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Risk assessment in patients with pulmonary arterial hypertension in the era of COVID 19 pandemic and the telehealth revolution: State of the art review

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Patients affected by pulmonary arterial hypertension (PAH) benefit from intensive, continuous clinical monitoring to guide escalation of treatments that carry the potential to improve survival and quality of life. During the coronavirus disease 2019 pandemic, the need for physical distancing has fueled the expeditious expansion of various telehealth modalities, which may apply in a unique manner to individuals with PAH. Performance of objective risk assessments in patients with PAH remotely via telemedical visits and other telehealth mechanisms is unprecedented and not yet rigorously validated. The uniquely high risk for rapid deterioration in patients with PAH demands a high degree of sensitivity to detect changes in functional assessments. In this review, several telehealth modalities for potential utilization in risk assessment and treatment titration in patients with PAH are explored, yet additional study is needed for their validation with the pre-pandemic care paradigm.
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The coronavirus disease 2019 (COVID-19) pandemic has posed unprecedented challenges in the management of patients with chronic diseases. Patients with pulmonary arterial hypertension (PAH) need close monitoring and serial evaluation, given their high risk for rapid deterioration, identification of which can trigger timely treatment intensification that attenuates disease progression. COVID-19 has adversely influenced the care of many patients with PAH, especially during periods in which stay-at-home policies may decrease a patient's confidence in the safety of an in-person visit. During such times, many PAH expert centers have adopted telemedical tools to evaluate these potentially complex patients. Before the emergence of COVID-19, telehealth comprised an important but generally non-dominant role in ambulatory health care. With the onset of the pandemic, the essentially instantaneous necessity of providing telehealth services to preserve physical distancing has opened the (virtual) door for remote healthcare access for many patients with PAH. Whereas telemedicine is generally used to refer to virtual visits with a health care provider,[1] the term "telehealth" may be more broadly defined as "technology-enabled health care management and delivery systems that extend capacity and access"[2].

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Telehealth also encompasses use of mobile technologies to support maintenance of health and wellness, sometimes termed mHealth. To the authors' knowledge, no study yet has demonstrated the effectiveness of the use of telehealth services to improve outcomes specifically in patients with PAH. Individuals affected by PAH rely on a uniquely aggressive multimodality evaluation at each point of healthcare contact to assess for any subtle worsening of the disease.

Current practice in the management of patients with PAH requires ongoing reassessment for risk of disease progression based on multiple types of data, including reported functional capacity, 6-minute walk test (6MWT) results, serum brain natriuretic peptide, and echocardiographic findings. Guidelines founded on the current body of evidence direct that that each patient with PAH undergo objective risk assessment during each office visit.[3–7] Although telemedical video visits (VVs) with providers may deliver ambulatory care as definitive in quality as an in-person visit for a variety of conditions, the ways in which the spectrum of telehealth services can meet the distinctive needs of patients with PAH has yet to be fully elucidated. In this review, several currently available telehealth modalities that can be utilized in the remote assessment of patients with PAH are explored, with recognition of the need for intensive further study to define and validate an optimal approach in this important population.

Impact of COVID-19 on PAH care

COVID-19 has brought unprecedented challenges to healthcare, especially in the management of chronic diseases such as PAH, which is often associated with delayed diagnosis[8] and, once diagnosed, warrants close monitoring. A recent study showed that during the mandated lockdown period, there was close to a 50% decline in new appointments for PAH evaluation, with similar reduction in the initiation of PAH-specific therapy, when compared with prior seasonally adjusted data.[9] Qaiser et al[10] recently discussed safety precautions for performing right heart catheterization for PAH evaluation during this pandemic. Another study evaluated a combination of 3 echocardiographic parameters including left atrial size, E:e' ratio, and presence of systolic interventricular septal flattening in discriminating pulmonary hypertension (PH) owing to left heart disease vs PH owing to a pulmonary vascular process.[11] The authors suggested that this information can be obtained from a routinely performed echocardiography; this may abrogate the need for travel for another echocardiogram dedicated for assessment of PAH.

Just as the diagnosis of PAH can be adversely impacted during the COVID-19 pandemic, so can the implementation of therapy. A recent survey from United States (US) PAH expert centers showed a hospitalization rate of 30% and mortality of approximately 12% in patients with PAH or chronic thromboembolic PH (CTEPH) infected with COVID-19.[12] This survey also demonstrated fewer clinic visits and increased use of telemedicine in patients with PAH, as well as decreased diagnostic testing in individuals suspected of PAH. Delayed referral, compounded with delayed assessment, has clear potential to harm the overall outcome of patients with PAH. Notably, the 12% mortality rate from COVID-19 among patients with PAH/CTEPH reported from this survey appears higher than that of the general population.[13] In contrast, in a recent commentary, Horn et al[14] speculated that PAH might be beneficial in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection because of protection provided by endothelin receptor antagonist therapy, which blocks the same angiotensin-converting enzyme 2 receptor needed for SARS-CoV-2 viral entry into the cell. Yet, critics of this hypothesis contend that it may provide false reassurance to patients with PAH who are at higher risk of poor outcomes.[15] Recent reports of COVID-19 infection affecting the pulmonary vasculature and right ventricle are intriguing, but the long-term impact of COVID-19 on PAH disease progression and outcomes has yet to be established.

