

A propensity-matched analysis of cardiac operation in patients with and without cardiac amyloidosis



Akshay Chauhan, MBBS,^a Kevin L. Greason, MD,^a Daniel D. Borgeson, MD,^b Austin Todd, MS,^c John M. Stulak, MD,^a Richard C. Daly, MD,^a Juan A. Crestanello, MD,^a and Hartzell V. Schaff, MD^a

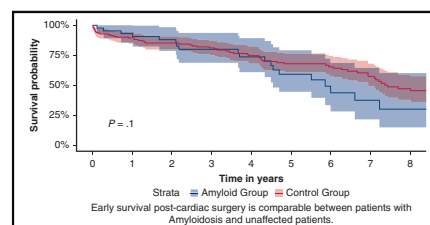
ABSTRACT

Objective: There are limited data on the outcome of routine cardiac operations in patients with cardiac amyloidosis. This study studied the impact of amyloidosis on early and late results of cardiac operations.

Methods: This was a retrospective, propensity-matched, case-control study of patients with cardiac amyloidosis undergoing cardiac surgery. Heart transplantation and ventricular assist implantation were excluded. Controls were patients without known cardiac amyloidosis matched on baseline patient characteristics, echocardiographic findings, and type of operation. Outcomes included operative complications and survival.

Results: In total, 42 patients with cardiac amyloidosis (amyloid group [AG]) were matched with 168 controls (CON group). The median left ventricular ejection fraction was 63% in the AG group (vs 64% CON). Aortic valve replacement and septal myectomy were the most common operations. Cardiopulmonary bypass ($P = .374$) and crossclamp ($P = .185$) times were similar in the 2 groups. Complication rates were similar in the 2 groups, including the need for mechanical circulatory support ($n = 1$ AG group vs $n = 1$ CON; $P = .361$) and intra-aortic balloon pump use ($n = 3$ AG group vs $n = 13$ CON; $P = 1.000$). There were no operative deaths. Survival was similar in the 2 groups at 1 year (AG 93% vs 89% CON; $P = .1$) but was worse in the AG at 5 years (59% vs 68% CON; $P = .1$).

Conclusions: Early procedural outcomes and 1-year survival are similar in patients with and without cardiac amyloidosis with preserved cardiac function. Diagnosis of amyloidosis should not be a contraindication to cardiac surgery. (JTCVS Open 2024;22:235-43)



Early survival postcardiac surgery is similar among patients with and without amyloidosis.

CENTRAL MESSAGE

Early outcomes of routine cardiac surgery in patients with cardiac amyloidosis are favorable, especially in cases with preserved cardiac function.

PERSPECTIVE

There is limited clinical experience with routine cardiac operations in patients with cardiac amyloidosis. This study has the potential to influence present clinical practice, where just a diagnosis of amyloidosis prohibits many surgeons from performing cardiac surgery fearing high morbidity and mortality.

Cardiac amyloidosis represents a rare pathologic condition, and its precise prevalence remains challenging to ascertain. It is characterized by the deposition of amyloid fibrils within the extracellular matrix surrounding myocardial cells, culminating in a restrictive variant of cardiomyopathy. Its principal etiologies are transthyretin amyloidosis (ATTR), chiefly originating from hepatic synthesis and associated with thyroxine transport, and

misfolded monoclonal immunoglobulin light chain amyloidosis (AL), stemming from aberrant clonal proliferation of plasma cells.^{1,2} The 1- and 3-year survival rates are usually poor, approximately 70% and 60%, respectively.³

Traditionally, the conventional wisdom is that intervening surgically in patients afflicted with cardiac amyloidosis is linked to heightened perioperative morbidity and mortality rates.⁴⁻⁶ Some research examining coincidental discoveries of amyloidosis in patients undergoing surgery has hinted at an alternative perspective that its prognosis may not be as worse as previously thought.^{7,8} Nevertheless, comprehensive data about the outcomes of routine cardiac procedures conducted in individuals with cardiac amyloidosis remain scarce. The present study assesses the effect of amyloidosis on both short-term and long-term outcomes in patients undergoing routine cardiac operations.

From the Departments of ^aCardiovascular Surgery, ^bCardiovascular Medicine, and ^cClinical Trials & Biostatistics, Mayo Clinic, Rochester, Minn.

Received for publication July 30, 2024; accepted for publication July 31, 2024.

Address for reprints: Akshay Chauhan, MBBS, Department of Cardiovascular Surgery, Mayo Clinic, 200 First St SW, Rochester, MN 55905 (E-mail: dr.akshaychauhan1990@gmail.com).

