Myocardial Effects of Propofol in Hamsters with Hypertrophic Cardiomyopathy

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Background: Propofol is a short-acting intravenous induction agent that induces cardiovascular depression but without significant effect on intrinsic myocardial contractility in various species. However, its effects on diseased myocardium remain unknown.

Methods: The effects of propofol (1, 3, and 10 µg·ml⁻¹) on the intrinsic contractility of left ventricular papillary muscles from normal hamsters and those with hypertrophic cardiomyopathy (strain BIO 14.6, aged 6 months) were investigated in vitro (Krebs-Henseleit solution, 29°C, pH 7.40, Ca¹⁺ 2.5 mmol·l⁻¹, stimulation frequency 3/min).

Results: Cardiac hypertrophy (143 ± 13%, P < 0.001) was observed in cardiomyopathic hamsters. The contractility of papillary muscles from hamsters with cardiomyopathy was less than that of controls, as shown by the decrease in maximum shortening velocity (−29%, P < 0.03) and active isometric force (−51%, P < 0.001). Propofol did not induce any significant effect on contraction, relaxation, and contraction-relaxation coupling under low and high loads in normal hamsters. The effects of propofol were not significantly different between normal hamsters and those with cardiomyopathy. A slight but significant increase in maximum unloaded shortening velocity was observed in cardiomyopathic hamsters at 3 µg·ml⁻¹ (4 ± 6%, P < 0.05) and 10 µg·ml⁻¹ (7 ± 6%, P < 0.05).

Conclusions: Propofol did not modify intrinsic myocardial contractility in normal hamsters, and no significant differences were observed between normal and cardiomyopathic hamsters. These results may be useful because, unlike propofol, most anesthetics decrease myocardial contractility. Nevertheless, indirect cardiac effects of propofol may be more important than its direct cardiac effects in patients with impaired cardiac function. (Key words: Anesthetics, intravenous: propofol. Heart: cardiomyopathy. Heart, papillary muscle: contractility; relaxation.)

PROPOFOL is a short-acting intravenous induction agent widely used for induction and maintenance of anesthesia, and sedation in the postoperative period and in the critically ill patient. Propofol induces cardiovascular depression, which is thought to be mainly related to a decrease in sympathetic activity¹ and a vasodilatory effect.²,³ The effects of propofol on intrinsic myocardial contractility remained debatable over a long period. Because of concomitant changes in preload, systemic resistance, sympathetic activity, and central nervous system activity, the precise effects of propofol on intrinsic myocardial contractility are difficult to assess in vivo. Most in vitro studies demonstrated that propofol has no significant isotropic effect in various species, including the rat,⁴ rabbit,⁵ and dog.⁶ The effects of propofol on diseased myocardium remain unknown. It has been demonstrated that the myocardial effects of anesthetic agents may differ between normal and diseased myocardium.⁸,⁹ The various strains of Syrian hamsters with hereditary cardiomyopathy offer an opportunity to investigate the effects of anesthetic agents on intrinsic myocardial contractility.⁸,⁹ Indeed, contractility, cellular biochemistry, molecular biology, and pathophysiology have been studied extensively in this model, the time course of heart failure is well known, and impairment in contractility is primarily due to cardiac muscle cell disease, and thus may be more relevant to clinical cardiomyopathies.¹⁰,¹¹ We therefore conducted an in vitro study of the effects of propofol on intrinsic contractility of left ventricular papillary muscles from normal hamsters and those with cardiomyopathy.

