A Single-Center, Prospective, Pilot Cohort Study of Preoperative Abnormal Sleep Patterns and Postoperative Delirium in Older Hispanic/Latino Patients Undergoing Cardiac Surgery.

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Research Article

Keywords: Pilot study, Hispanic/Latino, older patients, geriatric anesthesiology, postoperative delirium, abnormal sleep patterns, poor sleep quality, actigraphy

Posted Date: October 28th, 2023

DOI: https://doi.org/10.21203/rs.3.rs-3231303/v1

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Abstract

Background

Delirium occurs in 20–50% of older patients after cardiac surgery and is associated with prolonged intensive care and hospital length of stay, postoperative cognitive decline, and dementia. Preoperative abnormal sleep patterns are potentially modifiable risk factors that have been associated with an increased incidence of postoperative delirium. Hispanic/Latinos may be a particularly vulnerable population given their higher prevalence of risk factors for delirium including cognitive impairment, lower level of education, and sleep disturbances, as compared to non-Hispanic White adults. A largescale cohort study is needed to determine if altered sleep patterns increase the risk of delirium in older, Hispanic/Latino patients after cardiac surgery. The primary aims of this pilot study were to determine the feasibility of recruitment, retention, preoperative sleep actigraphy measurements, preoperative sleep questionnaire and cognitive batteries, and postoperative delirium testing.

Methods

We conducted a single-center, prospective, pilot cohort study of older Hispanic/Latino patients undergoing cardiac surgery with and without preoperative sleep disturbances and postoperative delirium from February 2020 to December 2021 at UHealth of the University of Miami, an academic tertiary center in Miami, FL. Patients underwent preoperative cognitive and sleep questionnaire testing and wore an actigraphy wristwatch with a sleep diary for 5 to 7 days prior to surgery. Postoperatively patients were tested for delirium for up to 7 days or hospital discharge. Feasibility of the study protocol was the primary objective of this pilot study.

Results

155 patients were screened, 40 met full inclusion criteria, and 14 patients were recruited. The mean age was 67.2 years old. Spanish was the preferred language in 21.4% of patients. Poor sleep quality was present in 78.5% of subjects. 57.1% of subjects experienced either delirium or subsyndromal delirium. Despite being conducted during the height of the COVID-19 pandemic, our pilot trial met our a priori thresholds for specific feasibility criteria.

Conclusions

The protocol was feasible and a future, definitive prospective cohort study of older Hispanic/Latino patients undergoing cardiac surgery with and without preoperative altered sleep patterns and an outcome of postoperative delirium will be planned.
Trial registration:
The study was registered at ClinicalTrials.gov on March 8, 2021 (NCT04786899)

BACKGROUND

Delirium occurs in 20–50% of older patients after cardiac surgery and increases intensive care unit length of stay and cost of health care by $44,000 per patient per year in the United States. Delirium is characterized by acute onset and fluctuating levels of inattention, altered mental status, and disorganized thinking. Delirium after cardiac surgery carries significant morbidity leading to increased cognitive impairment, decreased independence, and increased mortality in older patients. Although preventative treatments of delirium are available after surgery, limited preoperative treatments are available. The most consistent risk factors are largely nonmodifiable and include advancing age, cognitive impairment, dementia, lower level of education and surgery type. Evaluating novel risk factors for delirium will inform decisions about preoperative strategies to minimize delirium after cardiac surgery. Preoperative abnormal circadian and sleep patterns are potentially modifiable risk factors that have been associated with an increased rate of postoperative delirium.

