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Effects Of Thoracic Endovascular Aortic Repair On Cardiac Function At Rest

Nabeel Kassam

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EFFECTS OF THORACIC ENDOVASCULAR AORTIC REPAIR ON CARDIAC FUNCTION AT REST

A Thesis Submitted to the Yale University School of Medicine in Partial Fulfillment of the Requirements for the Degree of Doctor of Medicine

by

Nabeel Kassam 2024
Abstract

EFFECTS OF THORACIC ENDOVASCULAR AORTIC REPAIR ON CARDIAC FUNCTION AT REST

Nabeel Kassam, Afsheen Nasir, Syed Usman Bin Mahmood, Argyrios Gyftopoulos, Roland Assi

a. Hypothesis: We hypothesize that Thoracic Endovascular Aortic Repair (TEVAR) leads to a decline in cardiac function among post-operative patients. Our primary objective is to identify the changes of cardiac function to post-TEVAR patients at rest using echocardiography studies. With this knowledge, we aim to gain valuable insight into the post-op management of patients with the goal of strategizing post-op care to reduce complications and exacerbation to heart failure.

b. Methods: Chart review of the electronic medical record (EMR) was used to collect patient data, patient history, procedural information, outcomes, and echocardiogram parameters. To assess the impact of TEVAR, the echo parameters were then analyzed using a paired sample t-test, comparing pre-TEVAR and post-TEVAR echocardiograms. The alpha level for determining statistical significance was set at p=0.05 for two-sided comparisons.
c. Results: Between the pre-TEVAR echo and first post-op echo, average indexed left atrial volume for all patients (n=30) was 35.68 pre-TEVAR and increased to 35.75 post-TEVAR with a p-value of 0.97. Mitral E/A ratio decreased from 1.09 pre-operatively to 1.04 post-operatively. E/A ratio (n=29) with a p-value of 0.92. Average E/e' ratio increased from 10.59 pre-TEVAR to 10.69 post-TEVAR (n=32) with a p-value of 0.91. Tricuspid regurgitation pressure gradient (TRPG) increased from 24.02 pre-operatively to 26.96 post-operatively (n=22) with a p-value of 0.33. Between the pre-TEVAR echo and second post-op echo, the indexed left atrial volume increased on average by 3.62 after TEVAR (p=0.66). E/A ratio decreased by 0.03 across all patients on average (p=0.66), while E/e’ ratio decreased by 0.25 post-operatively (p=0.31). TRPG increased by 0.92 after TEVAR (p=0.84).

d. Conclusions: The data showed a slight upwards trend in TRPG after the first post-op echo. However, no statistically significant changes to diastolic function were seen in patients after TEVAR.
Acknowledgements:

We gratefully acknowledge Dr. Roland Assi for his invaluable contributions to our research endeavors. We extend our sincere appreciation to the Yale Office of Student Research for their generous funding support, which has been instrumental in facilitating the execution and progression of our research projects. Additionally, we express our gratitude to the National Institutes of Health for their financial backing, providing critical resources that have empowered us to delve into groundbreaking research that holds the potential to impact the field of medicine positively. Special recognition is also extended to the Department of Surgery for their unwavering support, both in terms of resources and mentorship.

Together, the collaborative support from Dr. Roland Assi, the Yale Office of Student Research, the National Institutes of Health, and the Department of Surgery has fortified our research endeavors. Their collective contributions underscore the importance of collaborative partnerships in driving scientific inquiry and advancing the frontiers of knowledge.
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Introduction:

In the ever-evolving landscape of cardiovascular interventions, Thoracic Endovascular Aortic Repair (TEVAR) has firmly established itself as the preferred modality for addressing descending thoracic aortic aneurysms, ushering in a new era in the management of aortic aneurysms and dissections while surpassing open surgery in terms of both early and mid-term outcomes. Studies have shown that mean survival was superior for TEVAR when compared to open surgical intervention and should be considered first line for repair of intact descending thoracic aortic aneurysms.¹

The paradigm shift brought about by TEVAR is underscored by its efficacy in mitigating short-term post-intervention complications, presenting a promising avenue for enhanced patient care. Clinical outcomes have shown that 30-day mortality, stroke, renal failure, and pulmonary complications are significantly decreased in TEVAR patients when compared to open surgical repair cases.² Benefits from the endovascular approach are most likely due to avoidance of thoracotomy or sternotomy incision, absence of aortic cross-clamping, decreased blood loss, and decreased end-organ ischemia.³

The increasing acceptance and utilization of TEVAR has allowed its therapeutic reach to extend beyond conventional boundaries, with endovascular surgical intervention now possible for treatment of type B aortic dissection with malperfusion or rupture, traumatic aortic transection, and penetrating aortic ulcer.⁴
This breadth of diseases that can be treated with TEVAR has also expanded the age demographic for the procedure. Cooke et al. found patients less than 50 years old were over two times more likely to undergo TEVAR due to a type B aortic dissection, but 22% less likely to have a thoracic aortic aneurysm compared to those greater than or equal to 50 years old.\(^5\)

However, amid the triumphs, a shadow of uncertainty looms over the long-term performance of cardiac function after TEVAR procedures. Long-term outcomes for TEVAR can be affected due to surgical materials or clinical follow-up. Despite the undeniable recent success of TEVAR in mitigating mortality and other adverse outcomes, a critical nuance emerges in the form of endograft materials.

