In Vivo Activity of the Right Ventricular Papillary Muscles[1] (35306)

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William Harvey, noting the "fleshy columns" of the heart, speculated that the trabeculae carnae and papillary muscles enable the ventricles to contract more effectually. He observed the meagerness of those structures in the right ventricle and related that observation to the minimal effort required of the right ventricle to propel blood through the lungs (1). The dynamic behavior of the right ventricle is known to be complex (2, 3); understanding of its internal components and their functions is necessary for a functional analysis. Since recent experimentation has been directed exclusively towards function of the left ventricular papillary muscles (4, 5), it was deemed necessary to investigate the right ventricular papillary muscles which have less than half the mass of their left side counterparts (6). This paper deals with the *in situ* contractile behavior of the right ventricular papillary muscles.

Material and Methods. Twelve mongrel dogs of either sex, weighing from 15 to 25 kg were anesthetized with phencyclidine hydrochloride (2 mg/kg im) and alpha-chloralose (80 mg/kg iv). Bilateral thoractomy was performed and the stellate ganglia and cervical vagosympathetic trunks were isolated. Under inflow occlusion a Walton-Brodie strain gauge arch was sutured onto the longitudinal surface of one right ventricular papillary muscle, exposed through an atriotomy. Either of the anterior or posterior papillary muscles were used, primarily the larger anterior one. At the end of each experiment autopsy was performed to verify the location of the gauge and the fact that the underlying musculature was taut. Similar gauges were sutured parallel to the fiber direction of the epicardium of both sinus and conus of the right ventricle. A unipolar electrode attached to one foot of the strain gauge was employed sometimes when measuring right ventricular sinus or left ventricular epicardial contractile force. A standard lead II electrocardiogram, as well as local epicardial electrograms were obtained; femoral and right ventricular sinus cavity pressures were measured with Statham P23Db transducers. Records were obtained via either a type R Dynograph or a Model 7 Grass Polygraph. Nerves were stimulated with a Grass 5-S stimulator with rectangular pulses of 4 V, 10 cps, and 5 msec duration. Digital coarctation of the ascending aorta or main pulmonary artery was performed in a manner to minimize arrhythmias, therefore, generally the coarctations were not severe or of long duration. Infusion of 50 ml of normal saline directly through the AV valve into the right ventricle was performed, often causing arrhythmias. Augmentor drugs were also infused rapidly into the right atrium—norepinephrine (1 μg/kg), isoproterenol (0.05 mg/kg), and phenylephrine (1 μg/kg).

Results. Figure 1 demonstrates the normal pattern of contraction of the right ventricular papillary muscle recorded by a strain gauge (RVP) as related to force generated in the right ventricular conus (RVC) and sinus (RVS) regions. The papillary muscle commenced its force development 60 msec after the Q-wave of the EKG while the sinus and conus regions began to develop force 5 msec later. The papillary muscle contraction began well after the force development of the left ventricular anterior epicardium. All of the recorded right ventricular regional forces in-

[1] Supported by Grant HE 08682 from the National Heart Institute of the National Institutes of Health.

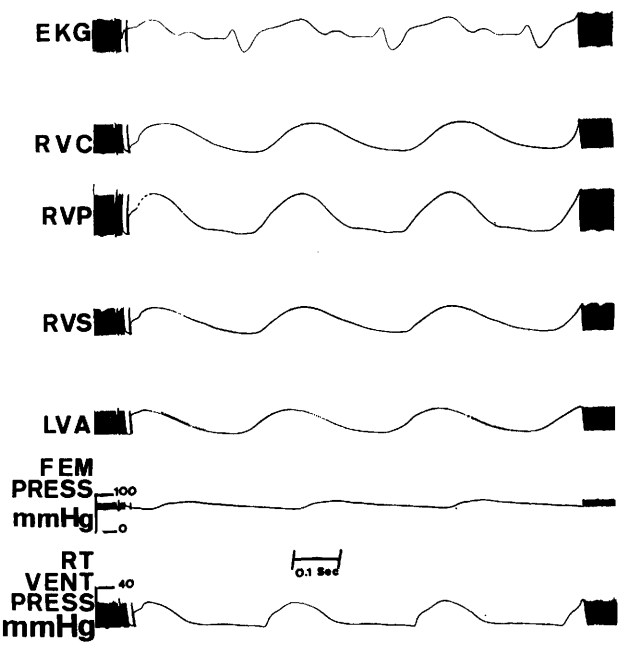

FIG. 1. An electrocardiogram (lead II), right ventricular conus epicardial force (RVC), right ventricular anterior papillary muscle force (RVP), right ventricular sinus epicardial force (RVS), left ventricular anterior epicardial force (LVA), femoral blood pressure, and right ventricular pressure traces. Note that onset of contraction is first in the left ventricular epicardium followed by the right ventricular regional forces.

creased in advance of the sinal intracavitary pressure and their period of sustained elevation exceeded the duration of the pressure elevation.

