Title

Is Ischemic Pre-Conditioning Present in Patients with Acute Coronary Syndrome and ECG Derived Moderate Sleep Disordered Breathing?

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Is Ischemic Pre-Conditioning Present in Patients with Acute Coronary Syndrome and ECG Derived Moderate Sleep Disordered Breathing?

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Is Ischemic Pre-Conditioning Present in Patients with Acute Coronary Syndrome and ECG Derived Moderate Sleep Disordered Breathing?

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Abstract

Background: Sleep Disordered Breathing (SDB) has been found to be associated with an increased risk of major cardiovascular events including Acute Coronary Syndrome (ACS). There is conflicting evidence that suggests SDB has a cardioprotective effect, via ischemic preconditioning, in patients with ACS when measured with cardiac troponin levels. This study was designed to examine whether troponin levels and or transient myocardial ischemia differed in patients with non-ST elevation (NSTE-ACS) with and without moderate SDB measured with 12-lead Holter electrocardiographic (ECG) data. **Purpose:** The purpose of this study was twofold: (1) examine the severity of myocardial injury using peak troponin levels between NSTE-ACS patients with and without Holter derived respiratory disturbance index (HDRDI) suggestive of moderate SDB; and (2) determine the frequency of transient myocardial ischemia between NSTE-ACS patients with and without a HDRDI suggestive of moderate SDB. **Method:** This was a secondary analysis from the COMPARE Study. A total of 110 hospitalized patients diagnosed with NSTE-ACS were included. SDB events were identified using 12-lead ECG Holter recordings using a combination of QRS, R-R intervals and the myogram. All 110 patients had at least eight hours of Holter recording. Moderate HDRDI suggestive of moderate SDB was defined as $\geq$15 HDRDI events per hour. Transient myocardial ischemia was defined as $\geq$1 millimeter (mm) of ST-segment ↑ or ↓, in $\geq$ 1 ECG lead, $\geq$ 1 minute. **Results:** Of the 110 NSTE-ACS patients included, 39% (n=43) had a HDRDI that was suggestive of moderate SDB. A higher proportion of males were in the moderate HDRDI group as compared to females (86% vs 14%; p=0.001). NSTE-ACS patients in the moderate HDRDI group had lower peak troponin levels than those without moderate HDRDI (6.8 ng/ml vs 10.2 ng/ml; p=0.037). There was a

trend for fewer transient ischemic events in the moderate HDRDI group as compared to those without moderate HDRDI, however, this was not statistically different (16% vs 30%; *p*=0.081). **Conclusions:** NSTE-ACS patients with moderate HDRDI suggestive of SDB have less cardiac injury as compared to NSTE-ACS patients without moderate HDRDI. There was a trend for fewer transient myocardial ischemic events in the moderate HDRDI group compare to those without moderate HDRDI, but the groups were not different. These findings corroborate prior studies suggesting a possible cardioprotective effect of SDB via a precondition mechanism in patients with ACS. Future research is needed to explore the underlying physiologic mechanisms of this findings.

