# GOOD NEWS FOR WAITING – BUT ONLY IF YOU KEEP WATCHING AND KNOW WHAT TO LOOK FOR

Lynda E. Rosenfeld, MD[1]

[1]Section of Cardiovascular Medicine, Yale University School of Medicine

**Short Title:** Ejection Fraction post coronary revascularization

**Word Count:** 1201

**Address for correspondence:**

Lynda E. Rosenfeld, MD

Section of Cardiovascular Medicine

Yale University School of Medicine

Dana 3, 789 Howard Avenue

New Haven, CT 06510

Phone: 203-737-4068

Email: lynda.rosenfeld@yale.edu

**Funding sources:** None

**Disclosures:** None relevant

**Keywords:** Implantable cardioverter-defibrillator, coronary artery bypass graft surgery, ejection fraction

**Abbreviations:**

CABG = Coronary artery bypass graft surgery

CMR = Cardiac magnetic resonance imaging

EF = Left ventricular ejection fraction

ICD = Implantable cardioverter-defibrillator

SCD = Sudden cardiac death

STICH = Surgical Treatment for Ischemic Heart Failure

Current guidelines[1] recommend delaying implantation of a primary prevention defibrillator (ICD) in patients with a preoperative left ventricular ejection fraction (EF) of ≤ 35% until at least 90 days after interventional or surgical revascularization both because competing risks may reduce the overall benefit of early device placement and there may be myocardial recovery during this period resulting in an EF >35%, the current cut off for such devices.

In this issue of the *Journal of Cardiovascular Electrophysiology*, Adabag, et al.,[2] utilizing data from the STICH (Surgical Treatment for Ischemic Heart Failure) trial, expand on their previous studies characterizing the potential for improvement of myocardial function after surgical coronary revascularization (CABG). The STICH trial[3], which, importantly, was reported in 2011, was meant to compare the use of then current guideline directed medical therapy alone with medical plus surgical therapy (either CABG alone or CABG and surgical ventricular reconstruction) in patients with coronary artery disease, heart failure and a reduced ejection fraction. The present report is limited to the 427 STICH patients, largely white and male, with a preoperative EF ≤ 35%, who underwent surgery (either CABG or CABG and surgical ventricular reconstruction) and had a technically good or excellent assessment of their EF both pre and 4 months post operatively using the same imaging modality (echo, cardiac magnetic resonance imaging (CMR) or radionuclide ventriculogram). The authors found that nearly 30% of patients had a significant postoperative improvement in EF defined as an EF > 35% and an absolute increase from baseline of > 5%. In almost 20% the EF improved to > 40%, but in only a very small number, 2.3%, was there complete normalization of the EF to > 55%. These changes were similar both in those having CABG alone or CABG plus surgical ventricular reconstruction. Significant improvement was, however, 2.2 times more likely (95% CI 1.41-3.43, p=0.0006) in patients with a

preoperative EF $\geq$ 25% than in those with a lower EF. A full 37.8% of patients with a preoperative EF of 30-35% had significant improvement while only 20.3% of those with an EF < 25% had similar benefit

These findings, while more robust, in that they are based on a larger number of patients in a randomized study, are not inconsistent with previous studies, dating back as far as the 1990s[4,5,6] which have shown a meaningful postoperative increase in EF in from 24 to 51% of patients. In none of these studies, including the present one, did patients have the benefit of current optimal guideline directed medical therapy including angiotensin-neprilysin inhibitors or sodium-glucose co-transporter 2 inhibitors which might be expected to further increase the number of patients having a "meaningful" improvement in EF - described by the authors as "obviating" the need for a guideline directed ICD. Thus, to optimally integrate these findings into our current management we still need more contemporary data on competing survival risks early post CABG, EF recovery, and a better understanding of the meaning of an improved, but less than normal EF with regard to sudden cardiac death (SCD).

Unfortunately, although the STICH trial was initially designed to include a preoperative assessment of myocardial viability, only 40% of the patients in the current analysis had such a study, limiting any conclusions about the utility of such testing in predicting postoperative improvement in myocardial function or SCD prognosis, though the identification of viable myocardium tended to be associated with a greater likelihood of myocardial recovery (33.9% vs 20.8% p=0.08).

In addition, it is well documented that SCD, though less common, does continue to occur in patients who have had recovery of their EF to > 35%[7,8,9]. In the present study, while EF improvement was associated with a 43% lower risk of all cause mortality when other variables were controlled for (hazard ratio 0.57, 95% CI 0.34-0.94; p=0.03), SCD risk was not significantly reduced (hazard ratio 0.83, 95% CI 0.35-1.94; p=0.66) though the numbers were small.

Thus, while validating previous studies and providing us with optimism with regard to the utility of CABG in improving myocardial function and overall survival in patients with significant left ventricular dysfunction and coronary artery disease, Adabag, et al's study leaves us with 3 unsettling and still unsettled issues:

1. What is the optimal way to identify which patients are most likely to have an improvement in EF post CABG? While preoperative EF may be a useful prognostic indicator, more data from studies examining viability and, perhaps more importantly, the presence of scar with contemporary imaging modalities are needed.
2. How do we recognize those patients who remain at heightened risk for SCD, even with a significant improvement in their EF, and who among those would most benefit from an ICD? We have struggled with this question for some time but if, as shown in the present study, improvement in EF results in improved overall survival not due just to a reduction in SCD, rather than "obviating" the need for an ICD, placing such a device may have added net benefit in some patients.

Hopefully newer imaging modalities and perhaps CMR and the identification of late gadolinium enhancement[10] may help provide an answer to both of these questions.

