The Correlations between Admission Heart Rate and Corrected QT Interval Prolongations with Coronary Artery Disease in Patients with Acute Coronary Syndrome

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

ABSTRACT

Background: Coronary heart disease is a major cause of mortality and this health problem is reaching pandemic in both developed, and developing countries. ACS carries significant morbidity and mortality and the prompt diagnosis, and appropriate treatment is essential. HR was identified as a risk predictor of ACS. Both continuous increase in high baseline heart rate and decrease in low baseline heart rate are associated with higher risk of CVD. Decreased heart rate could also cause dispersion of atrial repolarization which, in turn, initiate cardiovascular events.
Aim: The aim of this study was to assess the correlation between heart rate and severity of coronary artery disease in patient with acute coronary syndrome.
Patients and Methods: The retrospective study was conducted on 120 patients that fulfilled the inclusion criteria were recruited from Cardiology department in Tanta university hospitals presented with acute coronary syndrome.
Results: There was highly significant difference between both groups regarding *admission heart rate & QTc interval*. Both groups of low AHR< 60 bpm & high AHR >90bpm were significantly

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associated with severe CAD &.Mainly those patients with higher admission heart rate were more likely to have higher Syntax scores (severe coronary lesion). Also, patients with prolonged QTc had severe coronary artery diseases, higher SS & high probability to suffer adverse cardiac events more than patients without prolonged QTc interval.

Conclusion: The current study showed that QTc interval prolongation and admission HR are independent predictors of the severity of coronary artery disease in patients with acute coronary syndrome.

Keywords: Admission heart rate; QT Interval; coronary artery disease; acute coronary syndrome.

1. INTRODUCTION

Acute coronary syndrome (ACS) is the umbrella term for the clinical signs and symptoms of myocardial ischemia: unstable angina, non–ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI). The diagnosis and classification of ACS is based on a thorough review of clinical features, including electrocardiogram (ECG) findings and biochemical markers of myocardial necrosis [1].

ACS carries significant morbidity and mortality and the prompt diagnosis, and appropriate treatment is essential. Although mortality from ACS has declined substantially, it is still estimated that 40% of the patients who experience a coronary event will die within 5 years with the risk of death being 5 to 6 times higher in individuals who experience a recurrent event [2].

Heart rate (HR), a simple and easily measured clinical parameter, serves as a determinant of myocardial oxygen demand, coronary blood flow, and myocardial performance and plays a key role in the adaptation of cardiac output to metabolic needs [2].

Several clinical and epidemiological studies have reported that HR is an established predictor of cardiovascular (CV) morbidity and mortality in different patient populations with or without CV risks. An elevated HR influences and even participates in all stages of the CV disease continuum initiating from endothelial dysfunction and continuing via atherosclerotic lesion formation and plaque rupture to end-stage CV diseases [3].

Also HR may reflect other underlying processes leading to cardiovascular events. For instance, elevated heart rate reflects increased sympathetic activity, which is linked to an increased risk of obesity, diabetes, hyperlipidemia and hypertension [3].

Patients who have a higher HR, on the other hand, also demonstrate a higher number of angina attacks, uncontrolled systolic blood pressure, hospitalization for unstable angina, positive angiography and even hospitalization for HF. Elevated HR has been demonstrated to promote low and oscillatory endothelial shear stress, which was increasingly linked with plaque vulnerability and disruption in addition to platelet and leukocyte activation [4].

During the acute phase of ischemia, structural myocardial damage, electrolytic imbalance and an ion channel dysfunction in combination with an increased sympathetic activity may lead to a prolongation of the QT interval. Therefore, when approaching a patient with ACS, the prognostic role of corrected QT (QTc) interval prolongation should be considered [5].

2. METHODOLOGY

2.1.1 Patients and Methods

Patients population: 120 patients that fulfilled the inclusion criteria were recruited from cardiology department in Tanta university hospitals presented with acute coronary syndrome, divided into 2 groups according to SYNTAX Score (SS) [6].

