

## Late Sympathetic Reinnervation and Normalization of Canine Myocardial Beta-Adrenergic Receptor Density Following Denervation

**TO THE EDITOR:** We previously (1) reported up-regulation of myocardial beta-adrenergic receptors ( $\beta$ -AR) and the absence of significant sympathetic reinnervation up to 6 mo after intrapericardial denervation. We now report changes in myocardial sympathetic innervation and in  $\beta$ -AR density in the same dogs 2 yr later.

Five female beagle dogs were previously studied, 3–7 wk, 23–28 wk and 2 yr after denervation produced by the intrapericardial technique (2). To evaluate the sympathetic reinnervation, dogs underwent [ $^{123}$ I]MIBG scintigraphy. The heart-to-lung activity ratio (H/L) was used to quantify myocardial MIBG uptake. For PET determination of myocardial beta-AR density,  $^{11}$ C-CGP 12177 and a graphical method (3) were used.

Before surgery,  $\beta$ -AR concentration was  $33 \pm 4$  pmole/ml tissue. The MIBG H/L ratio was  $3.1 \pm 0.1$ . As previously reported,  $\beta$ -AR densities increased to  $68.9 \pm 15.7$  pmole/ml tissue and  $61.3 \pm 7.9$  pmole/ml tissue 3–7 wk and 23–28 wk after surgery, respectively. At the same time, MIBG H/L ratios were  $1.07 \pm 0.1$  and  $1.06 \pm 0.04$ , respectively. Two years after surgery, MIBG scintigraphy demonstrated a persistent decrease in ventricular sympathetic nerve uptake of the tracer (H/L =  $2.11 \pm 0.3$ ;  $p < 0.05$  versus presurgery). Beta adrenergic receptor density was  $29.4 \pm 2.2$  pmole/ml tissue, a value not different from that observed before surgery.

Following surgical denervation, early (1 mo) and late (6 mo) up-regulation of  $\beta$ -AR was observed (1,4), while MIBG myocardial uptake remained low. A partial reinnervation by the sympathetic nervous system usually occurs within the 6 mo to 1 yr following denervation (5). Kaye et al. demonstrated that the density of ventricular sympathetic neurons remained too low to restore normal ventricular norepinephrine levels 1 yr after denervation (5). Therefore, we did not perform any measurement at that time. Two years after surgery, partial ventricular sympathetic reinnervation occurred, as coarsely assessed by MIBG planar scintigraphy and the relatively insensitive H/L index. Despite this scintigraphic result, it is likely that myocardial norepinephrine content has returned to subnormal value since  $\beta$ -AR density is similar to that measured before surgery.

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### Clinically Silent Adrenal Masses

**TO THE EDITOR:** Some slight arithmetic errors seem to have slipped into the otherwise impressive series of adrenal images presented by Gross et al. (1) For instance, the article mentions 44 intra-adrenal neoplasms, whereas only 43 are represented in Table 1 of the original article. Similarly, 14 cases of adenoma with normal patterns are mentioned in Table 2, whereas the text implies that there are only 12. Finally, the number of adenomas is inconsistently given as 185 or 171.

More important, however, an error was made in data analysis. The authors define true-negative as a concordant pattern of imaging in adenoma or a normal pattern in periadrenal or pseudoadrenal masses. This implies that the imaging test is being judged with respect to the diagnosis of destructive adrenal lesions. In that case, however, the 14 adenomas which yielded symmetrical images can not be considered as false-negatives but should be viewed as true-negatives, because the scans in these cases do not raise the suspicion of a destructive lesion. In other words, even if these adenomas are misclassified as normal, their classification as cases without destructive adrenal lesions is correct. Table 1 gives the values for the test parameters that are obtained when these changes are considered.

Alternative analyses can be performed if the aim of the test is to diagnose adenoma or the presence of any adrenal lesion. The corresponding test parameters are also given in Table 1. As can be seen, the negative predictive value is quite different according to the purpose of the test. The absence of a discordant pattern (negative test for destructive lesion) is highly predictive (98%) for the absence of a destructive lesion, whereas the absence of a

**TABLE 1**  
Efficacy of NP-59 Scintigraphy for Different Diagnoses

Diagnosis	Destructive lesion	Adenoma	Any adrenal lesion
Sensitivity	93%	92%	92%
Specificity	100%	100%	100%
Accuracy	99%	94%	93%
Predictive value of a negative test	98%	80%	41%
Predictive value of a positive test	100%	100%	100%