Optimal timing for stage II: Waiting for Godot

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There is a relatively narrow window for second-stage surgery in patients after a Norwood procedure. Before 6 to 8 weeks of age, a superior cavopulmonary connection has an increased risk of failure due to hypoxia, superior vena cava congestion, and pleural effusions.¹⁻⁴ Beyond 6 months of age, most neonatal shunts are outgrown and cyanosis becomes limiting. In practice, stage 2 palliation usually is carried out between 4 and 6 months of age.⁵ Nonetheless, appropriate timing within this window is a common issue and may vary from patient to patient. In this issue of the *Journal*, Barron and colleagues⁶ from Birmingham Children's Hospital examine the outcomes of stage II surgery with a particular focus on the effects of age and weight, and whether the surgery is planned (elective) or unplanned. The study includes 297 patients who underwent operation between 2002 and 2014. All patients had undergone a Norwood procedure with right ventricle–pulmonary artery shunt. Among the 297 patients, 222 (75%) underwent planned stage II surgery, and 75 (25%) underwent unplanned stage II surgery. Unplanned surgery generally occurred because of worsening desaturation or clinical deterioration.

The study's primary finding is that neither age nor absolute weight was associated with early or late mortality, although lower weight-for-age Z score was associated with worse outcome. The strongest predictors of mortality were the need for atrioventricular (AV) valve repair, AV valve insufficiency, and poor ventricular function. Unplanned surgery occurred at a younger age (median 3.0 vs 5.5 months), with higher operative mortality (5.3% vs 1.3%; not statistically significant) and worse survival at 5 and 10 years. However, unplanned surgery covaried with AV valve insufficiency and ventricular function, so that it was not significant in the multivariable model.

This article has several strengths: It comes from a group with recognized experience and expertise. It includes a large number of patients who had a uniform approach to a Norwood procedure, all with a right ventricle–pulmonary artery shunt, with 100% complete follow-up. The finding that AV valve function and ventricular function are the primary determinants of outcome at stage II surgery confirms

Weight-for-age Z score in patients undergoing the Norwood procedure (courtesy of Dr Sinai Zyblewski).

Central Message

A large study of outcomes for stage II surgery examines the roles of age, weight, weight-for-age Z score, and timing of surgery. Delaying surgery for weight gain is unlikely to be productive.

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previous publications on the topic.^{7,8} The effect of weight-for-age Z score also is in line with a previous report.⁹

Like most surgical studies, this study has the limitation of including only patients who actually underwent surgery, without accounting for those who did not make it to stage II. For patients who have undergone a Norwood procedure, this is an important limitation. In practice, a patient after a Norwood procedure is subject to the competing risks of stage II surgery or death or transplant before stage II. A decision on the appropriate timing of stage II surgery should account for the relative likelihood of each of these outcomes. It might then be possible to define an optimal age for stage II that both minimizes interstage death and maximizes post-stage II survival. This approach has recently been taken in the Congenital Heart Surgeons' Society study of optimal timing of Stage II palliation after the Norwood operation, the results of which were presented at the Society of Thoracic Surgeons annual meeting in January of this year.¹⁰

What should we take away from this article? Are there patients in whom we should wait for growth before stage II surgery? Clearly, patients requiring unplanned surgery will have surgery when their clinical condition demands. For elective surgery, the authors' findings indicate that this is a forgiving operation: Neither age nor absolute weight has much effect on outcomes. A higher weight-for-age Z score at the time of surgery is desirable; however, we know that this value does not increase appreciably over the interstage period. Interstage growth occurs, but not disproportionately to age. In my program's recent

FIGURE 1. Weight-for-age Z score in 27 patients undergoing the Norwood procedure January 2012 to December 2016. Figure courtesy of Dr Sinai Zyblewski.

experience, mean weight-for-age Z score in patients who underwent the Norwood procedure was 0.03 at birth, -1.9 at the time of Norwood hospital discharge, and -1.7 at stage II, an interstage increase of only $+0.2$ (Figure 1). For comparison, in the current study a difference in weight-for-age Z score of $+1.4$ was necessary to achieve significance in the multivariable model, and even then it remained less important than function of the AV valve and ventricle. Other studies have documented weight-for-age Z score's resistance to positive change in patients with single ventricles. A National Pediatric Cardiology Quality Improvement Collaborative study of 465 patients found that weight for age Z score was -1.5 at Norwood discharge and -1.3 at stage II, an average increase of $+0.2$.¹¹ In a more diverse group of patients with functional single ventricles, the Infant Single Ventricle Enalapril Trial found a mean decrease in weight-for-age Z score of 0.37 from baseline to stage II.¹² It seems that waiting for growth to decrease stage II operative risk will put us in the position of the 2 characters in Samuel Beckett's play *Waiting for Godot*¹³: awaiting an event that never arrives. A low weight-for-age Z score may confer some operative risk,

but in an individual patient this is unlikely to improve over time.

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