.20%], 16 [4.98%], and 11 [3.43%] were found to have positive results for HCV, HIV, and HBV, respectively. Cigarette smoking 241 [75.08%] and cannabis 48 [14.95%] were the predominant concurrent substances used.

Over one-third 123 [38.32%] of the participants were on >150 mg of methadone dose, sixteen participants [5%] met the criteria for hypertension, while, 154 [47.98%] and 125 [38.94%] had pre-hypertension as per systolic and diastolic blood pressure parameters, respectively.

Table 3: Sociodemographic and Clinical Characteristics of Adults Attending at Itega Addiction Centre for Methadone Assisted Therapy in Dodoma region [N = 321]

Variables	Frequency [n]	Percentage [%]	Mean
Age [years]			
≤30	82	25.55	35.44±6.54
31-40	170	52.96	
>40	69	21.50	
Sex			
Male	308	95.95%	
Female	13	4.05%	
Marital status			
Married/in Union	72	22.43	
Single/never married	249	77.57	
Educational level			
Informal or incomplete primary school	16	4.98	
Primary	197	61.37	
Secondary	98	30.53	
Tertiary	10	3.12	
Employment status			
Employed	62	19.31	
Not employed	259	80.69	
Familial chronic illness			
Yes	38	11.84	
No	283	88.16	
HCV test status			
Negative	269	83.80	
Positive	52	16.20	
HBV test status			
Negative	310	96.57	
Positive	11	3.43	
HIV status			
Negative	305	95.02	
Positive	16	4.98	
Methadone dosage [mg]			
≤50	30	9.35	
51-100	122	38.01	
101-150	46	14.33	

Variables	Frequency [n]	Percentage [%]	Mean
>150	123	38.32	
Concurrently substance use prior MAT			
Heroin and cigarette	241	75.08	
Heroin and cannabis	48	14.95	
Heroin and alcohol	30	9.35	
Combination of other drugs	2	0.62	
Systolic pressure [mmHg]			
Normal [90-119]	157	48.91	**116.69±10.45**
Pre-HTN [120-139]	154	47.98	
HTN 1 [140-159]	7	2.18	
HTN 2 [≥160]	3	0.93	
Diastolic pressure [mmHg]			
Normal [60-79]	186	57.94	**75.50±7.24**
Pre-HTN [80-89]	125	38.94	
HTN 1 [90-99]	6	1.87	
HTN 2 [≥100]	4	1.25	
Other substances used while on MAT			
Smoking	208	81.57	
Cannabis	31	12.16	
Alcoholism	16	6.27	
BMI [kg/m^2]			**20.15±2.40**
Underweight [<18]	60	18.69	
Normal [18-24.9]	249	77.57	
Overweight [25-29.9]	12	3.74	
Depression			
No depression	100	31.15	
Minimal depression	124	38.62	
Mild depression	80	24.92	
Moderate depression	17	5.29	
Anxiety			
No anxiety	187	58.25	
Mild anxiety	98	30.52	
Moderate anxiety	34	10.59	
Severe anxiety	2	0.62	
Duration on Methadone in months [25,75th QR]			8[3,15]
Duration Heroin/Opioids in years			11.75±6.70

Prevalence of ECG Abnormalities among Adults with Opioid Use Disorder Attending at Itega Addiction Centre for Methadone Assisted Therapy in Dodoma region

The prevalence of participants with one or more ECG abnormality was 85 [26.47%]. [Figure 1].

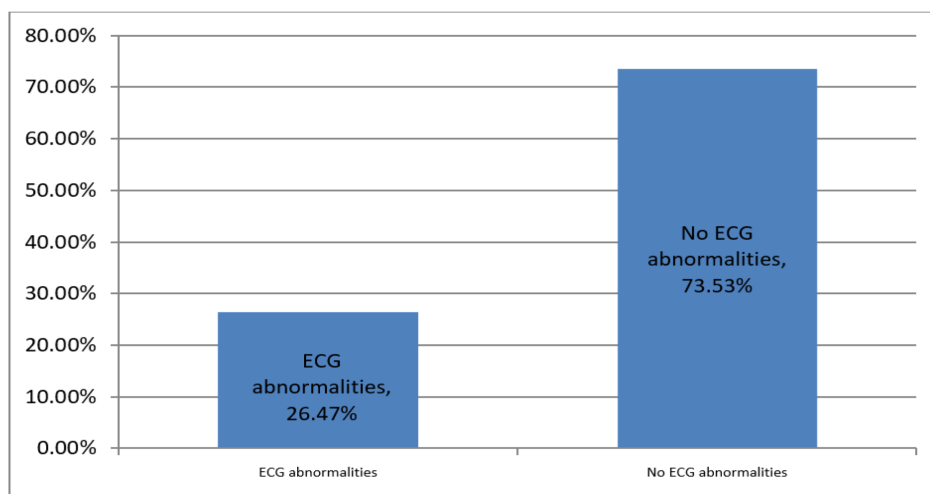

Figure 1: Prevalence of ECG Abnormalities among Adults with Opioid Use Disorder Attending at Itega Addiction Centre for Methadone Assisted Therapy in Dodoma region [N = 321]

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Identification of the ECG Abnormalities among Adults with Opioid Use Disorder Attending at Itega Addiction Centre for Methadone Assisted Therapy in Dodoma region

The most observed ECG abnormalities were sinus bradycardia 59 [18.4%] followed by prolonged QTc interval which accounted for 27 [8.4%] while other ECG abnormalities had a frequency of 2[0.6%] or less, see Table 4.

