REFERENCES


REPLY

We thank Drs. Arques and Roux for their comments concerning the increasing use of the deceleration time of the pulmonary venous early diastolic flow (PV-DT) in published reports. We agree that the PV-DT is a useful tool for estimating pulmonary capillary wedge pressure (PCWP) as a measure of the left ventricular (LV) filling pressure, especially in patients with normal sinus rhythm. As mentioned in our study (1), it is important to recognize the influence of several factors regarding use of pulmonary venous flow velocities in clinical practice.

When evaluating PV-DT to estimate PCWP, the influences of heart rate, mitral regurgitation (MR), atrial fibrillation (AF), and LV systolic function have to be taken into account. Of those factors, heart rate may have the largest influence on the PV-DT. Chirillo et al. (2) specifically paid attention to the two components of the deceleration slope of PV-DT. They speculated that the first component was mainly dependent on the initial driving pressure of the pulmonary venous flow, and the second component was affected by the duration of LV relaxation, LV compliance, and heart rate as reported by Little et al. (3). They found a strong correlation between the initial deceleration slope of PV-DT and PCWP during chronic AF with controlled ventricular rates. With faster heart rates, it would be difficult to separate the first and second components. Thus, PV-DT can estimate PCWP only when the heart rates are relatively slow. Matsukida et al. (4) have also reported that the PV-DT accurately predicted PCWP in patients with AF, whereas they only included patients with a heart rate of 60 to 80 beats/min. Both of the above investigators (2,4) excluded patients with AF and a rapid ventricular rate. It is well recognized that the loading conditions during AF are constantly changing; therefore, even when an average of consecutive several cardiac cycles of PV-DT is used, the value would vary depending on the selected beats.

The final issue is the effect of MR. Pozzoli et al. (5) reported that the PCWP can be reliably estimated by combining mitral inflow and pulmonary venous flow velocities even when MR was present. Although they have not evaluated PV-DT, the investigators have reported that the correlation between mitral deceleration time and PCWP was stronger in patients without MR. Furthermore, they have limited their results to apply to patients without atrial arrhythmias or tachycardia.

Thus, we conclude that the evaluation of the PV-DT for estimating PCWP is most useful in patients without MR with sinus rhythm and a relatively slower heart rate. As suggested by Drs. Arques and Roux, we believe that the improvement in the quality of pulmonary venous Doppler flow profile obtained by transthoracic techniques will enhance the future use of PV flow in clinical practice.

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REFERENCES


Glycoprotein IIb/IIIa Inhibitors and the Guidelines for Treatment of Non–ST-Elevation Myocardial Infarction

In a recent study published in the Journal (1) Peterson et al. found that with regard to use of glycoprotein (GP) IIb/IIIa inhibitors there was a low adherence to American College of Cardiology/American Heart Association guidelines (published in 2000) for treatment of non–ST-elevation myocardial infarction (2), and they
noted that increased use of this type of medication represents a target for quality improvement. The observation that most clinicians were not implanting recommendations from published guidelines is important, but conclusions regarding specific use of GP IIb/IIIa inhibitors are limited by the fact that the guidelines referenced in this study have already been superseded by new guidelines published in 2002 (3), which incorporate research showing the importance of adding clopidogrel to aspirin early in the treatment of acute coronary syndromes (4).

The role of GP IIb/IIIa inhibitors for treatment of acute coronary syndromes at this time is not clear. Therapy with clopidogrel has not been compared directly to therapy with GP IIb/IIIa inhibitors, and further data need to be obtained to determine the incremental value for adding GP IIb/IIIa inhibitors to aspirin/clopidogrel/heparin therapy (5). Recommendations may differ in patients with different prognostic risk (as assessed by clinical/laboratory variables at time of initial presentation) and whether an interventional or noninterventional approach is being used. In many cases, GP IIb/IIIa inhibitors may be a fourth element of antiplatelet/antithrombotic therapy to consider in patients with acute coronary syndromes.

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REFERENCES

REPLY
Dr. Coplan questions the evidence supporting glycoprotein (GP) IIb/IIIa inhibitors in the care of non–ST-elevation acute coronary syndrome (ACS). This doubt is remarkable given that GP IIb/IIIa agents have received more intensive investigation than nearly any other ACS treatment. More than 30,000 patients have been studied in six randomized trials of GP IIb/IIIa inhibitors. Three meta-analyses have summarized the trial results, each concluding that early use of GP IIb/IIIa agents resulted in a highly significant overall reduction in risk for death or myocardial infarction (1–3). Dr. Coplan is correct that the benefits tended to be greater in those patients with higher risk (as marked by positive cardiac markers, ST depression, or patients selected for interventional procedures, or those with other high-risk clinical features such as diabetes mellitus, heart failure, or advanced age). These findings are similar to those seen for many ACS interventions and argue for appropriate risk-based treatment strategies. Based on these findings, both the 2000 American College of Cardiology/American Heart Association Guidelines and the current 2002 Guidelines Update recommend the use of GP IIb/IIIa inhibitors in high-risk ACS patients (4,5). To this body of knowledge, our current study provided further confirmatory evidence that early use of GP IIb/IIIa inhibitors was associated with significantly lower inhospital mortality rates when used in a community-based non–ST-elevation patient population. These benefits were also seen in all patient subgroups including those receiving conservative, non-interventional care (6).

Dr. Coplan is correct that there are limited randomized trial data on the incremental value of other antiplatelet therapies (such as clopidogrel) in patients already receiving a GP IIb/IIIa agent or vice versa. However, in the absence of data, one cannot conclude which agent is superior and/or whether a combined approach may yield the best results. Specifically, use of intravenous (IV) GP IIb/IIIa inhibitors results in much more rapid and complete inhibition of platelet aggregation than an oral inhibitor such as clopidogrel. Yet clopidogrel can be continued after IV GP IIb/IIIa agents have been discontinued and still provide long-term benefits (in combination with aspirin) in patients with coronary disease (7). Whether first, second, third, or “fourth,” we would hope that clinicians would use all guidelines-indicated therapies to improve the outcomes of patients with ACS.

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