The SCA has accomplished so much over the last 35 years because of many who deserve credit. I would like to acknowledge all those who contributed their time and energy. I especially wish to thank the hard work of the committee members, past officers and members from the Board of Directors over the years who have worked so hard to bring our society to the place where it is now. I humbly ask that all in the society including my new executive team (Steve Konstadt, Scott Reeves and Linda Shore-Lesserson), the new incoming Board members (Michael Eaton, Jerry Levy, David Mazer) and sitting Board members (George Burgess, Albert Cheung, Kathy Glas, Glenn Gravlee, Colleen Koch, Marty London, Bob Marino, Rob Sladen, Peter Slinger, and Chris Troianos) continue to provide support in the years to come. As we enter an era of certain change for our profession, there is much to do. Together I am confident we will meet these challenges and turn opportunities to realities. It is with that spirit and confidence that I propose what you should expect from your society.

1. To be more attentive to membership needs. This is your society and the officers, Board of Directors, committees, task forces, working groups and administrative office work for you. The SCA will conduct a survey in the months ahead to better understand what your needs and expectations are and we will commit to prioritizing our actions to serving those needs.

2. To diligently continue to work toward developing state-of-the-art educational programs of value for the Cardiac, Thoracic and Vascular perioperative care team. An interactive website will facilitate our goal of outreach and enable us to build creative electronic educational opportunities including CME activities, dynamic education, reference and guideline library, video streaming, social media networking, Wiki links and blogging capabilities to enhance dynamic discussion and sharing of interesting cases. We will soon launch this new face of the SCA in the weeks to come. We will also build on our successes in leading standards for TEE education and provide interactive case presentation through the electronic platform. The SCA has recently teamed up with Heartweb, which will deliver on behalf of the SCA, comprehensive, self-directed professional development programs in echocardiography and clinical ultrasound. These programs will be the first On-line Clinical Ultrasound and Echocardiography Courses provided to its members by the SCA and will be called “SCA On-CUE”. These are based on the highly successful University of Melbourne distance education courses. We are very excited about this opportunity for our members, as this collaboration ushers in the ability for us to deliver high-quality and comprehensive echo knowledge which can be studied in your own time and location. The programs are divided into two levels, with Level I providing knowledge base to be a good basic sonographer with a TTE and surface ultrasound focus, and Level II follows on to provide additional knowledge for advanced diagnostic echocardiography including TEE. These programs will facilitate uptake of echocardiography to the wider Anesthesiology, Intensive Care and Emergency Medicine practitioners, as well as provide a comprehensive and consistent knowledge base to advanced practitioners such as Cardiovascular Anesthesiologists. These programs will complement our SCA conferences, workshops, and update meetings. While we are in the process of updating our respective websites, please go to www.heartweb.com or email colin.roys@heartweb.com for further information. Finally, our footprint in interdisciplinary education venues will be expanded. Programs such as our CPB course and team training will push ahead to develop even more interesting and valuable programs for our membership. I have asked a group led by Stan Sherman to explore opportunities that include working with other societies toward developing co-share web base, electronic and other novel education products.

3. To continue to focus on FOCUS. Through our close ties with the SCA Foundation (SCAF) focusing on patient safety has been clearly articulated by our investment and collective actions. It is important to our mission alignment and essential to further our role as a leader and standard bearer in CV anesthesia. The benchmark question, “Is this patient safe to anesthetize for this procedure, with this provider, at this time?” will be asked and answered with SCA and SCAF supported research. For those of you that have contributed to the SCAF, I say “good for you” and “thank you”. For those who have not yet contributed, I simply ask that you please consider the great things that could be done with your support. Paul O’Neill, our keynote speaker at the annual meeting in Savannah, spoke of “habitual excellence” and “theoretic limitations”. These concepts inspire further the SCA to lead our specialty in paving the way as the standard bearer in CV anesthesia. The benchmark question, “Is this patient safe to anesthetize for this procedure, with this provider, at this time?” will be asked and answered with SCA and SCAF supported research. For those of you that have contributed to the SCAF, I say “good for you” and “thank you”. For those who have not yet contributed, I simply ask that you please consider the great things that could be done with your support. Paul O’Neill, our keynote speaker at the annual meeting in Savannah, spoke of “habitual excellence” and “theoretic limitations”. These concepts inspire further the SCA to lead our specialty in paving the way as the standard bearer in CV anesthesia.
4. To continue to represent a standard of care for CV anesthesia that is both looked up to and sought. We will be the leaders for CV perioperative education to all who practice clinical anesthesia and will assume that responsibility as essential to our mission with great humility. We will work with the ASA committee on cardiac anesthesia to better understand the needs of the general anesthesiologist who provides anesthesia for the CV patient undergoing cardiac surgery. There is an important role for our society to educate and welcome all providers of CV anesthesia. We should embrace that role. We must continue to be proactive in being viewed as the standard for patient advocacy whenever and wherever cardiothoracic and vascular anesthesia is provided.

