

Virtual visits to optimize research trial offerings to heart failure patients



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BACKGROUND Clinical trials are crucial for development of new treatments that impact outcomes. Assessments used in heart failure trials include the 6-minute hallway walk test (6MWT) and timed up and go test (TUG).

OBJECTIVES We hypothesized that 6MWT and TUG performed virtually would be feasible and comparable to in-person functionality testing for heart failure patients.

METHODS This pilot study explored the use of virtual visits to collect functional information on patients living with heart failure. Patients were enrolled in an outpatient setting. Informed consent was obtained. Baseline testing consisted of patient-reported New York Hospital Association class, quality-of-life surveys (EQ-5D-5L, Kansas City Cardiomyopathy Questionnaire [KCCQ], Frailty Index for Elders), and cognitive assessments (Mini-Cog). Patients also completed an in-person TUG and 6MWT at baseline. Patients were issued supplies to set up TUG/6MWT courses at home. Follow-up video visits occurred 7 days and 14 days (\pm 3 days) postbaseline. Surveys (EQ-5D-5L, KCCQ, Frailty Index), TUG, and 6MWT were completed. Study staff reviewed 6MWT/TUG course set-up for accuracy and supervised patients during testing.

RESULTS Of the 94 patients enrolled, 74 patients completed all 6MWT assessments. One-way repeated measures ANOVA found no statistical difference between mean in-person and virtual 6MWT ($P = .45$). One-way repeated measures ANOVA found a statistical difference between mean TUG scores ($P = .03$). Patients were comfortable with the use of virtual visits (56%), would participate in research studies through telemedicine (98.7%), and found completing a virtual research visit to be not difficult (77.3%).

CONCLUSION Virtual administration of the 6MWT was shown to be feasible and acceptable to heart failure patients as compared to in-person functionality testing. This approach could be implemented into clinical care pathways for evaluation of heart failure patients, as well as adopted by industry-sponsored and investigator-initiated research studies in heart failure cohorts for data collection.

KEYWORDS Digital health; Heart failure; Telemedicine; Virtual visit

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Introduction

Patient participation in clinical trials is crucial for development of new treatments that impact patient outcomes. Barriers to patient enrollment have been discussed and reviewed in the literature. Common patient-specific factors identified that impede enrollment include out-of-state residence, trial duration, and intensive trial-related testing.^{1–3} Trial designs that accommodate patient needs while maintaining scientific integrity may improve enrollment and bolster patient participation.

Patients are more commonly utilizing virtual methods to communicate with and receive care from their physicians and care team. Virtual visits have been shown to be useful in a variety of inpatient and outpatient settings and patient populations, including for those living with heart failure. A

recent study has shown the usefulness and applicability of virtual visits to provide follow-up care for heart failure patients, after a hospital admission.⁴ Virtual visits can increase patient accessibility to care, overcoming barriers such as time, cost, and distance of travel. Virtual visits also serve to protect patients and providers during the coronavirus pandemic by reducing in-person exposure without sacrificing contact for clinical assessment and disrupting continuity of care.⁵

Functional tests commonly used as study endpoints in heart failure trials are the 6-minute hallway walk test (6MWT) and timed up and go test (TUG). The 6MWT provides reliable information about the patient's exercise tolerance and is useful to prognosticate and trend changes in patient functional capacity over time. Furthermore, the 6MWT is inexpensive and well tolerated by patients.⁶

The TUG test is a short test used commonly to quantify frailty through assessment of mobility and balance. The TUG test, like the 6MWT, can be repeated over time to track

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KEY FINDINGS

- Virtual functionality testing (6-minute walk test and timed up and go test) is feasible and acceptable for patients living with heart failure.
- Patients would participate in research studies if virtual visits and/or digital health components were integrated into study protocols.
- Issues regarding access to technology and experience with technology should be considered for successful implementation of virtual functionality testing on a broader scale in varied settings.

patient progress and performance can be used as an endpoint in a clinical trial.

Given the advent of telemedicine and the increasing use of virtual visits in clinical care, coupled with COVID restrictions in hospital facilities, it is reasonable to consider the integration of virtual options for completing study visits and assessments. A pilot study was designed to explore the use of virtual visits to collect functional information on patients living with heart failure. The aims of this study were to examine the feasibility and acceptance of virtual, at-home functionality assessments. We hypothesized that these would be feasible for patients to perform and similar to the patient's own baseline, in-person functionality testing.

