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# Point of care with serial N-terminal pro-B-type natriuretic peptide (NT-proBNP) for heart failure in patients with acute decompensation. An invited commentary

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ABSTRACT

Point-of-care (POC) Testing (POCT) is a medical diagnostic approach carried out outside the clinical laboratory and close to the patient. The results are used for the immediate clinical decision to improve patient care. Accreditation Canada and Diagnostic Accreditation Programs regulatory standards and the College of the American Pathologists for POCT have implemented several guidelines and certifications. POC in heart failure (POC-HF) will demonstrate that it is helpful to develop a preliminary understanding of the value of serial N-terminal **pro**-B-type **natriuretic peptide** (NT-proBNP) measurements in the diagnostic and therapeutic process in patients hospitalized with acute decompensation of heart failure. In addition, POC-HF will hopefully answer questions on the workability of this approach in clinical routine and the usefulness and justification to perform larger-scale studies investigating this strategy.

Heart failure is often defined as an abnormality of cardiac function, which is the basis for the incapability of the heart to pump blood to provide the oxygen requirements of the peripheral tissues. It is also defined as a failure performing at a level that is highly conditioned by an abnormally elevated filling pressure [1–3]. According to the American Heart Association (AHA), more than 6 million people in the United States live with this condition. It has been estimated that one in five adults aged 40 years or older will eventually develop heart failure in their lifetime [4,5]. Heart failure may have a systolic and a diastolic component. These two components of heart failure often co-exist in numerous patients with cardiac hypertrophy and dilatation, although generally speaking, systolic heart failure is the "classical" heart failure. This type of heart failure is characterized by an impairment of the inotropic state, which leads to weakened systolic contraction. This state, eventually, will promote a decrease in stroke volume and cardiac dilatation. In diastolic heart failure, there is an impairment of the relaxation of the ventricles, which leads to an increase of the ventricular diastolic pressure at an average diastolic volume.

Systolic or classical heart failure occurs in patients with idiopathic dilated cardiomyopathy. Conversely, restrictive cardiomyopathy is associated with multiple etiologies (e.g., genetic hemochromatosis and amyloidosis). Such a restrictive type seems to be often behind diastolic heart failure. In this setting, it has been reasonably substantiated that there is remodeling of the interstitial matrix. In the last few decades, it has been evidenced that genetic and epigenetic factors may enormously contribute to matrix metalloproteinases remodeling [6,7].

Several techniques are available to define an impairment of heart performance in humans. The most common forms of low-output heart failure are linked to arteriosclerosis, hypertension, congenital heart disease, and valvular disease. These conditions highlight an absolute or relative reduction in the failing pump. Consequently, there is an abnormality of peptides, ions, and excitation-contraction coupling. There is an alteration in calcium ions' delivery to the contractile sites with consequent impaired cardiac performance [8]. B-type natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) are peptides produced in small amounts in the heart. They are released in more significant amounts when the heart struggles to work harder. The precursor protein, pro-BNP, is split by the enzyme Corin to remove

; ACE, angiotensin-converting enzyme; AHA, American Heart Association; DAP, Diagnostic Accreditation Programs; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York Heart Association; POC, Point-of-care; POCT, Point-of-Care Testing; POC-HF, Point-of-Care in heart failure; QC, Quality Control.

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an inactive fragment, which is indeed called NT-proBNP. Subsequently, the active hormone BNP is released into the blood [9–13]. In the setting of pump failure and myocardial stress, a BNP test or NT-proBNP can be used, along with other biomarker tests of cardiac functionality. Both biomarkers are helpful in the scene of shortness of breath to differentiate between heart failure and non-cardiac etiologies, e.g., lung disease. The blood levels of these biomarkers have also been associated with the severity and degree of heart failure. Still, some subjects with chronic heart failure may demonstrate the persistence of the elevation of these markers and the impossibility to be used to monitor the response to therapy, including angiotensin-converting enzyme (ACE) inhibitors, beta-blockers, and diuretics.

Point-of-care (POC) Testing (POCT) is a medical diagnostic approach carried out outside the clinical laboratory and close to the patient. The results are used to improve patient care for the immediate clinical decision and reduce hospitalizations. Accreditation Canada and Diagnostic Accreditation Programs (DAP) regulatory standards and the College of the American Pathologists for POCT have implemented several guidelines and certifications. POCT standards and requirements are well defined and include equipment and supplies management, documentation of ordering and testing, quality control and quality assurance, compliance with testing procedures, and promptly reporting results with critical values [14]. They also added external proficiency testing, training, and continuous competency assessment for users. Each area where POCT is performed is also audited for compliance with standards. The certification of the laboratory workers also needs to be relevant and current.