These materials, while contributing to the overall efficacy of TEVAR, exhibit a stiffness that contrasts with the inherent compliance of the native thoracic aorta. The decreased elastance seen in post-operative patients may have downstream effects that were not foreseen or could have been mitigated. This discrepancy raises concerns about the potential impact on aortic compliance, a pivotal factor in minimizing cardiac impedance and workload during ejection.

Aortic compliance, a dynamic property affected by various factors such as smoking, high cholesterol, hypertension, and genetic predisposition, assumes heightened significance in the realm of cardiovascular health. Endovascular aortic stent grafting is known to decrease the compliance of the aorta while also
increasing the left ventricular afterload. The process of aortic stiffening, accelerated by multiple cardiovascular risks, holds implications for the development and progression of cardiovascular diseases.

Notably, preclinical investigations underscore the occurrence of acute aortic stiffening following TEVAR, precipitating consequences such as elevated pulse pressure, hypertension, compromised coronary perfusion, and the conceivable onset of heart failure through left ventricular hypertrophy and reduced ejection fraction. In fact, increased aortic stiffness secondary to stent grafts leads to heart failure in as many as 40% of patients who survive long-term.

Along with compliance issues, persistent concerns center around complications that continue to challenge the durability and efficacy of endografts, encompassing issues like device fracture, endoleak, thrombosis, and graft kinking. Endoleak is identified as the ongoing flow of blood and pressurization within the aortic segment affected by disease, which should be isolated by the endograft. There are five different types of endograft leaks including sealing failure, retrograde flow, device failure of the modular graft or fabric, passage of blood due to graft porosity, and continued aneurysm expansion without a leak visible with imaging.

A Type II endoleak, where retrograde flow through collateral vessels occurs into the perigraft space, is the most common type, accounting for about 75% of all endoleaks. Although Type II leaks are stable and expected to
decrease or thrombose over time, treatment may be required if symptoms persist or if the aneurysm continues to expand. Reintervention may be required to repair certain types of endoleaks, and open surgical repair is sometimes needed if the endovascular approach fails.7

According to Shin-Ah Son et al., endoleak was seen as the leading cause of reintervention in their propensity-matched TEVAR analysis.8 This potential outcome could significantly compromise the overall efficacy of TEVAR, posing a substantial challenge to its intended effectiveness. On the other hand, the leading cause of reintervention for open surgical repair was new onset aortic dissection or expansion, which perhaps poses as further evidence for the use of TEVAR over open repair.8

Less common than endoleak, endograft collapse is a rare complication that can be seen usually with younger patients with traumatic aortic dissection. Additional risk factors for endograft collapse include smaller distal aortic diameter, minimal intragraft aortic diameter, and certain types of endograft fabrics. The leading causes of collapse are off-label usage and endograft oversizing, with serious complications requiring emergent TEVAR or open surgical repair.7

These unresolved challenges dictate an ongoing need for vigilant follow-up and emphasize the imperative for further advancements in device development. With continued progression in medical devices, we have seen a large decrease in the overall amount and type of endoleaks experienced in the
post-operative course of TEVAR. Type III endoleak, which commonly arises due to inadequate overlap between the components of the graft, and Type IV endoleak, which is caused by graft porosity, have become more increasingly uncommon with improvements in graft material.\textsuperscript{7}

As the landscape of endovascular techniques and device design for aortic repair evolves, the elimination of graft complications remains a consistent goal with additional area for improved clinical outcomes. Continued research and dedication to these complications could help decrease additional causes of leaks such as inadequate graft sealing and retrograde blood flow.

We must also consider the insufficiently characterized nature of the longer-term interaction between cardiac physiology and graft materials, especially when considering the impact of repetitive stressors on endografts and their enduring mechanical durability. The progression in stent graft technology has not only facilitated advancements but also paved the way for innovative designs specifically crafted to surmount anatomic challenges. This evolution in stent graft design not only addresses existing anatomical obstacles but also extends the scope and applicability of TEVAR.