Methods

Virtual Visits to Optimize Research Trial Offerings to Heart Failure Patients ([ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT04064541) Identifier: NCT04064541) was an institutional review board–approved single-group assignment pilot study conducted at the Cleveland Clinic between August 2019 and March 2020.

Patients were enrolled in the outpatient setting. Male or female patients older than 18 years of age with a diagnosis of heart failure, including patients with heart failure with preserved ejection fraction (HFpEF) and with reduced ejection fraction (HFrEF) who personally owned or had an individual in their social support network with access to equipment (phone, computer, tablet) and an internet connection in order to perform a distance health research visit, were considered for enrollment. Patients with a history of heart transplant or left ventricular assist device, unstable angina, or myocardial infarction within the past month were excluded.

After informed consent was obtained, subjects completed an in-person baseline assessment consisting of New York Heart Association (NYHA) classification, surveys (EQ-5D-5L, Kansas City Cardiomyopathy Questionnaire [KCCQ], Frailty Index for Elders [FIFE], and Mini-Cog), TUG, and 6MWT. NYHA classification was collected utilizing a patient self-report format, whereby patients were presented with descriptions of each heart failure class and were asked to select which class they fell into based on their symptoms

(shortness of breath, fatigue, and volume overload) on the day of baseline visit. NYHA classes are as follows: 1 – no symptoms and no limitation of physical activity; 2 – mild symptoms and slight limitation in physical activity; 3 – significant limitation in activity owing to symptoms and comfortable only when resting; 4 – severe limitations in functional capacity, and symptoms even while at rest.⁷ NYHA classification was obtained at baseline and at follow-up visits to characterize the study sample and understand the breadth of limitations the patients would have with completing required testing throughout the study period.

The EQ-5D-5L is a survey instrument developed by Euro-QOL to examine a patient's health state at the time of administration. The survey consists of 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has 5 levels for the patient to choose from to describe their health state, which are as follows: no problems, slight problems, moderate problems, severe problems, and extreme problems.⁸

The KCCQ is a validated instrument used to measure the patient's perception of their health status with a focus on how heart failure symptoms impact quality of life.⁹ The EQ-5D-5L, KCCQ, and FIFE were obtained to characterize potential limitations and quality of life at time of enrollment.

Patients received one-on-one training using the Cleveland Clinic Express Care Online application, through which they would complete both at-home virtual visits. Each patient utilized the app and performed the baseline walk with the app and video connect to familiarize the patient with the software. Patients were instructed on how to set up the 6MWT and TUG course themselves to ensure they could perform the functional portion of the virtual visit in the home at follow-up. Patients were issued 2 cones and a measuring tape for marking the distances for the functional assessment tests at home.

The TUG test measures the time it takes for the patient to rise from a seated position, walk 3 meters forward, turn around, and return to the starting position. Times longer than 30 seconds to complete the test can be indicative of problems with walking and being independently mobile.^{10,11}

Follow-up visits occurred via virtual distance health visits (video chat), and occurred 7 days and 14 days (± 3 days) after baseline. Surveys (EQ-5D-5L, KCCQ, and FIFE), TUG, and 6MWT were completed. Study staff reviewed 6MWT/TUG course set-up for accuracy prior to start. Patients were supervised via video for the entirety of their 6MWT/TUG (Figure 1).

The 6MWT was conducted following guidance issued by the American Thoracic Society,⁶ which states that the test should be performed indoors, on a long, flat, and straight corridor. The suggested course length is 30 meters, or approximately 100 feet. Scripted verbal encouragement is provided to the patient by the test facilitator as well as monitoring for safety events that may require the walk to be paused or ended.

