Long-Term Clinical and Radiographic Outcomes in Patients With Clinically Isolated Aortitis

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Objective. The optimal management of patients with incidentally found clinically isolated aortitis (CIA) after aortic aneurysm repair is unclear. This study compared long-term surgical and clinical outcomes after surgical repair of thoracic aortic aneurysm between patients with CIA and patients with noninflammatory etiologies.

Methods. This is a matched cohort study. Patients with CIA were identified by histopathology following open thoracic aortic aneurysm repair. Two comparators without inflammation on pathology were matched to each patient by year of surgical repair. Outcomes included surgical complications, new vascular abnormalities on imaging, and death.

Results. One hundred sixty-two patients were included: 53 with CIA and 109 matched comparators. Median follow-up time was similar between groups (CIA 3.7 vs. comparator 3.3 years, P = 0.64). There was no difference in postoperative complications, surgical revision, or death between groups. Only 32% of patients with CIA saw a rheumatologist in the outpatient setting and 33% received immunosuppressive treatment. On surveillance imaging, no difference was seen in new or worsening aortic aneurysms, but there were significantly more vascular abnormalities in branch arteries of the thoracic aorta in patients with CIA (39% vs. 11%, P < 0.01).

Conclusion. Among patients who underwent surgical repair of a thoracic aortic aneurysm, patients with CIA were more likely than noninflammatory comparators to develop radiographic abnormalities in aortic branch arteries. Notably, there was no difference in risk of new aortic aneurysms or surgical complications despite most patients with CIA never receiving immunosuppression. This suggests that more selective initiation of immunosuppression in CIA may be considered after aortic aneurysm repair.

INTRODUCTION

Aortitis is an immune-mediated vasculitis affecting the aorta. Aortitis can be a manifestation of an underlying primary vasculitis, commonly giant cell arteritis (GCA) or Takayasu arteritis, but many other etiologies, such as autoimmune or infectious processes, have been implicated (1–3). Clinically isolated aortitis (CIA) refers to aortitis that exists without other vascular or infectious manifestations (4–6). Because of the absence of symptoms, patients with CIA are usually first identified based on histology after aneurysmal repair. Prior studies have reported a prevalence of aortitis incidentally found on surgical pathology to range from 2% to 12% (3,5,7–13).

The optimal approach to management of CIA after aneurysmal repair is still unclear. This is in large part due to the uncertainty about whether CIA represents a distinct disorder or the form fruste of a systemic vasculitis. Prior studies evaluating outcomes of CIA after surgical repair have demonstrated high rates of surgical revision and new vascular lesions. However, these studies were case series limited by small sample size or lack of a noninflammatory comparator group (5,8,10,12–16). Because surgical revision or new vascular lesions (eg, due to atherosclerosis) can occur in patients without vasculitis, understanding the additional risk of these outcomes in aortitis would inform management, particularly ongoing surveillance and immunosuppressive therapies. Furthermore, prior studies have had conflicting results regarding glucocorticoid treatment and future risk of reoperation or radiographic progression of vascular disease (5,8,10,13–15).

The goal of this study was to examine the immediate postoperative and long-term outcomes of patients with noninfectious CIA compared to patients with noninflammatory aortic aneurysms after undergoing open thoracic aortic aneurysm repair.
PATIENTS AND METHODS

Study design and participant identification. This study is a matched cohort study and was approved by the Institutional Review Board of the University of Pennsylvania. Study participants were identified in the University of Pennsylvania Health System (UPHS) pathology database after undergoing open thoracic aortic aneurysm repair between 2007 and 2017. Aortitis cases were identified on histopathologic review, defined by the presence of giant cells, granulomatous inflammation, or significant adventitial inflammation without evidence of concurrent infection. Patients with prior known autoimmune disease associated with aortitis (eg, GCA) and those undergoing endovascular repair or surgical revision of previous aortic repair were excluded. Patients with aortitis were then matched to two comparators without any evidence of significant inflammation on pathology who had a thoracic aortic aneurysm repair within 1 year of the aortitis patient’s surgical date. Matching was not performed for age and sex to minimize loss of patients, which would impact the power of the study, and to enable evaluation of these factors as potential effect modifiers. Patients needed to have at least one outpatient follow-up visit at UPHS to be included in this study, unless they died during hospitalization.