5. To commit to developing the next generation of leaders. Our society possesses the talent and expertise to develop forward thinking and we will actively seek out individuals who are interested in getting involved and build on the mission of the SCA for committee and leadership positions. Each committee chair will be asked to grow their committees and seek new members in the society to get involved. We are a volunteer organization and people who want to help are always welcomed. If you want to get involved in the society, the committee level is a great place to start. Please email the SCA office and let us know what your strengths are and how we can help you do what you want to do. Go to SCA's website for a list of committees in which you may wish to become involved.

6. To continue to strengthen relationships with other societies representing members of the global cardiovascular perioperative care team. For over the last decade, the SCA has had a strong, valuable, important and rewarding relationship with the Canadian Anesthesiologists Society, Cardiovascular Thoracic Section. This year we have broadened our global outreach and engaged the European Association of Cardiothoracic Anaesthesiologists (EACTA) community with a shared invitation to sit at each other’s boards. In the months ahead I will ask that we continue to explore opportunities with our colleges in Asia and Latin America. The growth in knowledge and need for education in cardiovascular and thoracic care is well beyond North America and the SCA should continue to represents the standard for patient advocacy in the world. We will also build on and strengthen our relationships and collaborations with the American Heart Association (AHA), Society of Thoracic Surgeons (STS), American Society of Anesthesiologists (ASA), International Anesthesia & Research Society (IARS) and SCAF.

7. To continue to pursue a path toward Cardiovascular Anesthesia Fellowship Certification. A special task force led by Dr. Mark Stafford-Smith will be asked to explore opportunities and challenges that lie ahead.

8. To recognize that public perception and understanding of the SCA is important. The SCA needs to communicate a more clear understanding of who we are and what we do within the cardiovascular and thoracic care specialty. We will explore current perceptions and define potential gaps from patient’s and our colleagues in cardiology and cardiovascular surgery to better understand what would be useful in assuring all are more savvy consumers of anesthesia services.

9. To be committed to the DATABASE project because it is important and will allow us to assume a leadership role in understanding best practice and provide a valuable resource that we should utilize to advance patient care and the practice of cardiovascular anesthesia. We have been working with the STS on formulating an agreement to incorporate adult CV anesthesia data fields into the existing STS database. These discussions will continue and be communicated to our society in the months ahead. In addition, the data fields themselves will be further refined by a working group led by Dr. Joseph Mathew which includes John Ellis, Marty London, Manny Fontes, David Reich, Nancy Nussmeier, Jake Abernathy and Stan Shernan.

10. To advocate that we be proud and identify who we are. Disclosing who we are to our patients is reasonable. Patients should know and have a right to know the credentials of the person who is taking care of them.

We are members of the SCA — we are Cardiovascular Anesthesiology. I looked forward to working for you in the years ahead.
The role of 3D TEE in perioperative diagnosis and decision-making

PRO

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Live or real-time three-dimensional (3D) transesophageal echocardiography (TEE) is now possible due to significant advances in TEE technology. A real-time 3D fully-sampled matrix array TEE (RT3D-MTEE) transducer is capable of three different 3D acquisition modes, allowing for flexibility in mode selection. Initial experiences with RT3D-MTEE show its usefulness and ability to augment conventional two-dimensional (2D) TEE. Evidence to support the role of RT3D-MTEE in clinical diagnosis and decision-making is quickly growing.

In addition to a 2D mode, a RT3D-MTEE transducer has three 3D acquisition modes: live 3D, 3D zoom, and full-volume. The live 3D mode portrays a small pyramidal segment in real time. The 3D zoom mode is also a live 3D mode, but the echocardiographer is able to define the location and size of the pyramidal segment. The ability to show a larger pyramidal segment is at the expense of frame rate. Both live 3D and 3D zoom modes do not require ECG gating. The full-volume mode acquires the largest 3D image, which is acquired over consecutive heart beats, thus requiring ECG-gating. The 3D mode selected depends on the structure being imaged. The ability to quickly transition between the 2D mode and the three 3D modes allows the echocardiographer to complete a comprehensive 2D exam with 3D images in a timely fashion.