Hispanic/Latino patients may be a particularly vulnerable population given their higher prevalence of risk factors for delirium including dementia, lower level of education, and sleep disturbances as compared to non-Hispanic White adults. Sleep disturbances are particularly important in Hispanic/Latino populations. Data from the Hispanic Community Health Study/Study of Latinos (HCHS/SOL), the largest study of Hispanic/Latino adults in the US, shows sleep disorders are highly prevalent in Hispanic/Latino populations. For example, 28% had insomnia and more than one-third had self-reported short sleep (< 6 hours) or long sleep duration (> 9 hours). Sleep disordered breathing was prevalent in 33% of males and 19% of females in the HCHS/SOL in comparison to 17% of middle-aged men and 9% of middle-aged women in the Wisconsin Sleep Cohort Study population on non-Hispanic White adults. Importantly, our group has found worse cognitive scores are associated with Hispanic/Latino adults with long sleep duration in age, sex, and obesity adjusted models. Although Hispanic/Latino people are the largest minority group in the United States, there is a disproportionately low number of research studies on delirium in Hispanic/Latino patients and an urgent need for future studies. The relationship between sleep disturbances and risk of postoperative delirium in Hispanic/Latino patients is unknown.

Abnormal circadian and sleep patterns, sleep fragmentation, and poor sleep quality, have been associated with postoperative delirium. Most studies have investigated sleep after the onset of delirium. Few studies, however, have investigated whether preoperative sleep fragmentation and poor quality of sleep leads to an increased rate of delirium. In one study of 50 English speaking patients undergoing non-cardiac surgery patients who developed delirium had a significantly higher percentage of time awake after sleep onset measured by wrist actigraphy, a measure of sleep fragmentation and poor sleep quality. Another cohort study of 101 older patients undergoing joint replacement, preoperative
sleep disruption, assessed with actigraphy and sleep questionnaires, carried a risk ratio of 3.1 (95% CI 1.34–7.17) of developing delirium. While we have shown many types of altered sleep patterns are common in Hispanic/Latino patients, we do not know which sleep patterns may increase the risk of delirium. Sleep fragmentation and short duration are of particular interest as sleep deprivation causes acute cognitive changes similar to delirium with impaired attention and executive function. Additionally, patients with delirium develop abnormal circadian and melatonin cycling with short, fragmented sleep patterns. A melatonin receptor single nucleotide polymorphism (SNP), rs10830963, common in Hispanic/Latino people, associates with altered circadian and melatonin cycling in non-Hispanic White patients. Our prior work found that the melatonin SNP correlated with delirium after cardiac surgery in non-Hispanic White patients.

A largescale cohort study is needed to determine if altered sleep patterns increase the risk of delirium in older, Hispanic/Latino patients after cardiac surgery. However, given the vulnerable nature of the target population, older patients undergoing a major surgery in an underrepresented population, it is imperative that we determine the feasibility of our protocol in a pilot study. The aims of the study were developed according to CONSORT extension to pilot and feasibility trials with modifications for a prospective cohort study.

**METHODS**

The primary aims of this pilot study were 1) to determine the proportion of approached, eligible patients who consented, 2) to determine the proportion of screened patients who consented, 3) to measure the number of days between surgery scheduling and admission date, 4) to determine the proportion of study participants retained, 5) to determine the proportion of study participants with adequate preoperative actigraphy data, 6) to determine the proportion of study participants who completed the sleep questionnaire battery, 7) to determine the proportion of study participants who completed the cognitive testing battery, and 8) to determine the proportion of postoperative days with daily delirium testing. The secondary aims of the study were 1) to investigate the prevalence of preoperative altered sleep patterns, 2) to determine the prevalence of the melatonin receptor SNP, and 3) to investigate the incidence of postoperative delirium and subsyndromal delirium.

**Study design:** We conducted a single-center, prospective, pilot, cohort study of older Hispanic/Latino patients undergoing cardiac surgery with and without preoperative sleep disturbances and postoperative delirium from February 2020 to December 2021.

Changes in methods after study commencement:

Our study was conducted during the height of the COVID19 pandemic in Miami, FL. During the various waves of the pandemic, when local incidence of COVID19 increased, recruitment would fall. To continue to assess the feasibility of the protocol, we amended our protocol to decrease the age for eligibility from 65 years of age to 50 years of age on June 17, 2021. In addition, we amended our protocol to allow a
minimum of 5 days between recruitment and surgery instead of a 7-day requirement. Finally, after 6 participants the cognitive battery was reduced from 5 to 3 total tests due to multiple complaints of increased burden by the participants.