Intervisit telehealth services in cardiovascular disease management

Use of telehealth services between provider visits has been widely explored in cardiovascular conditions. Although findings are generally auspicious, evidence of benefit is not uniform across prior studies of telehealth interventions in heart failure (HF), which raises concern regarding the generalizability of such interventions. Where promising evidence exists, there are logistical challenges to broad-scale implementation because of barriers in the translation of telehealth strategies into practice. In 2010, Inglis et al[16] published a meta-analysis of randomized controlled trials comparing structured phone support and/or non-invasive telemonitoring with usual care of patients with HF. Non-invasive telemonitoring interventions entailed objective review of blood pressure, weight, electrocardiograms, or rhythm strips. In this meta-analysis, both interventions resulted in a significant reduction in HF-related hospitalization. Telemonitoring reduced all-cause mortality (risk ratio: 0.66, 95% CI: 0.54−0.81, $p < 0.0001$), but phone-based support demonstrated no definite effect (risk ratio: 0.88, 95% CI: 0.76−1.01, $p = 0.08$).

Subsequently, the Telemonitoring to Improve Heart Failure Outcomes trial randomized patients recently hospitalized with exacerbated HF to a telephone-based interactive voice-response system that collected daily information about symptoms and weight, the results of which were reviewed by clinicians, or usual care.[17] This showed no significant difference between the intervention and usual care groups with respect to all-cause readmission or death within 180 days. Similarly, the Better Effectiveness After Transition−Heart Failure randomized clinical trial assessed the effectiveness of pre-discharge education, systematized telephone calls, and remote telemonitoring among patients hospitalized for HF across 6 academic medical centers in California.[18] Wireless electronic devices were used to transmit daily data, including patient blood pressure, heart rate, and weight to a nurse triage center, triggering a nurse

response if clinical attention was required on the basis of pre-defined parameters. The trial failed to show improvement in all-cause hospitalizations or mortality, but secondary analysis suggested improvement in 180-day quality of life scores because of the intervention. Another meta-analysis and systematic review by Feltner et al[19] examined 47 trials that employed telemonitoring services, phone-based support interventions, and home-visiting programs intended to prevent readmissions in patients with HF. In composite, structured phone-based interventions reduced HF-specific readmission and mortality, yet telemonitoring failed to improve 30-day readmission or 3- to 6-month all-cause readmissions.

Despite a lack of uniformity, the aforementioned studies based on remote check-ins and/or periodic vital sign telemonitoring between provider visits do support the potential benefit of these approaches in individuals with cardiovascular diseases such as HF. Continuous monitoring strategies including accelerometry and invasive pulmonary artery pressure measurement have been applied to patients with PAH and are discussed subsequently. Accelerometry devices (e.g., ActiLife, ActiGraph, LLC, Pensacola, FL) have been studied in patients with PAH, noting their potential to capture data complementary to the 6MWT, including duration of sedentary time in a patient's daily life. A single-center study using wrist-worn accelerometric devices demonstrated increased sedentary time among patients with PAH (mean: 92.1% of daily activity sedentary, $n = 20$) vs healthy controls (mean: 79.9% sedentary, $n = 30$; $p < 0.001$) over a 7-day monitoring period.[20] However, this study with small sample size and potential for selection bias likely has limited generalizability. A similar design was utilized by Zijlstra et al[21] in children, with the key finding that the accelerometric end-point of vector magnitude counts per minute was lower among children with PAH (647, $n = 29$) than healthy controls (921, $n = 60$; $p < 0.001$). On assessing the additional end-point of physical activity intensity, among categories of sedentary, light, moderate, and vigorous, the authors found that patients with PAH spent less time in moderate and vigorous activity states than controls. In post hoc analyses, vector magnitude counts per minute and time spent in combined moderate/vigorous and vigorous physical activity states were associated with poorer outcomes, such as freedom from non-elective PAH-related hospitalization, lung transplantation, or death, during the median follow-up period of 2.2 years ($p \leq 0.044$). New frontiers for telemonitoring of patients with HF include thoracic impendence assessment with remote dielectric sensing,[22] which is under investigation for home use (ReDS For Home, Sensible Medical Innovations, Ltd., Tenafly, NJ).[23] Portable impedance cardiography devices have also been applied to describe heart rate changes over time during the 6MWT in patients with PAH vs healthy controls.[24]

Although non-invasively assessed biometric and accelerometric data are obtained with relative ease, invasive monitoring such as the CardioMEMS HF system (Abbott, Abbott Park, IL), an implantable pulmonary artery pressure monitor, has also generated considerable interest among those who care for individuals with PAH. The key concept supporting the utility of this device is that measurable and actionable filling pressure elevations may long precede clinical decompensation[25] (Figure 1). Among 26 patients with PAH and New York Heart Association Class III or IV HF, the CardioMEMS HF system was safely used to monitor PAH therapy, with no apparent device-related serious adverse events.[26] Using trends of CardioMEMS HF device-generated data, the study showed significant reduction in pulmonary artery pressure and improved cardiac output as early as 1 month after implant (Figure 2). The study also showed significant improvement in functional class and quality of life scores within 1 year. Among other invasive devices, implantable loop recorders, which are widely used for arrhythmia detection, are under study for specific application to an HF population (e.g., Reveal LINQ, Medtronic, Dublin, Ireland).[27]

