Timing is everything—Or is it?

Carl Lewis Backer, MD

See related article on pages 205-10.

Anderson and colleagues¹ from New York Presbyterian/Morgan Stanley Children's Hospital present in this issue of the *Journal* an important and provocative article that could potentially have serious implications for the timing of stage 1 palliation in hypoplastic left heart syndrome. Their review of 134 neonates with hypoplastic left heart syndrome has led them to the conclusion that earlier stage 1 palliation is associated with better clinical outcomes and lower costs. For every day that surgery was delayed, the odds of major morbidity rose by 15.7% and the cost rose by 6.5%. The odds of mortality also increased for every day that surgery was postponed, peaking at day of life 6. This is an extremely interesting finding, because the timing of surgical intervention is a potentially modifiable variable. The cohort of patients analyzed is a very "clean" group, in that 82% of the patients had their conditions diagnosed prenatally and 72% were born at the center of Anderson and colleagues.¹ With hypoplastic left heart syndrome being the most expensive birth defect managed in the United States, finding the ideal age at operation becomes very important. If the hypothesis of Anderson and colleagues¹ is correct, practice patterns will be changing. Centers will need to develop a comprehensive institutional commitment of early stage 1 palliation in the first 3 to 5 days of life. Is timing everything? Should all patients with hypoplastic left heart syndrome undergo stage 1 palliation before day 5 of life?

Of course, other centers and groups have examined the timing of stage 1 palliation. The Society of Thoracic Surgeons Congenital Heart Surgery Database analysis included 2557 patients undergoing the Norwood operation.² Interestingly, the median age at operation was 6 days—the day at which the odds of mortality peaked in the Columbia series! In the Society of Thoracic Surgeons database analysis, prolonged preoperative stay (greater than 75th percentile) was *not* associated with postoperative complications.

From the Division of Cardiovascular-Thoracic Surgery, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, Ill; and the Department of Surgery, Northwestern University Feinberg School of Medicine, Chicago, Ill.

Disclosures: Author has nothing to disclose with regard to commercial support.

Received for publication Oct 6, 2014; accepted for publication Oct 8, 2014; available ahead of print Nov 7, 2014.

Address for reprints: Carl Lewis Backer, MD, Division of Cardiovascular-Thoracic Surgery, Ann & Robert H. Lurie Children's Hospital of Chicago, 225 E Chicago Ave, MC 22, Chicago, IL 60611 (E-mail: cbacker@luriechildrens.org).

J Thorac Cardiovasc Surg 2015;149:211-2

0022-5223/\$36.00

Copyright © 2015 by The American Association for Thoracic Surgery

<http://dx.doi.org/10.1016/j.jtcvs.2014.10.051>

The University of Michigan group analyzed the timing of stage 1 palliation for 124 patients with hypoplastic left heart syndrome.³ In their study of patients operated on between 2005 and 2010, *no association* was found between age at surgery and the primary composite end point of mortality or prolonged intensive care unit stay. There was also no association when analyzing mortality alone. The only statistically significant finding was that older age at surgery (≥ 8 days) was associated with a decreased likelihood of prolonged mechanical ventilation. No difference was found between the subgroup of patients who underwent intervention within 72 hours of birth and those who underwent surgery later. The Michigan group concluded that their data did not suggest a benefit to earlier stage 1 palliation for hypoplastic left heart syndrome.

Of even greater interest is the report from Seattle Children's Hospital.⁴ That group analyzed 105 consecutive patients undergoing stage 1 palliation between 2004 and 2011. Mortality was higher for infants operated on at younger than 7 days relative to infants operated on at older than 7 days (14% vs 3%). Median age was higher for operative survivors than nonsurvivors (12 days vs 5 days). That group concluded (and I would agree) that there may be intangible *center-specific effects*. Results from a given institution may not be generalizable to other institutions. The Seattle group recommended targeted specific internal reviews before proceeding with externally recommended changes in practice patterns.

With the increased availability of fetal diagnosis, we do have the potential to alter the timing of surgery, and that modifiable variable could have the potential to optimize the outcomes for our patients with hypoplastic left heart syndrome. On the basis of the available data, with conflicting reports from some of our finest centers, it is important for us to analyze this issue in further detail. It is possible that a more granular analysis of the Society of Thoracic Surgeons database or a prospective, randomized trial could provide the answer to this question. I thank Anderson and colleagues¹ for their provocative and potentially practice-altering article. Timing may not be everything, but it is certainly an important modifiable variable factor that should be optimized.

References

1. Anderson BR, Ciarleglio AJ, Salavitarab A, Torres A, Bacha EA. Earlier stage 1 palliation is associated with better clinical outcomes and lower costs for neonates with hypoplastic left heart syndrome. *J Thorac Cardiovasc Surg*. 2015;149:205-10.
2. Hornik CP, He X, Jacobs JP, Li JS, Jaquiss RB, Jacobs ML, et al. Complications after the Norwood operation: an analysis of the Society of Thoracic Surgeons Congenital Heart Surgery Database. *Ann Thorac Surg*. 2011;92:1734-40.

3. Kumar TK, Charpie JR, Ohye RG, Hirsch-Romano JC, Donohue JE, Yu S, et al. Timing of neonatal cardiac surgery is not associated with perioperative outcomes. *J Thorac Cardiovasc Surg*. 2014;147:1573-9.
4. Karamlou T, Sexson K, Parrish A, Welke KF, McMullan DM, Permut L, et al. One size does not fit all: the influence of age at surgery on outcomes following Norwood operation. *J Cardiothorac Surg*. 2014;9:100.