Studies of TEVAR outcomes using the Zenith Alpha Thoracic Stent Graft, one of the first low-profile devices used in treatment of thoracic aortic diseases. Many of the advantages of this graft rely on the graft material. However, the thinner woven polyester fabric and lower profile may lead to larger complications in the long run. Torsello et al. found a lower rate of aneurysmal sac growth and
migration with one case of distal stent graft migration and no stent fracture. One case of reintervention was necessary due to a combine Type IA and Type II endoleak.⁹

The challenges in device design are compounded by the cyclic deformations induced by the rhythmic pulsatility of the heart and fluctuations during respiration. While existing knowledge has successfully quantified morphologic changes in the thoracic aorta and left ventricle resulting from cardiac-induced motion, a significant gap persists in our understanding of how TEVAR specifically alters additional cardiac geometry and induces cardiac-related deformation from the pre- to post-TEVAR phases.

Moreover, research studies have systematically demonstrated and provided insights into the impact of exercise physiology on cardiac function. Evaluation during exercise stress echocardiogram has shown TEVAR possesses the ability to influence the interaction between the left ventricle and aorta through drastic geometrical changes. More specifically, TEVAR has been demonstrated to suppress left ventricular contractile capacity while also increasing cardiac afterload during exercise as evidenced by a significant increase in ventricular-arterial coupling.¹⁰

However, the effects of TEVAR at rest have yet to be studied effectively. By delving into the intricate interplay between TEVAR, aortic compliance, graft materials, and cardiac dynamics, this study aspires to provide a holistic and nuanced understanding of how TEVAR influences the structural and functional
aspects of the heart at rest. The research not only contributes to the expanding body of knowledge within cardiovascular medicine but also holds the potential to inform future refinements in TEVAR procedures at the surgical, mechanical, and clinical level, improve post-procedural care and follow-up through the utilization of a standardized echocardiogram schedule, and decrease adverse events in both short-term and long-term outcomes, ultimately optimizing patient care and advancing the field of cardiothoracic surgery.

**Statement of purpose:**

In our research endeavor, we postulate that Thoracic Endovascular Aortic Repair (TEVAR) potentially leads to a decline in cardiac function among post-operative patients. Our primary objective revolves around a meticulous analysis, delving into the nuanced realms of cardiac performance to identify the precise areas influenced by TEVAR and quantify the magnitude of this impact through advanced imaging techniques. We believe a decrease in diastolic function will be observed in post-TEVAR patients while at rest, as demonstrated by findings on echocardiogram.

Armed with this comprehensive understanding, our overarching aim is to furnish valuable insights that can contribute to the development of strategies for averting or alleviating the diminished cardiac function after surgical intervention, thereby effectively addressing and managing the adverse effects associated with TEVAR on the cardiovascular system.
Methods:

Student Contributions:

The procedures used in this study, including TEVAR and echocardiography, were conducted by faculty and staff of the Yale Cardiothoracic Surgery Department at Yale New Haven Hospital. The data from these procedures were collected through electronic medical record analysis completed by Nabeel Kassam and Argyrios Gyftopoulos, MD. The database was further edited by Syed Usman Bin Mahmood, MD and Afsheen Nasir, MD. Statistical analysis was completed by Afsheen Nasir, MD and Nabeel Kassam. The writing of this manuscript was completed solely by Nabeel Kassam with feedback and support from Roland Assi, MD.

Ethics Statement:

Ensuring the ethical and responsible conduct of research involving patients is paramount to upholding the principles of patient welfare, autonomy, and justice. In the realm of cardiac surgery research, it is imperative to prioritize the well-being and rights of individuals who entrust their health to the scientific community. Researchers must adhere to rigorous ethical standards, respecting the dignity, privacy, and confidentiality of cardiac surgery patients throughout the research process.
**Human Subjects Research:**

This study was approved by the Institutional Review Board on 3/2/17 under IRB Protocol ID 2000020356 and allows for medical record review of cardiac surgery patients. "The Committee finds that informed consent can be waived for this study per federal regulation 45 CFR 46.116(d). This part of the regulations states that 1) this research involves no more than minimal risk to the subjects, 2) the waiver or alteration will not adversely affect the rights and welfare of the subjects, 3) the research could not practicably be carried out without the waiver and 4) whenever appropriate the subjects will be provided with additional pertinent information after participation.

**Laboratory Animals:**

No laboratory animals were utilized during the ideation, data collection, or analysis of this study.

**Methods Description:**

**Retrospective Chart Review:**

The electronic medical record (EMR) was used to collect information on the procedures as well as outcomes post-operatively. Data was extracted from echocardiography pre-operatively where possible and compared to post-op echocardiography. Key parameters of cardiac function that were collected during
echocardiography include left atrial volume indexed to body surface area (LA Vol Index), left ventricular ejection fraction (LVEF), mitral E/A ratio, average mitral E/e’ ratio and tricuspid regurgitation pressure gradient (TRPG) among other parameters.

Patient demographics and pre-existing comorbidities were also extracted from the EMR. The admission and procedure notes were used to determine necessary information about the procedure. Chart review was also utilized to determine adverse outcomes and events after surgery. The main outcome studied was change in diastolic function post-TEVAR using paired analysis.

