

# Aortic Allografts: Bigger is not always better!

James C. Witten, MD

Cleveland Clinic Department of Thoracic and Cardiovascular Surgery, Miller Family Heart, Vascular and Thoracic Institute, Cleveland Clinic, Cleveland, OH

BIO-IMPLANT BRIEF

Aortic allografts are a valuable tool in certain situations for aortic valve and root reconstruction, most notably in cases of invasive aortic root endocarditis.<sup>1</sup> Proper sizing of aortic allografts is not widely discussed in the literature, and the temptation is to maximally upsize the implanted allograft. There are, however, downsides to the use of a larger allograft, with limited hemodynamic upside. The purpose of this article is to discuss allograft sizing and make the case for using smaller (normal-sized) allografts, when indicated.

## When to choose an allograft?

Due to their natural resistance to infection,<sup>2,3</sup> allografts are an excellent prosthesis choice for invasive aortic root endocarditis with significant circumferential involvement or root abscess, as well as for root/ascending graft infections.<sup>1,2</sup>

## How are allografts sized?

Allograft valve size is determined via the insertion of a Hegar dilator through the aortic valve annulus, such that the dilator fits through the annulus without distending it. The annulus diameter is reported in millimeter increments.

## How to choose an allograft valve size for my patient?

Allograft valve sizing should incorporate data from transthoracic echocardiography, gated CT angiography (when indicated), and intraoperative trans-esophageal echocardiography measurements of the aortic annulus, particularly the left ventricular outflow tract (LVOT). Intraoperatively, cylindrical valve sizers (Hegar dilator, preferentially) are used to size the LVOT.

An allograft is chosen to match the internal diameter of the LVOT to the internal diameter of the allograft; however, the allograft affords significant size flexibility. Some perform commissural plication for very large roots.<sup>4</sup> However, we find this rarely necessary. The allograft muscle should be trimmed so that the graft sits down into the LVOT. This allows for excellent hemostasis and argues against oversizing the valve. In most case series, the vast majority of allograft sizes fall below 25mm.<sup>5,6</sup> This is in line with normalized dimensions across age and body size, demonstrating a mean aortic annular diameter of  $22.4 \pm 2.7$ mm.<sup>7,8</sup>

## Do larger allografts improve hemodynamics?

A major benefit of aortic allografts is their excellent hemodynamics. Allografts are sized based on the internal diameter (ID; mm), and the lack of sewing ring means the outer diameter is only a few millimeters larger, facilitating placement of an appropriately sized allograft. Stented bioprosthetic valves are sized based on the midpoint to midpoint of the mounting stent. Thus, the true ID of a stented valve is less than the label size, and the outer diameter greater, given the stent and sewing ring. This means that, compared to the same labeled size of an allograft, a stented bioprosthesis has a smaller effective orifice area (EOA; cm<sup>2</sup>), and requires a larger root to seat.<sup>9</sup> See Table 1 below.

**Table 1.** Effective Orifice Area (cm<sup>2</sup>) of Biological Prostheses According to Label Size (mm).

Prosthesis	Graft Label Size (mm)				
	19	21	23	25	27
	Effective Orifice Area (cm <sup>2</sup> )				
Carpentier-Edwards® porcine	1.17	1.38	—	2.36	2.74
Hancock™ porcine	1.15	1.31	1.73	1.93	2.14
Hancock™ modified orifice (MO)	1.22	1.43	1.94	2.16	—
Hancock™ II	—	1.48	1.81	2.10	2.36
Carpentier-Edwards® pericardial	1.56	1.88	—	3.25	3.70
Freestyle™	1.84	2.17	2.69	3.41	3.75
Aortic allograft*	1.7	2.3	2.5	2.7	—

Effective Orifice Area (cm<sup>2</sup>) taken from *in vitro* studies on biological prostheses; table adapted with permission. Copyright 2017 Elsevier.<sup>10</sup>

\* Aortic allograft Effective Orifice Area (cm<sup>2</sup>) from *in vivo* echocardiographic data.<sup>11</sup>

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To avoid patient-prosthesis mismatch, the EOA should be indexed to body surface area (BSA) and greater than  $0.85 \text{ cm}^2/\text{m}^2$ .<sup>12</sup> Even a large patient with a BSA of  $2.5 \text{ m}^2$  only requires a size 21mm allograft to achieve this (Table 2).<sup>12</sup> While this index is a minimum, there is little hemodynamic or survival benefit to greatly exceeding this.<sup>12,13</sup>

**Table 2.** Body surface area and corresponding indexed effective orifice area to avoid patient-prosthesis mismatch.

Patient BSA (m <sup>2</sup> )	Minimal Valve EOA (cm <sup>2</sup> ) for Indexed EOA >0.85 cm <sup>2</sup> /m <sup>2</sup> (Ideal)
1.30	1.11
1.35	1.15
1.40	1.20
1.45	1.23
1.50	1.28
1.55	1.32
1.60	1.36
1.65	1.40
1.70	1.45
1.75	1.49
1.80	1.53
1.85	1.57
1.90	1.62
1.95	1.66
2.00	1.70
2.05	1.74
2.10	1.79
2.15	1.83
2.20	1.87
2.25	1.97
2.30	1.96
2.35	2.00
2.40	2.04
2.45	2.08
2.50	2.13