Eligibility requirements:

Sequential eligible people scheduled for cardiac surgery at the University of Miami, Miami Florida were recruited between February 2020 and November 2021. Inclusion Criteria were: 1), self-identify as Hispanic/Latino or preferred language as Spanish, 2) undergoing scheduled elective and urgent cardiothoracic surgery, and 3) 50 years of age and older. Exclusion Criteria were: 1) inability to consent, 2) preferred language other than English, Spanish or Portuguese, 3) emergency surgery, 4) anticipated discharge < 48 hours, 5) individuals < 50 years of age, 6) pregnant women, and 7) prisoners.

Setting: UHealth of the University of Miami is an academic tertiary center in Miami, FL with a large, 60%, Hispanic/Latino population.

Ethical approval, Registration and Funding:

The study was approved by the University of Miami Institutional Review Board (IRB) (eProst ID 20200942). The study was registered at ClinicalTrials.gov on March 8, 2021 (NCT04786899) This study received funding from the Miami Clinical and Translational Science Institute (Grant number: CTSI-Pilot-FY2021-05).

Recruitment and Informed Consent Process:

Each week, the study team reviewed a list of patients who were scheduled for cardiac surgery in the cardiothoracic clinic for age and estimated length of stay eligibility. The Internal Review Board (IRB) approved for the study team to search for each patient in the Electronic Health Record and review the patient demographics only. If a patient self-identified as Hispanic/Latino or their preferred language was Spanish, the study team then called the patient to assess for interest in participating in the study using IRB approved telephone scripts. Consent took place either virtually or in-person. The virtual consent process was approved by the IRB.

Study Procedures

Recruitment: We measured the number of eligible, approached, and consented patients in an on-going basis and at completion of the study. We gathered data on reasons for denial of participation, barriers to recruitment, and eligible: enrolled ratios to optimize recruitment in an ongoing basis. We measured the number of days between scheduling the surgery and the planned surgery date. The subjects were paid $50 after the preoperative study visit and an additional $50 at the completion of the study.

Retention: We measured how many participants completed the study once consented. We gathered data on reasons for withdrawal. We gathered data from all participants data on burden level of each part of
the study protocol.

Preoperative cognitive testing: Preoperative cognitive impairment is a major risk factor for the development of delirium and a potential confounder. Baseline cognitive was to be tested in all subjects. Baseline cognitive status was evaluated by a cognitive battery. This battery was given in-person if feasible. If not feasible due to COVID-19 and social distancing requirements, we gave the battery over video-call platform if the patient had a capable device and internet connection. If they did not have video-call capabilities, we planned to administer a modified battery over the phone. The original cognitive battery included Montreal Cognitive Assessment (MOCA) (Spanish version and telehealth or blind version as necessary),\textsuperscript{24,25} Hopkins Verbal Learning Test Revised (HVLTR),\textsuperscript{26} copy figure from Repeatable Battery for the Assessment of Neuropsychological Status (RBANS),\textsuperscript{27} Geriatric Depression Scale (GDS) (available in multiple languages including English, Spanish and Portuguese),\textsuperscript{28} and the FRAIL scale.\textsuperscript{29} The modified cognitive battery only included the MOCA, GDS, and the FRAIL scale. MK, a neuropsychologist at the University of Miami, developed the protocol for virtual cognitive test visits according to her clinical practice. She trained all clinical research coordinators and EMG in the cognitive test administration over a series of 3 training sessions.

