A Randomized Comparison of External and Internal Cardioversion of Chronic Atrial Fibrillation

We thank Dr. Ewy for his editorial comment on our study and would like to respond to the issues he raised. The first comment refers to the low success rate that we obtained with external shocks compared with the pioneering reports of Lown et al. Their initial report included only 10 patients who were undergoing mitral valve operation; sinus rhythm was restored in eight of these. The second report was a lecture, and the results of cardioversion are difficult to compare with the results of other reports. The duration of atrial fibrillation, number of sessions of cardioversion, and number of shocks per patient were not detailed; the energy delivered was not standardized. Whereas a majority of patients in our study had coronary artery disease, hypertensive heart disease, or dilated cardiomyopathy, valvular heart disease was the cause of atrial fibrillation in 70% of patients in the Lown report. Note that 35% of the patients in the external cardioversion group and 45% in the internal group in our study had a history of congestive heart failure, and 36% of patients in the external cardioversion group had failed previous electrical cardioversion attempts. Note also the long duration of atrial fibrillation in many patients in our study, with 43% of patients in the external cardioversion group having had atrial fibrillation for >2 years.

Dr. Ewy found our description of the external cardioversion technique not detailed enough. The paddles were standard size (3 x 5 in.) and were applied to the chest wall manually with firm pressure. The paddles were positioned in an anterolateral fashion and not apicoposteriorly as stated in his editorial. The purpose of our study was not to compare the "optimal technique of external cardioversion" (which to our knowledge has not been universally defined) with internal cardioversion but instead to compare a conventional method of external cardioversion with internal cardioversion. We are aware that electrode position, electrode size, and other parameters may influence the results of external cardioversion. Nevertheless, our study demonstrated that internal cardioversion is more effective than and as safe as conventional external cardioversion in patients with chronic atrial fibrillation.

Transvenous internal high-energy cardioversion of chronic atrial fibrillation is not an alternative to external cardioversion. It has proved to be safe and effective and serves as an additional tool to convert patients with chronic atrial fibrillation to sinus rhythm if external cardioversion fails. We hope Dr. Ewy will try this technique in his patients with chronic atrial fibrillation who fail to respond to external cardioversion.

Samuel Levy, MD
Fred Morady, MD
Marseille, France and Ann Arbor, Michigan

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5. Ewy GA: Effectiveness of direct current defibrillation: Role of paddle electrode size. II. Am Heart J 1977;93:674–675

Acute Reduction of Lipoprotein(a) by Tissue-Type Plasminogen Activator

We read with interest in the June 1992 Circulation the work of Hegele et al. on lipoprotein(a) [Lp(a)] reduction in patients with unstable angina treated with tissue-type plasminogen activator (t-PA) and/or heparin. The authors attributed this effect to t-PA and excluded a possible influence of the heparin given intravenously at the same time in a first group of patients because they did not observe any significant lowering effect on Lp(a) in their group of patients treated only with heparin.

We propose a different interpretation to emphasize the value of the heparin, which is indirectly supported by another study that does not demonstrate any effect on Lp(a) of isolated thrombolytic therapy and is directly supported by our own previous and recent experience with the Lp(a) and heparin relation.

Table 1 summarizes the results of our latest study regarding the effect of intravenous heparin on Lp(a) in patients with coronary artery disease treated with PTCA. It is evident that heparin infusion produced a very marked decrease of Lp(a) (the same order of values as seen by Hegele et al in their group of patients treated with t-PA and heparin) whose statistical significance (p < 0.001) persisted in blood samples taken at the end of PTCA and 4 hours later.

Similar reductions in Lp(a) values were first seen by us in patients with coronary heart disease who underwent coronary artery bypass graft surgery (studied before and after surgery) and, more recently, were also found in patients with chronic renal insufficiency during the course of hemodialysis. All these patients were given intravenous heparin; the resultant effect of the drug on Lp(a) was not dependent on the type of technical procedure and was possibly related to basal values of Lp(a).

We wonder whether the chance presence of cases previously treated with heparin might have had a part in the results reported by Hegele et al. In their 11 patients treated only with heparin, we noted significantly lower basal values of Lp(a) compared with those of the other group and four cases, noted by the authors, with a decrease of Lp(a), as we have observed in our patients, that might be ascribed only to the effect of heparin.