Table 4: Frequency Distribution of the ECG Abnormalities Among Adults with Opioid Use Disorder Attending at Itega Addiction Centre for Methadone Assisted Therapy in Dodoma region [N = 321]

ECG abnormalities*	Frequency [n]	Percentage [%]
Sinus bradycardia	59	18.4
QTc prolongation	27	8.4
Sinus tachycardia	2	0.6
Left ventricular hypertrophy	2	0.6
Left atrial enlargement	1	0.3
Right atrial enlargement	1	0.3

*An individual may have more than one ECG abnormality

Factors Associated with ECG Abnormalities

After adjusting for confounders, female sex [AOR = 0.05, 95% CI = 0.01-0.59, p = 0.017] and a month increase in the duration on MAT [AOR = 0.85, 95% CI = 0.74-0.96, p = 0.014] were significantly associated with decreased risk of ECG abnormalities.

Being underweight had a 1.24-fold increased risk for ECG abnormalities compared to normal weight but the difference was not significant [AOR = 1.24, 95% CI = 0.65-2.37, p = 0.506]. Also, having HBV and HIV infections had an increased risk for developing ECG abnormalities with 1.84- and 1.13-fold increased risk for acquiring ECG abnormalities, respectively. [Table 5].

Table 5: Factors Associated with ECG Abnormalities

Characteristic	COR [95% CI]	p-value	AOR [95% CI]	P-value
Age [years]				
≤30	**Reference**			
30-40	1.07[0.59-1.91]	0.823		
>40	1.09[0.58-2.04]	0.772		
Sex				
Male	**Reference**		**Reference**	
Female	0.23[0.07-0.73]	0.013	0.05[0.01-0.59]	**0.017**
Highest formal education attained				
Primary and below	Reference			
Secondary and higher	1.07[0.64-1.78]	0.803		
BMI [kg/m^2]				
Normal [18-24.9]	Reference			
Underweight [<18.0]	1.24[0.65-2.37]	0.506		
Overweight [≥25-29.9]	0.58[0.18-1.89]	0.366		
Systolic pressure				
Normal [90-119]	Reference			
Pre HTN [120-139]	1.14[0.69- 1.87]	0.599		
HTN 1 [140-159]	0.55[0.12- 2.56]	0.449		
HTN 2 [≥160]	Omitted			
Diastolic pressure				
Normal [60-79]	Reference			
Pre-HTN [80-89]	1.02[0.62-1.69]	0.924		
HTN 1 [90-99]	0.39[0.08-2.03]	0.269		
HTN 2 [≥100]	0.39[0.05- 2.90]	0.364		
Duration on heroin [years]	0.99[0.96-1.03]	0.913		
Duration on Methadone [months]	0.81[0.74-0.89]	0.0001	0.85[0.74-0.96]	**0.014**
Marital status				
Married/cohabiting	Reference			
Single/never married	1.33[0.75-2.33]	0.320		
Employment status				
Employed	Reference			
Not employed	1.35[0.74-2.45]	0.314		

Characteristic	COR [95% CI]	p-value	AOR [95% CI]	P-value
Education level				
Primary and below	Reference			
Secondary and Higher	1.07[0.64-1.78]	0.803		
Chronic illness in the family				
No	Reference			
Yes	0.65[0.32-1.32]	0.237		
HCV test status				
Negative	Reference		Reference	
Positive	0.48[0.25-0.88]	0.019	0.40[0.15-1.04]	0.061
HBV test status				
Negative	Reference			
Positive	1.84[0.39-8.68]	0.441		
HIV status				
Negative	Reference			
Positive	1.13[0.38-3.37]	0.814		
Drug which was being used concurrently prior MAT				
Heroin and smoking	Reference		Reference	
Heroin and Cannabis	0.52[0.27-0.98]	0.046	0..36[0.13-1.07]	0.068
Heroin and Alcohol	0.58[0.26-1.29]	0.188	0.88[0.21-3.61]	0.859
Combination of other drugs	0.34[0.02-5.50]	0.447	[omitted]	
Other drugs used while on Treatment				
Methadone and smoking	Reference		Reference	
Methadone and Cannabis	0.49[0.23- 1.06]	0.071	0.36 [0.13-1.01]	0.052
Methadone and Alcohol	0.52[0.18-1.46]	0.216	0.86[0.19-3.78]	0.839
Methadone dose used in mg categories				
≤50	Reference			
51-100	1.11[0.45-2.76]	0.814		
101-150	0.83[0.30-2.31]	0.723		
>150	0.75[0.30-1.84]	0.536		
Depression				
No depression	Reference			
Minimal depression	1.01[0.42-2.44]	0.974		
Mild Depression	1.05[0.38-2.89]	0.918		
Moderate depression	0.96[0.11-8.90]	0.976		
Anxiety				
No anxiety	Reference		Reference	
Mild anxiety	1.03[0.38-2.76]	0.957		
Moderate anxiety	2.72[0.94- 7.84]	0.064	0.47[0.13- 1.66]	0.244
Severe anxiety	Omitted			

Factors Associated with QTc Prolongation Among Adults with Opioid Use Disorder Attending at Itega Addiction Centre for Methadone Assisted Therapy in Dodoma region

Participants with moderate anxiety were almost fourtimes the odds of having QTc prolongation compared to those without anxiety [AOR = 3.65, 95% CI = 1.18-11.26, p = 0.024]. Being underweight significantly increased the risk of prolonged QTc interval compared to normal BMI [AOR = 2.90, 95% CI = 1.42-30.66, p = 0.027].