Clinical data. Two investigators were trained in consistent procedures and performed a chart review. A subset of patients were reviewed by both investigators to ensure consistent data collection. Electronic health records from UPHS and outside institutions were reviewed. Baseline demographic data and comorbid medical conditions were collected for all patients from outpatient surgical notes leading up to the index surgery. Inpatient surgical outcomes were abstracted from inpatient progress notes, operative notes, and discharge summaries, and long-term outcome data were obtained from outpatient primary care, surgical notes, and rheumatology office notes. Medication data were collected from inpatient and outpatient prescription lists. Computed tomography (CT) and magnetic resonance imaging (MRI) reports were reviewed to assess long-term radiographic outcomes. Involvement of or referral to a rheumatologist was ascertained from inpatient and outpatient documentation. If a patient did not follow-up with rheumatology within the UPHS system, evidence of rheumatology office visits at other health care systems were confirmed by documentation in the Care Everywhere interoperability platform on the Epic electronic medical record. This allows access to a patient’s electronic health records at other participating health care systems. In addition, telephone encounters were searched to look for documentation of office visits with a rheumatologist, and immunosuppression prescriptions were evaluated to see if the prescriber was a rheumatologist. Finally, eventual diagnosis of a systemic vasculitis was recorded and confirmed via application of established disease-specific classification criteria, such as the 1990 American College of Rheumatology (ACR) classification criteria.

Outcomes. Outcomes of interest during the index surgical hospitalization included length of stay, intra- or postoperative surgical complications, infection or revision, evaluation by rheumatologist, and immunosuppression administration. Long-term clinical outcomes included length of outpatient follow-up, rates of surgical and rheumatology follow-up, immunosuppression prescription, surgical revision, and mortality. Radiographic findings of interest included new or worsening aneurysmal changes, wall thickening, stenosis, occlusion, and thrombosis in the aorta and main aortic branches. Imaging changes were defined as new or worsening if interpreted as such by the radiologist in their imaging report when compared to previously completed vascular imaging. Radiologic changes that occurred within 6 months of surgery were not included in the analysis because these may not represent incident events.

Statistical analysis. Outcomes were compared between aortitis and noninflammatory groups using conditional logistic regression and conditional Poisson regression models. Cox proportional hazards regression models stratified by matched groups were used for time-to-event analyses. Multivariate models were adjusted for age, sex, rheumatology referral, and perioperative glucocorticoid use. Association of immunosuppressive treatment and rheumatology referral with outcomes was evaluated. A significance level of 0.05 was used for all tests of hypothesis. All statistical analyses were performed using Stata 14.1 (Stata Corp).

RESULTS

Cohort characteristics. A total of 1373 patients with available surgical tissue pathology from open thoracic aortic aneurysm repairs between 2007 and 2017 were identified in the UPHS pathology database. Fifty-five patients (4%) were identified as having aortitis on pathology, 53 of whom met inclusion criteria for the study. These patients were then matched with 109 comparators with noninflammatory aortic aneurysms for a total of 162 patients.

Compared to patients with noninflammatory aortic aneurysms, patients with aortitis were significantly older at the time of surgery (median age CIA 67 years vs. comparator 62 years, \( P = 0.02 \)) and more likely to be female (CIA 58% vs. comparator 25%, \( P < 0.01 \)) (Table 1). Patients with aortitis were more likely to have existing hypertension (CIA 84% vs. comparator 64%, \( P = 0.01 \)) but significantly less likely to have underlying coronary artery disease (CIA 18% vs. comparator 45%, \( P < 0.01 \)). There was no difference in other comorbidities, including hyperlipidemia, diabetes mellitus, cerebrovascular disease, or tobacco use history. Ninety-three percent of patients in each group had an ascending aortic aneurysm repaired. On postsurgical
histopathologic specimen review, 32% and 81% of patients with aortitis were found to have granulomatous inflammation and giant cells, respectively, whereas none of those findings were identified in comparators. Sixty-one percent of patients with aortitis had evidence of adventitial inflammation compared to 12% in the comparator group.