Figure 2 represents the results of stimulation of both right and left stellate ganglia upon force of contraction of the right ventricular papillary muscle (RVP), as compared with augmentation of contractile force in the epicardial region of the right ventricular sinus (RVS) and the anterior left ventricular epicardium (LVA). The change in contractile force signaled from a gauge sutured onto the right side of the interventricular septum (IVS) is also shown to permit comparison of this endocardial region response with that of the nearby papillary muscle. Electrical activation of both ventricles as well as right ventricular sinus pressures were also recorded. RVE represents an electrical unipolar recording from the right ventricular sinal epicardium and LVE the anterior left ventricular epicardial electrical activity; these two electrical activities began concurrently 5 msec after the onset of the Q wave of the EKG. The augmentation in contractile force for both the right ventricular papillary muscle and spetum was greater during right stellate than during left stellate stimulation. Also, the percentage change in contractile force in these two areas was greater than in the epicardial force recordings (RVS and LVA). The onset of contractile force of the papillary muscle, developing 30 msec later than that in the left ventricular epicardium, was nearly synchronous with contraction in the septal and sinus regions. This sequence of contraction did not alter during either right or left stellate ganglion stimulation although the interval between excitation and contraction shortened. The onset in right ventricular pressure rise always followed the initial increase in contractile force of the muscular components. Note that the papillary muscle response elicited by right stellate stimulation was considerably greater than that induced by the left. Average maximum systolic pressures developed in the right ventricle were also slightly higher, but not significantly so.

