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Cardiorespiratory Fitness After Open Repair for Acute Type A Aortic Dissection – A Prospective Study

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Abstract

Objective: Cardiorespiratory fitness (as measured by peak oxygen consumption [VO_{2peak}]) is an independent predictor of cardiovascular disease and all-cause mortality. Limited data exist on VO_{2peak} following repair for an acute type A aortic dissection (ATAAD) or proximal thoracic aortic aneurysm (pTAA). This study prospectively evaluated VO_{2peak}, functional capacity, and health-related quality of life (HR-QOL) following open repair.

Methods: Participants with a history of an ATAAD (n=21) or pTAA (n=43) performed cardiopulmonary exercise testing (CPX), six-minute walk testing, and HR-QOL at 3 (early) and 15 (late) months following open repair.

Results: The median age at time of surgery was 55-years-old and 60-years-old in the ATAAD and pTAA groups, respectively. Body mass index significantly increased between early and late timepoints for both ATAAD (p=0.0245, 56% obese) and pTAA groups (p=0.0045, 54% obese). VO_{2peak} modestly increased by 0.8 mLO2·kg−1·min−1 within the ATAAD group (P=0.2312) while VO_{2peak} significantly increased by 2.2 mLO2·kg−1·min−1 within the pTAA group

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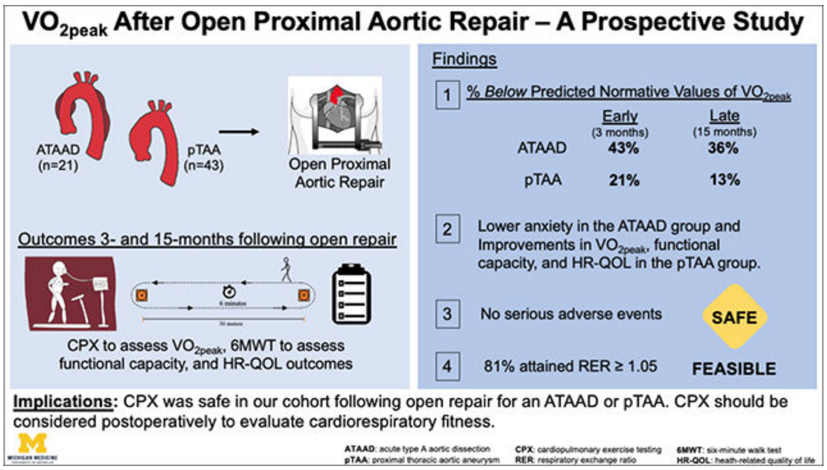
(P=0.0003). Anxiety significantly decreased in the ATAAD group whereas functional capacity and HR-QOL metrics (social roles and activities, physical function) significantly improved in the pTAA group (p values<0.05). There were no serious adverse events during CPX.

Conclusion: Cardiorespiratory fitness among the ATAAD group remained 36% below predicted normative values >1 year after repair. CPX should be considered post-operatively to evaluate exercise tolerance and blood pressure response to determine whether mild-to-moderate aerobic exercise should be recommended to reduce future risk of morbidity and mortality.

Graphical Abstract



Keywords

exercise testing; aortic dissection; cardiorespiratory fitness; thoracic aortic aneurysm

INTRODUCTION

Cardiac rehabilitation is a cornerstone of postoperative care for most cardiac surgery populations as there is long-standing evidence to support its efficacy at lowering cardiovascular-related mortality through improvements in cardiorespiratory fitness, reductions in hospitalizations, and improvements in quality of life[1]. In chronic cardiac conditions, cardiorespiratory fitness is considered a clinical vital sign with assessment recommended across all phases of clinical decision making[2,3]. At present, cardiorespiratory fitness is not clinically evaluated following open aortic repair for thoracic aortic disease, especially acute type A aortic dissection (ATAAD)[4]. The clinical importance of evaluating cardiorespiratory fitness in this setting is warranted as preliminary data from cross-sectional studies highlight that cardiorespiratory fitness (as measured by peak oxygen consumption, VO_{2peak}) is 34–40% below normative values[5,6].

This study prospectively evaluated cardiorespiratory fitness and health-related quality of life outcomes after open proximal aortic repair for an ATAAD or proximal thoracic aortic aneurysm (pTAA) at two postoperative timepoints (3- and 15-months) that align with clinical follow-up. We hypothesized that cardiorespiratory fitness would remain impaired greater than a year after repair, especially among ATAAD, given scant guidance on the need to evaluate cardiorespiratory fitness and on the value of implementing exercise training in this setting.

METHODS

Trial Design and Study Population

Eligible participants underwent open proximal aortic repair through sternotomy for an emergent ATAAD or elective pTAA. Society of Thoracic Surgery data elements from the University of Michigan Department of Cardiac Surgery Data Warehouse were utilized to determine pre-, intra-, and post-operative (defined as in-hospital postoperative events) outcomes as previously reported [7]. ATAAD and pTAA participants were evaluated at approximately 3 months (early timepoint) and 15 months (late timepoint) following open repair between March 2016 and July 2018 at the University of Michigan, Michigan Medicine (Supplemental Figure 1). Early and late timepoints were selected as they align with clinical guidelines for follow-up[8]. Eligible participants were >18 years of age, cleared by their aortic surgeon to perform cardiopulmonary exercise testing (CPX), and without a known syndromic diagnosis or underlying genetic predisposition (this phenotype confers an increased risk of dissection)[9]. All study procedures were reviewed and approved by the Michigan Medicine institutional review board (IRBMED, HUM00110749) and all participants provided written informed consent. Data supporting the findings of this study are available from the corresponding authors upon reasonable request.

The primary endpoint was change in VO_{2peak} which was evaluated using an electronic/motorized treadmill test performed by two advanced cardiovascular life support and American College of Sports Medicine–certified clinical exercise physiologists under the supervision of the interpreting cardiologist[10]. Expired gases were analyzed continuously by an Ultima CPX metabolic stress test system (MCG Diagnostics). After stable resting values had been achieved, participants were tested according to the Cornell protocol until patient request to stop due to fatigue, maximal effort, or clinical decision to terminate[10]. The Cornell protocol increases the treadmill speed and grade every two minutes with standardized metabolic equivalent increases per stage. VO_{2peak} was defined as the greatest VO_2 value for a given 30-sec interval; anaerobic threshold was calculated using standard methods[11]. Percent-predicted VO_{2peak} was calculated according to the Fitness Registry and the Importance of Exercise National Database (FRIEND) normative values for VO_2 (referred to as normative values from this point onward)[12]. A peak CPX was defined as a respiratory exchange ratio (RER) ≥1.05 [5,13–15]. Heart rate (HR) response was evaluated utilizing continuous 12-lead Mac 5000 ECG Monitoring system (GE Healthcare) and blood pressure response was measured manually by an auscultatory sphygmomanometer every two minutes during CPX procedures. Blood pressure termination criterion during CPX included a decrease in systolic pressure > 20mm Hg[16] or an increase ≥180 mm Hg systolic or ≥90 mm Hg diastolic pressure[4]. It is possible that blood pressure may have exceeded the upper-limit thresholds because of the time interval between blood pressure measurements. EKG termination criterion during CPX included ischemic EKG changes, complex ectopy, or second or third degree heart blocks[16]. Participants were not asked to discontinue medications prior to CPX. The criterion utilized to determine an abnormal HR recovery was ≤12 bpm (max HR – 1-min HR recovery) following a walking protocol[17]. Exercise breathing reserve indicates how closely ventilation approaches maximal ventilatory volume during exercise, and is calculated (1-[peak ventilation/maximal ventilatory volume])[16]. Echocardiography and computed tomography angiography (CTA) outcomes including left ventricular ejection fraction (LVEF), presence of moderate-to-severe aortic valve insufficiency, aortic diameters, and evidence of residual aneurysmal disease or distal dissection, particularly for ATAAD participants, were assessed[18].

