The Utility of Ambulatory Electrocardiographic Monitoring for Detecting Silent Arrhythmias and Clarifying Symptom Mechanism in an Urban Elderly Population with Heart Failure and Hypertension: Clinical Implications.

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Abstract

Background: Atrial and ventricular tachyarrhythmias, as well as bradyarrhythmias, in the elderly with heart failure (HF) and/or hypertension (HTN) have been well documented. However, the frequency of these arrhythmias, whether silent or symptomatic, and their association with subsequent cardiac events has not been well defined in patients 65 years or older with HF and other cardiovascular risk factors.

Objective: To assess the value of 2 weeks of remote, transtelephonic cardiac monitoring for detecting arrhythmias in an elderly, urban population living with HF.

Methods: Fifty-four patients with a history of systolic HF and/or HTN were consented and enrolled. All wore an auto triggered cardiac loop monitor for 2 weeks that captures EKG data and both silent and symptomatic arrhythmias were recorded.

Results: Mean age was 73 ± 6 years with 59% of subjects were females, 74% Hispanic, 22% black, and 4% white/other. All patients had HF and 94% had HTN. From the cardiac monitoring, 72% demonstrated ectopic atrial and ventricular activity, and 1 paroxysmal episode of atrial fibrillation was documented. In addition, 3 subjects had significant non-sustained ventricular tachycardia, and 4 individuals had severe bradycardia recorded on cardiac monitoring. These 7 individuals underwent placement of an implantable cardioverter defibrillator (ICD) or pacemaker based on the documented arrhythmias which may have otherwise gone undetected.

Conclusions: A substantial proportion of patients exhibited cardiac arrhythmias. Future morbidity was prevented because of the detection of arrhythmias on monitoring that led to specific therapies such as pacemaker or ICD implantation which otherwise may not have been implemented.

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Introduction

Atrial Fibrillation (AF) is the most common arrhythmia encountered in clinical practice affecting several million adults in the U.S. each year.\(^1\) AF is associated with an increased mortality rate as well as increased morbidity with reduced quality of life (QoL). Although most patients with AF are symptomatic, a significant minority of the elderly (up to ~30%) are asymptomatic when AF is recorded on their electrocardiogram.\(^1\) Nonetheless, asymptomatic AF is still significant as it has the same risk for thromboembolism as otherwise symptomatic AF and the same risk for developing a tachycardic induced cardiomyopathy when rate control is inadequate.\(^5\) Consequently and ideally, asymptomatic AF needs to be recognized despite its absence of symptoms and needs appropriate prophylactic therapy to be initiated if these important adverse outcomes are to be prevented. As AF is most common in older patients and in those with underlying cardiopulmonary disorders, including hypertension (HTN), heart failure (HF), diabetes, and coronary artery disease, patients with these characteristics are most likely to harbor asymptomatic “silent” AF. Similarly, such patients are more likely than younger healthier patients to also suffer clinically important and/or prognostically significant ventricular arrhythmias and bradyarrhythmias. Additionally, AF in older patients and in those with HTN and other high-risk markers is also a marker for an enhanced incidence of stroke and systemic embolism (SSE).

When AF is associated with symptoms, they often include fatigue, palpitations, dyspnea, dizziness, and/or exercise intolerance. However, these symptoms are non-specific in themselves as they are also commonly associated with other underlying chronic conditions such as HF, HTN, and/or diabetes, even in the absence of an arrhythmia.\(^6\) Thus such symptoms, which are frequent in the populations at most risk for AF, may or may not indicate the presence of AF but certainly do play a role in reducing QoL regardless of a dysrhythmic or other cause. Furthermore, many individuals with both HF and HTN are over 65 years of age which further increases their risk of developing AF as well as other arrhythmias and their associated morbidity and mortality risk and thus confounding symptom assessment. This number will likely continue to grow as our population continues to live longer with these and other chronic underlying diseases.