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List of Abbreviations

ACS: Acute Coronary Syndrome

AHI: Apnea Hypopnea Index

BBB: Bundle Branch Block

ECG: Electrocardiogram

HDRDI: Holter Derived Respiratory Disturbance Index

MI: Myocardial Infarction

NSTE-ACS: Non-ST elevation – Acute Coronary Syndrome

OSA: Obstructive Sleep Apnea

PSG: Polysomnography

SDB: Sleep disordered breathing

STEMI: ST-elevation myocardial infarction

Background

Recently published statistics from the American Heart Association estimate that every 41 seconds an American will experience an Acute Coronary Syndrome (ACS), or heart attack.[1] ACS affects approximately 15.5 million people in the United States (US) and is responsible for one-third of the total US deaths in people older than 35 years of age.[1] ACS refers to a group of cardiovascular events that includes ST-elevation myocardial infarction (STEMI); non-ST elevation-ACS (NSTE-ACS); and unstable angina.[1] There is evidence showing that sleep disordered breathing (SDB) is associated with an increased risk of major adverse cardiovascular events, including ACS.[2] The prevalence of SDB in patients with ACS is as high as 60%.[3] SDB, and the resultant arousal associated with apnea, is capable of modulating the autonomic nervous system through a number of mechanisms. During normal, undisturbed sleep, parasympathetic modulation of the heart predominates and myocardial electrical stability is enhanced.[4] This quiescence is disturbed during SDB and creates an autonomic profile in which vagal activity can lead to brady-arrhythmias and sympatho-excitation favoring ventricular ectopy.[5] These myocardial responses are likely to be more significant in ACS patients whose myocardia are vulnerable due to acute ischemia and excessive sympathetic stimulation. Physiologic responses to SDB that may exacerbate ACS include; hypoxia, arousal due to sympathetic activation, oxidative stress, and hypercoagulability.[6] [7] [8] Given these mechanisms, it has been hypothesized that ACS patients with SDB may have more severe myocardial damage and/or on-going myocardial ischemia.

There is debate, however, about whether the above mechanisms occur during intermittent hypoxemia (apnea) seen in SDB, specifically, obstructive sleep apnea (OSA). In one hospital based study that used respiratory polygraph to assess OSA, no association between OSA and cardiac events were found, but hospitalization was longer in those with OSA.[9] Interestingly, however, was the finding that peak plasma troponin levels were higher in patients

with SDB compared to those without SDB, suggesting infarct size was larger in those with SDB. This finding is counter to a study by Shah and co-workers who found that ACS patients with mild OSA (<5 events/hour) measured by polygraph, had lower troponin levels than those without SDB after adjustments for age, race, smoking and other cardiovascular risk factors and/or comorbidities.[10] The investigators suggested that OSA present prior to the acute ACS event may have a cardio-protective effect from "ischemic precondition", a finding supported in animal studies.[11] [12] [13] Similar to Shah's study, Sanchez-De-La-Torre and co-workers found that cardiac troponin levels were lower in ACS patients with severe OSA (>32 events/hour) as compared to those without OSA.[14] These two studies suggest that OSA may have a cardio-protective effect (i.e., less severe ischemia) in the early phase of ACS when measured with troponin biomarkers.

Conversely, studies examining cardiac function using magnetic resonance[15] and left ventricular angiography[16] at 3 months and 21 days respectively after an ACS event found that myocardial salvage, infarct recovery and left ventricular function was less in patients with moderate OSA (i.e., AHI >15) as compared to those without moderate OSA. Suggesting impaired cardiac function is seen weeks after an ACS event among patients with OSA.

In studies examining in-hospital clinical outcomes in ACS patients with SDB, two have linked SDB to increased cardiac events (e.g., death, MI, recurrent angina).[17] [18] However, these two studies screened for SDB using a self-report questionnaire and recurrent angina was measured by patient reported symptoms, rather than the non-invasive gold standard 12-lead electrocardiogram (ECG). Given the evidence suggesting that myocardial preconditioning is present in ACS patients with SDB using troponin blood levels, one might expect that transient myocardial ischemia, which occurs in 17% of ACS patients[19] would also be lower. However, no study to date has examined this using continuous 12-lead ECG Holter recordings. Findings from such a study could corroborate whether pre-conditioning exists and enhance our understanding of the underlying physiologic mechanisms of ischemia in ACS patients with SDB.

While the gold standard test used to diagnose SDB (both obstructive and non-obstructive) is polysomnography (PSG), this test is not practical in hospitalized ACS patients. In addition, while there are a number of SDB screening tools available (i.e., paper-based and device), these methods can also be cumbersome, and none can objectively measure transient myocardial ischemia. Our group and a number of other researchers, have examined ECG derived methods to identify abnormal respirations associated with SDB.[20 21 22 23 24 25] This method is intriguing given that hospitalized ACS patients have continuous ECG monitoring as standard of care. In this study, we take the novel approach of identifying moderate/severe SDB (AHI $\geq$15) using a Holter Derived Respiratory Disturbance Index (HDRDI). The continuous 12-lead ECG data also allowed our team the opportunity to objectively identify transient myocardial ischemia. Therefore, the purpose of this study was twofold: (1) examine the severity of myocardial injury using peak cardiac troponin levels between NSTE-ACS patients with and without moderate HDRDI SDB; and (2) determine the frequency of transient myocardial ischemia between NSTE-ACS patients with and without moderate HDRDI suggestive of SDB.