Group I (72 patients): Those with low syntax score (<22)

Group II (48 patients): Those with intermediate to high syntax score (>22)

2.1.2 Inclusion criteria

1. Symptoms of ischemia (e.g. chest discomfort, angina equivalent and silent ischemia).

2. Electrocardiogram (ECG) changes indicative of new ischemia (new ST-T changes or new left bundle branch block (LBBB).
3. Development of pathological Q-wave changes in the ECG.(32,42)

2.1.3 Exclusion criteria

1. Patients with previous MI or previous PCI.
2. Patients presented with cardiogenic shock.
3. Patients underwent CABG.
4. Patients with end stage renal failure (creatinine clearance <15 mL/min).
5. Patients with hematological disorders.
6. Patients with active hepato-biliary disease.
7. Patients with neoplastic diseases.
8. Patients with psychiatric disease
9. Patients with thyroid dysfunction.
10. Patients with connective tissue disorder.
11. Patients with recent major surgical procedure or trauma.
12. Patients with non-sinus rhythm on the first available resting ECG after admission.
13. Patients taking medications that might affect heart rate before admission e.g. (thyrotoxic & antiarrythmic drugs)
14. Patients with missing or unreadable ECGs, unreadable QT intervals.

All patients subjected to

1-An informed consent taken from all patients
2-Full history taking:

- Systemic hypertension
- Patient defined as having diabetes
- Dyslipidemia
- Smoking
- Family history of premature coronary artery diseases

3-Full Clinical examination:
4-Resting 12 leads ECG:

- Standard 12-lead ECG was obtained within 10 minutes of first medical contact (FMC) according to ESC guidelines 2017 [7].

5- Laboratory investigations:

- Admission HR Recording
- corrected QT interval (QTc)

6. Transthoracic Echocardiography:

- Assess LV systolic function.

- Assessment of regional wall motion by dividing LV into 17 segments and scoring each segment individually based on its motion and systolic thickening & detection of wall motion abnormalities.
- Detection of complications as LV dysfunction, mitral regurge & ventricular septal rupture [8].

Coronary Angiography: to detect culprit vessel & number of the affected vessels & calculate Syntax Score [6].

2.2 Statistical Analysis

Statistical presentation and analysis of the present study was conducted, using the mean, standard Deviation, unpaired student t-test, Paired t-test, ROC-curve, Logistic Regression and chi-square tests by (IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp.).

3. RESULTS

Regarding risk factors in the study population: Smoking: 57 patients of the study population were smokers. In group I: 21 patients (29.9%) were smokers, while in group II: 36 patients were smokers (75%). Smoking was statistically significant between the two groups (P value =0.004). Hypertension (HTN): 42patients of the study population were hypertensive. In group I: 12 patients were hypertensive (16.7%), while in group II: 30 patients were hypertensive (62.75%). HTN was statistically significant between both syntax groups (P value 0.003). Diabetes Mellitus (DM): 48 patients of the study population were diabetic. In group I: 12 patients were diabetic (16.7%), while in group II: 36 patients were diabetic (75%). DM was statistically highly significant between the two groups (P value =0.001). Dyslipidemia: 42 patients of the study population had dyslipidemia. In group I: 15patients had dyslipidemia (20.8%), while in group II: 27 patients (56.3%) had dyslipidemia. There was statistically significant difference between both groups. (P=0.001) (Table 1).

Electrocardiographic data: Regarding QTc: In group I (low SS): It ranged from 418-473 msec with mean of 435.08 ±12. 96 while, in group II(intermediate to high SS), it ranged from 439-482msec with higher mean of QTc (459.44 ±14.30). There was highly significant difference between both SYNTAX groups regarding range & mean of QTc interval with p value (0.001). By subclassifying the studied population according

to QTc: Group 1 (QTC < 440 msec): total patients was 54, 51 patients (70.8%) were included in group I (low syntax) while 3 patients (6.3%) were included in group II (inter to high syntax). Group 2 (QTc ≥ 440 msec): total patients was 66 patients, 21(29.2%) were included in group I (low syntax) While 45 patients (93.8%) were included in group II. There was significant difference between both syntax groups with p value (0.001) & patients with prolonged QTc intervals ≥440 msec had unfortunately suffered severe coronary lesion denoted by higher syntax scores than those without prolonged QTc (Table 2).

