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Happy 53rd birthday GIK: insulin, cake, and presents

Sheela Pai Cole, MD¹ and Eric R. Gross, MD, PhD¹

¹Department of Anesthesiology, Perioperative and Pain Medicine, School of Medicine, Stanford University, Stanford, CA 94305

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Nearly 53 years ago, the use of glucose, insulin and potassium (GIK) infusions were introduced into medical practice to reduce myocardial injury during a heart attack¹ 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 and colleagues determined patients subjected to a hyperinsulinemic, normoglycemic clamp had no outcome benefit when compared to patients undergoing standard insulin treatment for aortic valve replacement².

For the study, Duncan and colleagues used speckle tracking echocardiography (STE) to determine there were no differences in myocardial function between the groups (Figure 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 societies³. Further, 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 intraoperative work-flow to make this technique more useful within the operating room.

The hyperinsulinemic normoglycemic clamp, proposed almost 20 years ago⁴, is reported in clinical studies of cardiac bypass surgery to provide beneficial effects including an improvement of cardiac index⁵, reduction in inflammatory markers⁶ and lactate levels⁷. The HINGE trial, using a GIK infusion and supplemental insulin for patients undergoing aortic valve replacement, also found both biochemical and functional improvement for the GIK

Correspondence: Eric R Gross, MD, PhD, Stanford University, School of Medicine, Department of Anesthesiology, Perioperative and Pain Medicine, Telephone: 650-723-7442, Fax: 650-725-5840, ergross@stanford.edu..

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treatment arm⁸. The differences in effect seen for the treatment arm in prior studies compared to the study by Duncan and colleagues 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, since 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.

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References

1. Sodi-Pallares D, Testelli MR, Fishleder BL, Bisteni A, Medrano GA, Friedland C, De Micheli A. Effects of an intravenous infusion of a potassium-glucose-insulin solution on the electrocardiographic signs of myocardial infarction. *American Journal of Cardiology*. 1962; 9:166–181. [PubMed: 13914751]
2. Duncan AE, Kashy BK, Sarwar S, Singh A, Stnina-Adognrave O, Christoffersen S, Alfirevic A, Sale S, Yang D, Thomas JD, Gillinov M, Sessler DI. Hyperinsulinemic normoglycemia does not meaningfully improve myocardial performance during cardiac surgery: a randomized trial. *Anesthesiology*. 2015; X:XXX–XXX.
3. Voigt JU, Pedrizzetti G, Lysyansky P, et al. Definitions for a common standard for 2D speckle tracking echocardiography: consensus document of the EACVI/ASE/Industry task force to standardize deformation imaging. *Journal of the American Society of Echocardiography*. 2015; 28:183–93. [PubMed: 25623220]
4. Svedjeholm R, Huljebrant I, Hakanson E, Vanhanen I. Glutame and high-dose glucose-insulin-potassium (GIK) in the treatment of severe cardiac failure after cardiac operations. *Ann Thorac Surg*. 1995; 59:S23–30. [PubMed: 7840695]
5. Sato H, Hatzakorizan R, Carvalho G, Sato T, Lattermann R, Matsukawa T, Schricker T. High dose insulin administration improves left ventricular function after coronary artery bypass graft surgery. *J Cardiothoracic and Vascular Anesthesia*. 2011:1086–1091.
6. Koskenhara JK, Paukoranta PK, Kiviluoma KT, Raatikainen MJP, Ohtonen PP, Ala-Kokko TI. Metabolic and hemodynamic effects of high-dose insulin treatment in aortic valve and coronary surgery. *Ann Thorac Surg*. 2005; 80:511–517. [PubMed: 16039195]
7. Visser L, Zuurbier CJ, Hoek FJ, Opmeer BC, de Jonge E, de Mol AJM, van Wezel HB. Glucose, insulin and potassium applied as perioperative hyperinsulinaemic normoglycaemic clamp: effects on inflammatory response during coronary artery surgery. *British Journal of Anesthesia*. 2005; 95:448–457.
8. Howell NJ, Ashrafian H, Drury NE, et al. Glucose-insulin-potassium reduces the incidence of low cardiac output episodes after aortic valve replacement for aortic stenosis in patients with left ventricular hypertrophy. *Circulation*. 2011; 123:170–177. [PubMed: 21200004]
9. Kersten JR, Toller WG, Gross ER, Pagel PS, Warltier DC. Diabetes abolishes ischemic preconditioning: role of glucose, insulin and osmolality. *Am J Physiol Heart Circ Physiol*. 2000; 278:H218–224.

“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..”

Image: J.P. Rathmell

Speckle tracking echocardiography

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 semi-automated 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.