Although it was statistically significant, participants with pre-HTN by systolic pressure were almost twice more likely to associated with QTc prolongation compared with those with normal systolic pressure [AOR = 1.72, 95% CI = 0.69-4.27, p = 0.236]. Also, participants with mild anxiety had a 1.18-fold increased risk of getting QTc prolongation compared with those with no anxiety [AOR = 1.18, 95% CI = 0.42-3.31, p = 0.75]. [Table 5].

Table 6: Factors Associated with QTc Prolongation among Adults Attending at Itega Addiction Centre for Methadone Assisted Therapy in Dodoma region [N = 321]

Characteristic	COR [95% CI]	p-value	AOR [95% CI]	P-value
Age [years]				
≤30	Reference			
31-40	0.94[0.44-2.03]	0.880		
>40	0.91[0.40-2.08]	0.827		
BMI				
Normal [18-24.9]	Reference		Reference	
Underweight [<18]	1.70[0.79-3.64]	0.170	2.90[1.42- 30.66]	0.027
Overweight [≥25-29.9]	3.79[1.07-13.38]	0.038	1.02[0.02- 47.06]	0.990
Sex				
Male	Reference			
Female	0.51[0.07-4.05]	0.527		
Highest formal education attained				
Primary and below	Reference			
Secondary and higher	0.71[0.35-1.43]	0.337		
Systolic Pressure				
Normal	Reference		Reference	
Pre hypertension	1.42[0.74-2.74]	0.290	1.72 [.69-4.27]	0.236
HTN stage1	Omitted		Omitted	
HTN stage 2	5.44[1.33-17.90]	0.029	Omitted	
Diastolic Pressure				
Normal	Reference		Reference	
Pre hypertension	1.27[0.65-2.44]	0.474	1.08[0.44-2.62]	0.861
HTN stage1	Omitted		Omitted	
HTN stage 2	7.08[0.95-5.27]	0.056	Omitted	
Duration on Heroin/opioids in years	1.01[0.96-1.06]	0.529		
Duration on Methadone in months	1.10[0.98-1.23]	0.094	1.04[0.91-1.20]	0.541
Marital status				
Married/cohabiting	Reference			
Single/ever married	0.65[0.32-1.31]	0.226		
Employment status				
Employed	Reference			
Not employed	1.60[0.65-3.98]	0.308		
Education level				
Primary and below	Reference			
Secondary and Higher	0.71[0.35-1.43]	0.337		
Any chronic illness in the family				
No	Reference			
Yes	1.21[0.47-3.08]	0.691		
HCV test status				
Negative	Reference			
Positive	0.79[0.32-1.98]	0.620		
HBV test status				
Negative	Reference			
Positive	0.62[0.08-4.97]	0.654		
HIV status				
Negative	Reference		Reference	
Positive	0.45[0.14-1.47]	0.188	0.48[0.12-2.01]	0.316
Concurrent substance used prior MAT				
Heroin and smoking	Reference		Reference	
Heroin and Cannabis	1.35[0.58-3.16]	0.483	1.32[0.44-4.01]	0.617
Heroin and Alcohol	1.04[0.34-3.18]	0.942	1.06[0.21-5.26]	0.942
Combination of other drugs	6.77[0.41-11.1]	0.180	Omitted	
Substance used while on MAT				
Methadone and smoking	Reference			
Methadone and Cannabis	1.23[0.43-3.48]	0.688		

Characteristic	COR [95% CI]	p-value	AOR [95% CI]	P-value
Methadone and Alcohol	0.91[0.19-4.25]	0.913		
Methadone dose[mg]				
≤50	Reference			
51-100	1.35[0.36-5.00]	0.645		
101-150	1.09[0.24-4.97]	0.904		
>150	1.75[0.48-6.31]	0.395		
Depression				
No depression	Reference			
Minimal depression	1.02[0.42-2.44]	0.974		
Mild Depression	1.05 [0.38-2.89]	0.918		
Moderate depression	0.96[0.11-8.90]	0.976		
Anxiety				
No anxiety	Reference		Reference	
Mild anxiety	1.03[0.38-2.76]	0.957	1.18 [0.42- 3.31]	0.750
Moderate anxiety	2.72[0.94-7.84]	0.064	3.65[1.18-11.26]	0.024
Severe anxiety	Omitted		Omitted	

Factors Associated with Sinus Bradycardia

Under multivariable logistic regression, being underweight was significantly associated with the risk of sinus bradycardia compared to normal body weight [AOR = 5.19, 95% CI = 1.02-16.52, p = 0.048]. Also, increased level of anxiety, such as mild compared to no anxiety [AOR = 0.19, 95% CI = 0.06-0.58, p = 0.004]. Similarly, those who used cannabis while on methadone therapy were less likely to have sinus bradycardia compared to smoking cigarettes while on MAT [AOR = 0.23, 95% CI = 0.05-0.91, p = 0.037]. A month increase in duration on MAT was also found to be significantly associated with sinus bradycardia [AOR = 0.74, 95% CI = 0.63-0.87, p = 0.001] [Table 6].