2666-2736

Copyright © 2024 The Author(s). Published by Elsevier Inc. on behalf of The American Association for Thoracic Surgery. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<https://doi.org/10.1016/j.xjon.2024.07.019>

Abbreviations and Acronyms

AG	= amyloid group
AL	= light chain amyloidosis
ATTR	= transthyretin amyloidosis
CON	= control
ICU	= intensive care unit
IQR	= interquartile range

PATIENTS AND METHODS

This study received approval from the institutional review board at the Mayo Clinic (application #22-011427, date December 20, 2022). We reviewed the records of 51,282 patients who underwent cardiac surgery at our Clinic from January 1, 1998, to December 31, 2022. From that group of patients, we identified 99 (0.2%) patients with cardiac amyloid deposits. Patients undergoing heart transplantation ($n = 51$) and left ventricular assist device implantation ($n = 6$) were excluded from the study cohort.

Data were sourced from the Mayo Clinic electronic health record and our surgical database. All patients authorized the use of clinical data for research, and informed consent was waived. For comparison, a control (CON) group of patients without cardiac amyloidosis who underwent similar cardiac operations was also included in the study. Heart transplantation and left ventricular assist device implantation were also excluded from the CON group. The CON group was pulled from our Society of Thoracic Surgeons database, and 1:4 propensity score matching was performed to account for baseline differences between the 2 groups (demographics, comorbidities, year, and type of operation as mentioned in Table 1).

The histopathologic confirmation of amyloidosis was accomplished through the application of a Congo Red amyloid stain. The categorization of amyloid subtypes was achieved using liquid chromatography-tandem mass spectrometry-based proteomic analysis on peptides extracted from the Congo Red-positive, microdissected areas of the paraffin-embedded specimens.

The case (amyloid group [AG]) and CON groups were propensity matched on baseline characteristics, echocardiography findings, and type of operation (Table E1). The propensity scores were derived from a multivariable logistic regression using potential confounders. Nearest-neighbor matching was used, and the caliper width used for matching was the standard deviation of the scores multiplied by 0.2. The AG and CON groups were compared on intraoperative and postoperative course, complications, and survival.

Categorical variables are reported as number (percentage), and continuous variables are reported as median (range or 25th through 75th interquartile range [IQR]). Comparisons between groups were made using the Kruskal-Wallis test, χ^2 test, or Fisher exact test, as appropriate. For the primary outcome, unadjusted survival curves were constructed using the Kaplan-Meier estimator. All statistical analyses were done using RStudio, Version 4.1.3 (RStudio; PBC).

RESULTS

There were 42 patients identified with amyloidosis (AG group) who had an operation in the last 25 years. They were matched with 168 controls (CON group). The median patient age in the AG group was 76 years (IQR, 71-81), and 88% of them were male. All 42 patients were of White race. The median Society of Thoracic Surgeons Predicted Risk Of Mortality for cases was 2.6% (IQR, 1.5%-4.6%) versus 3.2% (IQR, 1.6%-6.6%) in controls ($P = .422$). Both

groups were well matched on additional baseline demographics and comorbidities (Table 1).

Type of amyloidosis was not ascertained in 4 patients. Of the remaining 38 patients, 30 (79%) had ATTR (transthyretin), 6 (16%) had AL (immunoglobulin light chain), and 2 (5.2%) had the atrial natriuretic factor amyloidosis subtype of amyloidosis. There were 11 cases (26%) diagnosed preoperatively, of which 5 (46%) were ATTR and 6 (55%) were AL subtype. These patients had myocardial biopsies done in outpatient clinic and referred to our department for various cardiac operations. The remaining 31 cases (74%) were diagnosed postoperatively on surgical tissue histopathology. Most of them were ATTR subtype ($n = 25$, 81%), and 2 had the atrial natriuretic factor amyloidosis subtype of amyloid deposition in tissue. Overall, 33 cases (78.6%) were diagnosed from myocardial tissue, 6 (14.3%) from left atrial appendage, 1 (2.3%) tricuspid valve leaflets, and 2 (4.6%) aortic valve leaflet tissue.

The baseline echocardiography in AG cases demonstrated a median ejection fraction of 63% (IQR, 55.2%-66.8%). Median diastolic dysfunction was grade 2 (IQR, 1-2.5), and median left ventricle mass index was 131.5 g/m² (IQR, 97.8-157.2 g/m²). Median diastolic dysfunction and left ventricular mass index were not available for the CON group cases.

