Is Center Specific Implantation Volume a Predictor of Clinical Outcomes with Mechanical Circulatory Support?

TOFY MUSSIVAND, DELPHINE A. HASLE, AND KEVIN S. HOLMES

This study examined the relationship between implant center volumes and survival rate for implantation of mechanical circulatory support (MCS) devices. Using the Novacor left ventricular assist system (LVAS) Registry, the study cohort consisted of 1,348 patients with established outcomes from 97 centers stratified by the implant center volume: 1–10 implants (n = 199, 65 centers), 11–25 implants (n = 189, 12 centers), 26–50 implants (n = 445, 13 centers), and more than 51 implants (n = 515, 7 centers). Regression and correlation analyses were performed.

Regression analysis found a negative impact on survival for centers performing 1–10 implants, with an odds ratio of 1.73 (95% confidence interval, 1.28–2.34; *p* < 0.001). Composite results from the first 10 implants of each larger volume center were then compared with the group with 1–10 implants, demonstrating that centers with larger volumes had superior results, even in the early patient experience (61% *versus* 46% transplanted/weaned, *p* < 0.001). However, when annualized outcomes (*i.e.,* outcomes by calendar year) were determined for each center, no significant correlation was found between the outcomes and annualized frequency of implantation (R^2 = 0.003, n = 422).

Although the total number of implants performed at a specific center appeared to impact clinical outcomes, no correlation was found between annualized frequency of implant and clinical outcome. *ASAIO Journal* 2004; 50:33–36.

The correlation between surgical volume and mortality has been debated for decades.[1] The increasing use of studies on surgical volume and its impact on the structure of the health care delivery system led to a major review of the supporting evidence by the U.S. Institute of Medicine in 2000.[2] The report concluded that although many large scale studies have been conducted for a variety of procedures[2,3] and most publications reported improved outcomes at higher volumes, the underlying reasons for this volume-outcome relationship remain unclear. Furthermore, it recognized that volume is not a direct measure of quality but is instead a proxy that may provide insight into quality. There is also great variability in results (*i.e.,* some low volume centers have excellent outcomes, whereas some large volume centers may have poor outcomes). This area of study has been the topic of much debate and controversy, particularly in relation to how the data are interpreted and used.[4–8] Most notably, there are concerns how volume-outcome studies are used in the rationalization of health care services.

Recently, the International Society of Heart and Lung Transplantation (ISHLT) proposed clinical standards for centers performing long-term mechanical circulatory support device implantation (*i.e.,* destination therapy).[9] This proposal was brought forward in response to the recent U.S. Food and Drug Administration (FDA) approval of a destination therapy indication for a mechanical circulatory support device and the panel review conducted by the U.S. Centers for Medicare and Medicaid Services (CMS) regarding reimbursement coverage for this new indication. The goal of the ISHLT proposal was to establish a methodology whereby the protection and benefit to the individual patient would be preserved as this new indication evolves and the technology is disseminated into the wider clinical community.

One specific criterion of the clinical standards proposed by ISHLT was mandatory reporting of implant volumes and outcomes (at 1 month, 6 months, and 12 months). Along with this requirement, the proposal also indicated that centers should "meet or exceed previously established target volumes and outcomes." (Deng et al,[9] p. 368) It is important to note that these "target volumes and outcomes" have yet to be determined. The proposal also recommended that CMS coverage for destination therapy only be provided to those centers that meet the proposed clinical standards.

Interestingly, a recent review of the literature found no mention of the volume-outcome relationship in the field of mechanical circulatory support. On the basis of the lack of available data, a review of this relationship was conducted using the Novacor LVAS Global Registry (World Heart Corporation), which currently consists of more than 1,450 mechanical circulatory support device implants conducted at 97 international centers.[10] This retrospective study was conducted to answer the clinical research question, "Do center specific implant volumes impact survival with left ventricular assist device support?"

From the University of Ottawa Heart Institute, Ottawa, Ontario, Canada.

Presented at the American Society for Artificial Internal Organs and International Society for Artificial Organs Joint Conference, June 19–21, 2003, Washington, DC.

Tofy Mussivand, Kevin Holmes, and Delphine Hasle are salaried employees, and Tofy Mussivand and Kevin Holmes are stock owners in the World Heart Corporation.

Submitted for consideration June 2003; accepted for publication in revised form September 2003.