TEE is invaluable in examination of the mitral valve (MV). The MV, including leaflet scallops, complex annulus, and sub-valvar structures, are well-visualized by RT3D-MTEE. Showing the MV with depth helps to define and localize MV lesions. Evidence suggests that RT3D-MTEE is superior to 2D TEE in evaluating individual MV segments and ruptured chordae. RT3D-MTEE images with color Doppler also provides more information about the mechanism and severity of MR. Recent literature includes data on the assessment of MR by the PISA and vena contracta methods using RT3D-MTEE. In addition to displaying the MV in detail, RT3D-MTEE also displays the MV with respect to surrounding structures, such as the left ventricular outflow tract. This ability to display the MV’s relationship to other structures in real-time may provide insight into the potential for SAM after MV repair. The additional information from RT3D-MTEE thus has the potential to help surgical decision-making regarding MV repair vs. replacement as well as to guide the surgical management of repair.

CON

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The availability of a matrix transesophageal echocardiography (TEE) probe capable of real-time three-dimensional TEE (RT3D TEE), there has added another dimension to the intraoperative echocardiographic examination, literally and figuratively. Currently the 3D technology is available as either rotational R-wave gated acquisition or as the ‘live’ 3D image acquired with matrix X7-2t TEE probe (Philips Medical Systems Andover MA). The traditional rotational image acquisition has been available for quite sometime for clinical use and has been extensively used for geometric analyses of intra-cardiac valves. Whereas the rotational 3D imaging technology is manufacturer non-specific, the matrix 3D TEE probes are currently produced by a single vendor. The unique nature of the 3D technology and commercial hype associated with its launch has also led to some unrealistic perceptions and expectations. For example, somehow this impression has been created that all imaging with the X7-2t probe is ‘live’. While this is only partly true because essentially all clinically meaningful 3D imaging with the X7-2t probe is based on R-wave gated reconstruction (as will be discussed later). While the RT3D TEE has certainly improved our visualization and assessment of mitral valve, the visualization of the rest of the cardiac structures is less than optimal.

The matrix array fully sampled transducer is a quantum leap ahead of the traditional sparsely sampled phased array transducer. However, the matrix nature of the transducer results in an introduction of an ‘elevational dimension’ to the existing two-dimensional (2D) scan plane. Therefore, currently the matrix 3D beam is merely a composite of multiple 2D scan planes and hence suffers from the same limitations and shortcomings. Therefore the quality of 3D images is based entirely on the quality of the 2D images i.e. perfect 3D images are obtained generally from patients with perfect 2D images. Hence, the 3D technology as it is currently available, is not a substitute for suboptimal image quality. Also after image acquisition and prior to the rendered image display the data goes through significant interpolation and smoothing, i.e., introduction of surfaces and contours based on gray scale of surrounding structures.

The 3D image acquisition leads to the projection of the volumetrically acquired 2D ultrasound data resulting in the creation of a ‘perception of
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In addition to evaluation of native valves, RT3D-MTEE is useful for the evaluation of prosthetic valves. The ability of RT3D-MTEE to show the entire MV en face with and without color Doppler provides information about ring dehiscence and paravalvular leaks. This is useful for planning and guiding the appropriate intervention, whether it is surgical or percutaneous.

The interatrial septum and left atrial appendage are also well-visualized by RT3D-MTEE. TEE has an integral role in percutaneous patent foramen ovale and atrial septal defect closures. Important parts of the exam include determining the number of defects, the size and shape of the defects, and the morphology of the surrounding tissue. RT3D-MTEE provides additional information by showing the atrial septal defect en face, thus being able to more accurately determine diameters and distance between defects or surrounding structures. The ability to visualize and measure the left atrial appendage in RT3D-TEE is useful in guiding occlusion devices as well as differentiating between thrombus and pectinate muscles.

Determining left ventricular size and function is part of the comprehensive 2D TEE exam. It has been demonstrated that RT3D echocardiography examination of left ventricular volumes is comparable to those obtained with cardiac MRI, CT, and radionuclide studies. The use of RT3D-MTEE to evaluate left ventricular size eliminates calculations based on geometric modeling and avoids the use of foreshortened and oblique imaging planes. Regional assessment of RT3D-MTEE images of the left ventricle may also prove to be useful in guiding resynchronization therapy and surgical correction of left ventricular aneurysms.

The use of RT3D-MTEE in surgical and procedural planning is evolving. The ability to acquire 3D data sets in addition to RT3D images allows the imaging physician to be more involved in both the planning and execution of various procedures. Emerging techniques for percutaneous repair of patent foramen ovale, atrial septal defects, mitral valves, and aortic valves will continue to benefit from RT3D-MTEE. The role of RT3D-MTEE will also grow with further improvements in spatial and temporal resolution.