Secondary endpoints were safety, functional capacity, and patient-reported outcomes (PROs). Safety was evaluated by the type and prevalence of serious (e.g., requiring hospitalization, life-threatening) and non-serious (e.g., musculoskeletal pain) adverse events during CPX[5]. Functional capacity was assessed by the six-minute walk test and measured by the six-minute walk distance (6MWD)[19]. Health-related quality of life (Patient Reported Outcomes Measurement Information System, PROMIS)[20], anxiety (Generalized Anxiety Disorder 7-Item, GAD-7 Scale)[21], pain (20-item Brief Pain Inventory)[22], sleep quality (Pittsburgh Sleep Inventory)[23], and physical activity (Godin-Leisure Time Exercise Questionnaire)[24] were also evaluated.

Statistical Analysis

The analysis provided descriptive information on demographic, clinical, and surgical outcomes in the overall population and amongst the ATAAD and pTAA groups. Results are presented as median (interquartile range (IQR): 25% and 75%) for continuous data and n (%) for categorical data. Means were utilized for percent of predicted and percent change. For repeated measurements on surgical outcomes, paired Wilcoxon signed-rank tests and McNemar's test were conducted to assess the difference for continuous and categorical variables, respectively, between early and late timepoints. The difference in anxiety level (ordinal variable) over time was evaluated by cumulative link mixed effects model with patient ID as random effect. Additionally, group by time interactions were evaluated by linear mixed model with group, timepoint, and group by timepoint as fixed effects and participant ID as random effect. Longitudinal analysis was performed for participants with complete data. Correlations between health-related quality of life measurements and the change in VO_{2peak} and 6MWD over time were evaluated using both Pearson correlation and Spearman correlation tests. All statistical calculations used SAS 9.4 (SAS Institute, Cary, NC) and R 3.4.2. Statistical significance was considered at $p<0.05$.

RESULTS

The analytic cohort consisted of 64 participants that underwent open proximal aortic repair through sternotomy for an emergent ATAAD (n=21) and elective pTAA (n=43). Median time from open repair to the postoperative CPX was 3.4 months (3.1, 3.6) for the ATAAD group and 3.2 months (3.0, 3.5) for the pTAA group. The postoperative CPX occurred a median of 15.9 months (13.0, 17.3) for the ATAAD group and 15.2 months (12.6, 15.7) for pTAA group following open repair. Fifty-one participants completed a CPX at both timepoints (ATAAD, n=16 and pTAA, n=35), with 13 participants lost to follow-up due to death (one death per group, n=2), contraindications to CPX at time of follow-up (e.g., hip arthroplasty, stroke, vertigo, type B intramural hematoma, n=4), and inability to re-contact (n=7). One participant in the ATAAD group and two participants in the pTAA group participated in cardiac rehabilitation between study timepoints.

Study Outcomes for ATAAD

Clinical Characteristics and Operative Outcomes—The ATAAD group was predominately male (86%) with a median age of 55 years. At the time of open repair, 24% of participants had moderate-to-severe aortic insufficiency and 14% had moderate-to-severe aortic stenosis. Regarding cardiovascular disease risk, 81% of participants had hypertension, 43% had peripheral vascular disease, and 9.5% had previous cardiac surgery (Table 1). Thirty-eight percent underwent aortic root replacement and 29% underwent a zone 1/2/3 arch replacement. The median cardiopulmonary bypass time was 216 minutes and hypothermic circulatory arrest was utilized in 100% of participants with predominantly (86%) antegrade cerebral perfusion. Nine and half percent of participants suffered a postoperative stroke and 9.5% had renal failure requiring dialysis; the median postoperative length of stay was nine days (Table 2).

Cardiorespiratory, Hemodynamics, and Functional Capacity—Body mass index significantly increased between early and late timepoints (28.7 vs 30.6 $kg \cdot m^{-2}$, p=0.0245), with 56% of participants classified as obese at the late timepoint. There was no change in median VO_{2peak} between early and late timepoints (18.3 to 19.1 $mLO_2 \cdot kg^{-1} \cdot min^{-1}$, p=0.2312). The average VO_{2peak} was 43% and 36% below age- and sex-predicted normative values at the early and late timepoints, respectively. There were no other significant changes in cardiorespiratory outcomes over time. The median RER was 1.1 with 62% (early) and 75% (late) of CPX studies meeting "peak" criteria as defined by a RER≥1.05. There were no significant differences over time for peak HR, systolic blood pressure, or diastolic blood pressure (Figure 1). The 1-minute HR recovery did not improve between the early and late timepoints (13 vs 14 bpm, p=0.11). There was no change in median 6MWD between the early and late timepoints (459 vs 502 m, p=0.14), with 80% of participants achieving age- and sex-predicted distance (Table 3).

Adverse Events and Diagnostic Imaging Outcomes—No serious adverse events requiring hospitalization were observed during CPX. A total of two participants at both timepoints required early CPX termination due to non-serious hypotensive responses (early, n=1; late, n=1) or electrocardiogram abnormalities (early, n=1; late, n=1) The same participants' experienced similar non-serious responses during CPX 1 and CPX 2 (Supplemental Table 1). There were no differences in LVEF or aortic insufficiency over time. Root, ascending, arch, and thoracic descending aortic diameters remained similar; however, the abdominal aortic diameter significantly increased between the early and late timepoints (30 vs 31.9 mm, p=0.005) (Table 4).

Health-Related Quality of Life Outcomes—Thirty-seven percent of participants reported moderate-to-severe anxiety at the early timepoint compared to 16% at the late timepoint (p=0.0061, Figure 2 and 3; Supplemental Table 2).

Study Outcomes for pTAA

Clinical Characteristics and Operative Outcomes—The pTAA group was predominantly male (86%) with a median age of 60 years. Eightyone percent of participants in the pTAA had ascending aortic aneurysms. At time of open repair, 48% of participants had moderate-to-severe aortic insufficiency and 28% had moderate-to-severe aortic stenosis. Regarding cardiovascular disease risk, 77% of participants had hypertension, 9.3% had peripheral vascular disease, and 19% had previous cardiac surgery (Table 1). Fifty-one percent of participants in the pTAA group underwent aortic root replacement and 16% underwent a zone 1/2/3 arch replacement. The median cardiopulmonary bypass time was 212 minutes with hypothermic circulatory arrest utilized in 37% of participants. Postoperative complication rates were low as 0% of participants suffered a stroke or had renal failure requiring dialysis; the median postoperative length of stay was six days (Table 2).