Figure 3 represents a comparison of the

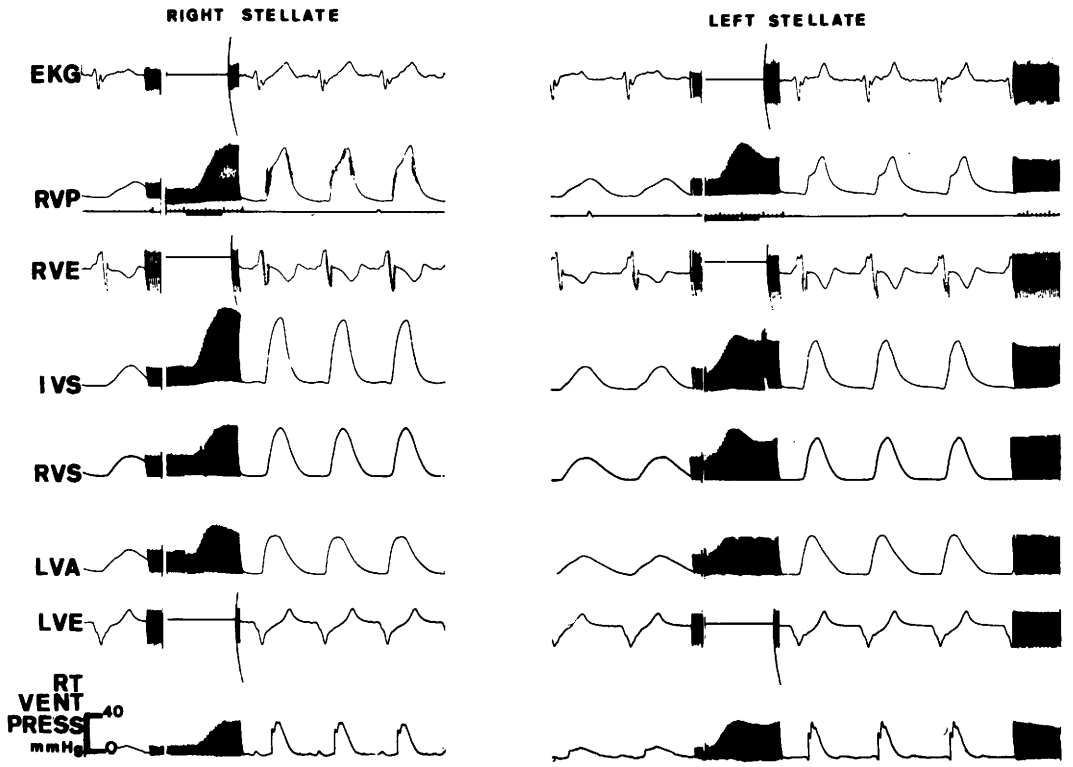

FIG. 2. The effects of stellate ganglia stimulations upon recordings of a canine electrocardiogram (EKG), right ventricular papillary muscle force (RVP), right ventricular epicardial electrogram (RVE), septal force from the right ventricle (IVS), right ventricular sinal epicardial force (RVS), anterior left ventricular epicardial force (LVA), left ventricular epicardial electrogram (LVE), and right ventricular pressure. Both the right papillary muscle and septum are augmented more during right stellate ganglion stimulation than during left stellate stimulation, although the chamber pressure rise was similar in both instances.

effects of two inotropic drugs with increasing right ventricular afterload (cross clamping of the pulmonary artery) and efferent vagal stimulation upon the right ventricular sinus force (RVS), right ventricular papillary muscle force (RVP), right ventricular conal force (RVC), left ventricular force (LVA), systemic pressure (FAP) and right ventricular sinal pressure (RVP). Intravenous norepinephrine (first arrow) elicited augmentation in both pressure and contractile force, the papillary muscle and conal regions being augmented in the greatest amount. Note the gradual increase in contractile force resulting from this combined inotropic and increased afterloading procedure as compared with the steep rises elicted by sympathetic nerve stimulation (Fig. 2). The onset of contraction in all regions became more nearly synchronous and rates of rise in contractile force and pressure were increased. A similar pattern of augmentation in contractile force subtended with the infusion of isoproterenol, the effects being greatest on papillary muscle contraction, onset times becoming nearly synchronous. However, systemic arterial pressure (FAP) did not rise while the rate of development of augmentation in force was more like that elicited by stellate stimulation. This is to be expected from this predominantly inotropic agent and is in contrast to the combined actions of norepinephrine on both myocardial muscle and vascular resistance. When the pulmonary artery was digitally coarcted (CCPA) so that a significant rise of intracavitary pressure occurred without ar-

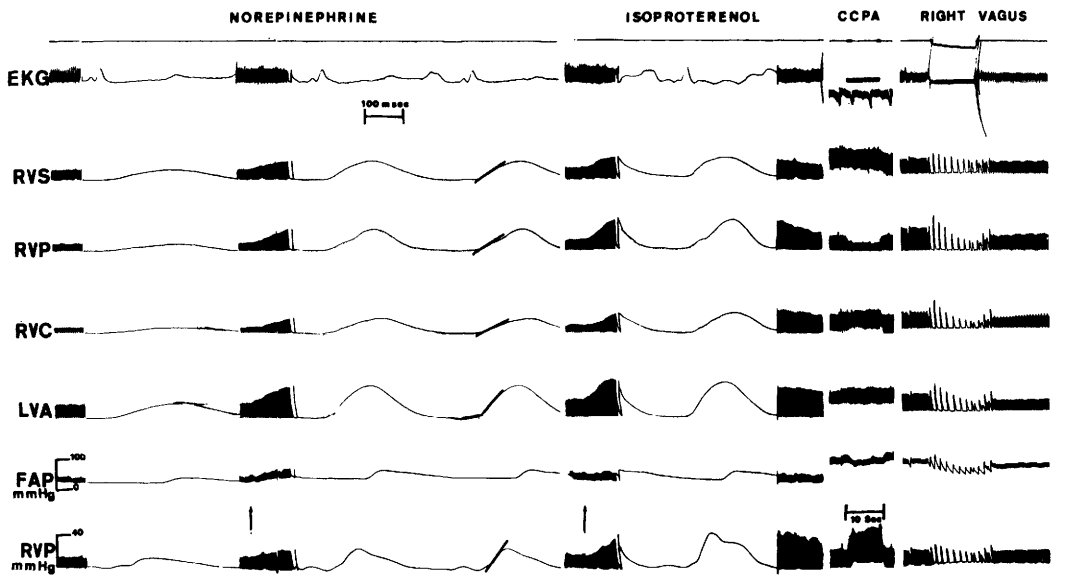

FIG. 3. The effects of norepinephrine, isoproterenol, cross clamping of the pulmonary artery (CCPA), and stimulation of the distal right vagus upon a standard EKG, right ventricular sinus epicardial force (RVS), right ventricular anterior papillary muscle force (RVP), right ventricular conal epicardial force (RVC), left ventricular anterior epicardial force (LVA), femoral artery pressure (FAP), and right ventricular pressue (RVP). The effects of norepinephrine and isoproterenol upon a deteriorated preparation demonstrate fairly similar force augmentations. Digital occlusion of the pulmonary artery, without arrhythmias, augmented right sided force, except in the papillary muscle. Also, distal vagal stimulation suppressed peak contractile force in the right ventricular papillary muscle.

