

# Wearable Devices in Pulmonary Arterial Hypertension: What Are We Trying to Learn?

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**Background:** Wearable technologies (accelerometers) are currently being evaluated as an alternative to the 6-minute walk test as an objective measure of functional status in pulmonary arterial hypertension (PAH). Multiple observational studies incorporating accelerometers have shown patients with PAH have low physical activity (PA) time.

**Implications for clinicians:** Despite widespread use of accelerometers, PA has not been shown to increase after adding vasodilator therapy, which suggests a behavioral component influencing activity. A decrease in PA from baseline may identify clinical worsening and someone at risk for future hospitalization. *Cardiac Effort*, the number of heart beats used during the 6-minute walk test/6-minute walk distance (beats per meter), has less variability than 6-minute walk distance and provides a comparable clinic measurement in the home setting. *Cardiac Effort* may provide a better remote measurement than changes in total daily activity when evaluating for clinical improvement.

**Conclusions:** The amount and duration of PA achieved in patients with PAH is likely related to a combination of right ventricular (RV) function, deconditioning, and environmental factors. Strategies to target all aspects are needed to improve PA. Further studies are needed to determine the optimal remote measure and monitoring period.

Pulmonary arterial hypertension (PAH) is a progressive vasculopathy that results in reduced cardiac stroke volume and impairment in gas exchange.<sup>1</sup> As a result, dyspnea on exertion and fatigue are often the first presenting symptoms. As PAH progresses and symptoms worsen, physical activity (PA) decreases, and deconditioning along with skeletal muscle dysfunction also contribute to worsening symptoms.<sup>2,3</sup> The 6-minute walk test (6MWT) is a commonly used test to monitor and objectively assess functional capacity in PAH<sup>4</sup>; 6-minute walk distance (6WMD) has significant prognostic value and is included in the major contemporary risk assessments.<sup>5,6</sup> Changes in 6MWD can also be helpful in detecting clinical improvement.<sup>7</sup> Variability in longer 6MWD can make detecting functional improvement difficult because the day-to-day variation may

equal or exceed improvements expected with therapeutic change.<sup>8,9</sup> During the pandemic, telemedicine and concerns about respiratory exposure decreased the number of 6MWTs performed. This accelerated already growing interest in using wearable technology to measure changes in PA as an alternative to 6MWT.

Wearable devices can measure multiple different parameters including PA, sleep, heart rate, oximetry, and respiratory rate.<sup>10</sup> They are being used in disease monitoring and screening as well as in outcomes assessment.<sup>10</sup> Accelerometers (to measure PA) passively collect data and can be attached to different areas of the body. In PAH, wearable devices have been primarily worn on the wrist,<sup>11–14</sup> hip,<sup>13,15,16</sup> chest and thigh,<sup>12,17</sup> and arm.<sup>18</sup> Activity counts are determined by changes in acceleration during a period

of time (epoch, typically 60 seconds); proprietary algorithms transform counts into activity classifications.<sup>19</sup> One of the most popular activity count classifications was developed on healthy individuals wearing a hip-based accelerometer walking on a treadmill.<sup>20</sup> The wrist- or hip-worn Actigraph has been the most widely used accelerometer in research with over 20 000 publications<sup>19</sup> and is commonly used in PAH.<sup>12–16,21</sup> Unfortunately, different proprietary algorithms between commercially available devices makes comparing output (step counts and activity time) extremely difficult.<sup>12,22</sup> Calculating vector magnitude ( $\sqrt{x^2 + y^2 + z^2}$ ) and mean amplitude deviation are 2 emerging ways to analyze postprocessed acceleration data.<sup>13,15,17</sup>

Physical inactivity remains a significant problem in the United States, with less than half of adults meeting the Centers for Disease Control and Prevention (CDC) and American College of Sports Medicine (ACSM) activity recommendation (>150 minutes of moderate intensity aerobic activity, 3.0–5.9