Methods

Study Design

This was a secondary analysis using data from the COMPARE study which evaluated the frequency of transient myocardial ischemia in 488 patients with suspected ACS. The primary study methods have been previously reported.[26] Briefly, the COMPARE Study was a prospective observational study conducted at three private hospitals in Northern Nevada and Northern California. The study was approved by each hospital's institutional review board and informed written consent was obtained from each patient at enrollment.

English speaking patients who presented to the emergency department, or within 8 hours after hospital admission, for symptoms suggestive of ACS (i.e., chest pain, shortness of breath, arm pain, diaphoresis, or symptoms at rest) were invited to participate in the study. Patients were excluded if they were: admitted for STEMI, comatose or obtunded, had a major psychiatric disorder, or were in isolation precautions. Also excluded were patients with left bundle branch block (BBB) or ventricular paced rhythms because these known ECG confounders make it difficult to determine if true myocardial ischemia is present.[26]

Sample

For this secondary analysis, only those patients enrolled in the COMPARE Study who were ultimately diagnosed with NSTE-ASC were included. The diagnosis of NSTE-ACS was defined using the standard definition of cardiac biomarker evidence of myocardial necrosis (e.g., positive CK-MB or troponin) without new ST-segment elevation.[27] At the time of the primary study, a troponin > 0.04 ng/ml was considered a positive test for NSTE-ACS. While the COMPARE Study enrolled a total of 488 patients, 110 (23%) were ultimately diagnosed with NSTE-ACS and are thus, included in this secondary analysis.

12-lead Holter Date Acquisition

A 12-lead ECG Holter recorder (H12+ Digital Holter Recorder Mortara Instruments, Milwaukee WI) was applied as soon as possible after presentation to the emergency department, or within 8 hours of admission for patients admitted during the time our research team was not present in the hospital. Prior to initiating Holter recording, a unique study identification number assigned at enrollment, was typed onto the Holter recorder. The 12-lead Holter recorders were “black boxes;” hence, the data was not available to clinicians for decision making and there were no alarms generated. In addition, the ECG data was analyzed after

hospital discharge. Prior to application of the Holter recorder, a research nurse carefully prepped the patient's torso to remove any dirt, oils or creams that may interfere with ECG signal quality, and chest hair was carefully clipped if necessary. Radiolucent ECG electrodes were applied in the Mason-Likar limb lead configuration so as to not interfere with chest X-rays. During the Holter recording, positional ECGs were obtained with patients assuming supine, right and left lying positions, which were used during off-line analysis to identify false positive ST-segment changes due to body position changes.[26] The Holter remained in place until discharge from the hospital. All of the patients were also monitored using the hospital's telemetry ECG system as per the hospital's protocol; thus, the standard of care was not interrupted by the research protocol. For the present study, all of the patients had at least eight hours of Holter recording.

A research nurse, present during the hours of 7 AM to 5 PM, rounded hourly on the patients enrolled to ensure that the Holter recorder was in place, that the ECG electrodes/lead wires had not been removed and/or the location of the electrodes had not been changed from the correct location. At these inspections, the research nurses also addressed any questions or concerns the patient and/or nurse had about the research protocol. This approach meant that reapplication of any electrode(s) that have fallen off or were taken off for procedures were promptly corrected. The research nurse also retrieved demographics, clinical history, procedures (i.e., treadmill test, cardiac cath. lab), medications, lab values and outcome data from the electronic health record.

ECG Analysis for Identifying Transient Myocardial Ischemia

Data from the Holter recorder was downloaded to a password protected research computer. The download was done at hospital discharge in patients admitted less than 24 hours, or at 24-hour intervals for those admitted longer than 24 hours because the card reader

had reached storage capacity. In these patients, a new card reader was replaced immediately in the Holter recorder to ensure that continuous 12-lead ECG data was recorded. The Holter recorder remained on the patient until: hospital discharge; the patient asked to have the device removed, which was rare; or the patient went to surgery.