Reprint requests: Dr. Tofy Mussivand, FRSC, Professor of Surgery and Engineering, University of Ottawa, Director & Chair, Cardiovascular Devices Division & Medical Devices, University of Ottawa Heart Institute, 40 Ruskin Ave, Rm. H560B, Ottawa, Ontario, Canada K1Y 4W7; E-mail tmussivand@ottawaheart.ca.

DOI: 10.1097/01.MAT.0000104847.87144.61

Table 1. Patient characteristics at Time of Implant and Mechanical Circulatory Support Durations for Each of the Four Implant Center Volume Groups

	1–10 Implants at 65 Centers	11–25 Implants at 12 Centers	26–50 Implants at 13 Centers	>51 Implants at 7 Centers
Number	199	189	445	515
Mean age (range)	47 years (13–75)	47 years (16–76)	49 years (14–78)	48 years (12–71)
Gender (male)	91%	94%	87%	90%
Etiology				
CM	64%	60%	57%	58%
IHD	26%	28%	36%	35%
Indication of use				
BTT	87%	95%	95%	92%
Mean duration (± SD)	123 days (± 175)	137 days (± 211)	114 days (± 170)	123 days (± 160)

CM, cardiomyopathy; IHD, ischemic heart disease; BTT, bridge to transplant; SD, standard deviation. No meaningful differences were observed between the groups.

Methods

Patients

All patients from the Novacor LVAS Global Registry were included in the study with the exception of those patients currently undergoing support with the device, as these patients do not yet have an established outcome (*i.e.,* transplantation, weaning, or death). The resulting study group consisted of 1,348 patients implanted with the Novacor LVAS between September 1984 and January 2003 at 97 international centers. The data from this study group represent more than 500 patient years of LVAS support.

Patients were stratified by implant center volume (*i.e.,* total number of Novacor LVAS implants): 1–10 implants (n = 199, 65 centers), 11–25 implants (n = 189, 12 centers), 26–50 implants (n = 445, 13 centers), and more than 51 implants (n = 515, 7 centers). Patient characteristics at the time of implant and the support durations for each of these four groups are shown in **Table 1**. No significant differences were observed in the baseline characteristics or support durations among these individual groups.

Definitions

For the purpose of this study, the following definitions were used:

Implant center volume: Total number of Novacor LVAS implants performed at a specific center, including patients currently undergoing support.

Frequency of implantation: Number of procedures (*i.e.,* Novacor LVAS implants) performed at a specific center in a 1 year period. This period was measured in calendar years (*i.e.,* January 1 to December 31).

Favorable outcome: Survival on the LVAS to either transplantation or weaning.

Survival rate: Percentage of patients with an established outcome experiencing a favorable outcome.

Table 2. Mantel-Haenszel Regression Analysis Comparing Survival Rate by Implant Center Volume

Center Volume	OR	95% CI
1–10 implants	1.73	1.28–2.34
11–25 implants	0.88	0.65–1.21
26–50 implants	0.89	0.71–1.13
> 51 implants	0.88	0.70–1.10

A negative impact on survival (OR 1.73, CI 1.28–2.34, $p < 0.001$) was observed in the implant center volume group with 1–10 implants. OR, odds ratio; CI, confidence interval.

Data Analysis

All statistical analyses were performed using SAS (SAS for Windows Version V.8e, SAS Inc, Cary, NC). Categorical values (gender, etiology, indication of use, outcome, and implant center volume group) were expressed as a percentage. Continuous variables were expressed as mean and range (age) or mean and standard deviation (support duration). Multivariate regression analysis (Mantel-Haenszel odds ratio with exact t-tests) was performed to predict the impact of implant center volume group on survival. Univariate analysis (Fisher's exact tests) was used to compare outcomes between different implant center volume groups. The relationship between frequency of implantation and survival rate was tested for statistical significance using Pearson's correlation coefficient. The level of significance used in this study was 0.05 for both exact tests and 0.5 for the correlation coefficients.

