Standard versus Intensive Monitoring Post-Myocardial Infarction Looking for New-Onset Atrial Fibrillation (SIMPL-AF)

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1. BACKGROUND:

Patients with atrial fibrillation (AF) who suffer an acute myocardial infarction (MI) are at increased risk for stroke (2% during index hospitalization), and mortality (14% 30-day mortality and 22% 1-year mortality) compared to those without AF.[1] In the TRACE trial, post-MI patients with AF during hospitalization had an increased 5-year mortality compared to those without AF (56%, OR 1.5).[2] Furthermore, AF post-MI has been associated with 30-day (HR 14.6) and long-term stroke (HR 2.29, mean follow-up 2.7 years).[3] Even transient AF in hospital has been associated with stroke at 1-year (10.2%, HR 5.1), thus representing a target for therapeutic intervention[4] In this study, patients were discharged home with only single or dual antiplatelet therapy despite eligibility for anticoagulation (mean age 70 years, 53% hypertensive, 34% diabetic). Thus, after an MI, AF is an important prognostic factor for predicting future events, including stroke and death.

1.1 New-Onset AF Post-MI

The prevalence of new AF post-MI is variably reported, with previous trial data reporting new AF in 3-7% of patients after extended follow-up (2-4 years).[2, 3] A community cohort using ECG records identified new AF in 3.7% 3-30 days post-MI, and in 12% after long-term follow-up (6.6 years). However, despite the prevalence of AF, the majority of these episodes are asymptomatic, as demonstrated in two recent studies using continuous monitoring via implantable cardiac monitors. The first study (CARISMA) enrolled post-MI patients with LV dysfunction (EF ≤40%) but no history of AF. The investigators demonstrated the risk of developing new AF was highest in the first 2 months post-MI (16%), with the prevalence of new-onset AF increasing to 28% at approximately 2 years follow-up.[5] The ARREST study enrolled 50 post-STEMI patients with LVEF ≥40% who received percutaneous revascularization (PCI) within 7 days following MI.[6] Over a 2-year follow-up, AF was newly detected in 58% of the study population, with a median time to first episode of 4.8 months. Importantly, in both these studies >90% of patients were unaware of their AF highlighting the importance of vigilant surveillance of cardiac rhythm. As such a substantial proportion of patients may have undiagnosed AF and remain at increased risk of stroke.[5, 6]

1.2 Limitations of Current Studies

A major difference between the aforementioned CARISMA and ARREST studies has to do with the method of surveillance. The CARISMA study utilized a loop recorder with an older AF detection algorithm that was reliant on ventricular rate. Specifically, AF was only detected at high heart rates (≥125 bpm) or in the presence of severe bradycardia (≤30 bpm). As many post-MI patients receive rate-slowing medications it is possible that they may not develop AF within the detection zones, and thus the prevalence estimate in this study likely represents an underestimate.[7] Using an improved detection algorithm (R-R interval assessment), the ARREST study identified a greater proportion of new onset AF in a potentially healthier population (LVEF ≥40%). However, in order to document this prevalence, patients were required to undergo an invasive procedure. The routine implantation of implantable loop recorders (ILRs) post-MI remains prohibitive due to its high cost and semi-invasive nature.

External loop recorders may fit the ideal niche for AF monitoring in post-MI patients. As relatively affordable devices, external loop recorders provide extended monitoring and is best suited for patients with arrhythmia recurrence within 3-4 weeks.[8] Furthermore, in contrast to patient activated external monitors (event recorders), external loop recorders have diagnostic rhythms for intelligent analysis and identification of AF, thus making the an ideal method to detect AF in asymptomatic patients, These devices have been used in syncope work-up and evaluation of palpitations, and more recently in the prolonged monitoring of cryptogenic stroke with great success.[9] A non-invasive but intensive monitoring strategy post-MI may effectively identify individuals who develop AF after discharge and are eligible for oral anticoagulation (OAC).

1.3 Targets for intervention
Dual antiplatelet therapy (DAPT), is routinely prescribed to patients after an acute coronary syndrome owing to its beneficial effects in the prevention of stent thrombosis, myocardial infarction, and death after acute coronary syndrome (ACS).[10-14] Unfortunately in the AF population, DAPT is inferior to OAC in the prevention of thromboembolic complications associated with atrial fibrillation or flutter (AF/AFL).[15-17] As such, the identification of AF in this population has the potential to significantly alter the clinical management of these patients, as well as potentially improve outcomes.

2. RATIONALE:
After an MI, patients discharged home in sinus rhythm may develop AF that is asymptomatic, undetected, and undertreated. Previous studies (CARISMA and ARREST) have demonstrate high rates of new-onset AF recorded on ILR, although the routine implantation of ILRs post-MI remains costly and invasive. The external loop recorder may effectively identify patients with new-onset AF through a validated diagnostic algorithm and targeted monitoring during a high-risk period (immediately after hospital discharge).