In the amyloid case group, 60% ($n = 25$) of the patients had coronary artery disease, 26% ($n = 11$) had hypertrophic obstructive cardiomyopathy, 19% ($n = 8$) had mitral stenosis, 45% ($n = 19$) had moderate-to-severe mitral regurgitation, 50% ($n = 21$) had aortic stenosis, 7.2% had severe aortic regurgitation, and 31% ($n = 13$) had severe tricuspid regurgitation. All of the patients underwent elective surgery. Two patients had redo cardiac surgery, one patient had undergone previous mitral valve repair, and the other patient had previous mitral and tricuspid valve repair. There were 8 patients (19%) who had previous percutaneous coronary intervention, 6 had pacemakers (14%), and 2 (5%) had AICD devices implanted previously. Among the cardiac procedures performed, aortic valve replacement was most common (45%, $n = 19$), followed by septal myectomy (38%, $n = 16$). Other operations were mitral valve replacement (19%, $n = 8$), mitral valve repair (14%, $n = 6$), and tricuspid valve repair in 16% ($n = 7$) patients.

The median skin incision time in the AG group was 231 minutes (IQR, 175.0-333.0 minutes) versus 237 minutes (IQR, 158.0-307.0 minutes) in the control group. Cardiopulmonary bypass was used in 95% ($n = 40$) of the AG group and 89% ($n = 149$) of the control group. The median cardiopulmonary bypass time was 86 minutes for the AG group and 79.5 minutes for the control group. The difference was not significant ($P = .235$). The median crossclamp time was 62.5 minutes for the AG group and 53.0 minutes for the control group ($P = .063$).

TABLE 1. Patient characteristics, diagnosis and operations performed

Characteristics	Cases (AG) (n = 42)	Controls (CON) (n = 168)	P value
Demographics			
Age, y (median Q1, Q3)	75.7 (70.7, 80.6)	77.6 (69.7, 82.6)	.488*
Male, n (%)	37 (88)	146 (87)	1.000†
Female, n (%)	5 (12)	22 (13)	
BMI, kg/m ² , median (Q1, Q3)	29.1 (27.4, 30.8)	28.3 (24.7, 31.9)	.539*
Race—White, n (%)	42 (100)	168 (100)	
STS Predicted Risk Of Mortality, %, median (Q1, Q3)	2.6 (1.5, 4.6)	4.1 (2.2, 7.9)	.105†
Comorbidities, n (%)			
Diabetes mellitus	7 (17%)	34 (20%)	.670*
Peripheral vascular disease	8 (19%)	33 (20%)	1.000*
Hypertension	35 (83%)	146 (87%)	.617*
Chronic renal failure	5 (12%)	15 (8.9%)	.560*
Cerebrovascular disease	13 (31%)	55 (33%)	1.000*
Cardiac characteristics, n (%)			
NYHA I	4 (9.5%)	10 (7%)	.444*
II	11 (26%)	29 (20%)	
III	21 (50%)	90 (63%)	
IV	6 (14%)	14 (9.8%)	
Previous myocardial infarction, n (%)	7 (17%)	28 (17%)	1.000*
Congestive cardiac failure within 2 wk, n (%)	6 (14%)	40 (24%)	.215*
Cardiogenic shock at time of surgery, n (%)	0 (0%)	0 (0%)	
Atrial arrhythmias, n (%)	14 (33%)	57 (34%)	1.000*
LV ejection fraction, median (Q1, Q3)	62.5 (55.2, 66.8)	63.0 (55.0, 69.0)	.766*
LV diastolic dysfunction, median (Q1, Q3)	2.0 (1.0, 2.5)	N/A	
LV mass index, median (Q1, Q3)	131.5 (97.8, 157.2)	N/A	
Diagnosis, n (%)			
Coronary artery disease	25 (60%)	115 (69%)	.278*
Hypertrophic obstructive cardiomyopathy	11 (26%)	53 (31%)	.577*
Severe mitral stenosis	8 (19%)	20 (12%)	.215*
Severe mitral regurgitation	10 (24%)	49 (29%)	.828*
Severe aortic stenosis	21 (50%)	90 (54%)	.731*
Severe aortic regurgitation	1 (2.4%)	6 (3.8%)	.259†
Severe tricuspid stenosis	0 (0%)	0 (0%)	
Severe tricuspid regurgitation	7 (17%)	34 (20%)	.406*
Previous cardiac surgery	2 (4.8%)	26 (16%)	.078*
Previous PCI	8 (19%)	35 (21%)	1.000*
Previous pacemaker	6 (14%)	14 (8.3%)	.246*
Operation, n (%)			
Coronary artery bypass grafting	14 (33%)	62 (37%)	.722*
Aortic valve replacement	19 (45%)	81 (48%)	.863*
Mitral valve replacement	8 (19%)	33 (20%)	1.000*
Mitral valve repair	6 (14%)	23 (14%)	1.000*
Tricuspid valve repair	7 (17%)	36 (21%)	.669*

(Continued)

TABLE 1. Continued

Characteristics	Cases (AG) (n = 42)	Controls (CON) (n = 168)	P value
Septal myectomy	16 (38%)	63 (38%)	1.000*
Skin incision time, min, median (Q1, Q3)	231.0 (175.0, 333.0)	232.0 (153.0, 321.0)	.496†
Cardiopulmonary bypass time, min, median (Q1, Q3)	86.0 (55.0, 125.5)	81.5 (36.2, 127.5)	.374‡
Crossclamp time, min, median (Q1, Q3)	62.5 (40.0, 99.8)	55.0 (28.8, 93.0)	.185‡

AG, Amyloid group; CON, control; BMI, body mass index, STS, Society of Thoracic Surgeons; NYHA, New York Heart Association; LV, left ventricular; N/A, not available; PCI, percutaneous coronary intervention. *Pearson χ^2 test. †Kruskal-Wallis rank sum test. ‡Fisher exact test.