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metabolic equivalent (MET), every week and strength training 2 or more days per week). Specifically, above 65 years old, PA levels decrease, with 61% of adults not meeting the CDC-ACSM recommendation and classified as physically inactive.<sup>23</sup> Light PA is classified as activities between 1.5 and 3 METs<sup>24</sup>; sedentary behavior is defined as <1.5 METs,<sup>25</sup> ie, sitting and watching television. It is possible to achieve the CDC-ACSM PA recommendation and spend a significant amount of time in sedentary behavior. Many accelerometers use METs as criteria for activity classification. It is worth highlighting that a 6MWD of 320 m (2 miles/h) would be classified as light activity even though, for some PAH patients, this exertion is at their physiologic limit. In that instance, they would never cross the threshold to moderate PA with an accelerometer because a walking speed of 3 miles/h (~480 m 6MWD) would be needed to generate enough activity counts. Since the 6MWD is the most physically demanding activity most patients do, baseline 6MWD may provide a rough estimate of what someone will do with home monitoring. External factors, such as anxiety and depression, likely influence PA level in a chronic disease state.<sup>26</sup>

Accelerometers have been used in PAH for over a decade. The initial reporting used an arm-based biaxial accelerometer and showed PAH patients had decreased daily steps and activity time compared with a control cohort.<sup>18</sup> A second report then found PAH patients had very high sedentary time measured by a hip-based accelerometer.<sup>15</sup> Since then, multiple observational studies have shown that PAH patients have low PA time measured by multiple different types of accelerometers worn on different areas of the body (Table 1). It also appears that scleroderma PAH patients also have less PA time than idiopathic PAH.<sup>18,3</sup> In contrast, 1 Spanish cohort of PAH patients had a high percentage (61%) of patients meeting the >150 minutes of moderate PA time.<sup>21</sup> Many patients with PAH are deconditioned at time of diagnosis from months of progressive symptoms; anecdotally, our patients report that ignorance about how to start an exercise program safely leads

to further deconditioning and persistent, often disabling, symptoms of dyspnea or fatigue even once they have begun effective therapy.

There have been few reports on the reproducibility of activity measurements in stable compensated patients with PAH.<sup>16,27,28</sup> Matura et al<sup>16</sup> used a hip accelerometer and found no difference in activity parameters when comparing two 1-week intervals within a 4-week period. Using a wrist accelerometer, Hemnes et al<sup>11</sup> suggested a Hawthorne effect as patients increased their activity during the initial monitoring period. They show how activity dropped over time, perhaps because they forgot about the device. To account for that, those authors excluded the first week of monitoring and used the second week to assess for changes. They found no change in activity after 12 weeks of monitoring in the control group. In the Effect of Selexipag on Daily Life PA of Patients with PAH (TRACE) study, using a wrist accelerometer, researchers found no change in a 14-day average (each monitoring period) after 24 weeks of placebo control.<sup>14</sup>

Accelerometers can be worn on multiple locations on the body. Wrist-based devices are the most used in research<sup>10</sup> and likely provide higher compliance and patient acceptance. Truncal monitoring (hip, chest, or thigh) logically produces information with less noise introduced by isolated forearm movements. We found that, in patients with PAH, there is significant discrepancy in PA time and daily steps measured when simultaneously wearing a chest or thigh and a wrist accelerometer. Surprisingly, we found wrist-based measurements correlated strongly with PAH variables of interest, which suggests that patients may use their arms to accomplish activities of daily living.<sup>12</sup> Further studies are needed on the best location for monitoring in PAH, balancing patient acceptance and meaningful data.

Accelerometer reported measurements (activity time, intensity, and daily steps) are associated with PAH variables of interest, specifically criteria included in risk scores. Not surprisingly, authors of multiple studies have shown a strong correlation between baseline 6MWD and PA (Table 1). Daily steps also have

a very high correlation with 6MWD,<sup>11,14</sup> while steps and PA time also associate with functional class. It would seem reasonable that PA might be related to right ventricular (RV) function. The data are mixed on NT-pro BNP and RV function correlating with activity parameters (Table 1).