3. PROPOSED RESEARCH
3.1 Hypothesis
Using a non-invasive but intensive monitoring strategy (30-day external loop recorder), we hypothesize that AF will be detected more frequently compared to standard care. Furthermore, intensive monitoring will result in higher rates of oral anticoagulation prescription (secondary outcome) compared to standard care.

3.2 Objectives
1) **Primary Objective -** To determine the incidence of new-onset AF at 30-days post-MI using an intensive monitoring strategy.
2) **Secondary Objectives**
   a) To determine the impact of intensive monitoring on oral anticoagulation rates at 90-days and 1-year after monitoring.
   b) To identify the risk factors for developing new-onset AF (i.e. demographics, MI characteristics, GRACE score).

c) To determine the variables associated with initiating or withholding anticoagulation in new-onset AF (i.e. CHADS$_2$, CHA$_2$DS$_2$-VASc, HASBLED scores).

3.4 Inclusion Criteria
1) Age 18 years or older.
2) Patients with ST-elevation myocardial infarction (STEMI) or Non-ST-elevation myocardial infarction (NSTEMI; Third Universal Definition of MI[18]) with or without PCI. All patients must have troponin elevation.
3) No history of AF during hospitalization, at discharge, or pre-existing AF documented on history (i.e. hospital records, previous hospitalization, ECG records).
4) No anticoagulation for AF or other indications (i.e. LV thrombus, heart valves, venous thromboembolism/deep venous thrombosis).
5) No concomitant disease expected to reduce expected lifespan to <2 yrs.

3.5 Exclusion Criteria
1) Patients receiving CABG surgery during this hospitalization or planned cardiac surgery within the next 3 months.
2) Patients with spontaneous coronary artery dissection (SCAD), non-atherosclerotic coronary disease (NACAD), and Takotsubo cardiomyopathy are excluded from this study.
3) Patients with contraindications to anticoagulation.
4) Patients with a chronic skin disorder on the upper torso, or an allergy to medical tape or glue.

3.6 Outcomes
1) **Primary Outcome**: development of atrial fibrillation or flutter lasting ≥30 seconds (consensus definition[19, 20]) detected using external loop recorder
2) **Secondary Outcome**: anticoagulation prescription, AF-related hospitalization, and a composite secondary outcome of all-cause hospitalization, re-infarction, stroke, and death at 90-days and 1-year after completion of monitoring

3.7 Methods
Upon enrollment, patients will be randomized (2:1 distribution for intensive monitoring, stratified by STEMI vs. NSTEACS) to receive standard care or intensive monitoring. Intensive monitoring entails wearing a Spiderflash (LivaNova) 30-day external cardiac monitor at discharge. A 30-day external cardiac monitor represents the most feasible, high-quality, non-invasive monitoring strategy possible, while maximizing the duration of uninterrupted monitoring beginning at discharge. Demographics, clinical characteristics, and risk factors for stroke and bleeding (i.e. CHADS$_2$, HASBLED) will also be collected at enrollment.

The research team will perform all aspects of SpiderFlash data acquisition and interpretation. The research team has purchased the SpiderFlash devices and the programming/analysis software. After patients have completed the 30-day recording, the information will be downloaded directly off the device (via SD card). There is no

industry involvement and no data transfer to a server or out of country. There is no relationship between the SpiderFlash provider and UBC/VCH, and no connection between the research team and SpiderFlash provider. All funds are provided by a research award attained by the trainee (CC).

Spiderflash ECGs will be interpreted by the trainee (CC, cardiology resident) with oversight from the supervising physician (JA). The reports will be distributed to the primary cardiologist and family physician. The standard care strategy includes a 12-lead ECG performed prior to discharge and at follow-up with the primary cardiologist (typically 4-8 weeks post-MI).

Cardiac medication review will be performed by the trainee (CC) at 90-days and 1-year post-monitoring (to allow adequate time for anticoagulant initiation). A telephone follow-up (15 min) and chart review will confirm anticoagulation status, and reasons for initiating or withholding anticoagulation.

Both the intensive monitoring and control groups will receive telephone follow-up at 90-days to assess prescription status. No additional care or clinic visits are scheduled for the control group. All additional data (including ECGs performed by primary cardiologist and confirmation of anticoagulation status) in the intervention and control group will be performed via electronic chart review of Cardiology EMR.

3.8 Sample Size Calculations and Statistical Analysis

Previous retrospective and cohort data has identified new-onset AF in 7-14% of patients in-hospital or within 2 days after MI.[4, 21] Between 3-30 days, new AF occurs in 3.7% when ascertained through an electronic ECG database, with the remainder of AF (12%) developing during long-term follow-up (6.6 years).[21] Thus, at 30-days post-MI, we anticipate that the standard care strategy will detect similar rates of AF to this cohort study (3.7%).