Results

As shown in **Table 2**, regression analysis demonstrated a negative impact on survival at those centers with 1–10 implants. The odds of experiencing a unfavorable outcome (*i.e.,* death) were 1.73 times greater in recipients from centers with 1–10 implants compared with those recipients from centers with more than 10 implants (odds ratio 1.73, 95% confidence interval, 1.28–2.34, $p < 0.001$). In terms of outcomes, **Figure 1** shows survival rates for each of the implant center volume groups. Again, centers with implant volumes with 1–10 implants had significantly worse results, with just 91 of 199 patients (46%) achieving a favorable outcome (*i.e.,* transplan-

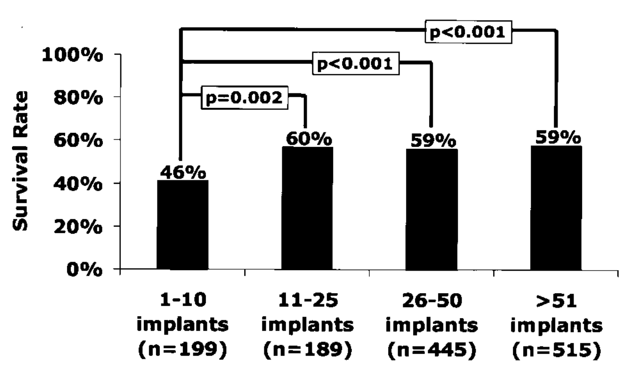

Figure 1. Patient survival rate by implant center volume group. Survival rate was significantly lower in the group with 1–10 implants. No differences were observed between each of the other implant center volume groups.

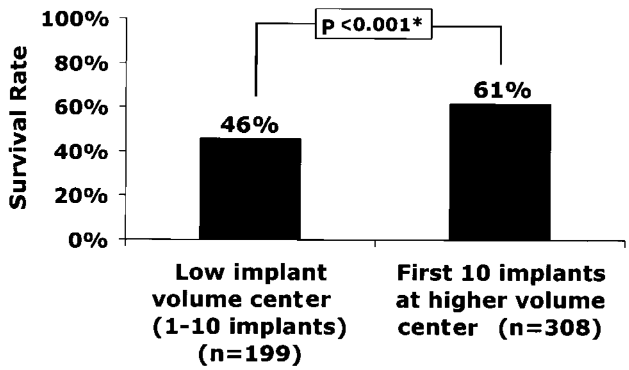

Figure 2. Comparison of the survival rate in the group with 1–10 implants to a group consisting of the first 10 implants performed at each of other centers from the higher volume implant groups.

tation or weaning). The survival rate at centers with implant volumes with 1–10 implants (46% transplant/weaned) was significantly lower than all other implant volume groups; 11–25 implants (60% transplant/weaned, $p = 0.002$), 26–50 implants (59% transplant/weaned, $p < 0.001$), and more than 51 implants (59% transplant/weaned, $p < 0.001$).

To assess whether these results were somehow related to one of the historical explanations of the volume-outcome relationship (*i.e.,* a learning curve or practice makes perfect[2]), further analysis was conducted that compared the results from the group with 1–10 implants with the results for the first 10 implants of each center performing more than 10 implants. As shown in **Figure 2**, centers with larger volumes had superior results (61% *versus* 46% transplant/weaned, $p < 0.001$), even during their early patient experience with this device (*i.e.,* first 10 implants).

Because a major use of any established volume-outcome relationship is to determine volume targets or thresholds to achieve a certain level of favorable clinical outcome, annualized results (*i.e.,* results by calendar year) are often used. Using the entire database (n = 1,348), annualized implant center volumes and survival rates were determined for each of the 97 implanting centers for each calendar year. These data were plotted to assess the correlation, whether any, between survival rate and implant frequency (number of implants/year). As shown in **Figure 3**, this analysis demonstrated no correlation between the frequency of implantation and the survival rate ($R^2 = 0.0037$, n = 422).

Because targets or thresholds are often applied to individual centers, an *ad hoc* examination of annualized outcomes at individual centers was conducted. Respected, well-established, and capable mechanical circulatory support programs were analyzed. **Figure 4** shows a representative 10 year sample of data from a single center. Not surprisingly, the intercenter results were similar to the analysis of the entire database in that there was no correlation between survival rate and frequency of implantation. However, the data did clearly demonstrate a wide variation in outcomes from year to year within individual centers.