3. Lastly, and very importantly, although almost 30% of the patients in the current study had an improvement in their post operative EF to > 35%, 70% did not and almost 80% of those with a pre operative EF < 25% continued to have current indications for a primary prevention ICD. Historically, guideline directed primary prevention ICDs have been significantly underutilized[11,12] and in many studies less than 20% of patients eligible for these devices actually receive them. The active follow up necessary to improve this outcome is very challenging – especially if we are waiting 3-4 months after surgery, when patients often are feeling better and want to get on with

their lives – to make a decision to go ahead with an ICD. There are multiple points at which the chain of events needed to ensure appropriate device implantation can be broken: Patients need initiation and titration of optimal guideline directed medical therapy, a follow up postoperative measure of EF must be scheduled, completed, and reviewed. Appropriate patients must then be scheduled for evaluation by an electrophysiologist, that appointment must be kept, and after discussion with and education of the patient a decision must be made to whether to place an ICD and that procedure, if indicated, must be carried out.

In sum, the study of Adabag, et al., provides us with important and heartening information that our present practice to wait 90 days after CABG to place a primary prevention ICD in a patient with a reduced preoperative EF and heart failure is reasonable. It also challenges us to use contemporary techniques to better define ways to predict EF improvement post CABG, and to continue to work on refining the answer to the question of who will benefit most from a primary prevention ICD. Perhaps most importantly, it demands that we recognize that these findings create a complicated care path for both physicians and patients to adhere to and necessitates that we take the extra steps to “keep an eye on our patients” and see that this process is carried through to completion.

**References:**


1. Al-Khatib SM, Stevenson WG, Ackerman WG, Bryant MJ, Callans DJ, Curtis AB, Deal BJ, Dickfeld T, Field ME, Fonarow GC, Gillis AM, Granger CB, Hammill SC, Hlatky MA, Joglar JA, Kay GN, Matlock DD, Myerburg RJ, Page RL. 2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death. Circulation 2018;138:e272-e391.
2. Adabag S, Carlson S, Gravely A, Buelt-Gebhardt M, Madjid M, Naksuk N. Improvement of Left Ventricular Function with Surgical Revascularization in Patients Eligible for Implantable Cardioverter Defibrillator. J Cardiovasc Electrophys….
3. Velazquez EJ, Lee KL, Deja MA, Jain A, Sopko G, Marchenko A, Ali IS, Pohost G, Gradinac S, Abraham WT, Yii M, Prabhakaran D, Szwed H, Ferrazzi P, Petrie MC, O'Connor CM, Panchavinnin P, She L, Bonow RO, Rankin GR, Jones RH, Rouleau J-L, STICH Investigators. Coronary-artery bypass surgery in patients with left ventricular dysfunction. N Engl J Med 2011;364:1607-1616.
4. Elefteriades JA, Tolis G, Jr, Levi E, Mills LK, Zaret BL. Coronary Artery Bypass Grafting in Severe Left Ventricular Dysfunction: Excellent Survival With Improved Ejection Fraction and Functional State. J Am Coll Cardiol 1993;22:1411-1417.
5. Vakil K, Florea V, Koene R, Kealhofer JV, Anand I, Adabag S. Effect of Coronary Artery Bypass Grafting on Left Ventricular Ejection Fraction in Men Eligible for Implantable Cardioverter-Defibrillator. Am J Cardiol 2016;117:957-960.
6. Koene RJ, Kealhofer JV, Adabag S, Vakil K, Florea VG. Effect of coronary artery bypass graft surgery on left ventricular systolic function. J Thorac Dis 2017;9:262-270.
7. Naksuk N, Saab A, Li J-M, Florea V, Akkaya M, Anand IS, Benditt DG, Adabag S. Incidence of Appropriate Shock in Implantable Cardioverter-Defibrillator Patients with Improved Ejection Fraction. J Cardiac Fail 2013;19:426-430.

8. Zhang Y, Guallar E, Blasco-Colmenares E, Butcher B, Norgard S,Nauffal V, Marine JE, Eldadah Z, Dickfeld T, Ellenbogen KA, Tomaselli GF, Cheng A. Changes in Follow-Up Left Ventricular Ejection Fraction Associated with Outcomes in Primary Prevention Implantable Cardioverter-Defibrillator and Cardiac Resynchronization Therapy Device Recipients. J Am Coll Cardiol 2015;66:524-531.
9. Adabag S, Patton KK, Buxton AE, Rector TS, Ensrud KE, Vakil K, Levy WC, Poole JE. Association of Implantable Cardioverter Defibrillators With Survival in Patients With and Without Improved Ejection Fraction. JAMA Cardiol 2017;2:767-774.
10. Disertori M, Rigoni M, Pace N, Casolo G, Mase M, Gonzini L, Lucci D, Nollo G, Ravelli F. Myocardial Fibrosis Assessment by LGE Is a Powerful Predictor of Ventricular Tachyarrhythmias in Ischemic and Nonischemic LV Dysfunction. J Am Coll Cardiol Img 2016;9:1046-1055.
11. Narayanan K, Reinier K, Uy-Evanado A, Teodorescu C, Chugh H, Marijon E, Gunson K, Jui J, Chugh SS. Frequency and Determinants of Implantable Cardioverter Defibrillator Deployment Among Primary Prevention Candidates With Subsequent Sudden Cardiac Arrest in the Community. Circulation 2013;128:1733-1738.
12. Cho Y, Cho S-Y, Oh I-Y, Lee JH, Park JJ, Lee H-Y, Kim KH, Yoo B-S, Kang S-M, Baek SH, Jeon E-S, Kim J-J, Cho M-C, Shae SC, Oh B-H, Choi D-J. Implantable Cardioverter-defibrillator Utilization and Its Outcomes in Korea: Data from Korean Acute Heart Failure Registry. J Korean Med Sci. 2020;35:e397.