Using an ILR, new-onset AF was detected in 16% at 2-months (approx. 8% at 1-month, CARISMA).[5] However, in the CARISMA study, AF was only detected when HR ≥125 bpm, effectively missing AF at slower rates (<125 bpm).[5] Up to half of patients (49%) with AF post-MI have heart rates ≤94 bpm.[7] Thus, we anticipate that an intensive monitoring strategy (30-day external cardiac monitor) will detect higher rates of AF (16%) after 30-days (double ILR rate given the heart rate limitations).

With a 2:1 randomization to intensive monitoring and using a 5% significance level (α=0.05), **216 patients** (144 patients with intensive monitoring and 72 patients with standard care) are required to have a 80% power (1-β=0.80) of detecting an increase in new AF (primary outcome) from 3.7% (standard care) to 16% (intensive monitoring). Accounting for a 5% drop-out, the final sample size is **240 patients (120 patients per group)**.

Statistical analysis will be performed using an intention-to-treat analysis for patients randomized to the intensive monitoring or standard care strategy. Regression analysis

will be used to compare rates of AF at 30-days between both groups. Time-to-event analysis will be used to compare the time to development of AF in both groups.

4. FEASIBILITY
4.1 Recruitment
There are approximately 310 STEMI/year in the health region (308-341/year, regional data[22]) with at least 4 NSTEACS per 1 STEMI (1240 NSTEACS/year, including transfers, regional data[23]). Patients will be excluded based on LVEF>40% (66% ineligible[24]), pre-existing AF (9%[21]), in-hospital AF (14%[4]), LV thrombus (8%[25]), and other factors (i.e. heart valves/VTE; uncommon, ≤1%[26]). 368 patients/year will meet enrollment eligibility. Using an enrollment rate of 66%, 20 patients will be enrolled per month (10 for intensive) and the target (264 patients) will be met in 13 months.

Patient recruitment will be overseen by Cardiology Research Manager, Jackie Chow, and Cardiology Clinical Research Coordinator, Andrew Starovoytov.

Patients will be recruited directly from the Vancouver General Hospital Coronary Care Unit (CCU). The Cardiology research nurses (Andrew Starovoytov and Jackie Chow) routinely screen patients admitted to the CCU for study eligibility. This process is well-established for a number of ongoing studies that operate in the CCU.

In this study, prospective participants will be identified upon admission to the CCU meeting the eligibility criteria. Study participants will be approached by Andrew and Jackie for consent to participate in the study.

4.2 Randomization and Blinding
Patients will be recruited from the Vancouver General Hospital Cardiac Care Unit (CCU) and St. Paul's Hospital Cardiac Intensive Care Unit (CICU). Randomization will be performed using a central randomization system (integration through RedCap) in a 1:1 manner, and will be implemented using an online access (RedCap) system. A back-up randomization will be available through sealed envelope in case of database issues. The allocation sequence will be generated by the co-investigator and Database expert (AS). Patients will not be blinded to the monitoring device. Physicians will blinded to patient identity, but will only review results for patients that received the monitoring device.

4.3 Device Purchase and Interpretation
The investigator and co-investigators have met with industry to purchase the SpiderFlash devices for specific use in this study. A reduced price for 10 SpiderFlash devices ($1150.00) was negotiated and the devices have been purchased, with delivery expected in May 2017.

SpiderFlash device interpretation will be performed initially by technicians that are working with the software for other clinical services. Technician interpretation of the SpiderFlash will be overseen by Operations Manager, Faisal Aziz. Technician reports

are subsequently reviewed by the investigator and co-investigator, blinded to patient demographics and details. All reports will be sent to the primary cardiologist for all enrolled patients.

4.4 Potential Issues and Mitigating Strategies
1) Patients may develop AF in-hospital and revert to sinus rhythm prior to discharge: these patients are excluded (AF already diagnosed, no role for intensive monitoring as per primary outcome).
2) Impact on anticoagulation: all test results will be communicated with the primary cardiologist and family physician. This study does not prescribe anticoagulation and will not influence the prescribing physicians- rather, all information will be communicated to the primary cardiologist or family physician.
3) Impact on stroke: this pilot study allows for the planning of a subsequent intervention with cardiovascular endpoints.

4.5 CCS-Bayer Resident Vascular Award and Funding
This project is co-led by a trainee (CC) and received full funding and won first prize at the CCS-Bayer Resident Vascular Award trainee competition in October 2016, receiving $30,000 funding ($20,000 + $10,000 presentation bonus). There is significant motivation to support this project from a local and divisional level, including commitment from various faculty and research staff at Vancouver General Hospital.

4.6 Research Infrastructure
The coordinating centre is the UBC Division of Cardiology, Cardiology Research at Vancouver General Hospital (located at Gordon and Leslie Diamond Health Care Centre). This research project will be performed at two sites in British Columbia with supervisors at each site (Vancouver General Hospital: JA, KG; St. Paul's Hospital: AK, MD). Each site benefits from a large referral base for STEMI and NSTEACS from across the province. There is established research support for the screening and enrollment of patients (research nurses are supportive). This project is financially supported by the UBC Division of Cardiology, with divisional research funds (CAPP) to support the purchase and donation of 10 Spiderflash monitors to this project.

