Compression Wraps as adjuvant therapy in the management of acute systolic heart failure (CATAS-HF trial)

8/1/2020

- Study Protocol & Statistical Analysis Plan

NCT# NCT04095416

STUDY TITLE: Compression wraps as adjuvant therapy in the management of acute systolic heart failure (CATAS-HF)

● STUDY AIM, BACKGROUND, AND DESIGN ABSTRACT

Our goal is to measure the application of lower extremity compression wrapping as adjuvant therapy to diuresis in the management of patients hospitalized for acute systolic heart failure. Use of compression wrapping will be assessed through randomized parallel intervention clinical trial of patients admitted to Henry Ford Hospital I5 Cardiology service for management of acute systolic heart failure presenting with lower extremity edema. Enrolled patients will be managed with standard medical therapy, with (intervention) or without (control) the adjuvant use of lower extremity compression wrapping. Efficacy of the intervention will be analyzed for the following primary endpoints: 1) Percentage difference in weight before and after diuresis 2) Percent difference in Brain natriuretic peptide (BNP) from admission to discharge; 3) Difference in length of admission in days . Our hypothesis is adjuvant use of lower extremity compression wraps to standard medical therapy increases percentage of weight reduction achieved with diuresis, increases percent reduction in BNP after diuresis, and decreases total length of stay for patients hospitalized with acute systolic heart failure.

Lower extremity compression wraps are a low cost inpatient intervention when managing fluid overload in patients hospitalized for acute systolic heart failure, and presenting with lower extremity edema. Also, compression stockings are mainstay devices in the outpatient setting for improving symptoms of lower extremity edema in chronic systolic heart failure. However, the utility of compression wraps in managing patients hospitalized for acute systolic heart failure, and transitioning to the use of compression stockings for symptom management upon discharge, has not been thoroughly assessed. Current practice suggests use of lower extremity compression wraps can facilitate intravenous diuresis while inpatient, achieve more optimal discharge dry weight, and lower BNP levels prior to discharge. Demonstrating efficacy of such a low-cost, low-risk intervention in decreasing hospital stay and achieving more favorable patient outcomes will have considerable impact on standard practice.

● SUBJECT POPULATION AND ELIGIBILITY

Inclusion criteria: patients age greater than 18 and less than 85 years of age, admitted to I5 with Acute Systolic Heart Failure, and an ejection fraction of less than 50% as determined by echocardiogram within 6 months, requiring inpatient management with intravenous diuretic therapy. Must have a diagnosis of acute systolic heart failure (by ICD coding) on admission, of any underlying etiology. Must have documentation of pitting edema on primary assessment.

Exclusion criteria: patients who do not meet inclusion criteria, who cannot tolerate IV diuresis, who cannot wear or tolerate lower extremity compression stockings or wraps; active diagnosis of ESRD on dialysis or peripheral neuropathy; ejection fraction greater than 50% as evaluated by echocardiogram within 6 months.

Control population: Patients meeting inclusion criteria, managed on I5 for acute systolic heart failure with standard medical therapy without the use of lower extremity compression wraps.

This will allow direct comparison of the effect of intervention (lower extremity compression wraps) on the previously listed endpoints on the same patient population.
Since this study evaluates an already established component of standard medical practice, there will be no discrimination of patient populations in enrollment outside of the inclusion and exclusion criteria.
Patients will be enrolled exclusively based on inclusion and exclusion criteria, undergoing randomization into intervention or control groups. No screening tools will be used.

● STUDY PROCEDURES

The study will be an internally funded, parallel-intervention clinical trial studying the use of lower extremity compression stockings as adjuvant therapy to standard medical care in management of patients admitted for acute systolic heart failure. There will be two arms, intervention and control. 120 patients will be enrolled in the study, 60 to each arm, to achieve power above 80% with an alpha of 0.05, measuring continuous primary endpoints of average percent reduction in weight after diuresis, average change in BNP from admission to discharge, and average length of admission in days.
Data will be collected by Henry Ford personnel, for 120 patients previously admitted after January 2018 and managed on the HF Main cardiology I5 floor meeting inclusion criteria and managed with standard medical therapy without the use of compression stockings, and will undergo review by research team for enrollment into the control group. If additional patients are needed to achieve enrollment number of 60 control subjects, patients will be enrolled and randomized prospectively by the research team. Data collected retrospectively will be performed through Epic health medical record and charted on Excel spreadsheet, and will include admission length of stay, daily weights, daily urine outputs, daily diuretic dose and type(s) used, admission BNP, and discharge BNP. Research team will also perform chart review on enrolled patients to evaluate for 30-day readmission rate.
The intervention arm will include patients enrolled and randomized by the research team meeting inclusion criteria, and managed on HF Main cardiology I5 floor. This population will receive bilateral lower extremity compression wraps (ACE bandages) on day 1 of admission in addition to standard medical therapy. Data will be collected by the research team through Epic health medical record and will be charged on Excel spreadsheet, and will include admission length of stay, daily weights, daily urine outputs, daily diuretic dose and type(s) used, admission BNP, and discharge BNP. These charts will also undergo review by research team to evaluate for 30-day readmission rate.
Co-investigators will be responsible for retrospective and prospective data review for control population. Both co-investigators and sub-investigators will be responsible for enrolling patients in the study and collecting above mentioned data points. Nursing staff on the floor will undergo teaching on application of ACE compression wraps, and will be responsible for capturing physician order for wrap application and executing order, which will mark the beginning of the trial enrollment.
Data analysis will be conducted through the Division of Biostatistics and Research Epidemiology and will include descriptive statistics and univariate comparisons between treatment groups. T-test and ANOVA with post-hoc analysis will be used to evaluate for difference in the means of each endpoint previously listed for each treatment group. Patient information will be de-