**Statistical Methods:**

The statistical methodology employed in this study involved the meticulous collection and thorough analysis of data utilizing Microsoft Excel. The inclusion criteria for patients in the study stipulated the availability of both pre-TEVAR and post-TEVAR echocardiograms, thus ensuring a comprehensive and complete dataset for analysis. Patients lacking either pre- or post-TEVAR echocardiograms were deliberately excluded from the study to maintain data integrity.

Furthermore, a stringent approach was taken to eliminate potential sources of bias by excluding patients with incomplete echocardiogram results. Specifically, individuals with more than two missing echo variables were deemed ineligible for inclusion in certain analyses, as conducting a paired analysis on such cases would not be methodologically sound.
Identification and handling of outliers were integral to the robustness of the statistical analysis. Outliers were identified based on their deviation of more than 3 standard deviations from the mean, ensuring that extreme data points did not unduly influence the overall results. This meticulous outlier detection process contributes to the reliability and validity of the statistical findings.

To assess the impact of TEVAR, a paired sample t-test was employed, comparing relevant parameters from pre-TEVAR and post-TEVAR echocardiograms. This statistical test provides a robust means of evaluating the significance of any observed differences. The alpha level for determining statistical significance was set at p=0.05 for two-sided comparisons, adhering to conventional standards in the field.

**Transparent reporting of results:**

211 TEVAR procedures were completed at Yale New Haven Hospital between October 2019 and October 2022. With a total of 146 unique patients undergoing TEVAR, 96 of them had undergone a pre-operative echocardiogram. A total of 63 of the patients underwent a post-operative echocardiogram, while only 34 patients underwent both procedures. This results in only 23% of patients who underwent TEVAR meeting the inclusion criteria for our study.
Table 1: Number of patients undergoing echocardiography studies

<table>
<thead>
<tr>
<th>Procedure Type</th>
<th>Patients (n=146)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-op echocardiograms</td>
<td>96</td>
</tr>
<tr>
<td>Post-op echocardiograms</td>
<td>63</td>
</tr>
<tr>
<td>Pre-op and post-op echocardiograms</td>
<td>34</td>
</tr>
</tbody>
</table>

Of the 34 patients with at least one echo before and one echo after TEVAR, 25 were male and 9 were female. The average age of male patients was 61 years old, while the average age of female patients was 65 years old.

Table 2: Patient Demographics

<table>
<thead>
<tr>
<th>Gender</th>
<th>All patients</th>
<th>&lt;65 years old</th>
<th>&gt;= 65 years old</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>25</td>
<td>17</td>
<td>8</td>
</tr>
<tr>
<td>Female</td>
<td>9</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
Indication for patients undergoing TEVAR procedure include aortic dissection, aortic aneurysm, and penetrating aortic ulcer. The most common indication was aortic dissection with 74% of patients (n=25) undergoing TEVAR due to this cause.

Most patients (n=13) underwent elective TEVAR procedure, amounting to 45% of the patient sample. There were 8 patients that underwent urgent TEVAR, comprising 28% of the sample, and another 8 patients that underwent Emergent TEVAR, again comprising 28% of the sample population.

<table>
<thead>
<tr>
<th>TEVAR Indication</th>
<th>Patients (n=34)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic Dissection</td>
<td>25</td>
</tr>
<tr>
<td>Aortic Aneurysm</td>
<td>4</td>
</tr>
<tr>
<td>Penetrating Aortic Ulcer</td>
<td>7</td>
</tr>
</tbody>
</table>

TEVAR: Thoracic Endovascular Aortic Repair

Table 4: Surgical status of TEVAR procedure
<table>
<thead>
<tr>
<th>Status</th>
<th>Patients (n=29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urgent</td>
<td>8</td>
</tr>
<tr>
<td>Emergent</td>
<td>8</td>
</tr>
<tr>
<td>Elective</td>
<td>13</td>
</tr>
</tbody>
</table>

TEVAR: Thoracic Endovascular Aortic Repair

Table 5: Prior cardiothoracic interventions in patients undergoing TEVAR

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Patients (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sternotomy</td>
<td>9</td>
</tr>
<tr>
<td>Coronary Artery Bypass Graft</td>
<td>3</td>
</tr>
<tr>
<td>Aortic Valve Replacement</td>
<td>4</td>
</tr>
<tr>
<td>Aortic Valve Repair</td>
<td>2</td>
</tr>
<tr>
<td>Open Aortic Repair</td>
<td>9</td>
</tr>
<tr>
<td>Endovascular Aortic Repair</td>
<td>5</td>
</tr>
</tbody>
</table>

TEVAR: Thoracic Endovascular Aortic Repair
32% of the patients (n=11) had a history of prior cardiac intervention including sternotomy, coronary artery bypass graft, aortic valve replacement, aortic valve repair, and prior aortic intervention. 9 patients underwent previous open aortic repair, while 5 patients had a previous TEVAR procedure.