Overall, telehealth services have demonstrated variable success in the management of chronic HF between visits with health care providers. However, such research is lacking yet critical in PAH management in the era of COVID-

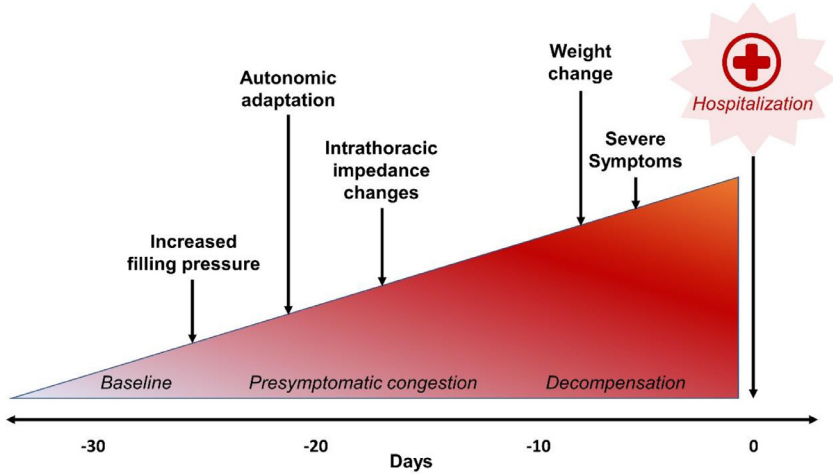


Figure 1 Framework of heart failure pathophysiology depicting an archetypal progression from baseline to pre-symptomatic congestion and eventual hospitalization for decompensation. Adapted from Adamson, 2009.[25]

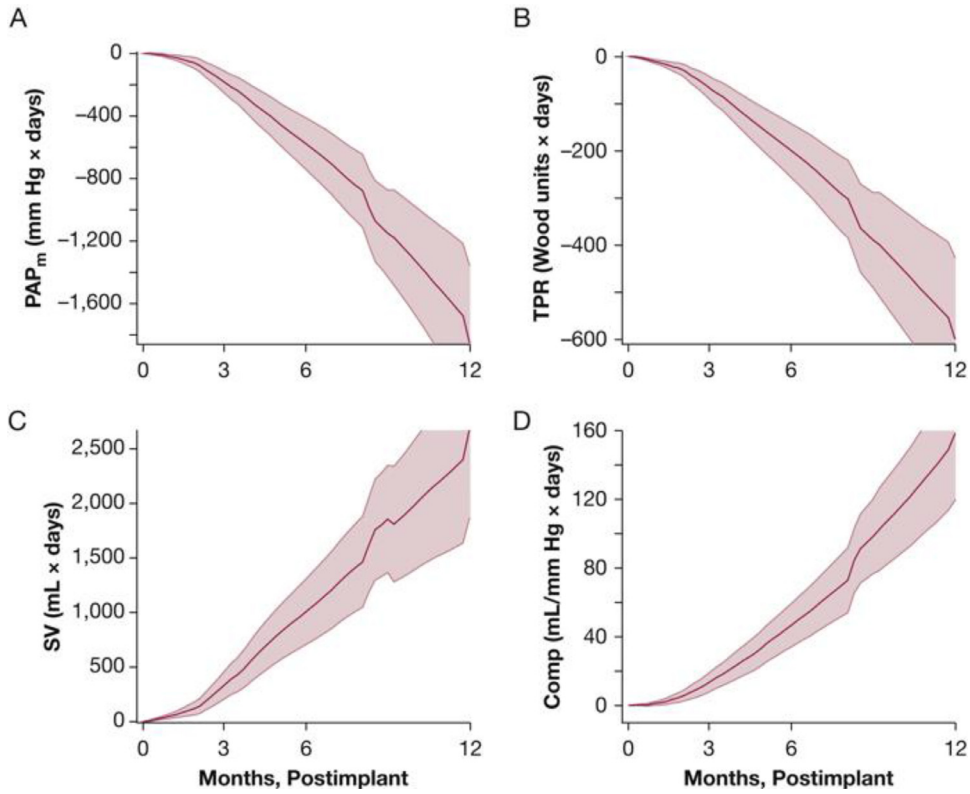


Figure 2 Cumulative hemodynamic response over time among a cohort of patients at single institution. PAP_m, TPR, right ventricular SV, and Comp are shown as mean (solid line) ± standard error (shaded envelope) of the cumulative change over time. All $p < 0.05$ at 12 months, relative to baseline. Reproduced from Benza et al, 2019.[26] Comp, compliance; PAP_m, mean pulmonary artery pressure; SV, stroke volume; TPR, total pulmonary resistance.

19, the success of which depends on the quality and depth of clinical and biometric information gathered.