Patient study characteristics were described using mean and standard deviation (SD) (Table 1). A 1-way repeated

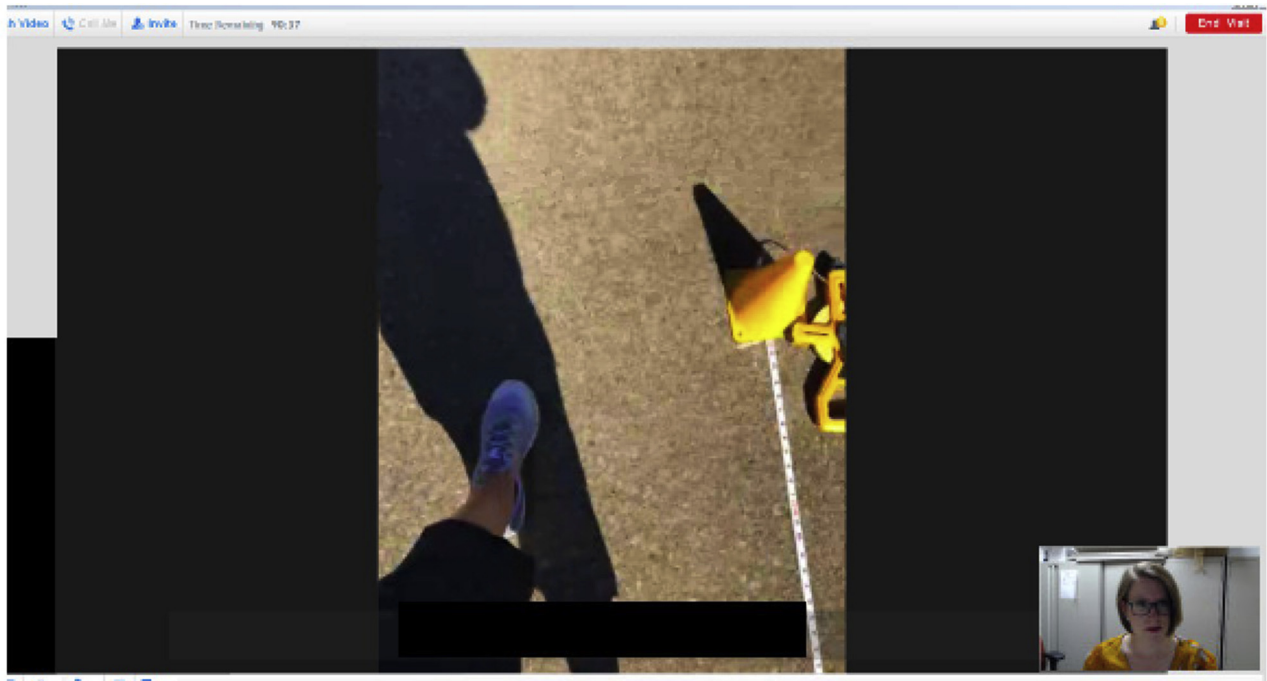


Figure 1 Virtual visit showing 6-minute walk test (6MWT). Screen shot from video virtual visits between study coordinator (right lower corner) and subject. Study coordinator has reviewed course set-up and is supervising patient during 6MWT.

measures ANOVA was planned to compare mean differences between in-person and virtual 6MWT/TUG scores.

Results

A total of 94 patients were consented for this study. Demographics and baseline characteristics of the study sample are described in [Table 1](#). The study population consisted of predominantly male (64.9%) subjects, with a mean age of 58 (SD 11.32) years. The subjects recruited comprised a variety of heart failure stages at baseline ranging from NYHA class I to class III. The majority of subjects completed high school or further education, had no cognitive impairment, and lived with 1 or more person(s) in their household ([Table 1](#)).

Of the 94 patients consented, 74 patients completed all 6MWT assessments and were therefore included for final functionality test analysis. Mean 6MWT scores at baseline, day 7, and day 14 were 1052.3 ft, 1107.6 ft, and 1080.3 ft, respectively ([Figure 2](#)). One-way repeated measures ANOVA found no statistical difference between mean scores from in-person and virtual follow-up time points ($P = .45$). Mean TUG scores at baseline, day 7, and day 14 were 9.3 seconds, 10.83 seconds, and 9.7 seconds, respectively ([Figure 3](#)). One-way repeated measures ANOVA found a statistical difference between mean TUG scores at each time point ($P = .03$). Differences in the TUG test mean results can be attributed to a video delay that affected millisecond timing.