Cardiorespiratory, Hemodynamics and Functional Capacity—Body mass index significantly increased the between early and late timepoints (30.4 vs 31.2 kg·m^{-2}, p=0.0045) with 54% of participants classified as obese at the late timepoint. There was a significant increase in median VO_{2peak} between early and late timepoints (20.2 to 22.4 mL.kg^{-1}.min^{-1}, p=0.0003). The average VO_{2peak} was 21% and 13% below age- and sex-predicted normative values at the early and late timepoints, respectively. There were significant increases in peak ventilation (66.5 vs 73.9 L.min-1, p=0.0162) and METs (5.8 vs 6.4, p=0.0128) between the early and late timepoints. Median RER at both timepoints was 1.2 with 90% (early) and 94% (late) of CPX studies meeting “peak” criteria as defined by a RER≥1.05. There were no significant differences over time for peak HR, systolic blood pressure, or diastolic blood pressure (Figure 1). There was a significant increase in median 6MWD between the early and late timepoints, (480 vs 492 m, p=0.01), with 90% achieving age- and sex-predicted distance (Table 3).

Adverse Events and Diagnostic Imaging Outcomes—No serious adverse events requiring hospitalization were observed during CPX. A total of three participants at the early timepoint and two participants at the late timepoint required early CPX termination due to non-serious hypotensive responses (early, n=2; late, n=1) or electrocardiogram abnormalities (early, n=1; late, n=1). The same participants experienced similar non-serious responses during CPX 1 and CPX 2 (Supplemental Table 1). There were no differences in LVEF or aortic insufficiency between timepoints. Root, ascending, arch, thoracic descending, and abdominal aortic diameters remained similar between timepoints (Table 4).

Health-Related Quality of Life Outcomes—The pTAA group significantly improved PROMIS measures of satisfaction with social roles and activities (p=0.0105) and physical function (p=0.0214) between the early and late timepoints (Figure 2; Supplemental Table 2). PROMIS measure of satisfaction with social roles and activities was positively associated with improvements in VO_{2peak} within the pTAA group (correlation=0.57; p=0.005) using Pearson correlation test. Marginal significance was identified using Spearman correlation between PROMIS measure of satisfaction with social roles and activities and improvement of VO_{2peak} (p=0.064) within pTAA group. There were no significant correlations between

PROMIS measures of satisfaction and participants' improvements in 6MWD between timepoints, but non-statistically significant correlations of improvement in 6MWD with higher satisfaction were observed across all PROMIS measurements (e.g., psychosocial, social activities, and physical function, and fatigue) (Figure 3).

DISCUSSION

We prospectively evaluated VO_{2peak} response following open proximal aortic repair for an ATAAD or pTAA. Our findings show the following: i) significantly lower anxiety and increased BMI with no change in VO_{2peak} among the ATAAD group between 3- and 15-months postoperatively. VO_{2peak} remained 36% below age- and sex-matched normative values > 1 year following open repair; ii) no serious adverse events during CPX procedures, providing additional evidence to support the safety and feasibility of CPX and mild-to-moderate aerobic exercise in this setting for participants cleared by a cardiac surgeon or cardiologist; and iii) significant improvements in VO_{2peak}, functional capacity, and health-related quality of life measures were noted among the pTAA group between 3- and 15-months following open repair (Figure 4).

VO_{2peak} was on average 43% less than predicted normative values at the 3-month follow-up after open repair for an ATAAD. Over the course of one year, body mass index significantly increased and no significant change in VO_{2peak} was observed (mean, 18.4 to 19.5 $mL{\cdot}kg^{-1}$ min^{-1}, 36% below predicted normative values). Our findings corroborate the initial work of Delsart et al. that reported a mean VO_{2peak} of 19.2 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$ among 105 type A and B aortic dissection participants approximately two years following hospitalization or open repair[6]. At this juncture, preliminary studies show reduced VO_{2peak} and increased BMI one to two years following an aortic dissection[5,6,15]. These outcomes typically are interwoven although the effects are cumulative leading to an increased risk of cardiovascular morbidity and mortality[25–28]. Recently, Delsart et al. showed that a low VO_{2peak} (<70% of predicted) among 165 type A and B dissection survivors was an independent predictor of a major cardiac event occurrence (i.e., cardiovascular death, stroke, acute coronary syndrome, hospitalization for cardiac failure, and coronary or peripheral artery revascularization) over a 39 month follow-up period[29].

VO_{2peak} provides an objective assessment of the integrative capacity of the cardiovascular, pulmonary, hematopoietic, and musculoskeletal systems to transport and use oxygen[11], and thus, it is widely considered a reflection of overall health[2], with numerous empirical studies highlighting the association between reduced VO_{2peak} and future risk of cardiovascular morbidity and mortality[25,30,31]. The exact mechanisms of reduced VO_{2peak} among ATAAD survivors was not assessed in this study, although all ATAAD participants (with the exception of one, LVEF=43%) had a normal LVEF (>50%, range 50–60%), normal pulmonary function (>20% breathing reserve)[16], and 80% had no history of peripheral vascular disease. Indirect causes of reduced VO_{2peak} could be that: i) the acute event and complex surgical repair likely exacerbated declines in exercise leading to weight gain and exercise intolerance, and ii) fear that exercise may increase the risk of disease progression[32,33,34]. We observed significantly lower generalized anxiety between timepoints; however, we did not directly assess anxiety related to exercise and thus, further investigation is warranted. Current recommendations advise against strenuous resistance or isometric exercise and competitive sports due to concerns that elevations in blood pressure may cause progression of the patent false lumen, aortic expansion, and rupture[8]. At present, there is no confirmatory data to show that low-to-moderate intensity exercise is unsafe[4].

Aerobic exercise training is a prototypical strategy that maintains and restores homeostasis and can prevent or reduce the risk of numerous chronic diseases as observed in numerous epidemiological studies[35–38]. Post-dissection rehabilitation appears justified given findings of reduced VO_{2peak} and increased BMI > 1 year following open repair. Additional findings from this cohort show that participants are able to perform incremental exercise (81% attained a RER ≥1.05) without serious adverse events, which aligns with tolerability (i.e., more than 80% of participants achieve peak criteria) and safety (i.e., no exercise-related deaths and an approximate 15% nonserious adverse event rate) data observed in other populations[39]. Preliminary findings from Corone et al.[40] and Fuglsang et al.[15] show beneficial effects of moderate-intensity exercise-based cardiac rehabilitation following open repair for an ATAAD. However, these studies are limited by sample size, lack of randomization, minimal details outlining the exercise prescription, and quantitative assessment of VO_{2peak}.

We contend that the path forward involves a well-designed randomized controlled trial, utilizing submaximal CPX to assess exercise tolerance to guide low-to-moderate-intensity aerobic exercise prescriptions. Careful and continued monitoring of systolic and diastolic blood pressures (for hyper- and hypotensive responses) during CPX procedures and aerobic exercise are paramount to ensure safety. We recommend that intervention align with the post-operative clinical follow-up and utilize available diagnostic imaging data (echocardiography and CTA) to ensure optimal aortic valve function and stable aortic diameters, by comparing serial CTA imaging, prior to CPX procedures to ensure safety.

Novel data on a cohort of pTAA participants is also presented, showing that pTAA participants appear to more spontaneously recover based on significant improvements in VO_{2peak}, functional capacity, and patient-reported quality of life – PROMIS metrics: social roles/activities and physical function over time, which were not observed among the ATAAD group. It is unclear why VO_{2peak} recovers more exponentially after open repair for a pTAA as neither diagnosis meet eligibility criteria for insurance reimbursement of cardiac rehabilitation and exercise recommendations in this setting vary among cardiac surgeons. The pTAA group had a substantial percentage of patients with preoperative aortic valve disease (Table 1). Thus, improvements in VO_{2peak}, functional capacity and health-related quality of life may be secondary to improved hemodynamic function as the majority of these patients now have “normal” aortic valves and aortas and can perform activities of daily living with far fewer symptoms and/or fear.