All patients in the study had prior comorbidities prior to undergoing TEVAR. Hypertension was the most common comorbidity with 68% of patients (n=23) having hypertension prior to surgical intervention followed by dyslipidemia with 41% of patients (n=14).

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>Patients (n=34)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>23</td>
</tr>
<tr>
<td>Diabetes</td>
<td>5</td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>8</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>3</td>
</tr>
<tr>
<td>Congestive Heart Failure</td>
<td>3</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>14</td>
</tr>
<tr>
<td>Chronic Kidney Disease</td>
<td>6</td>
</tr>
</tbody>
</table>
Figure 1: Individual changes in indexed left atrial volume pre- and post-operatively.

LA: left atrial

Figure 2: Individual changes in Mitral E/A ratio pre- and post-operatively.
Average indexed left atrial volume for all patients (n=30) was 35.68 pre-TEVAR and increased to 35.75 post-TEVAR with a p-value of 0.97. Indexed left
atrial volume increased in 16 patients post-operatively and decreased in 14 patients, which can be seen visually in Figure 1.

Mitral E/A ratio decreased from 1.09 pre-operatively to 1.04 post-operatively. E/A ratio (n=29) with a p-value of 0.92. E/A ratio increased in 12 patients while decreasing in 12 patients. The ratio remained the same in 5 patients. The comprehensive details and findings for E/A ratio are encapsulated in Figure 2.

Figure 3 serves as an illustrative visual depiction presenting the intricate findings related to the E/e’ ratio. Average E/e’ ratio increased from 10.59 pre-TEVAR to 10.69 post-TEVAR (n=32) with a p-value of 0.91. E/e’ ratio increased in 16 patients after TEVAR and decreased in 15 patients. The ratio remained the same for 1 patient.

In Figure 4, findings for the tricuspid regurgitation pressure gradient can be found. TRPG increased from 24.02 pre-operatively to 26.96 post-operatively (n=22) with a p-value of 0.33. The gradient increased in 15 patients, decreased in 6 patients, and remained the same in 1 patient post-TEVAR.

Between the pre-TEVAR echo and first post-op echo, the indexed left atrial volume increased on average by 0.07 after TEVAR. E/A ratio decreased by 0.04 across all patients on average, while E/e’ ratio increased by 0.10 post-operatively. Tricuspid regurgitation pressure gradient increased by 2.94 after TEVAR. All changes measured on echocardiogram for indexed left atrial volume,
E/A ratio, E/e’ ratio, and tricuspid regurgitation pressure gradient were not statistically significant with p-values well above 0.05.

Table 7: Echocardiogram parameters for pre-op echo and first post-op echo

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pre-op echo</th>
<th>Post-op echo 1</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indexed LA Volume</td>
<td>35.68</td>
<td>35.75</td>
<td>0.97</td>
</tr>
<tr>
<td>Mean</td>
<td>17.73</td>
<td>14.98</td>
<td></td>
</tr>
<tr>
<td>Std Dev</td>
<td>1.09</td>
<td>1.04</td>
<td>0.92</td>
</tr>
<tr>
<td>E/A (n=29)</td>
<td>0.37</td>
<td>0.37</td>
<td></td>
</tr>
<tr>
<td>E/e’ (n=32)</td>
<td>10.59</td>
<td>10.69</td>
<td>0.91</td>
</tr>
<tr>
<td>TRPG (n=22)</td>
<td>24.02</td>
<td>26.96</td>
<td>0.33</td>
</tr>
<tr>
<td>Mean</td>
<td>8.23</td>
<td>10.96</td>
<td></td>
</tr>
<tr>
<td>Std Dev</td>
<td>24.02</td>
<td>26.96</td>
<td>0.33</td>
</tr>
</tbody>
</table>

LA: left atrial; TRPG: Tricuspid Regurgitation Pressure Gradient

Table 8: Echocardiogram parameters second post-op echo

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Post-op Echo 2</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indexed LA Volume</td>
<td>39.30</td>
<td>0.66</td>
</tr>
<tr>
<td>Mean</td>
<td>16.13</td>
<td></td>
</tr>
<tr>
<td>Std Dev</td>
<td>39.30</td>
<td></td>
</tr>
</tbody>
</table>
Between the pre-TEVAR echo and second post-op echo, the indexed left atrial volume increased on average by 3.62 after TEVAR. E/A ratio decreased by 0.03 across all patients on average, while E/e’ ratio decreased by 0.25 post-operatively. Tricuspid regurgitation pressure gradient increased by 0.92 after TEVAR. All changes measured on echocardiogram for indexed left atrial volume, E/A ratio, E/e’ ratio, and tricuspid regurgitation pressure gradient were not statistically significant with p-values well above 0.05.