Table 1. Baseline characteristics of cohort

|                              | All (N = 162) | Aortitis (n = 53) | Comparator (n = 109) | P     |
|------------------------------|--------------|-------------------|----------------------|-------|
| Age at surgery               | 65 (55-74)   | 67 (59-76)        | 62 (54-71)           | 0.02  |
| Female sex                   | 58 (36%)     | 31 (58%)          | 27 (25%)             | <0.01 |
| Race                         |              |                   |                      |       |
| White                        | 128 (79%)    | 37 (70%)          | 91 (83%)             | 0.05  |
| Black                        | 13 (8%)      | 7 (13%)           | 6 (6%)               | 0.09  |
| Asian                        | 3 (2%)       | 2 (4%)            | 1 (1%)               | 0.25  |
| Other                        | 18 (11%)     | 7 (13%)           | 11 (10%)             | 0.73  |
| Comorbidities                |              |                   |                      |       |
| Hypertension                 | 112 (70%)    | 43 (84%)          | 69 (64%)             | 0.01  |
| Coronary artery disease      | 58 (36%)     | 9 (18%)           | 49 (45%)             | <0.01 |
| Hyperlipidemia               | 85 (53%)     | 26 (51%)          | 59 (55%)             | 0.88  |
| Diabetes mellitus            | 16 (10%)     | 7 (14%)           | 9 (8%)               | 0.39  |
| Cerebrovascular disease      | 14 (10%)     | 4 (13%)           | 10 (9%)              | 0.56  |
| Tobacco history              |              |                   |                      |       |
| Current smoker               | 22 (14%)     | 8 (16%)           | 14 (13%)             | 0.60  |
| Former smoker                | 60 (39%)     | 20 (40%)          | 40 (38%)             | 0.93  |
| Never smoker                 | 72 (47%)     | 22 (44%)          | 50 (48%)             | 0.78  |
| Location of aneurism repair  |              |                   |                      |       |
| Ascending aorta              | 150 (93%)    | 49 (93%)          | 101 (93%)            | 0.96  |
| Aortic arch                  | 6 (4%)       | 2 (4%)            | 4 (4%)               | 0.64  |
| Descending thoracic aorta    | 6 (4%)       | 2 (4%)            | 4 (4%)               | 0.64  |
| Histopathologic findings     |              |                   |                      | N/A   |
| Granulomatous inflammation   | 17 (10%)     | 17 (32%)          | 0%                   |       |
| Giant cells                  | 43 (27%)     | 43 (81%)          | 0%                   |       |
| Adventitial inflammation     | 49 (30%)     | 36 (68%)          | 13 (12%)             |       |

Note: Values are expressed as median (interquartile range) or absolute value (%).
Abbreviation: N/A, not applicable.

Figure 1. Immediate and long-term surgical complications in patients with clinically isolated aortitis (CIA) compared to patients with noninflammatory aortic aneurysms. A, There was no significant difference between groups with respect to surgical complications or death during the index surgical hospitalization. B, Survival without surgical revision was similar between groups as shown in this Kaplan–Meier curve. All P values are greater than 0.05.
Length of stay and surgical complications. There was no difference in length of hospitalization between groups (adjusted incidence rate ratio (IRR) 1.06, 95% confidence interval [CI] 0.95–1.19, \( P = 0.28 \)). During the hospitalization, there was no significant difference in rates of postoperative complications between groups, including graft leak, aortic dissection, graft or nongraft infection, aortic dissection, and organ or limb ischemia (Figure 1A). Rates of surgical revision (CIA 8% vs. comparator 5%, \( P = 0.48 \)) and death (CIA 4% vs. comparator 3%, \( P = 0.66 \)) during the index hospitalization were also similar, even after adjusting for age, sex, treatment, and rheumatology referral.

Median long-term follow-up time was similar between groups (CIA 3.7 vs. comparator 3.3 years, \( P = 0.64 \)). Surgical follow-up was robust, with 94% of patients overall following up at least once as an outpatient. There was no significant difference between groups with respect to rate of surgical revision (CIA 6% vs. comparator 9%, \( P = 0.55 \)), median time to revision after initial surgical procedure (CIA 36 months vs. comparator 44 months, \( P = 0.49 \)) (Figure 1B), or death (CIA 11% vs. comparator 12%, \( P = 0.97 \)) in the long term. No difference remained between groups with respect to the above surgical complications and death, even after adjusting for possible confounders.

Rheumatologic evaluation and immunosuppression. During the index surgical admission, 30% of patients with aortitis were seen by a rheumatologist and another 17% were referred within 4 weeks of discharge. Twenty-one percent of patients with aortitis were started on systemic glucocorticoids during their initial inpatient stay. Although nearly all patients saw their surgeon at least once in the outpatient setting, only 32% of patients with aortitis had a documented follow-up visit with a rheumatologist (Figure 2).