identified prior to data analysis. Data for enrolled patients will be saved on secure Henry Ford Health System servers on Microsoft OneDrive cloud servers and shared among research team. Identifiers will include MRNs to access patient charts, collect and verify data, and perform review for 30-day readmission rates. Data will be stored for the entirety of the study, and promptly discarded in accordance with HFHS regulation at the completion of the study tentatively scheduled for January 2021. Data collected on patients excluded from the study will be discarded at the time of exclusion in accordance with HFHS regulation. Missing or incomplete data will prompt withdrawal of particular patient from study, and will factor into final data analysis as an intention to treat value.
Total time of subject enrollment in the study: duration of hospital stay. No additional visits or follow-up testing is required.
Literacy and language barrier concerns will be handled on a case-by-case basis, primarily using standard communication methods of translator services.

● **ANTICIPATED RISKS**

There are no significant anticipated risk beyond standard of care risk in management of patients with acute systolic heart failure. Intervention includes an already established therapy on patients with lower extremity edema. We are simply testing the formal efficacy of this intervention in an interventional study.

● **ANTICIPATED BENEFITS**

Anticipated benefits include: decreased length of stay, decreased amount of diuretic used, increased percentage of weight achieved through diuresis; greater percent of BNP reduction; decreased 30-day readmission rate.

● **RENUMERATION/COMPENSATION**

No compensation offered

● **COSTS**

There is no additional cost anticipated for this study outside of standard medical management of acute systolic heart failure and any additional medical conditions treated during the hospital admission.

● **ALTERNATIVES**

Intervention does not involve offering an established efficacious therapy to patients, and conversely control group is not being withheld from any known therapy that affects morbidity/mortality. No known alternatives.

● **CONSENT PROCESS AND DOCUMENTATION**

Co-investigators and sub-investigators enrolling patients will be responsible for obtaining consent from patients prior to enrollment. This will involve presentation of consent document with description of study. Patients will have the opportunity to privately ask questions and receive answers at the time of enrollment after the study is described to them in detail, including risks and benefits. There will be no duress or undue influence, as intervention is already a standard of medical practice. Patients will have the opportunity to refuse intervention. Patients will not be enrolled if they have diminished capacity or learning disability, or impairment of any kind. If patient is non-English speaking, consent form will be translated using standard translator services (in person translator, translator phone). Consent documentation will be stored on the Henry Ford secured OneDrive Microsoft cloud server. This information will only be accessible by research team. Information will be stored for the entirety of the study, and promptly discarded in accordance with HFHS regulation at the completion of the study tentatively scheduled for January 2020. Information collected on patients excluded from the study will be discarded at the time of exclusion in accordance with HFHS regulation.

● WITHDRAWAL OF SUBJECTS

Patients withdrawn from study will be notified, and information gathered from enrollment period will be analyzed as intention to treat. All information will be destroyed appropriately at the time of withdrawal.

● PRIVACY AND CONFIDENTIALITY

Patient information will be stored without identifiers. Access to patient chart will be provided to healthcare providers caring for patients during hospitalization, as well as co-investigators and PI of the study. Research team will then use a master key to remove identifiers. Data will be collected and pooled using this master key, and stored on secured HF servers under password protection for use by research team exclusively.

Important HIPAA Concerns

If you will be using, disclosing or accessing the health record (medical record, mental health or substance abuse records, etc) for research purposes, then HIPAA applies. If you are accessing medical records or PHI for screening purposes, HIPAA regulations apply and investigators will need to obtain prospective HIPAA authorization or apply for a waiver of HIPAA authorization for the screening activities, as applicable, depending on the nature of the study.

If accessing PHI for screening purposes and providing written authorization, describe how authorization will be obtained for the screening portion, who will obtain it or request and justification for a request for HIPAA waiver for recruitment purposes. If you are requesting waiver of HIPAA for screening purposes, describe the confidentiality procedures that will be used.

For more information on HIPAA authorization guidance, visit: https://www.hhs.gov/hipaa/for-professionals/privacy/guidance/research/index.html

NOTE: You may also need to obtain a waiver of documentation of informed consent (ie, signed consent) for screening purposes if you do not meet the requirements for waiving consent provided in the Consent Process section.

● DATA AND SAFETY MONITORING PLAN

PI and co-investigators will be directly involved in the enrollment of each subject. The intervention is low-risk and already a component of standard medical care. Nurses and sub-investigators will be allowed to care for enrolled patients under standard medical care. Each patient will be assessed at the start of enrollment, and at the end of hospitalization for compliance with standard medical care, as is the practice of all patients at Henry Ford Hospital. All adverse events and harm/near miss/sentinel events will be reported immediately to IRB. No such events are anticipated.

● QUALIFICATIONS OF THE INVESTIGATOR(S)

Principal Investigator, Cori Russell, MD is an ABMS certified physician in Cardiovascular Medicine, and Internal Medicine.
Joseph Miller, MD is an ABMS certified physician in Emergency Medicine and Internal Medicine
Tarek Makki MD is a current fellow in Cardiovascular Medicine and ABMS certified physician in Internal Medicine
Co-investigators Raef Fadel and Carina Dagher are residents of Henry Ford Hospital.
Sub-investigators are residents, nursing staff, and medical students of Henry Ford Hospital.

● REFERENCES

Be sure that any sources cited in the Study Aim, Background and Design section are included in your bibliography. Conversely, make sure that you have included references in this section that support your hypothesis or research purpose.