

## EXPERIMENTAL GALLOP RHYTHM IN SHEEP WITH GOUSIEKTE: CORRELATION OF CHANGES IN AMPLITUDE WITH HAEMODYNAMIC PARAMETERS

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### ABSTRACT

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To investigate the correlation of haemodynamic parameters with the intensity of the gallop sound ( $S_3$ ), use was made of right heart catheterization with a Swan-Ganz catheter to measure the pulmonary and right atrial pressures. The cardiac output was determined with the thermodilution method. A radiocardiogram was obtained after a bolus injection of technetium pertechnetate. The cardiopulmonary flow-index was obtained from the simultaneous recordings of the radiocardiogram and an electrocardiogram. With the haemodynamic parameters, heart sounds were recorded simultaneously and externally with a microphone.

Eight Merino sheep were dosed with dried *Pachystigma pygmaeum* (Schltr) Robyns plant material through rumen fistulas until the clinical symptoms of heart failure such as gallop sounds, systolic murmurs and haemodynamic symptoms as well as increases in end diastolic pressure and decreases in stroke volume, appeared. After the appearance of the symptoms the sheep were treated symptomatically to delay the development of the cardiomyopathy. The changes in haemodynamic parameters before and after treatment were used and correlated with the intensity of the gallop sounds on a 6 point criterium scale. The results in brief show that, for gallop sound intensities between 0 and 6 on the criterium scale, most of the haemodynamic parameters correlate with the intensity of the gallop sounds, except the cardiac output, cardiopulmonary blood volume and the systemic and pulmonary vascular resistances. The haemodynamic parameters correlate better with the intensities of the gallop rhythm between 0 and 3.

It is evident from this study that the model of heart failure in sheep is useful to study heart sounds and may also be valuable in the study of the genesis of the gallop sound.

### INTRODUCTION

Ventricular gallop sounds despite remarkable advances in the understanding of cardiac physiology, are still a much debated subject. Because of the conspicuousness of abnormal heart sounds, the clinical correlation and physiological meaning are important.

A review of the literature on gallop sounds revealed that the physiological and clinical aspects of gallop sounds are complex and still to a great extent unknown (Van de Werf, Minten, Carmeliet, De Geest & Kesteloot, 1984; Shaver, Reddy, Alvares & Salerni, 1987; Ozawa, Smith & Craige, 1983 a and b). Although gallop sounds are an indicator of cardiac failure, the relation between haemodynamic parameters, pathological changes and gallop sounds are not clear. Functional and structural aspects of the ventricular wall, changes in blood flow, changes in pre- and afterload, even in mechanical effects as a cause of cardiac movement may play a role in the development of pathological and physiological ( $S_3$ ) sounds. It is important to develop and evaluate experimental models for investigating hypothesis regarding gallop sounds.

In this study cardiac failure was evoked experimentally in sheep, and haemodynamic changes were manipulated and correlated with gallop sounds. The usefulness of this animal model as well as the relation between haemodynamic parameters and the intensity and nature of the gallop sounds, were investigated.

### MATERIALS AND METHODS

The experimental procedures for this study consisted of inducing a cardiomyopathy (gousiekte) after dosing sheep daily through ruminal fistulas with 9-13 gm/kg body mass dried *Pachystigma pygmaeum* (Schltr) Robyns plant material (Theiler, Du Toit & Mitchell,

1923). The method of inducing experimental cardiac failure in sheep is described in previous publications (Pretorius & Terblance, 1967; Pretorius, Terblanche, Van der Walt & Van Ryssen, 1973; Van der Walt, Van Rooyen, Cilliers, Van Ryssen & Van Aarde, 1981; Kellerman, Coetzer & Naude, 1988). From these results the following were concluded: This experimental cardiac failure is a typical congestive heart failure characterized by cardiac dilation, systolic murmurs, typical haemodynamic symptoms such as increases in end diastolic pressure and decreases in stroke volume (SV) and the development of gallop sounds. About 2 weeks before the experimental procedures started, 8 adult Merino sheep were anaesthetised with pentobarbital sodium and subcutaneous arterial loops were surgically made from the carotid arteries and fistulas were implanted in the rumens of the sheep.