History and remote physical examination during telemedical visits

A VV is a synchronous communication between a patient and healthcare provider utilizing technology that provides real-time, 2-way audio and visual interaction. Telecommunication platforms may be integrated within the electronic health record, third-party business-oriented videoconferencing mechanisms, or medically optimized solutions touting Health Insurance Portability and Accountability Act compliance, some with the option for the patient to initiate the interaction by responding to a text message invitation (e.g., Updox, Doximity Dialer Video, Doxy.me). Before the COVID-19 pandemic, such VVs were already a viable method for performing ambulatory office-based care remotely, particularly in the period after hospital discharge, with a trend toward lower no-show rates compared with traditional visits among patients with HF.[28] VVs are also demonstrably effective among Veterans Affairs patients.[29] In fact, Veterans Affairs has served as a key pioneer for telehealth advancements well before the COVID-19 era. In general, many patients find VVs convenient and appreciate access to their providers without having to incur the risk of viral exposure associated with travel or presence in a healthcare facility. Contrarily, some patients voice valid concerns regarding lack of a hands-on physical examination. Yet, healthcare providers learn much from observing the general appearance and behavior of the patient and may still capture certain findings such as the skin examination, including the appearance of wounds, catheter sites, device implant incisions, extremity swelling, or rashes; breathing patterns; and physical movement. A recent study compared the remote assessment of jugular venous pulsation (JVP), an arguably essential part of the physical examination of a patient with PAH or HF, to the bedside assessment of JVP in patients with systolic left heart failure.[30] The study showed that bedside and remote JVP estimates were comparable ($R^2 = 0.635$) and significantly correlated with invasively measured right atrial pressure, despite a lower level of confidence among the remote evaluators in their estimates. Yet, this level of confidence may have been simply because of decreased familiarity with the process of remote evaluation.

Telemedical exams may also supply information not readily available during in-person office visits, such as views into the patient's home environment (if the patient agrees to share this), including physical barriers that could increase the risk of falls such as stairs or imposing furniture. It is noteworthy that risk stratification tools (e.g., The US Registry to Evaluate Early and Long-Term PAH Disease Management [REVEAL] 2.0 and the European Society of Cardiology/European Respiratory Society) used for prognostication in patients with PAH do not include physical examination findings, although the REVEAL 2.0 does

incorporate heart rate and systolic blood pressure, which can be easily performed by a patient at home.

Although smartphones have become increasingly ubiquitous in society, many individuals remain without access to the resources needed to perform VVs. Particularly in rural communities, the availability of high-speed internet or mobile data networks may be insufficient, and regardless of population density, some individuals cannot afford to own or maintain connectivity for any camera-enabled device. Even with an operational video device, some patients may not feel confident in their ability to use it. This factor can be especially prominent under the circumstances of a medical visit subject to the time pressures of practicing medicine. Certain patients may even fear potential embarrassment or exposure of cognitive impairment if they are unable to launch a videoconference in the moment successfully. In those patients unable or unwilling to participate in VVs, audio-only telephone encounters are an alternative.

Regardless of whether video or only phone-based interaction is used, clinical history taking is essential in the ambulatory assessment of patients with PAH. Information collected during the interview helps in determination of functional capacity, informing suspicion for potential disease progression. Historical points collected during a telemedical visit should be similar to in-person encounters and focused on determination of functional capacity, presence of dyspnea or other symptoms at a given activity level, knowledge of PAH drug treatment, therapeutic adherence, and potential adverse effects, particularly in patients who are on continuous IV prostacyclin therapy. Activity assessment in patients who are spending most of their time at home can be challenging; of course, the need for physical distancing has led to increased time at home for most individuals. This effect has led to often substantial cardiopulmonary deconditioning for those who previously performed the bulk of their most physically exertional activities outdoors or otherwise removed from the home (e.g., walking or ascending stairs in workplaces, grocery stores, or other shopping environments). Notably, a recent study by Salvi et al[31] supported the 6MWT as feasible in the home environment using device-based applications, but such tools have yet to undergo validation among individuals with PAH.

The distinction between deconditioning-related dyspnea and worsening of underlying PAH is critical yet often difficult. Information about weight gain may be important, and especially if decompensation is considered imminent, serial assessment of body weight can be highly useful. Any available patient-acquired biometric data such as weight, blood pressure, oxygen saturation, heart rate, or cardiac rhythm tracings generated by wearable devices (e.g., Apple Watch[32,33]) should be incorporated, to the extent reliable. As previously noted, heart rate and blood pressure are integral elements of the REVEAL 2.0 risk prediction tool. When telemedical visits are scheduled, patients and/or their family members and caregivers may be reminded to use any available biometric devices and generally prepare for the visit as much as possible to maximize the objective information available to the provider and, in doing so, optimize the quality of care to the fullest extent achievable remotely.