Table 7: Factors Associated with Sinus Bradycardia Among Adults with Opioid Use Disorder Attending at Itega Addiction Centre for Methadone Assisted Therapy in Dodoma region

Characteristic	COR [95% CI]	P-value	AOR [95% CI]	P-value
Age				
≤30	Reference			
31-40	1.15[0.55-2.39]	0.709	1.08[0.31-3.84]	0.898
>40	0.94[0.45-1.97]	0.863	1.05[0.21-5.35]	0.957
BMI				
Normal [18-24.9]	Reference			
Underweight [<18]	2.49[0.94-6.57]	0.065	5.19[1.02- 16.52]	**0.048**
Overweight [≥25]	2.49[0.31- 19.76]	0.388	1.47[0.15- 14.23]	0.746
Systolic Pressure				
Normal	Reference			
Pre-hypertension	1.78[0.94- 3.35]	0.073	0.31[0.11- 0.86]	0.025
HTN stage1	0.31[0.07- 1.48]	0.144	0.27[0.0-4.41]	0.362
HTN stage 2	0.47[0.04- 5.38]	0.546	Omitted	
Diastolic Pressure				
Normal	Reference			
Pre-hypertension	1.46[0 .77- 2.80]	0.304	1.50[0.56-4.01]	0.412
HTN stage 1	0.22[0.04- 1.11]	0.026	Omitted	
HTN stage 2	Omitted		Omitted	
Duration on Heroin/opioids in years	1.00[0.95-1.04]	0.927		
Duration on Methadone in months	0.78[0.70-0.88]	0.001	0.74[0.63-0.87]	0.001
Sex				
Male	Reference			
Female	0.28[0.09-0.91]	0.035	0.14[0.05- 1.22]	0.075
Marital status				
Married/cohabiting [in union]	Reference			
Single/ Ever married	1.045[0.51-2.11]	0.903		
Highest formal education attained				
Primary and below	Reference		Reference	
Secondary and higher	0.64[0.35-1.18]	0.151	1.31 [0.42- 4.03]	0.631

Characteristic	COR [95% CI]	P-value	AOR [95% CI]	P-value
Employment status				
Employed	Reference		Reference	
Not employed	2.15[1.10-4.20]	0.025	2.85 [0.76- 5.77]	0.117
Any chronic illness in the family				
No	Reference		Reference	
Yes	0.48[0.22-1.08]	0.076	0.61 [0. 17-2.28]	0.472
HCV test status				
Negative	Reference		Reference	
Positive	0.39[0.19-0 .78]	0.008	0.37[0.11-1.32]	0.129
HBV test status				
Negative	Reference			
Positive	1.97[0.25- 15.72]	0.523		
HIV status				
Negative	Reference			
Positive	0.73[0.16- 3.30]	0.682		
Concurrent substances used prior MAT				
Heroin and smoking	Reference	Reference		
Heroin and Cannabis	0.64[0.29- 1.41]	0.274		
Heroin and Alcohol	0.55[0.22- 1.39]	0.214		
Combination of other drugs	Omitted			
Substance used while on MAT				
Methadone and smoking	Reference		Reference	
Methadone and Cannabis	0.47[0.20-0.13]	0.092	0.23[0.05-0.91]	0.037
Methadone and Alcohol	0.59[0.18- 1.92]	0.379	0.92[0.13-6.70]	0.937
Methadone dose[mg]				
≤50	Reference			
51-100	2.17[0.79-5.92]	0.13		
101-150	1.44[0.46-4.51]	0.526		
>150	1.39[0.53-3.66]	0.496		
Depression				
No depression	Reference			
Minimal depression	1.63[0.75-3.50]	0.216		
Mild Depression	[Omitted]			
Moderate depression	[Omitted]			
Anxiety				
No anxiety	Reference			
Mild anxiety	0.24[0.11-0.52]	0.001	0.19[0.06-0.58]	0.004
Moderate anxiety	Omitted		Omitted	
Severe anxiety	Omitted		Omitted	

DISCUSSION

The study observed a 24.47% prevalence of ECG abnormalities, with sinus bradycardia 59[18.4%], and QTc prolongation 27[8.4%] being the most prevalent of the ECG abnormalities.

The prevalence of ECG abnormalities varies across the globe with higher rates of ECG abnormalities in MAT centers being reported. A 61% prevalence was reported in Austria[21]. Martell et al reported a prevalence of 48.3% among 118 patients with opioid use disorder on methadone treatment [22], a prevalence of 54% in the United States of America[23], and 59.3% in India[34]. The variations in study population, may explain the diversity in prevalence, while this study had younger, a study in India reported include opioid users who were older and with comorbid non-cardiac medical conditions[34, 35].

The role of aging as an independent risk ECGs abnormalities including greater QTc has been demonstrated[22],[24]. Aging processes may affect the molecular determinants of the QT interval or alter the myocardium with increased myocardial fibrosis previously observed in the Multi-Ethnic Study of Atherosclerosis study[25]. Aging is also associated with alterations in the amount of sympathetic and parasympathetic tone, which can alter myocardial repolarization and the duration of the QTc [26]. Despite of interaction with other factors, opioid drugs in general can uniquely affect the ECG and can lead to the development of cardiac arrhythmias and QTc interval prolongation being the most significant side effect [30].