In the AG group, 1 patient who underwent coronary artery bypass grafting required extracorporeal membrane oxygenation support because of low cardiac output (vs 0.6% in CON group, $P = .361$), and 3 patients (7.1%) needed intra-aortic balloon pump therapy (vs 7.7% in CON group, $P = 1.000$). Median length of intensive care unit (ICU) stay for the AG group was 31.0 hours (IQR, 22.4-65.7 hours) and 27.7 hours (IQR, 21.0-60.5 hours) for the CON group ($P = .579$). The median length of hospital stay was 7 days for the AG group and 6 days for the CON group ($P = .100$). Amongst the AG group, the 30-day

readmission rate was 4.9% ($n = 2$) and 10.3% ($n = 15$) in the CON group ($P = .371$). There was no operative death or 30-day mortality in the AG group (vs 5.4% CON group, $P = .209$).

Among complications, 17 patients (41%) of the AG group had atrial fibrillation in the postoperative period (vs 30% CON, $P = .268$), and 4 (10%) had significant cardiac events (cardiac arrest, low cardiac output, cardiogenic shock) (vs 5.4% CON, $P = .298$). One patient (2.4%) had a stroke, 2 (4.8%) had renal failure requiring dialysis, and 5 (11.9%) required prolonged ventilation. A single

TABLE 2. Postoperative course and complications of the patients

Variables	Cases (AG) (n = 42)	Controls (CON) (n = 168)	P value
Postoperative course			
Length of ICU stay, h, median (Q1, Q3)	31.0 (22.4, 65.7)	27.7 (21.0, 60.5)	.579*
Length of hospital stay, d, median (Q1, Q3)	7.0 (6.0, 9.8)	6.0 (4.5, 10.0)	.100*
Readmission within 30 d of surgery	2 (4.9%)	15 (10.3%)	.371†
Operative mortality	0 (0.0%)	10 (6.0%)	.218‡
30-d mortality	0 (0.0%)	9 (5.4%)	.209‡
Complications			
Atrial fibrillation	17 (41%)	51 (30%)	.268†
Significant cardiac event (cardiac arrest, low cardiac output, cardiogenic shock)	4 (9.5%)	9 (5.4%)	.298‡
ECMO	1 (2.4%)	1 (0.6%)	.361‡
IABP	3 (7.1%)	13 (7.7%)	1.000†
Wound infection	1 (2.4%)	1 (0.6%)	.361‡
Sepsis	0 (0.0%)	5 (3.0%)	.585‡
Stroke	1 (2.4%)	1 (0.6%)	.361‡
Renal failure	2 (4.8%)	10 (6.0%)	1.000†
Dialysis	2 (4.8%)	8 (4.8%)	1.000‡
Pneumonia	3 (7.1%)	9 (5.4%)	.710†
Prolonged ventilation	5 (12%)	26 (16%)	.639†
Multiorgan failure	0 (0.0%)	3 (2.5%)	.569‡

AG, Amyloid group; CON, control; ICU, intensive care unit; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump. *Kruskal-Wallis rank sum test. †Pearson χ^2 test. ‡Fisher exact test.

patient developed sternal wound infection with sternal dehiscence. A permanent pacemaker was implanted in 3 patients (7.1%) of the AG group for heart block. No patient had a reoperation in the AG group on follow-up. The distribution and frequency of complications were similar in the 2 groups (Table 2).

The median follow-up period was 5.8 years (IQR, 2.9-10.1), and it was complete. The 1-year survival for AG group was 93% and CON was 89% ($P = .1$); however, the survival for the AG group fell to 59% at 5 years compared with the control group at 68% ($P = .1$) (Figure 1). The survival for preoperatively diagnosed cases of cardiac amyloidosis was 91% at 1 year and 49% at 5 years. And for cases discovered incidentally by histopathology, survival was 94% at 1 year and 62% at 5 years ($P = .17$) (Figure 2). The survival for ATTR type amyloidosis was 90% at 1 year and 60% at 5 years. AL subtype had similar survivals, 100% at 1 year and 56% at 5 years. ($P = .65$) (Figure 3).