The ECG data were analyzed using the H-scribe Analysis System (Mortara Instruments, Milwaukee, WI). The H-scribe software displays 24 hours of ECG recordings and identifies ST-segment changes that meet the ST-segment threshold criteria for transient myocardial ischemia. We define transient myocardial ischemia using the standard definition of > 1millimeter (mm) of ST-segment elevation or depression, in >1 ECG lead(s), lasting > 1minute.[26] The ECG analysis for identifying transient myocardial ischemia was performed using a semi-automated approach. All of the H-Scribe computer software events were over-read by the principal investigator (MMP) who carefully examined changes to the ST-segment trend (elevation or depression) during the entire monitoring period in all 12-ECG leads. 12-lead ECGs were printed out and compared pre, during and post ischemia to confirm the diagnosis. The human annotator was blinded to demographics, clinical history and/or clinical outcomes. In cases where there were questions about whether transient myocardial ischemia was present or absent, two co-investigators from the parent study reviewed the ECG data and consensus was reached.[19]

Holter Derived Respiratory Disturbance Index (HDRDI)

Continuous high resolution 12-lead ECG data was used to generate a Holter Derived Respiratory Disturbance Index (HDRDI) using the entire length of Holter recording. The HDRDI algorithm was developed by our co-author a biomedical engineer (DM) at the Center for Physiologic Research. The HDRDI method has been used to identify Cheyne-Stokes respirations and periodic breathing and has been published by both our research group and others.[22] [20] The HDRDI algorithm uses QRS morphology changes, heart rate and ECG-derived

myogram signals that are associated with inspiration and exhalation (i.e., tidal volume changes) to generate respirations. When the normal pattern of respirations are interrupted, for example during apnea followed by arousal to break the apnea, the associated ECG changes generate a HDRDI event. The algorithm events allow us to calculate the number of HDRDI events per hour, which is used as an equivalent to an apnea hypopnea index (AHI). Of note, because we do not measure nasal flow as is used in polygraph testing, we are unable to differentiate obstructive from central sleep apnea; hence, we use the term HDRDI suggestive of SDB. **Figure 1** is an example of both normal and abnormal breathing events using our algorithm-based approach from 12-lead ECG recordings.

For this study, we selected patients who were identified as having a moderate HDRDI if they exhibited 15 or more events per hour. The group of NSTE-ACS patients with moderate HDRDI were compared to those without this measure to determine the peak troponin I level (ng/ml) and the presence of transient myocardial ischemia measured from continuous 12-lead Holter recordings.

Diagnosis of NSTE-ACS

Venous blood samples were obtained in all of the patients per the hospital's protocol to rule in/out NSTE-ACS. Typically, three samples were obtained in a patient over the course of an 18 to 24-hour timeframe. The hospital's troponin I test was considered positive for NSTE-ACS if it was >0.04 ng/ml. For this study, we used the highest troponin level, or peak, to compare those with and with-out a moderate HDRDI suggestive of SDB.

Statistical Analysis

Data was analyzed using SPSS 27.0 (International Business Machines Corporation [IBM] Corporation 2009; version as of 2021). Descriptive statistics were used to report

demographics including age, body mass index, gender and ethnicity. These same statistics were used to examine clinical information including medical history, prior angina, coronary arterial bypass graft surgery, coronary arterial disease, current smoker, diabetes, ejection fraction, hypertension, percutaneous coronary intervention and prior myocardial infarction. In addition, ACS variables of interest included blood pressure and heart rate upon admission, the number of angina episodes in the last 24 hours, length of hospital stay and total Holter monitoring time. Peak troponin I was compared among the two groups with and without moderate HDRDI using the Students t-Test. A Pearson Chi-square test was used to compare whether patients with/without moderate HDRDI had more transient myocardial ischemia events as compared to those without HDRDI. Values are expressed as means $\pm$ standard deviations and percentages for the entire sample, and by presence/absence of a moderate HDRDI. Categorical variables were analyzed, and *p*-values reported, using a Pearson-Chi Square analyses. A p value of <0.05 was used as the critical value to determine whether there were statistical differences.