Authors of 2 reports assessed activity in patients with PAH during the COVID pandemic.<sup>12,30</sup> The first used a pedometer to measure steps. They classified activity as low or moderate to high using 5000 steps as a cutoff. Interestingly, patients segregated almost equally into the 2 classifications; there was no difference in NT-pro BNP between groups, and the low activity group had an impressively high 6MWD of 503 m.<sup>30</sup> In our cohort, we also found low PA time and daily steps; NT-pro-BNP was correlated ( $r = -0.50$ ) with total PA time but even stronger with patient-reported inactivity time ( $r = 0.76$ ).<sup>12</sup> While it seems clear that physiologic capacity (RV function) influences PA, behavioral factors also influence PA.

There are few longitudinal observational studies in which authors evaluate PA and daily steps in patients with PAH. Marvin-Peek et al<sup>29</sup> used a wrist accelerometer and found daily steps were negatively correlated with clinical worsening. Interestingly, they found 6MWD was not associated with clinical worsening; higher daily steps and longer 6MWD were associated with maintenance of functional class. Sehgal et al<sup>28</sup> found in their cohort that a decline in activity occurred over 4 weeks preceding hospital admission. Both studies suggest there may be an opportunity to intervene and prevent hospitalization if providers recognize a decline in activity. The Pulmonary Hypertension Association Registry (PHAR) is now incorporating physical activity in PAH (AC-TiPH) as an ancillary study.<sup>31</sup> One goal of the study is to evaluate home activity monitoring on adult and pediatric participants in PHAR with accelerometers every 6 months to determine whether PA is associated with health care utilization and/or outcomes in PH.

Accelerometers are also being used to assess for clinical improvement in PAH.<sup>11,13,14,32</sup> Unlike 6MWD, a mean-

**Table 1.** Studies Incorporating Activity Monitoring in PAH

Reference	No. patients	Age (y)	SPD or PA time (min/%)	6MWD (m)	FC (II/III)	NT-pro BNP	Activity correlation		
							RV	QOL	6MWD
Mainguy et al <sup>18</sup>	25 total		Step: 5041 (3357) 3234 (2437)			NA	No	NA	Yes
	Idiopathic: 15	47 (15)		401 (89)	11/4				
	CTD: 10	58 (10)		349 (129)	5/5				
Pugh et al <sup>15</sup>	20 total Idiopathic: 7 CTD: 7	54 (14)	Sedentary: 92% Light: 6.8% Moderate: 1.1% >3 METs: 7.5 min	NA	10/7	NA	No	NA	Yes
Matura et al <sup>16</sup>	15 total Idiopathic: 5 CTD: 4	51 (16)	Sedentary: 611, 84% Light: 73, 10% Moderate: 18, 2%	413 (66)	12/3	216 (65, 531)	NA	Yes	Yes
Cascino et al <sup>27</sup>	35 total	61 (12)	Steps: 4391 (2442)	460 (107)	NA	NA	NA	Yes	Yes
Sehgal et al <sup>28</sup>	30 enrolled with 23 having usable data.	50 (13)	Steps: 5847 (3321)	401 (102)	14/11	268 (85, 754)	No	Yes	Yes
Minhas et al <sup>13</sup> (Phantom)	55 total Idiopathic: 27 CTD: 13	61 (10)	Steps: 3860 (2830) Sedentary: 610 (508–680) Light: 165 (131–190) Moderate: 8 (2–13) VM: 355 600 (158 400)	424 (113)	35/16	NA	Yes	Yes	Yes
Minhas et al <sup>13</sup> (Penn)	60 total Idiopathic: 30 CTD: 18	50 (18)	Steps: 7960 (2710) Sedentary: 333 (255–396) Light: 236 (207–260) Moderate: 16 (12–29) VM: 1 860 000 (613 800)	403 (129)	28/27	NA	No	No	Yes
Lachant et al <sup>12</sup>	22 total		Steps: 3254 (5781)				No	No	Yes
	Treatment naïve idiopathic 4/CTD 2	61 (13)		395 (229, 429)	3/3	1827 (112, 3852)			
	Treatment intensification idiopathic 3/CTD 2	53 (17)		377 (152, 498)	1/5	2029 (50, 3845)			
	Stable idiopathic 6/CTD1	53 (15)		381 (352, 459)	10/0	214 (137, 360)			
Gonzalez-Saiz et al <sup>21</sup>	75 total Idiopathic: 31 CTD: 13	48 (14)	Sedentary: 600 (125) Light: 137 (61) Moderate: 30 (21)	NA	15/22	510 (904)	No	NA	NA
Marvin-Peek et al <sup>29</sup>	41 total	47 (40–57)	Steps: 4656 (3649–6256)	427 (360, 480)	26/15	NA	No	NA	No

