end-tidal carbon dioxide partial pressure of 30–35 mmHg). CI was estimated by dye dilution method using 10 mg of indocyanine green as an indicator (DDG1001; Nihon Kodens Inc., Tokyo, Japan). Subsequently, carbon dioxide was added to the inspiratory gases, so that PaCO₂ rose to approximately 55 mmHg. The same set of measurements was repeated in each patient.

MAP, CI and HR responses to hypercapnia in the clonidine-propofol subgroup were significantly attenuated compared with those in the other three subgroups (Figure). Plasma norepinephrine concentrations (but not epinephrine concentration) were significantly lower in clonidine-propofol patients.

The cardiovascular effects of hypercapnia are suppressed in patients given clonidine prior to propofol anesthesia, perhaps due to the profound suppression of sympathetic nervous system activity. The hemodynamic response to hypercapnia depends on the level and extent of any sympathetic blockade.⁵ The interaction between the basal anesthetic agent and clonidine (given as a premedicant) can apparently modify the hemodynamic response to hypercapnia to a significant extent.

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The early detection of bupivacaine toxicity in dogs

To the Editor:

We read with interest the article of Kim *et al.*¹ «Continuous mixed venous oxygen saturation, not mean blood pressure, is associated with early bupivacaine cardiotoxicity in dogs». In 1988, we conducted similar work,² also showing that cardiac output appeared to be the first and the most affected hemodynamic variable, whereas mean systemic blood pressure remained unchanged because of the compensatory increase in systemic vascular resistance.

In fact, bupivacaine *iv* primarily impairs cardiac intraventricular conduction^{3,4} enhancing QRS duration, as noted in Kim *et al.*'s Table and Figure 2.¹ Contractile deficiency occurs only later.

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REPLY:

We thank Freysz *et al.* for their comments. Though there is a some similarity in the experimental design between the two studies,^{1,2} we think the point of the articles is different.

In our article,¹ we intended to show that continuous mixed venous oxygen saturation correlated well with cardiac output in the early and late phases of bupivacaine intoxication. Mean blood pressure (MBP) was maintained in the early phase of bupivacaine-induced cardiotoxicity. MBP decreased abruptly and correlated