rhythmias, the right ventricular pressures (both systolic and diastolic) were elevated and the right ventricular chamber became distended. Although right ventricular sinus and conus forces were minimally augmented, the papillary muscle force was greatly depressed. Depression of force in all regions occurred with distal right vagal stimulation; this was particularly evident in the right ventricular papillary muscle and conus epicardial muscle. Note the sustained suppression in contractile force with gradual recovery following cessation of stimulation.

Table I lists the effects of eight different interventions upon maximum heart rate (HR), systemic systolic pressure, epicardial contractile force, and rate of force development of the right ventricular sinus and conus, right ventricular papillary muscle, the anterior left ventricular epicardium, and right ventricular sinus cavity pressure. Standard error of the mean accompanies each value. Stimulation of either right or left stellate ganglion elicited an augmentation of papillary muscle force considerably greater than that occurring simultaneously in epicardial muscle segments. Right sympathetic stimulation augmented papillary muscle force of contraction, as well as dF/dt, considerably more than did the left sympathetics ($p = 0.001$). Norepinephrine consistently elicited maximal changes in contractile force, not only of the papillary muscles but in the epicardial segments and in intracavitary pressures as well. Neosynephrine, an agent acting strongly on the peripheral vascular bed, elevated systemic arterial pressure markedly but had only moderate influences upon the papillary muscles of the right ventricle, and upon right ventricular pressure. Isoproterenol, presumably acting primarily at the beta receptors in the heart, elicited little or no elevation in systemic pressure but induced a powerful inotropic action on the papillary muscles. The purely afterloading procedure of coarctation of the pulmonary artery, in-

TABLE I. Alterations in Ventricular Contractile Responses.

Group	N	HR	Systemic (systolic) BP	Sinus		Conus		Right ventricular papillary muscle		Left ventricular anterior		Right ventricular pressure	
				Force	*dF/dt*	Force	*df/dt*	Force	*dF/dt*	Force	*df/dt*	(mm Hg)	(mm Hg/ msec)
Control	12	141 ± 10	102 ± 6	100 ± 11	100 ± 15	100 ± 10	100 ± 14	100 ± 19	100 ± 16	100 ± 5	100 ± 9	12.5 ± 1.5	0.35 ± 0.02
Right stellate	12	176 ± 13	120 ± 12	170 ± 5	194 ± 60	190 ± 30	200 ± 36	330 ± 40	257 ± 51	210 ± 20	253 ± 51	33 ± 6	1.3 ± 0.4
Left stellate	12	150 ± 12	126 ± 4	160 ± 10	212 ± 12	170 ± 20	201 ± 72	210 ± 20	206 ± 66	170 ± 60	238 ± 59	31 ± 3	1.14 ± 0.28
Norepi-nephrine	12	164 ± 10	152 ± 7	250 ± 30	277 ± 17	310 ± 42	616 ±104	320 ± 30	277 ± 92	291 ± 24	330 ± 66	36 ± 4	1.09 ± 0.31
Neosy-nephrine	10	137 ± 12	172 ± 23	230 ± 30	180 ± 26	221 ± 20	280 ± 6	220 ± 30	141 ± 33	200 ± 20	107 ± 21	29 ± 2	0.66 ± 0.21
Isopro-terenol	10	172 ± 10	115 ± 10	230 ± 30	213 ± 43	180 ± 20	133 ± 11	350 ± 30	275 ± 62	220 ± 20	188 ± 31	42 ± 5	1.79 ± 0.57
Cross clamp PA	10	136 ± 9	64 ± 5	150 ± 20	116 ± 12	120 ± 70	105 ± 18	190 ± 40	171 ± 52	130 ± 2	87 ± 21	38 ± 6	0.93 ± 0.20
Cross clamp aorta	10	137 ± 10	59 ± 5	110 ± 5	114 ± 20	120 ± 2	103 ± 18	130 ± 20	147 ± 21	140 ± 20	110 ± 31	17 ± 2	0.46 ± 0.11
Infuse saline	6	138 ± 5	104 ± 8	140 ± 20		120 ± 18		120 ± 14		140 ± 10		18 ± 2	

TABLE II. Onset of Contraction and Pressure Rise After Q Wave (msec).