The mechanism of QTc prolongation due to opioid use is explained by inhibition of the Human ether a go-go related gene[hERG][31]. Also, negative chronotropic effects via Ca^{+} channel antagonism and anticholinesterase effect explain the mechanisms of opioid-induced cardiac arrhythmias[27].

Similar to our study, QTc prolongation and sinus bradycardia are also observed to be the most common abnormalities among people with opioid addiction, [22, 23, 27, 28] , while few others report ST abnormalities to be the most common ECG abnormalities [21]. Other less common ECG abnormalities with smaller proportion include Brugada syndrome, sinus tachycardia and ST changes [29]. While the study may suggest high prevalence of sinus bradycardia based on the criteria of a pulse rate of < 60 beats a minute, this may be a normal observation in healthy young adults and old people above 65 years. Healthy young adults have increased vagal tone which could be the cause of sinus bradycardia at rest [32]. Nevertheless, the observed over-representation of sinus bradycardia in the study population could also be linked to the effect of heroin acting centrally on the vasomotor center to increase parasympathetic and reduce sympathetic activity [28] and also through slowing down the sinus node which is responsible for the regulation of cardiac electrical activity [33].

Several factors are also associated with ECG abnormalities; previous studies have linked higher dosage of methadone to QTc prolongation[27]. A study in Iran showed 54.6% prevalence of QTc prolongation which is attributed to a higher dosage of methadone compared to the dosage of < 150mg provided for majority of our participants [36]. Interestingly, a month unit increase in the duration of methadone in a course of two years use was associated with less ECG abnormalities in our study, participants who are on longer duration of methadone use in years are observed to have higher prevalence of ECG abnormalities[23]. While the observation may suggest cardiovascular benefit of methadone treatment at least in the early phase of MAT, prolonged use of methadone may have be linked to ECG abnormalities. Being an opioid, chronic use of Methadone could be linked to cardiotoxicity related to several ECG abnormalities including QT dispersion, torsades-de pointes, pathological U waves, ventricular bigeminy, Takotsubo syndrome, Brugada like syndrome and coronary artery diseases[37,38].

Our study showed that being male had a positive association with ECG abnormalities. Generally, males are observed to have higher cardiovascular risk at relatively younger age [40] compared to female counterparts who are exposed to cardioprotective endogenous estrogen during fertile period although the benefit is lost post-menopausal [41].

Increased levels of anxiety were associated with QTc prolongation but inversely associated with sinus bradycardia. Although Piccirillo et al showed that anxiety even at moderate levels was associated with QTc prolongation [44] other studies found no association [43]. Anxiety is thought to disturb cardiac autonomic balance and related increased risk of cardiac arrhythmia [45] and also mediate increase in QTc interval variability via adrenergic mechanisms[46], atrial fibrillation[47], and coronary heart diseases [48]. The physiological mechanism of anxiety in causing cardiovascular diseases includes inflammation, endothelial dysfunction, platelet dysfunction, and autonomic dysfunction[49]. Anxiety state can also trigger an increase in neurotransmitters such as dopamine and epinephrine which cause an increased heart rate[50].

However, in a meta-analysis done in Australia, it has been shown that anxiety disorders are associated with sinus bradycardia[51].

Regarding being underweight, compared to those with normal body weight, those who were underweight had a positive association with both QTc prolongation and sinus bradycardia.

It was observed that there was an increased risk of getting QTc prolongation similar to the meta-analysis study which was done in Colombia in a population of underweight adults, it was found that being underweight was associated with QTc prolongation [52]. In another prospective case-control study, it was found being underweight was associated with QTc prolongation [53]. This is similar to the findings in another study done in Italy which also reported that being underweight was associated with QTc prolongation [54]. The mechanism of QTc prolongation in underweight individuals may be explained by micronutrients, macronutrients deficiencies, and electrolytes imbalances[53],[55].In a study by Alem et al, it was found that BMI was associated with electrolyte imbalance whereby those who were underweight were more likely to have electrolyte imbalances[56].Another study which was done in Italy, had shown an association of hypokalaemia with the occurrence of QTc prolongation and ventricular arrhythmias among underweight population[57]. In a cross-sectional study which was done in Korea being underweight was seen as an independent risk factor for cardiovascular diseases. [58].In a longitudinal study on ECG abnormalities among the underweight, loss of cardiac muscle mass has also been shown as a possible cause of occurrence of cardiac conduction defects[59]. Another study on malnutrition had also shown loss of cardiac muscle mass as a cause of ECG abnormalities among the underweight population[60].

While the positive association of being underweight and sinus bradycardia among opioid users in this study was similar to the finding in a study which was done among underweight individuals in which it was

observed that sinus bradycardia was common [61]. Sinus bradycardia is a common phenomenon in the underweight population as the body's parasympathetic nervous systems try to conserve energy[53].In a meta-analysis on the effect of BMI on the autonomic nervous system, weight loss was seen to cause changes in the metabolic profile which could be the main driver in parasympathetic increases with weight loss. Also, the negative energy balance has a role in the variation of the autonomic nervous system with weight loss[62].