Results

Table 1 shows the demographic, clinical characteristics, Holter recording time and hospital length of stay in the 110 NSTE-ACS patients included in the study. Of the entire sample, 43 (39%) had moderate HDRDI suggestive of SDB. There was no statistical differences between the groups for age, body mass index, or race. There was a higher proportion of males with moderate HDRDI compared to males without moderate HDRDI (86% versus 57%; p = 0.01). The opposite was found in females (moderate HDRDI = 14% versus no = 43%; p = 0.001). A higher proportion of patients with a moderate HDRDI had a history of angina (moderate HDRDI = 58% versus no = 36%; p = 0.022). Whereas a higher proportion of patients without moderate HDRDI had a higher rate of diabetes (no = 37% versus moderate HDRDI = 19%; p = 0.037). The other clinical history characteristics were not different by group. Admission

blood pressure (systolic and diastolic) and the presence of 2 to 3 angina events in the last 24 hours was not different by group, but patients with moderate HDRDI had a lower admission heart rate as compared to those without moderate HDRDI (moderate HDRDI = 75 beats/minute versus no = 82 beats/minutes; p = 0.026). There was no difference between the groups with regards to length of hospitalization and total Holter recording time.

Table 2 shows group comparisons for peak troponin and transient myocardial ischemia. NSTE-ACS patients with moderate HDRDI had lower peak troponin levels than those without moderate HDRDI (moderate HDRDI = 6.8 ng/ml versus no = 10.2 ng/ml; p=0.037). There was a trend for a lower proportion of transient myocardial ischemic events in the moderate HDRDI group, but this difference was not statistically significant (moderate HDRDI = 16% versus no = 30%; p=0.081).

Discussion

This study in 110 NSTE-ACS showed that 39% had moderate HDRDI suggestive of SDB captured using continuous 12-lead Holter recordings. Peak troponin was lower in the moderate HDRDI group as compared to those without moderate HDRDI. There was a trend for fewer transient myocardial ischemic events, but the differences were not statistically different.

The findings from our study with regards to lower peak troponin levels in ACS patients with a HDRDI suggestive of moderate SBD are consistent with both Shah et al.[10] and Sanchez-de-la-Torre et al.[14]. In all three studies, peak troponin levels were obtained in the early phase of ACS (i.e., <24 hours). Both Shah et al., and Sanchez-de-la-Torre et al. used similar respiratory polygraphy devices to identify ACS patients with SDB. Shah et al., used an apnea hypopnea index of $\geq$5 (mild) and 35% met these criteria, whereas Sanchez-de-la-Torre et al., like our study, used an AHI of $\geq$15 (moderate). Of note, our rate of SDB (39%) was half that reported in the Sanchez-de-la-Torre et al., which was 70% in their study. Our study used a novel approach

to identify SDB by using 12-lead Holter recordings, but these proportional differences may suggest the ECG derived method may undercount apnea episodes. Regardless of these differences, our study corroborates the findings that there may be a cardio-protective effect from ischemic precondition in ACS patients with SDB.

Our findings are opposite of those of Barbe and co-workers.[9] In their study, patients with moderate/severe SDB had higher peak troponin levels than those who did not have moderate/severe SDB. This might be explained by the sample. Barbe et al., included patients with both STEMI and NSTE-ACS, whereas our study included only NSTE-ACS patients. Patients in their study also had respiratory polygraph 48-72 hours after admission, which is well past the time when we recorded our HDRDI, which similar to the time frame of Shah et al., and Sanchez-de-la-Torre et al. It is unclear when troponin levels were drawn in the Barbe et al., study, but our study used those obtained within 24 hours of admission, which was also done in the Shah et al., and Sanchez-de-la-Torre et al. study. Therefore, when during the course of ACS troponins are obtained in relation to when OSA is diagnosed may impact these findings. In an animal study done by Murry et al.,[11] intermittent episodes of ischemia had a protective effect on the myocardium during the early course of ischemia, but they found that the myocardium eventually had sustained damage. In other words, brief myocardial ischemia only delays myocardial cellular death. Thus, based on these findings it is unclear whether intermittent hypoxia associated with SDB in the early stages of ACS truly protects the myocardium or only delays more severe myocardial damage. Whether this leads to long term untoward outcomes is not entirely known.[28] Further studies are needed to better understand these intriguing physiological mechanisms.

