The Inotropic Effect of Cyclopropane Anesthesia upon the Intact Dog Heart

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The effect of cyclopropane anesthesia on the intrinsic state of the myocardium of the intact heart was determined by means of force–velocity relations in 14 dogs. The maximal intrinsic velocity ($V_{\text{max}}$), an index of myocardial contractility, was obtained before and during anesthesia by extrapolating either the force–velocity curve using stress calculation or the isovolumic force–velocity curve using the simplified formula of $(dP/dt)/k_p$ as the contractile element velocity. Cyclopropane (arterial blood concentration ranging from 9 to 46 mg/100 ml) did not cause any significant change in $V_{\text{max}}$ in either shape or position of the force–velocity curves. The average change in $V_{\text{max}}$ was $-6$ per cent ($P > 0.2$). These findings indicate that cyclopropane anesthesia does not alter myocardial contractility. (Key words: Myocardial contractility; Cyclopropane anesthesia; Force–velocity relations.)

Assessment of myocardial function in intact subjects during administration of general anesthetic agents has been difficult. The problem has been to separate changes in fundamental function of the heart as a muscle from those of cardiac output and its related hemodynamics. Most studies of the effects of cyclopropane upon the heart and circulation have been concerned primarily with indices of cardiac response related to changes in venous return. These hemodynamic measures are related to the performance of the heart as a pump, but not to changes in the intrinsic contractile state of the myocardium (i.e., contractility).

Recent studies show that changes in myocardial performance in vivo during anesthesia are determined by the force–velocity relationship. Accordingly, the present study was undertaken to determine the effects of cyclopropane upon the intrinsic contractile properties of the intact dog heart by means of measuring force–velocity relations.

Methods

Fourteen dogs (weights $17.8 \pm 0.70$ kg), each serving as its own control, were studied. The dogs were anesthetized with a chloralose–urethan solution (chloralose: 150 mg/kg; urethan: 750 mg/kg) injected intravenously. The trachea of each dog was intubated with a cuffed endotracheal tube after intravenous administration of gallamine triethiodide (Flaxedil) (40 mg, i.v.). Controlled ventilation (with 100 per cent oxygen) was maintained throughout the experiment. A sternum-splitting thoracotomy was performed, and the root of the aorta exposed for placement of a non-cannulating blood flowmeter probe.

Aortic and ventricular pressures were monitored with wide-bore cannula attached to Statham P23Db transducers. The rate of left ventricular pressure development $(dP/dt)$ was computed continuously with an electronic differentiator, the amplitude of which was a linear function of frequency to 40 cycles/sec. A thermistor was inserted in the descending aorta for measurements of the left ventricular ejection fraction by means of the thermodilution technique. All values were recorded with the electrocardiogram on a multichannel oscillograph (Sanborn Model 560) at a paper speed of 200 mm/sec. Using Simpson's rule, stroke volume was computed by integrating the area under the ejection-rate curve.

Before and during cyclopropane anesthesia, two methods were used for assessment of the
maximal intrinsic velocity of shortening ($V_{\text{max}}$) as an index of myocardial contractility. The first was related to a stress (or tension) calculation from data obtained in a single isovolumic left ventricular contraction, previously described in detail (Method I). In brief, an isovolumic left ventricular contraction was produced by a sudden occlusion of the aorta in order to obtain data necessary for calculation of instantaneous force–velocity relations. Analyses of force–velocity relations were made at 5-msec intervals through systole. All computations derived for calculation of contractile element velocity ($V_{\text{cm}}$) and ventricular tensile force ($F$) were made by means of an IBM system 360 model 30 digital computer. $V_{\text{max}}$ was obtained by extrapolation of the curve to zero stress.

In the second method, $V_{\text{max}}$ was obtained by extrapolating the isovolumic force–velocity curve, constructed by plotting $(dP/dt)/kP$ against the corresponding intraventricular pressure ($P$) in a manner described previously (Method II).²

### Results

**Force–Velocity Relations**

Effects of cyclopropane anesthesia on force–velocity relations, using stress calculation (Method I), were studied during 27 determinations in five dogs. Each force–velocity curve was constructed by plotting average values of myocardial force per unit of length of circumference ($F_{\text{cm}}$) against those of shortening velocity of the contractile element ($V_{\text{cm}}$) in cm/sec. Figure 1 represents the force–velocity curves obtained in one dog before and during cyclopropane anesthesia.