Group	No. of animals	Sinus force	Conus force	RV papillary muscle force	Left ventricular force	p value pap. vs left vent.	Right ventricular pressure onset time
Control	12	51 ± 4	53 ± 4	55 ± 6	49 ± 3	NS	72 ± 6
Right stellate	12	37 ± 5	46 ± 6	37 ± 5	31 ± 4	NS	60 ± 6
Left stellate	12	41 ± 5	35 ± 3	46 ± 6	33 ± 5	0.001	52 ± 7
Norepinephrine	12	45 ± 3	44 ± 3	46 ± 7	29 ± 4	0.001	60 ± 5
Cross clamp pulmonary art.	10	48 ± 5	52 ± 8	49 ± 6	37 ± 4	0.05	61 ± 4
Cross clamp aorta	10	46 ± 4	56 ± 8	52 ± 8	30 ± 7	0.010	62 ± 9

duced nearly maximal elevations in intraventricular pressure but had relatively little influence upon the papillary muscles or the muscles of the overlying epicardium. However, to avoid serious arrhythmia during accompanying distension of the right ventricle, the coarctation was generally not severe. In some instances (Fig. 3), this maneuver induced apparent suppression in contractile force of the papillary muscles. These data clearly show that the papillary muscles respond strongly to procedures having positive inotropic effects and that they are less profoundly influenced by essentially afterloading or preloading maneuvers.

Table II presents the average time interval between the Q wave of the ECG and the onsets of contraction as measured by the strain gauge arch on both epicardial and endocardial muscle segments as well as onset of pressure rise in the right ventricle. Highly significant ($p = 0.001$) reductions in onset times of RV papillary muscle contraction are revealed between control values (first row) and those induced during right stellate stimulation (second row). Similar shortening of onset times for the right ventricular sinus and conus, as well as left ventricular force are evident. However, reduction in onset time of papillary muscle contraction was not significant as a result of left stellate stimulation, although changes in the other ventricular parameters were significant ($p = 0.001$). It is further evident that systemic afterloading procedures failed to induce significant changes in the RV papillary muscle onset of contraction, even though the alterations in left ventricular force were generally apparent.

Comparing the onset of contraction in all of the right ventricular segments, it is apparent that all contracted more nearly synchronously during electrical excitation of the right stellate ganglion. This was distinctly less characteristic of left stellate stimulation, but it is of interest to note that the latter procedure consistently and preferentially influenced the conal portion of the ventricle. It is also of interest that stellate stimulations and norepinephrine injection exerted consistently greater influence on the left ventricular musculature. The onset of contraction in the papillary muscle, which always preceded the initial rise in intracavitary pressure, occurred after the commencement of contraction in the anterior epicardium of the left ventricle. Essentially heterometric changes (coarctation of pulmonary artery and aorta) clearly shortened the onset time of contraction in the left ventricle, but had no such consistent effect in any of the right ventricular test segments. Thus, it is again apparent that the right ventricular papillary muscles show active changes in dynamic behavior during many different experimental interventions. They further appear capable of acting quite independently of other right or left ventricular structures.

Discussion. The dynamic actions of *in situ* papillary muscles have, until recently, been analyzed upon primarily theoretical grounds. Previously, recordings of the chorda tendinea in the left ventricle (7) showed onset of tension to occure approximately simultaneously with initial rise in intraventricular pressure, but this did not elucidate the papillary muscle function. Direct recordings of con-

traction of the *in situ* papillary muscle (4) have demonstrated their late onset of contraction in the left ventricle. Due to their size, the right ventricular papillary muscles lend themselves to *in vitro* experimentation (8, 9). However, *in vivo* function of these muscles has not heretofore been studied. It is quite clear that they represent functionally active elements with differential responses to specific experimental manipulations. Augmentation in force of papillary muscle contraction was significant ($p < 0.001$) for all of the homeometric interventions.

