

PROTOCOL Changes from Version 1.2 (June 16, 2017) for Version 1.3 (April 16, 2021)

4.2.7 Six Minute Walk Test (50)

Six minute walk test will be performed in accordance with American Thoracic Society guidelines. **Continuous pulse oximetry should be used throughout the test.** Resting O₂ sat and heart rate will be obtained and again at the end of the walk test. A Borg Dyspnea score will also be acquired.

4.2.11 Right Heart Catheterization

C. Challenges (74-76)

2. Inhaled NO (78-83)

- a. Performed in all patients except with PCWP $\geq$ 25 mmHg or those with mPAP $<$ 20 mmHg
- b. Inhale iNO 40 ppm (added on to 100% oxygen) for 5 minutes
- c. Record measurements from B1, B2, B3, and B5
- d. Stop iNO and 100% oxygen
- e. ~~5-minute washout period.~~

3. Fluid challenge (84-86)

- a. Performed in all patients except with baseline RA $\geq$ 15 or PCWP $\geq$ 18 mmHg or having an invasive CPET (selection likely based on center availability of invasive CPET)
- b. Infuse 500 ml of 37°C 0.9% saline intravenously over 105 min
- c. Record measurements from B1, B2, B3, and B5
- d. Complete study.

4.2.12 Cardiopulmonary Exercise Testing (CPET) (87-94)

At some of the centers the CPET will be invasive (90), adding:

- Radial artery line (optional)
- IJ or brachial vein pulmonary artery line
- Hemodynamics (RAP, PAP, PCW and AO, if available) obtained at each workload increment. These measurements will be captured during spontaneous breathing and during a brief expiratory pause if possible.
- Cardiac output ~~will~~can be obtained by ~~thermodilution (all sites) or~~ direct Fick ~~when~~(if) possible.

4.4 Longitudinal Follow-up

All patients, or their designated contacts, will be contacted by telephone and/or letter at least annually up to 10 years after enrollment ~~up to the end of the study (maximum of 3.5 years)~~ if not seen at the enrolling center for follow-up. Vital status and occurrence/date of any lung, heart or heart-lung transplantation will be determined from this contact or by using center medical records. Cause of death will be ascertained by the site investigators.