dogrel (300 mg) followed by a daily dose of 75 mg for a minimum of 6 weeks (2). We further justify this anticoagulation regimen by the relative state of hypercoagulation we have previously described, which follows off-pump coronary artery bypass surgery (3). Because of variation on conduit size as well as distal runoff, we no longer routinely use the gray (4.5 to 5.0 mm) or green (5.0 to 5.5 mm) connectors but limit our practice to the blue (5.5 to 6.0 mm) and purple (6.0 to 7.0 mm) devices.

The authors do note that the published incidence of saphenous vein graft failure using conventional suture technique at one year is 15%. Their reported incidence of graft occlusion with this Food and Drug Administration-approved product is one-fifth of this value. It is also interesting to note that in those patients with early graft occlusion, the phenomenon occurred in all grafts. This observation may simply represent poor quality conduit, poor distal runoff, hypercoagulation, or all of the above.

We continue to employ the symmetry device in our surgical practice using the aforementioned protocol. There is no doubt that use of the connector avoids the significant manipulation of the ascending thoracic aorta so often associated with catastrophic cerebral vascular accidents.

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REPLY

We agree that device size may account for some cases of anastomotic device failure, although these data became available only this month (February 2004), showing a 20.8%, 8.5%, 14.7%, and 0.0% failure rate in gray, green, blue, and purple sizes, respectively, although these were not statistically different from each other (1). In our report (2), mostly green or blue devices were used, but after appreciating that some patients were developing anastomotic device stenosis, only blue and purple were used. The quality of the veins and distal targets was felt to be adequate. In addition, all occlusions were at the proximal anastomoses, rendering poor distal runoff or technical problems with the distal anastomosis less likely. All patients received aspirin 325 mg and clopidogrel 75 mg on the day of the surgery. The aspirin was given indefinitely, and the clopidogrel was continued for two to three months.

Although the historical incidence of graft failure is higher than in our report, our study was a clinical and not an angiographic study. Thus, we did not evaluate the true incidence, which is likely underestimated. In addition to the studies pointed out in our study, a recent angiographic (three month) report shows that 11%, 5%, and 7% of grafts were either occluded, had >50% stenosis or <50% stenosis, respectively (19 of 81, or 23% saphenous vein graft [SVG]) (1). Of note, 18.6% of patients had recurrent cardiac symptoms, including three cardiac deaths. We have also identified an additional three patients and six SVGs with variable amounts of anastomotic device stenosis or occlusion in whom coronary artery bypass graft was performed in 2002, the time period reported in our article. Two patients were treated with sirolimus-eluting stents (2 SVGs and native left circumflex obtuse marginal coronary artery, respectively), and the other with medical therapy.

An important clinical consequence of anastomotic device stenosis is its aggressive nature, which appears diffuse and severe with involvement of all SVGs. This is in contrast to in-stent restenosis, which is more variable and only rarely leads to involvement of all stents. In this regard, patients with anastomotic device stenosis can present with global ischemic episodes that lead to myocardial infarction and death, which is also unusual with coronary in-stent restenosis. With the publication of additional reports describing anastomotic device stenosis (1,3), we would reemphasize increased oversight by regulatory agencies and adequately powered, randomized controlled trials of such devices, similar to coronary stent trials.

We believe that these devices will ultimately find their niche in clinical practice, as the imperative to reduce stroke during coronary artery bypass grafting is obviously critically important and has been reflected by the rapid acceptance of such devices by cardiovascular surgeons. However, improvements in the design of such devices seem to be required to improve outcomes (i.e., anti-proliferative drug coatings, improved loading and deliverability, and so forth). Pending further studies showing long-term efficacy, we continue to advise limiting their use to patients with a clearly increased risk of stroke during aortic cross-clamping. In patients in whom the device needs to be placed, the use of the largest devices, prolonged dual anti-platelet agents, careful follow-up, communication between cardiothoracic surgeons and cardiologists when the device is implanted, and ischemia testing in the first two to six months are warranted. The treatment of anastomotic device stenosis will continue to evolve as we learn more about this new iatrogenic disease.
3. Fuertes J, Lozano I, Turiel JM, Llosa JC, Suarez E, de la Tassa CM. Vitamin K antagonist therapy (VKA) based on their heart valves who had either high-intensity or low-intensity thromboembolism among patients with mechanical heart valves. Modelling techniques are essential to evaluate the burden of the competing risks of bleeding and thromboembolism and their consequences during the lifetime of the patient.

Optimal Target International Normalized Ratio For Patients With Mechanical Heart Valves

Vink et al. (1) compared the occurrence rates of bleeding and thromboembolism among patients with mechanical heart valves who had either high-intensity or low-intensity vitamin K antagonist therapy (VKA). Based on their findings of lower combined bleeding and thromboembolic occurrence rates in the high- versus low-intensity VKA group, they concluded that “both aortic and mitral valves will benefit from a treatment strategy with a target INR higher than 3.0.” This is a controversial conclusion because most recent publications recommend a valve-specific and lower target international normalized ratio (INR) (2,3). Therefore, we closely studied Vink’s analyses and have the following comments.

When trying to identify the optimal target INR for patients with mechanical heart valves, not only the occurrence rates of bleeding and thromboembolism but also the consequences of these events need to be considered. It may well be possible that although the combined occurrence rates of bleeding and thromboembolism are lower in the high-intensity VKA group, the combined mortality associated with bleeding and thromboembolism is lower in the low-intensity VKA group.

We repeated the reported meta-analysis for the aortic valve replacement group, and we pooled the mortality rates of bleeding and thromboembolism from those studies that reported on mortality resulting from these events (11 of the 21 studies in the low-intensity and 5 of the 9 studies in the high-intensity VKA group). We found in the low-intensity VKA group versus the high-intensity VKA group, a pooled mortality rate for bleeding of 12% (95% confidence interval [CI] 7.7% to 16.3%) versus 20% (95% CI 13.3% to 26.6%; p = 0.05), for valve thrombosis 27% (95% CI 12% to 42%) versus 33% (95% CI 3.5% to 63.5% p = NS), and for thromboembolism 14% (95% CI 9.6% to 18.4%) versus 14% (95% CI 8.3% to 19.7% p = NS). We entered the occurrence rates and mortality rates of bleeding, valve thrombosis, and thromboembolism from the meta-analysis in a microsimulation model that we previously developed (4) to estimate patient prognosis after aortic valve replacement with mechanical prostheses, and we simulated 10,000 life histories of a 56-year-old (mean age in meta-analysis) male patient after aortic valve replacement in order to estimate the expected lifetime risk of death due to bleeding, valve thrombosis, and thromboembolism for either a low-intensity or high-intensity anticoagulation regimen. We found that the combined lifetime risk of death due to bleeding, valve thrombosis, and thromboembolism in the low-intensity versus the high-intensity VKA group was 6.3% versus 7.8% (p = NS). This shows that, when considering the mortality due to bleeding and thromboembolic events, for aortic valve patients nothing is gained by a target INR higher than 3.0.

In conclusion, a meta-analysis of only bleeding and thromboembolic event rates is methodologically insufficient to determine the optimal anticoagulation regimen for patients with mechanical heart valves. Modelling techniques are essential to evaluate the burden of the competing risks of bleeding and thromboembolism and their consequences during the lifetime of the patient.

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