Results in the other four dogs were similar to those shown in figure 1. Mean values of $V_{\text{max}}$ before and during cyclopropane anesthe-
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Figure 2. Mean values of $V_{\text{max}}$ (maximal velocity of shortening) on the left and those of $P_e$ (maximal isometric force) on the right before (open bars) and during (hatched bars) cyclopropane anesthesia.

Hemodynamic Effects

Pertinent data are summarized in Table 1 and Figures 3-6. During cyclopropane anesthesia, cardiac output fell 26 per cent ($P > 0.05$). Average stroke volume was reduced 6 per cent ($P > 0.05$). Heart rate decreased significantly during anesthesia, the average change being $-19.4$ per cent ($P < 0.05$). Mean aortic pressure was reduced by 12.9 per cent ($P > 0.1$). The average change in left ventricular rate of pressure rise (LV $dP/dt$) during anesthesia was $-44.7$ per cent ($P < 0.01$). Percentage changes in left ventricular end-diastolic pressure and volume were $-3.8$ ($P > 0.5$) and $+36.0$ ($P > 0.05$), respectively.

Discussion

Results of the present study indicate that cyclopropane anesthesia does not alter the maximal intrinsic velocity of shortening ($V_{\text{max}}$), an index of myocardial contractility, in the intact dog heart. Also, hemodynamic changes

| Table 1. Hemodynamics in Five Dogs before and during Cyclopropane Anesthesia |
|---------------------------------|---------------------------------|-----------------|
|                                | Control                         | During Anesthesia |
|                                | (Mean ± SE)                     | (Mean ± SE)     |
| Cardiac output (l/min)         | 0.93 ± 0.18                     | 0.68 ± 0.04     |
| Stroke volume (ml/beat)        | 5.0 ± 1.0                       | 4.6 ± 0.3       |
| Heart rate (beats/min)         | 180 ± 4.9                       | 130 ± 7.2       |
| Mean aortic pressure (mm Hg)   | 101 ± 1.0                       | 88 ± 1.3        |
| Maximum LV $dP/dt$ (mm Hg/sec) | 1717 ± 526                      | 949 ± 65        |
| LVED pressure (cm H$_2$O)      | 5.2 ± 1.1                       | 5.4 ± 0.7       |
| LVED volume (ml)               | 28 ± 2.3                        | 24 ± 2.3        |

$P > 0.05$
Fig. 3. Mean values of cardiac output on the left and those of stroke volume on the right before (open bars) and during (hatched bars) anesthesia.

Fig. 4. Average values of mean aortic pressure and heart rate before (open bars) and during (hatched bars) anesthesia.

Fig. 5. Mean values of maximal rate of left ventricular pressure rise (LV dp/dt) before (open bar) and during (hatched bar) anesthesia.

do not correlate with changes in the inotropic state of the myocardium (myocardial contractility). The high reproducibility of $V_{\text{max}}$ determined by Method I and Method II in dogs anesthetized with basal anesthetics alone has been reported. Results of the present study are in accord with our previous findings of unchanged left and right ventricular function curves (i.e., relationship between the ventricular end-diastolic pressure and external stroke work) during cyclopropane anesthesia in the intact dog. At any given myocardial force, the velocity of shortening of the contractile element ($V_{\text{ce}}$) during anesthesia was unchanged compared with that in the control state. Since the product of force and velocity is the contractile element power, cyclopropane
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Fig. 6. Mean values of left ventricular end-diastolic (LVED) pressure on the left and those of volume on the right before (open bars) and during (hatched bars) anesthesia.

\[ \pm 1 \text{SEM} \]

LVED Pressure

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\( P > 0.5 \)

LVED Volume

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\( P > 0.05 \)

did not alter the rate of doing work (i.e., power). Findings of unaltered maximal velocity and contractile element power during anesthesia indicate that the intrinsic contractile properties of the myocardium (contractility) are not altered.