Regarding Admission Heart Rate(AHR): In group I: HR ranged from 42-120 bpm with mean of 75.29 ±15.49 bpm while in group II, it ranged from 35 -130 bpm with mean of 90.31 ±31.19. By sub classifiction of the study population according to admission heart rate: There was three heart rate groups: Group A:{HR<60bpm} included 21 Patients: 9 patients (42.9%) had low SS & 12 patients (57.1%) had (intermediate to high SS). Group B: {HR 60-90 bpm} included 60 patients: 54 patients (90 %) had (low ss)& 6 patients (10%) had (Intermediate – high SS). Group C:{HR >90 bpm}: included 39 patients: 9 patients (23.1%) had low SS & 30 patients (76.9%) (inter- high SS) (Table 2).

Table 1. Comparison between the two studied groups according to risk factors

Risk factors			Group I (Low SS) (n=72)	Group II (Intermediate to high SS) (n=48)	X^2	P-value
Smoking	No	N	51	12	24.261	0.004*
		%	70.8%	25.0%		
	Yes	N	21	36		
		%	29.2%	75.0%		
HTN	No	N	60	18	26.593	0.003*
		%	83.3%	37.5%		
	Yes	N	12	30		
		%	16.7%	62.5%		
DM	No	N	60	12	40.833	0.001*
		%	83.3%	25.0%		
	Yes	N	12	36		
		%	16.7%	75.0%		
Dyslipidemia	No	N	57	21	15.879	0.001*
		%	79.2%	43.8%		
	Yes	N	15	27		
		%	20.8%	56.3%		

X^2: Chi square test: p value statistically significant at p ≤ 0.05 DM: diabetes mellitus, HTN: hypertension

Table 2. Comparison between the studied groups regarding QTc & HR

			Group I (Low SS) (n=72)	Group II (Intermediate to high SS) (n=48)	t. test	p. value
QTc (msec)	Range		418 – 473	439 – 482	9.844	0.001*
	Mean ± S. D		435.08 ± 12.96	459.44 ± 14.30		
QTc (msec)	G1 < 440 (total=54)	N	51	3	48.535	0.001*
		%	70.8%	6.3%		
	G2 ≥ 440 (total =66)	N	21	45		
		%	29.2%	93.8%		
HR (bpm)	Range		42 – 120	35 – 130	3.565	0.049*
	Mean ± S. D		75.29 ± 15.49	90.31 ± 31.19		
AHR (bpm)	A < 60 (total =21)	N	9	12	47.225	0.001*
		%	12.5%	25.0%		
	B. 60 – 90 (total =60)	N	54	6		
		%	75.0%	12.5%		
	C ≥ 90 (total =39)	N	9	30		
		%	12.5%	62.5%		

HR: heart rate, QTc: corrected QT interval

Regarding Angiographic data: Regarding number of diseased vessels: SVD (single vessel disease): In group I: 39 patients (54.2%) had SVD while no patients of group II. Two-vessel disease: In group I: 27 patients (37.5%) while 15 patients of group II (31.3%) had two vessel disease. Three-vessel disease (MVD):6 patients (8.3%) in group I, while 33patients (68.8%) of group II had MVD. Multi vessel disease was more prevalent in intermediate to high SS group & there was highly statistically significant difference between both groups regarding number of vessels lesion p value 0.001. Regarding left main lesion: In group II, 15 patients (31.3%) had left main, while no patients had left main in group I. There was significant difference between both groups with p value 0.003. Regarding proximal LAD lesion: 27patients of group I (37.5%) had proximal LAD, while 42 patients (87.5%) of group II. Proximal LAD lesion was more associated with Intermediate to high SYNTAX scores. There was significant difference between groups with p value of 0.002. (Table 3).

ROC curve analysis was done to pick up the best cutoff values of QTc & admission heart rate to predict severity of coronary artery disease which revealed that admission heart rate (AHR) more than 80 bpm is a predictor of severity of CAD with sensitivity 75%, specificity 67% & accuracy 70%, While QTc $\geq$ 450 msec is a predictor of severity of CAD & incidence of major cardiovascular events with sensitivity 81%, specificity 92%, & accuracy 88%. (Table 4).