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Lastly, the mechanism for aortic allograft failure is typically regurgitation, not progressive stenosis, compared to stented bioprosthetic valves.<sup>5</sup> As stented bioprosthesis leaflets become rigid and calcified, the EOA decreases and the patient and LV are subject to progressive aortic stenosis.<sup>14,15</sup> The tendency is thus to upsize stented bioprostheses as much as possible to compensate for this, which is unnecessary for allografts given their mode of failure.<sup>12</sup>

## Are there durability implications to implanting larger allografts?

Larger allograft size is an independent predictor of worse durability.<sup>5,16</sup> See Figure 1 and Table 3. Allografts >24mm have nearly twice the risk of explant for structural failure than 21-22mm grafts.

Larger allografts also frequently equate to older donors, as aortic valve diameter increases with age;<sup>17</sup> donor age is an independent predictor of worse durability.<sup>5,18</sup> Even in younger donors, a larger allograft may potentially be associated with abnormal aortic connective tissue, if they fall outside normalized values for patient size.<sup>7</sup>

**Figure 1.** Allograft durability stratified by donor allograft size

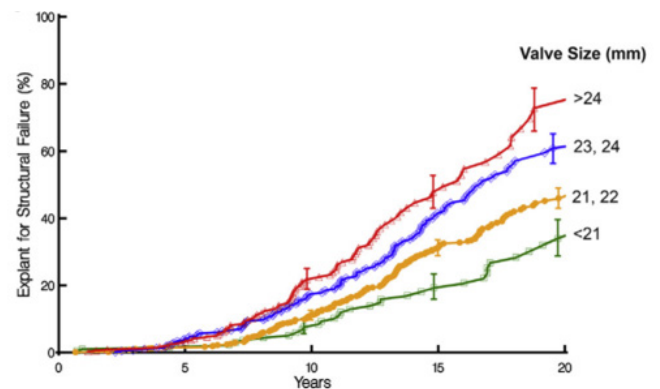


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**Table 3.** Factors associated with higher mean gradient after allograft aortic valve replacement.

Factor	Estimate ± SE	P
Donor Age	0.39 ± 0.066	<0.0001
Donor female	0.24 ± 0.044	<0.0001
Allograft size	0.038 ± 0.0042	<0.0001
Recipient Age	-0.171 ± 0.020	<0.0001

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## Is a larger allograft better for future procedures (transcatheter valve-in-valve)?

Experience with transcatheter valve-in-allografts has been limited to small case-series.<sup>19,20</sup> This is not advocated for several reasons. First, the predominant mechanism of allograft failure is aortic insufficiency; this remains a challenge for performing transcatheter aortic valve replacement (TAVR).<sup>5</sup> Leaflet calcification, leaflet tears, and the allograft leaflet height may also preclude TAVR. Additionally, allograft degeneration often involves extensive calcification of the allograft root, putting the patient at higher risk for embolic complications.<sup>19,21</sup> Lastly, the experience at my institution with allograft reoperations has demonstrated excellent outcomes with radical explants followed by a conventional Bentall operation.<sup>19</sup> For these reasons, allograft oversizing for the purpose of future TAVR is not recommended.

## Conclusions:

- Aortic allografts have excellent hemodynamics and are a valuable tool for invasive aortic root infective endocarditis.
- Appropriate sizing of the left ventricular outflow tract usually equates to a normal (21-24mm) allograft.
- Larger allografts offer little hemodynamic upside.
- In our experience, larger allografts degenerate faster.
- There is limited utility to over-sizing allografts for future transcatheter interventions at present.