DISCUSSION

In this study, we report our experience with 42 patients diagnosed with amyloidosis who received cardiac operation at Mayo Clinic over the past 25 years. The demographic profile of the cases primarily comprised White male patients in their seventies. All these patients underwent routine cardiac operations, most commonly aortic valve replacement and septal myectomy. The cardiac function in the case group was well preserved, as indicated by a median ejection fraction of 62%. When compared with a matched control group without amyloidosis, there was no difference in rates of complications, length of ICU, or

hospital stay. There was no 30-day mortality in our amyloid case cohort. Examining survival outcomes, we observed a comparable 1-year survival between the AG and CON groups. However, a more noticeable difference emerged at 5 years, with patients having amyloidosis exhibiting a poorer survival rate (59% vs 68% in the CON group). We postulate that the progression of amyloidosis disease burden could explain the decrease in survival of these patients at 5 years and beyond.

Although no statistical difference between the total incision time and duration of cardiopulmonary bypass between the case and control group was detected in our study, we did observe longer cardiopulmonary bypass time in procedures of patients with amyloidosis. No specific reason could be identified; however, we note that the heart is usually hypertrophic in cases with amyloid deposition, as suggested by the high median left ventricle mass index in our case group. This might contribute to difficulty in positioning and exposure of the enlarged heart, leading to a longer bypass time. Also, the length of hospital and ICU stay was marginally longer in patients with amyloidosis. This trend could be attributed to the greater percentage of adverse cardiac events (low cardiac output, cardiac arrest, cardiogenic shock, need for extracorporeal membrane oxygenation support) noted after surgery in this group, although this difference was not found to be significant in our study.

There is considerable variability in the reported outcomes of aortic valve replacement in patients with amyloidosis. Although some studies and case reports demonstrate positive results with comparable outcomes,⁵⁻⁷ others report greater mortality and low cardiac output in these patients.^{9,10} Our study includes some of the patients with

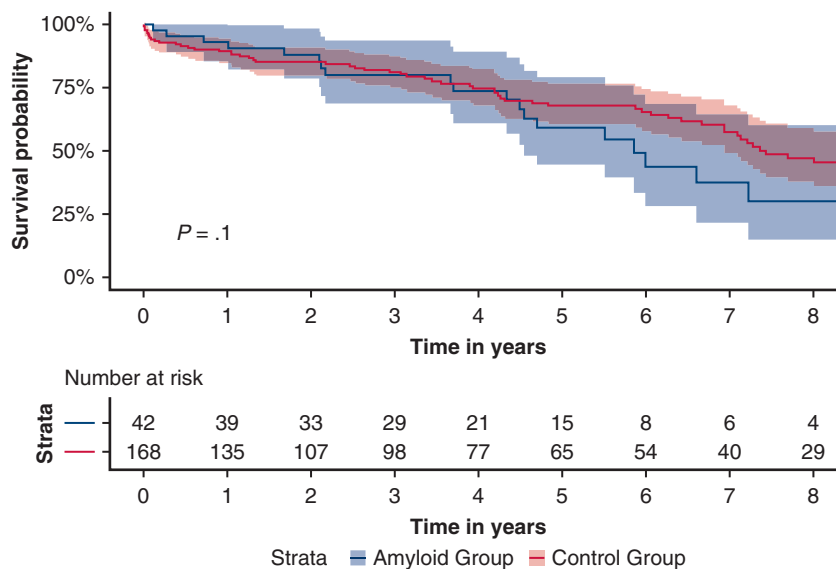


FIGURE 1. Kaplan-Meier survival curve for matched patients undergoing cardiac surgery without amyloidosis (CON, control) compared with that for our cohort of patients with amyloidosis (AG, cases). 95% confidence interval is shown.