Those who smoked cigarettes were more likely to have sinus bradycardia compared to those who used cannabis while on MAT. Nicotine which is the main constituent of cigarettes is a potent blocker of the cardiac A-Type K^+ channels which cause-effect on cardiac physiology and induce arrhythmias including sinus bradycardia [63]. However, nicotine can induce cardiovascular effects causing tachycardia by stimulation of sympathetic neurotransmission, as nicotine stimulates catecholamine release by activation of nicotine acetylcholine receptors localized on peripheral postganglionic sympathetic nerve endings and the adrenal medulla[64,65].

Conclusion

The prevalence of ECG abnormalities in this study is quite significant and requires preventive measures such as screening in this population to prevent morbidity and mortality. Sinus bradycardia and QTc prolongation were the most commonly found types of ECG abnormalities. Males were more likely to have ECG abnormalities. Also, being underweight had an increased risk for both sinus bradycardia and QTc prolongation. There was also a negative association for developing sinus bradycardia for participants with mild anxiety.

Recommendation

ECG screening should be incorporated for opioids users on MAT before during and even after the therapy. There is a need of conducting a longitudinal study among opioids users on MAT in Tanzania to establish possible behavioural and ECG changes.

Limitations

The cross-sectional study design was used hence we cannot establish a causal relationship between predictor and outcome variable. A single 12-lead ECG was used for QTc measurements which might not be able to capture diurnal variations in QTc.

The presence of prolonged QTc interval was observed among MAT patients, however, it is hard to define how much of this QTc prolongation is the result of heroin use and how much of it is the result of the effect of other risks factors. This study lacked a genetic component as genetic testing was not conducted for the evaluation of genetic mutations and polymorphism as factors influencing QTc prolongation.

In this study, some of the possible confounders such as underlying medical condition, serum electrolytes, urine drug screen, and serum methadone levels, were not measured. Also, concomitant use of QT-altering medications that were not identified in the study might affect statistics. There was a large difference between the number of men and women enrolled in the study. This may under power the conclusions in the study due to a low number of females.

Ethical issues

Ethical approval was obtained from the University of Dodoma. Permission to conduct the study was obtained from Itega addiction Centre. The participants were free to withdraw from the study at any point in time. Participants found with ECG abnormalities were scheduled for cardiology clinic for further investigation and follow up.

References

1. World Drug Report 2019: 35 million people worldwide suffer from drug use disorders while only 1 in 7 people receive treatment [Internet]. United Nations: Office on Drugs and Crime. [cited 2022 Jul 16]. Available from: //www.unodc.org/unodc/en/frontpage/2019/June/world-drug-report-2019_-35-million-people-worldwide-suffer-from-drug-use-disorders-while-only-1-in-7-people-receive-treatment.html
2. NATIONAL GUIDELINES FOR THE MANAGEMENT OF HIV AND AIDS 6th 2017 – NACP-National AIDS Control Programme [Internet]. [cited 2022 Jul 17]. Available from: https://nacp.go.tz/download/national-guidelines-for-the-management-of-hiv-and-aids/
3. Lipari RN. Key Substance Use and Mental Health Indicators in the United States: Results from the 2018 National Survey on Drug Use and Health. 2018;82.
4. Singleton JH, Abner EL, Akpunonu PD, Kucharska-Newton AM. Association of Nonacute Opioid Use and Cardiovascular Diseases: A Scoping Review of the Literature. J Am Heart Assoc. 2021 Jul 6;10[13]: e021260.
5. Ghuran A, Nolan J. Recreational drug misuse: issues for the cardiologist. Heart. 2000 Jun 1;83[6]:627–33.
6. Behzadi M, Joukar S, Beik A. Opioids and Cardiac Arrhythmia: A Literature Review. Med Princ Pract. 2018;27[5]:401–14.
7. Anchersen K, Clausen T, Gossop M, Hansteen V, Waal H. Prevalence and clinical relevance of corrected QT interval prolongation during methadone and buprenorphine treatment: a mortality assessment study. Addict Abingdon Engl. 2009 Jun;104[6]:993–9.
8. Kusumoto FM, Schoenfeld MH, Barrett C, Edgerton JR, Ellenbogen KA, Gold MR, et al. ACC / AHA / HRS GUIDELINE 2018 ACC / AHA / HRS Guideline on the Evaluation and Management of