Abbreviations: 6MWD, 6-minute walk distance; CTD, connective tissue disease; FC, functional class; MET, metabolic equivalent; NA, not applicable; PA, physical activity; PAH, pulmonary arterial hypertension; QOL, quality of life; RV, right ventricular; SPD, steps per day; VM, vector magnitude count.

ingful change in PA or steps is not yet known in PAH. Authors are using different devices and location, making comparisons difficult. They also have different criteria for acceptable wear time. The largest clinical trial to date that incorporated activity as an endpoint in PAH is the TRACE study.<sup>14</sup> After 24 weeks of placebo-controlled selexipag, authors found no significant change in nonsedentary (light) PA, moderate to vigorous PA, or steps per day (Table 2). They also found no change in 6MWD, NT-pro BNP, or PAH-Symptoms and

Impact scores. In contrast, Hemnes et al<sup>11</sup> evaluated the effect of a behavioral intervention on increasing activity. After 12 weeks, they found the intervention group increased steps more than the control group (Table 2). Interestingly, there was no difference in 6MWD. This suggests there may be a strong behavioral aspect to activity in PAH; pharmacologic interventions alone may not be enough to increase PA even if capacity for PA is increased. Dr. Evan Brittain<sup>33</sup> is now evaluating whether incorporating customized text messages

of encouragement based on daily activity improves health-related quality of life in PAH in the study MOBILE Health InterVENTion in PAH (MOVE PAH). In this single-centered study, instead of just monitoring activity, they are using Fitbit Application Program Interface to create encouraging text messages that will be sent 3 times/day based on the current daily activity metrics. One hundred stable patients with PAH will be randomized to receive the text intervention or not for 24 weeks. Interestingly, the outcomes being assessed are

**Table 2.** Clinical Trials Incorporating Activity Monitoring in PAH

Author	No. Patients	Age (y)	Steps/day or PA time, min (%)		6MWD (m)	FC (II/III)	NT-pro BNP/BNP	Activity correlation		
			Baseline	Change				RV	QOL <sup>a</sup>	6MWD
Howard et al <sup>14</sup>	Selexipag: 53 Idiopathic: 40 CTD: 8	49 (15)	Sedentary Koster: 394 (101)	1.1 (-16, 18)	453 (130)	33/20	207 (36, 9811)	NA	NA	Yes
			Freedson: 666 (102)	-13.3 (-33, 6)						
			MVPA: 118.5 (58)	0.3 (-9.1, 9.6)						
			11.5% (5.5)	0.3 (-0.7, 1.2)						
			Steps: 3729 (2327)	0.3 (-317, 316)						
	Placebo: 55 Idiopathic: 42 CTD: 10	50 (14)	Sedentary Koster: 397 (122)	-17 (-33, 0.04)	450 (99)	41/14	162 (16, 3871)	NA	NA	NA
			Freedson: 651 (115)	-27 (-46, -8)						
			MVPA: 115 (67)	-2.0 (-11, 7)						
			11% (6)	0.3 (-0.6, 1.2)						
			Steps: 3238 (2038)	-202 (-512, 109)						
Hemnes et al <sup>11</sup>	Intervention: 20 Idiopathic: 13 CTD: 3	47 (41-54)	Steps: 4611 (3322, 8619)	1409 (-32, 2220)	431 (396, 456)	15/2	28 (10, 54)	NA	NA	NA
			Total activity: 227 (128-325)	10 (-36, -58)						
			Moderate: 4.3 (1.8, 13.3)	1.6 (-5.1, 16.1)						
	Control: 22 Idiopathic: 18 CTD: 4	47 (36-58)	Steps: 4709 (3795, 6135)	-149 (-1010, 735)	442 (362, 494)	12/3	53 (16, 90)	NA	NA	NA
			Total activity: 216 (184, 254)	-16 (-44, 29)						
			Moderate: 3.4 (0.3, 10.9)	-0.6 (-4.5, 1.4)						

Abbreviations: 6MWD, 6-minute walk distance; CTD, connective tissue disease; FC, functional class; MVPA, moderate vigorous physical activity; NA, not applicable; PA, physical activity; QOL, quality of life; RV, right ventricular function.