The steering committee includes the principal investigator and co-investigators listed in this application. Enrollment will be performed by the Cardiology Research staff (AS, JC) and trainee (CC). The endpoint adjudication committee will be attend through consensus of the principal investigator (JA) and trainee (CC). The data management team will include the co-investigator (AS) with expertise in data management and RedCap Database development and the trainee (CC).

The trainee (CC) leading this project has significant research experience, and has participated in multiple prospective and retrospective projects in the field. He has written a review of loop recorders in syncope, and is writing a review of novel technologies for detecting AF. He has received multiple awards, including from the Canadian Stroke Prevention Intervention Network (C-SPIN) and the Cardiac Arrhythmia Network of Canada (CANet), and twice attended the C-SPIN Annual Clinical Trials workshop. The

supporting mentor and supervisors have extensive experience in clinical trials and AF research, and the trainee has collaborated with them on various occasions. Together, these supports and experiences provide an exceptional research environment for the design, coordination, and completion of this research project.

4.7 Research Database Development
The investigators will be using a RedCAP database for the storage of all patient information, including demographics, baseline, and follow-up variables collected in the case report forms. The RedCap system will provide anonymization and generate unique study ID numbers for all participants in this study. The RedCAP system is used in several site-specific and multicenter studies at the University of British Columbia, and will be managed by Clinical Research Coordinator, Andrew Starovoytov. Data will be entered by the principal investigator (JA), co-investigator (CC, AS). Access to the final trial dataset will include the principal investigator and all co-investigators.

4.8 Data Monitoring Committee
The Data Monitoring Committee includes two co-investigators that will not be involved in data collection or analysis (AK, KG). The Data Monitoring Committee will review the status of the trial every 6 months to ensure no difference in outcomes including mortality or re-hospitalization between the intensive monitoring and control groups. Stopping guidelines include an excess of mortality (2x) in either group. The Data Monitoring Committee will make the final decision to terminate the trial.

4.9 Ethical Considerations
The ethics application for this underway. The complete study protocol has been submitted and received initial review from the UBC/Vancouver Coastal Health Clinical Research Ethics Board (CREB). All data collection sheets and patient consent forms have been submitted and included in the appendix of this application.

Protocol modifications will be submitted as soon as possible to the ethics committee/institutional review board for approval. The principal investigator or trainee will inform all co-investigators in the event of any protocol modifications.

This project will be conducted in compliance with the protocol and principles laid down in the Declaration of Helsinki, Good Clinical Practice (GCP), as defined by the International Conference on Harmonization (ICH) where applicable, along with all other local regulatory requirements. Before study initiation, the enrolling center must have written and received approval/favorable opinion from the Institutional Review Board/Independent Ethics Committee (IRB/IEC) for the protocol, and data collection forms.

4.10 Publication and Presentation
Once completed, the investigators will communicate trial results with participants through publication. Publication and manuscript preparation will involve the principal investigator and all co-investigators. There are no anticipated publication or presentation restrictions.

APPENDICES.
APPENDIX 1. Enrollment Case Report Form.

<u>DEMOGRAPHICS</u>

Study Site _____
(VGH = 1; SPH = 2)

Study ID _____

Year/Month of Birth _____
(YYYY-MM)

Gender ☐ Female ☐ Male

Age at enrolment (years): _____

Date of Enrollment _____
(YYYY-MM-DD)

Signature of Person Completing CRF _____ Date: _____

<u>INCLUSION CRITERIA</u> (patient must meet all criteria to be eligible for study)
1) Age 18 years or older.
2) Patients with ST-elevation myocardial infarction (STEMI) or Non-ST-elevation myocardial infarction (NSTEMI; Third Universal Definition of MI18) with or without PCI. All patients must have troponin elevation.
3) No history of AF during hospitalization, at discharge, or pre-existing AF documented on history (i.e. hospital records, previous hospitalization, ECG records).
4) No anticoagulation for AF or other indications (i.e. LV thrombus, heart valves, venous thromboembolism/deep venous thrombosis).
5) No concomitant disease expected to reduce expected lifespan to <2 yrs.

<u>EXCLUSION CRITERIA</u>
1) Patients receiving CABG surgery during this hospitalization or planned cardiac surgery within the next 3 months.
2) Patients with spontaneous coronary artery dissection (SCAD), non-atherosclerotic coronary disease (NACAD), and Takotsubo cardiomyopathy are excluded from this study.
3) Patients with contraindications to anticoagulation.
4) Patients with a chronic skin disorder on the upper torso, or an allergy to medical tape or glue.