There are limitations that need to be considered when interpreting the findings. First, the findings are from a single center and the sample size is relatively small, possibly limiting the statistical power to assess changes in VO_{2peak}. Second, selection biases may exist given that participants were cleared by their cardiac surgeon prior to participating and only participants motivated to voluntarily participate in supervised CPX to evaluate cardiorespiratory fitness were recruited. These factors may affect the generalizability of our findings to all postsurgical participants in this setting. It is possible that the general population of ATAAD participants could be worse. Thirdly, three participants (n=2, pTAA; n=1, ATAAD) completed cardiac rehabilitation which may have also resulted in study bias. Lastly, it can be argued that VO_{2peak} was reduced compared with normative values since participants attaining an RER of <1.05 were included. To address this point, we evaluated participants achieving only an RER ≥1.05 (range RER 1.07–1.36), and VO_{2peak} remained 36% below normative values (among peak CPX) >1 year following open repair for an ATAAD.

CONCLUSION

Cardiorespiratory fitness among the ATAAD group remained 36% below predicted normative values >1 year after repair, whereas the pTAA group experienced a significant improvement in cardiorespiratory fitness, which was only 13% below predicted normative values > 1 year after repair. Cardiopulmonary exercise testing was safe and feasible following open aortic repair in this setting for patients cleared to participate by their cardiac surgeons. Cardiac surgeons and cardiologists managing ATAAD participants post-operatively should consider CPX to assess exercise tolerance and blood pressure response to determine whether mild-to-moderate aerobic exercise should be recommended to reduce future risk of morbidity and mortality (Video).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Glossary of Abbreviations:

(ATAAD)	acute type A aortic dissection
(CPX)	cardiopulmonary exercise testing

(FRIEND Registry)	Fitness Registry and the Importance of Exercise National Database
(HR)	heart rate
(LVEF)	left ventricular ejection fraction
(PROs)	patient reported outcomes
(pTAA)	proximal thoracic aortic aneurysm
(VO_{2peak})	peak oxygen consumption
(RER)	respiratory exchange ratio
(6MWD)	six minute walk distance

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PERSPECTIVE STATEMENT

Cardiopulmonary exercise testing (CPX) is safe and feasible following open repair for an ATAAD or pTAA in patients cleared by their cardiac surgeons. Cardiac surgeons and cardiologists should consider CPX to evaluate exercise tolerance and blood pressure response and determine if mild-to-moderate aerobic exercise should be recommended to reduce future morbidity/mortality in post-repair ATAAD patients.

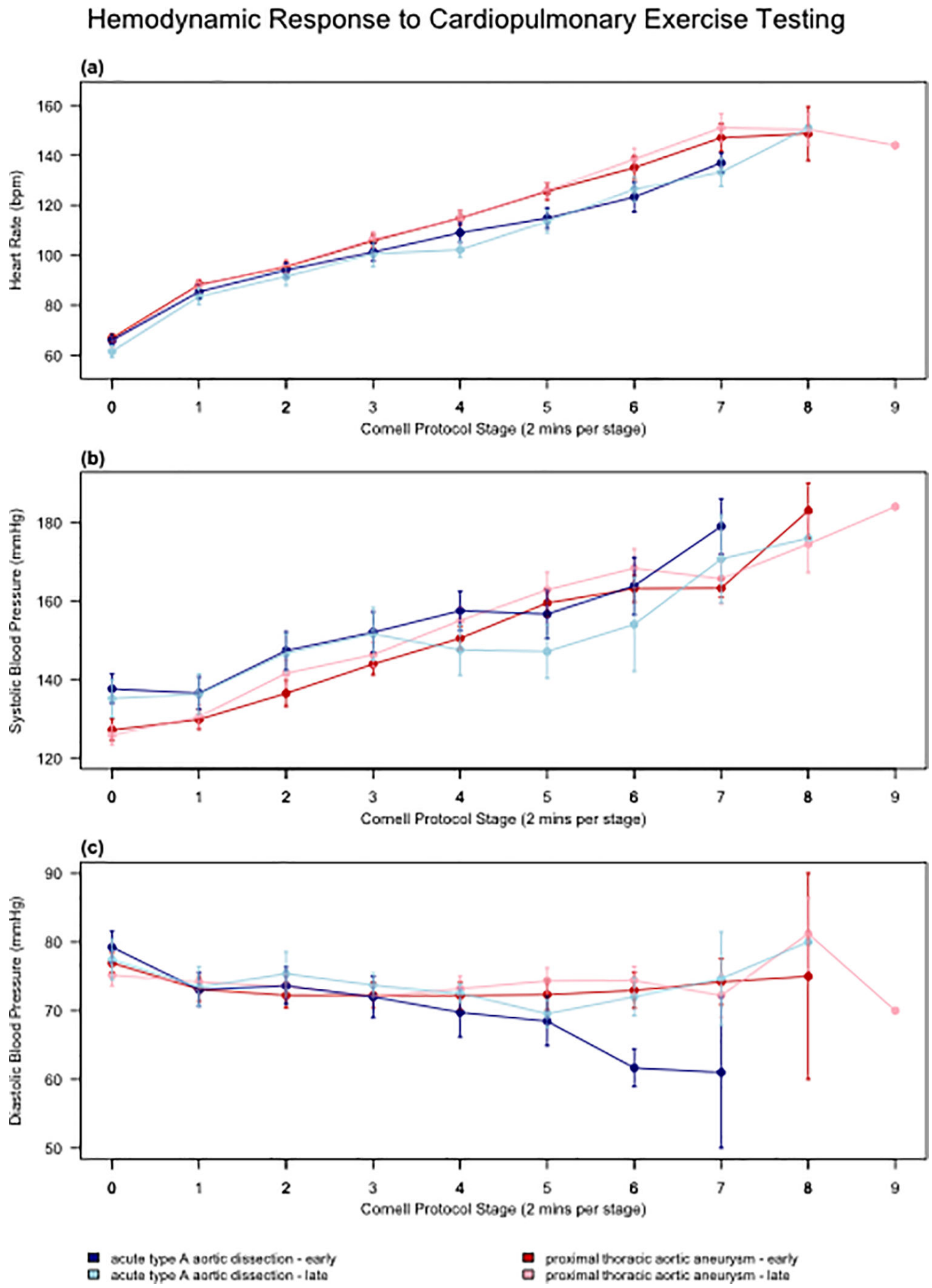


Figure 1: Heart rate and blood pressure responses to cardiopulmonary exercise testing.

Heart rate and blood pressure responses to cardiopulmonary exercise testing for ATAAD and pTAA groups from Timepoints Early and Late. ATAAD=acute type A aortic dissection; DBP=diastolic blood pressure; pTAA=proximal thoracic aortic aneurysm; SBP=systolic blood pressure.