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Received from Laboratoire d’Anesthésiologie, Département d’Anesthésie-Réanimation, Groupe hospitalier Pitié-Salpêtrière, Université Paris VI, Paris; the Institut National de la Santé et de la Recherche Médicale Unité 275, LOA-ENSTA-Ecole Polytechnique, Palaiseau; and Service de Physiologie, Hôpital de Bicêtre, Université Paris Sud, Le Kremlin-Bicêtre, France. Submitted for publication July 15, 1994. Accepted for publication October 27, 1994. Supported by Institut National de la Santé et de la Recherche Médicale (Contrat de Recherche Externe 92-0413) and the Association Française contre la Myopathie. Dr. M. Lejay was the recipient of a fellowship grant from the Fondation pour la Recherche Médicale.
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Materials and Methods

Animals
Six normal Syrian hamsters (strain F1B) and nine cardiomyopathic Syrian hamsters (strain BIO 14.6) were used in the current study (Bio Breeders, Fitchburg, MA). In this strain, all animals of both sexes develop hypertrophic cardiomyopathy from the age of 6 weeks. Care of the animals conformed to the recommendations of the Helsinki Declaration, and the study was performed in accordance with the regulations of the official edict of the French Ministry of Agriculture. All animals were 6 months of age. Body weight (BW), heart weight (HW), and left ventricular weight (LVW) were determined at the moment of killing. HW/BW and LVW/BW ratios were calculated. Cardiac hypertrophy was determined by dividing the HW/BW value of each cardiomyopathic hamster by the mean HW/BW value in normal hamsters.

Experimental Protocol
Twenty-two left ventricular papillary muscles (1–2 from each hamster) were studied. After brief anaesthesia with ether, the hearts were quickly removed and left ventricular papillary muscles were carefully excised and suspended vertically in a 200-ml jacketed reservoir with Krebs-Henseleit bicarbonate buffer solution containing (mmol·L⁻¹) NaCl 118, KCl 4.7, MgSO₄ 1.2, KH₂PO₄ 1.1, NaHCO₃ 25, CaCl₂ 2.5, and glucose 4.5. The Krebs-Henseleit solution was daily prepared with highly purified water (Ecopure, Bioblock, Illkirch, France). The jacketed reservoir was maintained at 29°C with a thermostatic water circulator (Polystat 5HP, Bioblock) and a continuous monitoring of the solution temperature (Pt100 temperature probe, Bioblock). Preparations were field-stimulated at 3/min by two platinum electrodes with rectangular wave pulses of 5-ms duration just above threshold. The bathing solution was bubbled with 95% O₂/5% CO₂, resulting in a pH of 7.40. After a 90-min stabilization period at the initial muscle length at the apex of the length-active isometric tension curve (Lₘₐₓ), papillary muscles recovered their optimal mechanical performance, which remained stable for many hours.

Control values of each mechanical parameter were recorded. Because propofol is insoluble in aqueous media, we tested the commercially available form of propofol in which a soya bean emulsion is the solvent (Diprivan, Zeneca Pharma, Cergy-Pontoise, France). The solvent has been shown to be devoid of significant effect on intrinsic myocardial contractility.⁴ Concentrations of propofol during anesthesia range from 1 to 10 μg·ml⁻¹.¹²,¹³ Propofol is highly bound (96–98%) to plasma protein, but this does not seem to influence its rapid disappearance from the blood and extensive tissue distribution.¹³ Thus, three concentrations of propofol were tested in a cumulative manner: 1 μg·ml⁻¹ (5.6 μmol·L⁻¹), 3 μg·ml⁻¹ (16.8 μmol·L⁻¹), and 10 μg·ml⁻¹ (56.4 μmol·L⁻¹), with 15 min elapsing between each dose, as previously reported in rat myocardium.⁴

Electromagnetic Lever System and Recording
The electromagnetic lever system has been described previously.¹⁴ Briefly, the load applied to the muscle was determined by means of a servomechanism-controlled current through the coil of an electromagnet. Muscular shortening induced a displacement of the lever, which modulated the light intensity of a photoelectric transducer. All analyses were made from digital records of force and length obtained with a computer, as previously described.⁴ The recording speed was one A/D (12 bits) conversion every 1 ms, for a total recording time of 500 ms.

