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Point of care with serial NT-proBNP measurement in patients with acute decompensated heart failure as a therapy-monitoring during hospitalization (POC–HF): Study protocol of a prospective, unblinded, randomized, controlled pilot trial

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ABSTRACT

Despite important advances in diagnosis and medical therapy of heart failure (HF), disease monitoring and therapy guidance remains to be based on clinical signs and symptoms. NT-proBNP was repeatedly demonstrated to be a strong and independent predictor of morbidity and mortality in patients with HF. Only few – and conflicting – data are available on the efficacy of serial measurement of NT-proBNP as a tool for treatment monitoring in HF. These data are limited to the outpatient setting. Currently, no data are available on the effects of this approach in patients hospitalized for acute decompensated HF. The goal of this study is to explore whether the availability of serial NT-proBNP measurements may influence treatment decisions in patients with acute decompensated HF, and whether this leads to more rapid dose adjustments of prognostically beneficial medical therapies and earlier hospital discharge. In the intervention group, serial measurements of NT-proBNP every second business day are performed and made available to the treating physician, while no serial measurements are available in control group. HF therapy is left at the discretion of the treating physician. The primary endpoints are defined as the effects of monitoring NT-proBNP on medical HF therapy decisions, including type and dosing of medical therapies and the rapidity of adjustments, length of hospital stay, and evaluation of the changes in NT-proBNP values. Additional secondary endpoints include incidence of electrolyte imbalances and renal failure, changes in NYHA functional class, vital signs, body weight, quality of life, incidence of adverse events, transfer to Intensive Care Units, and mortality.

1. Introduction

Increased wall stress on the cardiac atrium and ventricle are pathophysiological hallmarks of heart failure (HF). Increased wall stress and myocyte stretching induce the synthesis of the preprohormone of B-type natriuretic peptide (BNP). BNP is secreted from cardiomyocytes as a prohormone (proBNP). In circulation, proBNP is further processed by proNP convertases to inactive NT-proBNP and active BNP [1]. Physiological effects of BNP include diuresis, natriuresis, vasodilation, and antagonism of the renin–angiotensin-aldosterone system (RAAS) and the sympathetic nervous system, thus playing a critical role in the maintenance of cardiovascular homeostasis, and may also have the actions of anti-hypertrophy, anti-fibrosis and anti-inflammation in the myocardium [2–5].

Together with typical signs and symptoms of HF such as dyspnea, reduced exercise tolerance, fatigue, peripheral edema, elevated jugular

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venous pressure, lung congestion, cardiomegaly in chest x-ray, ECG and echocardiographic changes such as left ventricular hypertrophy and/or dilation, increased natriuretic peptides (NP; e.g. BNP > 100 pg/ml/NT-proBNP > 300 pg/ml) can be used as diagnostic tools in patients with suspected acutely decompensated HF [6,7]. Increased NPs are not only diagnostic for HF but are also associated with increased mortality and morbidity, e.g. with NT-proBNP values greater than 986 pg/mL predicting death at 1 year [8,9]. Moreover, a decrease in these peptides appears to be a beneficial prognostic factor of outcome in HF, particularly in patients admitted for acute decompensated HF [10]. However, it is important to note that increased NPs should always be interpreted in connection with clinical signs and symptoms, as well as other laboratory parameters, since increased NP may be found in diseases other than HF such as renal dysfunction, anemia, stroke, or pulmonary diseases [9].

Optimal medical HF therapy consists of diuretics, nitrates and/or digoxin for symptomatic improvement together with inhibitors of the RAAS, i.e. angiotensin converting enzyme inhibitors, angiotensin receptor blockers (ARB), mineralocorticoid receptor antagonists, and beta-blockers (BBL) as prognostically beneficial therapies [6]. Recently, the neprilysin inhibitor sacubitril in combination with an ARB was successfully introduced as a novel prognostically beneficial therapy in HF with reduced ejection fraction [11]. Beneficial therapies of heart failure are associated with a decrease in BNP, but patients are often treated with a lower dose than recommended [12].