4. DISCUSSION

In the current study DM had significant impact on severity of CAD with higher prevalence in group II than group I (75% versus 16.7%) with P value =0.001. This is concordant with study conducted by Ma et al. [3] showed that 342 patients (38.7%) were diabetic & DM was significant on severity of CAD with p value (<0.001).

Also the study conducted by Cherku et al [9] stated that DM was highly significant between the study population.

In contrast to the current study: the study conducted by Nabati et al. [5] showed that 56 (35%) patients were diabetic. DM was non significant between the study population with p value 0.945.

Regarding hypertension (HTN) & Smoking: in the current study 42 patients were hypertensive & 57 patients were smokers. HTN& smoking were significant between both groups with P value (0.003 &0.004) respectively.

Table 3. Comparison between both groups regarding angiographic data

Angiographic data			Group I (Low SS) (n=72)	Group II (Intermediate to high SS) (n=48)	X^2	P-value
Number of vessels lesion	Single vessel	N	39	0	67.628	0.001*
		%	54.2%	0.0%		
	Two vessels	N	27	15		
		%	37.5%	31.3%		
	Multi vessels	N	6	33		
		%	8.3%	68.8%		
Left main lesion	No	N	72	33	25.714	0.003*
		%	100.0%	68.8%		
	Yes	N	0	15		
		%	0.0%	31.3%		
Proximal LAD	No	N	45	6	29.463	0.002*
		%	62.5%	12.5%		
	Yes	N	27	42		
		%	37.5%	87.5%		

Table 4. ROC curve analysis of AHR & QTc cut off values with Syntax score

	Cutoff	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy
AHR	80bpm	0.915	75%	67%	60%	80%	70%
QTC	450ms	0.704	81%	92%	87%	88%	88%

AHR: admission heart rate & QTc: corrected QT interval.

This was concordant with study conducted by Ge et al. [10] showed that (57. 2%) were hypertensive & (71.2 %) were smokers & Smoking & HTN was with significantly impact on severity of CAD & higher in patients with multi vessel disease than those patients without MVD with p value (<0.001&0.049% respectively.

In contrast to the present study: the study conducted by Nabati et al [5] stated that HTN was non significant between the studied population with p value (0.299).

In the present study 56.3% of patients in group II had dyslipidemia while 20.8% in group I (low SS) & there was significant difference between both groups regarding dyslipidemia with P value =0.001) & so that dyslipidemia exhibit significant association with severe CAD.

Also in the current study: There was three heart rate groups: group A <60bpm, group B HR 60-90 bpm&group C HR >90 bpm.

The 3 heart rate groups were compared according to Syntax Score, ACS type &site of MI showed that prevalence of higher SS>22 was (76.9%) of group C{HR >90 bpm} versus 57.1% in group A {HR <60bpm} while (50%) of group B {HR 60-90bpm}.

There was significant difference between the heart rate groups & SYNTAX score with p value (0.001).

Both groups of lower HR< 60 bpm & higher HR >90bpm were significantly associated with severe coronary artery disease & Mainly those with higher admission heart rate were more likely to have higher Syntax scores.

This was concordant with study conducted by Jensen et al. [11] showed that patients with highest & lowest AHR were at high risk with cut off value of AHR > 80 bpm & above. Also, AHR<50 bpm should be considered as high-risk heart rate.

Also concordant with studies conducted by Zhang et al. [12] & Yilmaz et al. [13] showed that a strong relation between heart rate & SS which was significantly higher in patients with AHR> 80 Bpm.

Also this was concordant with study conducted by Ma et al. [3] showed that AHR was independently & significantly correlated with SS

with p value <0.001, thus elevated AHR was independent predictor of high SS & may be used to identify patients with ACS with high atherosclerotic plaque burden.

Also this was concordant with studies conducted by Ma et al. [3] Chen et al. [14] Choudhary et al. [15] Xu et al. [16] Diaz et al. [17] & Bangalore et al. [18] stated that there was highly significant correlation between the heart rate & severity of CAD & study conducted by Ho et al. [19] showed that patients with higher heart rate are at high risk for severe coronary lesion so more likely to cardio vascular events particularly heart failure, arrhythmias & all –cause mortality.