In terms of treatment, 33% of patients with aortitis were started on glucocorticoids at some point postoperatively, with a median initiation at 5 days (interquartile range [IQR] 3–14 days) after their procedure. The median initial dose (in prednisone mg equivalent) was 60 mg with a median duration of therapy of 10 months (IQR 6–16 months). Thirteen percent of those with underlying aortitis were started on another form of immunosuppression, which started at a median of 6 months from the index surgery. This included methotrexate, azathioprine, tumor necrosis factor \( \alpha \) inhibitors, and rituximab. There was no association between postoperative initiation of glucocorticoids and/or other immunosuppressives and future surgical or radiographic outcomes.

A number of patients with CIA were ultimately classified as having a systemic vasculitis during the long-term follow-up period. Using definitions based on the 1990 ACR classification criteria, we found that 7 of 53 (13%) patients with aortitis were classified as GCA, whereas another five were diagnosed with polymyalgia rheumatica but did not meet strict classification criteria for GCA. Of the patients classified as having GCA, only two had headache and none developed vision loss. One patient (2%) was classified as having Takayasu arteritis and one (2%) was identified as having immunoglobulin G4–related disease according to the clinician.

Longitudinal changes in radiographic imaging. Of the 53 patients with CIA included in this study, 44 of 53 (83%) had available preoperative imaging. Seventeen of forty-four (39%) had complete baseline vascular imaging at the time of enrollment:

![Figure 2. Outpatient follow-up and immunosuppression initiation in patients with clinically isolated aortitis (CIA) vs. patients with noninflammatory aortic aneurysms. Bar graphs show the proportion of patients with at least one surgical or rheumatologic follow-up visit after hospital discharge, as well as treatment initiation at any point during the follow-up period. Both groups had high rates of follow-up with their surgical teams, but only 32% of patients with CIA saw a rheumatologist. Thirty-three percent of patients with CIA were started on glucocorticoids, whereas 13% received some other form of immunosuppression (eg, methotrexate, azathioprine, tumor necrosis factor \( \alpha \) inhibitors).]
14 study participants had thoracoabdominal computed tomography angiography (CTA) and three had thoracoabdominal CT with intravenous contrast. Patients with aortitis had a significantly larger number of radiographic imaging studies performed during the long-term follow-up period (CIA 5 vs. comparator 4, \( P = 0.01 \)), but the median time between the first and last imaging study was the same in each group (39 months) (Table 2).

| Table 2. Radiographic (CT or MRI) changes during follow-up in patients with aortitis vs. noninflammatory comparators |
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| | All (N = 131) | Aortitis (n = 44) | Comparator (n = 87) | \( P \) |
| Total number of imaging studies performed | 4 (3–7) | 5 (3–8) | 4 (2–6) | 0.01 |
| Time between first and last imaging study, months | 39 (20–65) | 39 (15–62) | 39 (23–67) | 0.92 |
| Changes in aorta |  |  |  |  |
| New or worsening changes in aorta on imaging | 57 (44%) | 18 (41%) | 39 (45%) | 0.37 |
| Location of new or worsening changes in aorta |  |  |  |  |
| Aortic root | 1 (1%) | 0% | 1 (1%) | 0.32 |
| Aortic arch | 31 (24%) | 8 (18%) | 23 (26%) | 0.24 |
| Descending thoracic aorta | 33 (25%) | 16 (36%) | 17 (20%) | 0.12 |
| Abdominal aorta | 26 (20%) | 9 (20%) | 17 (20%) | 0.88 |
| Abnormality identified in aorta |  |  |  |  |
| Aneurysm | 58 (44%) | 18 (41%) | 39 (45%) | 0.67 |
| Stenosis or occlusion | 2 (2%) | 1 (2%) | 1 (1%) | 0.62 |
| Wall thickening | 1 (1%) | 1 (2%) | 0% | 0.16 |
| Thrombosis | 8 (6%) | 5 (11%) | 3 (3%) | 0.09 |
| Changes in arteries that branch from aorta |  |  |  |  |
| New or worsening changes in branches of aorta on imaging | 43 (33%) | 20 (45%) | 23 (26%) | 0.03 |
| Location of new or worsening changes in branch artery |  |  |  |  |
| Arteries above celiac axis | 27 (21%) | 17 (39%) | 10 (11%) | <0.01 |
| Carotid artery | 7 (5%) | 6 (14%) | 1 (1%) | 0.02 |
| Subclavian artery | 6 (5%) | 4 (9%) | 2 (2%) | 0.11 |
| Brachiocephalic artery | 9 (7%) | 7 (16%) | 2 (2%) | 0.02 |
| Celiac artery | 14 (11%) | 9 (20%) | 5 (6%) | 0.02 |
| Arteries below celiac axis | 24 (18%) | 10 (23%) | 14 (16%) | 0.37 |
| Superior mesenteric artery | 7 (5%) | 4 (9%) | 3 (3%) | 0.20 |
| Renal artery | 8 (6%) | 4 (9%) | 4 (5%) | 0.33 |
| Inferior mesenteric artery | 5 (4%) | 4 (9%) | 1 (1%) | 0.06 |
| Iliac artery | 17 (13%) | 7 (16%) | 10 (11%) | 0.50 |
| Other | 18 (14%) | 9 (20%) | 9 (10%) | 0.09 |
| Abnormality identified in branch artery |  |  |  |  |
| Aneurysm | 25 (19%) | 12 (27%) | 13 (15%) | 0.13 |
| Stenosis or occlusion | 23 (18%) | 12 (27%) | 11 (13%) | 0.04 |
| Wall thickening | 6 (5%) | 6 (14%) | 0% | <0.01 |
| Thrombosis | 4 (3%) | 4 (9%) | 0% | 0.01 |