Finally, an estimated 20% of strokes are secondary to embolism from AF with about 20% of these being fatal. Importantly, stroke, both fatal and non-fatal, may be the initial clinical presentation of AF the latter resulting from either new onset AF or previously asymptomatic AF. Stroke and systemic embolism in patients with AF can be substantially reduced with prophylactic anticoagulation (warfarin); however, in those with asymptomatic AF, its recognition would be required to allow for treatment initiation.

As advances in the treatment and management of HTN and HF continue to improve and mortality rates from these disorders decline, practitioners will need to recognize which subgroups of patients and which symptom patterns may be most likely to have or to be associated with underlying cardiac arrhythmias and such practitioners may need to consider routine screening of some manner in at-risk populations in order to detect the presence of clinically important but still “silent” arrhythmias deserving of more intensive follow up and evaluation and to best understand the basis for symptoms as a guide to their reduction. More specifically, how frequently asymptomatic AF or other significant but “silent” dysrhythmias might occur in individuals with multiple underlying risk factors, such as older age, HTN, HF but without arrhythmic symptoms or prior SSE, for example, is currently unknown. Also poorly understood at present is what impact aging and chronic diseases such as HTN and HF have on the frequency and nature of self reported individual symptoms, or the frequency with which they are associated with an underlying arrhythmia. Similarly, little research has been done to assess whether modest and tolerable periods of continuous ambulatory ECG monitoring (e.g., 14-30 days) in patients with risk factors for clinically important arrhythmias but no history of any arrhythmia, might demonstrate its presence. If frequent, then a positive impact on therapy initiation and outcome may be expected, similar to screening blood tests or imaging studies for many cancers in men and women. It is therefore, a logical extrapolation of the above to question whether ambulatory recording of two weeks or so would be useful and cost-effective in
detecting previously unrecognized AF or other important dysrhythmias in at-risk individuals prior to SSE thus becoming a useful screening tool for the potential prophylactic anticoagulation for SSE prevention and/or whether it would be clinically helpful in symptom evaluation so as to improve QoL with targeted therapy. Towards this end we initiated the herein described pilot study.

**Material and Methods**

**Study Subjects**

The study was a prospective feasibility pilot with an anticipated enrollment of at least 50 subjects which was conducted in a consecutive cohort of consenting patients aged 65 years or older seen in the outpatient cardiac clinic of New York-Presbyterian Hospital. Informed consent was obtained from all subjects under an IRB-approved protocol, prior to participation. Inclusion criteria for study participation was age 65 years or older plus a history of HF and/or HTN but no prior history of arrhythmias. Subjects who agreed to participate were asked to wear an auto-triggered external memory-loop EKG recorder for 14 days and to transmit EKG strips via their home phone line in order to document the frequency and duration of arrhythmias, both silent and symptomatic. In addition, subjects were also requested to press an event recorder button on the monitor when symptomatic and to record any associated symptoms in a diary. We sought to determine whether AF or other significant underlying arrhythmias were present frequently enough to warrant a larger study so as to demonstrate a more precise incidence of their occurrence and the cost-eff ectiveness of this approach to arrhythmia detection, and to determine how often potentially arrhythmia associated symptoms in this population were actually arrhythmia related.

**Cardiac Monitoring Methods**

All subjects were given a LifeStar AF Express® monitor [Figure 1] along with instructions in English or Spanish on how to transmit data from their device over the phone to a central receiving service for analysis. This auto-triggered memoryloop recording system was chosen because it has previously been demonstrated to be tolerable by most patients and more eff ective than either 24-hr Holt-
Further review and management. During the beginning of the monitoring period, (baseline enrollment in the cardiac clinic) all subjects were given and instructed to keep a daily diary of symptoms (including date and time of occurrence). However, most subjects chose not to complete the diary; rather, they reported their individual symptoms for the 24-hr period to the technician at the time of daily phone transmissions as well as when capturing a recording during a period of symptoms.