Con, continued from page 3

depth’ on a flat screen, i.e. there is no actual depth in the image. This is the source of the ‘parallax error’ i.e. inaccurate linear measures on a projected 3D image due to inability to generate perfectly parallel images. Therefore, when making linear measures on 3D data sets, the operator has to resort to the 2D images within the volumetric data for accuracy. Similarly, 3D image acquisition is associated with significant compromise in the frame rate leading to deterioration in the temporal resolution. Whereas, R-wave gated volumetric acquisition can improve the frame rate but it is significantly less than achieved during conventional 2D imaging. Similarly, incorporation of color-flow Doppler also leads to significant deterioration in image quality and frame rate making the image suboptimal. Furthermore, the size of the color sector cannot be changed, and the operator has to make adjustment in line density to increase the size of the region of interest to locate the regurgitant jets with a significant trade off in spatial resolution.

When ‘live’ imaging mode is used, a pyramidal shaped beam called the ‘frustum’ is emitted from the transducer. The width of the frustum is so narrow in this mode that it does not encompass any cardiac structure in totality e.g. both commissures of the mitral valve cannot be seen simultaneously. To overcome this, the ‘live zoom’ mode can be used, but this is again associated with a significant reduction in frame rate. To overcome reduction in frame rate and image quality, R-wave gated volumetric imaging can be performed. However, the R-wave gating depends upon the patient being in a stable rhythm, lack of motion and electrical interference during acquisition to achieve an optimal spatial and temporal synchronization of the echocardiographic frames. Patient or probe motion and cautery use can lead to spatial mis-alignment, i.e. the ‘stitch artifact’, or temporal mis-alignment when the heart rate is irregular, i.e. the systolic frames get aligned with the diastolic frames.

Utilization of RT3D TEE has certainly improved mitral valve imaging. However, the accuracy of identification of prolapsed scallops and localization of regurgitant mitral regurgitant is more than 90% by experienced echocardiographers when using 2D TEE. Therefore the incremental benefit of RT3D TEE over conventional 2D imaging is not so significant. There are some reports of measuring dimensions of atrial septal defects, left atrial appendage, vena contracta and proximal isovelocity surface area with RT3D echocardiography. These are however, preliminary reports and lack large scale validation studies. Also, to make accurate linear measures, perfectly orthogonal multi-planar reformatted 2D slices have to be dissected out of the volumetric data sets, i.e. linear measures are made on 2D images. Therefore, the real advantage of 3D imaging may lie in its ability to provide perfect 2D images.

There is also significant deterioration of image quality in the ‘far field’ of the scan plane during RT3D echocardiography. Hence, it is very difficult to visualize the aortic and tricuspid valves and the left and right ventricular apices. Due to deterioration in image quality, it is difficult to differentiate an actual tissue defect from an image dropout. The volumetric nature of left and right ventricular imaging is often quoted as a major advantage of 3D imaging, but this assumption is based on data acquired from computerized tomography (CT) and magnetic resonance imaging (MRI). There are no studies validating RT3D echo data on ventricular volumes by demonstrating a favorable correlation with similar volumetric data acquired from CT and MRI. Our ability to perform geometric analyses of the mitral valve on 3D data sets is also based on identification of anatomical landmarks on 2D frames and then projecting them on to the rendered 3D image.

In summary, acquisition of 3D echocardiography equipment and expertise in its performance and interpretation is associated with a significant cost and learning curve. Whether it is worth the additional cost and makes any difference in outcome remains to be seen. The available technology is produced by a single vendor. It was formally introduced in 2008, and in the last three years, it has progressed little beyond providing en-face of the mitral valve and anecdotals reports of its clinical utility. Lack of competition in the form of another alternative system in the market may be responsible for the slow progress. The volumetric nature of the echocardiographic data provides with unlimited opportunities to analyze the heart on engineering principles and to move beyond mere visualization. By using this technology to only generate ‘pretty pictures’, we may be selling this technology short. To overcome the aforementioned limitations of the 3D technology, the computational power of the equipment has to be significantly increased to overcome the reductions in frame rate and beam width and simultaneously decreasing patient exposure to ultrasound. Also an ideal 3D system would incorporate the flow information within the volumetric data, thus providing real-time Doppler information for accurate calculation of stroke volume and volume to regurgitant jets and quantification of stenosis.
Simultaneous Hybrid Revascularization Versus Off-Pump Coronary Artery Bypass for Multivessel Coronary Artery Disease


Reviewers: Sean Kiley, MD and Yong G. Peng, MD, PhD
University of Florida, Gainesville, FL

Background

The authors of this study sought to compare a simultaneous hybrid coronary revascularization procedure to conventional off-pump coronary bypass (OPCAB). They did this by recording early and midterm clinical outcomes of patients who had the hybrid procedure and comparing these values with those in a propensity-matched subset of patients that underwent OPCAB.