Note: Values are expressed as median (interquartile range) or absolute value (%). Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging.

There was a large proportion of patients who developed new or worsening aortic aneurysms outside of the site of surgery on longitudinal imaging in both the aortitis and noninflammatory groups (CIA 41% vs. comparator 45%, \( P = 0.37 \)). Seventeen patients with CIA had new lesions identified in either the aorta or aortic branches during follow-up. Thirteen (76%) of these patients had baseline preoperative imaging of the affected areas that did not show evidence of any vascular abnormality at that time (10 patients had CTA, two had noncontrast CT, and one had CT with IV contrast). There were significantly more vascular abnormalities in the aortic branch arteries in the aortitis group versus the noninflammatory comparators during long-term follow-up (CIA 45% vs. comparator 26%, \( P = 0.03 \)). The discrepancy in aortic branch abnormalities was most profound when examining branch arteries of the thoracic aorta (CIA 39% vs. comparator 11%, \( P < 0.01 \); hazard ratio 2.70 [95% CI 1.05–6.93], \( P = 0.03 \)), including the carotid, subclavian, brachiocephalic, and celiac arteries (Table 2, Figure 3). There was no significant difference in development of branch arterial abnormalities below the celiac axis (CIA 23% vs. comparator 16%, \( P = 0.37 \)). Results were similar when adjusting for potential confounders. In addition, glucocorticoid or immunosuppression initiation was not associated with aortic or aortic branch abnormalities. Similar results were found when examining the subgroup who did not receive immunosuppressive therapies.

**DISCUSSION**

Appropriate management of CIA after surgical repair of the primary lesion remains unclear. Understanding the risk of new vascular lesions and surgical outcomes in patients with untreated,
incidentally found aortitis would inform clinical approaches to disease surveillance and use of immunosuppressive therapies. We leveraged a cohort of patients with aortitis with matched comparators and detailed clinical data to investigate these important questions. Although previous studies have reported high rates of surgical complications and distal aortic aneurysms developing in CIA, our study showed that rates of these outcomes were actually very similar to those in patients with noninflammatory aortic aneurysms despite a majority of patients with aortitis remaining off immunosuppressive therapy. The only difference in vascular outcomes between groups was a higher risk of branch artery abnormalities on imaging in patients with CIA.