Preoperative Sleep testing

Actigraphy: We obtained 5 to 7 days of wrist actigraphy data using an Actiwatch Spectra Pro (Philips Respironics, Murrysville, PA), a research grade actigraph. Philips Actiware 6.1.1.3 (Respironics Inc, Murrysville, PA) software was used. The Spectra Pro is lightweight and waterproof. The participants were to press the event marker button on the device during wake-sleep transitions. Wake-sleep transitions were also determined from the actigraphy data if participants did not push the event marker button. Raw acceleration signals were converted into activity counts over 30 sec time epochs. Actiware automatically computed wake thresholds, the minimum number of activity counts required to score an epoch as awake. The Actiware software also has a sleep interval detection algorithm, and sleep duration was calculated once a rest interval was set. The wake-sleep transitions and sleep intervals were manually reviewed and validated by the research team. Sleep duration, wake after sleep onset (WASO), and sleep efficiency were our key variables. WASO is the total number of minutes scored as awake within sleep intervals during a 24-hour day. Sleep efficiency is the total sleep time divided by the time in bed and multiplied by 100. We defined normal sleep efficiency as >85%, slightly poor sleep efficiency as 75-84%, moderately poor sleep efficiency as 65-74%, and severely poor sleep efficiency as <65%.\textsuperscript{30} We derived 24-hour rest-activity rhythm metrics estimated from activity counts over multiple days to determine the timing and stability of such rhythms. Each participant was also asked to complete a sleep diary.

Sleep questionnaires:

The Pittsburgh sleep quality index (PSQI) was given to each patient to assess for the presence of poor sleep quality in the 4-week time interval prior to surgery. It is a validated and commonly used self-rated questionnaire. A cut-off score of 5 has a sensitivity of 89.6% and specificity of 86.5% in distinguishing good and poor sleepers.\textsuperscript{30} It consists of 19-item scale
that provides seven component scores (ranges 0-3): subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, use of sleeping medications, and daytime dysfunction. The PSQI is available in multiple languages including English, Spanish, and Portuguese and includes a version specifically for Hispanic/Latino patients in the USA.\textsuperscript{31}

The Insomnia Severity Index (ISI) was administered.\textsuperscript{32} The ISI, a 7-item self-report questionnaire, assesses the nature, severity and impact of insomnia. Severity of sleep onset, sleep maintenance, and early morning awakening problems, sleep dissatisfaction, interference of sleep difficulties with daytime functioning, noticeability of sleep problems by others, and distress caused by the sleep difficulties are evaluated. A 5-point Likert scale is used to rate each item (0 = no problem; 4 = very severe problem), for score of 0 to 28. We planned a cutoff of > 10 for insomnia (sensitivity of 86.1% and specificity of 87.7% in community samples).\textsuperscript{32} The ISI is available in multiple languages including English, Spanish and Portuguese.

The Epworth Sleepiness Scale (ESS) was administered. The ESS is a validated brief self-administered questionnaire which is used both clinically and research settings to measure the subject’s usual level of daytime sleepiness or average sleep propensity.\textsuperscript{33} The ESS asks the patient to rate the likelihood of falling asleep during 8 common situations like “watching television,” “sitting and reading,” and “sitting and talking to someone.” For each situation, the patient rates on a 4-point ordinal scale the chance of dozing from “No chance of dozing” to “high chance of dosing.” Scores of > 6 are consistent with excessive daytime sleepiness. The ESS is available in multiple languages including English, Spanish, and Portuguese.

The STOP-BANG score was administered to assess the risk of sleep disordered breathing. The STOP-BANG score is one of the most widely used scores to assess for the risk for obstructive sleep apnea (OSA).\textsuperscript{34} The questionnaire has 8 questions. The risk of OSA is scored as low, intermediate, or high depending on which questions are answered yes and the total answered yes. The Stop-Bang is available in multiple languages including English, Spanish and Portuguese.

Genetic testing for rs10830963 polymorphism: A blood sample was drawn during the patient’s hospital stay. The UHealth Center for Genome Technology provided DNA extractions, quantitation, and storage of the DNA. A taqman allelic discrimination assay for the variant was performed. All genotypes were done in duplicate with appropriate controls to ensure proper clustering and genotype calling. The prevalence of both the risk allele (G) and risk genotype (GG) were determined.

Postoperative Delirium Testing

The Confusion Assessment Method (CAM) was given twice per day along with chart review until discharge to identify the presence of delirium. All clinical research coordinators and research assistants were trained by MK, a neuropsychologist, and EMG, expert in delirium, according to the CAM training manual.\textsuperscript{35} The CAM-ICU was given to the patient while in the intensive care unit (ICU) and intermediate care unit.\textsuperscript{36} The CAM-ICU is the validated version to be used in this setting. The CAM-ICU is available in
multiple languages including English, Spanish, and Portuguese. The Long CAM was planned to be given to the patient when not in an intensive care setting. Delirium was defined as the patient having evidence of both acute onset of change in cognition or fluctuating course (CAM Feature 1) and inattention (CAM Feature 2) and either altered consciousness (CAM Feature 3) or disorganized thinking (CAM Feature 4). Subsyndromal delirium was defined as the patient having any of the four features but not meeting criteria for delirium. The duration of delirium in days was recorded. Team meetings occurred once per month to review delirium testing and documented observations to adjudicate delirium results.

Data collection from both patient interview and medical record review included demographic variables, medical comorbidities, home medications, surgery type, anesthesia type, administered medications, perioperative complications, and pain scores.

Feasibility to proceed with future definitive trial

Feasibility of the study protocol was the objective of this pilot study. Investigators had established a priori threshold for specific feasibility criteria. These were the following: (a) the proportion of approached patients participating in the pilot study would be 30% or greater, (b) the proportion of enrolled subjects who were retained until the end of the study would be 70% or greater, (c) the proportion of 5 days or more of actigraphy data would be 80% or greater, (d) the proportion of complete sleep questionnaire battery would be 80% or greater, (e) the proportion of complete cognitive battery would be 80% or greater, and (f) the proportion of subjects with daily delirium testing would be 80% or greater.

Sample size: Since this was a pilot study, a sample size calculation was not performed. The researchers aimed for 15 to 30 participants because it was felt this would be a large enough sample to inform them about the practicalities of recruitment, retention, study procedures in a perioperative study on sleep and delirium in older Hispanic/Latino patients undergoing cardiac surgery. While a sample size of a future definitive study at this time cannot be calculated, the goal would have a pilot sample of about 10% the size of the larger scale study.

Blinding: Because the primary goal of the pilot study was to assess feasibility of the protocol and because we had limited research staff, blinding of the results of the sleep questionnaire and cognitive batteries during delirium testing was not always possible. However, the clinical research staff were blinded to the results of the actigraphy and melatonin receptor SNP data during delirium testing.

Analytical Methods:

For the primary feasibility aims of the study descriptive statistics were performed for eligible patients who consented, approached patients who consented, number of days between scheduling of the surgery and surgery date, the retention of study participants, the adequacy preoperative actigraphy data, the completion of the sleep questionnaire battery, the completion of the cognitive battery, and the completion postoperative delirium testing. For the secondary patient specific aims, descriptive statistics were performed for sleep duration, wake after sleep onset, sleep efficiency, poor sleep quality, insomnia,
excessive daytime sleepiness, melatonin receptor SNP risk allele and genotype, and postoperative delirium. We also included age, education level, surgery type, and length of postoperative stay. Descriptive statistics were conducted for all these study variables.

**RESULTS**

**Participant flow**

There were 155 patients who met initial eligibility of age (> 65 years prior to 06/17/2021 and > 50 years afterwards), self-identification as Hispanic/Latino or preferred language listed as Spanish, and surgery scheduled five or more days later (Figure 1). Ninety-two of these patients preferred Spanish and 63 either preferred English or were equally comfortable with both languages. No eligible patients preferred Portuguese only. The research staff attempted to contact 76 of the screened patients, which 22 preferred Spanish. We successfully contacted 45 patients of which 14 preferred Spanish. Of those, 4 were determined to be ineligible as the participant could not understand the nature of the research study and were unable to consent. Twenty-six patients declined to participate. Most participants declined due to feeling overwhelmed by undergoing cardiac surgery during the COVID-19 pandemic and not wanting to add any more stress prior to surgery. Three patients declined to participate due to the genetic testing of the melatonin receptor SNP. One patient agreed to participate but then his surgery was cancelled prior to his scheduled informed consent visit, and he was no longer eligible for the study. Fourteen patients consented to participate of which three preferred Spanish.

**Study period:** Recruitment occurred from February 12, 2020 until November 3, 2021 and data collection was stopped on December 31, 2021.

Baseline data are shown in Table 1. The mean age was 67.2 years. Spanish was the preferred language in 21.4% of patients. The cohort was highly educated. However, 42.9% screened positive for cognitive impairment on the MOCA. Frailty and prefrailty were prevalent at 14.3% and 42.9% respectively. 41.7% of patients screened positive for depression.

Table 1: Baseline Characteristics
<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Age (years)</td>
<td>67.2 (SD = 8.68)</td>
</tr>
<tr>
<td>Female</td>
<td>7/14 (50%)</td>
</tr>
<tr>
<td>Spanish preferred language</td>
<td>3/14 (21.4%)</td>
</tr>
<tr>
<td>Education attainment &gt; 12 years</td>
<td>12/14 (85.7%)</td>
</tr>
<tr>
<td>Length of Stay*</td>
<td>5.29 (SD = 2.05)</td>
</tr>
<tr>
<td>Minimally invasive Valvular Surgery</td>
<td>13/14 (92.8%)</td>
</tr>
<tr>
<td>Coronary Artery Bypass Graft Surgery</td>
<td>1/14 (7.1%)</td>
</tr>
<tr>
<td>Cognitive screen positive</td>
<td>6/14 (42.9%)</td>
</tr>
<tr>
<td>Frail</td>
<td>2/14 (14.3%)</td>
</tr>
<tr>
<td>PreFrail</td>
<td>6/14 (42.9%)</td>
</tr>
<tr>
<td>Depression screen positive $</td>
<td>5/12 (41.7%)</td>
</tr>
</tbody>
</table>

SD = Standard Deviation, n=14 except $Depression scale n=12, *Length of Stay was calculated until study completion which was up to 7 days postoperative or discharge.

Primary Feasibility Outcomes

Primary feasibility outcomes are shown in Table 2. The number of days between surgery scheduling and admission date ranged between 5 and 105 days as initial screening for eligibility excluded any patients with surgeries scheduled less than 5 days out. The median number of days was 20. 32.2% (50/155) had surgery scheduled between 5 and 15 days out, and another 34.2% of patients (53/155) had surgery scheduled between 15-25 days out. Key feasibility outcomes to determine feasibility of a larger scale study are as follows. The proportion of approached eligible patients participating in the pilot study was 14/40 (35%). The proportion of enrolled patients who were retained until the end of the study was 14/14 (100%). The proportion of adequate actigraphy data was 12/14 (85.7%). The proportion of complete sleep questionnaire was 14/14 (100%). The proportion completing the cognitive battery was 13/14 (92.9%). Of note the cognitive battery was changed from 5 total tests to 3 after 6 patients. The proportion of patients with daily delirium testing was 62/63 (98.4%) of total hospital days that study participants were eligible for delirium testing. One hospital day was missed when a patient’s surgery was moved up 3 days and the study team was not made aware until postoperative day 1. Twice daily testing occurred in 47/63 hospital days as we did not have enough funding for research staff for twice daily weekend testing during the pilot trial. Only the CAM-ICU was given to patients as all patients’ entire hospital stay occurred in the intensive care unit or intermediate care unit and no patients spent time on regular surgical floor.

Table 2: Primary Feasibility Outcomes
<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
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<tbody>
<tr>
<td>Proportion of eligible, approached patients who consented (n=30)</td>
<td>14/30 (35.0%)</td>
</tr>
<tr>
<td>Proportion of screened patients who consented (n=155)</td>
<td>14/155 (9.0%)</td>
</tr>
<tr>
<td>Median number of days between scheduling and surgery date</td>
<td>20</td>
</tr>
<tr>
<td>Proportion of recruited patients retained until study completion (n=14)</td>
<td>14/14 (100%)</td>
</tr>
<tr>
<td>Proportion of patients with acceptable actigraphy data (n=14)</td>
<td>12/14 (85.7%)</td>
</tr>
<tr>
<td>Proportion of sleep questionnaire battery completion (n=14)</td>
<td>14/14 (100%)</td>
</tr>
<tr>
<td>Proportion of cognitive battery completion (n=14)</td>
<td>13/14 (92.9%)</td>
</tr>
<tr>
<td>Daily postoperative delirium testing (n hospital days = 63)</td>
<td>62/63 (98.4%)</td>
</tr>
<tr>
<td>Twice daily postoperative delirium testing (n hospital days = 63)</td>
<td>47/63 (74.6%)</td>
</tr>
</tbody>
</table>

Secondary Patient Specific Outcomes

Secondary patient specific outcomes are shown in Table 3. The prevalence of preoperative altered sleep patterns was high. Poor sleep quality as defined by the PSQI score of greater than or equal to 6 was present in 78.5% of patients. Excessive daytime sleepiness as defined by Epworth Sleepiness Scale score greater than 10 was present in 7% of patients. The mean sleep duration of patients was 7.76 hours (SD = 0.79). Interestingly the patients had large differences between their minimum and maximum sleep epochs. The mean difference between the minimum and maximum sleep epoch was 4.36 hours (SD =1.31). Sleep efficiency was slightly poor, with the mean sleep efficiency of 80.18 (SD =8.72). The mean WASO was 45.25 minutes (SD =11.25), which equaled a mean of 9.24% (SD 1.52) time spent awake after sleep onset. The prevalence of the melatonin receptor SNP risk allele, G, was 6/14 (42.9%). No patients were homozygous for G. The incidence of postoperative delirium was 4/14 (28.6%) with another 4 patients experiencing subsyndromal delirium. In total, 57.1% of patients experienced either delirium or subsyndromal delirium.

Table 3: Secondary Patient Outcomes
<table>
<thead>
<tr>
<th>Sleep Quality Measure</th>
<th>Proportion</th>
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<tbody>
<tr>
<td>Proportion with Poor sleep quality</td>
<td>11/14 (78.5%)</td>
</tr>
<tr>
<td>Proportion with Insomnia screen positive</td>
<td>2/14 (14.3%)</td>
</tr>
<tr>
<td>Proportion with Excessive Daytime Sleepiness</td>
<td>5/14 (35.7%)</td>
</tr>
<tr>
<td>Proportion with OSA screen positive</td>
<td>4/14 (28.6%)</td>
</tr>
<tr>
<td>Mean sleep duration (hours)*</td>
<td>7.76 (SD = 0.79)</td>
</tr>
<tr>
<td>Mean difference in maximum and minimum sleep durations (hours)*</td>
<td>4.36 (SD = 1.31)</td>
</tr>
<tr>
<td>Mean Wake After Sleep Onset (minutes)*</td>
<td>45.25 (SD = 11.25)</td>
</tr>
<tr>
<td>Mean Sleep Efficiency*</td>
<td>80.18 (SD = 8.72)</td>
</tr>
<tr>
<td>Melatonin Receptor SNP (rs10830963) risk allele (G)</td>
<td>6/14 (42.9%)</td>
</tr>
<tr>
<td>Subsyndromal Delirium</td>
<td>4/14 (28.6%)</td>
</tr>
<tr>
<td>Delirium</td>
<td>4/14 (28.6%)</td>
</tr>
</tbody>
</table>

SD = Standard Deviation; n=14 except *Actigraphy data n=11

**DISCUSSION**

Interpretation: Despite being conducted during the height of the COVID-19 pandemic, our pilot trial met our a priori thresholds for specific feasibility criteria. (a) The proportion of approached patients participating in the pilot study would be 30% or greater, and ours was 35%. (b) The proportion of enrolled patients who were retained until the end of the study would be 70% or greater, and ours was 100%. (c) The proportion of patients with acceptable actigraphy data would be 80% or greater, and ours was 85.7%. (d) The proportion of complete sleep questionnaire battery would be 80% or greater, and ours was 100%. (e) The proportion of complete cognitive battery would be 80% or greater, and ours was 92.9%. (f) The proportion of patients with daily delirium testing would be 80% or greater, and ours was 98.4%. Therefore, a future, definitive prospective cohort study of older Hispanic/Latino patients undergoing cardiac surgery with and without preoperative altered sleep patterns and an outcome of postoperative delirium will be planned. The protocol is planned to be modified by increasing the age of eligibility to 65 years of age and older.