<table>
<thead>
<tr>
<th></th>
<th>E/A (n=23)</th>
<th>E/e' (n=23)</th>
<th>TRPG (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.06</td>
<td>10.34</td>
<td>24.94</td>
</tr>
<tr>
<td></td>
<td>0.41</td>
<td>3.35</td>
<td>9.43</td>
</tr>
<tr>
<td></td>
<td>0.66</td>
<td>0.31</td>
<td>0.84</td>
</tr>
</tbody>
</table>

LA: left atrial; TRPG: Tricuspid Regurgitation Pressure Gradient

Table 9: Months between pre-op to post-op echo

<table>
<thead>
<tr>
<th></th>
<th>Post-op echo 1 (n=34)</th>
<th>Post-op echo 2 (n=28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>12.35</td>
<td>20.07</td>
</tr>
<tr>
<td>Std Dev</td>
<td>12.92</td>
<td>15.31</td>
</tr>
</tbody>
</table>
The average number of months between patients’ pre-operation echo and first post-op echo was on average 12.35 months with a standard deviation of 12.92 months. Between the pre-op echo and second post-op echo, an average of 20.07 months had passed with a standard deviation of 15.31 months.

Discussion:

In our comprehensive investigation into the impact of Thoracic Endovascular Aortic Repair (TEVAR) on cardiac function, we meticulously compared resting echocardiograms obtained before the procedure with those conducted post-TEVAR. Despite the inherent variability in individual changes among patients, a discernible overarching trend in the entire cohort for alterations in left atrial volume indexed to body surface area, mitral E/A ratio, and average E/e’ ratio was notably absent. Intriguingly, some patients had drastic changes in their cardiac measurements, but the observed alterations in individual measurements could not be solely attributed to the effects of TEVAR, indicating a nuanced interplay of factors influencing cardiac dynamics.

An intriguing non-significant observation emerged regarding the tricuspid regurgitation pressure gradient, where an initial upward trend was noted post-TEVAR, only to revert back to preoperative levels during the subsequent follow-up echocardiogram. This fluctuation hints at the dynamic nature of cardiac parameters and raises questions about the transient effects of TEVAR on specific aspects of cardiac function.
One plausible explanation for the lack of a significant trend post-surgical intervention might stem from the possibility that TEVAR exerts minimal to no discernible effects on resting heart function. Previous research has demonstrated potential impacts on cardiac contractility following TEVAR, particularly during exercise stress echocardiogram.\(^{10}\) However, it is essential to acknowledge that the changes observed in cardiac function during exercise could be predominantly influenced by the heightened physiological demands imposed by exercise itself, potentially overshadowing the direct effects of TEVAR during rest.

Furthermore, the absence of statistically significant changes might also be attributed to the relatively short duration between surgical intervention and the initial follow-up echocardiogram (approximately one year), with the secondary follow-up occurring at an average of 20 months post-TEVAR. If TEVAR-induced cardiac remodeling were to manifest and result in abnormal echocardiogram readings, the current observation period might not suffice to capture the complete spectrum of these potential changes. Extended and more prolonged follow-up with the cohort is imperative to unravel the true temporal effects of TEVAR on cardiac function.

Another crucial aspect affecting the interpretability of our results is the considerable standard deviation observed for both the initial post-operative echocardiogram and the subsequent follow-up. This variability underscores the absence of a standardized protocol for post-procedure echocardiogram timing, potentially influencing the consistency and reliability of the data. In the absence of a universally accepted timeframe for conducting follow-up studies post-
TEVAR, deriving meaningful comparisons from the dataset becomes inherently challenging.

Given the retrospective nature of our study, the inability to establish a uniform and standardized period for patients to receive post-procedure care underscores a potential limitation that future studies should proactively address. Implementing a standardized and well-defined schedule for post-TEVAR follow-up assessments would enhance the validity and generalizability of results, minimizing the impact of disparate timeframes on data interpretation.

The study, while providing valuable insights, grapples with a limitation inherent in its inclusion criteria, as only 23% of patients undergoing TEVAR at our institution met the stringent requirements for participation. This modest inclusion rate necessitates caution in extrapolating conclusions to a broader population, emphasizing the importance of recognizing the study's constraints. The limited representation of patients poses a challenge in generalizing findings, urging the need for additional research endeavors to expand the pool of participants adhering to the study's inclusion criteria.

To address this limitation and enhance the robustness of our conclusions, future studies should be initiated, aiming to increase the number of patients meeting the inclusion criteria. By broadening the participant pool, subsequent investigations can offer a more comprehensive understanding of the impact of TEVAR on cardiac function, capturing a more diverse range of responses to this intervention. The imperative for longer follow-up periods and an augmented
sample size becomes apparent, as these factors are pivotal in uncovering nuanced and sustained changes in cardiac dynamics post-TEVAR.