Although several studies have looked at radiographic changes in the aorta during the long-term surveillance of patients with CIA, few have focused on abnormalities seen in the major aortic branch arteries. A 2009 case series by Liang et al was the first to extensively report on additional vascular imaging findings in patients with noninfectious ascending aortitis (8). In their study of 64 patients (81% CIA), 72% had other vascular abnormalities identified by the time of their ascending aortic aneurysm repair. These included other aortic aneurysms as well as stenosis or ectasia of major branch arteries, the latter two being found in 42% of patients. More recently, Clifford et al found that 26% of patients with CIA developed branch artery abnormalities over a mean follow-up of 56 months (14). Both of these studies lacked a noninflammatory comparator group which is important because atherosclerosis can result in similar changes on imaging. Accordingly, the noninflammatory comparator group in our study, which had a higher prevalence of coronary artery disease at baseline, also developed branch artery abnormalities of the aorta although to a lesser degree compared to the aortitis group. Our study significantly adds to the literature by demonstrating that major aortic branch vessel abnormalities are significantly more likely to occur in patients with aortitis compared to those without. This difference was even more pronounced when assessed anatomically, with branch arteries above the celiac axis showing the greatest discrepancy between groups (CIA 39% vs. comparator 11%, $P < 0.01$). This suggests that in the long term patients with aortitis may benefit from surveillance vascular imaging, such as magnetic resonance angiography or CT angiography.

A surprising finding of this study was the lack of robust involvement of a rheumatologist for patients diagnosed with CIA. Despite more than 90% of patients having follow-up with their surgical team as an outpatient, less than one-third of patients saw a rheumatologist in the outpatient setting and only a third received glucocorticoid therapy. Although it is possible some rheumatology visits may have been missing in this database, a similarly low rate of referral to a rheumatologist was observed during hospitalization and at discharge (in which there were no missing data). Our findings contrast with a study of a surgical cohort of nearly 200 patients with aortitis at the Mayo Clinic by Prasad et al in which 61% of surviving patients had a rheumatologist actively participate in their care (15). This difference might reflect regional or hospital-level variations in practice. Increased awareness of the need for rheumatologist consultation may be beneficial for this population. Linking these patients with a rheumatologist is important given the potential for longer-term complications related to an underlying vasculitis and possible need for more nuanced medical management.

A minority of the patients with CIA in our cohort went on to receive an eventual rheumatologic diagnosis. Our findings are similar to those in a previous cohort of 196 patients with aortitis,
in which 11% of those with CIA were ultimately diagnosed with GCA and 3% were diagnosed with Takayasu arteritis (14). In our cohort, 13% of patients initially classified as having CIA eventually developed manifestations sufficient for classification of GCA within a few years of their surgery. In our study, the majority of patients with CIA did not receive any immunosuppression after their index surgery and still did not have any significant difference in surgical outcomes or radiographic main aortic disease compared to noninflammatory comparators. Similar findings were found in a study by Rojo-Leyva et al that showed that patients with CIA can often have favorable outcomes even in the absence of immunosuppressive therapy (5). Although prevention of branch artery disease (eg, carotid or subclavian artery narrowing) is important, involvement of these arteries is generally not life-threatening and, if detected early, can be managed with immunosuppressive therapies. The lack of a difference in severe life-threatening vascular outcomes between CIA and noninflammatory aortopathies suggests that widespread immunosuppression of all surgically repaired CIA may not be necessary. Rather, close clinical and radiographic surveillance in this population and more selective initiation of immunosuppression may be sufficient.

Almost half of patients in each group developed new or worsening radiographic changes in the aorta, mainly aneurysms, during long-term follow-up. Although patients with aortitis tended toward having more aortic wall thickening and thrombosis, the numbers were too small to meet statistical significance. Clifford et al (14) reported a similar rate (45%) of new aortic aneurysms after surgery in patients with CIA and Zehr et al (16) found that 46% with GCA had prior or new descending thoracic and/or thoracoabdominal aneurysms. However, in studies by Rojo-Leyva et al (5) and Miller et al (10) only 15% to 17% of patients developed new aneurysms during long-term follow-up. Differences in patient population and frequency of surveillance imaging may explain these discrepancies.

Several studies have suggested that patients with ascending noninfectious aortitis are predisposed to the development of distal aortic disease over time (5,7,12,16,17). In one study by Wang et al, 47% of patients with ascending aortitis had distal aortic events after their initial surgical repair (“events” defined as new aortic surgical procedures, new >5.0-cm aortic aneurysms, ruptured aortic aneurysms or new aortic dissections) versus just 7% in the noninflammatory control group, although only 15 patients with aortitis were included (12). Zehr et al similarly reported distal aneurysms in 46% of their cohort (16). In our study, patients with aortitis tended to have more changes involving the descending thoracic aorta when compared to noninflammatory comparators although the difference was not statistically significant (36% vs. 20%, P = 0.12). Lastly, the lack of a significant difference between groups with respect to surgical complications, surgical revision, and death during both the index hospitalization and long-term follow-up as well as the absolute incidence of these events is consistent with what has been reported in other prior studies (3,15,16,18,19).