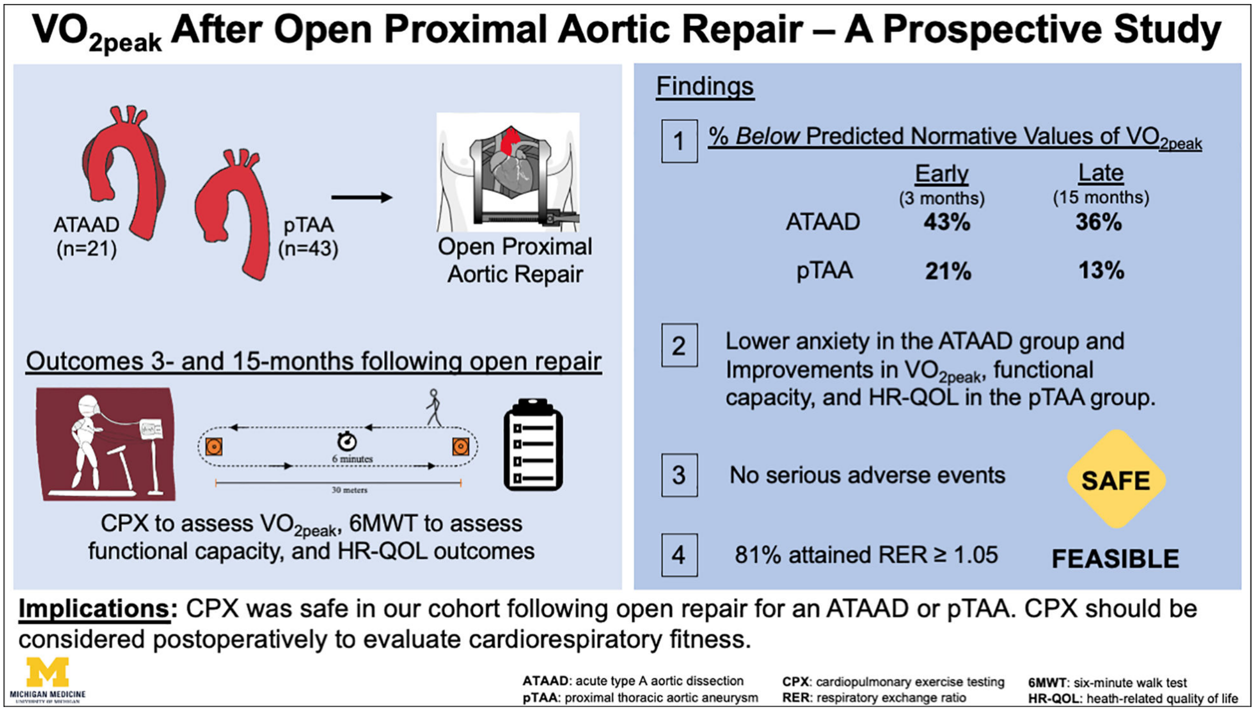


Figure 2: Health-related quality of life outcomes.

Health-related quality of life outcomes for ATAAD and pTAA groups for timepoints Early and Late. P-values for differences between early and late timepoints in social activities and physical function in the pTAA group were derived from paired Wilcoxon signed-rank tests. ATAAD=acute type A aortic dissection; pTAA=proximal thoracic aortic aneurysm.

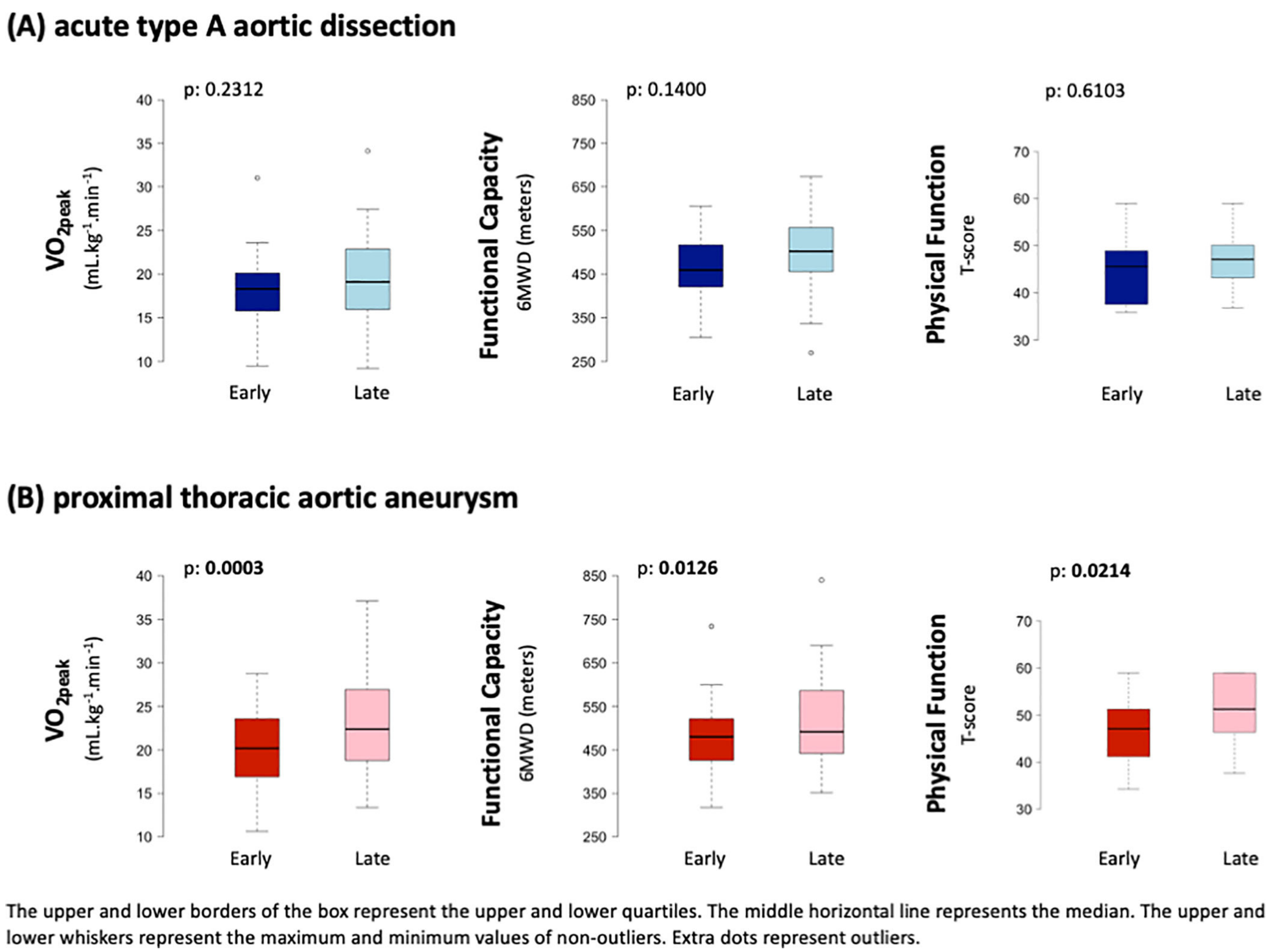


Figure 3: (Central Picture):

VO_{2peak}, functional capacity, and physical function remained similar from three months fifteen months following aortic repair in the ATAAD group; however, VO_{2peak}, functional capacity, and physical function significantly improved from three to fifteen months after open aortic repair in the pTAA group. The upper and lower borders of the box represent the upper and lower quartiles. The middle horizontal line represents the median. The upper and lower whiskers represent the maximum and minimum values of non-outliers.