PATIENT MEETS ALL INCLUSION AND EXCLUSION CRITERIA:

Signature of Investigator: _____ **Date:** _____

PAST MEDICAL HISTORY

Hypertension ☐ YES ☐ NO

Diabetes ☐ YES ☐ NO
    If yes, Type? ☐ Type 2 ☐ Type 1
    Insulin-use ☐ YES ☐ NO

Dyslipidemia ☐ YES ☐ NO

Coronary Disease (before enrolment) ☐ YES ☐ NO
    Prior MI ☐ YES ☐ NO
    Prior PCI ☐ YES ☐ NO
    Date of Last MI/PCI: _____
                             (YYYY-MM)
    Prior CABG ☐ YES ☐ NO
    Date of CABG: _____
                            (YYYY-MM)

Heart Failure (prior to enrolment ACS) ☐ YES ☐ NO
    Ejection Fraction (EF): ☐ Reduced EF (HFrEF, LVEF <40%)
                       ☐ Preserved EF (HFpEF, LVEF >40%)
    If Reduced EF, last documented EF before current MI: _____ %

Prior Stroke/CVA ☐ YES ☐ NO
    If so, what type? ☐ Ischemic ☐ Hemorrhagic
                   ☐ TIA ☐ Other
    How many strokes? _____
    Most recent stroke: _____
                        (YYYY-MM)

Carotid Artery Disease ☐ YES ☐ NO
Peripheral Vascular Disease ☐ YES ☐ NO
(i.e. femoral, aortic aneurysm including AAA, TAA)

Renal Disease (i.e. GFR <60 mL/min) ☐ YES ☐ NO
    GFR at enrollment: _____ mL/min

Liver Disease (i.e. documented cirrhosis) ☐ YES ☐ NO

Thyroid Disease ☐ YES ☐ NO
    If yes, on replacement? ☐ YES ☐ NO
    Last TSH _____
    Date of Last TSH _____
                     (YYYY-MM)

Cancer/Malignancy ☐ YES ☐ NO
    If so, type and stage (if available): _____
    Active Cancer? (i.e. treatment within past 6 months) ☐ YES ☐ NO

SOCIAL HISTORY

Smoking history: ☐ YES ☐ NO

    Current smoker ☐ YES ☐ NO

    If quit, date: _____

        (YYYY-MM)

    Years smoked: _____

Regular Alcohol Use ☐ YES ☐ NO

    Drinks per week: _____

Illicit Drug Use ☐ YES ☐ NO

    Drugs used: _____

CURRENT MYOCARDIAL INFARCTION

Date of MI _____

        (YYYY-MM)

Date of Admission _____ (if different from date of MI)

        (YYYY-MM)

Type of MI ☐ STEMI ☐ NSTEMI

LVEF ≤ 40% ☐ YES ☐ NO

    On left ventriculogram ☐ YES ☐ NO

    On echocardiogram ☐ YES ☐ NO

    Other modality: _____

    Lowest LVEF measured _____ %

    Modality used: ☐ LVgram ☐ Echo ☐ Other: _____

CORONARY ANGIOGRAM

Cath Performed? ☐ YES ☐ NO

    Date of Cath _____

        (YYYY-MM)

    PCI performed ☐ YES ☐ NO

    Number and location of stent(s) _____

    Type of stents ☐ DES ☐ BMS

Number of vessels with disease (≥70%)

    ☐ single-vessel ☐ two-vessel ☐ three-vessel ☐ left main ☐ prior CABG

ECHOCARDIOGRAM (closest to discharge)

Echo Performed? ☐ YES ☐ NO

    Date of Last Echo _____

        (YYYY-MM)

Valvular abnormalities (please describe)

_____

_____

Left atrial size and dimensions
        Volume (indexed)   _____

        Dimension   _____

OTHER RELEVANT INVESTIGATIONS
(i.e. if patient had another imaging modality to document LV dysfunction)

_____

_____

ARRHYTHMIAS

Ventricular arrhythmias   ☐ YES   ☐ NO

        If yes, shocked?   ☐ YES   ☐ NO

Did patient have cardiac arrest?   ☐ YES   ☐ NO
(either out-of-hospital or in-hospital cardiac arrest)

CARDIAC MEDICATIONS

Please list medications on discharge prescription (or as close to discharge as possible)

Antiplatelet(s)   ☐ ASA   ☐ Clopidogrel   ☐ Ticagrelor   ☐ Prasugrel

Beta-blocker   ☐ YES, name: _____   ☐ NO

ACE Inhibitor   ☐ YES, name: _____   ☐ NO

ARB   ☐ YES, name: _____   ☐ NO

MRA   ☐ YES, name: _____   ☐ NO

Diuretic   ☐ YES, name: _____   ☐ NO

Statin   ☐ YES, name: _____   ☐ NO

Other medications   ☐ Hydralazine   ☐ Nitrates (i.e. isosorbide dinitrate,
        ☐ Sacubitril/valsartan   isosorbide mononitrate, nitro patch)
        ☐ Ivrabradine   ☐ Others: _____

*Please contact Chris Cheung (email: ccheung@alumni.ubc.ca, phone: 604-715-8173, pager: 604-707-3086)
or Dr. Jason Andrade (jason.andrade@vch.ca) with questions surrounding enrollment or eligibility.

APPENDIX 2. Follow-up Case Report Form.