A root cause analysis is usually initiated in case of any nonconformity issues. Despite substantial advances in diagnosis and medical therapy of heart failure, disease monitoring and therapy guidance remain based on clinical signs and symptoms. There is evidence that NT40 proBNP has a robust and independent predictor of morbidity and mortality in patients with heart failure. Only a few – and probably conflicting – data seems to be available on the efficacy of NT-proBNP serial measurement as a tool for treatment monitoring in heart failure. Dr. Zuesli et al. targeted the serial size of NT-proBNP as a tool for treatment monitoring in heart failure patients hospitalized for acute decompensation of heart failure [15]. This study aimed to investigate whether the availability of serial NT-proBNP measurements may influence treatment decisions in these patients. Besides, it examined whether this procedure will lead to more rapid dose adjustments of beneficial medical therapies and earlier hospital discharge. As primary endpoints, the effects of monitoring NT-proBNP, including type and dosing of medical treatments and the rapidity of adjustments, stay length in hospital, and evaluation of the changes in NT-proBNP values, have been clearly defined.

Further, secondary endpoints will include incidence of electrolyte imbalances and occurrence of renal failure, changes in the NYHA (New York Heart Association) functional class, vital signs, body weight, quality of life, the rate of adverse events transfer to Intensive Care Units, and mortality data. A phone call informs the physician of a study member if the NT-proBNP has not decreased by 10% or more between the two measurements. This study (POC-HF) is a pilot and feasibility study. Data from this study will allow the estimate of effect sizes. POC-HF will demonstrate that it is helpful to develop a preliminary understanding of the value of serial NT-proBNP measurements in the diagnostic and therapeutic process in patients hospitalized with acute decompensation of heart failure. In addition, POC-HF will hopefully answer questions on the workability of this approach in clinical routine and the usefulness and justification to perform larger-scale studies investigating this strategy. Further, this study will delineate the adequate sample size, develop budgets, and pinpoint potential research collaborators in the setting of future larger-scale studies.

The Cobas h232 NT-proBNP POC test (Roche Diagnostics, Basel, Switzerland) has been demonstrated to be an accurate, user-friendly and appropriate test in primary care [16]. In assessing Dr. Zusli et al.'s work, we emphasize that POCT for NT-proBNP in the Roche Cobas h232 system to be used by Zusli et al. [15] has a measuring range of 60–9000 ng/L. It takes 12 min before the measurement is done. POCT measures have been advocated to be used for medical decision-making during the hospitalization of heart failure patients instead of by regular laboratory measurements. Although healthcare quality and policy regulators may see some positivity, speed may be no need. The timing of measurements is every two days in the study of Zusli [15]. On the other hand, a study assessed NT-proBNP measures during hospitalization [17]. More than 30% NT-proBNP reduction in acute decompensated heart failure at discharge predicts a favorable prognosis. Stienen et al. [17] studied 25 consecutive patients with acute decompensated heart failure with NT-proBNP >1,700 ng/L. The cumulative percentage of patients attaining the target increased gradually during admission to 22 patients (88%) in a median of 3 days. The authors conclude that a target >30% NT-proBNP reduction is gradually attained before discharge, and rebound NT-proBNP increases to levels off-target occur in up to 33% of patients with acute decompensated heart failure who initially attained target early during admission. There is a continuous decline in NT-proBNP during hospitalization. In further assessing NT-ProBNP, what may be the rationale behind a clinical decision making on declining levels of NT-proBNP. Is the "wait and see" policy enough? To identify when NT-proBNP declines until a preset target? The suggested target of 10% change in NT-proBNP may be part of a normal variation. Moreover, Zusli et al. [15] also fail to mention the NT-proBNP guided randomized study on showing acute decompensated heart failure in patients when they were stabilized. A therapy decision was made exclusively depending on whether or not the patients had reached the target of more than a 30% decrease in NT-proBNP, as noted previously [18]. This randomized trial seemed to have failed to change the outcome. Thus, despite positive considerations, some criticisms make the pilot study of Zusli et al. [15] an exciting study but afflicted with several caveats.

Overall, POCT preserves or enhances the quality of patient care while meeting hospital and laboratory accreditation standards. The Laboratory Director is the duly authorized officer responsible for POCT within the hospital and implementing any policies, processes, and procedures related to POCT. The POCT coordinator or lead is primarily responsible for coordinating POCT evaluations, developing strategies and practices, establishing a training program, assisting with implementations, and highlighting and monitoring the quality control (QC) and proficiency programs. Further, the POCT coordinator will regularly conduct competency evaluations, recommend retraining on an as-needed basis, troubleshoot and manage documentation and delineate the range of interaction with an advisory management group, including multidisciplinary representatives from the laboratory, administration, and nursing teams.

## Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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