Mechanical Parameters
Conventional mechanical parameters at Lₘₐₓ were calculated from three twitches. The first twitch was isotonic and was loaded with the preload corresponding to Lₘₐₓ. The second twitch was abruptly clamped to zero-load just after the electrical stimulus; the muscle was released from preload to zero-load with a critical damping to slow the first and rapid shortening overshoot resulting from the recoil of series passive elastic components, as previously reported;¹⁴ the maximum unloaded shortening velocity (Vₘₐₓ) was determined from this twitch. The third twitch was fully isometric at Lₘₐₓ.

The mechanical parameters characterizing the contraction and relaxation phases, and the coupling between contraction and relaxation are defined as follows.

Contraction Phase. We determined Vₘₐₓ using the zero-load clamp technique; maximum extent of shortening (Dₐₘₐₓ) and maximum shortening velocity (Vₘₐₓ) of the twitch with preload only; maximum isometric active force normalized per cross-sectional area (AF); and the peak of the positive force derivative normalized per cross-sectional area (+dF/dt) (Vₘₐₓ and AF tested the inotropic state under low and high loads, respectively).

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Relaxation Phase. We determined maximum lengthening velocity of the twitch with preload only \(\text{L}_{\text{max}}, \text{Vr}\) and the peak of the negative force derivative at \(\text{L}_{\text{max}}\) normalized per cross-sectional area \((-\text{dF}/\text{dt}^{-1})\). These two parameters tested the lusitropic state under low- and high-loading conditions, respectively. Because changes in the contraction phase induce coordinated changes in the relaxation phase, variations in contraction and relaxation must be considered simultaneously to quantify drug-induced changes in lusitropy. Therefore, indexes of contraction-relaxation coupling have been developed.\(^{16}\)

Contraction-Relaxation Coupling. Coefficient R 1 = \(\frac{\text{Vc}}{\text{L}_{\text{max}}, \text{Vr}}\) tests the coupling between contraction and relaxation under low load. Under isometric conditions, the amplitude of sarcomere shortening is twice that observed under isometric conditions.\(^{17}\) Because of the lower sensitivity of myofilament for calcium when cardiac muscle is markedly shortened under low load, relaxation proceeds more rapidly than contraction, apparently due to the rapid uptake of calcium by the sarcoplasmic reticulum (SR). Thus, R1 (contraction-relaxation coupling under low load) is significantly less than 1 and tests SR function. Coefficient R2 = \((\text{+dF}/\text{dt}^{-1})/(-\text{dF}/\text{dt}^{-1})\) tests the coupling between contraction and relaxation under high load. When the muscle contracts isometrically, sarcomeres shorten very little.\(^{17}\) Because of a higher sensitivity of myofilament for calcium,\(^{18}\) the relaxation time course is determined by calcium unbinding from troponin C rather than by calcium sequestration by the SR. Thus, R2 (contraction-relaxation coupling under heavy load) is greater than 1 and reflects myofilament calcium sensitivity.

At the end of the study, the muscle cross-sectional area was calculated from the length and weight of papillary muscle, assuming a density of 1. Shortening and lengthening velocities were expressed in \(\text{L}_{\text{max}} \cdot \text{s}^{-1}\), force in \(\text{mN} \cdot \text{mm}^{-2}\), and force derivative in \(\text{mN} \cdot \text{mm}^{-2} \cdot \text{s}^{-1}\).

Statistical Analysis

Data are expressed as mean ± SD. Control values in normal hamsters and those with cardiomypathy were compared by means of the Student's t test. The effects of propofol in normal hamsters and those with cardiomypathy were compared by repeated-measures analysis of variance and Student-Newman-Keuls test. All P values were two-tailed, and a P value of less than 0.05 was required to reject the null hypothesis. Statistical analysis was performed on a personal computer using PCSM software (Deltasoft, Meylan, France).

