Correspondence

Letters to the Editor must not exceed 400 words in length and may be subject to editing or abridgment. Letters must be limited to three authors and five references. They should not have tables or figures and should relate solely to an article published in Circulation within the preceding 12 weeks. Only some letters will be published. Authors of those selected for publication will receive prepublication proofs, and authors of the article cited in the letter will be invited to reply. Replies must be signed by all authors listed in the original publication.

Assessment of Atrioventricular Junction Ablation and VVIR Pacemaker Versus Pharmacological Treatment in Patients With Heart Failure and Chronic Atrial Fibrillation

To the Editor:

We congratulate Brignole et al1 on their study. In particular, we found ourselves in agreement with their emphasis on the importance of a randomized controlled trial in this field, a void which they have sought to fill. We are somewhat puzzled by their choice of control, however, and fear that it points to a gulf between the electrophysiology community and the heart failure community.

Whilst it appears that the electrophysiologist’s reaction to the copresentation of atrial fibrillation and congestive heart failure is to reach for his ablation catheter, our reaction to the copresentation of atrial fibrillation and congestive heart failure is to book an anaesthetist and reach for the defibrillator. We were surprised that nowhere did Brignole et al even mention the word “cardioversion,” and neither did Dr Scheinman in his editorial,2 despite the fact that he drew attention to the remarkable results that can be achieved with restoration of sinus rhythm.3 It may be that cardioversion had been attempted in a number of patients (some might not even accept the diagnosis of “chronic” atrial fibrillation until electrical cardioversion has been tried and has failed), but nowhere is this information supplied. The mean duration of arrhythmia was fairly long but was exceeded by its standard deviation, so both groups must have included patients who had had atrial fibrillation for a relatively short time. We are not even told whether all the patients were still in atrial fibrillation at the end of the trial.

We are not aware of a randomized controlled trial comparing the results of electrical cardioversion and medical therapy in patients with atrial fibrillation and congestive heart failure. The safety and efficacy of electrical cardioversion are so well founded that we would consider it unethical to conduct such a trial. The safety and efficacy of ablation and pacemaker insertion are not so well founded, however, and it would appear to us that the ideal comparison would be between ablation and cardioversion, not between ablation and medication. To have randomized half their patients to medication alone under these circumstances seems to us questionable.

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Response

We believe the electrophysiologist’s reaction to the copresentation of atrial fibrillation and congestive heart failure is the same as that of the specialist in heart failure: namely, to make every effort to restore and maintain sinus rhythm for as long as possible. However, at least 12% of paroxysmal atrial fibrillation is considered intractable despite multiple-drug therapy and repeated cardioversions.1 Moreover, in epidemiological studies, about 60% of patients with atrial fibrillation have a chronic form. In most cases, the main problem is not converting to sinus rhythm but maintaining it for a long time and avoiding the adverse effects of therapies necessary to obtain that goal. Thus, current treatments often fail to maintain stable sinus rhythm. That was the case with our patients who underwent AV junction ablation only when reasonable attempts to restore stable sinus rhythm (including repeated cardioversions) had failed. The median duration of chronic atrial fibrillation of the enrolled patients in our study was 2.5 years, and before the development of the chronic form, most patients had had a history of paroxysmal tachyarrhythmias lasting 9±6 years (median, 7 years). Admittedly, some patients were enrolled a relatively short time after the development of chronic atrial fibrillation (minimum of 6 months) when it seemed clear that sinus rhythm could not be maintained due to frequent relapses, adverse effects of antiarrhythmic drugs, and/or severity of heart failure that required a prompt intervention. All of the patients remained in atrial fibrillation throughout the study.