Functional capacity assessment during telemedical visits

One of the most significant challenges in the evaluation of patients with PAH during telemedical visits is assessment of functional capacity. As previously introduced, in routine clinical practice, detailed history taking focusing on the patient's activities of daily living and a formal 6MWT is the guideline-supported standard of care in the longitudinal management of patients with PAH[4,6,7] and has been shown to predict long-term outcomes.[34,35] Objective activity assessment obtainable remote to a health care facility has not been standardized among patients with PAH. However, several potential options may augment the subjective assessment. The Duke Activity Status Index (DASI) was derived in 1989 to assess functional capacity in subjects undergoing cardiac exercise testing.[36] DASI is a self-administered 12-point questionnaire intended to determine the respondent's effort tolerance based on whether he or she reports the ability to complete certain physical activities. Items chosen for inclusion in the DASI tool represent a broad range of cardiovascular stressors and several dimensions of personal health status (Figure 3). Use of DASI has been validated in patients with cardiopulmonary diseases such as HF and chronic obstructive pulmonary disease.[37,38] Although not yet validated for use in patients with PAH, application of DASI or other questionnaire-type functional status measures to patients with PAH warrants further exploration.

Beyond metrics based on self-report, a possible surrogate for the traditional 6MWT is the incremental shuttle walk test (ISWT), which is an exercise test that patients can perform in a self-directed fashion.[39,40] The objective of the ISWT is to walk as long as tolerated, from start to finish of a 10-meter course and back, keeping to the speed indicated by recorded audio indicators (beeps). Each single beep signals the end of a shuttle, and each triple beep signals an increase in walking speed. The participant is directed to stop walking only when he or she becomes too breathless to maintain the required speed or can no longer keep up with the set pace. A progressive and maximal self-directed test, the ISWT has been validated against 6MWT results,[41] as have other smartphone app-based self-directed 6MWTs.[42,43] The most significant concern is assurance of the safety of the patient during testing, a factor that can potentially be ameliorated by training a family member or caregiver to supervise the patient during the test. In addition, these tests have yet to be formally validated in the home setting. Overall, functional capacity evaluation outside of a health care setting is a critical feature of PAH management in the era of COVID-19, the optimization of which requires utilization of patient-provided history and possibly functional questionnaires, self-directed exercise

Is the patient able to	
1. take care of self, i.e. eating, dressing, bathing or using the toilet?	2.75
2. walk indoors, such as around the house?	1.75
3. walk 1-2 blocks on level ground?	2.75
4. climb a flight of stairs or walk up a hill?	5.50
5. run a short distance?	8.00
6. do light work around the house, such as dusting or washing dishes?	2.70
7. do moderate work around the house, such as vacuuming, sweeping floors, or carrying in groceries?	3.50
8. do heavy work around the house, such as scrubbing floors, or lifting or moving heavy furniture?	8.00
9. do yardwork like raking leaves, weeding or pushing a power mower?	4.50
10. have sexual relations?	5.25
11. participate in moderate recreational activities like golf, bowling, dancing, doubles tennis, or throwing a baseball or football?	6.00
12. participate in strenuous sports like swimming, singles tennis, football, basketball or skiing?	7.50

The highest score is 58.2, which corresponds to 9.89 metabolic equivalents (METs).

Figure 3 The Duke Activity Status Index. METS, metabolic equivalents.

testing such as the ISWT, and potentially novel technologies, to be discussed subsequently.

Patient-reported outcomes for remote assessment in PAH

In the last few years, there has been growing evidence to support the use of patient-reported outcomes (PROs) in the management of PAH. The objective of PRO use is to assess the patient's quality of life and to involve the patient's own perspective in disease management. Patient perspective is the patient's experience of PAH and its impact on him/her and caregivers, including symptomatic, intellectual, psychosocial, spiritual, and goal-oriented dimensions of the disease and its treatment.[44] Table 1 lists some of the commonly derived and validated PROs used in the PAH population. Because PROs emphasize the patient's perception of symptoms, use of a PRO tool can provide critical information in conjunction with a telemedical evaluation. McCabe et al[45] retrospectively applied the Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR) tool on patients with idiopathic PAH (IPAH) and CTEPH to assess the predictability of clinical decline. At study enrollment, total CAMPHOR scores demonstrated a significant predictive effect on clinical decline in patients with IPAH and CTEPH (hazard ratios: 1.03 [95% CI: 1.01−1.05] and 1.04 [95% CI: 1.02−1.06], respectively, per unit score increase). In addition, CAMPHOR subscales were independent predictors of outcomes, although this effect was diluted after adjusting for the prognostic effect of 6MWT and New York Heart Association class. Moreover, serial CAMPHOR assessments did not add predictive value of clinical decline but still informed physicians of important changes in self-reported symptoms. Later, the PAH-Symptoms and Impact questionnaire was developed, which encompasses 4 symptom domains (respiratory symptoms, tiredness, cardiovascular symptoms and other symptoms) and 5 impact domains (physical activities, daily activities, social impact, cognition and emotional impact)[46]; this tool was validated in the SYMPHONY study. Data from 278 patients (79% female; mean age, 60 years) were analyzed. A total of 11 symptom items across cardiopulmonary and cardiovascular symptoms and 11 impact items across physical and cognitive/emotional areas were assessed. Analysis confirmed that PRO scoring was unaffected by oxygen use, internal consistency and reliability was high for all 4 domains (Cronbach's alpha > 0.80), and scores were highly reproducible in stable