The sheep were dosed for 7 to 28 days with plant material until the gallop rhythm appeared. The sheep were then treated symptomatically and use was made of positive inotropic agents, such as dobutamine hydrochloride<sup>1</sup>, in doses of 0,497-15,92  $\mu\text{g}/\text{kg}/\text{min}$  with a mean dose of 8,21  $\mu\text{g}/\text{kg}/\text{min}$  and vasodilators, such as sodium nitroprusside<sup>2</sup>, in doses of 0,67-1,44  $\mu\text{g}/\text{kg}/\text{min}$  with a mean dose of 1,06  $\mu\text{g}/\text{kg}/\text{min}$ . In some cases furosemide<sup>3</sup>, was injected intravenously in combination with sodium nitroprusside in doses of 20 or 40 mg. The sheep were treated with the drugs to delay the development of the cardiomyopathy and to ensure that all sheep would show gallop rhythms. All the haemodynamic recordings were made on unanaesthetised animals after they were suspended in a normal upright position in a canvas cradle.

The heart sounds were recorded with a microphone<sup>4</sup> and amplifier on a chart recorder. The microphone was positioned and the sensitivity and filter chosen to record the different components of the first ( $S_1$ ) and second ( $S_2$ )

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<sup>4</sup> Elema EMT 25c

heart sounds. The amplitudes of the gallop sounds were measured and quantified according to a 6 point criterium scale in the following manner:

- 0 No gallop ( $S_3$  or  $S_4$ )<sup>5</sup> visible
- 1 Uncertain, very small amplitude, intermittent
- 2 Very small amplitude, smaller than  $S_2$ , constant
- 3 Small amplitude (same order as  $S_2$ ), clearly visible
- 4 Medium amplitude
- 5 Amplitude nearly the amplitude of  $S_1$
- 6 Amplitude greater than  $S_1$

In all the experiments a 7F-110 cm Swan-Ganz double lumen thermodilution catheter was positioned in the pulmonary artery after percutaneous jugular vein catheterization. Cardiac output (CO) was determined by using the thermodilution technique with a cardiac output computer.<sup>6</sup> The cardiopulmonary flow-index (CPFI) which is the quotient of the cardiopulmonary transit time and the period of the heart beat, was determined from the simultaneous recording of a radiocardiogram and an ECG (Van der Walt *et al.*, 1981). The radiocardiogram was obtained after the injection of a bolus of 0,074 GBq-0,185 GBq <sup>99m</sup>Technetium pertechnetate through the proximal opening of the Swan-Ganz catheter. The cardiopulmonary blood volume (CPBV) was calculated as the product of the CPFI and the stroke volume (SV) (Van der Walt *et al.*, 1981) which was determined with thermodilution. The distending pulmonary pressure (DPP) was calculated from the mean pulmonary arterial pressure (PAP) and the pulmonary capillary wedge pressure (PCWP) by averaging the 2 pressures,  $(PAP + PCWP)/2$ . The mean arterial pressure (MAP) was determined through the arterial loop with a 21G needle. The systemic (SVR) and pulmonary (PVR) vascular resistances, as well as the left ventricular stroke work (LVSW), were calculated from the haemodynamic parameters which were measured directly.

The results obtained after treatment were analysed with a BMDP-8-D-analysis programme (Dixon, 1983) to

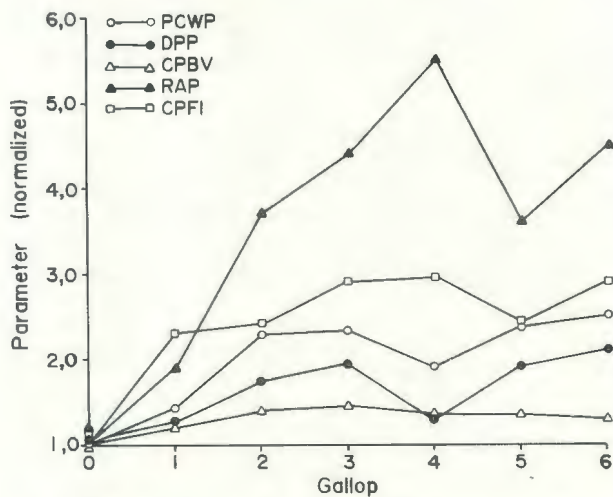


FIG. 1 The relationship of pulmonary capillary wedge pressure (PCWP), distending pulmonary pressure (DPP), cardiopulmonary blood volume (CPBV), right atrial pressure (RAP) and the cardiopulmonary flow index (CPFI) with the intensity of the gallop rhythm