Results

HW and LVW were not significantly different between normal hamsters and those with cardiomypathy. However, the HW/BW and LVW/BW were significantly greater in cardiomypathic hamsters, indicating marked cardiac hypertrophy (table 1). The intrinsic mechanical performance of papillary muscles from hamsters with cardiomypathy was significantly lower during isometric (AF, \(+\text{dF}/\text{dt}^{-1}\)) and the isotonic (\(\text{Dl}_{\text{max}}, \text{V}_{\text{max}}\)) twitches (table 2). R1, which tests the contraction-relaxation coupling under low load, and thus SR function, was not significantly different between the two groups. In contrast, R2, which tests the contraction-relaxation coupling under high load, and thus the myofilament calcium sensitivity, was significantly lower in cardiomypathic hamsters than in controls.

Propofol induced no significant inotropic effect on normal muscles as shown by the absence of changes in \(\text{V}_{\text{max}}\) (fig. 1) and active isometric force (fig. 2). No differences in these inotropic parameters were observed between normal hamsters and those with cardiomypathy (figs. 1 and 2), but a slight significant increase in \(\text{V}_{\text{max}}\) was noted at 3 \(\mu\text{g} \cdot \text{mL}^{-1}\) (+4 ± 6%) and 10 \(\mu\text{g} \cdot \text{mL}^{-1}\) (+7 ± 6%) propofol in cardiomypathic muscles (fig. 1). Because contractile properties varies from one papillary muscle to another in cardiomypathy hamsters, papillary muscles were divided into two groups: those with a severe myocardial failure (\(i.e., \text{AF}\) of less than 25 \(\text{mN} \cdot \text{mm}^{-2}\); \(n = 6; \text{AF} = 16 ± 8 \text{mN} \cdot \text{mm}^{-2}\)) and those with a moderate myocardial failure (\(n = 7, \text{AF} = 32 ± 6 \text{mN} \cdot \text{mm}^{-2}\)). At the highest concentration

Table 1. Characteristics of Normal Hamsters and Those with Cardiomypathy

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal Hamsters (n = 6)</th>
<th>Cardiomypathic Hamsters (n = 9)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>BW (g)</td>
<td>135 ± 6</td>
<td>94 ± 17</td>
<td>0.001</td>
</tr>
<tr>
<td>HW (mg)</td>
<td>396 ± 24</td>
<td>390 ± 51</td>
<td>NS</td>
</tr>
<tr>
<td>LVW (mg)</td>
<td>275 ± 29</td>
<td>267 ± 40</td>
<td>NS</td>
</tr>
<tr>
<td>HW/BW (10^-3)</td>
<td>2.92 ± 0.10</td>
<td>4.17 ± 0.36</td>
<td>0.001</td>
</tr>
<tr>
<td>LVW/BW (10^-3)</td>
<td>2.03 ± 0.17</td>
<td>2.85 ± 0.24</td>
<td>0.001</td>
</tr>
<tr>
<td>Cardiac hypertrophy (%)</td>
<td>100</td>
<td>143 ± 13</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Data are mean ± SD.

NS = not significant; BW = body weight; HW = heart weight; LVW = left ventricular weight.
Table 2. Characteristics of Left Ventricular Papillary Muscles from Normal Hamsters and Those with Cardiomyopathy