Follow-Up and Outcomes Assessment

Follow-up evaluations were conducted during semi-annual visits and by chart review. Subjects were considered to have had a cardiac event if they experienced a myocardial infarction (MI) or unstable angina, underwent coronary revascularization with CABG or percutaneous cardiac intervention, underwent insertion of a device to control arrhythmias, exhibited exercise induced symptoms of cardiac ischemia or HF, such as angina, or dyspnea on exercise stress testing, developed clinically recognized AF, AFL, VT, or had a syncopal episode.

Data Analysis

Statistical analyses were performed using SAS 8.2 (SAS Institute, Cary, NC). Clinical data are reported as means and standard deviations for continuous variables and as frequencies for categorical variables. Kaplan-Meier event-free survival curves were constructed and Cox proportional hazard models were used to determine the effect of the presence of ectopic activity in both univariate and multivariable models. Multivariable analyses were performed adjusting for potentially confounding risk factors such as age, gender and body mass index (BMI). A p value < 0.05 was used for significance in all analyses.

Results

The demographic and clinical characteristics of the study population are listed in [Table 1]. From August 2006 until December 2007 a total of 54 subjects successfully performed ECG strip transmissions from home. The mean age was 73 ± 6 yrs (39% > 75 yrs); 59% were female, 74% were Hispanic, 22% were African-American, and 4% were self reported as white or other. All subjects with HF had systolic heart failure (class II-III) and 94% also had a history of HTN. The mean ejection fraction was 49% ± 13. Hyperlipidemia was present in 65%, 46% had diabetes, and 4% were active smokers. The baseline mean blood pressure was 139 ± 17 / 77 ± 11 mmHg. The mean body mass index (34.0 ± 8.6) was above normal. A total of 29% of subjects reported being hospitalized in the last year -- most for shortness of breath or chest pain rather than an arrhythmia while 27% had visited an emergency room and 52% had seen a physician in the last 4 weeks. In the last 4 weeks 45% reported palpitations, 50% resting shortness of breath, 70% shortness of breath with exercise. B-type Natriuretic Peptide (BNP) levels were not routinely collected in those hospitalized or in the out patient clinical setting. Most subjects were on one or more medications: 73% were on a beta blocker, 67% were taking an ACE inhibitor or angiotension receptor blocker, and 16% were taking a calcium channel blocker. These medications were prescribed by their primary physician in the cardiac clinic to treat their underlying cardiac conditions. We recognize that the use of these medications may have reduced the incidence of atrial and ventricular arrhythmias detected on cardiac monitoring and/or the aware-

| Table 1: Demographic and Clinical Characteristics of the Study Population |
|-------------------|-----------------------------------------------|
| Demographics     | Number of Subjects who successfully Transmitted |
| Age (year's± SD) | 73 ± 6                                         |
| Females          | 32(59%)                                        |
| Race/Ethnicity   |                                               |
| Hispanic         | 40(74%)                                        |
| Afircan-American | 12(22%)                                        |
| Caucasian/Other  | 2(4%)                                          |
| Clinical Characteristics |                        |
| HF               | 54(100%)                                       |
| HTN              | 51(94%)                                        |
| Hyperlipidemia   | 35(65%)                                        |
| Diabetes         | 25(46%)                                        |
| Former Smokers   | 19(35%)                                        |
| Current Smokers  | 2(4%)                                          |
| BMI(kg/m²)       | 34 ± 86                                        |
| Mean Systolic Blood Pressure(mmHg) | 139 ± 17                                      |
| Mean Diastolic Blood Pressure(mmHg) | 77 ± 11                                       |
Figure 2: Documented episode of atrial fibrillation captured in a female patient who was asymptomatic while wearing the monitor. Circles represent isolated premature ventricular beats.
ness of them and hence made our results more modest than they might otherwise have been in the absence of such medications.