Patient acceptance was assessed by exit interview ([Table 2](#)). A majority of patients were comfortable with the use of virtual visits (56%), believed that the care they would

receive in a virtual visit is as good as an in-person visit (60%), and would be more willing to participate in research studies if they could do so via distance health (98.7%), and patients found the act of completing a study via virtual visit to be not difficult (77.3%).

Discussion

This study demonstrates that functionality testing can be completed at home by heart failure patients. The virtual 6MWT and TUG test may be an appropriate choice for clinicians in a multitude of areas of clinical specialties and in both an inpatient and an outpatient setting. Clinicians may consider adopting the virtual functionality testing as shown here in conjunction with other assessments done during a virtual visit (medication reconciliation, visual jugular venous pressure assessment, and visual edema assessment) to allow for a comprehensive overview of patient status. The use of virtual visits in the care of the heart failure patient has grown exponentially in the past decade, particularly with the advent of the COVID-19 pandemic. Outpatient care providers, cardiac rehabilitation services, and care coordination services post hospital discharge can all utilize digital health and virtual visits to provide care for heart failure patients. At-home functionality testing such as the 6MWT and TUG can provide a glimpse into patient functional status and quality of life that dives further than patient-reported symptoms, and can be used to drive clinical decision-making. The at-home delivery of the 6MWT and TUG tests is advantageous for patients and providers in terms of cost, ease, and acceptance. These quick tests can be done in and around the home in a relatively short period of time, with little to no

Table 1 Patient characteristics at baseline (in-person visit)

| Characteristic | Result (N = 94 patients) |
|--|-----------------------------|
| Sex, n (%) | |
| Male | 61 (64.9) |
| Female | 33 (35.1) |
| Race (%) | |
| Black/African American | 16 (17.0) |
| White | 77 (81.9) |
| American Indian | 1 (1.1) |
| Age, mean (SD) | 58.64 (11.32) |
| Heart failure diagnosis, n (%) | |
| Ischemic cardiomyopathy | 16 (17.0) |
| Nonischemic cardiomyopathy | 78 (83.0) |
| LVEF %, mean (SD) | 41.04 (14.30) |
| NYHA heart failure class, n (%) | |
| 1 | 41 (43.6) |
| 2 | 25 (26.6) |
| 3 | 28 (29.8) |
| Education level, n (%) | |
| Postgraduate degree | 4 (4.3) |
| Graduate degree | 13 (13.8) |
| Bachelor's degree | 23 (24.5) |
| Associate or some college | 36 (38.3) |
| High school education | 15 (16.0) |
| Middle school education | 1 (1.1) |
| Primary school education | 1 (1.1) |
| Other | 1 (1.1) |
| Hearing impairment, n (%) | |
| No hearing aid | 82 (87.2) |
| Hearing aid | 12 (12.8) |
| Social support, n (%) | |
| Lives alone | 25 (26.6) |
| Lives with 1 or more person | 68 (72.3) |
| Other | 1 (1.1) |
| Mini-Cog / cognitive scores, n (%) | |
| Cognitive impairment | 4 (4.3) |
| Intact | 90 (95.7) |
| KCCQ total score, mean (SD) | 46.99 (10.54) |
| Frailty Index for Elders assessment, n (%) | |
| At risk for frailty | 28 (30.8) |
| Frail | 34 (37.4) |
| No frailty | 29 (31.9) |
| EQ-5D-5L: mobility, n (%) | |
| No problems | 65 (69.9) |
| Has problems | 28 (30.1) |
| EQ-5D-5L: self-care, n (%) | |
| No problems | 82 (87.2) |
| Has problems | 12 (12.8) |
| EQ-5D-5L: usual activities, n (%) | |
| No problems | 47 (50.0) |
| Has problems | 47 (50.0) |
| EQ-5D-5L: pain, n (%) | |
| No pain | 54 (57.4) |
| Has pain | 40 (42.6) |

KCCQ = Kansas City Cardiomyopathy Questionnaire; LVEF = left ventricular ejection fraction.

equipment necessary, other than the patient's phone, tablet, or smart device. As patients become more familiar with the use of technology through its continued integration into everyday life, including healthcare, use of virtual methods to communicate with healthcare providers and at-home functionality testing may become more commonplace.