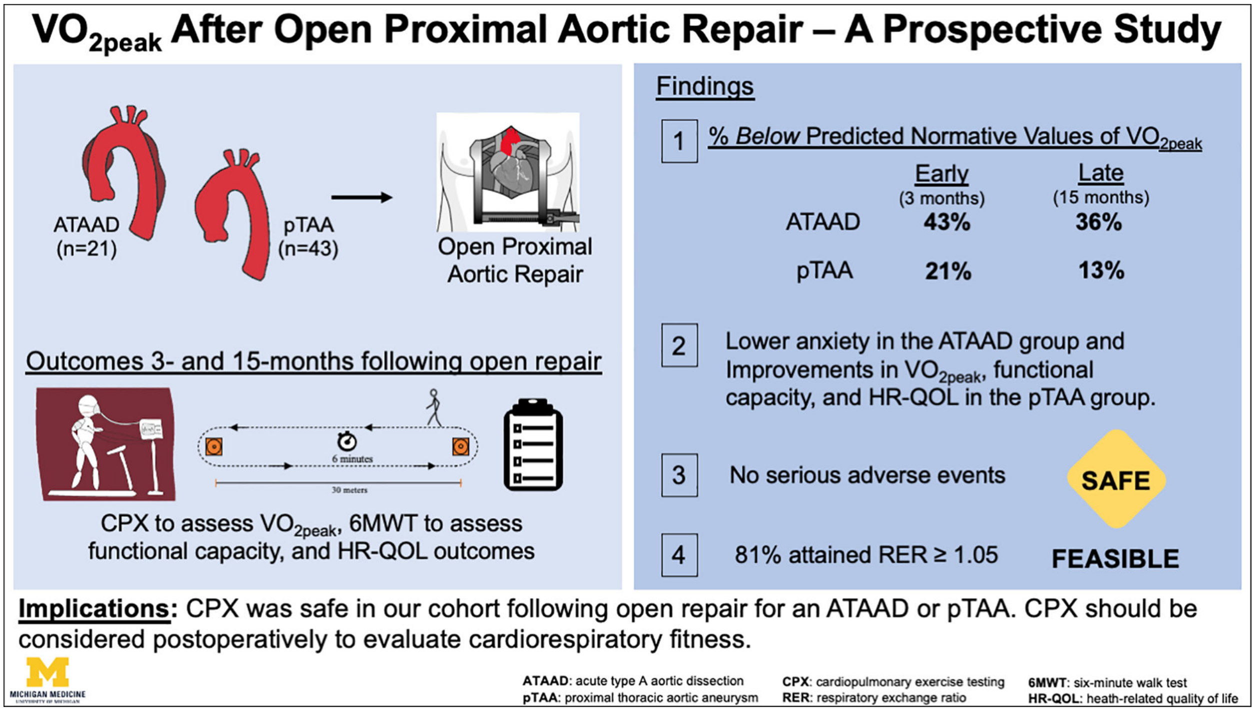
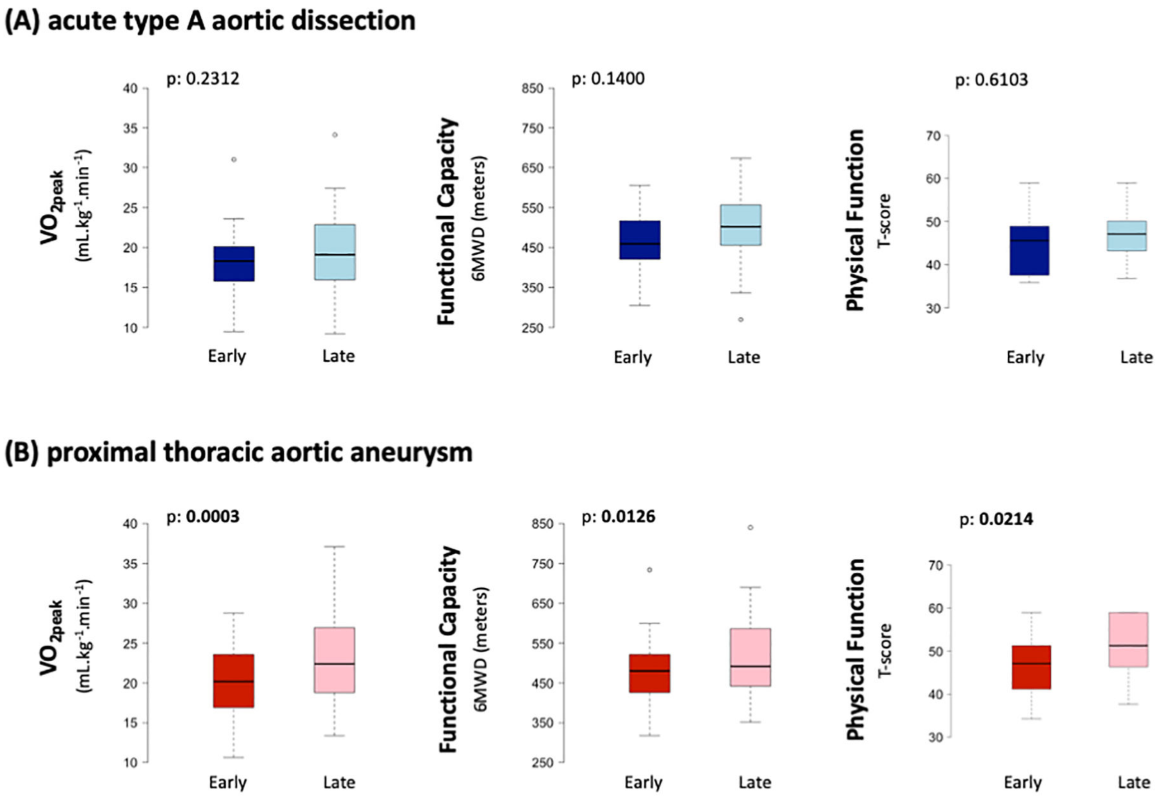


Figure 4: (Graphial Abstract):

Peak oxygen consumption (VO_{2peak}), functional capacity, and health-related quality of life outcomes were prospectively (3- and 15-months) evaluated following open repair. Significant improvements in VO_{2peak}, functional capacity, and HR-QOL metrics (social roles and activities, physical function) were observed within the pTAA group. There were no serious adverse events during CPX procedures. P-values were derived from paired Wilcoxon signed-rank tests. The upper and lower borders of the box represent the upper and lower quartiles. The middle horizontal line represents the median. The upper and lower whiskers represent the maximum and minimum values of non-outliers.

ATAAD=acute type A aortic dissection; pTAA=proximal thoracic aortic aneurysm; CPX=cardiopulmonary exercise test; 6MWT=Six minute walk test; HR-QOL=health-related quality of life; cardiorespiratory fitness=VO2peak; RER=respiratory exchange ratio.



The upper and lower borders of the box represent the upper and lower quartiles. The middle horizontal line represents the median. The upper and lower whiskers represent the maximum and minimum values of non-outliers. Extra dots represent outliers.

CENTRAL PICTURE.

VO_{2peak}, functional capacity, and physical function improved in pTAA but not ATAAD group.

CENTRAL MESSAGE

VO_{2peak} remained 36% below normative values >1 year after ATAAD repair. CPX should be considered to evaluate exercise tolerance and blood pressure response to determine if exercise should be recommended.