Patients With Bradycardia and Cardiac Conduction Delay. 2019.
9. Surawicz B, Childers R. AHA / ACCF / HRS Recommendations for the Standardization and Interpretation of the Electrocardiogram. JAC. 2009;53[11]:976–81.
10. Rapid Interpretation of EKG's - 6th Edition [2000].pdf.
11. Webb J, Humphries K, Sutandar A. How long is too long? J Invasive Cardiol. 2001;13[10]:673.
12. Yanowitz FG. Introduction to. 2018; 0:1–91.
13. Fawzi MCS, Ngakongwa F, Liu Y, Rutayuga T, Somba M, Kaaya SF. screening of depression in Tanzania. 2020;9–14.
14. Psychiatry G, Nyongesa MK, Mwangi P, Koot HM, Cuijpers P, Newton CRJC. The reliability, validity and factorial structure of the Swahili version of the 7 - item generalized anxiety disorder scale [GAD - 7] among adults living with HIV from Kilifi, Kenya. Ann Gen Psychiatry. 2020;1–10.
15. Mark PRG. ©Prof. Roger G. Mark, 2004. 2004;
16. Dahlberg P, Diamant UB, Gilljam T, Rydberg A, Bergfeldt L. QT correction using Bazett's formula remains preferable in long QT syndrome type 1 and 2. Ann Noninvasive Electrocardiol. 2021;26[1]:1–8.
17. Silva EP, Martins RR. QTc interval prolongation in critically ill patients: Prevalence, risk factors and associated medications. 2018;1–12.
18. Goldenberg I, Moss AJ, Zareba W. QT Interval: How to Measure It and What Is "Normal." :333–6.
19. Sijs H Van Der, Kowlesar R, Klootwijk APJ, Nelwan SP, Vulto AG, Gelder T Van. Clinically relevant QTc prolongation due to overridden drug – drug interaction alerts: a retrospective cohort study. 2009;
20. Arunachalam K, Lakshmanan S, Maan A. Impact of Drug Induced Long QT Syndrome: A Systematic Review. 2018;10[5]:384–90.
21. Wallner C, Stöllberger C, Hlavin A, Finsterer J, Hager I, Hermann P. Electrocardiographic abnormalities in opiate addicts. 2008;[August 2006]:1987–93.
22. Martell BA, Arnsten JH, Krantz MJ, Gourevitch MN. Impact of Methadone Treatment on Cardiac Repolarization and Conduction in Opioid Users. 2004;171–4.
23. Yoon G, Batres-y-carr T. Long QTc During Methadone Maintenance. 2017;00[00]:1–6.
24. Chang L ren, Lin Y hsuan, Kuo TBJ, Ho Y cheng, Chen S horng, Chang H chieh W, et al. Progress in Neuro-Psychopharmacology & Biological Psychiatry Cardiac autonomic modulation during methadone therapy among heroin users: A pilot study. Prog Neuropsychopharmacol Biol Psychiatry. 2012;37[1]:188–93.
25. S Chen JXYZWLXW. Role of different concentrations of morphine after coronary perfusion for myocardial protection. WIMJ Open. 2014;1[3]:107–10.
26. Pfeifer A, Weinberg R, Best D, Halter B, Re- M. Differential Changes of Autonomic Nervous System Function with Age in Man. 1993;75[August]:249–58.
27. Behzadi M. Opioids and Cardiac Arrhythmia: A Literature Review. 2018; 7616914115:401–14.
28. Ghuran A, Nolan J. Recreational drug misuse: issues for the cardiologist. 2000;627–33.
29. Sheibani M, Zamani N, Hassanian H. Electrocardiographic Findings in Mortalities Due to Pure Methadone Toxicity. Cardiovasc Toxicol. 2018;0[0]:0.
30. Etaee F, Tobin M, Vuppala S, Komaki A, Delisle BP, Di Biase L, et al. Effects of opioid receptor agonist and antagonist medications on electrocardiogram changes and presentation of cardiac arrhythmia: review article. J Interv Card Electrophysiol 2021. 2021 Oct 21;1–30.
31. Titus-Lay EN, Jaynes HA, Tomaselli Muensterman E, Walroth TA, Ott CA, Desta Z, et al. Methadone-associated QT interval prolongation in patients undergoing maintenance therapy in an urban opioid treatment program. Pharmacotherapy. 2021 Mar 1;41[3]:238–46.
32. Dobrzynski H, Anderson RH, Atkinson A, Borbas Z, Souza AD, Fraser JF, et al. Pharmacology & Therapeutics Structure, function and clinical relevance of the cardiac conduction system , including the atrioventricular ring and out fl ow tract tissues. Pharmacol Ther. 2013;139[2]:260–88.
33. Saeed M, Tripathi D, Chaudhari S. Marked Symptomatic Sinus Bradycardia with New Onset First-Degree Atrioventricular Block after Concomitant Methadone and Trazodone Use. Am J Ther. 2018;25[5]:E575–7.
34. Mirakbari SM, Javadi HR, Allami A, Yazdi Z, Katebi K. Opium-associated QT Interval Prolongation: A Cross-sectional Comparative Study. Indian J Crit Care Med. 2021 Jan 18;25[1].
35. Rabkin SW, Cheng XBJ, Thompson DJS. Detailed analysis of the impact of age on the QT interval. J Geriatr Cardiol. 2016;13[9]:740–8.
36. Soroosh D, Neamatshahi M, Zarmehri B, Nakhaee S, Mehrpour O. Drug-induced prolonged corrected QT interval in patients with methadone and opium overdose. 2019; 3:10–4.
37. Leavitt SB, Krantz MJ. * Methadone Maintenance Treatment. 2001;
38. Alinejad S, Kazemi T, Zamani N, Hoffman RS, Mehrpour O, Artery C, et al. Review article: A SYSTEMATIC REVIEW OF THE CARDIOTOXICITY OF. 2015;577–600.
39. Ouali S, Guermazi O, Guermazi F, Ben M, Halima B, Boudiche S. Drug Abuse-Induced Cardiac Arrhythmias: Mechanisms Mechanisms and Management and Sana. 2018;
40. Bolijn R, Ter Haar CC, Harskamp RE, Tan HL, Kors JA, Postema PG, et al. Do sex differences in the prevalence of ECG abnormalities vary across ethnic groups living in the Netherlands? A cross-sectional