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal Hamsters (n = 10)</th>
<th>Cardiomyopathic Hamsters (n = 12)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>L_max (mm)</td>
<td>3.2 ± 0.8</td>
<td>2.9 ± 0.6</td>
<td>NS</td>
</tr>
<tr>
<td>CSA (mm²)</td>
<td>0.70 ± 0.16</td>
<td>0.83 ± 0.19</td>
<td>NS</td>
</tr>
<tr>
<td>RF/TF</td>
<td>0.13 ± 0.05</td>
<td>0.25 ± 0.19</td>
<td>NS</td>
</tr>
<tr>
<td>Dl_max (% L_max)</td>
<td>18 ± 2</td>
<td>12 ± 4</td>
<td>0.001</td>
</tr>
<tr>
<td>V_max (L_max · s⁻¹)</td>
<td>3.32 ± 0.32</td>
<td>2.34 ± 0.69</td>
<td>0.03</td>
</tr>
<tr>
<td>maxVo (L_max · s⁻¹)</td>
<td>2.15 ± 0.22</td>
<td>1.42 ± 0.51</td>
<td>0.001</td>
</tr>
<tr>
<td>maxVr (L_max · s⁻¹)</td>
<td>2.69 ± 0.52</td>
<td>1.72 ± 0.74</td>
<td>0.002</td>
</tr>
<tr>
<td>AF (mN·mm⁻²·s⁻¹)</td>
<td>51 ± 18</td>
<td>25 ± 11</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Data are mean ± SD.
NS = not significant; L_max = initial length; CSA = cross-sectional area; RF/TF = ratio of resting force to total force; Dl_max = maximum extent of shortening; V_max = maximum unloaded shortening velocity; maxVo = maximum shortening velocity; maxVr = maximum lengthening velocity; AF = isometric active force normalized per CSA; +dF·dt⁻¹ = peak of the positive force derivative normalized per CSA; -dF·dt⁻¹ = peak of the negative force derivative normalized per CSA; R1 = maxVo/maxVr; R2 = +dF·dt⁻¹/-dF·dt⁻¹

Fig. 1. Comparison of the effects of propofol on maximum unloaded shortening velocity (V_max) of papillary muscles from normal hamsters and those with cardiomyopathy. Data are mean ± SD. Between-group difference was not significant (NS). *P < 0.05 versus control values.

Fig. 2. Comparison of the effects of propofol on isometric active force (AF) normalized per cross-sectional area of papillary muscles from normal hamsters and those with cardiomyopathy. Data are mean ± SD. Between-group difference was not significant (NS).

of propofol (10 μg·ml⁻¹), there was no significant difference in the percent change in AF between papillary muscles with severe myocardial failure (113 ± 8%) and those with moderate myocardial failure (102 ± 10%).

Under isotonic conditions, propofol had no significant lusitropic effect (maxVr, data not shown) in normal hamsters, resulting in no significant changes in contraction-relaxation coupling (R1), and no significant differences were noted between normal hamsters and those with cardiomyopathy (fig. 3). Under isometric conditions, propofol had no lusitropic effect (−dF·dt⁻¹, data not shown) in normal hamsters, resulting in no significant changes in contraction-relaxation coupling (R2), and no significant differences were noted between normal hamsters and those with cardiomyopathy (fig. 4).

Discussion

In the present study, we observed that propofol induced no significant effects on the intrinsic mechanical properties of left ventricular papillary muscles from normal hamsters and that there were no significant differences in the effects of propofol in normal hamsters and those with cardiomyopathy.

Numerous studies indicate that propofol administration is associated with cardiovascular depression.¹⁹,²⁰

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However, the precise effects of propofol on myocardial contractility remain debatable. The effects of a drug on intrinsic myocardial contractility are difficult to assess in vivo because of changes in heart rate, preload, and afterload, especially with anesthetic agents known also to decrease oxygen demand and central nervous system activity, and consequently cardiac output. Moreover, propofol is known to markedly decrease preload and sympathetic activity. Most recent in vitro studies observed that propofol has no significant inotropic effect on myocardium in various species, including the rat, rabbit, and dog. Nevertheless, it is clear that a negative inotropic effect can be observed with propofol in the ferret and guinea pig myocardium, and in certain experimental conditions that are associated mainly with ischemia. The mechanisms of the negative inotropic effect of propofol in the guinea pig and the ferret myocardium have been explained. Propofol appears to decrease calcium availability within the myocardium, based upon studies in ferrets in which there is no change in the myofilament calcium sensitivity. Depression of the cardiac action potential plateau and duration in guinea pig myocardium suggest that calcium current may be depressed, but this effect does not occur in rat myocardium. However, it should be pointed out that Azuma et al. tested supratherapeutic propofol concentrations (i.e., up to 600 mol·l\(^{-1}\)) in guinea pig myocardium, and that Park and Lynch were unable to demonstrate depression of action potential duration and rate of depolarization at lower concentrations in the guinea pig, suggesting that the effect of propofol on calcium cardiac currents is modest. Our study showed that propofol induced no significant effect on intrinsic myocardial contractility in the hamster, as previously reported in rat, rabbit, and dog myocardium.