In the present study, we also found that the maximum slope of left ventricular systolic pressure (LV dP/dt) decreased significantly during anesthesia in spite of unchanged maximal intrinsic velocity. Recently, the usefulness and limitations of the rate of rise of intraventricular pressure (dP/dt) in the evaluation of myocardial contractility have been described.\(^8\) Ventricular dP/dt depends upon many influences unrelated to alteration in the isotropic state of the heart. At a given intrinsic isotropic state (contractility), the loading conditions under which the heart operates alter the maximal ventricular dP/dt.\(^9\) Thus, when ventricular end-diastolic pressure and volume (preload) are elevated by the augmentation of venous return, the maximal dP/dt increases. Ventricular dP/dt is also affected by alteration of mean aortic pressure (afterload). Therefore, changes in the mean aortic pressure unassociated with those of ventricular contractility influence the rate of the rise of ventricular pressure.\(^9\)\(^-\)\(^10\) Thus, the finding of a decreased maximal dP/dt with unaltered maximal velocity during cyclopropane anesthesia, as observed in the present study, strongly suggests that changes in maximal dP/dt are related to decreases in mean aortic pressure (afterload), and not to changes in contractility. It is evident that the use of maximum rate of intraventricular pressure alone for assessment of myocardial contractility during anesthesia\(^11\) is not warranted.

Our recent studies of isolated cat papillary heart muscle preparations revealed that cyclopropane causes the smallest reductions in both maximal velocity and maximal isometric force of the five anesthetics studied (cyclopropane, Ethane, diethyl ether, methoxyflurane, and halothane). These studies were done at the equipotent level using partial pressures of anesthetics at the minimum alveolar concentrations (MAC).\(^12\) It has been suggested that cyclopropane causes an increase in activity of the sympathetic nerves supplying the heart,\(^12\) evoking a positive isotropic effect on the myocardium.\(^4\)\(^-\)\(^14\) Thus, unaltered myocardial contractility, as evidenced in the present study by unchanged maximal intrinsic velocity, may indicate that the direct negative effect of cyclopropane on the myocardium is antagonized by the indirect effect of the anesthetic on the extrinsic cardiac control mechanism.

References

2. Li TH, Esten B: Effect of cyclopropane anesthesia on cardiac output and related hemodynamics in man. ANESTHESIOLOGY 18:15, 1957

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**Anesthesia**

**TRACHEAL STENOSIS** Prolonged assisted respiration through a tube inserted into the trachea may result in laryngeal and tracheal stenosis. The mechanism is as follows: during inspiration, the trachea is stretched lengthwise and the larynx descends by several millimeters; during expiration, the opposite movement occurs. This creates friction between the balloon and the trachea. Two stenotic rings were seen in one patient whose endotracheal tube had two cuffs that were intermittently inflated. Endotracheal tubes with mobile cuffs have been designed. The balloon is connected to the tube by an elastic membrane; therefore, the balloon fits the wall of the trachea and the tube can easily follow tracheal movements. Other measures to prevent laryngeal and tracheal stenosis in patients needing prolonged ventilatory assistance should be developed. (Kleinsasser, O.: *Endotracheal Catheters with Mobile Cuffs to Avoid Pressure Lesions of the Tracheal Wall*, *Der Anästhesist* 18: 382 (Nov.) 1969.)

**HEPATIC NECROSIS** Biopsy and necropsy materials from patients who became jaundiced after halothane anesthesia were analyzed and compared with tissues from 81,000 autopsies of patients who had received other anesthetics. Eight cases of massive hepatic necrosis were found: three of the patients had had pre-existing viral hepatitis, and one had had serum hepatitis. The remaining four had all received halothane, and no other process could be invoked as a cause for the hepatic disease. Massive hepatic necrosis was never seen postoperatively except when halothane had been the anesthetic. This indicates that the relationship between halothane anesthesia and hepatic necrosis is not fortuitous. The data incriminate obesity as well as recent previous exposures to halothane as risk factors. The histologic evidence suggests that hepatic necrosis is not a simple sensitization to halothane, but that the initial exposure may produce idiosyncratic necrosis of insufficient extent to produce recognizable signs. (Peters, R. L., and others: *Hepatic Necrosis Associated with Halothane Anesthesia*, *Amer. J. Med.* 47: 748 (Nov.) 1969.)