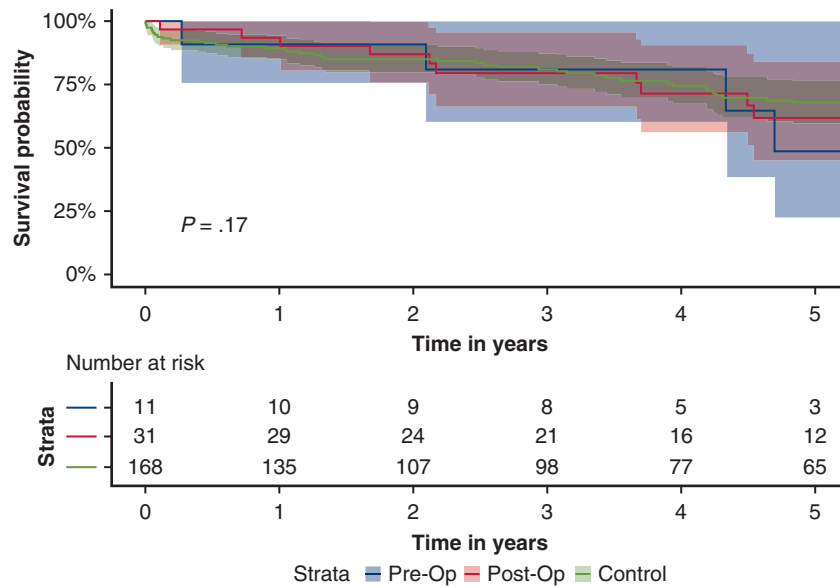


FIGURE 2. Kaplan-Meier survival curve for matched patients undergoing cardiac surgery without amyloidosis (CON, control) compared with that for our cohort of patients with amyloidosis diagnosed preoperatively (*Preop*) and postoperatively (*Postop*). 95% confidence interval is shown.

amyloidosis previously studied by Java and colleagues⁷ at our institution for results of surgical and transcatheter aortic valve replacement. That study concluded there was a low risk of operative morbidity and mortality in patients with amyloidosis undergoing aortic valve replacement. Another study showed similar good outcomes on experience with septal myectomy in incidentally discovered amyloidosis from our department.⁸ Experience with mitral valve surgery in such populations is limited. A study done by Xu and colleagues¹¹ found the prevalence of incidental amyloidosis in

mitral valve surgery to be 0.2%, with no operative mortality and good outcomes. However, some case reports of valve replacement do report death attributable to low cardiac output.^{6,12} These patients had hypertrophied myocardium, suggesting extensive myocardial involvement by amyloidosis. Low cardiac output after coronary bypass has also been reported in patients with amyloidosis.^{13,14}

There is an overall limited amount of literature related to experience with routine surgeries in these patients, and what is available is often limited to case reports and small case

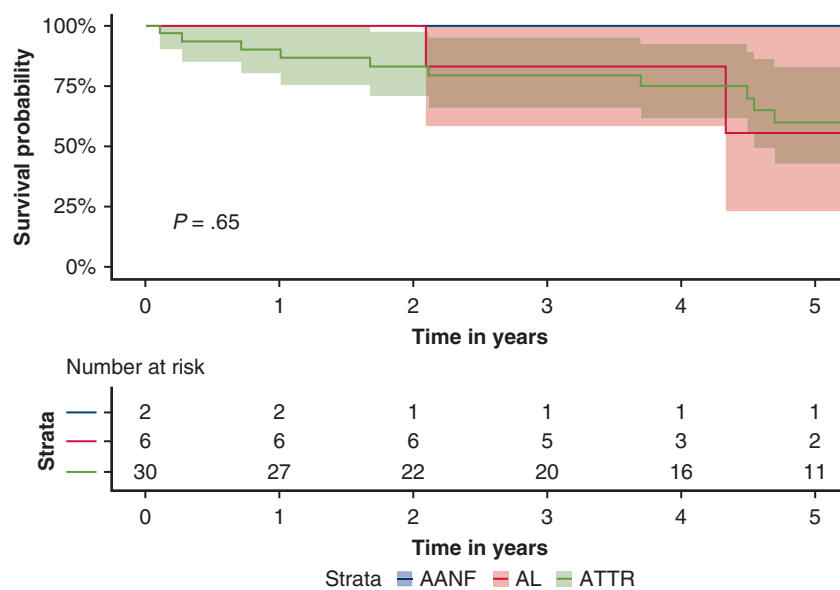


FIGURE 3. Kaplan-Meier survival curve for patients with different subtypes of amyloidosis undergoing cardiac surgery. *AANF*, Atrial natriuretic factor type amyloid; *AL*, light chain-type amyloid; *ATTR*, transthyretin type amyloid, 95% confidence interval is shown.

series. Smith and colleagues¹⁵ reviewed the results of non-transplant surgery in cardiac amyloidosis. They concluded that these patients have increased incidences of peri- and postoperative complications, especially low cardiac output, leading to significant mortality. The reason for this has been postulated as secondary to restrictive physiology and diastolic dysfunction associated with the amyloid deposition in the myocardium. However, in our study, we identified no association, and the short-term results were good, with no 30-day mortality.

The prognosis of individuals with amyloidosis can be significantly influenced by the specific subtype of amyloid identified in operative specimens. Amyloid infiltration in patients with ATTR (senile) amyloidosis is often restricted to the heart, and patients with this subtype have survived longer. In contrast, patients with AL amyloidosis typically have systemic involvement and, thus, have much worse survival.^{1,8,16} In our study, 5-year survival was worse (40%) for patients who were preoperatively diagnosed, the majority with AL type of amyloidosis, and they might have more generalized and aggressive disease. In contrast, survival was better in patients with incidentally discovered amyloid, as most of them were senile ATTR subtype, which has a more benign course.