In contrast to the current study, the study conducted by Özilhan et al. [20] demonstrated that AHR may not be an optimal variable for determining the coronary anatomy, complexity & severity because many factors like anemia, anxiety, inflammatory process & baseline rate can affect AHR.

Regarding to QTC In the current study: In (low SS) group I, the mean QTc was 435.08 ±12. 96msec while, in group II the mean was 459.44 ±14.30 ms.

There was highly significant difference between both Syntax groups regarding QTc with P value 0.001.

In the current study the study populations were classified according to QTc into 2 groups: group 1 (QTc <440 msec) included 54 patients & group 2 (QTc > 440 msec) included 66 patients.

They were compared regarding severity & incidence of MACE: In the current study (68.2%) of patients with prolonged QTc >440 had severe CAD & higher SS versus 5.6% of patients with QTc<440msec.

This was concordant with a study conducted by Helmy et al. [21] demonstrated that there was significant correlation between QTc prolongation & QTc dispersion with severity of CAD denoted by higher SS.

Also this was concordant with study conducted by Akgumus et al. [22] showed that QTc values significantly high in patients with severe CAD (multi vessel disease) compared to patients with mild CAD (Single Vessel Disease) with mean of (471±52 ms) versus (443 ±48 ms) with p value 0.001.

Regarding incidence of major adverse cardiac events (MACE): 13 patients of group 2 (QTc > 440 ms) suffered MACE: (18.2%) had fatal arrhythmia, (22.7 %) had Acute heart failure, (9.1%) recurrent ischemia, (4.5 %) death & (4.5%) suffered resuscitated cardiac arrest.

There was significant difference between groups of QTc regarding incidence of cardiac events with p value 0.023 & higher incidence of MACE was in patients with prolonged QTc interval > 440ms.

In the current study: there was highly significant difference between groups regarding number of diseased vessels. Also Patients of (intermediate - high SS) group were more likely to have multi vessel disease than patients of (low SS) group (68.8%versus 8.3%) with p value 0.001

This was concordant with studies conducted by Cherku et al. [9] & Hindieh et al. [23] showed that the individuals with multi-vessel diseases (MVD) are associated with higher burden of angiographic CAD severity Compared with those with non –MVD with P value 0.047.

Also concordant with the study conducted by Xenogiannis et al. [24] showed that 80% of patients who suffered cardiogenic shock or acute heart failure severe coronary lesion in the setting of ACS have MVD.

In the current study the prevalence of left main, MVD& Proximal left anterior descending (LAD) was more frequent with (intermediate-high SS) patients: as (31.3%) of patients had left main lesion, (87.5%) had proximal LAD lesion, while in group I (low SS): no patients had left main & (37.5%) had proximal LAD.

There was highly significant difference between Syntax groups regarding left main coronary artery (LMCA) & LAD lesion as culprit vessel with P value (0.003 & 0.002).

This was concordant with study conducted by Hammami et al. [25] showed that patients with 70% stenosis of proximal LAD had highly severe coronary stenosis.

Also concordant with studies conducted by Ma et al. [9], Rahmani et al. [26], Khandelwal et al. [27], & Wang et al. [28], showed significant difference between the study population regarding left main & proximal LAD lesion.

5. CONCLUSION

The current study showed that QTc interval prolongation and admission HR are independent predictors of the severity of coronary artery disease in patients with acute coronary syndrome.

LIMITATIONS OF THE STUDY

1. Relatively small sample size of this study.
2. The results were obtained from only one center (Tanta University Cardiology department) hence the data may not be applicable to all patients.
3. The studied patients weren't compared regarding medications e.g., antiplatelet or statins.
4. No long term follow up.
5. Some factor like anemia, anxiety and infection that may affect heart rate weren't included in the study. Also, psychiatric diseases (e.g. anxiety disorders) that may affect QTc were excluded in the current study.

CONSENT AND ETHICAL APPROVAL

- Informed written consent was obtained from all patients after full explanation of benefits and risks of the study.
- The study was approved by the ethics committee of Tanta University.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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