Study Site _____ Study ID _____

(VGH = 1; SPH = 2)

Date of Follow-up _____ Which period? ☐ 3-month ☐ 1-year

(YYYY-MM)

Alive at Follow-up ☐ YES ☐ NO, cause of death: _____

date of death: _____

(YYYY-MM)

Signature of Person Completing CRF _____ Date: _____

ANTIPLATELET/ANTICOAGULANT PRESCRIPTION

Antiplatelet ☐ ASA ☐ Clopidogrel ☐ Ticagrelor ☐ Prasugrel

Anticoagulant ☐ YES, name: _____ ☐ NO

dose: _____

CLINICAL OUTCOMES (since enrollment or last follow-up)

Myocardial Infarction ☐ YES ☐ NO

    With PCI ☐ YES ☐ NO

    Date of Last MI/PCI: _____

(YYYY-MM)

    With CABG ☐ YES ☐ NO

    Date of CABG: _____

(YYYY-MM)

Stroke/CVA ☐ YES ☐ NO

    If so, what type? ☐ Ischemic ☐ Hemorrhagic ☐ TIA ☐ Other

    Date of Stroke/CVA: _____

(YYYY-MM)

Atrial Fibrillation (patient reported) ☐ YES ☐ NO

    Symptomatic? ☐ YES ☐ NO

    If symptomatic, number of episodes: _____

Cardiac Arrest ☐ YES ☐ NO

    Date of cardiac arrest: _____

(YYYY-MM)

Re-hospitalization (since discharge ☐ YES ☐ NO
or last-follow-up)

    Reason for re-hospitalization ☐ Stroke ☐ MI ☐ Heart Failure

    ☐ Other: _____

    Date of re-hospitalization: _____

(YYYY-MM)

Emergency Room Visits (without hospitalization, since discharge or last follow-up)

        ☐ YES   ☐ NO

        Reason for ER Visit   ☐ Cardiac (i.e. chest pain, shortness of breath, palpitations)

                ☐ Other: _____

INVESTIGATIONS (since discharge or last follow-up)
ECHOCARDIOGRAM

Echo since discharge/last follow-up? ☐ YES   ☐ NO

        Date of Last Echo   _____

                    (YYYY-MM)

LV ejection fraction: _____ %

        Change in LV function: ☐ Increase   ☐ Decrease

PATIENT SATISFACTION
(Complete at 3 month follow-up if patient received the intensive monitoring strategy)

Did the patient complete full duration of monitoring (30 days)?

        ☐ YES   ☐ NO

        If not, how many days?   _____

Please rate the comfort of wearing the SpiderFlash device (score from 1-10, 10 is very comfortable)

        Rating (1 to 10)   _____

        If not comfortable why not?   _____

Did the patient have any difficulty using the device?

        ☐ YES   ☐ NO

        What difficulties?   _____

Does the patient prefer intensive monitoring over no monitoring?

        ☐ Prefers intensive monitoring   ☐ Prefers less monitoring

        Why or why not?   _____

Did the patient feel satisfied with the care they received as part of the study?

Please rate your satisfaction (score from 1-10, 10 is very satisfied).

        Rating (1 to 10)   _____

        If not satisfied, why not?   _____

APPENDIX 3. STUDY CONSENT FORM.

Participant Information and Consent Form

Vancouver
CoastalHealth
Promoting wellness. Ensuring care.

Protocol Title:	Does Intensive Monitoring Improve Diagnosis and Treatment of Atrial Fibrillation after Myocardial Infarction **(SIMPL-AF)**
Principal Investigator:	Dr. Jason G Andrade
Co-investigators:	Doctors: Christopher C. Cheung, Kenneth G. Gin, Andrew D. Krahn, Marc W. Deyell. Research Managers: Jackie Chow and Andrew Starovoytov. Operations Manager: Faisal Aziz. All investigators are members of the Vancouver Hospital Division of Cardiology and the Department of Medicine of the University of British Columbia (UBC).
Funding:	This project is supported by the Canadian Cardiovascular Society-Bayer Resident Vascular Research Award and the UBC Division of Cardiology.

Invitation and background

You are being invited to consider participating in this research study because you had a myocardial infarction (heart attack) and being discharged home. Patients that suffer a heart attack are at higher risk for developing a cardiac arrhythmia (irregular heart beats) after leaving hospital. An area of the heart damaged during a heart attack may create abnormal electric currents making heart work very fast or slow. These arrhythmias can lead to palpitations (feeling of heart racing), fainting, and some could be life threating. Because of the arrhythmias, patients in the hospital wear cardiac monitors and are observed for at least 2 days.

Although all patients will receive cardiac monitoring during their hospital stay, cardiac monitoring is currently not available once patients are discharged home. Without monitoring at home, patients may develop an arrhythmia that is not detected or unrecorded. Since the arrhythmia may only happen from time-to-time, they may not be detected by periodic monitoring or appointments with the family doctor or cardiologist.