**Recorded Arrhythmias and Symptoms**

Table 2 presents the type and frequency of arrhythmias that were detected on cardiac monitoring and the subsequent treatment. Ectopic activity was detected in 72% of subjects but only 31% were symptomatic, including 9% with palpitations and 7% with dizziness. One documented episode of atrial fibrillation was captured in a female patient who was asymptomatic while wearing the monitor [Figure 2] but for whom therapy was then instituted. In addition, 3 subjects had 4 to 6 beat runs of self-terminating ventricular tachycardia that contributed to a decision to implant an ICD for primary prevention of sudden cardiac death. Figure 3 shows one strip of frequent ventricular ectopy captured by the LifeStar AF Express® in one of these subjects during the study. Four subjects underwent permanent pacemaker placement for severe bradycardia: one for a prolonged pause, and the other 3 individuals for advanced AV block. Figure 4 shows an example of an AV block captured during the monitoring period. Therefore, in 8/54 subjects (15%), a significant, otherwise unanticipated dysrhythmia of clinical importance was detected during the two week period of continu-

**Figure 3:** Strip of frequent ventricular ectopy captured by the LifeStar AF Express® in this study, coupled with the subject’s low ejection fraction, led to placement of an ICD

**Figure 4:** Asymptomatic second degree AV block captured by the LifeStar AF Express® on a subject while sleeping, which led to placement of a permanent pacemaker
uous ECG monitoring. The most common symptoms reported by subjects were palpitations/heart racing in (9%) and dizziness/lightheadedness in 7%. These symptoms correlated with isolated ventricular or atrial ectopic beats in 28%. In addition, one subject with palpitations had NSVT, while one subject who reported dizziness/lightheadedness was noted to have second degree AV block. The AF event was without associated symptoms.

Follow-up

Subjects were followed for a median of 32 months (range 24 – 40 months). During that time, 15 subjects (28%) experienced cardiac events in addition to the 8 subjects (15%) noted above in whom either AF was detected or a device was implanted for a detected bradycardic or VT episode during monitoring. Two of these 15 subjects suffered a MI or unstable angina, 1 underwent CABG, and 8 developed exercise induced symptoms of cardiac ischemia confirmed on stress testing. Finally, the same individual who suffered the MI also had a NSTEMI in the setting of new onset unrecognized AF. One individual required hospitalization for a rapid symptomatic 2:1 atrial flutter. Of note, the individual with atrial flutter had sinus bradycardia on cardiac monitoring. The two subjects who suffered cardiac events were not wearing the loop recorder at the time of these events which occurred outside the 14 day monitoring period. However, during their initial 14 day recording period baseline ST/T waves were unremarkable. Finally, the individual who suffered the NSTEMI was noted to have frequent premature atrial contractions and atrial runs on cardiac monitoring. The Kaplan-Meier survival curve for cardiac events in these 15 subjects is shown in Figure 5. The presence of atrial and ventricular ectopic activity during cardiac monitoring was not significantly associated with increased risk of a cardiac event in this population with already established hypertension and heart failure in the univariate analysis (HR = 3.03,

<table>
<thead>
<tr>
<th>Arrhythmia</th>
<th>Frequency</th>
<th>Treatment</th>
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<tbody>
<tr>
<td>Silent AF</td>
<td>1/54 (2%)</td>
<td>Watchful frequent cardiac monitoring for future events, ASA initiation</td>
</tr>
<tr>
<td>Bradyarrhythmias</td>
<td>4/54(7%)</td>
<td>Implantation of a pacemaker (1 pause, and 3 AV blocks)</td>
</tr>
<tr>
<td>Non-sustained Ventricular Tachycardia</td>
<td>3/54(6%)</td>
<td>Implantation of an ICD</td>
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Figure 5: Kaplan-Meier Survival Curve for Cardiac Events. The frequency of individuals without cardiac events is presented over time.

Table 2: Type and Frequency of Arrhythmias Detected and Subsequent Treatment
95% C.L. 0.68 – 13.47) or a” er adjusting for age, gender, and BMI (HR = 2.53, 95% C.L. 0.53 – 12.02) (recognizing that 8 subjects with detected AF, VT, or a significant bradycardia/AV block underwent therapy as noted above which might have prevented some additional long-term outcome events). Only female gender was significant in the multivariable model (HR = 0.25, 95% C.L. 0.07 – 0.86, p = 0.03). The power to detect a significant effect for the presence of ectopic activity was 36%.