Cardiac amyloidosis exhibits a range of variability in involvement and presentation, which poses challenges in decision-making regarding surgical intervention. The outcomes of these patients depend on various factors like the degree of myocardial and systemic involvement of the amyloid, type of amyloid, and cardiac function. Also, the incidental discovery of mild amyloidosis after surgery should not be worrisome and usually carries a good prognosis. All these factors should be considered before planning routine cardiac surgery in patients with or suspected to have amyloidosis.

The medical treatment of amyloid continues to advance, with several medications recently receiving approval for the treatment of amyloid cardiomyopathy. Notably, the use of tafamidis has shown significant benefits, including improved survival at 18 months, enhanced performance in the 6-minute walk test, and sustained improvements in quality of life over 5 years of treatment when compared with a placebo.^{17,18} In addition to tafamidis, there are now gene silencers available that intervene earlier in the cascade, effectively preventing the formation of TTR amyloid.¹⁹ With encouraging results, we anticipate that there will be a surge in the number of patients seeking these therapies in the future. This heightened interest is poised to translate into improved postsurgery survival rates for patients undergoing treatment.

Specific limitations constrain the study, one of the most significant being the relatively modest size of our patient cohort. This renders our study vulnerable to type 2 statistical error. Cardiac amyloidosis manifests with varying

degrees of cardiac involvement, and accurately predicting the extent of involvement through conventional tissue biopsy methods remains elusive. Also, being a chronic disease, its effects on heart would certainly be present preoperatively, even though the diagnosis was not known at that stage. Because of these reasons, the outcomes of these patients tend to exhibit significant variability and pose challenges for prediction and generalization. Therefore, it seems imperative to study larger patient cohorts undergoing cardiac surgery, particularly those with rarer subtypes of amyloidosis.

CONCLUSIONS

Early outcomes in patients with cardiac amyloidosis undergoing routine cardiac surgery are favorable, with 1-year survival comparable with unaffected patients. Notably, the subtype of amyloid may also influence overall prognosis. It is also important to emphasize that the diagnosis of amyloidosis should not serve as an absolute contraindication to cardiac surgery, especially in patients with preserved cardiac function. Although primary amyloidosis may carry an increased risk of low cardiac output early postoperatively, and even though the 5-year survival tends to fall below expected, offering surgery to these patients with amyloidosis will provide them with symptom relief from various pathologies without adding unnecessary operative risk.

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

References

1. Fontana M, Banypersad SM, Treibel TA, et al. Differential myocyte responses in patients with cardiac transthyretin amyloidosis and light-chain amyloidosis: a cardiac MR imaging study. *Radiology*. 2015;277(2):388-397.
2. Merlini G, Bellotti V. Molecular mechanisms of amyloidosis. *N Engl J Med*. 2003;349(6):583-596.
3. Moayedi Y, Duero JP, Foroutan F, Alba AC, Ross HJ, Delgado D. (561) - Predictors of survival in patients with cardiac amyloidosis. *J Heart Lung Transplant*. 2017;36(suppl 4):S217.
4. Arora S, Patil NS, Strassle PD, et al. Amyloidosis and 30-day outcomes among patients with heart failure. *JACC CardioOncol*. 2020;2(5):710-718.
5. Terada Y, Wanibuchi Y. Aortic valve replacement in a patient with cardiac amyloidosis. *Ann Thorac Surg*. 1996;62(5):1571-1572.
6. Schwartz JG, Ghidoni JJ. Unsuspected amyloidosis and cardiac arrest following mitral valve replacement. *Int J Cardiol*. 1985;9(4):485-487.
7. Java AP, Greason KL, Dispenzieri A, et al. Aortic valve replacement in patients with amyloidosis. *J Thorac Cardiovasc Surg*. 2018;156(1):98-103.
8. Helder MR, Schaff HV, Nishimura RA, et al. Impact of incidental amyloidosis on the prognosis of patients with hypertrophic cardiomyopathy undergoing septal myectomy for left ventricular outflow tract obstruction. *Am J Cardiol*. 2014;114(9):1396-1399.