Atrial fibrillation (irregular beats from the upper chamber of the heart) is the most common type of arrhythmia after a heart attack. Atrial fibrillation can lead to a sensation of palpitations, and over the long term, can also increase the risk of suffering a stroke. Individuals that develop atrial fibrillation may benefit from the initiation of a blood thinner (anticoagulant) to reduce the risk of stroke.

In this research study, individuals will be randomly assigned to receive an additional 30-day continuous monitor or standard medical care. Half of participants will be randomly assigned to use the 30-day continuous monitor to detect for cardiac arrhythmias once you have been discharged from hospital. The monitoring results will be shared with your primary cardiologist and family physician, and you will also have access to the information after collection is completed. The information will tell us more about what happens to your heart rhythm after going home, and whether you have any cardiac arrhythmias, including atrial fibrillation. We are planning enroll 264 subjects at Vancouver General hospital.

Your participation is voluntary

It is a basic requirement of clinical research that a person who participates in the study of a new medical condition or treatment gives his or her informed consent to such participation. This

consent must be based on an understanding of the procedures and risks involved. Please take your time in making your decision. If you decide to participate you will be asked to sign the last page of this form. You may choose not to participate, or you may withdraw from participation in the study at any time after you are enrolled without providing any reason. In either case, your standard medical care will not be affected by this decision

Who is conducting the study
This study is conducted by Dr. Jason Andrade and a group of cardiologists under the University of British Columbia (UBC). This project is supported by the Canadian Cardiovascular Society-Bayer Resident Vascular Research Award and the UBC Division of Cardiology.

Who can participate in this study
Your medical history will be reviewed to determine that you meet all the criteria to participate in this study. The study doctor or staff will discuss them with you. You can participate if you:
- Are 18 years or older;
- Had a heart attack during this hospital admission;
- Have no history of atrial fibrillation in the past;
- Are not taking anticoagulants (type of blood thinner medication) for another reason

You should not participate if you:
- Have chronic skin disorder on your upper torso;
- Are allergic to medical tape or glue;
- Received cardiac surgery (bypass surgery) during this hospitalization or have planned cardiac surgery within next 3 months;
- Had an atypical heart attack or disorder (called "spontaneous coronary artery dissection", "non-atherosclerotic coronary disease" or "Takotsubo cardiomyopathy");
- Are unable to take anticoagulation (type of blood thinner medication) for any reason

What does the study involve?
If you agree to participate in the study we will ask you sign this consent form before you leave the hospital. You will be randomized (like flipping a coin) and assigned to be in one of two groups: the standard of care group (without extra monitoring) or monitored group.

Subjects in the monitored group prior to leaving hospital will be trained how to apply and use the SpiderFlash 30-day monitoring device. SpiderFlash is small medical device with three electrodes (wires) attached to your skin with special stickers. We ask that you disconnect the device and wires during showering, bathing, and swimming. You will be provided with extra stickers to reconnect the device, if any leads fall off. This device will begin recording your heart electrical activity (ECG or electrocardiogram) immediately and will continue for the next 30-days.

If you are randomly assigned to receive the SpiderFlash device, you will receive training on wearing the device for the first time. This training will take between 30-60 minutes and will occur during your hospital stay. At home, routine changing of the leads is anticipated to take 5-10 minutes per day.

After 30 days we will see you in our research clinic for a follow-up visit and ask you to return the device. Your monitoring device will be analyzed and reviewed by the study investigators, and all results will be forwarded to your primary cardiologist and family physician. You will be asked about your current symptoms and any new health issues or hospital visits. We will also collect names of you current cardiac medications. This visit will take approximately 40 minutes of your time.

At 3 months and 1 year after your discharge your will be contacted on the phone to review your current symptoms, new health problems and review your cardiac medications. This phone interview will take 15 minutes. At this time, your health records will also be reviewed for prescription information, electrocardiograms, new health issues, and hospital visits. You will have

to dedicate about a total of 2 hours beyond that required for standard treatment (not including travel time) to complete the study.

What if the monitor detects an arrhythmia?
If you are randomly assigned to receive the 30-day monitor, the monitoring results will be forwarded to your primary cardiologist and family physician. If atrial fibrillation is detected, your primary cardiologist and family physician will have this information and treat you accordingly. Although patients with atrial fibrillation may benefit from taking a blood thinner (anticoagulant) to prevent stroke, this should only be started if it is consider safe in your circumstance. Thus, these medications will not be started as part of the research protocol- the final decision will be made by your primary cardiologist or family physician. If the 30-day monitor detects any other arrhythmias, your primary cardiologist and family physician will also have this information and treat you accordingly.

What are the possible harms and discomforts?
Potential risks associated with participation in this study are discomfort, redness or irritation under the electrodes when using the SpiderFlash device. We will simply ask you to disconnect the device if it causes you significant skin discomfort.

What are the potential benefits of participating?
You may not have any direct benefits from this study. You may experience better care from specialists, however, this is not guaranteed. You may be contributing to the medical knowledge about your heart condition. Information regarding any important changes discovered with your monitoring device will be forwarded to your doctors.