Industry-sponsored and investigator-initiated clinical trials may choose to consider at-home functionality testing when developing study protocols. The 6MWT is used widely in many heart failure trials to ascertain the effect of the drug or device in question on a patient's functional capacity. When patients are unable to return to the study site for follow-up, this important endpoint data point remains missing. Allowing for functionality testing to be done at home via virtual visit will allow for continued collection of data, including functionality, even when patients cannot or will not return to the study site for follow-up. Broadly, utilizing virtual methods to conduct study visits allows for a larger population of patients to consider clinical trial enrollment, as they are less encumbered by the time, distance, and cost it takes to travel to study sites frequently for study-related visits.

The sample of heart failure patients in this study were predominantly NYHA class I and II and with a mix of frailty index (FIFE) scores, with only a small percentage of the patient population identified as at risk for frailty or defined as frail at baseline. It was not expected by the study authors that the patients enrolled in this study would decompensate quickly during the study follow-up period, given the patients were a low-heart failure acuity group (NYHA class I–III). The TUG and FIFE are 2 assessments that could be performed prior to the consideration of virtually-administered testing to identify patients who may be at risk for falls or other injuries.

A statistically different mean between the 3 study time points was found for the TUG test in this patient population. The difference in patient TUG tests over the follow-up period could be attributed to video delay that affected millisecond timing. For future studies considering timed testing through a virtual method, this problem should be taken into consideration in study design. To ensure the test has validity and to overcome this technological barrier, the patients could potentially videotape themselves doing the TUG test and send it to their physician to review as part of their virtual visit.

Inclusion of patients of a wide variety of age and educational attainment are some of the study's strengths. Systematic bias was controlled in this study by the distribution of study instructions to each patient and each study coordinator to ensure study methodology was followed consistently.

Additional limitations included a small sample size. The onset of the COVID-19 pandemic and subsequent visit restrictions limited patient recruitment. The small sample size also was limited in diversity of sex and race. A larger sample size of patients with more severe stages of heart failure would aid in the potential generalizability of this study in a broader heart failure patient population.

Further research is needed to explore the applicability of at-home virtual functionality testing in more greatly decompensated heart failure patients.

At the beginning of the study, many patients and care providers were not familiar with the Cleveland Clinic Express Care Online application, which led to some difficulty with patient enrollment and completion of study visits. Careful instruction and training of patients and staff members alleviated

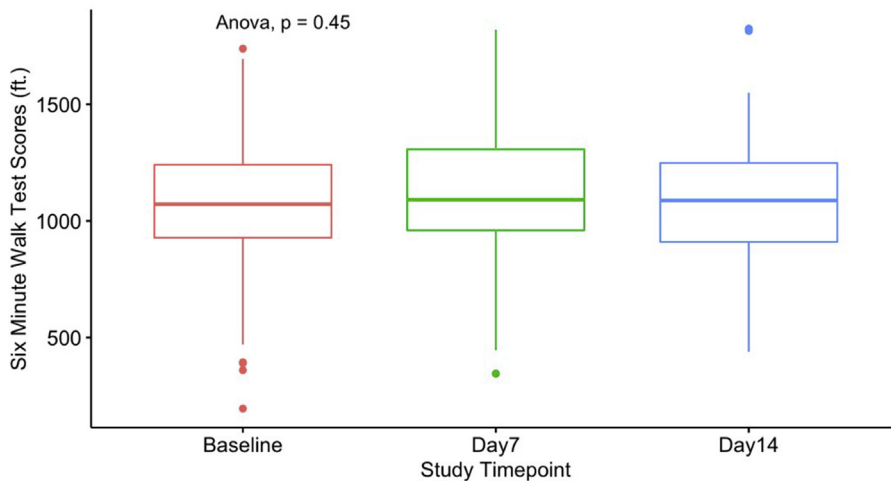


Figure 2 Six-minute walk test results.

the upfront burden of the technological learning curve. However, this potential barrier should be taken into consideration in future studies.

The validity of the tests performed in this study could be improved by implementing a randomized controlled trial design. The patient population in this study was selected for their relevance and current use of 6MWT and TUG tests in heart failure clinical trials currently performed at the study site. This convenience sampling could be viewed as an additional limitation in the study.