Our study went a step beyond prior studies in that we also examined transient myocardial ischemia measured using the non-invasive gold standard 12-lead ECG. Two prior hospital-based studies, Correia et al. and Jesus et al., found higher rates of recurrent angina,

measured by patient reported symptoms, in ACS patients with moderate/severe SDB. Interestingly, they showed that these patients experienced more cardiac events.[17] [18] Importantly, studies using continuous ECG recordings have shown that transient myocardial ischemia is asymptomatic in as many as 70% of ACS patients;[19] hence, myocardial ischemia have not been examined in a comprehensive way in the above two cited studies. Overall, 27 (25%) of our 110 NSTE-ACS patients had transient myocardial ischemia, which is higher than the rate in both the Correia et al., and Jesus et al., studies. While we found a trend for a lower proportion of transient myocardial ischemia events in the moderate HDRDI group as compared to those without moderate HDRDI, this difference was not statistically significant. This is likely due to the small size of our sample but is nonetheless an interesting trend in the same direction as troponin, that should be examined in a future study.

Limitations

One limitation of our study was the use of an ECG method to identify SDB. However, there have been a number of studies that have evaluated the ECG derived methods to identify abnormal respirations associated with SDB.[20] [21] [22] [23] [24] [25] As mentioned previously an ECG method for detection of SDB represent an interesting and convenient method for research into the possible mechanisms of SBD during ACS and possibly even a screening tool given that ECG monitoring is a standard of care for hospitalized ACS patients. Continuous ECG data also allows for examination of other important pathophysiological mechanisms, such as ischemia. Our sample was small and only included NSTE-ACS patients during a short timeframe after the acute ACS event. Additional studies examining all types of ACS that evaluate this phenomenon during the latter part of hospitalization and post discharge is warranted. Such a study should also examine transient myocardial ischemia.

Conclusion

In conclusion, our findings and that of others shows that peak troponin levels are lower in ACS with mild or moderate SDB in the early phase of ACS, which suggests there may be a cardio protective effect from SDB. However, these findings may only occur in the initial phase of ACS since others have found that myocardial damage is higher when measured after the acute event. Hence, myocardial cellular death may only be delayed in these patients. A future research study that examines both early and late phases of ACS in patients with and without SDB would build our understanding of this topic.

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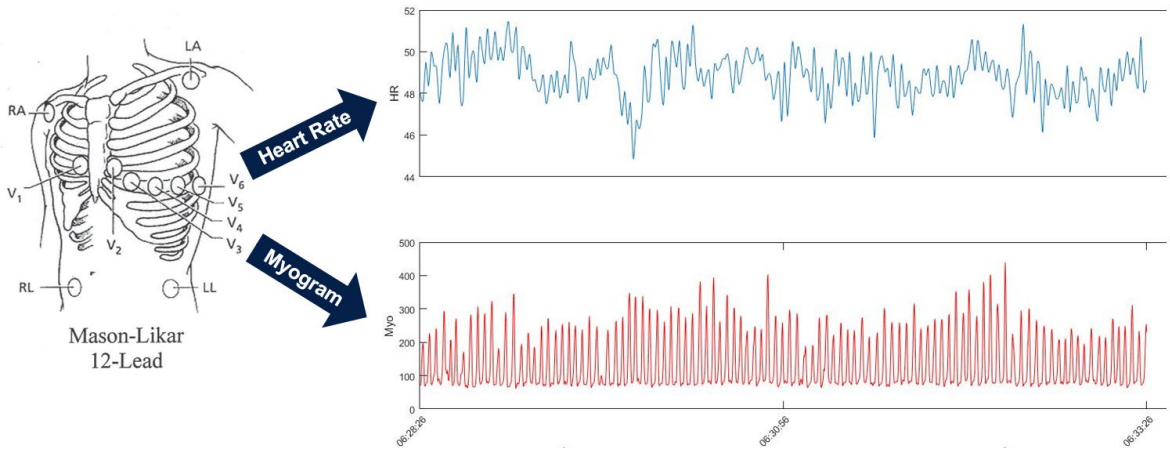
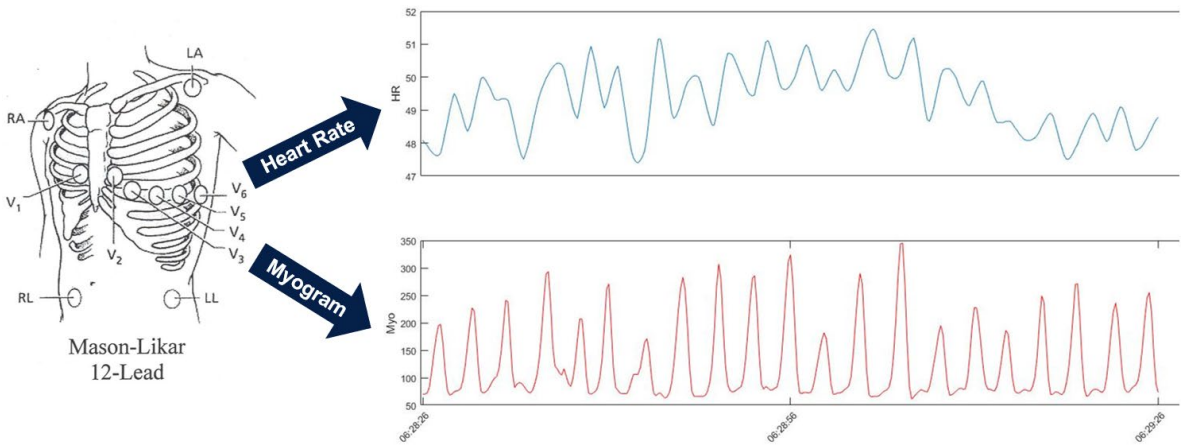


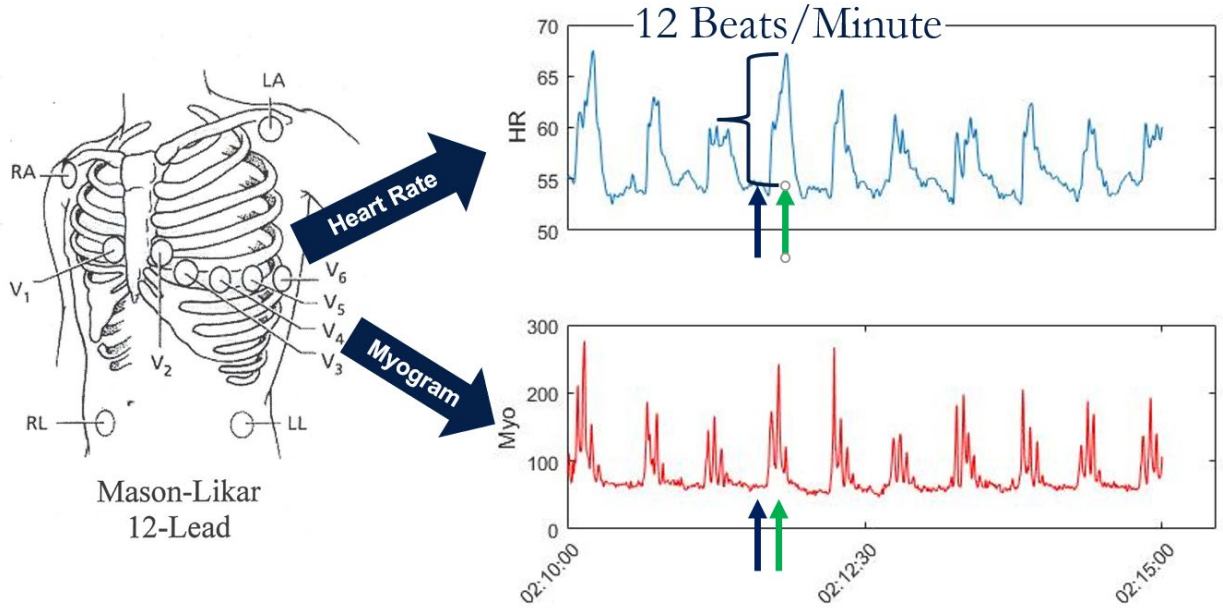
A. Normal respiratory rate during a five-minute time period.