Table 1 PAH-Specific Health-Related QoL Tools in PAH

Reference	PAH-specific QoL tool	Domains	Number of variables	Recall period
A	CAMPHOR	Overall symptoms (energy, breathlessness, mood), functioning, quality of life	65	Today
B	MLHFQ	Physical, emotional	21	4 weeks
C	LPH	Physical, emotional	21	1 week
D	CHFQ	Dyspnea, fatigue, emotional function, mastery	20	2 weeks
E	emPHasis-10	Dyspnea, fatigue, emotional function, mastery Unidimensional	10	At the moment
F	PAH-SYMPACT	Respiratory symptoms, tiredness, cardiovascular symptoms, other symptoms, physical activities, daily activities, social impact, cognition, emotional impact	41	24 h for symptoms; 7 days for impacts

Abbreviations: CAMPHOR, Cambridge Pulmonary Hypertension Outcome Review; CHFQ, Chronic Heart Failure Questionnaire; emPHasis-10, 10-question survey proposed by the Pulmonary Hypertension Association UK; LPH, Living with Pulmonary Hypertension questionnaire; MLHFQ, Minnesota Living with Heart Failure Questionnaire; PAH, pulmonary arterial hypertension; QoL, quality of life; SYMPACT, Symptoms and Impact.

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patients (intraclass correlation coefficient: 0.84−0.94). Correlations with the CAMPHOR questionnaire and the 36-item Medical Outcomes Study Short Form Survey were moderate to high (r = 0.34−0.80). The questionnaire consistently differentiated patients with varying disease severity levels and was sensitive to improvements in clinician- and patient-reported disease severity.[47]

In another study of 54 consecutive newly diagnosed patients with PAH who received first-line endothelin receptor antagonists or phosphodiesterase 5 inhibitor, a baseline Short Form-36 Physical Component Summary (PCS) score >32 was associated with a better survival rate than a score <32 ($p = 0.04$). Moreover, patients exhibiting a PCS score ≥38 after 16 weeks of treatment demonstrated a superior 3-year survival rate vs those who scored <38 on the PCS ($p = 0.016$).[48] Given the treatment-related benefits in health-related quality of life (HRQoL) observed in patients with PAH, mounting evidence implicates a future role for improved HRQoL as a prognostic marker in PAH.[49] A recent study from the Pulmonary Hypertension Association Registry showed that patients with PAH judged at high risk by COMPERA and REVEAL 2.0 risk assessment tools had a greater risk of death and hospitalization and had worse disease-specific HRQoL, as assessed by the emPHasis-10 and Medical Outcome Study Short Form-12 general physical and mental component scores.[50] Another randomized study (NCT03078907) of selexipag vs placebo in patients with functional class II PAH used accelerometry (GT9X Link, ActiGraph) and PAH-Symptoms and Impact to assess daily physical activity.[51] Although this study did not meet its primary end-point, it did provide important insight into using accelerometers and PROs in assessing activity in patients with PAH. As such, these findings are intriguing and suggest a potential role for PRO tools in management of PAH, telemedical or otherwise.

Remote monitoring using telehealth devices in PAH

Many devices that individuals may own and maintain on their persons regularly easily obtain objective measures of physical activity, the preeminent example of which is step counting. The essentially ubiquitous example of this is the smartphone. For example, the Apple iPhone harbors a Health app that summarizes step estimates derived from accelerometric and other embedded sensors, generated with movement of the device when carried.[52] Android-based and other smartphones offer similar options. However, the smartphone itself is one of a myriad of other wearable items that collect activity and other biometric information that may be linked to a smartphone or computer, devices that include not only smart watches or wrist-worn bands (examples of such manufacturers include Fitbit, Garmin, Withings, and Polar) but also a variety of technology-enabled products.[53] Examples of other novel accessories include earphones, necklaces, hats, and even smart shirt garments, most of which provide some combination of biometric data

such as steps taken, heart rate, and respiratory variability. Much of the available new and often pricey technology is marketed toward individuals with high physical functioning and adequate discretionary financial resources. However, in the coming years, the wearable boom will undoubtedly result in new products, the data output from which providers can harness for the management of individuals with PAH and other chronic cardiopulmonary diseases.

Biometric data collected by personally owned devices, often even without the awareness of the wearer/user, constitute a vast untapped resource in the management of individuals with cardiovascular disease. Most healthcare systems currently lack the infrastructure for healthcare providers, nurses, and other staff to access and utilize the wealth of biometric information being stored on personal devices. To present a clinical example, consider a 40-year-old woman with chronic PAH who at baseline is managed on oral therapy and has Class II symptoms; she owns a smartphone and wears a smart bracelet (e.g., Fitbit) most of the time, which measures her steps and heart rate continuously. In March, she stopped walking her dog as regularly and avoided shopping for groceries herself because of perceived risk of SARS-CoV-2 exposure, for which reason she also rescheduled her routine follow-up visit with her PAH provider. In May, she found herself with increased swelling and then breathless while dressing or cleaning dishes; later, she was hospitalized in June with syncope. It is likely that this patient's healthcare providers would have observed several key biometric trends over the months of decompensation, had the data from her smartphone and smart band (e.g., Fitbit) been available for review. For example, decreased step count, increased resting heart rate, decreased heart rate variability, and (if assessed/recorded) increased body weight may have developed (Figure 4). Slow and subtle changes in such parameters that may be imperceptible to the patient may be uncovered by automated analysis or machine learning, and significant deviations could potentially generate notifications to health providers.