Methods

One hundred and four consecutive patients (mean age 61.8+/−10.2 years) with multivessel coronary artery disease underwent elective simultaneous coronary revascularization at Fuwai Hospital. Using propensity score methodology, these patients were matched with 104 patients who had undergone off-pump coronary artery bypass grafting through median sternotomy during the same period. These groups were compared by in-hospital clinical outcomes and freedom from major adverse cardiac or cerebrovascular events at a mean follow-up of 18+/−7.9 months.

Results

The hybrid procedure required longer operative time and incurred higher in-hospital costs, but had shorter median intubation time (11.6+/− 6.3 vs 13.8+/− 6.8 hours, p=0.02), intensive care unit length of stay (34.5+/−35.6 vs 55.3+/−46.4 hours, p < 0.001), and postoperative in-hospital length of stay (8.2+/− 2.6 vs 9.5+/− 4.5 days, p=0.01). The hybrid group had significantly less chest tube drainage (789 +/-389 vs 834+/− 285 mL, p = 0.005) and need for blood transfusion (28.8% vs 51.9%, p > 0.001). At a mean follow-up of 18 months, freedom from major adverse cardiac or cerebrovascular events favored the hybrid group (99.0% vs 90.4%; p= 0.03).

Conclusions

Compared with conventional off-pump coronary artery bypass grafting, simultaneous hybrid coronary revascularization shortens recovery time and has superior outcomes at a mean follow-up of 18 months. Simultaneous hybrid coronary revascularization provides a safe and reproducible alternative for selected patients with multivessel coronary artery diseases.

Comments

Utilizing multivariate logistic regression propensity scoring analysis, the authors of this study performed a retrospective cohort study comparing the outcomes of two separate coronary revascularization approaches: 1. Conventional off-pump coronary artery bypass grafting (OPCABG) and 2. hybrid coronary revascularization. There were 104 consecutive patients matched to an equal number of patients from a pool of 967 patients that had undergone OPCAB during the same time period. Although the authors went to great effort to match revascularized anatomy and comorbidities, it was made evident that patients undergoing the hybrid procedure were specifically chosen due to perceived favorable anatomy for the procedure and subjects’ selection bias may be inevitable. Despite the limited sample size, the authors concluded that the hybrid procedure, at minimum, is a safe and reproducible alternative for coronary revascularization. The authors further claim the hybrid operation to be superior using in-hospital resources with good midterm outcomes. The midterm follow up results, like neurological events and readmission rates were compelling, however the results from the hybrid group did not translate to increased survival. The single death reported in the OPCAB group was caused from cancer.

Overall, the results of this study suggest that there may be promise in the described hybrid procedure. At this time, there is a limitation of resources, or may be even the high cost, which will prevent most institutions from taking advantage of this novel technique. The procedure requires an operating suite that has to be equipped with angiography capability as well as a support for cardiopulmonary bypass if needed. Although the study demonstrated decreases in utilizing hospital resources during the immediate postoperative period, overall cost and OR time were increased in this procedure. Considering the modern trend of minimally invasive procedures for high risk patient populations, the hybrid operation would seem likely to garner appeal in the future clinical practice. There is clear need for prospective randomized trials to provide long-term follow up data to justify the superiority of this innovation.

Radial artery grafts vs. saphenous vein grafts in coronary artery bypass surgery: A randomized trial


Reviewer: Hong Liu, MD
UC Davis Health System, Sacramento, CA

Background and Objective

Arterial grafts are thought to be better conduits than saphenous vein grafts for coronary artery bypass grafting (CABG) based on experience with using the left internal mammary artery to bypass the left anterior descending coronary artery. The efficacy of the radial artery graft is less clear. This study is to compare 1-year angiographic patency of radial artery grafts vs. saphenous vein grafts in patients undergoing elective CABG.

Methods

A multicenter, randomized controlled trial was conducted from February 2003 to February 2009 at 11 Veterans Affairs medical centers among 757 participants (99% men) undergoing first-time elective CABG. The left internal mammary artery was used to preferentially graft the left anterior descending coronary artery whenever possible; the best remaining recipient vessel was randomized to radial artery vs. saphenous vein graft. The primary end point was angiographic graft patency at 1 year after CABG. Secondary end points included angiographic graft patency at 1 week after CABG, myocardial infarction, stroke, repeat revascularization, and death.

