Low-dose anticoagulation therapy can be used safely with new design mechanical heart valve

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Less aggressive anticoagulation therapy, combined with low-dose aspirin, can be used safely in conjunction with a newer generation mechanical heart valve. These findings from the first phase of a randomized clinical trial are published in *The Journal of Thoracic and Cardiovascular Surgery*, an official publication of the American Association for Thoracic Surgery.

Patients under 65 years of age requiring heart valve replacement have had to choose between a mechanical valve that may last a lifetime but requires aggressive anti-clotting treatment with warfarin, and a biological (cow or pig) valve that does not require warfarin treatment but will need replacement in 10-20 years. Aggressive anti-clotting treatment is accompanied by significant risk of bleeding, while inadequate treatment can result in an increased incidence of stroke.

Therefore, the choice between valve types for physicians and patients narrows to one of avoidance of the risk, pain, and costs of reoperation for valve obsolescence versus avoidance of the lifetime composite risk of bleeding and thromboembolism and the nuisance of ongoing anticoagulation management. Both valve types can develop complications which, although rare, can result in reoperation, stroke, or death.

The US Food and Drug Administration (FDA) approved a randomized

trial to test the safety of less aggressive anti-clotting treatment than the American Heart Association/American College of Cardiology guidelines currently recommend, in patients implanted with a newer generation On-X heart valve. "This is a bileaflet mechanical valve approved by the FDA, which is designed to function with less anticoagulation, or in some cases, antiplatelet therapy only," explains John D. Puskas, MD, Professor of Cardiothoracic Surgery at the Icahn School of Medicine at Mount Sinai, and Chairman of the Department of Cardiothoracic Surgery, Mount Sinai Beth Israel, New York, NY.

In this first phase of the three-phase Prospective Randomized On-X Anticoagulation Clinical Trial (PROACT), conducted under an FDA investigational device exemption, 375 aortic valve replacement patients with elevated risk factors for clotting were randomized into control (190) and test (185) groups from September 2006 to December 2009 at 33 US centers. Patients in the control group received standard treatment of warfarin to maintain a target range of the International Normalized Ratio (INR) of 2.0-3.0. Patients in the treatment group received low-dose warfarin, targeting an INR of 1.5-2.0, after an initial 90 postoperative days of standard therapy. All patients received 81 mg aspirin daily.

The patients were followed up by in-person visits at three months, six months, and one year after surgery and then annually for between five and eight postoperative years to accrue the necessary 800 patient-years of follow-up mandated by the FDA. During these visits, electrocardiography or echocardiography was performed as required by the protocol and as clinically indicated. All patients maintained with warfarin therapy were followed up using weekly home INR testing through a central telephone or online database.

"The results show that anticoagulation may be safely reduced in patients following aortic valve replacement with this approved bileaflet

mechanical prosthesis," says Dr. Puskas. "INR can be safely maintained between 1.5 and 2.0. With low-dose aspirin, this resulted in a significantly lower risk of bleeding, without a significant increase in thromboembolism. In high-risk recipients of On-X valves, the INR should be assiduously kept above 1.5 to maximize the safety and effectiveness of this therapeutic change," he concludes.

The investigators caution that results from the present trial should not be extrapolated to other prostheses, mechanical mitral valve replacements, or patients undergoing double aortic valve/mitral valve replacement. The present standard of care for all mechanical AVR patients outside the PROACT study remains conventional anticoagulation, as indicated by the American Heart Association/American College of Cardiology guidelines.

Two further phases of PROACT are planned. The second will be used to compare current anticoagulant therapy versus aspirin and/or clopidogrel only in selected lower risk patients requiring atrial valve replacement. The third will compare standard anticoagulation therapy versus INR goal of 2 to 2.5 in patients requiring mitral valve replacement.

More information: "Reduced anticoagulation after mechanical aortic valve replacement: Interim results from the Prospective Randomized On-X Valve Anticoagulation Clinical Trial randomized Food and Drug Administration investigational device exemption trial," by John Puskas, MD, MSc, FACS, FACC; Marc Gerdisch, MD; Dennis Nichols, MD; Reed Quinn, MD; Charles Anderson, MD; Birger Rhenman, MD; Lilibeth Fermin, MD; Michael McGrath, MD; Bobby Kong, MD; Chad Hughes, MD; Gulshan Sethi, MD; Michael Wait, MD; Tomas Martin, MD; and Allen Graeve, MD, on behalf of all PROACT Investigators (DOI: dx.doi.org/10.1016/j.jtcvs.2014.01.004), *The Journal of Thoracic and Cardiovascular Surgery*, Volume 147, Issue 4.

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