HF continues to represent a large and increasing burden to national and international healthcare systems affecting several millions of patients in Europe alone [13–16]. Despite the important advances in the medical therapy of HF, therapy monitoring is still based on signs and symptoms of this syndrome. Several trials have investigated the value of serial measurement of NPs for disease and therapy monitoring of HF in the outpatient setting, demonstrating mixed results [17–26]. Though NT-proBNP was repeatedly demonstrated to be a strong and independent predictor of morbidity and mortality in patients with HF and a decrease in NT-proBNP during hospitalization for acute decompensated HF represents a beneficial prognostic factor, no data are available on the effects of repetitive NT-proBNP measurements in patients hospitalized for acute decompensated HF [6,12]. However, it is conceivable that such measurements may trigger a faster dose- and/or medication-increase in patients with HF, in particular when complemented by safety parameters such as electrolytes and creatinine.

Therefore, the goal of the POC-HF study is to investigate whether the availability of serial NT-proBNP measurements influences treatment decisions in hospitalized patients with acute decompensated HF, and whether this leads to more rapid dose adjustments of prognostically beneficial therapies and earlier hospital discharge.

2. Material and methods

POC-HF is an ongoing prospective, unblinded, single center, 2-arm randomized controlled pilot trial. It is performed at the Cantonal Hospital Baselland, Liestal, as single-center study and will include at least 50 patients hospitalized for acute decompensated HF. Patients are randomized to either the intervention arm (POC available group) investigating the effect of serial NT-proBNP measurements in addition to receiving care as usual, or to the control arm receiving only care as usual (Control group).

The study was approved by the Ethical Committee (EC) of Northwestern and Central Switzerland (Ethikkommission Nordwest-und Zentralschweiz, EKNZ) and is registered at www.swissethics.ch (BASEC-ID 2017–01030).

2.1. Study design

The study design is depicted in Fig. 1 with each element detailed in the following sections.

2.2. Study endpoints

The primary endpoint of this study is defined as the effects of monitoring NT-proBNP on medical HF therapy decisions, including type and dosing of medical therapies and the rapidity of adjustments, length of hospital stay, and evaluation of the changes in NT-proBNP values.

Secondary endpoints are defined as the incidence of electrolyte imbalances and renal failure, changes in NYHA functional class, vital signs, body weight, quality of life, incidence of adverse events, transfer to Intensive Care Units, and mortality.

2.3. Eligibility

Eligibility criteria are aimed at ensuring participant safety and balancing internal validity with real world applicability (see Table 1).

2.4. Screening and recruitment

The members of the study team screen the files of all newly admitted patients for eligibility on a daily basis. All patients admitted with acute decompensated HF to the University Department of Medicine of the Cantonal Hospital Baselland, Liestal, and hospitalized on one of two predefined general medical wards are eligible for inclusion into the study. Patients fulfilling all inclusion criteria in the absence of all exclusion criteria (see Table 1) are provided with further detailed information on the study as well as with the informed consent form. Patients are given sufficient time for their decision and it is clearly communicated that participation in the study is voluntary and that in case of refusal to participate, treatment will in any case be according to current guidelines throughout the entire hospitalization. Patients with acute decompensated HF requiring immediate intensive care are not eligible for inclusion into the study and are not included.

2.5. Randomization

After having obtained informed consent, patients are randomized in a 1:1 ratio to either the intervention or the control group. Randomization is performed using closed envelopes containing a paper sheet with either the letter A or B. The letter A stands for the control group and the letter B for the intervention group. These envelopes are mixed initially, numbered for order purposes and the order is maintained throughout the study. The name of the patient will be written down on the envelope. Then it will be opened and the patient will be allocated to the study group according to the letter in the envelope.

2.6. Study procedures

All patients undergo an inclusion and a discharge visit. General demographic data, including age, gender, nationality, smoking status, alcohol consumption, current profession, exercise behavior, allergies, medication, HF history and comorbidities are recorded. Assessment of vital signs and body weight are performed together with an ECG, laboratory tests (NT-proBNP, potassium, sodium and creatinine). QoL is assessed using the SF-12, KCCQ, and MLWHFQ questionnaires [27–29]. Women who are potentially able to get pregnant have to undergo a pregnancy test prior to inclusion into the study to rule out pregnancy.