Table 1.

Preoperative Characteristics and Comorbidities

	All Participants n=64	ATAAD n=21	pTAA n=43
Age (years)	57 (49, 64)	55 (47, 59)	60 (53, 65)
Sex, male	55 (86)	18 (86)	37 (86)
Body mass index (kg/m^2)	29.9 (26.6, 33.8)	28.7 (26.6, 32.6)	30.6 (26.6, 35.2)
Aortic valve indications			
Aortic insufficiency, mod-to-severe	24 (41)	4 (24)	20 (48)
Aortic stenosis, mod-to-severe	13 (25)	2 (14)	11 (28)
Bicuspid aortic valve	23 (36)	1 (4.8)	22 (51)
Thoracic aortic aneurysm			
Root	26 (41)	7 (33)	19 (44)
Ascending	43 (67)	8 (38)	35 (81)
Arch	16 (25)	4 (19)	12 (28)
Descending	1 (16)	0 (0)	1 (2.3)
Max diameter (cm)	5.3 (4.7, 5.6)	5.1 (4.5, 5.5)	5.3 (4.7, 5.7)
Risk Factors			
Hypertension	50 (78)	17 (81)	33 (77)
Dyslipidemia	39 (61)	7 (33)	32 (74)
Peripheral vascular disease	13 (20)	9 (43)	4 (9.3)
Smoking history, former/current	35 (55)	12 (57)	23 (53)
Diabetes	10 (16)	1 (4.8)	9 (21)
Chronic lung disease	6 (9.4)	0 (0)	6 (14)
Chronic kidney disease	4 (6.2)	2 (9.5)	2 (4.6)
On dialysis	2 (3.1)	1 (4.8)	1 (2.3)
Coronary artery disease	20 (31)	3 (14)	17 (40)
History of myocardial infarction	6 (9.4)	0 (0)	6 (14)
History of stroke	3 (4.7)	0 (0)	3 (7.0)
History of heart failure	8 (12)	1 (4.8)	7 (16)
Heart failure within 2 weeks of operation	2 (3.1)	0 (0)	2 (4.7)
NYHA classification			
I	41 (64)	18 (86)	23 (53)
II	17 (27)	2 (9.5)	15 (35)
III	5 (7.8)	1 (4.8)	4 (9.3)
IV	1 (1.6)	0 (0)	1 (2.3)
Previous cardiac intervention	14 (22)	2 (9.5)	12 (28)
Previous cardiac surgery	10 (16)	2 (9.5)	8 (19)

Data presented as median (25%, 75%) for continuous data and n (%) for categorical data.

Abbreviations: ATAAD=acute type A aortic dissection; NYHA=New York heart association; pTAA=thoracic aortic aneurysm.

Table 2.

Intraoperative Details and Postoperative Outcomes

	All Participants n=64	ATAAD n=21	pTAA n=43
Intraoperative			
Valve/Root Procedure			
Aortic valve replacement	13 (20)	0 (0)	13 (30)
Root replacement	30 (47)	8 (38)	22 (51)
Aortic valve/root repair	17 (27)	11 (52)	6 (14)
Ascending replacement	60 (94)	21 (100)	39 (91)
Arch Procedure			
Hemiarch replacement	24 (37)	14 (67)	10 (23)
Zone 1/2/3 replacement	13 (20)	6 (29)	7 (16)
Concomitant surgery			
CABG	5 (7.8)	1 (4.8)	4 (9.3)
Mitral valve	2 (3.1)	0 (0)	2 (4.7)
Tricuspid valve	0 (0)	0 (0)	0 (0)
CPB time, minutes	212 (172, 256)	216 (188, 267)	212 (166, 250)
Cross-clamp time, minutes	153 (123, 186)	156 (109, 191)	152 (128, 186)
Hypothermic circulatory arrest	37 (58)	21 (100)	16 (37)
HCA time, minutes	27 (21, 35)	28 (21, 41)	26 (19, 34)
Cerebral Perfusion			
None	27 (42)	0 (0)	27 (63)
Antegrade	22 (34)	18 (86)	4 (9.3)
Retrograde	8 (12)	1 (4.8)	7 (16)
Both	7 (11)	2 (9.5)	5 (12)
Postoperative			
Reoperation for bleeding	1 (1.6)	1 (4.8)	0 (0)
Myocardial infarction	0 (0)	0 (0)	0 (0)
Cerebrovascular accident	2 (3.1)	2 (9.5)	0 (0)
TIA	0 (0)	0 (0)	0 (0)
Atrial fibrillation	18 (28)	4 (19)	14 (33)
Pneumonia	2 (3.1)	2 (9.5)	0 (0)
New-onset renal failure	4 (6.2)	2 (9.5)	2 (4.6)
Requiring dialysis	2 (3.1)	2 (9.5)	0 (0)
On dialysis at discharge	1 (1.6)	1 (4.8)	0 (0)
Deep sternal wound infection	0 (0)	0 (0)	0 (0)
Sepsis	0 (0)	0 (0)	0 (0)
Gastrointestinal complications	0 (0)	0 (0)	0 (0)
Hours ventilated	8.4 (5.6, 13.1)	11.6 (7.2, 26.6)	7.6 (5.0, 12.6)
Prolonged ventilation, >24 hrs	8 (12)	6 (29)	2 (4.6)
Hours intubated	17.3 (14.3, 23.0)	18.6 (16.4, 34)	16.5 (12.5, 20.6)

	All Participants n=64	ATAAD n=21	pTAA n=43
Reintubation	0 (0)	0 (0)	0 (0)
Postoperative length of stay (days)	6 (5, 9)	9 (6, 11)	6 (5, 8)
Total length of stay (days)	7 (5, 11)	11 (7, 14)	6 (5, 9)

Data presented as median (25%, 75%) for continuous data and n (%) for categorical data.

Abbreviations: ATAAD=acute type A aortic dissection; CABG=coronary artery bypass graft; CPB=cardiopulmonary bypass; HCA=hypothermic circulatory arrest; pTAA=thoracic aortic aneurysm; TIA=transient ischemic attack.

Zone 1 arch replacement=the arch is divided between the innominate and LCC arteries with replacement of the innominate artery to its bifurcation; Zone 2 arch replacement=the arch is divided between the LCC and left subclavian arteries with replacement of the innominate and LCC arteries; and Zone 3 arch replacement (total arch replacement)=the arch is divided distal to the left subclavian artery with replacement of all arch branch vessels.

Table 3.