The process of regular integration of such biometric mHealth data into the electronic health record of the patient's medical home is now feasible and in clinical use at certain institutions (e.g., MyChart Fitness Tracker, Epic Systems, Verona, WI). Often, biometric data are combined from various sources into a centralized interface (Table 2). For example, the user's primary smartphone mHealth application (e.g., Apple Health, Google Fit) collects and summarizes data from internal sensor sources and may integrate with output from any other smart devices or wearables that the user has linked. With the user's permission, the mobile application specific to the patient's health system (e.g., MyChart mobile, Epic Systems) can access the mHealth data and generate applicable summaries or alerts at the discretion and order of the managing healthcare provider. Commercial third-party, web- or app-based solutions providing interactivity between mHealth data and care providers are also available (e.g., Tholomeus).[54] Regular

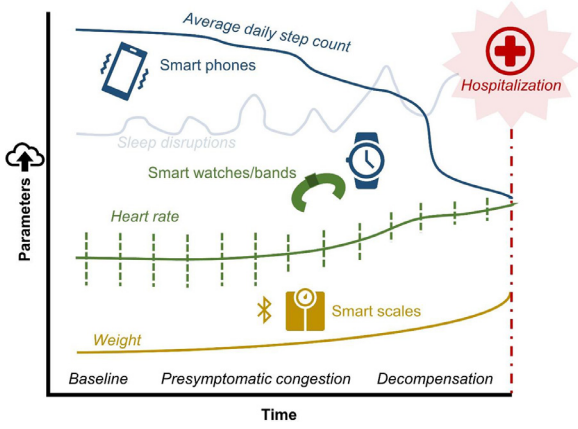


Figure 4 Conceptual diagram depicting the potential for technology-enabled devices to track and identify disturbances in biometric data before a decompensated state of cardiovascular disease.

Table 2 Examples of Biometric Parameters Used in MHealth and Potential Consumer-Marketed Data Sources for Each

Parameter	Potential sources of data
HR: Average resting, min, max, variability	Smart watch or band with photo-plethysmographic sensor Other wearable device or clothing (e.g., ring, pendant, shirt, chest band, earphones) Manual entry from unlinked BP cuff or pulse oximeter
BP	Smart/linked BP cuff, wrist or arm Manual entry from unlinked BP cuff
Step count; distance ambulated	Smart watch or band acquiring accelerometric and/or GPS data Smartphone (carried for sufficient duration of day/period of physical activity) Other wearable device or clothing (e.g., ring, pendant, shirt, earphones) Manual entry from unlinked pedometer/step counter
Oxygen saturation	Smart pulse oximeter Manual entry from unlinked pulse oximeter
Sleep pattern	Smart watch, band, or other wearable worn during sleep
Cardiac rhythm	Smart watch or band with appropriate capability (e.g., Apple Watch) Non-worn/intermittently applied smart device (e.g., AliveCor KardiaMobile)

Abbreviations: BP, blood pressure; GPS, global positioning system; HR, heart rate; min, minimum; max, maximum.

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use of such mHealth data integration has been pioneered by several institutions[55] and is now undergoing rapid dissemination, with applicability to many patients with PAH.

Even an act as seemingly simple as serial assessment of body weight can be potentially optimized by emerging smart technologies. Patients who weigh themselves daily may or may not record the result, and fewer still might have the log of serial weights available at the time of an in-person or telemedical visit. Use of scales that automatically record; store (e.g., via Bluetooth bridging with the patient's smartphone); and, with the process described above, link the results of serial body weight measurements can greatly improve the ability of providers to act on the data, such as via diuretic titration or guidance regarding dietary sodium or fluid intake restrictions. The same concept applies to pulse oximetric data as well. In addition, patients with PAH with comorbid arrhythmias can potentially benefit from use of cardiac rhythm monitoring devices, particularly when there is low arrhythmia awareness or if distinguishing between low-grade ectopy and sustained arrhythmias such as atrial fibrillation is clinically challenging and management-defining. Smart watches or bands and external periodically activated devices (e.g., AliveCor KardiaMobile) may serve this purpose (Table 2). A study evaluating clinical outcomes using simultaneous digital tracking of daily physical activity, heart rate, and inhalation behavior in patients with PAH treated with inhaled iloprost is underway.[56] This provocative study will provide insight into clinical outcomes, daily physical activity, and quality of life in patients with PAH and inform future research on wearable technology in this population.

Overall, although copious, data obtained from personal, consumer-marketed devices should be vetted with ongoing study to ensure adequate validity to support medical decision making. Even if data such as step count or distance walked are not perfectly accurate on an absolute basis, evaluation for trends may still be extremely informative on an individualized level, where each patient may serve as his or her own internal control. As previously discussed, medically validated and/or implantable monitoring devices may be complementary in certain situations.