<sup>5</sup>  $S_4$  sound is seen as a low intensity low frequency vibration with probably an atrial systolic origin.  $S_4$  sounds are found in sheep with heart failure with low heart rates. With higher heart rates  $S_3$  and  $S_4$  can summate  
<sup>6</sup> Edwards model 9520A

show the correlation between haemodynamic parameters and the gallop rhythm. A BMDP 9R (analysis of variance programme) (Dixon, 1983) was also used on the data to show which haemodynamic parameters correlate

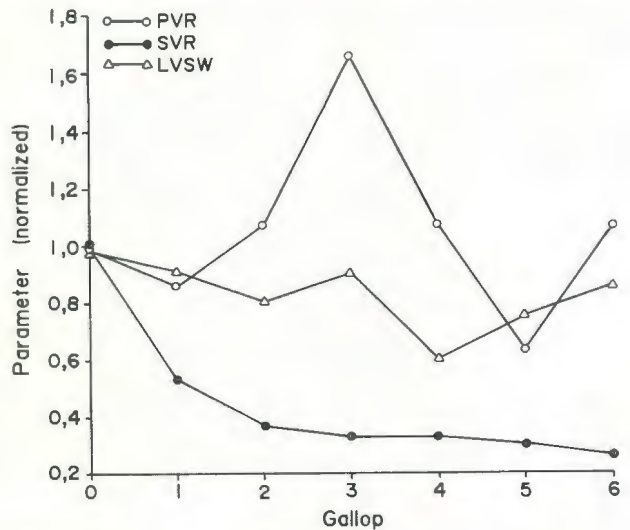


FIG. 2 The relationship of the pulmonary vascular (PVR) systemic vascular resistance (SVR) and left ventricular stroke work (LVSW) with the intensity of the gallop rhythm

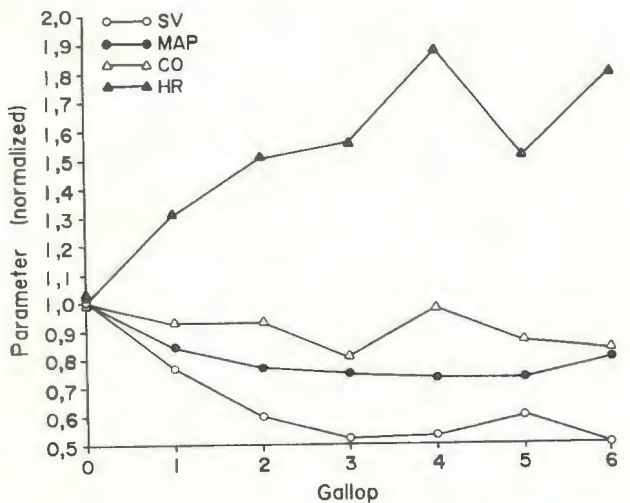


FIG. 3 The relationship of the stroke volume (SV), mean arterial pressure (MAP), cardiac output (CO) and heart rate (HR) with the intensity of the gallop rhythm

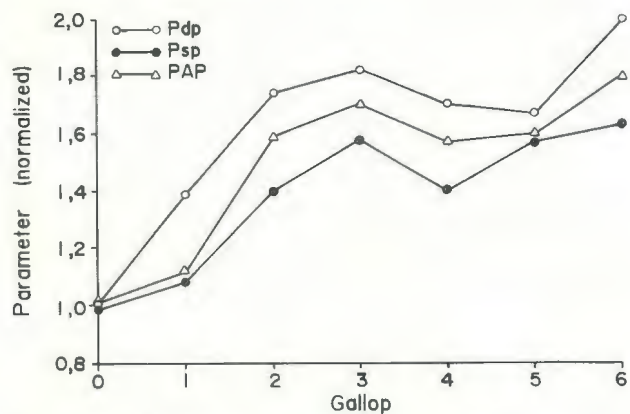


FIG. 4 The relationship of the pulmonary diastolic (Pdp), pulmonary systolic (Psp) and mean pulmonary artery pressure (PAP) with the intensity of the gallop rhythm