Results

Analysis included 733 patients (366 in the radial artery group, 367 in the saphenous vein group). There was no significant difference in study graft patency at 1 year after CABG (radial artery, 238/266; 89%; 95% confidence interval [CI], 86%-93%; saphenous vein, 239/269; 89%; 95% CI, 85%-93%;
adjusted OR, 0.99; 95% CI, 0.56-1.74; P = .98). There were no significant differences in the secondary end points.

Conclusion
Among Veterans Affairs patients undergoing first-time elective CABG, the use of a radial artery graft compared with saphenous vein graft did not result in greater 1-year patency.

Comments
CABG is one of the most common operations performed in the U.S. There were 163,048 patients who had CABG surgery in 2008. The success of CABG depends on the long-term patency of the arterial and venous grafts. About 6% of patients undergoing CABG have radial artery grafts. In this study, the authors demonstrated that there was no difference in angiographic patency between radial artery grafts and saphenous vein grafts in men one year after surgery compared to the RAPS study which demonstrated an improved 1-year patency of radial artery grafts compared with saphenous vein grafts (92% vs. 86%). Although most clinicians assume that arterial grafts have a better patency rate than vein grafts, this study showed that there was more disease in the radial artery grafts at 1 week and at 1 year despite the similar patency rates. Another interesting finding in this study is a lower vein graft patency when endoscopic harvesting was used which is also against common wisdom. This study also showed no significant difference with on-pump vs. off-pump surgery for radial artery graft patency. However, it showed a higher vein graft patency on-pump consistent with the results from other studies. These findings could be the result of a higher percentage of diabetics. Patients with diabetes are prone to the development of atherosclerosis and calcification in their grafted arteries. Since this is just a one-year follow-up, longer follow-up will be necessary to determine whether radial artery grafts are truly of benefit in diabetic patients.

**Standard vs. High-Dose Clopidogrel Based on Platelet Function Testing After Percutaneous Coronary Intervention: The GRAVITAS Randomized Trial**


**Reviewer: Mojca Remskar Konia, MD**

*University of Minnesota, Minneapolis, MN*

**Abstract Excerpt**

The study by Price and co-authors is a multicenter, randomized, double-blind, active-control trial performed in 83 centers in the United States and Canada. Inclusion criteria consisted of patients after PCI with 1 or more drug-eluting stents for the treatment of stable coronary artery disease or non-ST elevation acute coronary syndrome. Major exclusion criteria included use of periprocedural glycoprotein IIb/IIIa inhibitors, planned future use of oral anticoagulants and bleeding prior to platelet function testing.

Study screened 5429 patients with VerifyNow P2Y12 platelet function test 12 to 24 hours after percutaneous coronary intervention (PCI), at 30 days and 6 months. Of these, 2214 patients had high on-treatment platelet reactivity during the initial test, defined as 230 P2Y12 reaction units (PRU), and 3215 did not have a high on-treatment reactivity. The high on-treatment group was randomized to receive high-dose clopidogrel (600 mg followed by 150 mg daily for 6 months) in 1109 patients and standard-dose clopidogrel (loading dose of placebo, followed by 75 mg and placebo tablet daily) in 1105 patients. A randomized group of 586 patients without high on-treatment reactivity was assigned to receive standard-dose clopidogrel. All patients received 75 to 162 mg of Aspirin. The primary end-point was a composite of death from cardiovascular causes, nonfatal myocardial infarction, or stent thrombosis. The main safety outcome was severe or moderate bleeding according to the Global Utilization of Streptokinase and t-PA for Occluded Coronary Artery (GUSTO) definition. Analysis of the efficacy was performed based on the time to the first event on an intention-to-treat basis. Safety analysis was performed with patients who received at least one dose of the study drug. Survival curves were obtained using Kaplan-Meier method and survival differences were compared with the use of log-rank test stratified by acute coronary syndromes.

There were no differences in primary end points between high and standard dose clopidogrel groups (2.3% of patients in high-dose group vs. 2.3% in standard-dose group – HR, 1.01; 95% CI, 0.58-1.76; P=0.97). Also safety of the two regimens did not differ (1.4% of patients in high-dose vs. 2.5% in standard-dose, HR, 0.59; 95% CI, 0.31—1.11; P=0.1). High-dose clopidogrel provided a 22% (95% CI, 18-26%) absolute reduction in the rate of high on-treatment reactivity at 30 days (62%, CI, 59-65% vs 40%, 95% CI, 37-43%; P<0.001). In 38% of patients initial high on-treatment platelet reactivity was observed to decrease by 30 days when treated with high-dose clopidogrel. Authors conclude that high-dose clopidogrel does not reduce incidence of death from cardiovascular incidents as compared to standard-dose clopidogrel.