Pilot trial Limitations: The pilot trial was limited by the loss of our Spanish speaking clinical research coordinator. This limited which patients we were able to recruit and led to selection bias for Hispanic/Latino patients who spoke English proficiently. This may be why our cohort was highly educated. The feasibility of the protocol may be different in a more representative sample of patients who preferred Spanish. However, of the 3 patients who preferred Spanish, all 3 completed all study procedures. This limitation can be overcome during a larger, definitive study by ensuring all clinical research coordinators, research associates and assistants are fluent in Spanish.
In addition, the pilot trial was limited by decreasing the age of eligibility to 50 years old to continue adequate recruitment. Younger patients may more readily be able to follow the protocol. However, despite lowering the age of eligibility, the mean age of our study was 67.2 years with only 3 patients being less than 60 years old.

The pilot trial was also limited by the unique clinical, research and societal changes that occurred during the COVID-19 pandemic. It is possible that surgeries were scheduled further out from clinic visits than would occur not during the pandemic. This may change the total amount of patients who are eligible for a future, larger scale study. However, the primary reason given by patients in declining to participate was the not wanting to add any stress prior to undergoing Cardiac surgery, specifically during the pandemic as they expressed fears of contracting SARS-CoV2 and complicating their surgery and fears of being alone in the hospital after surgery. A subsequent larger, definitive study likely would be able to overcome this as the COVID-19 pandemic is resolving.

Generalizability: Our protocol, methods and data are of only one pilot study. Despite this, we feel that our detailed description of recruitment and cognitive testing over video-platform may be replicated in other pilot studies in different settings and patient populations.

**CONCLUSION**

The protocol was feasible and a future, definitive prospective cohort study of older Hispanic/Latino patients undergoing cardiac surgery with and without preoperative altered sleep patterns and an outcome of postoperative delirium will be planned.

**Abbreviations**

CAM: Confusion Assessment Method; ESS: Epworth Sleepiness Scale; GDS: Geriatric Depression Scale; HCHS/SOL: Hispanic Community Health Study/Study of Latinos; HVLTR: Hopkins Verbal Learning Test Revised; IRB: Internal Review Board; ISI: Insomnia Severity Index; MOCA: Montreal Cognitive Assessment; PSQI: Pittsburgh sleep quality index; OSA: obstructive sleep apnea; RBANS: Repeatable Battery for the Assessment of Neuropsychological Status; SD: Standard Deviation; SNP: single nucleotide polymorphism; WASO: wake after sleep onset

**Declarations**

**Funding:** This study received funding from the Miami Clinical and Translational Science Institute (CTSI) (Grant number: CTSI-Pilot-FY2021-05).

**Conflicts of Interest:** The authors declare that they have no conflicts of interest.

**Availability of data and material:** Raw data will be made available upon request to Dr. Elizabeth Mahanna-Gabrielli. Given the limited number of participants in this pilot study, raw data will not be
publicly deposited into a data repository, as identification of the individual patients may be possible.

**Authors contributions:** EMG designed and executed the study protocol, gathered, and analyzed data, and wrote, edited, and approved the manuscript. TL gathered data and wrote the first draft of the manuscript. CS recruited subjects, executed the protocol, gathered data, and edited and approved manuscript. JL gathered data and wrote the first draft of the manuscript. MK designed the cognitive battery and trained the research staff in cognitive testing. MF assisted in recruiting subjects, executing the protocol, edited and approved the manuscript. JL assisted in recruiting subjects, executing the protocol, and approved the manuscript. AR designed the study protocol, analyzed data, edited and approved the manuscript.

**Ethics approval:** The study was approved by the University of Miami Institutional Review Board (IRB) (eProst ID 20200942) on 9/5/2020.

**Consent to participate:** All study subjects consented to participate

**Consent for publication:** All study subjects consented for their data to be used in publication.

**References**


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**Figures**
Figure 1

Patient Flow Diagram

Supplementary Files

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