Discussion

In this review of the volume-outcome relationship for implantation of mechanical circulatory support devices, no evidence of either a typical learning curve (**Figure 2**) or correlation between annualized frequency of implantation and survival rate (**Figure 3**) was found. Although the regression analysis showed that centers that performed 1–10 implants in total had inferior survival rates (**Figure 1**), this may simply be a weakness in dataset construct caused by some or all of the confounding factors (*i.e.,* factors that make it not logically possible to separate the contribution of any single causal factor

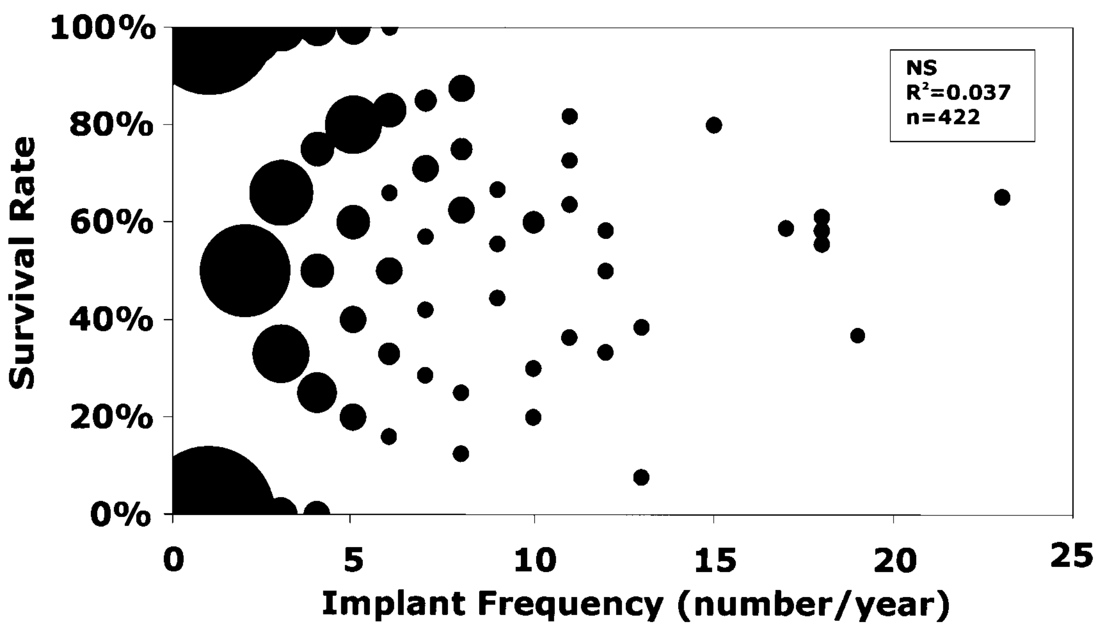

Figure 3. Annualized outcomes for each center and each calendar year. Bubble size reflects the number of common data points. No correlation was found between survival rate and frequency of implantation.

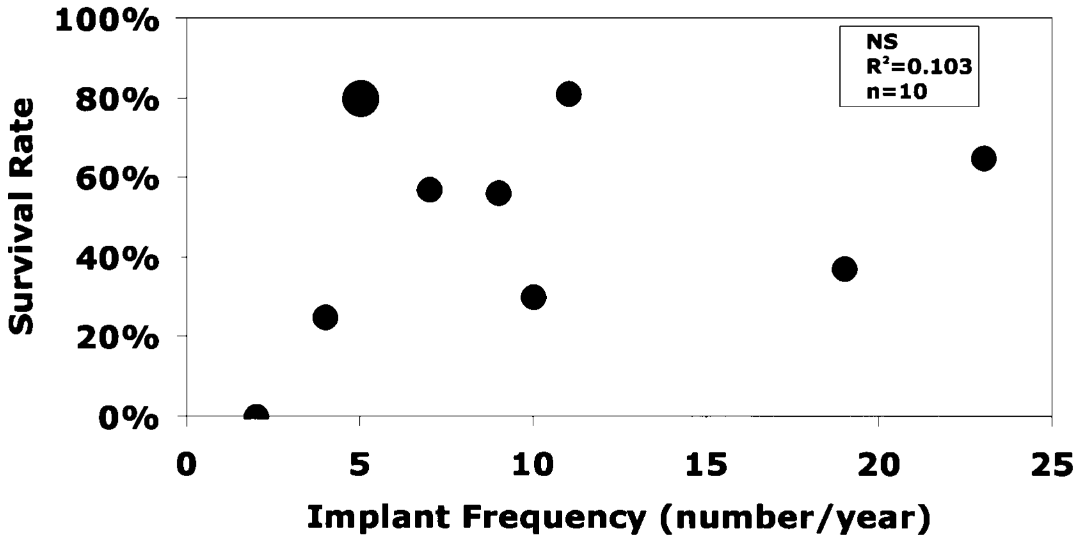

Figure 4. Annualized outcomes for a representative individual center for each calendar year. Bubble size reflects the number of common data points. No correlation was found between survival rate and frequency of implantation, and wide data variability was observed.