TABLE 1 The correlation between haemodynamic parameters and the gallop rhythm (a) Gallop 0-6; (b) Gallop 0-3; (c) Gallop 4-6. According to Pearson's product moment correlation coefficient, values above 0.32 show a significant correlation of 95 % between gallop rhythm and haemodynamic parameters, where: cardiopulmonary flow index (CPFI); heart rate (HR) in beats/min; cardiac output (CO) in l/min; stroke volume (SV) in ml; pulmonary capillary wedge pressure (PCWP), pulmonary diastolic pressure (Pdp), pulmonary systolic pressure (Psp), distending pulmonary pressure (DPP) and mean pulmonary artery pressure (PAP) in kPa; cardiopulmonary blood volume (CPBV) in ml; right atrial pressure (RAP) and mean arterial pressure (MAP) in kPa; systemic vascular resistance (SVR) and pulmonary vascular resistance (PVR) in dynes.s.cm<sup>-5</sup>; left ventricular stroke work (LVSW) in g-M/stroke

Parameter	CPFI	HR	CO	SV	PCWP	Pdp	Psp	DPP	PAP	CPBV	RAP	MAP	SVR	PVR	LVSW
TABLE 1a Correlation coefficient	*0,37	*0,68	-0,14	*-0,50	*0,53	*0,45	*0,47	*0,49	*0,46	0,26	*0,55	*-0,47	-0,25	0,02	*-0,58
TABLE 1b Correlation coefficient	*0,49	*0,69	-0,16	*-0,61	*0,64	*0,57	*0,56	*0,65	*0,58	*0,42	*0,67	*-0,66	-0,22	0,19	*-0,71
TABLE 1c Correlation coefficient	0,16	-0,15	-0,29	-0,08	*0,40	0,25	0,22	*0,51	0,22	-0,10	-0,23	0,25	*0,43	0,0	-0,17

best with the gallop rhythm. According to Pearson's product, moment correlation coefficient, values above 0,32 show significant correlations of 95 % between the gallop rhythm and the haemodynamic parameters.

## RESULTS

After the development of the cardiomyopathy in 8 sheep the intensity of the gallop sound, which is a clinical symptom of the disease in the later stage of heart failure, was correlated with haemodynamic parameters obtained after right heart catheterization. The results show that certain haemodynamic conditions have an influence on the intensity of the gallop rhythm. From Fig. 1 it is clear that an increase in right atrial pressure (RAP) has a direct relationship with the intensity of the gallop rhythm up to 4 on the criterium scale.

The RAP starts decreasing with an increase in intensity above 4. The decreases in RAP can probably be related to the treatment of the sheep which started at that stage. The CPFI, PCWP, DPP and the CPBV also show relationships with the intensity of the gallop rhythm.

In Fig. 2 it is indicated that with a decrease in the LVSW and SVR the intensity of the gallop rhythm increased. With an increase in PVR the intensity of the gallop also increased to 3 on the criterium scale.

In Fig. 3 it is indicated that with a decrease in the CO, MAP and the SV as a result of the development of heart failure, the intensity of the gallop rhythm increased up to 6 on the criterium scale. With an increase in HR as a result of compensation, the intensity also increases.

From Fig. 4 it is evident that the intensity of the gallop rhythm increased with an increase in the pulmonary pressures. The pulmonary pressures increased probably as a result of congestion of the lungs. The above figures indicate correlations between the haemodynamic parameters measured and the intensity of the gallop rhythm.

From statistical analysis of the haemodynamic data and the intensity of the gallop rhythm it is evident from Table 1a that for intensities of the gallop rhythm between 0 and 6 the HR (0,68,  $P < 0,05$ ), LVSW (-0,58,  $P < 0,05$ ) RAP (0,55,  $P < 0,05$ ), PCWP (0,53,  $P < 0,05$ ), SV (-0,50,  $P < 0,05$ ), DPP (0,49,  $P < 0,05$ ), Psp (0,47,  $P < 0,05$ ), MAP (-0,47,  $P < 0,05$ ), PAP (0,46,  $P < 0,05$ ), Pdp (0,45,  $P < 0,05$ ) and the CPFI (0,37,  $P < 0,05$ ) show significant correlations with the gallop rhythm.