Propofol did not modify contraction-relaxation coupling under low load (R1). Under isometric conditions, the amplitude of sarcomere shortening is twice that observed in isometric conditions, and the time course of isotonic relaxation occurs earlier and more rapidly than that of isometric relaxation, partly through two mechanisms: (1) the easier removal of calcium from troponin C, due to a decrease in myofilament calcium sensitivity, and (2) the rapid uptake of calcium by the SR. Under low load, the SR appears to play a major role in the regulation of isotonic relaxation. Our results therefore suggest that propofol did not modify the uptake of calcium by the SR. This result contrasts with that previously obtained in rat myocardium. Indeed, in rat myocardium, propofol increased R1, suggesting a decrease in the uptake SR function. Two hypotheses can explain this discrepancy: (1) the effects of propofol on SR function were too small in hamster myocardium to be detected; indeed, the effects of propofol in rat myocardium were moderate because it did not induce

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Fig. 3. Comparison of the effects of propofol on contraction-relaxation coupling under low load (R1 = \(\frac{\text{max Ve}_\text{max Vr}}{}\)) of papillary muscles from normal hamsters and those with cardiomyopathy. Data are mean ± SD. Between-group difference was not significant (NS).

Fig. 4. Comparison of the effects of propofol on contraction-relaxation coupling under high load (R2 = \(\frac{\text{max Ve}_\text{max Vr}}{}\)) of papillary muscles from normal hamsters and those with cardiomyopathy. Data are mean ± SD. Between-group difference was not significant (NS).
any significant negative inotropic effect; (2) the effects of propofol on SR function did not occur in hamster myocardium; it is well known that the contribution of SR function to contractility is higher in the rat than in other species.25

The contraction-relaxation coupling under high load (R2) was not modified by propofol. Under isometric conditions and because of the slight sarcomere shortening, myofilament calcium sensitivity is less decreased than in isotonic conditions and becomes the limiting step that appears to play a major role in the regulation of the time course of isometric relaxation. The absence of any lusitropic effect of propofol under high load suggests that it did not modify the myofilament calcium sensitivity, as previously reported in rat myocardium.4

Genetically induced cardiomyopathy in Syrian hamsters is characterized by the progressive occurrence of focal myocardial degeneration, fibrosis, and calcifications during the life of the animal.10,11 At age 30–40 days, histologic lesions become apparent and myocardial performance decreases. Further cardiac changes include hypertrophy and/or dilation, depending on the strain, then congestive heart failure and death. In our study, myocardial contractility was markedly impaired in cardiomyopathic muscles, as reflected by the decrease in Vmax and AF (table 2). The decreased myocardial contractility in cardiomyopathic hamsters may be explained by the decreased activity of G proteins;26 decreased sarcoplasmic Ca++ and Na++-K+ ATPase activities,27 alterations in Na-Ca exchange,28 decreased conductance28 and density29 of voltage-sensitive calcium channels, alterations in the creatine kinase system,30 modifications in myofilament calcium sensitivity,30 alteration in actin regulatory proteins,41 and iso- myosin shift.52 Nevertheless, a decrease in SR function is not observed in all strains, and the strain used in the current study (BIO 14.6), which develops hypertrophic cardiomyopathy, has been shown to exhibit normal SR function.53 In the current study, the lack of significant increase in R1 is consistent with these results and concords with results previously obtained in another strain with hypertrophic cardiomyopathy (UMX 7.1).44 In contrast, R2 of hamsters with cardiomyopathy was lower than that of the controls, suggesting that myofilament calcium sensitivity was lower in hamsters with cardiomyopathy, as previously reported.8,9,34