to the observed effects). First, the survival data are unadjusted for age, etiology, comorbidity, etc. Second, because the group with 1–10 implants would be relatively new implanting centers (at least for this device), there are other issues such as natural bias early on toward implanting in sicker patients. In addition, some centers with poor initial results may have a tendency to abandon the technology. Finally, previous experience with other devices cannot be accounted for in this study. Many of these limitations are a result of the lack of important data elements required to conduct a comprehensive study on this topic.

Admittedly, these confounding factors are significant limitations to this study. However, many are simply a result of the limited parameters available through this type of database. Moreover, the technology is relatively new and evolving with just more than 14,000 reported cases worldwide in the past two decades. However, the significant size of this dataset helps to provide some important insight into these issues. Most notably, the wide variability in annualized outcomes both in the entire dataset (**Figure 3**) and in the selected intercenter analysis (**Figure 4**) sheds important information of the potential for annualized targets.

Based on this preliminary analysis of 1,348 patients supported with a single device type and given the lack of other available literature on the volume-outcome relationship in the use of mechanical circulatory support, setting meaningful targets for volume and outcomes for individual centers may prove extremely difficult at this time. This is where community style databases such as the ISHLT Mechanical Circulatory Support Device (MCSD) database,[11–13] which includes different devices, will play a vital role because some of the confounding factors may be able to be removed in future analysis. The ISHLT MCSD database will certainly play a central role in the evolution of the mechanical circulatory support field, and, therefore, all centers should be encouraged to participate fully in this important undertaking.

Acknowledgment

This manuscript would not have been possible without the valuable contributions of all the Novacor LVAS investigators who contribute data on an ongoing basis to the Novacor LVAS Global Registry.

References

1. Luft HS, Bunker JP, Enthoven AC: Should operations be regionalized? The empirical relation between surgical volume and mortality. *N Engl J Med* 301: 1364–1369, 1979.
2. Hewitt M for the Committee on Quality of Health Care in America and the National Cancer Policy Board: *Interpreting the Volume-Outcome Relationship in the Context of Health Care Quality: Workshop Summary.* Washington, DC: Institute of Medicine, 2000.
3. Birkmeyer JD, Siewers AE, Finlayson EV, *et al:* Hospital volume and surgical mortality in the United States. *N Engl J Med* 346: 1128–1137, 2002.
4. Shahian DM, Normand SL: The volume-outcome relationship: From Luft to Leapfrog. *Ann Thorac Surg* 75: 1048–1058, 2003.
5. Epstein AM: Volume and outcome—It is time to move ahead. *N Engl J Med* 346: 1161–1164, 2002.
6. Barone JE, Risucci DA, Savino JA: Volume and outcome. *N Engl J Med* 347(correspondence): 693–696, 2002.
7. Khuri SF, Daley J, Henderson W, *et al:* Relation of surgical volume to outcome in eight common operations: Results from the VA National Surgical Quality Improvement Program. *Ann Surg* 230: 414–429, 1999.
8. Birkmeyer JD: Relation of surgical volume to outcome. *Ann Surg* 232 (correspondence): 724–725, 2000.
9. Deng MC, Young JB, Stevenson LW, *et al:* Destination mechanical circulatory support: Proposal for clinical standards. *J Heart Lung Transplant* 22: 365–369, 2003.
10. Loisance DY, Jansen PG, Wheeldon DR, Portner PM: Long-term mechanical circulatory support with the wearable Novacor left ventricular assist system. *Eur J Cardiothorac Surg* 18: 220–224, 2000.
11. Deng MC, Loebe M, El-Banayosy A, *et al:* Mechanical circulatory support for advanced heart failure: Effect of patient selection on outcome. *Circulation* 103: 231–237, 2001.
12. Kirklin JK: The importance of the mechanical circulatory support database: A plea for commitment. *J Heart Lung Transplant* 20: 803–804, 2001.
13. Deng MC: Mechanical circulatory support device database of the International Society for Heart and Lung Transplantation. *Curr Opin Cardiol* 18: 147–152, 2003.