9. Treibel TA, Fontana M, Gilbertson JA, et al. Occult transthyretin cardiac amyloid in severe calcific aortic stenosis: prevalence and prognosis in patients undergoing surgical aortic valve replacement. *Circ Cardiovasc Imaging*. 2016;9(8):e005066.
10. Seki T, Hattori A, Yoshida T. Hemodynamic deterioration after aortic valve replacement in a patient with mixed systemic amyloidosis. *General Thorac Cardiovasc Surg*. 2017;65(8):470-473.
11. Xu B, Godoy Rivas C, Rodriguez ER, et al. Unrecognized cardiac amyloidosis at the time of mitral valve surgery: incidence and outcomes. *Cardiology*. 2019;142(4):253-258.
12. Engelmeier RS, O'Connell JB, Subramanian R. Cardiac amyloidosis presenting as severe mitral regurgitation. *Int J Cardiol*. 1983;4(3):325-327.
13. Zacek P, Medilek K, Lonsky V, Laco J, Nova M, Dominik J. Cardiac amyloidosis in the cardiosurgical operating room—a rare but fatal trap. *Thorac Cardiovasc Surg*. 2007;55(2):65-67.
14. Massoudy P, Szabo AK, Dirsch O, Wienecke H, van de Wal HJ, Jakob HG. Amyloid of heart and lungs in a patient with low output syndrome after coronary artery bypass grafting. *Herz*. 2003;28(5):453-456.
15. Smith A, Balmforth D, Treibel TA, Lall K, Oo A, Ambekar S. Cardiac amyloidosis in non-transplant cardiac surgery. *J Card Surg*. 2021;36(8):2901-2910.
16. Ng B, Connors LH, Davidoff R, Skinner M, Falk RH. Senile systemic amyloidosis presenting with heart failure: a comparison with light chain-associated amyloidosis. *Arch Intern Med*. 2005;165(12):1425-1429.
17. Elliott P, Drachman BM, Gottlieb SS, et al. Long-term survival with tafamidis in patients with transthyretin amyloid cardiomyopathy. *Circ Heart Fail*. 2022;15(1):e008193.
18. Maurer MS, Schwartz JH, Gundapaneni B, et al. Tafamidis treatment for patients with transthyretin amyloid cardiomyopathy. *N Engl J Med*. 2018;379(11):1007-1016.
19. Adams D, Tournev IL, Taylor MS, et al. Efficacy and safety of vutrisiran for patients with hereditary transthyretin-mediated amyloidosis with polyneuropathy: a randomized clinical trial. *Amyloid*. 2023;30(1):1-9.

Key Words: amyloidosis, cardiac surgery

TABLE E1. Prematching and postmatching data of case and control group with SMD values

Characteristics	Case	Control	SMD
Prematching			
n	42	26,463	
Age, y, mean (SD)	75.09 (8.51)	68.25 (13.22)	0.614
Gender—female	5 (11.9)	9523 (36.0)	0.588
Race—White	42 (100.0)	25,253 (95.4)	0.310
BMI, mean (SD)	29.17 (4.98)	29.93 (6.21)	0.136
Diabetes	7 (16.7)	7106 (26.9)	0.249
Chronic renal failure	5 (11.9)	1091 (4.1)	0.290
Hypertension	35 (83.3)	19,825 (74.9)	0.208
Peripheral vascular disease	8 (19.0)	4091 (15.5)	0.095
Cerebrovascular disease	13 (31.0)	4423 (16.7)	0.339
CABG	14 (33.3)	12,581 (47.5)	0.293
Aortic valve replacement	19 (45.2)	12,467 (47.1)	0.038
Mitral valve replacement	8 (19.0)	2931 (11.1)	0.224
Mitral valve repair	6 (14.3)	1761 (6.7)	0.251
Tricuspid valve repair	7 (16.7)	1250 (4.7)	0.394
Myectomy	16 (38.1)	4196 (15.9)	0.518
Year of surgery, mean (SD)	2015.14 (6.08)	2010.78 (6.74)	0.680
Postmatching			
n	42	168	
Age, mean (SD)	75.09 (8.51)	75.92 (9.27)	0.094
Gender—female	5 (11.9)	22 (13.1)	0.036
Race—White	42 (100.0)	168 (100.0)	<0.001
BMI, mean (SD)	29.17 (4.98)	28.98 (5.82)	0.035
Diabetes	7 (16.7)	34 (20.2)	0.092
Renal failure	5 (11.9)	15 (8.9)	0.098
Hypertension	35 (83.3)	146 (86.9)	0.100
Peripheral vascular disease	8 (19.0)	33 (19.6)	0.015
Cerebrovascular disease	13 (31.0)	55 (32.7)	0.038
CABG	14 (33.3)	62 (36.9)	0.075
Aortic valve replacement	19 (45.2)	81 (48.2)	0.060
Mitral valve replacement	8 (19.0)	33 (19.6)	0.015
Mitral valve repair	6 (14.3)	23 (13.7)	0.017
Tricuspid valve repair	7 (16.7)	36 (21.4)	0.121
Myectomy	16 (38.1)	63 (37.5)	0.012
Year of surgery, mean (SD)	2015.14 (6.08)	2015.24 (6.31)	0.015

SMD, Standardized mean difference; SD, standard deviation; BMI, body mass index; CABG, coronary artery bypass grafting.