Because of the complex action of anesthetic agents on cardiac muscle and because of the various pathologic changes observed in the myocardium of cardiomyopathic hamsters, it is not easy to predict the mechanical effects of anesthetic agents on this diseased myocardium. Indeed, it has been demonstrated that the mechanical effects of ketamine6 and etomidate9 differ in normal and hamsters with cardiomyopathy. In contrast, in the current study, we observed that the mechanical effects of propofol did not differ in left ventricular papillary muscles from normal and cardiomyopathic hamsters. Although the effect of propofol on Vmax was not significantly different in both groups, a slight but significant increase in Vmax was noted in cardiomyopathic hamsters. This slight effect must be interpreted with caution. Three hypotheses may explain this slight increase in Vmax: (1) propofol actually increased Vmax; (2) the increase in Vmax was related to a slight increase in Vmax with time in cardiomyopathic hamsters despite a prolonged recovery period before drug testing; it should be pointed out that such a slight increase in Vmax was also previously noted with etom- idate in hamsters with cardiomyopathy;2 (3) the increase in Vmax was related to the solvent, which may have served as a metabolic substrate in cardiomyopathic muscle, as previously suggested.52 In any event, this very moderate increase in Vmax without significant changes in active isometric force has probably no clinical relevance. Because hamsters with cardiomyopathy were relatively young (age 6 months) and because myocardial abnormalities are more prominent in end-stage disease, it is possible that the result would have been different had the animals been older and sicker. However, myocardial abnormalities are not homogeneous among different hamsters of the same age and are not homogeneous within the entire myocardium of each hamster. We observed several deaths in 6-month-old hamsters, and thus, when studying older hamsters with cardiomyopathy, one cannot rule out the hypothesis that these older hamsters had less severe cardiomyopathy. It is the reason why we divided papillary muscles into two groups, those with severe myocardial failure and those with moderate myocardial failure, and we observed that the effect of propofol did not significantly differ between these two groups.

The following points must be considered in the assessment of the clinical relevance of our results. First, because this study was conducted in vitro, it dealt only with intrinsic myocardial contractility. Observed changes in cardiac function after in vivo propofol administration also depend on modifications in venous return, afterload, and compensatory mechanisms. This point should be of special importance in patients with cardiomyopathy whose cardiac function does not de-
pend only on intrinsic contractility but also on preload, afterload, and sympathetic activity. Second, this study was conducted at 29°C at a low-stimulation frequency; however, papillary muscles must be studied at this temperature because stability of mechanical parameters is not sufficient at 37°C and at a low frequency because high-stimulation frequency induces core hypoxia. Moreover, higher stimulation rates frequently induce extrasystoles in cardiomyopathic muscles, resulting in an unreliable recording of mechanical parameters. Third, it was performed on hamster myocardium, which differs from human myocardium. In hamster myocardium as in rat, a negative staircase effect is observed (an increase in stimulation frequency decreases force), contractility is high, and myosin isoforms are predominantly of the V1 type. Furthermore, because propofol is highly bound to plasma protein and because the bathing solution was protein-free, the concentrations tested might be considered high.

In conclusion, in studies conducted on isolated left ventricular papillary muscle, propofol did not modify intrinsic myocardial contractility in normal hamsters, and no significant differences were observed between normal hamsters and those with cardiomyopathy. These results could be important because most anesthetic agents decrease myocardial contractility and propofol is widely used for the sedation of critically ill patients whose cardiac function may be impaired. However, the indirect effects of propofol may be more important than its direct cardiac effects in such conditions.

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