**Comments**

The significant individual variability in response to clopidogrel treatment is well established (1). In fact, one in five patients undergoing elective PCI exhibit high on-treatment platelet reactivity to both aspirin and clopidogrel. These are the patients at highest risk for atherothrombotic events (2). One possible explanation for significant inter-individual variability in response to clopidogrel may be genetic difference in the functional activity of CYP2C19 enzyme, which metabolizes clopidogrel, the prodrug, to its active metabolite (3). Carriers of a reduced function CYP2C19 are more likely to have high on-treatment reactivity of platelets as compared to people with normal CYP2C19 enzyme. If the decreased enzyme activity, and therefore less of the metabolized active drug, was the only explanation for increased risk of cardiovascular events we would expect an increased clopidogrel dose to improve platelet inhibition. As demonstrated in the presented study the increased clopidogrel dose does not work for these patients (4). We must, therefore, consider additional contributing factors. It may very well be that an alternative approach with a different medication such as prasugrel may be needed in these patients. In spite of the observed absence of the effect of increasing clopidogrel dose in GRAVITAS study, however, the individualized management of patients based on platelet functioning testing should still be considered. In fact the non-individualized management in the GRAVITAS study may be considered a limitation of the study. It may be that management with a goal of specific platelet inhibition target is the appropriate strategy. When interpreting the presented study we also need to consider that in spite of the fact, that inclusion criteria did not exclude high-risk patients, the study population ended up being a low-risk population. We may therefore not transfer conclusions of this study into a high-risk population. An additional interesting observation of the study was the decrease of high on-treatment platelet reactivity with time in 38% of patients by 30 days when treated with high-dose clopidogrel. The observed dynamic nature of platelet reactivity, may warrant an increased emphasis on timing of measurement on the level of reactivity and its association with adverse events and further studies to increase understanding of clinical,
procedural and genetic predictors of the early resolution of high on-treatment platelet reactivity after PCI, as suggested by the authors of presented study.

**References:**


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**Soluble Guanylate Cyclase α1 is Required for the Cardioprotective Effects of Inhaled Nitric Oxide**


**Reviewers:** Yasuko Nagasaka, MD, PhD and Theodore A. Alston, MD, PhD Massachusetts General Hospital, Harvard Medical School

**Abstract**

Inhaled NO was developed at MGH as a selective pulmonary vasodilator. However, researchers there find the gas to have other applications. This laboratory paper explores the mechanism by which iNO protects ischemic hearts of mice from reperfusion injury.

Anesthetized wild-type (WT) mice and mice deficient in the soluble guanylate cyclase α1 subunit (sGCα1(-/-)) mice were subjected to cardiac ischemia for 1 h followed by 24 h of reperfusion. Inhaled NO (80 ppm) was started 10 min after left coronary ligature and continued until 10 min after ligature release. NO decreased MI area by 41% in WT mice (p = 0.002) but not in sGCα1(-/-) mice.

Irradiation and bone marrow transplantation were performed to restore WT marrow-derived cells to sGCα1(-/-) mice. Breathing NO decreased MI area by 39% in sGCα1(-/-) mice carrying WT marrow (p = 0.03).

Therefore, the cardioprotective effect of iNO requires the presence of one of the NO receptor, the α1 isozyme of soluble guanylate cyclase. Presumably, cGMP is a second messenger for this benefit. Furthermore, marrow-derived cells are key mediators of the ability of NO to reduce cardiac ischemia-reperfusion injury.

**Comments**

Because breathing NO can decrease PVR without altering systemic blood pressure, it was initially proposed that the actions of inhaled NO were limited to the lungs. However, marrow-derived cells such as platelets and leukocytes can be “tamed” while transiting through iNO-exposed lungs. This is perhaps the major mechanism by which iNO attenuates ischemia/reperfusion injuries of tissues.

Additionally, NO, when breathed, may be carried in the blood stream as NO-metabolites capable of extra-pulmonary effects (1). For instance, though binding of NO to heme iron can proceed to NO destruction and met-heme formation, the heme can alternatively release some of the NO. Also, thiol groups of protein can reversibly carry NO as N-hydroxy-N-nitroso adducts (figure) (2). These and other NO products (3) might be beneficially carried from the lungs to the coronary arteries.