Moreover, the findings underscore the importance of incorporating post-operative echocardiograms into the standard of care for individuals undergoing TEVAR. The potential for alterations in cardiac function necessitates a proactive approach, wherein post-operative monitoring becomes an integral component of patient management. The non-invasive nature of the study allows for patients to undergo echocardiogram as needed for observation.

As data accumulates over time, discernible trends may emerge, guiding not only clinical decisions but also informing the development of tailored surgical interventions as some patients have already undergone multiple aortic repairs. The integration of emerging trends into clinical practice ensures a dynamic and patient-centered approach, allowing for preemptive interventions when warranted.

The prospect of worsening effects on diastolic function underscores the importance of proactive management strategies. If subsequent data confirms an adverse trajectory, early interventions can be implemented to forestall the onset of heart failure and mitigate other potential adverse outcomes. This proactive stance aligns with the overarching goal of optimizing patient care and underscores the clinical significance of ongoing research endeavors in the realm of TEVAR and its impact on cardiac health.
In essence, while our study provides a valuable foundation, its limitations emphasize the need for continuous exploration and refinement. By expanding participant numbers, extending follow-up periods, and integrating standardized post-operative echocardiograms into routine care, future investigations can contribute to a more nuanced understanding of the intricate dynamics surrounding TEVAR and its implications for cardiac function.

This iterative approach not only refines our understanding of the subject matter but also establishes a foundation for more targeted and effective clinical interventions. As we delve deeper into understanding the intricate interplay between TEVAR and cardiac function, future research endeavors must navigate these challenges to offer a more comprehensive and nuanced comprehension of the long-term effects of TEVAR on the cardiovascular system.

**Challenges & Limitations:**

The journey of this study has been marked by a multitude of challenges, spanning both methodological intricacies and operational hurdles. Navigating through these obstacles has been a testament to the resilience and dedication of the research team. Methodologically, the study grappled with challenges rooted in the intricacies of data acquisition. The availability of data posed a significant hurdle, compounded by the dynamic and fluctuating nature of the information. The vast breadth of data, spanning a considerable time period, presented complexities in ensuring uniformity and consistency throughout the study.
On the other hand, several cases requiring urgent or emergent intervention did not allow for pre-operative echocardiograms to be feasibly collected, resulting in a gap in data regarding the pre-TEVAR status of some patients. For this subset, our insights into cardiac function were limited to data obtained through transesophageal echocardiograms. Additionally, this data was biased as these patients were undergoing severe stress prior to an emergent/urgent surgery. This data could not be meaningfully utilized to compare with resting echocardiogram post-TEVAR.

The inherently transient nature of many variables collected added another layer of complexity to the study. Diverse time points for data collection, both pre- and post-operation, introduced variability across patients. The lack of standardized measures for the timing of post-operative echocardiograms further compounded the challenge, influenced by factors beyond the researchers' control, such as patient schedules, procedural availability, and the retroactive nature of the study.

This variability extended to other parameters, such as blood pressure, which fluctuates not only throughout the day but also over months after a significant surgical intervention. The singular data point obtained for blood pressure merely scratches the surface of its ever-evolving nature, making it a snapshot into a constantly changing landscape. Given many of the parameters measured on echocardiogram were in continuous fluctuation, the snapshot collected at each follow-up only gives us a small insight into the continuous function of the heart.
The study also grappled with the sheer volume of variables collected, presenting a potential source of error due to the extensive information extracted from the electronic medical record. The richness of data, while promising for a comprehensive analysis, necessitated meticulous attention to detail and thorough scrutiny to prevent inadvertent errors.

The large number of variables collected for the study may also underscore any significant trends observed. With well over twenty total variables collected paired with a significance level of 0.05, the probability of finding a statistically significant trend somewhere in the data by total random chance is quite high. The approach of having a high volume of statistical variables studied may lead to type 1 error that must be corroborated in future studies.

Operationally, the research undertook its course during the challenging backdrop of a global pandemic. The unforeseen circumstances brought about delays in accessing data and disrupted the general workflow of the research team. The pandemic's impact on hospital and research resources and logistics added an additional layer of complexity, requiring adaptability and resilience from the research team.

Despite these formidable challenges, the research team remained steadfast in their commitment to unraveling the intricacies of TEVAR-induced effects on cardiac dynamics. The acknowledgment of these hurdles serves as a testament to the transparency and rigor underlying the study, with each obstacle
serving as a stepping-stone towards refining the scientific process and contributing to the advancement of knowledge in the field.

In the relentless pursuit of a robust and productive research process, we confronted and navigated through a myriad of challenges, employing strategic solutions to fortify the integrity of our study. A significant facet of this resilience was our proactive approach to addressing the intricacies arising from the urgent and emergent nature of many cases involved in the study. A crucial decision point emerged in determining the optimal utilization of data derived from these patients.