Patients allocated to the intervention group (POC-available group) undergo serial measurements of NT-proBNP every second business day. To account for changes in electrolyte concentrations and renal function frequently seen with HF therapies, potassium, sodium, and creatinine

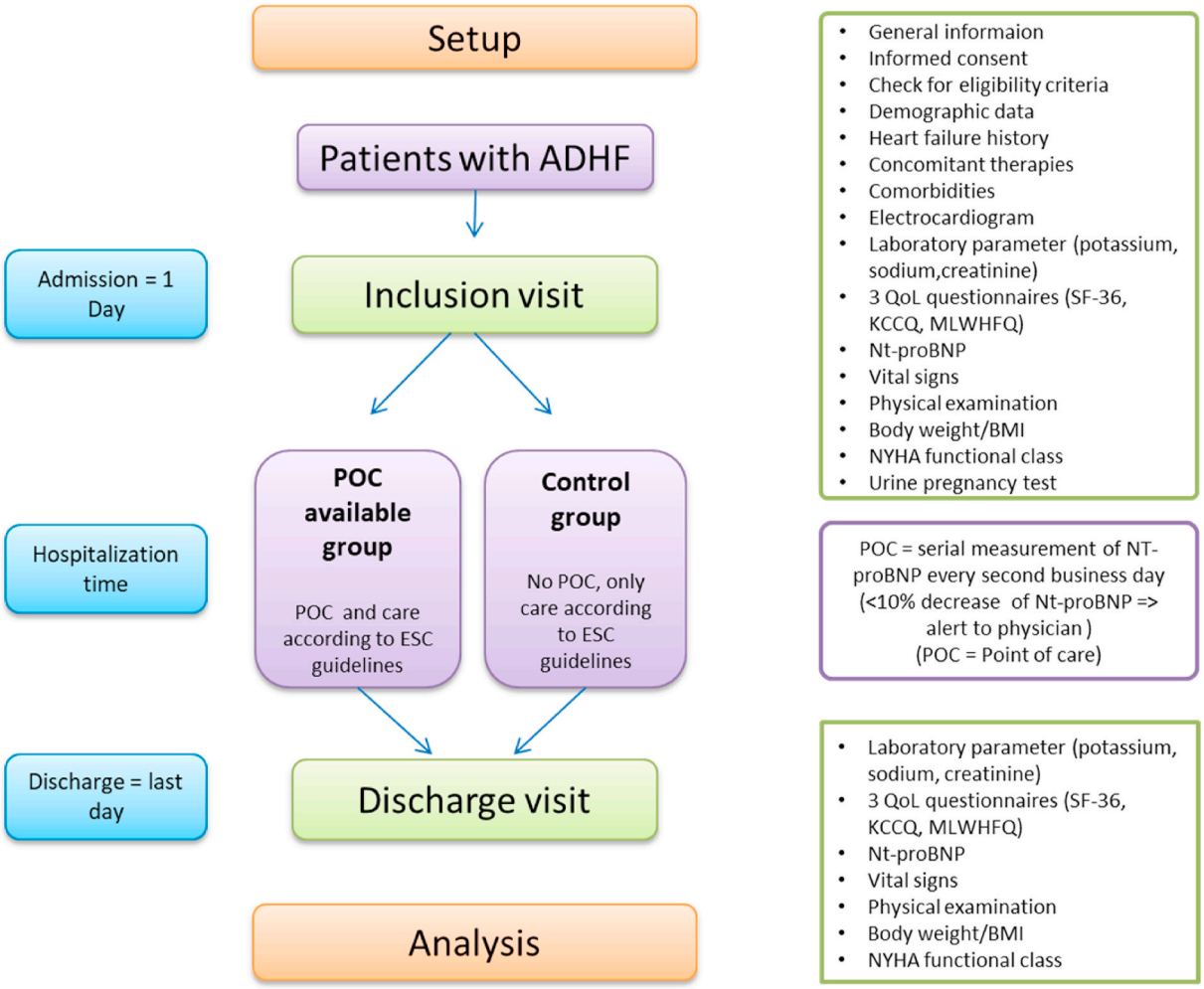

Fig. 1. ADHF = Acute decompensated heart failure; ESC = European Society of Cardiology; KCCQ = Kansas City Cardiomyopathy Questionnaire; MLWHFQ = Minnesota Living With Heart Failure Questionnaire; NT-proBNP = N-terminal pro-hormone B-type Natriuretic Peptide; NYHA = New York Heart Association; POC = Point of Care; SF-36 = Short Form (36) Health Survey.

are measured at the same time points. This interval was chosen to account for the slow changes observed for creatinine. At each blood sampling, 10 ml of blood is collected in a standard lithium-filled blood collection tube followed by immediate analysis of NT-proBNP, sodium, potassium, and creatinine using the following point-of-care laboratory devices:

Cobas 232 POC system [30].
FUJI DRI-CHEM NX500 FV [31].

Test results are provided directly to the responsible physician via e-mail. The physician is alerted by a phone call of a study member if the NT-proBNP has not decreased by 10% or more between two measurements. Diagnostic and therapeutic decisions are at the discretion of the responsible physician and based on the 2016 ESC guidelines on the diagnosis and therapy of HF as established at the Cantonal Hospital Baselland, Liestal [6]. No specific recommendations with regards to therapy are provided by the study team.

Patients allocated to the control group will undergo the same measurements at inclusion and discharge visit. Since no serial NT-proBNP measurements are performed in the control group, diagnostic and therapeutic decisions are guided by clinical signs and symptoms. However, as in the intervention group, diagnostic and therapeutic decisions in the control group are based on the current 2016 ESC guidelines on the diagnosis and therapy of HF as established at the Cantonal Hospital Baselland, Liestal [6].

The study-related procedures are summarized in Table 2. In order to minimize bias introduced by differences in executing and interpreting technical exams, all study related measurements and procedures are performed in a centralized manner at the Cantonal Hospital Baselland, Liestal.

2.7. Primary and secondary endpoints

As outlined above, the primary endpoints include the effects of monitoring NT-proBNP on medical HF therapy decisions, including type and dosing of medical therapies and the rapidity of adjustments, length of hospital stay, and evaluation of the changes in NT-proBNP values.

Secondary endpoints include the incidence of electrolyte imbalances and renal failure, changes in NYHA functional class, vital signs, body weight, quality of life, incidence of adverse events, transfer to Intensive Care Units, and mortality.

2.8. Patient safety

We expect a low incidence of adverse events (AE) and serious adverse events (SAE), as the study procedures are safe and performed according to protocols established at the Cantonal Hospital Baselland, Liestal. Moreover, functional status of patients will most likely improve

Table 1
Inclusion and exclusion criteria.

Inclusion Criteria	Exclusion Criteria
• Informed consent as documented by the patient's signature • Acute deterioration of signs and symptoms of chronic HF indicating acute decompensated heart failure (NYHA functional classes II-IV), such as: ◦ dyspnea ◦ paroxysmal nocturnal dyspnea ◦ reduced exercise tolerance ◦ fatigue ◦ peripheral edema (lower leg, ankle) ◦ elevated jugular venous pressure ◦ displacement of the apical impulse ◦ crackles ◦ wheezing (cardiac asthma) ◦ third/fourth heart sound • Lung congestion or cardiomegaly in chest X-ray • Signs of electrocardiographic and/or echocardiographic structural and/or functional abnormalities • NT-proBNP > 1000 pg/ml [9]	• age <18 years • women, who are pregnant or breast feeding • intention to become pregnant during the course of the study • lack of safe contraception, defined as: female participants of childbearing potential, not using and not willing to continue using a medically reliable method of contraception for the entire study duration, such as oral, injectable, or implantable contraceptives, or intrauterine contraceptive devices, or who are not using any other method considered sufficiently reliable by the investigator in individual cases (female participants who are surgically sterilized/hysterectomized or post-menopausal for longer than 2 years are not considered as being of child bearing potential) • known or suspected non-compliance, drug or alcohol abuse • inability to follow the procedures of the study, e.g. due to language problems, psychological disorders, dementia, etc. • participation in another intervention study within 30 days before and during the present study • enrolment of the investigators, their family members, and other persons involved in the study • unstable angina pectoris • uncontrolled brady- or tachyarrythmia • severe uncorrected valvular disease • acute myocardial infarction or acute coronary syndrome, transient ischemic attack or stroke within the last 3 months • clinical evidence of current malignancy with exception of basal cell or squamous cell carcinoma of the skin, and cervical intraepithelial neoplasia • currently receiving systemic chemotherapy and/or radiotherapy • COPD (chronic obstructive pulmonary disease) grades III-IV according to the GOLD (global initiative for chronic obstructive lung disease) classification • significant musculoskeletal disease limiting exercise tolerance • active infection • immunosuppressive medical therapy

during the course of the study. Nevertheless, in case of any AE during hospitalization, an immediate presentation of the participant to a physician is guaranteed. In the unlikely case of a SAE, the research project will be set on hold and the patient closely be followed until resolution or stabilization. Participants with on-going SAEs at the time of study termination will be further followed-up until recovery or stabilization of the disease.

2.9. Statistical analysis

2.9.1. Determination of sample size

POC-HF is a pilot and feasibility study. Since no previous studies have been performed addressing serial NT-proBNP measurements in an inpatient setting, a formal sample size calculation is not possible. According to our estimation based on the number of patients hospitalized for acute decompensated heart failure in previous years and taking into account that only patients hospitalized on the pre-defined trial wards are eligible for the study, we assumed that inclusion of around 50 patients into this study within the pre-planned time frame of one year for study completion may be realistic. Data from this study will allow the estimate of effect sizes and thus a sample size calculation.

2.9.2. Data processing

The full analysis set (FAS) will include all patients randomized to the trial, regardless of compliance. The per protocol set (PPS) will include all patients from the FAS, who have been discharged without previous withdrawal of informed consent or other reasons to be excluded from the study and who complied with their assigned study procedures (i.e. blood sampling, 80% compliance).

2.9.3. Datasets to be analyzed

Datasets to be analyzed will include the FAS as well as the PPS. The FAS will include all patients randomized to the trial, regardless of compliance. The PPS will include all patients from the FAS, who have been discharged without previous withdrawal of informed consent or other reasons to be excluded from the study and who complied with their assigned study procedures (i.e. blood sampling, at least 80% compliance). No subgroup analyses are planned.

2.9.4. Planned analysis

The primary analysis will be done on the FAS and based on the intention to treat (ITT) principle. Patient data will be analyzed according to the group to which they were assigned. Data will be presented as the mean ± standard deviation in case of normally distributed values, median and interquartile range in case of non-normally distributed values, or percentage in case of categorical variables at all time points. Both absolute and relative differences between groups and time-dependent absolute and relative changes will be calculated and presented.

Data of patients dropping out of the trial or not complying with treatment will be considered “censored”. The probability of censoring will be calculated based on baseline characteristics. Inverse probability of censoring weights will be used to weight patients with full data in the main analysis [32]. Thus, only patients from the FAS with complete data will be used in the model described below. Interest lies in significant differences between the treatment and the control group, which will be tested using Student's t-test and Chi2-tests where applicable. As a sensitivity analysis, the analysis above will be repeated on the PPS. No weighting will be performed here, as the data set excludes all censored patients. Missing NT-proBNP values will be imputed based on predicted values from a linear regression model including selected baseline variables [32,33].

Relative group and time effects on medication dosages will be analyzed using a non-parametric approach for the analysis of longitudinal data in a rank-based pattern. For this, the R package ‘nparLD’ will be used with a F1-LD-F1 experimental design, consisting of the whole-plot factor ‘group’ (intervention or control) and the sub-plot factor ‘time’ (n-th day of hospitalization) [34]. The relative marginal effects of group, time, and the interaction thereof will be analyzed by means of a classical Wald-type statistic (WTS) and an analysis of variance (ANOVA) type statistic, which is robust to outliers and accurately controls the type I error rate even for small sample sizes [35]. Repeated measures ANOVA will be used for the analysis of serial measurements. Therefore, the zero hypotheses will be no treatment effect, no time effect and no interaction between treatment effect and time.

Statistical analysis will be done using SPSS version 23 (International Business Machines Cooperation (IBM), Vulkanstrasse 106, 8010 Zürich, Switzerland) and R (The R Project for Statistical Computing, Boston, USA).

2.9.5. Deviations from the original statistical plan

If substantial deviations of the analyses as outlined in these sections are needed for whatever reason, the protocol will be amended. All deviations of the analyses from the protocol or from the detailed analysis plan will be listed and justified in a separate section of the final statistical report.

Table 2
Study-related procedures.

Examination	Inclusion visit (Randomization)		Visit 1		Visit 2		Visit 3		Visit 4		Visit 6		Visit 7 [a]		Discharge visit	
Time	Day 1		Day 3		Day 5		Day 7		Day 9		Day 11		Day 13		Day 15	
Intervention group (I) Control group (C)	**I**	**C**	**I**	**C**	**I**	**C**	**I**	**C**	**I**	**C**	**I**	**C**	**I**	**C**	**I**	**C**
Patient information, informed consent	x	x													x	x
In-/Exclusion criteria	x	x													x	x
Demographic data	x	x													x	x
Heart failure history	x	x													x	x
Concomitant therapies	x	x													x	x
Comorbidities	x	x													x	x
Electrocardiogram	x	x													x	x
Laboratory tests	x	x	x	x [b]	x	x [b]	x	x [b]	x	x [b]	x	x [b]	x	x [b]	x	x
QoL questionnaires	x	x													x	x
NT-proBNP	x	x	x		x		x		x		x		x		x	x
Vital signs	x	x	x		x		x		x		x		x		x	x
Physical examination	x	x													x	x
Body weight/BMI	x	x	x		x		x		x		x		x		x	x
NYHA functional class	x	x													x	x
Urine pregnancy test	x	x														
Change in medication/therapy	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Adverse events (AE)/Serious adverse events (SAE)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Transfer to Intensive Care Unit	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Mortality	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure [6]. The final decision is left at the discretion of the treating physician.

[a] Number of days and visits depends on duration of hospitalization.

[b] Laboratory tests should be performed according to the recommendations set out by the 2016.

2.10. Ethical aspects

As outlined above, the study was approved by the Ethical Committee of Northwestern and Central Switzerland (Ethikkommission Nordwest-und Zentralschweiz, EKNZ) and is registered at www.swissethics.ch (BASEC-ID 2017–01030). All procedures performed in this study are in accordance with the ethical standards of the EKNZ and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

In detail, prior to inclusion into the study, each patient is comprehensively informed about the nature of the study, its purpose, the procedures involved, the expected duration, the potential risks and benefits, and any discomfort it may entail. In addition, each patient is informed that participation in the study is voluntary, that he/she may withdraw from the study at any time with no need of justification, and that withdrawal of consent will not affect his/her subsequent medical assistance and treatment. Furthermore, the patient is informed on an obligatory basis that his/her medical records may be examined by authorized individuals other than their treating physician.

All study participants receive a patient information sheet and a consent form describing the study and providing sufficient information for patients to make an informed decision about their participation in the study. The possibility to contact investigators by e-mail or telephone to ask for further details is provided. The patient is given sufficient opportunity to read and consider the statement before signing and dating the informed consent form and receives a copy of the signed document. A signed consent form from each patient is obtained before the patient is submitted to any study procedures. The consent form will also be signed and dated by the investigating physician and will be retained as part of the study records.

Participants are given the possibility to withdraw from the study at any time without need for justification. In the case of withdrawal, a written withdrawal letter is appreciated. The reasons for withdrawal will be documented if the patient is willing to provide them. The analysis plan will deal with most of the withdrawals, if possible, by trying to identify patients with a higher risk of withdrawal. In addition, participants are going to be excluded from the study in case of any new diagnosis of concomitant disease directly affecting therapeutic decisions with regards to heart failure (e.g. cancer, pulmonary hypertension, etc.) or making a further participation in the study impossible (e.g. unexpected surgery, trauma, etc.).

2.11. Safety and reporting

During the entire duration of the study, all AE will be collected, fully investigated and documented in source documents and CRFs. Total study duration comprises the time from the participant's signature of the informed consent until the completion of the last protocol-specific procedure.

A SAE is defined as any unfavourable event for which a causal relationship to sampling of biological material or the collection of health related personal data cannot be ruled out, and which requires hospitalization or prolongation of an inpatients' hospitalization, results in persistent or significant disability or incapacity, or is life-threatening or results in death. In addition, important medical events that may not be immediately life-threatening or result in death, or require hospitalization, but may jeopardize the patient or may require intervention to prevent one of the other outcomes listed above, will also be considered as serious. If a SAE occurs the research project will be set on hold and the SAE followed until resolution or stabilization. Participants with ongoing SAEs at study termination will be further followed-up until recovery or stabilization of the disease after termination. Any occurring SAE will be reported within 48 h to the responsible ethical committee (EC).

If any other immediate safety and protective measures become necessary during the conduct of the research project, the sponsor will report them within 7 days to the responsible EC with an explanation of the circumstances, which led to the interference. In addition, the following safety outcomes will be recorded regularly throughout the hospitalization: SAEs, laboratory parameters (potassium, sodium, creatinine), ECG, vital signs (blood pressure, heart rate), change in actual medication or necessary intervention, infections, GP/cardiologist contacts, and death.

