Wearable technology for detection of COPD exacerbations: feasibility of the Health Patch

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To the Editor:

We found the article by Finney *et al*. [1] in your esteemed journal regarding the potential of an electronic diary and wristband accelerometer in detecting COPD exacerbations to be of great interest. The study demonstrates the feasibility of using digital technology for symptom and activity monitoring in COPD, suggesting its potential for early exacerbation detection. We believe that incorporating heart rate variability (HRV) measurements could enhance the effectiveness of such monitoring. Nonetheless, we acknowledge the challenges associated with implementing this technology, and recognise that several issues must be addressed before these technologies can be integrated into daily care. In this letter, we aim to share our thoughts and insights derived from both literature and our recent research findings.

The focus on wearable devices in COPD management is increasing. A recent systematic review by Shah *et al*. [2] highlighted various uses of these devices, including the early detection of COPD exacerbations. For this objective, a variety of parameters were investigated, including physical activity, body temperature, home air quality and saturation, as well as respiratory and heart rates. In addition, HRV may also be a valuable parameter for use in the detection of COPD exacerbations. HRV refers to the fluctuations in the time intervals between consecutive heartbeats, and HRV provides insight into the balance between sympathetic and parasympathetic activity. Generally, low HRV is associated with sympathetic activity. When sympathetic activity predominates, heart rate typically is increased and typically more constant, leading to decreased HRV. This indicates diminished bodily resilience, and challenges in adapting to changing situations. Therefore, low HRV is indicative of existing or potential health issues or the presence of inflammation. HRV can be evaluated across both time and frequency domains. Time domains provide information about long-term and short-term fluctuations and are often used for general assessments of HRV. Frequency domains reveal specific rhythmic patterns, including respiratory influences and baroreceptor reflexes [3, 4]. A recent systematic review indicated a general decrease in HRV parameters among COPD patients, suggesting a predominance of sympathetic activity [5]. Sympathetic hyperactivity in COPD may arise from a variety of pathophysiological changes, such as recurrent hypoxaemia, hypercapnia, fluctuations in airway obstruction-induced pressure, elevated respiratory effort, systemic inflammation, or the use of beta-sympathomimetic medications [6]. One could hypothesise that this sympathetic activity is even stronger during exacerbation compared to stable disease. Therefore, HRV might have the potential to serve as a promising indicator for early detection of COPD exacerbations. However, only one study conducted a comparison of HRV between stable disease and exacerbation, using short ECG measurements every 3 months for a period of 2 years, yielding mixed results regarding the differences in various HRV parameters during these states [7]. To the best of our knowledge, wearable monitoring of HRV has never been performed for the purpose of early detection of COPD exacerbations.

An example of a wearable device capable of measuring HRV continuously for several days is the Health Patch (2M Engineering, Valkenswaard, the Netherlands). This device, attached to a patient's left chest side, monitors heart and respiratory rates by using a one-lead ECG and bioimpedance measurement, respectively. The patch consists of an electrode patch and a data recorder. The recorder can wirelessly connect to the Health Patch application on either a computer or tablet (figure 1a) [8, 9].

We conducted a proof-of-concept study to assess the usability and feasibility of the Health Patch in distinguishing exacerbations from stable disease. Ethical approval for this study was granted by the United

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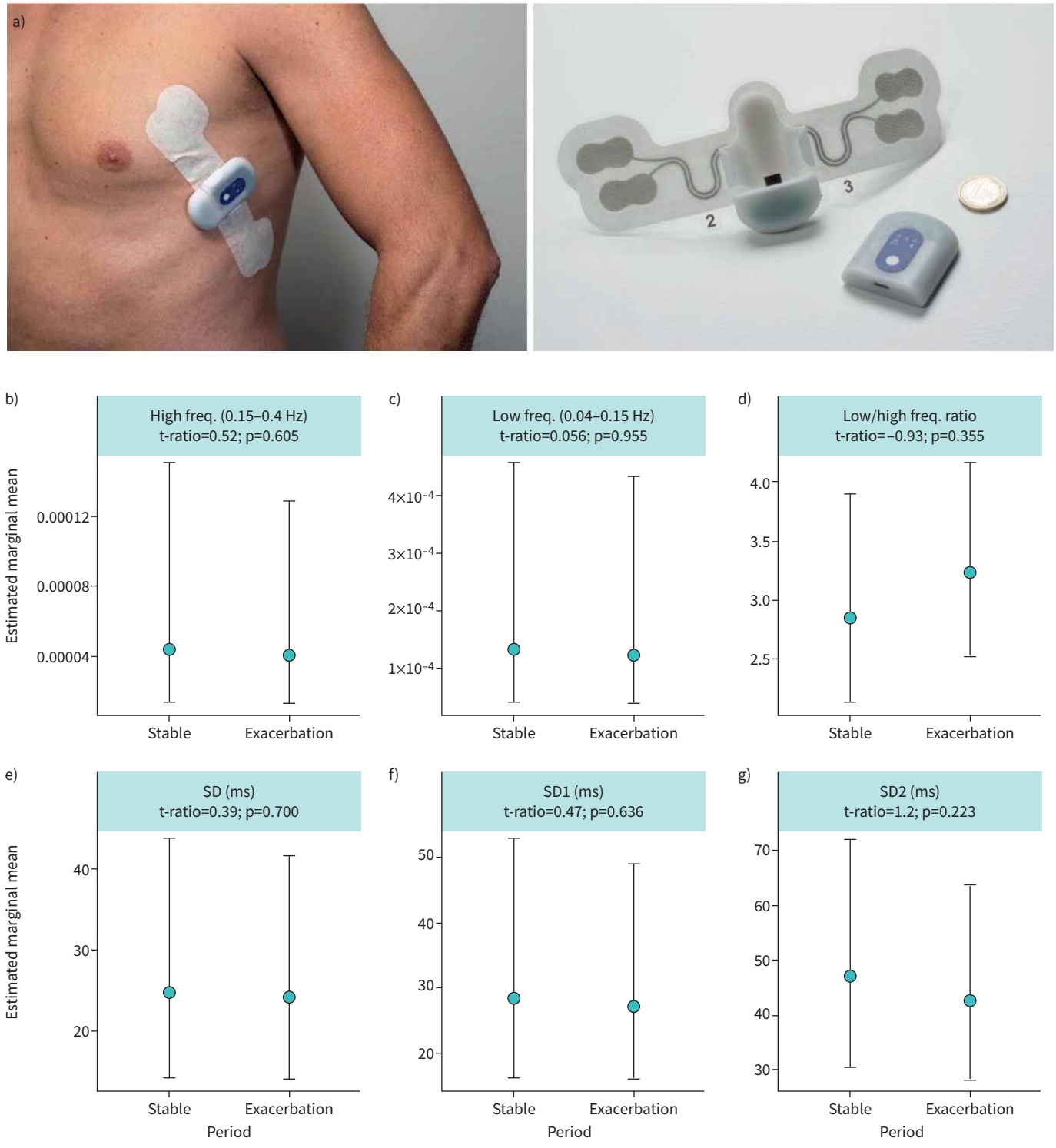

FIGURE 1 a) Health Patch prototype for clinical studies. b–g) Heart rate variability (HRV) measurements during exacerbation and stable disease. Frequency domain measurements: b) high frequency measurements; c) low frequency measurements; d) low/high frequency ratio. Time domain measurements: e) Standard Deviation of normal heartbeats (SD); f) SD1 (measuring short-term HRV); g) SD2 (measuring short- and long-term HRV).

Medical Research Ethics Committees (NL70290.100.19). 15 patients with a confirmed diagnosis of COPD were included during an exacerbation in the outpatient clinic of the Franciscus Gasthuis and Vlietland Hospital in Rotterdam, the Netherlands. They were asked to wear the Health Patch for 3 days. Clinical assessment included questionnaires, blood tests and spirometry. A questionnaire created by the developer

evaluated the feasibility of the Health Patch. After 6 weeks, when the patients' conditions stabilised, all assessments were repeated during the second study visit.

Unfortunately, we experienced a significant loss to follow-up due to the prolonged instability of the patients' clinical status following their exacerbation (n=6). Consequently, these patients were either unable or unwilling to visit the hospital for the second study visit. Furthermore, we encountered various technical obstacles regarding usability of the patch's research platform in four of the nine patients that completed both study visits. Technical issues and incomplete data collection, similar to those highlighted by Finney *et al*. [1] regarding connectivity problems, were observed. Data were extracted from the device once the wearing period had concluded, revealing instances where the device had not been switched on properly or data were insufficient due to improper attachment of the patch to the patient's chest. These challenges may have emerged because the patch is primarily a feasibility research platform, as opposed to a commercial device. Although the Health Patch was successfully applied in other studies, the device has not been previously tested in this specific population, so it is possible that the device is not yet well-suited for users with physical characteristics commonly observed in COPD patients (such as lower body mass index, older age or drier skin). We were unable to identify any significant correlations between these parameters and data quality, most likely due to the limited sample size. Certain issues could be addressed directly during this proof-of-concept study. For instance, the application was improved by providing visibility into whether the device was actively recording. As next steps, implementing the recommendation by Finney *et al*. [1] to automatically synchronise devices with the backend server, along with continual hardware advancements, could help in early identification of technical issues and, ideally, prevent them in future studies.

Ultimately, paired data from five patients were suitable for assessment of HRV, with each patient acting as their own control, as high inter-patient variability was observed. Linear mixed-effect models, incorporated with a corARMA correlation structure to account for autocorrelation, were used to analyse the average short-term night-time HRV calculated over 5-min intervals. Autocorrelation indicates that HRV intervals are influenced by previous intervals, making them interdependent [3]. Time domain measurements included the standard deviation of normal heartbeats, SD1 (measuring short-term HRV), and SD2 (measuring short- and long-term HRV). Frequency domain measures comprised low-frequency (LF) and high-frequency (HF), along with the LF/HF ratio. In the mixed-effect models (n=5), certain HRV metrics indicate a trend toward reduced HRV during exacerbation compared to stable disease (figure 1b–g). For instance, the SD2 metric is lower during exacerbation, with an estimated marginal mean difference between exacerbation and stable disease of −4.53 (95% CI −13.7, 4.61). Although this difference is not statistically significant (p=0.223), the t-ratio of 1.2 suggests a potential effect that likely did not achieve statistical significance due to the small sample size. The t-ratio shows the observed effect relative to data variability or standard error. A higher t-ratio, such as 1.2, indicates a stronger effect, implying it is probable that it will attain statistical significance with a larger sample size.

Much like the findings of Finney *et al*. [1], where a majority of patients deemed the wearable monitor device "easy" or "very easy" to use (71%) and the data "informative" or "very informative" (58%), our results suggested that, in general, patients exhibited good tolerance toward the Health Patch. The usability questionnaire for the Health Patch was completed by all but one participant during the first and/or second study visit (n=14). In two patients, some responses to the questionnaire items were missing. 85.7% of the patients reported no irritation of the skin during either period when the patch was worn (n=12). The predominant discomfort mentioned in some instances was attributed to the removal of the patch: 41.7% reported a score below 5 on a scale of 0 to 10 (0 indicating significant pain, and 10 indicating no pain). However, 91.7% of the patients (11 out of 12) expressed willingness to wear the device again if needed.

Although we identified certain trends in physiological changes in HRV between COPD exacerbations and stable disease, conclusive evidence is lacking due to a small sample size, and its clinical significance remains uncertain. Furthermore, our study highlights the obstacles of bench-to-bedside implementation of wearable digital devices. For subsequent studies, in response to the significant loss to follow-up resulting from prolonged clinical instability, we propose extending the interval between study visits and offering home visits as needed. Furthermore, future studies should consider the high dropout rate among this fragile patient population. Technical enhancements in the devices themselves should be considered to make them more suitable in this specific patient population. Throughout this study, the computer application underwent further development to clarify whether the device was measuring or not. As a next step, it would be convenient if the program clearly indicates when there is an issue with the device and what exactly this issue entails. Furthermore, as suggested by Finney *et al*. [1], enabling remote monitoring of the device during the wearing period would be helpful. After these technical improvements, a prospective study involving a larger patient cohort is warranted to evaluate the usability of the Health Patch, further

investigate the role of HRV in early detection of COPD exacerbations, and explore additional parameters beyond HRV that may serve as markers for a COPD exacerbation, for example respiratory rate variability. Considering continuous advancements and growing clinical evidence, using wearable devices such as the Health Patch could offer valuable support for managing and preventing exacerbations in the future.

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