Discussion

Our protocol was designed as a pilot study to attempt to determine if clinically important previously unrecognized arrhythmias exist frequently in patients who would appear to be at increased risk, such as the elderly with HTN and/or HF, as well as how frequently symptoms commonly encountered in a HF and HTN population, have a dysrhythmic basis. It was conducted in an elderly population in a single center outpatient cardiac population, which serves a primarily lower socioeconomic Hispanic population. All subjects who were enrolled had multiple underlying cardiovascular risk factors for both arrhythmias and future cardiac events as well as disease-related reasons for symptoms, but no previously recognized arrhythmia. In this setting, our pilot study suggests that a two week period of monitoring of elderly without previously recognized dysrhythmias but with at-risk conditions such as HTN or HF can be of clinical value, and cost effective. Of the 54 patients enrolled, 72% had some form of an arrhythmia detected with 8 subjects having a clinically significant dysrhythmia, including silent AF, significant bradycardia/AV block, and VT. Notably, only 28% of the detected dysrhythmias were symptomatic. Despite the absence of previously recognized arrhythmias, once arrhythmias of clinical importance are detected by such monitoring the existing guidelines for pacemaker and ICD implantation and/or AF antithrombotic therapy can be initiated, as was the case in 8 of our 54 subjects—a not trivial minority. Monitoring is helpful in distinguishing symptoms that are related to underlying CAD/HF vs. an underlying arrhythmia hence, it has a role in patients with symptoms. Depending on the type of monitoring used it may also have a role in assessing prognosis. A 14 day period seems feasible and tolerable by most elderly individuals. As compared with 24 hour Holter recordings, loop recorders are able to record a greater amount of data and provide a more comprehensive evaluation of patients underlying heart rhythm over time. Any fixed duration is arbitrary and increased yield has to be balanced with value and feasibility.

Anticoagulation of AF is particularly important in the population we studied as all had HF and/or HTN, all were at least 65 years old, and 39% were above 75 yrs of age, meaning that all had a CHADS2 score of at least 1, and most had a score of at least 2, such that if AF detected in this population would generally indicate the need for anticoagulation with warfarin. Thus, even in this small series, our results are clinically enticing as regards their importance to prophylactic clinical therapy. For example, if our observation of an approximately 2% incidence of silent AF in this high-risk population is representative of what would be found in a larger series, and given an approximately 3-6% yearly risk of stroke/systemic embolism in patients with their CHADS2 scores, then there would be approximately 100 patients with silent AF detected per 5000 patients studied, which would allow for prophylactic anticoagulation and event prevention in 4/5000 patients. The cost of the AF express device used in this investigation for a 2 week period of cardiac monitoring was $125 and yielded a total of 7 events that would have otherwise not been detected or treated. Despite the upfront cost of the auto-triggered device, the yield offsets the initial cost, and is similar to other investigations that found the use of an external loop recorder, beneficial when confirming a diagnosis of syncope or pre-syncope, in an ambulatory community setting.11 This also appears to be within the cost effectiveness of other screening procedures such as mammography and PSA determination.