Recognizing that measurements obtained during transesophageal echocardiograms immediately preceding major surgeries might not accurately reflect typical cardiac function, we made a choice to exclude these readings from our analysis. This proactive measure, while introducing a reduction in the overall sample size, served to eliminate potential confounding variables that could have skewed the study's outcomes.

Navigating the temporal landscape post-surgery presented another set of challenges, notably in the absence of a standardized post-operative echocardiogram protocol for every patient. In response, we opted for a comprehensive approach, considering all echocardiograms collected post-operatively for our analysis. This decision, while introducing variability, allowed us to capture the diverse timelines of post-operative data collection and undertake a more thorough comparison with pre-operative measurements.
The intricacies surrounding blood pressure measurements further underscored the need for meticulous decision-making. Given the multiple blood pressure readings available post-surgery, we strategically aligned our approach by anchoring our analysis to the time of echocardiograms. This decision ensured a standardized and consistent reference point, ignoring potential fluctuations taken during follow-up visits or assessments for other medical concerns.

To fortify the robustness of our data and maintain a vigilant stance against inadvertent errors, we leveraged the strength of collaboration within our team. Multiple team members undertook a comprehensive review of the voluminous data, serving as a collective assurance mechanism to verify accuracy and enhance the reliability of our findings.

The manifold challenges encountered throughout this study have inevitably given rise to certain limitations that warrant a nuanced consideration of the generalizability and interpretative scope of our findings. One significant limitation arises from the exclusion of the most severe cases, where pre-operative echocardiograms were not feasible due to the urgent or emergent nature of their medical conditions. The absence of baseline data for this subset prevents the ability to run a paired t-test and therefore utilization of the data in our analysis.

However, the lack of inclusion of this subset introduces an element of unpredictability, potentially influencing outcomes in ways that are not readily discernible without further analysis. The possibility that these cases may harbor
the most drastic changes in cardiac function implies that our current outcomes might be underscored by not encompassing urgent and emergent cases without pre-operative data. Exploring the transesophageal echocardiogram data available specifically for this cohort could have yielded insightful results, albeit potentially hampered by a limited sample size that might not contribute meaningfully to the overall findings.

A further limitation surfaces in the underutilization of several transient blood pressure readings, each of which holds equal validity but introduces a layer of variability that could significantly impact other variables collected, such as aortic elastance and end-systolic elastance. A more refined estimation of blood pressure could have been achieved through the calculation of an average of all measures taken.

Alternatively, daily blood pressure measurements could have been implemented, allowing for standardization. However, such an intervention might incur increased medical costs and pose as an ethically questionable imposition on patients, raising concerns about medical necessity and increased waste of the already limited healthcare resources.

Additional limitations stem from the temporal dynamics inherent in our data collection process. The inclusion of data from both pre-COVID and post-COVID periods introduces a potential confounder, as the pandemic may have caused delays in medical care, potentially affecting cardiac function and adverse outcomes, consequently influencing our findings.
The protracted duration over which data was collected spans several years, during which the field of cardiothoracic surgery and medicine at large may have witnessed notable changes, encompassing advancements in surgical techniques and shifts in patient management practices. This nuance will affect any additional patients who are added to our database and will also create variability for any teams hoping to replicate our study. These temporal distinctions introduce an element of inconsistency that must be acknowledged in the interpretation of our results.

Moreover, the diverse array of surgeons and medical staff attending to each patient introduces another layer of complexity. While the aim is to provide standardized care, the inherent variability in the approaches of different healthcare professionals may have contributed to some of the differences observed in outcomes. Acknowledging these limitations is crucial in tempering the generalizability of our findings and fostering a comprehensive understanding of the intricate interplay between methodological constraints and the multifaceted landscape of cardiac surgery research.

Dissemination:

While a preliminary step in knowledge dissemination has been taken through the creation of a handful of abstracts derived from our ongoing work, it is important to note most of these abstracts have thus far been confined to
circulation within the internal network of the Yale Cardiothoracic Surgery Department.

One abstract had been submitted to the European Association of Cardio-Thoracic Surgery in the past year, but unfortunately our work was not accepted. Regrettably, the fruits of our labor have not yet been unveiled on a national scale, withholding the broader scientific community from the opportunity to engage with and scrutinize our findings.

The meticulous process of sharing our study’s outcomes with patients is currently pending, as the study requires more patient follow-up and definitive conclusions. Even with enough data and analysis, we would like to have the study replicated in another cohort of patients outside of the Yale New Haven Health system to determine the accuracy and generalization of our study’s results.

Currently, we are awaiting thorough review and approval from both the Department of Surgery and the Office of Student Research at Yale before sharing the info with the scientific community. This deliberate approach aligns with the commitment to adhere to ethical and procedural standards, ensuring that the dissemination of information is not only timely but also comprehensive and considerate of all stakeholders involved.
References:


