

# Happy 53rd Birthday GIK

## Insulin, Cake, and Presents

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**N**EARLY 53 yr ago, the use of glucose, insulin, and potassium (GIK) infusions were introduced into medical practice to reduce myocardial injury during a heart attack<sup>1</sup> and subsequently applied to cardiac surgery. What particular component(s) of GIK, the glucose, insulin and/or potassium, provide myocardial benefits for cardiac surgery continues to be studied and questioned. In this month's *ANESTHESIOLOGY*, Duncan *et al.*<sup>2</sup> determined that patients subjected to a hyperinsulinemic normoglycemic clamp had no outcome benefit when compared with patients undergoing standard insulin treatment for aortic valve replacement.

For the study, Duncan *et al.* used speckle-tracking echocardiography (STE) to determine that there were no differences in myocardial function between the groups (fig. 1 for more detailed explanation). As shown by the authors, STE provides valuable information including myocardial strain and strain rate. However, to apply this technique for routine clinical practice, a number of challenges need to be addressed. Currently, STE remains an offline “after-the-fact” modality in most centers. The software is not standardized between machines, and the data-sampling software used is proprietary. This continues to be an ongoing discussion among industry and echocardiography governing societies.<sup>3</sup> Furthermore, STE remains vulnerable to high signal noise, such as artifacts secondary to aortic valve calcium deposits. This perhaps explains why some of the images were discarded for interpretation in this study. Eventually, these limitations will be solved by ongoing improvements in machines, better practitioner understanding, and incorporation of STE into



***“In combination with measures considered potentially to reduce myocardial injury during cardiac surgery, ... controlling glucose may provide enough of a beneficial effect without a need to implement hyperinsulinemia.”***

intraoperative work flow to make this technique more useful within the operating room.

The hyperinsulinemic normoglycemic clamp, proposed almost 20 yr ago,<sup>4</sup> is reported in clinical studies of cardiac bypass surgery to provide beneficial effects including an improvement of cardiac index<sup>5</sup> and reduction in inflammatory markers<sup>6</sup> and lactate levels.<sup>7</sup> The Hypertrophy, Insulin, Glucose and Electrolytes (HINGE) trial, using a GIK infusion and supplemental insulin for patients undergoing aortic valve replacement, also found both biochemical and functional improvements for the GIK treatment arm.<sup>8</sup> The differences in effect seen for the treatment arm in prior studies compared with the study by Duncan *et al.* may be dependent upon the timing, dose(s), duration of treatment, and biochemical markers assessed. It is also worth considering that localization, post-translational modification, and activity of cellular proteins may be important to evaluate rather than total protein levels because protein turnover is likely limited during the treatment window. Regardless, a number of additional biochemical and functional parameters measured in this study had no significant differences between the two groups.

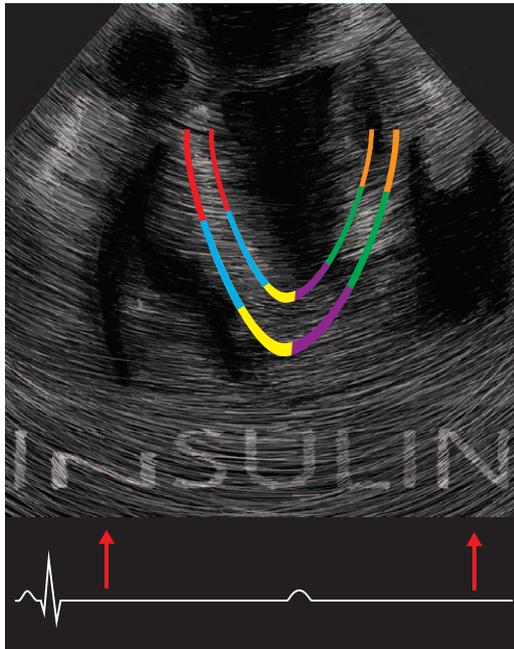
The findings of this study may imply that the benefit of insulin to minimize myocardial injury during cardiac bypass is its role in glycemic control. A strong correlation preclinically between the level of hyperglycemia and the degree of myocardial injury ( $R^2 = 0.96$ ) has been shown.<sup>9</sup> Compared with GIK treatments during cardiac surgery decades ago, anesthesiologists now are more vigilant to replete potassium and also maintain tighter glycemic control. In combination with measures considered potentially

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**Fig. 1.** Speckle-tracking echocardiography (STE). Called speckles, these are 20- to 40-pixel elements seen distributed throughout the myocardium on echo. Each speckle can be identified and followed accurately over a number of consecutive frames. STE is a semiautomated process, performed offline by applying endocardial border detection software at peak systole in the acquired images. STE involves tracking the geometric shift of each speckle and calculating strain and strain rate to represent regional wall motion (such as in an area of one of the six segments colored for the left ventricle above). In simplistic terms, looking at the letter “N” in insulin, STE is a means to measure how the “N,” or speckle, is changed in geometry from systole (*first red arrow*) to diastole (*second red arrow*) in a specific region of the myocardium. Collating the values from all the segments of the myocardium can create a diagram analogous to a conventional 17-segment model.

to reduce myocardial injury during cardiac surgery, such as cardioplegia, remote conditioning, moderate hypothermia, and administering volatile anesthetics and opioids, controlling glucose may provide enough of a beneficial effect without a need to implement hyperinsulinemia. Granted, the GIK debate and GIK iterations, including the hyperinsulinemic clamp, are far from over. Rest assured many additional GIK studies will be celebrated in the future with insulin, cake (dextrose), and presents (new techniques).

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### Competing Interests

The authors are not supported by, nor maintain any financial interest in, any commercial activity that may be associated with the topic of this article.

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