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## References

1. AATS Surgical Treatment of Infective Endocarditis Consensus Guidelines Writing Committee Chairs, Pettersson GB, Coselli JS, et al. 2016 The American Association for Thoracic Surgery (AATS) consensus guidelines: Surgical treatment of infective endocarditis: Executive summary. *J Thorac Cardiovasc Surg.* 2017;153(6):1241-1258. e29. doi:10.1016/j.jtcvs.2016.09.093.
2. Witten JC, Houghtaling PL, Shrestha NK, et al. Aortic allograft infection risk. *J Thorac Cardiovasc Surg.* 2023;165(4):1303-1315.e9. doi:10.1016/j.jtcvs.2021.04.086.
3. Preventza O, Mohamed AS, Cooley DA, et al. Homograft use in reoperative aortic root and proximal aortic surgery for endocarditis: A 12-year experience in high-risk patients. *J Thorac Cardiovasc Surg.* 2014;148(3):989-994. doi:10.1016/j.jtcvs.2014.06.025.
4. Northrup WF, Kshetry VR. Implantation technique of aortic homograft root: emphasis on matching the host root to the graft. *Ann Thorac Surg.* 1998;66(1):280-284. doi:10.1016/s0003-4975(98)00411-1.
5. Witten JC, Durbak E, Houghtaling PL, et al. Performance and Durability of Cryopreserved Allograft Aortic Valve Replacements. *Ann Thorac Surg.* 2021;111(6):1893-1900. doi:10.1016/j.athoracsur.2020.07.033.
6. Mokhles MM, Rajeswaran J, Bekkers JA, et al. Capturing echocardiographic allograft valve function over time after allograft aortic valve or root replacement. *J Thorac Cardiovasc Surg.* 2014;148(5):1921-1928.e3. doi:10.1016/j.jtcvs.2014.04.023.
7. Capps SB, Elkins RC, Fronk DM. Body surface area as a predictor of aortic and pulmonary valve diameter. *J Thorac Cardiovasc Surg.* 2000;119(5):975-982. doi:10.1016/S0022-5223(00)70092-4.
8. Kouchoukos NT, Blackstone EH, Hanley FL, Kirklin JK. Anatomy, Dimensions, and Terminology. In: *Kirklin/Barratt-Boyes Cardiac Surgery.* 4th ed. Elsevier/Saunders; 2013:1-66.
9. Blackstone EH, Cosgrove DM, Jamieson WRE, et al. Prosthesis size and long-term survival after aortic valve replacement. *J Thorac Cardiovasc Surg.* 2003;126(3):783-796. doi:10.1016/s0022-5223(03)00591-9.
10. Yoganathan AP, Heinrich RS, Fontaine AA. Fluid dynamics of prosthetic valves. In Otto CM, ed. *The Practice of Clinical Echocardiography.* 6th edition. Elsevier; 2022.
11. Eriksson MJ, Källner G, Rosfors S, Ivert T, Brodin LA. Hemodynamic performance of cryopreserved aortic homograft valves during midterm follow-up. *J Am Coll Cardiol.* 1998;32(4):1002-1008. doi:10.1016/s0735-1097(98)00352-0.
12. Pibarot P, Dumesnil JG. Hemodynamic and clinical impact of prosthesis-patient mismatch in the aortic valve position and its prevention. *J Am Coll Cardiol.* 2000;36(4):1131-1141. doi:10.1016/s0735-1097(00)00859-7.
13. Dismorr M, Glaser N, Franco -Cereceda Anders, Sartipy U. Effect of Prosthesis-Patient Mismatch on Long-Term Clinical Outcomes After Bioprosthetic Aortic Valve Replacement. *J Am Coll Cardiol.* 2023;81(10):964-975. doi:10.1016/j.jacc.2022.12.023.
14. Dvir D, Bourguignon T, Otto CM, et al. Standardized Definition of Structural Valve Degeneration for Surgical and Transcatheter Bioprosthetic Aortic Valves. *Circulation.* 2018;137(4):388-399. doi:10.1161/CIRCULATIONAHA.117.030729.
15. VARC-3 WRITING COMMITTEE, G n reux P, Piazza N, et al. Valve Academic Research Consortium 3: updated endpoint definitions for aortic valve clinical research. *Eur Heart J.* 2021;42(19):1825-1857. doi:10.1093/eurheartj/ehaa799.
16. Takkenberg JJM, van Herwerden LA, Eijkemans MJC, Bekkers JA, Bogers AJJC. Evolution of allograft aortic valve replacement over 13 years: results of 275 procedures. *Eur J Cardiothorac Surg.* 2002;21(4):683-691. doi:10.1016/S1010-7940(02)00025-8.
17. Kitzman DW, Scholz DG, Hagen PT, Ilstrup DM, Edwards WD. Age-Related Changes in Normal Human Hearts During the First 10 Decades of Life. Part II (Maturity): A Quantitative Anatomic Study of 765 Specimens From Subjects 20 to 99 Years Old. *Mayo Clin Proc.* 1988;63(2):137-146. doi:10.1016/S0025-6196(12)64946-5.
18. O'Brien MF, Harrocks S, Stafford EG, et al. The homograft aortic valve: a 29-year, 99.3% follow up of 1,022 valve replacements. *J Heart Valve Dis.* 2001;10(3):334-344; discussion 335.
19. Witten JC, Umana-Pizano J, Houghtaling PL, et al. Aortic root allograft reoperations. *J Thorac Cardiovasc Surg.* Published online February 15, 2023:S0022-5223(23)00164-2. doi:10.1016/j.jtcvs.2023.02.009.
20. Sedeek AF, Greason KL, Nkomo VT, et al. Repeat aortic valve replacement for failing aortic root homograft. *J Thorac Cardiovasc Surg.* 2019;158(2):378-385.e2. doi:10.1016/j.jtcvs.2018.11.107.
21. Nowicki ER, Pettersson GB, Smedira NG, Roselli EE, Blackstone EH, Lytle BW. Aortic Allograft Valve Reoperation: Surgical Challenges and Patient Risks. *Ann Thorac Surg.* 2008;86(3):761-768.e2. doi:10.1016/j.athoracsur.2008.01.102.

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