analysis of the population-based HELIUS study. BMJ Open. 2020;10[9]:5–11.
41. Maas AHEM, Schouw YT Van Der, Regitz-zagrosek V, Swahn E, Appelman YE, Pasterkamp G, et al. Red alert for women ' s heart : the urgent need for more research and knowledge on cardiovascular disease in women. 2011;1362–8.
42. Solhaug V, Molden E. Individual variability in clinical effect and tolerability of opioid analgesics – Importance of drug interactions and pharmacogenetics. Scand J Pain. 2017; 17:193–200.
43. Hu MX, Lamers F, Penninx BWJH, de Geus EJC. Association between depression, anxiety, and antidepressant use with T-Wave amplitude and QT-interval. Front Neurosci. 2018;12[JUN].
44. Piccirillo G, Cacciafesta M, Lionetti M, Nocco M, Di Giuseppe V, Moisè A, et al. Influence of age, the autonomic nervous system and anxiety on QT-interval variability. Clin Sci. 2001;101[4]:429–38.
45. Kelmanson IA. High anxiety in clinically healthy patients and increased QT dispersion: a meta-analysis. 2016;
46. Pohl R, Yeragani VK. QT interval variability in panic disorder patients after isoproterenol infusions. Int J Neuropsychopharmacol. 2001;4[1]:17–20.
47. Lampert R, Haven N. HHS Public Access. 2016;48[6]:1000–5.
48. Roest AM, Martens EJ, de Jonge P, Denollet J. Anxiety and Risk of Incident Coronary Heart Disease. A Meta-Analysis. J Am Coll Cardiol. 2010;56[1]:38–46.
49. Celano CM, Daunis DJ, Lokko HN, Campbell KA, Huffman JC. Anxiety Disorders and Cardiovascular Disease. Curr Psychiatry Rep. 2016;18[11].
50. Zarrindast MR, Khakpai F. The Modulatory Role of Dopamine in Anxiety-like Behavior. Arch Iran Med. 2015 Sep;18[9]:591–603.
51. Chalmers JA, Quintana DS, Abbott MJA, Kemp AH. Anxiety disorders are associated with reduced heart rate variability: A meta-analysis. Front Psychiatry. 2014;5[JUL]:1–11.
52. Vargas C. Alteraciones electrocardiográficas en anorexia nervosa : revisión crítica de la literatura. Rev Colomb Psiquiatr. 2015;44[1]:33–40.
53. Winston AP. The clinical biochemistry of anorexia nervosa. Ann Clin Biochem. 2012;49[2]:132–43.
54. Milano W, Capasso A. Cardiovascular alterations in eating disorders. 2018;3[2]:1–3.
55. Maguire A, Douglas I, Smeeth L, Thompson M. Determinants of cholesterol and triglycerides recording in patients treated with lipid lowering therapy in UK primary care. Pharmacoepidemiol Drug Saf. 2007;16[May]:228–228.
56. Alem A, Edae CK, Kelta Wabalo E, Abera Tareke A, Ayalew Bedanie A, Reta W, et al. Factors influencing the occurrence of electrolyte disorders in cancer patients. SAGE Open Med. 2021; 9:205031212110528.
57. Facchini M, Sala L, Malfatto G, Bragato R, Redaelli G, Invitti C. Low-K+ dependent QT prolongation and risk for ventricular arrhythmia in anorexia nervosa. Int J Cardiol. 2006;106[2]:170–6.
58. Park D, Lee JH, Han S. Underweight: another risk factor for cardiovascular disease? A cross-sectional 2013 Behavioral Risk Factor Surveillance System [BRFSS] study of 491,773 individuals in the USA. BRFSS Cent Dis Control Prev. 2017;48[September].
59. DiVasta AD, Walls CE, Feldman HA, Quach AE, Woods ER, Gordon CM, et al. Malnutrition and hemodynamic status in adolescents hospitalized for anorexia nervosa. Arch Pediatr Adolesc Med. 2010;164[8]:706–13.
60. El-Sayed HL, Nassar MF, Habib NM, Elmasry OA, Gomaa SM. Structural and functional affection of the heart in protein energy malnutrition patients on admission and after nutritional recovery. Eur J Clin Nutr. 2006;60[4]:502–10.
61. Yahalom M, Spitz FM, Roguin N, Turgeman Y, Heno N. The Signi fi cance of Bradycardia in Anorexia Nervosa. 2013;1[212].
62. Costa J, Moreira A, Moreira P, Delgado L, Silva D. Effects of weight changes in the autonomic nervous system: A systematic review and meta-analysis. Clin Nutr. 2019;38[1]:110–26.
63. Liang H yueh, Chang S sheng, Wang Y chen, Liang W miin, D P, Lane H yuan, et al. Gender-Specific Differences in Susceptibility to Low-Dose Methadone-Associated QTc Prolongation in Patients with Heroin Dependence. :7–10.
64. Haass M, Kübler W. Nicotine and sympathetic neurotransmission. Cardiovasc Drugs Ther. 1997;10[6]:657–65.
65. Page SJ, Zhu M, Appleyard SM. Effects of acute and chronic nicotine on catecholamine neurons of the nucleus of the solitary tract. Am J Physiol - Regul Integr Comp Physiol. 2019;316[1]: R38–49.

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