One major strength of this study was that it assessed only those patients who were incidentally found to have aortitis after their index surgery, a unique clinical situation encountered by rheumatologists. Many prior studies on aortitis included patients with known systemic vasculitis or other rheumatologic disease who may have already been on perioperative immunosuppression and seeing a rheumatologist, something that could very well skew short- and long-term postoperative outcomes in those cohorts (3,15,16). Another strength of this study was the inclusion of a relatively large number of patients with aortitis as well as matched noninflammatory comparators, which allowed for better risk assessment associated with aortitis. In addition, some of the studies with larger patient cohorts included patients with index surgeries starting as early as 1955, making the outcomes data potentially less relevant and reliable given improvements in medical care and surgical techniques (5,19). Finally, we had fairly robust and detailed follow-up data which allowed comprehensive evaluation of long-term outcomes.

There are several limitations to this study. Our cohort was from a multihospital health system that serves a specific region within the United States; this may limit the generalizability of our results to other populations. Imaging technique and interpretation were not standardized and therefore may have affected results, although we expect this bias to be similar between groups. Differentiating vasculitis from advanced atherosclerosis on imaging is often challenging, and obtaining serial histopathology is not feasible or ethical; therefore, this study could not validate that branch artery abnormalities in the CIA group were related to their autoimmune disease. However, comparison to a noninflammatory comparator group gives us more confidence that some of the differences in outcomes may have been related to aortitis. Because of the retrospective design of this study, there was potential for selection bias. None of the patients included in the study had a prior diagnosis or symptoms suggestive of a systemic vasculitis. However, because patients with aortitis were not seen by rheumatologists prior to surgery and comprehensive vascular imaging was not always obtained prior to surgery, pre-existing diagnoses of systemic vasculitis may have been missed. Our study mimics the clinical scenario often confronted by rheumatologists in real-world practice when evaluating patients with incidentally discovered aortitis. Reassuringly, even among patients who saw rheumatology after surgery, the majority of patients continued to have a diagnosis of CIA. Furthermore, none of the patients diagnosed with GCA postoperatively by the rheumatologist developed visual loss, and few had any cranial symptoms, suggesting that presurgery evaluation by rheumatology likely would not have changed management in the majority of the cases. We also could not completely exclude the possibility of patients in the comparator group having underlying aortitis beyond their pathology findings; however, this misclassification
would bias to the null (and therefore underestimate differences) and the aortitis prevalence in our cohort matches that seen in other previously published studies (3–5,7–13). Ascertainment bias may have occurred given the larger number of imaging studies performed in patients with aortitis; however, the median amount of time between the first and final imaging study was the same between groups, so any imaging findings would ultimately be captured in each group. Not all patients had abdominal imaging, so it is possible that some abdominal vascular abnormalities were missed because of surveillance bias. Although groups were not matched for type of aortic surgery performed, surgical location did not differ between groups and likely did not contribute to any outcome differences. In addition, all surgeries performed were open procedures and endovascular repairs were excluded. Rates of outcome may have been under- or overestimated because of missing data although we expect missingness would be nondifferential.

In summary, this study showed that patients with aortitis are more likely to develop aortic branch artery abnormalities after aneurysmal surgery compared to patients with noninflammatory aortic aneurysms, suggesting ongoing disease progression in a subgroup of patients with aortitis after the index surgery. No significant difference in surgical revision, mortality, or new or progressive aortic disease was noted between groups. These findings support the involvement of a rheumatologist and long-term imaging surveillance in the ongoing care of patients with CIA. Importantly, this study shows that the natural history of CIA tends to stay localized to the primary vascular lesion (mainly the ascending aorta) and thoracic branch arteries and does not result in a higher risk of life-threatening complications such as additional aortic aneurysms or surgical complications. Although further studies examining the impact of immunosuppression on outcomes are needed, this suggests that more selective initiation of immunosuppression in CIA may be considered after the aortic aneurysm has been repaired.

AUTHOR CONTRIBUTIONS
All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Mayer had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Mayer, Quimson, Rhee.
Acquisition of data. Mayer, Sperry, Quimson, Rhee.
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