Pragmatic challenges and potential barriers

With the advent of widespread telemedical provider visit use during the COVID-19 pandemic, in the US there existed considerable initial uncertainty regarding the reimbursement support for such service. In the first several months of pandemic-related telehealth expansion, there existed a striking differential in reimbursement and provider work credit for telephone-only vs VVs. For example, a telephone check-in for an established patient (code G2012), defined as a 5−10 minute audio call not related to another service in the preceding 7 days nor necessitating the next available in-person service, would receive 0.25 work relative value units (wRVU). This can be contrasted to established level 3 or level 4 VVs, which by submitting the E/M code commensurate for the complexity of medical decision making and a telehealth modifier, garner 0.97 (99213) and 1.5 (99214) wRVU, respectively, which are currently equivalent to the in-person visits. For new patients, the discrepancy was wider still. Such structure strongly incentivized performance of VVs in place of an audio-only call, and thus patients with no reliable access to VV technology could have been subject to their provider experiencing financial pressure to shorten their sessions. Consequently, even if a longer evaluation were medically indicated, the lack of a known mechanism to reimburse for the more thorough care could result in a suboptimal service. Fortunately for patients in such a situation, on April 29, 2020, Centers for Medicare and Medicaid Services announced increased reimbursement for longer periods of telephone-based care,[57] including codes 99442 (11−20 minutes) and 99443 (21−30 minutes) which had previously been covered by some private payers; the changes, retroactive to March 1, 2020, resulted in increased reimbursement for telephone-based encounters from approximately $14−$41 to $46−$110.[58] Such a maneuver may help resolve the previously perceived telephone time reimbursement ceiling and promote enhanced patient-provider telemedical interactions. Suggested legislation to ensure some, if not equivalent, reimbursement for telemedical evaluation and management visits has been introduced.[59,60]

Although current technology supports essentially effortless high-quality audiovisual communication between individuals who may be geographically remote, in the US, providers practicing across state lines must cautiously navigate the issue of state licensure requirements. Many state medical boards have allowed ad hoc practice of medicine for their residents by providers licensed in other states during the COVID-19 public health emergency without any additional medical board correspondence or documentation; others require at least provider registration of the out-of-state medical license, whereas still others inflexibly require the standard licensing procedures. For patients who routinely traverse state lines to receive medical care, this phenomenon may strain ongoing healthcare access with their established medical home.

Even when the stringency of physical distancing and personal protective equipment use can be relaxed in the future, telemedical visits will likely forever remain a more prominent aspect of medicine, with an inextinguishable benefit of mitigating transportation barriers for many patients, including those with PAH and HF. Some providers and patients may consider a model in which in-person and telemedical visits are rotated or interspersed based on each patient's individual needs (including the reason for visit and anticipated magnitude of benefit of an in-personal physical examination for the visit objective), transportation efforts, and technological device and network access and ease of utilization.

Beyond telemedical providers' visits, the method in which providers and health systems receive reimbursement for review and action based on patient communication within a secure portal or mHealth biometric data continues to evolve. There is currently a billing structure for the time, effort, and expertise that providers invest in responding to

and managing medical issues resulting from correspondence volunteered by patients via secure messaging portals. Codes 99421, 99422, and 99423 reimburse the provider for 5−10, 11−20, or 21 or more minutes, respectively, of time spent in evaluating and managing complaints described by established patients within secure messaging (over a 7-day period) and result in 0.25−0.80 wRVU. Such a fee structure can provide a helpful paradigm for patients who may need considerable support navigating medical concerns between provider (in-person or synchronous telemedical) visits, such as individuals with PAH. By utilizing this method of care as a billable service, providers may feel more comfortable justifying extended time, as appropriate, to evaluate and respond to patient concerns thoroughly. Patients should be notified of and consent to such billing, as with telemedical visits and in-person care. Finally, regarding mHealth data review, there is also a method in which providers may be reimbursed for "collection and interpretation of physiological data (e.g., ECG, blood pressure. . .)" (code 99091) requiring a minimum of 30 minutes of time. Undoubtedly, care systems and payers must continue to evolve and adapt to provide adequate reimbursement for review of mHealth data that can be leveraged to optimize patient care.

Conclusions

Patients with PAH represent a unique population of individuals in whom subtle changes in functional status may associate with impactful changes in prognosis. In this era of increased physical distancing to decrease infectious risk, patients, providers, and health systems must embrace novel methods of providing medical care. Synchronous telemedical visits should thoroughly evaluate aspects of symptomatology that could signal disease progression, and augmentation with standardized assessments such as DASI and various PROs may be complementary in some cases. Self- or caregiver-directed functional tests such as the ISWT or smartphone app-based 6MWT may provide objective functional assessment when presentation for a formal 6MWT is not feasible. A wealth of physiological data, oftentimes already being collected by the personal devices of patients with PAH (in particular, smartphones and smart watches/bands) such as step count, heart rate, blood pressure, body weight, and/or oxygen saturation, usually remains obscured from the view of healthcare providers. This issue necessitates rapid evolution in healthcare systems coupled with patient and provider education to harness the vast source of mHealth data to identify changes that could indicate disease progression and trigger therapeutic intensification, in particular among patients with PAH and other cardiovascular diseases.

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