We know from epidemiological studies2 that atrial fibrillation is associated with morbidity and mortality, and we have reason to hope that outcomes will improve if we can achieve permanent sinus or atrial paced rhythm. Nevertheless, epidemiological studies are unable to show whether a strategy aimed at preventing atrial fibrillation and maintaining sinus rhythm is better than another that allows control of the ventricular rate. New nonpharmacological therapies (which encompass surgical or catheter ablation procedures, implantable atrial defibrillator, and preventive pacemakers) are under investigation and may be able to maintain sinus or atrial paced rhythm when conventional treatments have failed. Placebo-controlled trials with warfarin have shown a substantial reduction in stroke rates, but we do not yet know enough about the risk-benefit ratio of these new therapies, which can only be determined from controlled clinical trials after they have shown promise in mechanistic and pilot studies. The benefits of sinus rhythm to reduce stroke, heart failure, hospitalization, and death and to improve symptoms, exercise capacity, and functional status should be quantified by controlled clinical trials. We hope that the National Heart, Lung, and Blood Institute will take responsibility for conducting and monitoring that trial.3 We conclude that the best strategies for management of atrial fibrillation have yet to be defined.

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Minimally Invasive Coronary Bypass Surgery: An Example for Optimal Teamwork Between Cardiologists and Cardiac Surgeons?

To the Editor:

At our institution, where we offer minimally invasive coronary bypass surgery alone or in combination with balloon angioplasty (hybrid revascularization), we also experienced powerful public demand for minimally invasive procedures. Much time was and will be spent to inform patients with single or multiple coronary vessel disease about the different revascularization options actually available. In accordance with Bonchek and Ullyot,1 we also are waiting for study results comparing minimally invasive coronary surgery with standard CABG in similar clinical settings. However, during our preliminary experiences with minimally invasive coronary surgery combined with coronary angioplasty,2 the most striking step toward optimal therapeutic approach was achieved through intensive and critical patient selection between cardiac surgeons and interventional cardiologists. In the absence of comparative studies, we do not consider minimally invasive approaches as an alternative to well-documented standard operation strategies in multiple-vessel disease, but on the basis of our experience, we see a “niche” for critically selected patients profiting from minimally invasive revascularization procedures.

In our opinion, only ameliorated teamwork between cardiologists and cardiac surgeons, evaluating the individual patient’s clinical situation and procedure-related risk, will provide the best revascularization strategy.

Correspondence

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January 1998 in New Orleans, La.3 Since 1995, we have applied our ultra–fast-track methods to all open heart surgical patients and have observed excellent outcomes, with most discharges occurring between postoperative days 1 and 4. Currently, >70% of our surgical cases are safely discharged within this time frame. These cases comprise the full spectrum of an active, adult cardiac surgical practice, including a high percentage of emergency cases as well as high-complexity/high-risk operations (eg, acute aortic dissection, Ross procedure, Bentall, redo CABG, and multiple comorbidities).

In our opinion, the standard operation using conventional techniques endorsed by Drs Bonchek and Ullyot remains the operation of choice in almost all cases owing to its superior exposure, broad applicability, and time-tested results. We believe recent developments in ultra–fast-track protocols only reinforce its superiority.

Minimally Invasive Heart Surgery

To the Editor:

We fully agree with the recent editorial by Drs Bonchek and Ullyot concerning minimally invasive heart surgery.1 Published comparisons between minimally invasive surgery and “standard” operations can be misleading and inappropriate.2–4 Indeed, the purported benefits of earlier discharge and cost savings can be similarly achieved with conventional cardiac surgical techniques, as was reported at the Society of Thoracic Surgeons meeting in

Constitutive Expression of phVEGF165 After Intramuscular Gene Transfer Promotes Collateral Vessel Development in Patients With Critical Limb Ischemia

To the Editor:

Baumgartner et al1 reported a significant advance in angiogenic gene therapy. They induced collateral neovascularization in 10 critically ischemic limbs by injection of vascular endothelial growth factor (phVEGF165) into the muscles of the ischemic limbs. The effect of the therapy was demonstrated by a significant rise in ankle-brachial index, newly visible collateral blood...
vessels on the contrast angiogram, healing of the patients’ former ulcers, and improvement in pain-free walking time. The authors cautiously claim that such improvement has not previously been achieved spontaneously or with medical therapy in patients with critical limb ischemia.

This may very well be so, but we had a corresponding experience in May 1992 with a 72-year-old male with critical ischemia in 1 limb. He was unsuitable for any type of vascular surgery and had no other alternative than amputation, when he underwent percutaneous corticotomy (cutting of the cortex, preserving the intramedullary circulation) on both the tibial and fibular bones. The bones were slowly moved posteromedial and posterolateral by transverse distraction osteogenesis by use of an Ilizarov ring fixator device.