<sup>a</sup>Both studies collected QOL data but did not compare it to activity.

changes in Short Form Survey (SF-36), emPHasis-10, change in a supervised home-based 6MWD and Borg Dyspnea Score, resting heart rate, and time to clinical worsening. This strategy of incorporating real-time monitoring with text messaging may prove to be a better strategy to improve mobility in PAH.

We are clearly in our infancy in studying accelerometers to measure PA in PAH. Commonly used algorithms were primarily developed on a young healthy population,<sup>20</sup> and the thresholds used to classify activity may be inappropriate to use in a group of PAH patients. The step count feature may not be accurate in patients with altered gaits (eg, scleroderma) or patients who require a walker or oxygen. There are still many unknowns about the best device or location and the wear duration (per day and

days per period). Some agreement and conformity will be required, or it will be very hard to compare results from different studies. We are also still determining which features of PA are most stable, most sensitive to a (favorable) therapeutic change, and most predictive of a clinical event. Wrist-based devices likely have a higher compliance rate than truncal devices but will report more isolated forearm movement in the measurements. It remains unclear whether this is good or bad.

In the past, the 6MWT was performed routinely with clinic or research visits. During the pandemic, investigators studied a home 6MWT on an outside 30 m walking space with a team member monitoring it remotely.<sup>34</sup> While an important proof of principle, this approach is probably not scalable. We

have previously reported on a strategy to heart rate monitoring continuously during the 6MWT and measure cardiac effort (CE),<sup>17,35,36</sup> which is the (number of heart beats used during the 6MWT)/6MWD (beats/m). Cardiac effort is more reproducible than 6MWD, tracks with clinical improvement, and correlates with RV function.<sup>35,36</sup> We have also found that a chest-based electrocardiogram heart rate monitor is more accurate and has less data loss than wrist-based devices that incorporate photoplethysmography.<sup>17,35</sup> Using a combination of chest accelerometry and electrocardiogram heart rate monitoring, we had patients perform unsupervised 6MWTs in the home setting on a variable-length course of their choosing.<sup>17</sup> The median walking length was 40 feet. We found that 6MWD was lower in the

home setting (than clinic), but after adjusting for heart rate, CE was reasonably similar to that measured in the clinic. Cardiac effort allows for a measurement that can be repeated frequently at home and compared with values from clinic. This could help with drug titration and identify clinical worsening. Given the behavioral factors, which seem to affect PA measures, a standardized test like CE may home in on physiologic limitations or improvements related to RV function with less burden (no requirement to wear a device all the time).

Finally, the data illustrating the behavioral component for reduced PA in PAH patients suggest an opportunity for meaningful intervention. Novel strategies, such as the electronic encouragement studied by Hemnes et al,<sup>11</sup> are likely useful to help improve PA in patients. We as providers can also be sources of encouragement: the PHA sponsored a set of professionally produced exercise videos (5 Videos To Safely Start a Home Exercise Routine) to help promote PA, aerobic conditioning, and strength in patients with PAH who were unable to attend pulmonary rehabilitation.<sup>37</sup> Perhaps wearable devices could be used to design remote rehabilitation programs to push patients toward safe limits and allow them to track their progress toward more PA (and perhaps better quality of life).

In summary, PA is low in our patients, and the available evidence suggests that this is at least in part due to physiologic limitations (RV function). We have much to learn about how to study PA, and there is clearly a behavioral component to reduced PA which will confound attempts to use PA as a measure of clinical improvement in therapeutic studies. Standardized home exercise testing (with CE as the measure) may be closer to the heart of the matter in terms of studying physiologic limits and the risk for clinical worsening, but wearable devices could help us disseminate and measure exercise interventions which could be of real value to our patients.

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