In addition, our results provide some insight as to how often in a population such as ours, which is extremely typical demographically of patients in major clinical trials of AF such as AFFIRM, ATHENA, and RACE, symptoms consistent with an arrhythmia actually have a dysrhythmia associated with them.12-14 Our observations confirm that self reported symptoms of palpitations, and lightheadedness/dizziness may be associated with an
Ectopic activity consisting of primarily isolated premature atrial and ventricular beats, which were multifocal with occasional couplets were noted in 72% of our older-aged subjects with HF and/or HTN during their EKG transmissions, with 31% of subjects reporting they were symptomatic just prior to the recording to the technician receiving the data via the telephone transmission. The symptoms noted most frequently included palpitations (9%) and dizziness (7%). These findings are consistent with those reported in the early years of using loop recorders in clinical practice that demonstrated the highest yield of NSVT, atrial and ventricular ectopy in those experiencing symptoms of palpitations and dizziness referred for monitoring.\textsuperscript{15} In those who experienced events in our series one individual complained of palpitations and dizziness referred for monitoring. Although the presence of ectopic activity during 2 weeks of cardiac monitoring was not significantly related to subsequent cardiac risk, the power of this preliminary pilot feasibility study was clearly low due to limited sample of elderly subjects who were capable of wearing the monitor for a two week period and able to change EKG leads daily and transmitting daily strips utilizing their home telephone, which many noted to be too complex. It is also most likely that the presence of a heart failure history, itself a potent marker of subsequent events, overwhelmed any additional prognostic value to detected arrhythmias in our population, and the 2 week monitoring period was too short to allow us to analyze if overall arrhythmia-burden (a product of frequency and time in an arrhythmia) might have been of prognostic value, rather than just the presence or absence of an arrhythmia. Finally, it should be noted that in our initial investigation the detection of arrhythmias led to implantation of either a pacemaker or ICD in 7 subjects that may have otherwise remained silently at risk and would not have undergone immediate appropriate clinical care. It thus remains plausible that in the absence of this investigation, adverse outcomes would have occurred that would have changed the observed rates of our arrhythmia-event associations. Finally, our observations were useful to the patients enrolled in our trial as noted by the frequency of clinical intervention and by implication there may be value to similar detection in additional populations with other underlying cardiovascular disorders, or even in those whose only risk marker is age, which remains another study to consider.

Additional Possible Limitations

Even though a bilingual research assistant/translator was present in the cardiac clinic during enrollment to enhance patient understanding of our study, many individuals choose not to participate due to a wide variety of reasons (lack of interest, viewed the study as burdensome and of no direct benefit to them). The reason for refusal was not systematically collected on all subjects as many declined to give a reason. This is a potential area that warrants further investigation. Finally, many subjects reported they simply forgot to keep the requested daily diary of symptoms, but instead verbally reported symptoms at the time of EKG transmission, when prompted by a technician over the phone. Notably, however, subsequent to the completion of our study, newer wireless technology has become more widely available that could be used in future investigations which would be less burdensome to the patient and yield
even greater data for correlation to underlying symptom and other clinical parameters. Finally, as noted earlier, it is possible that the medications taken by our subjects for their underlying HF and/or HTN could have reduced the number of arrhythmias we might have detected and/or altered their perception. However, this is limitation in any such a real-life scenario.

Conclusion

This study was novel in that it explored the utility of cardiac arrhythmia screening in a primary underserved urban elderly population living with two chronic diseases HF and HTN. Cardiac monitoring demonstrated most of the subjects experienced isolated atrial and premature beats during the two week cardiac monitoring period. In this at-risk population previously unrecognized AF was also recorded. Given the nature of this population, its implications for anticoagulation and SSE prevention are substantial. Significant bradycardia and non sustained ventricular tachycardia were also recorded; these led to implantation of a pacemaker or ICD in patients who otherwise would not have received them, or gotten them as early, possibly preventing additional adverse clinical outcomes during follow up. Thus, our study raises the question as to whether we should be monitoring more closely the at-risk elderly with or without symptoms to determine if in fact their symptoms are related to an underlying arrhythmia vs. a chronic condition such as HF or HTN and to detect silent but prognostically and/or therapeutically important arrhythmias. Future research aimed at replicating this pilot work is needed in larger more diverse patient population; living with chronic diseases is needed. Finally, the role of access to cardiac care, depression, anxiety, and knowledge regarding their underlying cardiac conditions and medication compliance as well as other socio-demographic variables which can all impact on cardiac outcomes, symptoms, and QOL warrants further investigation.

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References