We found that the toe pressure rose from 10 to 40 mm Hg and ankle pressure from 95 to 128 mm Hg (ankle-brachial index from 66% to 80%) 1.5 years after the operation. Newly formed collaterals were demonstrated on the contrast angiogram. His ulcers healed, his resting pain vanished, his toenails and hair started to grow, and he regained an infinite pain-free walking time.

Today, he is still without pain in the limb that was operated on, and the distal blood pressures at toe and ankle levels are 50 and 100 mm Hg, respectively, but he is starting to experience ischemic symptoms in the other limb; therefore, we are contemplating a second corticotomy and of course hoping for similar success. What actually is the course of this success? We can only speculate that surgical distraction osteogenesis also promotes angiogenesis. Distraction osteogenesis is known to give rise to the formation of multiple new small blood vessels in the calf muscle, thereby creating a sustainable low-pressure vessel area in which blood flow is high enough to nourish the foot and lower limb.

In patients who undergo distraction osteogenesis for limb shortening, the total limb blood flow increases by a factor of 5 to 7 during distraction. Distraction osteogenesis probably produces many local growth factors, of which some are angiogenic, and one may be VEGF. Debatable, but possible.

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Long-Term Oral Anticoagulant Therapy in Patients With Unstable Angina or Suspected Non–Q-Wave Myocardial Infarction

To the Editor:

A striking thing that emerges from the report by Anand et al of the OASIS pilot study1 relates to the differences in the control arms in phase 1 (randomization to coumadin or standard care a mean of 6 days after study entry) and phase 2 (randomization to coumadin or standard care a mean of 26 hours after study entry). It is difficult to reconcile why the placebo composite event rate of cardiovascular death/new myocardial infarction/refractory angina at 6 months in phase 1 (3.9%) is so much lower than the placebo composite event rate at 3 months in phase 2 (12.1%). How can getting placebo early or late make such a difference? At first glance, the protocol modifications instituted in phase 2 (cited by the authors by way of explanation) all relate to the dosing and administration of warfarin and ought not to really affect control event rates.

So what are the more subtle differences between the 2 control arms? In phase 1, heparin/hirudin therapy had been discontinued by the time randomization took place, whereas in phase 2 heparin/hirudin was still ongoing (and could be continued for up to 72 hours). Also, the “event clock” started much earlier in phase 2 than in phase 1. Could the higher control event rate in phase 2 be because the investigators were capturing far more early events that otherwise would have been counted as part of the heparin/hirudin randomization in phase 1?

Three important additional pieces of information are really necessary to help sort out this dilemma. First, what is the breakdown of individual components of the composite end points in phases 1 and 2? Is the driving end point (as I suspect) a much higher incidence of refractory angina in the phase 2 control patients? Second, what is the timing of the end-point events? Figure 2 (cumulative event rates in phase 2) indicates that all of the differences between groups occurred early (within 2 weeks or so), suggesting an early “window of vulnerability.” How do the phase 1 data (particularly in the control group) look in comparison? Might this not be construed as really an expression of a high number of recurrent events in the 26-hour-plus period after initiation of heparin/hirudin? Finally, were there any interactions between heparin/hirudin and coumadin/placebo in phase 2?

An even more intriguing question is raised by the phase 2 data in Figure 2. If the differences between coumadin and placebo all occur over the first 2 weeks or so, and the event curves then track parallel, couldn’t one argue that only 2 weeks of therapy with coumadin (rather than 3 to 6 months) may be necessary in patients with acute coronary syndromes? Again, this reinforces a “window of vulnerability,” a finite period within which there is a high risk for recurrent events.

It would be a mistake to broadly infer that coumadin therapy (particularly long-term therapy) is of benefit in acute coronary syndromes. I believe the more important message that emerges from the work of Anand et al is that there is an opportunity to improve the early-phase management of patients with acute coronary syndromes. The benefits of long-term coumadin therapy have yet to be established.

With additional data from the OASIS Pilot study, I hope we can begin to tease out the answers to some of the nagging questions.

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