The interesting work of Hegele et al. gives us the opportunity to propose and discuss our hypothesis, which is still in progress and requires further contributions. We hope that it will not be the object of merely speculative discussions and that the data hitherto collected will be considered sufficient for attributing to heparin this "Lp(a)-trapping" or "Lp(a)-clearing" effect, which is not yet well known to clinicians and which does not exclude a synergism with t-PA.
TABLE 1. Mean Values of Lp(a), Cholesterol, Triglycerides, and C Reactive Protein in 30 Patients Treated With Heparin (10,000 IU) During PTCA

<table>
<thead>
<tr>
<th></th>
<th>Before PTCA</th>
<th>End of PTCA</th>
<th>4 Hours after PTCA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lp(a) (mg/dl)</td>
<td>58.57±41.55</td>
<td>16.92±10.72*</td>
<td>21.15±11.72*</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>176.83±41.66</td>
<td>168.13±24.42</td>
<td>175.61±29.43</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>145.80±102.39</td>
<td>88.10±64.34*</td>
<td>105.61±49.74</td>
</tr>
<tr>
<td>CRP (µg/ml)</td>
<td>96.24±28.21</td>
<td>101.38±104.42</td>
<td>166.76±11.20</td>
</tr>
</tbody>
</table>

Lp(a), lipoprotein(a); PTCA, percutaneous transluminal coronary angioplasty; CRP, C-reactive protein.

*p<0.001.

Manlio Di Lorenzo, MD
Paolo Salvini, MD
Servizio di Cardiologia Ospedale S. Camillo, Rome

Maria Levi Della Vida, MD
Elvira Maddaloni, MD
Laboratorio Ricerche Cliniche Ospedale S. Camillo, Rome

References


Reply

Di Lorenzo et al have provided some interesting data that suggest that an acute reduction of plasma lipoprotein(a) [Lp(a)] concentration might be attributable to an effect of intravenous heparin alone, in the absence of tissue-type plasminogen activator (t-PA). In our study,1 which was randomized, double-blind, placebo-controlled, and analyzed with a repeated-measures design, there was no significant change over time in Lp(a) in the group that received heparin without t-PA. The group that received t-PA had a significant reduction in Lp(a) compared both with baseline and with the placebo group. We could not discount an interaction between heparin and t-PA, since both groups received heparin. In the group that received heparin alone, however, there was no significant change of Lp(a) from baseline.

Di Lorenzo et al are correct in saying that Qiu et al2 showed no effect after 6 hours of thrombolytic therapy on plasma Lp(a). Although this is at variance with our results, we note that our significant differences were seen at 12 hours. Furthermore, most subjects that Qiu et al studied received streptokinase, and only five received t-PA in the single-chain form. Although the small number of subjects studied confounds the interpretation of this discrepancy, it is possible that the reduction in Lp(a) that we observed was specific to double-chain t-PA but not other thrombolytic agents such as streptokinase or even single-chain t-PA.

The mean reduction in Lp(a) that Di Lorenzo et al report is significant, but it is based on observations in 30 subjects who received intravenous heparin in conjunction with percutaneous transluminal coronary angioplasty (PTCA). They have no control group of subjects who received only heparin, which makes it difficult to claim that the reduction they observed was caused by heparin alone. Furthermore, the dosage of heparin that they used was much higher than the dose our patients received (10,000 units versus 4,000 units). They give no indication of the timing of heparin administration. It is also possible that there are differences in the heparin preparations used. Our patients all received intravenous heparin sodium from a porcine source (Heparlein). In addition, our Lp(a) determinations in the t-PA and placebo groups at baseline are not statistically different, although the baseline Lp(a) in the group that received heparin alone was slightly higher than the Lp(a) in the t-PA group.

The lowering of the other lipids, particularly triglycerides, that Di Lorenzo et al observed is certainly compatible with an acute effect of heparin. Our protocol included the measurement of several analytes that were unaffected by treatment. This served as a control for nonspecific changes in the plasma fluid volume that might have confounded interpretation of the results.

Others have shown that Lp(a) can vary widely after myocardial infarction and invasive procedures.3 It is possible that the acute changes in Lp(a) seen in other clinical situations could result from an endogenous response to tissue injury and that this effect could be mimicked or enhanced by thrombolytic therapy. The subjects that we reported4 had unstable angina with no evidence of tissue injury. Di Lorenzo et al do not report results from a control group that received either PTCA without heparin or heparin without PTCA. They cannot exclude the possibility that the acute effect of systemic neurohumoral response to PTCA or an interaction between the effects of heparin and PTCA resulted in the acute reduction of Lp(a) that they observed. The basis for and practical implications of acute fluctuation of Lp(a) in the setting of coronary heart disease and thrombolytic therapy clearly requires further study.

Robert A. Hegele, MD
Michael R. Freeman, MD
Anatoly Langer, MD
Philip W. Connelly, PhD
Paul W. Armstrong, MD
Divisions of Endocrinology and Metabolism and Cardiology
Department of Medicine
St. Michael’s Hospital
Toronto

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Corrected Data and Analysis of Hemodynamic Variables Influencing Plasma Endothelin

In February 1992, we published our observations regarding plasma level of endothelin in normal subjects and patients with congestive heart failure, demonstrating a strong correlation between the plasma level of endothelin and the extent of pulmonary
Acute reduction of lipoprotein(a) by tissue-type plasminogen activator.
M Di Lorenzo, P Salvini, M Levi Della Vida and E Maddaloni

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