



6-minute walk test variability may be reduced by a structured training and monitoring program, potentially facilitating detection of treatment effects



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BACKGROUND

The 6-minute walk test (6MWT) is well established for evaluation of functional exercise capacity in patients with conditions such as pulmonary hypertension, peripheral arterial disease and heart failure. Its popularity as an endpoint in heart failure trials has increased in parallel with health authority acceptance of the test as a measure of patients' function. Minimizing variability is key to the successful conduct and outcome of trials with 6MWT endpoints. We assessed the impact on walking distance variability of a structured training and monitoring program.

METHODS

After systematically observing conduct of 6MWT worldwide, our core lab developed a multifaceted approach including inspection and standardization of the walking course, standardized training, review of the first 3 tests for each test administrator and random tests thereafter, standardized data collection methods, and assessment of intra-test inconsistencies with feedback. Variability of walking distance using this structured approach is descriptively compared with 6MWT data from the literature.

RESULTS

In a multicenter trial which used the structured program, the standard deviation (SD) of distance walked was 21.7% of the mean at baseline and 22.6% at Week 4 (Table 1); least squares mean standard error was 4 meters (m).

For comparison, we reviewed 2018-19 reports of 6MWT not utilizing this structured approach and identified 5 multicenter studies of patients with heart failure which reported mean and SD of distance walked (Table 2). Baseline distance walked ranged from 104 to 385 m (weighted mean 220.4 m); SD of distance walked ranged from 28% to 135% of distance walked (weighted mean 70.9%).

Table 1. Distance walked by placebo-allocated subjects in a multicenter study utilizing the structured training/monitoring program (EQuIP®) compared with historical data

	With structured program (n~100)		2018-19 Historical weighted average	
	Mean distance walked (SD), m	SD% of Mean	Mean distance walked (SD), m	SD% of Mean
Baseline	337.4 (73.14)	21.7%	220.4 (56.0)	70.9%
4 weeks	345.4 (78.16)	22.6%		
Change from baseline	8.0 (40 .11)			

Table 2. Summary of 6MWT in patients with heart failure reported 2018-19 in EMBASE

	n	Mean baseline		
		distance walked (m)	SD	SD% of mean
CoQ10	123	321	90	28.0
LVAD registry	319	104	140	134.6
Ferric carbomaltose	436	271	107	39.4
IV iron replacement in pts with LVAD	33	231	115	50.0
Testosterone	15	385	107	27.8

LIMITATIONS

- Considerations when comparing trial data to the literature:
- Single vs multicenter
 - Sample size
 - Extent of functional impairment (distance walked)
 - Impact of underlying disease, eg ataxia, neuropathy, pulmonary manifestations
 - How variability is reported

CONCLUSIONS

- Standardization of the 6MWT walking course, structured training of test administrators and monitoring of test quality may reduce test variability which could improve accuracy of treatment effect assessment and possibly require smaller sample sizes
- A randomized comparison vs usual conduct is needed

DISCLOSURES

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