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MONITORIA: The start of a new era of ambulatory heart failure monitoring? Part I – Theoretical Rationale

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Abstract Heart failure (HF) is a multifactorial chronic syndrome with progressive increasing incidence causing a huge financial burden worldwide.

Remote monitoring should, in theory, improve HF management, but given increasing morbidity and mortality, a question remains: are we monitoring it properly?

Device-based home monitoring enables objective and continuous measurement of vital variables and non-invasive devices should be first choice for elderly patients. There is no shortage of literature on the subject, however, most studies were designed to monitor a single variable or class of variables that were not properly assembled and, to the best of our knowledge, there are no large randomized studies about their impact on HF patient management. To overcome this problem, we carefully selected the most critical possible HF decompensating factors to design MONITORIA, a non-invasive device for comprehensive HF home monitoring.

MONITORIA stands for MOnitoring Non-Invasively To Overcome mortality Rates of heart Insufficiency on Ambulatory, and in this paper, which is part I of a series of three articles, we discuss the theoretical basis for its design.

MONITORIA and its inherent follow-up strategy will optimize HF patient care as it is a promising device, which will essentially adapt innovation not to the disease but rather to the patients.

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MONITORIA: o início de uma nova era na monitoração da insuficiência cardíaca? Parte I – Fundamentação teórica

Resumo A insuficiência cardíaca (IC) é uma síndrome crónica multifatorial com incidência progressivamente crescente e grande impacto financeiro a nível mundial.

Teorizou-se que a telemonitorização contribuiria para uma melhor abordagem da IC. Contudo, face à crescente morbimortalidade desta síndrome, é pertinente colocar uma questão: será que estamos a monitorizar a IC adequadamente? A monitorização ambulatória, por meio de dispositivos, permite uma avaliação objetiva e contínua de diversos parâmetros vitais, sendo preferíveis os dispositivos não invasivos no caso dos pacientes idosos.

Na literatura abundam artigos sobre estes dispositivos. Contudo, a maioria foi desenhada para monitorizar uma única variável ou uma classe de variáveis incorretamente reunidas. Além disso, até à data, não temos conhecimento de ensaios clínicos randomizados e controlados com intuito de avaliar o impacto destes dispositivos na abordagem da IC e seus *outcomes*. No sentido de tentar ultrapassar este problema, nós selecionamos cuidadosamente os fatores mais críticos nas exacerbações de IC, para desenhar o Monitoria, um dispositivo não invasivo para monitorização abrangente da IC em ambulatório.

Monitoria significa ***MO***nitoring ***N***on-***I***nvasively ***T***o ***O***vercome mortality ***R***ates of heart ***I***nsufficiency on ***A***mbulatory e neste artigo, que é a parte I de uma série de três artigos, nós pretendemos discutir os fundamentos teóricos que estiveram na base do seu desenho.

O Monitoria e a estratégia de *follow-up* que lhe é inerente aprimorará a abordagem do doente com IC, sendo um dispositivo promissor, essencialmente, por implicar um ajuste da inovação ao doente real, e não à sua doença ou a um conceito teórico de doente.

Introduction

Heart failure (HF) is a multifactorial chronic syndrome affecting over 23 million people worldwide[1] and its incidence is growing and causing a major financial and economic burden. Despite significant innovation in therapy (pharmaceutical and device-based) and developments in monitoring protocols, recurrent hospitalization, morbidity and mortality due to HF, remain high. Perhaps we are not yet monitoring HF properly, predicting it in a timely fashion or sensitively enough, or are not treating the correct decompensating factor.

Currently, there are reports in the literature on possible decompensation, factors in HF. Among these, increases in heart rate, as well as a rise in ventricular filling pressures,[2] both occurring shortly before an acute HF decompensation are the preponderant ones. Besides these, low heart rate variability, atrial and ventricular arrhythmias, high respiratory rate (as ventilatory oscillation) and pulmonary congestion[3,4] are the other main parameters believed to predictors of precipitating HF.

It has been theorized that remote monitoring could be used to improve HF management in a scalable and cost-effective manner. In fact, ambulatory follow-up of HF patients has been shown to be cost-effective,[5,6] even when it involved home visits by health care professionals. It correlated with reduced readmission and mortality rates.[6] The question is: are we monitoring the right parameters and in the right way?

Improved technology and effective predictive models can predict sudden decompensation events. Early detection of any alteration using telemonitoring of multiple vital parameters may avoid severe decompensation requiring hospital admission. Multiple parameter simultaneous detection and analysis might lead to more relevant findings, increasing sensitivity and specificity, when compared to single measurements.

Home monitoring of HF may be performed by the patient, by the healthcare provider or by a device. The latter has the advantage of being objective (and without bias), and of allowing for continuous measurements and monitoring. Moreover, the patient may not be able to self-monitor as a significant portion of HF patients have cognitive dysfunction,[7,8] Cognitive dysfunction is more prevalent as more symptomatic is the HF.

In published literature, there are many studies reporting on invasive and non-invasive devices, wired or wireless, wearable or not, designed for ambulatory monitoring of some vital variables such as heart rate, respiratory rate, peripheral oxygen saturation, pulmonary systolic arterial pressure, thoracic bioimpedance, and skin odor, among others. However, most have neither been validated nor are they applicable in clinical practice.[9] There have been no large randomized studies on the impact of these devices on HF patient mortality. On the other hand, nowadays, devices are designed to monitor a single variable or a single class of variables and there is an absence of multisensory devices that can provide a comprehensive perspective on HF, conducting to its full control.

Patients with implantable devices, such as implantable cardiac defibrillators or cardiac resynchronization therapy devices, with or without defibrillator, could be in an advantageous position because their devices can already be monitored continuously. However, despite some authors reporting the benefits of this kind of monitoring,[10–15] others have not consistently demonstrated an improvement in clinical outcomes.[16,17] Moreover, healthcare units responsible for deploying these devices continue to show a very low rate of remote monitoring, favoring instead the classic approach of periodic device interrogation, at scheduled clinic appointments, without any monitoring in the meantime.

Additionally, invasive techniques are expensive and most of them are not suitable to be used either on a routine basis or at home. Their benefit must also be balanced against safety concerns: the invasive nature of implants, with the risk of associated complications and need for sedation; thromboembolic events, antithrombotic therapy and bleeding risk; infectious complications; and the possibility of device extraction related complications. However, in the community, the necessary professional support for home monitoring of these invasive devices, is not universally available and remains costly and difficult to scale. Telemonitoring without implantable devices is perhaps a better option for elderly advanced patients, in whom the risk is likely to outweigh the benefit.

Therefore, we theorize that in this era of aggressive technological evolution, the future for successful follow-up in HF (essentially by reducing hospitalization rates and mortality) should be based on improving non-invasive devices for home monitoring of a specified array of vital and physiologic parameters, integrated in a comprehensive decision-based algorithm. Against this backdrop, we designed a non-invasive device that we believe will revolutionize outpatient follow-up, the management of HF, and its outcome.

This device - MONITORIA - will provide non-invasive, remote monitoring of HF patients by capturing vital and electrophysiologic, hemodynamic and chemical signs, and physical activity levels. With this monitoring device, its inherent predictive algorithm and the follow-up program we are implementing (named the GENICA project), it will be possible to detect early signs of decompensation more quickly, act on them and stabilize patients at home, avoiding hospitalization.

Objectives

The objective of our investigation is to develop the most appropriate device for home monitoring of chronic HF. That device is MONITORIA and for simplicity we choose to separate the discussion around MONITORIA into three articles. In part I, we aim to explain the theoretical foundation and rationale regarding MONITORIA's development. Part II and part III will be published separately: a paper concerning the specifications of the device's design and a paper presenting the MONITORIA prototype and validation tests, respectively.

Literature review and rationale for design of MONITORIA

As stated above in the introduction, the incidence of HF is increasing and its management still involves substantial direct and indirect costs, mainly related to recurrent hospitalizations caused by HF decompensation. We have therefore considered the hypothesis that we are not monitoring these patients properly.

To overcome this problem, we carefully selected the most critical possible decompensating factors to design a device to accurately and non-invasively monitor HF patients, while being comfortable for them, not interfering in their normal daily activities. The parameters we choose to monitor with MONITORIA, and the rationale behind our choices, are outlined in this article.

Transthoracic impedance (and by inference net lung impedance)

Extravascular lung water is a crucial parameter for management of heart failure. Arad et al.[18] found a correlation between lung water and clinical data, as well as signs of congestion on chest X-rays[18,19] in HF patients.

In the literature there are several reports on studies, some dealing with transthoracic impedance and others with lung impedance, showing overall positive results in HF outcomes. Shochat et al.[20] showed a significant reduction in the incidence of HF decompensations, all-cause mortality, cardiovascular deaths and mortality due to HF. Additionally, in the Impedance-HF trial, the authors noted a significant increase in pulmonary congestion as early as two weeks before acute HF hospitalization, with a very sharp deterioration the week prior to admission, and even more during the three days prior to admission. In fact, non-invasive measurements of transthoracic impedance showing a decrease in transthoracic impedance (equivalent to an increase in lung water) have been proven to be superior to weight gain in detection of early stages of decompensation.[21,22]

However, we must be cautious as discussions in the literature are not homogeneous, and in some cases, authors use the terms transthoracic impedance or lung impedance interchangeably, creating some confusion, even reporting similarities between them.[23]

Net lung impedance, which is the impedance of interest, comprises only a small fraction of the overall transthoracic impedance.[20] Subtraction of the chest wall impedance from the transthoracic impedance yields the net lung impedance.[24,25]

Moreover, usually as we have already pulmonary congestion in patients with HF when we are assessing them for the first time, sometimes it is not possible to determine the baseline lung impedance (BLI) but rather the instantaneous lung impedance (ILI). It has been described elsewhere that BLI should be defined as impedance in asymptomatic patients in New York Health Association (NYHA) class I, with no congestion on chest X-rays and a low-normal six-minute walking test.

In addition, ILI measured in absolute values (Ω) depends on the individual anthropometric characteristics, as well as on the location and type of electrodes and device used. Con-

sequently, another concept emerged as being more relevant than ILI – ΔLIR – a variation of lung impedance. Shochat et al.[20] demonstrated accurate management of therapeutics (diuretics) based on this variation, and previously Shochat M et al.[24] had found that ΔLIR reliably predicted hospitalizations for HF decompensation due to pulmonary congestion (PC) and risk of death and was found to be more sensitive and discriminative than NYHA functional class.

Nevertheless, over the years, ΔLIR progressively decreases (becoming more negative) in patients with multiple re-hospitalizations, resulting in the development of a certain amount of tolerance and patient adaptation to a higher degree of PC. Therefore, a pre-specified decrease in ΔLIR as predictor of hospitalizations due to PC becomes less relevant. To overcome this, we can also use ΔLIR year, which reflects trends in lung impedance variation over a year. Shochat et al. found that patients who experienced a higher degree of long-standing PC (ΔLIR year in the range of -30 to -70% vs. 0% to -30%) had a higher probability of PC-associated hospitalization and death.

Electrocardiographic data: heart rate and heart rate variability, T wave amplitude variability, electric conduction abnormalities, atrial and ventricular arrhythmias, myocardial ischemia

HF exacerbations do not only occur because of PC. When aiming for a better control of chronic HF in ambulatory care, we should pay attention also to the other components of this complex syndrome, such as the neurohormonal system. One way to do this, non-invasively, is by analyzing heart rate (HR) and heart rate variability (HRV).

The neurohormonal control system of the heart, comprising the autonomic nervous system (with sympathetic and parasympathetic limbs) and the renin-angiotensin-aldosterone system, detects a change in status and responds long before the patients develop symptoms that would traditionally require medical attention. This occurs several days to weeks before the patients decompensate enough to require hospitalization.[26]

Heart rate is controlled by a balance between the parasympathetic and sympathetic limbs of the autonomic nervous system. Yet, resting heart rate is typically dominated by vagal tone (parasympathetic). In HF, myocardial systolic dysfunction triggers compensatory sympathetic hyperactivity which, in the early phases, aims to preserve cardiovascular homeostasis. However, HF, over the years, has been associated with a chronic blunted response by some of the sympathoinhibitory reflexes normally involved in the vagal control of heart rate, whereas sympathoexcitatory reflexes from atrio-ventricular baroreceptors, arterial chemoreceptors, and metaboreceptors from the skeletal muscle are abnormally activated.[27,28] Hence, the initially present balance breaks down in more advanced phases of HF, which then reflects the imbalance of the two limbs of the autonomic system. It is indicative of an underlying pathophysiological process. The global effect is a persistent increase in resting HR and nighttime HR and a decrease in HRV.

However, if in the past it was believed that elevated HR in HF was an epiphenomenon of sympathetic hyperactivity, nowadays, experimental and clinical evidence suggests that elevated HR, per se, may have a pathogenic role in HF, at least in individuals with reduced ejection fraction.[29]

In fact, persistently elevated resting HR increases myocardial oxygen demand, reduces diastolic duration with impaired coronary perfusion time, downregulates β-adrenergic receptors with suppressed signal transduction, leads to ventricular dilatation, mitral regurgitation, and myocyte replacement with fibrosis; changes the extracellular matrix, impairs intracellular calcium handling and excitation-contraction coupling mechanisms, and leads to accumulation of oxygen free radicals,[30,31] among other deleterious effects, including a direct association with the presence, severity and progression of coronary atherosclerosis, increasing the likelihood of disruption of preexisting plaques.[32]

Accordingly, as reported in the literature, elevated resting HR is associated with increased risk of cardiovascular death, hospitalization and mortality,[33,34] and reducing it, irrespective of treatment used,[35,36] results in improved clinical outcomes.[35–38] The best protection was observed for those with HR <60 bpm or a >10 bpm reduction in HR at 28 days after treatment initiation.

On ECG, HR is determined by the intervals between adjacent QRS (R-R intervals, measured in ms), but the time between these is not always the same, generating the HRV, defined as the fluctuation in the degree of HR around its mean value, reflecting the regularity of heart beats. HRV is a standard non-invasive method for assessing autonomic nervous system function,[39,40] and is a powerful prognostic indicator of arrhythmic events following myocardial infarction. Lower HRV is frequently related to poorer autonomic function.

Sympathetic activity is associated with the low frequency range (0.04-0.15 Hz), while parasympathetic activity is associated with a higher frequency range (0.15-0.4 Hz) of modulation frequencies of HR. The difference in frequency range is an important marker identifying the contribution of sympathetic and parasympathetic systems.

Politano et al.[41] described different methods to determine HRV: time-domain methods, frequency-domain methods, short-term recording and long-term recording. Frequency-domain methods seem to be the best. The clinical use of HRV was first described in 1963, however it became a strong prognostic factor in HF during the 1990s. In HF, reduced or abnormal HRV reflects sympathovagal imbalance and is an indicator of increased risk of mortality.[42–44]

Another important prognostic risk factor is T wave heterogeneity (repolarization heterogeneity) as this has been shown to be a promising predictor of arrhythmias in patients with dilated cardiomyopathy.[45] Nearing et al. demonstrated that increased levels of T wave heterogeneity clearly preceded the development of T wave alternans (by 15 min) and ventricular tachycardia (by 30-45 min).[46]

Electrical conduction abnormalities, mainly left and right bundle branch as well as nonspecific intraventricular conduction delay (defined as QRS duration ≥110 ms without fulfilling the criteria of either bundle branch block) and their role in the pathophysiology and prognosis of HF, have not been well established, and until recently study findings have been controversial. Nonetheless, Tolppanen et al.[47] clearly demonstrated the long-term impact of these

conduction abnormalities on HF outcomes, discerning some differences between acute HF and acute decompensations of chronic HF. They found that right bundle branch block was associated with de novo acute HF and intraventricular conduction delay was an independent predictor of poor prognosis in patients with acute decompensations of chronic HF. The effect on mortality of both conduction abnormalities was related to impairment of left ventricular systolic function. Curiously, left bundle branch was not associated with poorer long-term survival overall.

Patients with chronic HF have a high incidence of atrial and ventricular arrhythmias, which seriously affect their lifespan and quality of life. Preventing arrhythmias and timely treating them can have a stabilizing effect on HF, avoiding the potentially lethal outcome of ventricular arrhythmias. We therefore hypothesize that continuous monitoring of these patients, looking carefully for certain predictive electrophysiological variables (see before on the electrocardiographic data section), is the future for successfully defeating the public health Goliath that is HF. Fortunately, most of the abnormal cardiac events such as myocardial ischemia, acute myocardial infarction and fatal arrhythmias can be diagnosed through continuous electrocardiogram analysis.[48]

Right atrial and left atrial pressures

It is important to determine right atrial pressure (RAP) in an HF monitoring follow-up program, because, as Pellicori et al.[49] demonstrated in the SICA-HF program, it accurately identifies ambulatory patients with HF who have more severe congestion and a worse outcome.

Yet, most patients with acute decompensation have PC secondary to elevated left atrial pressure (LAP).[50] Hence, continuous monitoring of LAP may also provide an excellent method of HF monitoring. There is an ongoing trial (LAP-Top-HF study) designed to assess the role of implantable LAP monitoring in association with guiding therapeutics in HF.[51] Nevertheless, we aim to accurately monitor LAP, as well as RAP, in a non-invasive way, using the MONITORIA device.

In fact, currently there are innovative methods to assess hemodynamic parameters such as these, non-invasively, such as those based on near-infrared energy. The discovery of near-infrared energy dates to the beginning of the 19th century, but it is only recently that interest has grown in near-infrared spectroscopy (NIRS) as a tool for medical research with a wide range of clinical applications.[52,53] NIRS works by projecting near-infrared light with a light emitting diode (LED) placed, for example, on the chest, and analyzing the back-scattered light captured with a photo-sensor tuned to the same frequency bandwidth. The absorption of near-infrared light is determined mainly by hemoglobin. Once the pressure is measured, is compared with a zero-reference, using another electrode placed near the first one.

Systemic arterial blood pressure

The prognostic value of blood pressure differs substantially between HF with reduced left ventricular ejection fraction (LVEF) and HF with preserved LVEF, as clearly reported in the literature.

Low systolic blood pressure (SBP), probably as a surrogate marker of low stroke volume, has been demonstrated as a predictor of death and HF hospitalization in HF with reduced ejection fraction patients.[54] By contrast, apparently, there is no relationship between SBP and outcome in HF with preserved ejection fraction patients. Some reports have shown that incrementally higher SBP had protective properties among these patients.

In fact, in HF patients with preserved ejection fraction, SBP may not be a good measure to characterize hemodynamic status because, independent of SBP values, there may be differences in their underlying stroke volume and arterial mechanics, with varying influences on clinical HF manifestations.

Contrary to SBP, low (<60 mmHg) diastolic blood pressure (DBP) has been shown to be associated with an adverse outcome, especially HF hospitalizations and a trend toward higher all-cause mortality, either in HF with reduced ejection fraction[55] or in HF with preserved ejection fraction.[54] However, excessively high DBP (>90 mmHg) may still be associated with an increased risk of atherosclerosis in HF patients with preserved ejection fraction.[56]

Among HF patients with preserved ejection fraction, a low DBP may be a surrogate marker of chronic non-cardiovascular disease besides diastolic dysfunction. Previous studies had shown a bidirectional ''J curve'' relationship between DBP and risk. This can be explained by the fact that in HF patients with preserved ejection fraction both coronary artery disease and left ventricular hypertrophy are common and low DBP could provoke myocardial ischemia because of reduced coronary perfusion pressure,[57] particularly in the context of impaired microcirculation.

With regard to pulse pressure (PP) in HF patients with reduced ejection fraction, a higher PP (in the range of 50 to 60 mmHg) has been associated with the best outcome, compared to those with the lowest PP. In these patients, PP was a surrogate marker of stroke volume. In HF patients with preserved ejection fraction, a PP between 50 and 60 mmHg was associated with the best outcome, while PP in the highest and lowest quartiles was associated with a worse outcome. The higher PP values in these patients were probably related to a lower DBP and a higher prevalence of general vascular disease, and the lower values of PP were likely related to lower stroke volume.[54]

As discussed above, the importance of monitoring blood pressure (BP) during follow-up of HF patients is clear. It does, however, need to be performed in a non-invasive way similar to other electrophysiological and hemodynamic variables.

Non-invasive measurement of blood pressure using traditional auscultatory method provides adequate data for many applications in medicine, but has some limitations for continuous home monitoring: this method only provides intermittent measurements; the inflation of the cuff may disturb the patient and as a consequence, alter the BP; and varied errors can arise because of the conditions imposed in order to obtain accurate measurements. Thus, alternative non-invasive methods were investigated.

Photoplethysmography (PPG) is one of these alternative methods, which use pulse wave velocity (PWV) and pulse transit time (PTT) approaches. PWV is the speed of a pressure pulse propagating along the arterial wall and can be calculated from PTT.[58] This method has been investigated

using a combination of ECG and PPG signals,[59] and, more recently, impedance cardiography[60] data. Several studies based on different technical solutions have shown a high correlation between PTT and BP. Globally, using this method we measure the time from ECG R-peak to the pulse wave reached at a peripheral artery. By placing the PPG sensor on the chest, the measurements are taken in superficial skin capillaries, and we can guarantee the patient for the patient as well as avoid some errors like the effect of peripheral vasoconstriction.

The addition of impedance cardiography to help in calculations of BP using the PPG method, contributed largely to obtaining more accurate measurements, mainly because it abolishes the pre-ejection period component (see below) in calculations of PTT.

Impedance cardiography (ICG) is a non-invasive method based on Ohm's law that determines changes in thoracic fluid content based on changes in the conductivity/resistance to propagation of an electrical impulse across the thorax. ICG waveforms are the basis of ICG data provided to clinicians and are described in detail in literature.[61] ICG measures certain parameters directly whereas others are calculated. Directly measured parameters include heart rate, thoracic fluid content, velocity index, acceleration index, pre-ejection period and left ventricular ejection time. Calculated parameters include stroke volume, stroke index, cardiac output, cardiac index, systemic vascular resistance, systemic vascular resistance index, left cardiac work index and systolic time ratio.[62]

Pre-ejection period

The pre-ejection period is an index that links electrical and mechanical cardiac activity and is obtained by simultaneous recording of the electrocardiogram and impedance cardiogram. It is defined as the interval between the onset of ventricular depolarization (Q-wave onset in the ECG) and the opening of the semilunar valves, i.e., ventricular contraction (sharp upstroke in the dz/dz or B-point in the impedance cardiogram).

When left ventricular failure occurs, the pre-ejection period lengthens (reduced left ventricular pressure during ventricular contraction) and the left ventricular ejection time shortens. Non-invasive assessment of pre-ejection period and left ventricular ejection time could assist the safe and accurate prescription of diuretics as well as other guideline-directed therapies for patients with HF, as we have described above.

Cardiac output

Recalling simple pump-function terms, HF is a syndrome in which the heart is performing on a depressed Frank-Starling curve relating stroke volume (or cardiac output) to ventricular diastolic filling (pressure or volume). Hence, its natural history implies progressive, albeit variable, reduction in cardiac output, and most of its signs/symptoms and complications are related to this factor. Nowadays, it is possible to assess this parameter non-invasively, using technologies such as impedance cardiography.[62,63]

Peripheral oxygen saturation

Peripheral oxygen saturation (SpO2) is the measurement of oxyhemoglobin (HbO2) percentage in arterial blood, reflecting the levels of blood oxygenation. Currently, non-invasive measurement of SpO2 by pulse oximetry is well stablished, enabling its use as an important biomedical sign in daily clinical practice. In fact, one of its well-known applications is in polysomnographic studies. And, it was, partially, thanks to these studies that a significant portion of HF patients were found to suffer from arterial oxygen desaturation, mainly during the nocturnal period.[64] It has also been observed that this desaturation, as well as troubled breathing (like Cheyne-Stokes respiration), gets worse in HF decompensations, returning to normal or improving significantly after treatment.

In HF patients, the occurrence of severe and prolonged oxygen desaturation decreases myocardial efficiency and increases oxygen consumption, contributing to progression or exacerbation of left ventricular failure. Besides this, some authors reported increased risk of ventricular arrhythmias in the presence of severe hypoxemia.[65] Correction of hypoxemia had shown to improve cardiopulmonary hemodynamics.[64–66] For this reason, it is essential to include SpO2 in any ambulatory HF monitoring system.

A non-invasive pulse oximeter is based on an optical process to detect SpO2, and is composed of a red and an infrared LED, and photodiode sensors.[67] In order to obtain SpO2, the red wavelength must be in a range within a region where the absorption of Hb and HbO2 are markedly different (Fontaine et al. suggested an optimal wavelength near to 660 nm[68]); and the region for the infrared light must turn around a wavelength where the absorption coefficients of Hb and HbO2 are practically the same (between 940 nm and 960 nm as stated by some authors).[68,69]

Pulse oximeters may be characterized as being transmission-based or reflectance-based. In transmission-based pulse oximetry, LED and a photodiode are placed on opposite sides of a substrate, which in turn can be attached across the fingertip, earlobe or foot. In reflectance-based pulse oximetry, the LEDs are placed together on the same probe surface. This method is intended to be used on body locations where pulse oximetry through transmission is not feasible, like in the chest. In fact, for continuous home monitoring purposes, a pulse oximetry sensor catching SpO2 from the chest would be much more suitable rather than the traditional fingertip oximeter, not interfering with patient's daily activities nor suffering misleading readings because of low cardiac output states.

Concerning reflectance-based pulse oximetry, there is still little supporting evidence that SpO2 can be accurately captured from the chest. However, the prototype built by Fontaine et al.[68] is promising, and accurately measures SpO2 from the chest, within an error of +/-1%.

Respiratory rate

Respiratory rate (RR) has been shown to be an important predictor of cardiac arrest, respiratory adverse events and intensive care unit admission. In HF patients, RR increases in HF decompensations and, in advanced stages, episodes

of apnea may occur, among other ventilatory problems such as ventilatory oscillation. For this reason, RR should also be included in any HF monitoring follow-up program.

Skin sodium content

The rationale for measuring sodium in sweat is based on a report from 1956,[70] in which sweat sodium excretion was equivalent to sodium intake among patients with HF. However, this might have occurred because the HF patients then were not on optimal medication, and reduced urine output and very small quantities of urine sodium, perhaps because of hyperaldosteronism were observed. Measurements of sodium on skin may function, to a certain extent, as a surrogate marker of dietary sodium intake, and may therefore help guide the choice of therapy in HF patients, chiefly diuretics.

Patient's physical activity levels

Physical activity (PA) is defined as any bodily movement produced by skeletal muscles resulting in energy expenditure beyond resting expenditure.[71]

The effects of PA seem to be different for men and women with HF. Rahman et al.[72] found a U-shaped association between PA and HF risk in men, but previous studies using the same construct for PA evaluation did not find this kind of association in women. In fact, men with the lowest levels of PA (<38 metabolic equivalents of task (METs) h/day) and those with the highest levels (>57 METs h/day) had, respectively, up to 44% and 25% higher risk of HF, compared to those with median levels of PA (41 METS h/day). Moderate levels of PA were associated with a lower risk of future HF. Women with very high levels of PA did not show any increased risk. In contrast, exercise training in individuals with HF was associated with a larger risk reduction of all-cause mortality and hospital stay in women compared with men.[73]

Monitoring daily PA levels may provide us with valuable information not only concerning current state of cardiovascular fitness and risk for worsening of HF but also indicating impending acute decompensations and deterioration of global health status.

Brief discussion and future work

At present, despite technological and pharmacological innovations, HF continues to be a Goliath of public health, bearing a substantial economic and social burden. We hypothesize that what is lacking in this fight against HF is, above all, a united strategy, one that encompass the most relevant innovations to date and constructs a comprehensive follow-up program based on an accurate algorithm for early detection of acute decompensation.

Therefore, more important than a blinded pursuit of miraculous technological/pharmacological innovation, is to be aware of and attentive to what is happening in the world, to the small but significant efforts made by each individual that treats HF patients and to gather all this information and knowledge under the umbrella of a global multidisciplinary monitoring strategy.

Feasibility

The model is still under construction and being testing, so its feasibility in real clinical practice is limited to theoretical speculation. However, based on the data retrieved to date, despite some limitations as outlined below, we think it will be feasible.

Conclusion

In this paper we present the theoretical foundation to build what we believe could be the best device for home monitoring of HF patients. Essentially because it will provide a real-time comprehensive picture of the disease and, hence, optimized control. We named this device MONITORIA and the technical specifications of its design are described in another paper, part II of this series of three articles (see the objectives section).

Limitations

The first limitation is that MONITORIA topic is separated into three articles, namely I-Theoretical Rationale, II-Technical Specifications and III-Validation. The second limitation is related to the device's complex technical specifications and the need for wearing a vest continuously. And the third arises from possible difficulties in interpretation of some parameters, especially those indirectly derived from others, as well as potential interaction between sensors, given their multiplicity.

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Conflicts of interest

The authors have no conflicts of interest to declare.

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