What if new information becomes available that may affect my decision to participate?
You will also be advised of any new information that becomes available that may affect your willingness to remain in this study.

What are the alternatives to participating?
If you chose not to participate in the study and develop symptoms of irregular heart-beat your doctor might give you a similar type of a monitoring device called Holter monitor. There will be no disadvantages should you decide not to participate in this study.

What happens if I decide to withdraw my consent to participate?
Participation in this study is voluntary. If you decide not to participate, this will not affect your medical care. You may discontinue participation in the study at any time without penalty or loss of benefits to which you are otherwise entitled. The Investigator will retain any data collected up to the point of a subject's withdrawal from the study such that the data itself cannot be withdrawn. In no way does signing this form waive your legal rights, nor relieve the investigator or involved institutions from their legal and professional responsibilities.

How will my taking part in this study be kept confidential?
Your confidentiality will be respected. However, research records and health or other source records identifying you will be inspected in the presence of the Investigator, or his or her designate, by representatives of the UBC Clinical Research Ethics Board for the purpose of monitoring the research. By signing this form you are authorizing such access to your medical records. No information or records that disclose your identity will be published without your consent, nor will any information or records that disclose your identity be removed or released without your consent unless required by law.

You will be assigned a unique study number as a participant in this study. This number will not include any personal information that could identify you (e.g., it will not include your Personal Health Number, SIN, or your initials, etc.). Only this number will be used on any research-related information collected about you during the course of this study, so that your identity will be kept confidential. Information that contains your identity will remain only with the Principal Investigator

and/or designate. The list that matches your name to the unique study number that is used on your research-related information will not be removed or released without your consent unless required by law.

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to insure that your privacy is respected. You also have the legal right of access to the information about you that has been provided to the sponsor and, if needed, an opportunity to correct any errors in this information. Further details about these laws are available on request to your study doctor

What happens if something goes wrong?
Since no experimental treatment will be used in this research study, we do not anticipate any side effects as a result of participating in this study. By signing this form, you do not give up any of your legal rights and you do not release the study doctor, participating institutions, or anyone else from their legal and professional duties. If you become ill or physically injured as a result of participation in this study, medical treatment will be provided at no additional cost to you. The costs of your medical treatment will be paid by your provincial medical plan.

What will the study cost me?
All research-related tests that you will receive during your participation in this study will be provided at no cost to you. You will not be paid for your participation in the study.

Who do I contact if I have questions about the study during my participation?
If you have any questions or desire further information about this study before or during participation, you can contact Dr. Jason Andrade at (604) 875-5069.

Who do I contact if I have any questions or concerns about my rights as a participant?
If you have any concerns or complaints about your rights as a research participant and/or your experiences while participating in this study, contact the Research Participant Complaint Line in the University of British Columbia Office of Research Ethics by e-mail at RSIL@ors.ubc.ca or by phone at 604-822-8598 (Toll Free: 1-877-822-8598).

After the study is finished
The study results will be compiled and reported in a medical journal. A description of this clinical trial will be available on http://www.ClinicalTrials.gov. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Does Intensive Monitoring Improve Diagnosis and Treatment of Atrial Fibrillation after Myocardial Infarction (SIMPL-AF) **Participant Consent**

My signature on this consent form means:
- I have read and understood the information in this consent form.
- I have had enough time to think about the information provided.
- I have been able to ask for advice if needed.
- I have been able to ask questions and have had satisfactory responses to my questions.
- I understand that all of the information collected will be kept confidential and that the results will only be used for scientific purposes.
- I understand that my participation in this study is voluntary.
- I understand that I am completely free at any time to refuse to participate or to withdraw from this study at any time, and that this will not change the quality of care that I receive.
- I authorize access to my health records as described in this consent form.
- I understand that I am not waiving any of my legal rights as a result of signing this consent
- I understand that there is no guarantee that this study will provide any benefits to me.

I consent to participate in this study

_____   _____   _____
Name of Participant: Signature: Date

I have explained the purpose of this research, the study procedures, identifying those that are investigational, the possible risks and discomforts, as well as the potential benefits and have answered any questions regarding the study. The subject meets all inclusion and exclusion criteria for the study and freely agrees to participate.

_____   _____   _____   _____
Person Obtaining Consent: Signature   Study role   Date

_____   _____   _____
Principal Investigator or   Signature: Date
designated representative

Was the participant assisted during the consent process in one of ways listed below? ☐ Yes ☐ No
☐ The consent form was read to the participant, and the person signing below attests that the study was accurately explained to, and apparently understood by, the participant.
☐ The person signing below acted as an interpreter/translator for the participant, during the consent process (please check if an interpreter/translator assisted during the consent process).
☐ If this consent process has been done in a language other than that on this written form, with the assistance of an interpreter/translator, indicate language: _____

_____   _____   _____
Signature of Person Assisting   Signature: Date
in the Consent Discussion

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