B. One-minute time period from selected five-minute tracing.

Figure 1.1 Recording of heart rate and myogram for five minutes with normal breathing

Illustrates simultaneous recordings of heart rate (top right figure HR Y-axis) and the myogram (bottom right figure Myo Y-axis) for five minutes (X-axis) of normal breathing using a 12-lead electrocardiographic Holter recording. The top image (A) is a five-minute recording of a normal respiratory rate. The bottom image (B) zooms in on a one-minute time period, selected from the five-minute tracing, showing 21 breaths/minute.



C. Five-minute abnormal breathing period.

Figure 2.1 Recording of abnormal breathing during a five-minute period

Image (C) shows a five-minute abnormal breathing period. The blue arrow denotes when no breathing (apnea) occurs and the green arrow denotes clearing of the airway obstruction resulting in a myogram peak and corresponding heart rate acceleration of 12 beats/minute.

Table 1.1 Demographics and clinical characteristics

Demographic and clinical characteristics of 110 non-ST elevation acute coronary syndrome patients without and with moderate sleep disordered breathing (≥15 events/hour) Holter derived respiratory disturbance index (HDRDI).

Variable	Entire Sample N = 110 (%) n (%)	No Moderate HDRDI n = 67 (61%) n (%)	Yes Moderate HDRDI n = 43 (39%) n (%)	P-Value
Demographics				
Age (mean)	65 ± 12	66 ± 13	63 ± 11	0.290
BMI (mean)	29.9 ± 5.2	29.7 ± 5.3	30.1 ± 4.9	0.731
Sex				
Female	35 (32)	29 (43)	6 (14)	**0.001**
Male	75 (68)	38 (57)	37 (86)	**0.001**
Race				
American Indian or Alaskan Native	3	1 (2)	2 (5)	0.524
Black/African American	1	1 (2)	0	
Pacific islander	1	1 (2)	0	
White	105	64 (96)	41 (95)	
Clinical History				
Angina	49 (45)	24 (36)	25 (58)	**0.022**
CABG	22 (20)	14 (21)	8 (19)	0.769
CAD	62 (56)	39 (58)	23 (54)	0.626
Current Smoker	65 (59)	42 (63)	23 (54)	0.338
Diabetes	33 (30)	25 (37)	8 (19)	**0.037**
EF	57 ± 11	55 ± 12	58 ± 9	0.600
HTN	69 (63)	45 (67)	24 (56)	0.230
PCI	41 (37)	29 (43)	12 (28)	0.104
Prior MI	40 (36)	27 (40)	13 (30)	0.284
Presenting ACS Variables				
Admission Systolic Blood Pressure	145 ± 27	142 ± 27	151 ± 25	0.076
Admission Diastolic Blood Pressure	84 ± 16	82 ± 17	87 ± 15	0.098
Admission Heart Rate	79 ± 18	82 ± 20	75 ± 13	**0.026**
Presence of 2 to 3 angina events in last 24 hours	32 (29)	18 (27)	14 (33)	0.521
Hospitalization Variables				
Average Length of Hospitalization (hours)	88 ± 86	95 ± 86	77 ± 86	0.278
Total Holter Monitoring Time (hours)	37 + 19	39 ± 21	34 ± 15	0.152

BMI = body mass index; CABG = coronary artery bypass Graft; CAD = coronary artery disease; EF = ejection fraction; HTN = hypertension; PCI = percutaneous coronary intervention; MI = myocardial infarction; ACS = acute coronary syndrome

Table 2.1 Comparison of peak troponin and transient myocardial ischemia

Comparison of peak troponin and transient myocardial ischemia among 110 non-ST elevation acute coronary syndrome patients - no versus yes moderate sleep disordered breathing ($\geq$15 events/hour) using a Holter derived respiratory disturbance index.

Total n = 110	**No Moderate HDRDI n = 67 (61%)**	**Yes Moderate HDRDI n = 43 (39%)**	**P-Value**
Highest Troponin I (mean)	10.2 ng/ml	6.8 ng/ml	**0.037**
Transient Myocardial Ischemia	20 (30%)	7 (16%)	0.081

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