The data gathered in this pilot study can serve as a basis for future research into the successful translation and implementation of digital health solutions for heart failure patients and patients enrolled in clinical trials.

Conclusion

The virtual administration of the 6MWT was shown to be feasible in this study population. The functionality testing

was compatible to in-person administration. This approach could be adopted by industry-sponsored and investigator-initiated research studies in heart failure cohorts. This potential for implementation is timely and useful during the limitations and risks of in-person care during the COVID-19 pandemic. Increasing clinical trial enrollment by diminishing access barriers will improve patient care by including a more diverse patient population in study enrollment and decrease study follow-up attrition rates.

Attrition and loss to follow-up are threats to internal and external validity of clinical trials. The use of virtual visits and telemedicine can aid in the completion of clinical trials by facilitating data collection and bridging gaps in access to care.

Additional studies are warranted to examine the applicability of at-home functionality testing. Patient, provider, and industry feedback is appreciated to understand value of and challenges to the wider-scale implementation of virtual visits in clinical research.

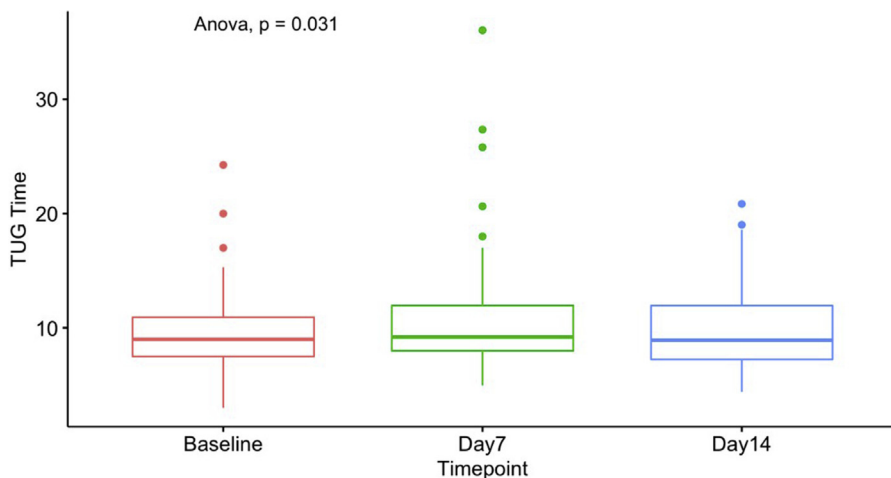


Figure 3 Timed up and go (TUG) test results.

Table 2 Patient experience with virtual visit

| Experience | Result (N = 91 patients) |
|---|-----------------------------|
| Comfortable with virtual visit, n (%) | |
| Extremely comfortable | 42 (56.0) |
| Very comfortable | 29 (38.7) |
| Moderately comfortable | 4 (5.3) |
| Had previously done virtual visits = Yes, n (%) | 8 (10.7) |
| Comfortable with new technology, n (%) | |
| Extremely comfortable | 25 (33.3) |
| Very comfortable | 27 (36.0) |
| Moderately comfortable | 19 (25.3) |
| Slightly comfortable | 3 (4.0) |
| Not comfortable | 1 (1.3) |
| Found the quality of the virtual visit to be acceptable to in-person visit = Yes, n (%) | 45 (60.0) |
| Needed additional guidance = Yes, n (%) | 8 (10.7) |
| Would participate in a research study with virtual visits = Yes, n (%) | 74 (98.7) |
| Difficulty rating of doing study visit virtually, n (%) | |
| Extremely difficult | 1 (1.3) |
| Moderately difficult | 4 (5.3) |
| Slightly difficult | 12 (16.0) |
| Not difficult | 58 (77.3) |

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Disclosures

Laurie Ann Moennich, MPH, CPH: none; Barbara Bittel, BSN, RN, CCRP: none; Jerry D. Estep, MD, FACC, FASE: none.

Authorship

All authors attest they meet the current ICMJE criteria for authorship.

Patient Consent

All patients provided written informed consent.

Ethics Statement

The authors designed the study and gathered and analyzed the data according to the Helsinki Declaration guidelines on human research. The research protocol used in this study was reviewed and approved by the institutional review board at the Cleveland Clinic.

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