Cardiopulmonary Exercise Test Outcomes Among Groups

	ATAAD (N=21)			pTAA (N=43)			Group by Time Interaction
Variables	**Early**	**Late**	**p-value***	**Early**	**Late**	**p-value***	**p-value†**
Resting Outcomes							
BMI, $kg \cdot m^{-2}$	28.7 (26.1, 30.1)	30.6 (27.4, 32.9)	0.0245	30.4 (26.6, 34.5)	31.2 (27.7, 37.7)	0.0045	0.3131
Anaerobic Threshold Outcomes							
VO_2, $mL.kg^{-1}.min^{-1}$	12.4 (10.9, 15.4)	13.9 (12.4, 15.4)	0.1025	13.5 (12.6, 15)	14.4 (13, 15.8)	0.0132	0.8021
RER	0.9 (0.8, 0.9)	0.9 (0.8, 0.9)	0.0958	0.9 (0.8, 0.9)	0.9 (0.8, 1)	0.3034	0.5697
VE/VCO_2 slope	28 (25.5, 33.5)	27.8 (24.2, 30)	0.2338	28.5 (25, 30)	28 (25.2, 30)	0.4758	0.2990
Peak Outcomes							
VO_{2peak}, $mL.kg^{-1}.min^{-1}$	18.3 (15.8, 20.1)	19.1 (16.8, 22.8)	0.2312	20.2 (17, 23.5)	22.4 (18.8, 26.9)	0.0003	0.1405
VO2, $mL.min^{-1}$	1638 (1281, 2070)	1849.5 (1539.8, 2235.2)	0.0833	1924 (1498.8, 2221)	2120.5 (1926.5, 2683.5)	0.0001	0.1489
RER	1.1 (1, 1.1)	1.1 (1.1, 1.2)	0.6908	1.2 (1.1, 1.2)	1.2 (1.1, 1.3)	0.3958	0.4220
VE_{peak}	52.7 (36.6, 58.6)	55 (43.2, 66.5)	0.8603	66.5 (51.5, 82.8)	73.9 (63.7, 86.2)	0.0162	0.2144
VE/ VCO_2 slope	24.7 (22.8, 29.6)	24.4 (22.7, 27)	0.0744	27.2 (23.6, 30.5)	25.9 (24, 28.7)	0.2944	0.5655
Predicted VO_{2peak}-FRIEND	33.84 (27.71, 36.04)	31.86 (26.35, 33.90)	0.0213	28.91 (24.22, 31.51)	27.96 (23.80, 31.74)	0.0052	0.3900
% predicted, VO_{2peak}-FRIEND	0.60 (0.49, 0.65)	0.68 (0.57, 0.74)	0.0788	0.73 (0.66, 0.82)	0.81 (0.70, 0.96)	0.0004	0.4758
METs	5.2 (4.5, 5.9)	6 (4.9, 8.4)	0.1705	5.8 (4.9, 7)	6.4 (5.5, 8)	0.0128	0.7647
RPE	15 (13, 16)	14 (12, 16)	0.7500	16 (15, 17)	15.5 (15, 17)	0.7424	0.6377
PRP	183.8 (162, 244)	188.7 (156.3, 250.2)	0.9799	228.2 (173.9, 258.5)	236.5 (201.2, 278.5)	0.5043	0.2423
CPX Time (min:sec)	545 (461, 684)	615 (450, 723.5)	0.7173	643 (590, 790.8)	720 (600, 836)	0.0720	0.2775
Heart Rate, bpm	115 (107, 133)	121.5 (104.8, 133)	0.7331	131 (118, 150)	137.5 (124.5, 159)	0.2561	0.2788
SBP, mmHg	170 (148, 182)	167 (147.5, 190)	0.4496	164 (158, 173)	167 (156, 185.5)	0.8530	0.7902
DBP, mmHg	68 (62, 80)	75 (69.5, 80)	0.1658	70 (63, 80)	70 (68, 80)	0.8288	0.1561
Recovery Outcomes							
1 min-HR, bpm	13 (7, 18)	14 (10.8, 19.2)	0.1108	11 (7, 15)	15.5 (11.2, 20.8)	0.0280	0.7652
% abnormal, 1 min-HR	9 (43%)	5 (31%)	0.0833	22 (54%)	9 (26%)	0.0522	0.5727
6 Minute Walk Test Outcomes							
6MWD, meters	459 (420, 517)	502 (456, 556)	0.1400	480 (426, 522)	492 (443, 585)	0.0126	0.4214
% predicted, 6MWD	0.8 (0.6, 0.8)	0.8 (0.7, 0.9)	0.1164	0.9 (0.8, 1)	0.9 (0.8, 1)	0.0089	0.3371
Pulmonary Function Outcomes							

	ATAAD (N=21)			pTAA (N=43)			Group by Time Interaction
Variables	Early	Late	p-value*	Early	Late	p-value*	p-value†
MVV	116 (96, 141)	138 (109.5, 152.5)	0.9818	132.5 (108.8, 146.8)	137 (114.8, 148)	0.1945	0.1023
Breathing Reserve, L	66 (32.3, 86.7)	75.5 (59.8, 92.4)	0.4060	59.3 (49.2, 71.7)	57.4 (41.4, 74.7)	0.2114	0.0246
% Breathing Reserve	55 (37, 65)	59 (46, 68)	0.1633	48 (37, 54)	43 (36, 52)	0.0979	0.0201

Abbreviations: ATAAD, acute type A aortic dissection; BMI, body mass index; CPX, cardiopulmonary exercise testing; DBP, diastolic blood pressure; FRIEND, fitness registry and the importance of exercise national database; HR, heart rate; MET, metabolic equivalent; MVV, maximal voluntary ventilation; PRP, pressure-rate product; RER, respiratory exchange ratio; RPE, rated perceived exertion; SBP, systolic blood pressure, pTAA, thoracic aortic aneurysm; VO_{2peak}, peak oxygen uptake; 6MWD, 6-minute walk test distance.

Data are reported as median (interquartile range) or n (%).

*P-values for continuous and categorical variables were derived from paired Wilcoxon signed-rank test and McNemar's test, respectively.

†P-values for group by time interactions were derived from linear mixed model.

Table 4.

Time Differences in Diagnostic Imaging Outcomes Among Groups

	ATAAD (N=21)			pTAA (N=43)			Group by Time Interaction
Variables	**Early**	**Late**	**p-value***	**Early**	**Late**	**p-value***	**p-value†**
LVEF	60 (56.2, 60)	60 (60, 62.8)	1.0000	60 (54.2, 60)	60 (55, 65)	0.2129	0.4818
Aortic Insufficiency	1 (6%)	2 (18%)	0.3173	1 (3%)	0 (0%)	1.0000	0.0558
Aortic Diameters (mm)							
Sinus	38.3 (33.9, 42.2)	37.6 (34.4, 42.7)	0.6659	38.5 (35.2, 42.5)	38.6 (35.6, 42.3)	0.1339	0.1590
Mid Ascending	30 (29.6, 32.5)	30.1 (28.5, 33.3)	0.4973	32.8 (31, 33.3)	32 (30.8, 34)	0.9904	0.5250
Proximal Arch	32 (29.1, 33)	31.9 (28.5, 33.4)	0.6462	33 (32, 36.2)	34 (32, 36.9)	0.6567	0.6265
Mid Arch	32 (29.4, 36)	33.9 (32, 35.2)	0.0711	31 (28.9, 34.1)	31 (28, 33.4)	0.8190	0.1756
Mid Descending	31.8 (27.1, 36.5)	31.4 (28.6, 34.9)	0.8445	27 (25.2, 30.3)	26.6 (24, 28.8)	0.0880	0.6145
Abdominal	30 (24, 32.5)	31.9 (26.8, 40)	0.0049	26.2 (24, 29)	24.7 (23.2, 28.1)	0.2291	$2*10^{-5}$

Abbreviations: ATAAD, acute type A aortic dissection; CT, computed tomography; LVEF, left ventricular ejection fraction; pTAA, proximal aortic aneurysm.

Data are reported as median (interquartile range) or n (%)

*P-values for continuous and categorical variables were derived from paired Wilcoxon signed-rank test and McNemar's test, respectively.

†P-values for group by time interactions were derived from linear mixed model.