The benefit of iNO against cardiac ischemia/reperfusion injury likely depends primarily on reaction of the gas with sGCα1 of the marrow-derived cells in the blood stream. However, NO metabolites may travel from the lungs to the heart (and to marrow-derived cells therein).

It is attractive to suppose that this safely inhaled drug could attenuate myocardial injury in patients. In theory, iNO could be started in any setting (including out-of-hospital), even before IV access is achieved.

Hopefully, the miracle drug will prove to save an expanded constellation of lives.

**References**


Figure. Though hemoglobin scavenges NO, initial reactions of NO with heme iron and with protein thiol groups are reversible.

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**Sodium Nitroprusside Enhanced Cardiopulmonary Resuscitation Improves Survival with Good Neurological Function in a Porcine Model of Prolonged Cardiac Arrest**


**Reviewers:** Magdalena Bakowitz, MD, MPH, and Theodore A. Alston, MD, PhD Massachusetts General Hospital, Harvard Medical School

**Abstract**

Large doses of epinephrine are standard adjuncts to CPR. Iconoclastic researchers in Minnesota report that a vasodilator may be better than a vasopressor. They refer to their experimental approach as “snappy CPR,” using SNPcPR as an acronym for a sodium nitroprusside-enhanced technique.
The method has three components: active chest compression/decompression with the aid of an airway inspiratory impedance device, lower abdominal binding to divert more blood flow to vital organs, and arterial vasodilation with nitroprusside to promote blood flow.

Twenty-four anesthetized and intubated pigs were electrically fibrillated, subjected to 8 min of untreated VF, and then supported for 25 min by one of three approaches: standard compression/decompression and ventilation, the same enhanced by an airway inspiratory impedance device and an abdominal binder, and the latter plus nitroprusside. The first group received 0.5 mg of epinephrine every 5 min, the second group received no vasoactive drug, and the third received 1 mg of nitroprusside every 5 min.

Twenty-four-hour survival with good neurologic function in these groups of eight pigs each was 0 in the first group, 1 (12.5%) in the second group, and 6 (75%) in the third group. The difference in survival as well as neurologic function between the second group and the third group reached statistical significance (p = 0.04). Of note, the only difference in design of these two protocols was the addition of nitroprusside. Coronary perfusion pressure, carotid blood flow, end-tidal CO2, and blood pH were the highest in the nitroprusside group.

Comments

Two strategies to aid an injured heart are to increase its diastolic perfusion pressure or to decrease its afterload. Any given drug can achieve one goal or the other but not both (though an IABP can do both). The present experiments call this pharmacological dilemma to mind.

One would like to have seen more variations examined in these experiments. For instance, a fourth group might have been managed with the aids of the airway inspiratory impedance device, and abdominal binder, and epinephrine. There was no such group. It would also be interesting to compare nitroprusside with vasopressin instead of epinephrine. Perhaps nitroglycerine or some other vasodilator would be better than nitroprusside, especially since nitroprusside releases cyanide. In any event, the innovative Lurie group has once again served cardiovascular anesthesiologists rich food for thought and research activity.
Support Our Profession

Cardiovascular anesthesiology, as we all agree, is a vastly rewarding profession. The SCA Foundation exists to ensure that our profession remains at the forefront of medicine. We do so through:

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Below are recent activities of the SCA Foundation announced at the SCA Annual Meeting

2011 Research Grants Awarded

At the 2011 SCA Annual Meeting, the SCA Research Committee and the SCA Foundation announced the recipients of the 2011 research grants. We would like to recognize the International Anesthesia Research Society (IARS) for their contribution to make these named grants possible.

SCA/IARS Starter Grants

Jayant Nick Pratap
Cincinnati Children’s Hospital Medical Center
“Randomized trial of near-infrared spectroscopy to guide intraoperative and intensive care management during children’s heart surgery”

Jan Stumpner
University of Wuerzburg
“The functional role of calcium/calmodulin kinase II in ischemic and anesthetic-induced cardiac protection”

SCA/IARS Mid-Career Grant

Diederik van Dijk
University Medical Center Utrecht, The Netherlands
“The effect of dexamethasone on cognitive decline after cardiac surgery”

Foundation Activities at the 2011 Annual Meeting

By Joyce A. Wahr, M.D.

We had a wonderful 2011 SCA Annual Meeting in Savannah! For those of you unable to attend this year, we would like to share information about the events that were supported by the SCA Foundation. We hope that you can join us next year in Boston.