The pattern of contraction of the right ventricular papillary muscle was found to differ in important ways from that of the left ventricular papillary muscles. The onset of contraction of these muscle segments is correlated with that of the sinus of the right ventricular musculature (Table II); similarity in onset of contraction times becomes evident during augmentation of contraction via sympathetic nerve stimulation or norepinephrine infusion. This fact supports the concept that the right ventricular papillary muscles function independently from their counterparts which arise from the septal wall of the left ventricle. That is, their actuation is identified with contraction in the right ventricular wall. The time of peak tension generation follows a similar time sequence (Fig. 1). The activation of these muscles during stellate stimulation also indicates a purely right ventricular function; right stellate stimulation augments force in the right ventricular papillary muscles more consistently and more intensely than does left stellate stimulation ($p > 0.001$). This is also consistent with the finding of an earlier report that the right stellate ganglion effects the right ventricular epicardium more than the left ganglion (2). When comparing the relative increase in force during stellate nerve activation or drug induced inotropism (5) in the papillary muscles of both ventricles, it is evident that the anterior left ventricular papillary muscle is capable of a greater increase in force. Norepinephrine elicted an increase of 320% in contracile force of the right ventricular papillary muscle, a magnitude of change comparable to that of the conus but exceeding that of the sinus. Norepinephrine has been shown (10) to augment force of contraction in the papillary muscles of the left ventricle by 282 and 398% for the posterior and anterior muscles, respectively. Each of these influences of vascular perfusion of elevated catecholamine to the papillary muscle was highly significant ($p = 0.001$), but there was no significant difference in responses between the papillary muscle of the right and left ventricles. Differences in mass of the papillary muscles from the two ventricles demonstrated that in dogs weighing 19.3 $\pm$ 6.0 kg the combined weight of all right ventricular papillary muscles was 0.5 $\pm$ 0.1 g; whereas the anterior left ventricular papillary muscle weighed 2.1 $\pm$ 0.68 g and the posterior left ventricular papillary muscle, 0.98 $\pm$ 0.14 g (6). These data confirm the impressions of Harvey recorded almost 350 years ago (1).

Although the anterior and posterior right ventricular papillary muscles do not appear to differ functionally, it is evident that their maximum development of contractile force is augmented minimally during preloading and afterloading conditions (Table I). Infusion of saline into the right ventricle and pulmonary coarctation are frequently accompanied by ectopic sites of activation, but force in the papillary muscle are found to be only slightly augmented. When the pulmonary artery was slightly coarcted without ectopic foci of activation, again only minimal augmentation occurred in papillary muscle force. When more severe coarctation was performed, especially without ectopic foci of excitation, depression of papillary muscle force was regularly observed (Fig. 3). This is in sharp contradistinction to the left ventricular papillary muscle response to afterload. Once again this is conceivably due to the meagerness of the right sided muscles which are working against a relatively greater load from their chordae tendineae. Right stellate stimulation, as well as infusion of norepinephrine or isoproterenol, augmented papillary muscle contraction to a greater extent than the bulk (sinus) of right ventricular musculature ($p < 0.001$). This was not true of the responses to left stellate stimulation or infu-

sion of neosynephrine which proved not to be significantly different from those of sinus (epicardial) musculature. Similar capabilities have been reported in the left ventricular papillary muscles (4).

These data controvert the notion that the right ventricle is primarily a passive region of the heart (11). Tension exerted upon the chordae tendineae conceivably not only prevents valvular prolapse, but may also serve to augment pressure generating capabilities of the right ventricle. Complex interactions probably occur during changing dynamics of systole. The patterns of contraction of the right ventricular papillary muscles are related specifically to the dynamics of the right ventricular sinus and are functionally distinct from those in the left ventricle.

Summary. Strain gauge recordings of *in situ* right ventricular papillary muscle behavior demonstrate their active contraction in well programmed coordination with other portions (conus, sinus, and right interventricular septal wall) of the right ventricle. Their activity is not directly associated with contraction of anterior epicardial segments of the left ventricle, but is associated with right ventricular sinus contraction. Electrical excitation of the right stellate ganglion elicits clear and discrete augmentation of the right ventricular papillary muscles while comparable excitation of the left stellate induces significantly lesser responses. Responses to positive inotropic agents (norepinephrine, isoproterenol) are sharp and strong while changes in activity accompanying afterloading (neosynephrine, coarctation of pulmonary artery and the aorta) and preloading (rapid saline infusion) are less intense. Alterations in contractile patterns, particularly those associated with time of onset of contraction, are closely associated with similar events in the sinus region, but are often divorced from simultaneous behavior of the conus. In clear distinction from the left ventricle in which papillary muscle contraction occurred concurrently with elevation in intraventricular pressure, the papillary muscles of the right ventricle contract some 10 to 20 msec before intraventricular pressure begins to rise.

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Received July 9, 1970. P.S.E.B.M., 1971, Vol. 136.