2.12. Current status of the study

POC-HF was approved by the EKNZ on 28-12-2017. Recruitment started in March 2018. Due to organizational reasons, recruitment had to be paused from December 2018 on and was restarted in August 2019. Due to significantly lower than expected inclusion rates and the restrictions imposed during the Covid19 pandemic, patient recruitment and data collection are expected to be completed by December 2020.

3. Discussion

The goal of the ongoing POC-HF Pilot study is to investigate whether regular NT-proBNP measurements may alter HF treatment and time of hospitalization in patients admitted for acute decompensated HF.

According to current ESC guidelines, disease monitoring and therapy guidance in patients with HF are based on signs and symptoms of HF, complemented by regular measurements of creatinine, blood urea nitrogen, and electrolytes at least every 1–2 days while in the hospital and before discharge from the hospital [6]. Introduction of NPs into clinical routine evaluation of patients with HF has considerably improved the accuracy of HF diagnosis [6]. Moreover, NPs are powerful predictors for adverse outcomes in patients with HF [6,9]. Reduction of natriuretic peptides during hospitalization was demonstrated to be associated with improved outcomes [10]. On the other hand, trials investigating the value of serial measurements of NPs for HF disease and therapy monitoring have delivered mixed results [17–26]. Surprisingly, though it is conceivable that repetitive NT-proBNP measurements in the acute in-hospital setting may be associated with improved outcomes, the value of this approach has never been tested.

Therefore, we have initiated the POC-HF study, which is based on the assumption that the availability of serial NT-proBNP measurements, in addition to laboratory parameters already recommended by guidelines, may influence treatment decisions in patients with acute decompensated HF leading to a more rapid dose adjustments of prognostically beneficial therapies and earlier hospital discharge.

As further objectives, we will investigate the effect of therapy monitoring with NT-proBNP on the change of the NT-proBNP and the dosing and variations made to medical HF therapies from admission to hospital discharge compared to the control group. Additional exploratory endpoints include the incidence of electrolyte imbalances, renal failure, length of hospital stay, NYHA functional classification, vital signs, body mass index and body weight, QoL, adverse events, transfer to Intensive Care Unit, and mortality.

POC-HF is a pilot and feasibility study. Since no previous studies have been performed addressing the effects of the availability of serial NT-proBNP measurements on treatment decisions in an inpatient setting, an estimation of expected effects sizes and a formal sample size calculation was not possible. Based on the annual number of hospitalizations for acute decompensated HF at our institution and the requirements of the study protocol, we assumed that the inclusion of around 50 patients appears to be realistically achievable within the initially planned time frame of the study.

As a pilot study, the interpretation and the generalizability of the expected results of POC-HF may certainly be limited because of the relatively small number of patients that will be included as well as by the fact that it is a single-center study. Since hospital care is accessible to all patients in Switzerland irrespective of their socio-economic status, we do not expect a substantial bias by socio-economic inequalities. However, patient populations differ between rural and urban areas and between academic and community hospitals with regards to their characteristics. In this respect, the generalizability of the expected results of this pilot, e.g. for a broad application in the clinical routine respectively for the development of health care policies and guidelines, will certainly be limited until confirmed in larger studies.

Nevertheless, POC-HF is needed and useful to develop a preliminary understanding of the value of serial NT-proBNP measurements in the diagnostic and therapeutic process in patients hospitalized with acute decompensated HF. Results from POC-HF will allow to answer open questions on the feasibility of this approach in clinical routine as well as the feasibility and the justification to perform larger-scale studies investigating this strategy. In addition, POC-HF may provide preliminary data to adjust and refine the strategy with respect to the optimal time interval between the repetitive NT-proBNP and safety measurements. Moreover, this study will help to estimate adequate sample sizes, develop budgets, timelines and to identify research collaborators for future larger-scale studies.

4. Conclusions

Given the fact that disease monitoring and therapy guidance in patients with acute decompensated HF is still based on clinical signs and symptoms together with the dismal prognosis of these patients, investigating optimized approaches is urgently needed. The expected results from POC-HF may have the potential to provide the basis for the development as well as a broader investigation of the value of this approach.

5. Publications and dissemination policy

Results of this study will be published at national and international scientific meetings as well as in peer-reviewed journals. Data will be made accessible to other researchers upon reasonable request and based on a description of the research question intended to be answered.

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Competing interests

PH was an employee of Synlab Suisse AG, Switzerland, at the time of study initiation.

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