The CO, CPBV, SVR and the PVR did not show any correlation with the gallop rhythm for intensities between 0 and 6. It is evident from Table 1b for intensities between 0 and 3 that the LVSW (-0,71,  $P < 0,05$ ), HR (0,69,  $P < 0,05$ ), RAP (0,67,  $P < 0,05$ ), MAP (-0,66,  $P < 0,05$ ), DPP (0,65,  $P < 0,05$ ), PCWP (0,64,  $P < 0,05$ ), SV (-0,61,  $P < 0,05$ ), PAP (0,58,  $P < 0,05$ ), Pdp (0,57,  $P < 0,05$ ), Psp (0,56,  $P < 0,05$ ), CPFI (0,49,  $P < 0,05$ ) and the CPBV (0,42,  $P < 0,05$ ) correlate significantly with the gallop rhythm. For intensities between 0 and 3 there is no significant correlation between the CO, SVR and the PVR with the gallop rhythm. For gallop rhythm intensities between 4 and 6 there is no correlation between most of the parameters and the gallop rhythm, although the PCWP (0,40,  $P < 0,05$ ), DPP (0,51,  $P < 0,05$ ) and the SVR (0,43,  $P < 0,05$ ) show significant correlations with the gallop rhythm.

## DISCUSSION

The aim of this study was to show correlations between the intensity of the pathological S<sub>3</sub> sound and



changes in haemodynamic parameters as well as to determine which parameters are predisposing to  $S_3$ . Correlations between haemodynamic parameters and the intensity of the gallop sound can be expected because there was a delay in the development of the cardiomyopathy as a result of the symptomatic treatment of the sheep. In this way the experimental model may resemble human heart failure more closely.

For intensities between 0 and 3 on the criterium scale it is evident that the LVSW correlates best with the intensity of the gallop sound. The good correlation between the heart rate and the intensity of the gallop sound is also expected, because the heart rate, although secondary to heart failure is a sign of compensation. The CPFI, which can be obtained noninvasively, without right heart catheterization, also show significant correlations with the intensity of the gallop sound except for intensities between 4 and 6 on the criterium scale. One would expect that because at the higher intensities, treatment had already been used to delay the development of the cardiomyopathy. According to Van der Walt *et al.* (1981), the CPFI is sensitive to evaluate treatment of heart failure, and at that stage the decrease in CPFI because of the treatment, will result in no correlation with the intensity of the gallop sound. The significant correlation of the filling pressures with the gallop rhythm at higher intensities is expected because at that stage the heart becomes very dilated and congested, which impedes the normal filling of the heart. Table 1 shows that the correlation values of intensities between 0 and 3 are much higher than the other intensities, therefore the haemodynamic parameters correlate better with the intensities of the gallop rhythm between 0 and 3.

The combination of parameters (Table 2) show, that the HR, PCWP, DPP, PAP, Psp and the SV give the best description of the gallop rhythm with intensities between 0 and 6.

TABLE 2 Correlation of a combination of parameters with the gallop rhythm with intensity between 0 and 6. Heart rate (HR) in beats/min; pulmonary capillary wedge pressure (PCWP), distending pulmonary pressure (DPP), mean pulmonary artery (PAP) and pulmonary systolic pressure (Psp) in kPa; stroke volume (SV) in ml

Haemodynamic parameter	Regression coefficient	Standard deviation	Relative contribution to $R^2=0,59898$
HR	2,1570	0,7824	0,08467
PCWP	2,3745	0,9205	0,07412
DPP	-2,6288	1,1020	0,06339
PAP	-5,2042	2,3145	0,05632
Psp	5,5529	2,7203	0,04642
SV	-1,5560	0,8365	0,03855
Interception constant for regression coefficient			-0,1233

The above-mentioned haemodynamic parameters describe 59 % ( $R^2=0,599$ ) of the information of the gallop rhythm. From Table 3 it is evident that for intensities from 0 to 3, the HR, Psp, RAP, SV and the CPBV describe the gallop rhythm best.

These parameters describe 73 % ( $R^2=0,730$ ) of the information of the gallop rhythm.

Although it was not the aim of this study to investigate the mechanism of the production of the gallop sound, it is possible to speculate on the genesis of the gallop sound. Considering the possible explanations for the

TABLE 3 Correlation of a combination of parameters with the gallop rhythm with intensity between 0 and 3. Heart rate (HR) in beats/min; pulmonary systolic pressure (Psp), right atrial pressure (RAP) in kPa; stroke volume (SV) and cardiopulmonary blood volume (CPBV) in ml

Haemodynamic parameter	Regression coefficient	Standard deviation	Relative contribution to $R^2=0,730$
HR	1,9898	0,6147	0,09431
Psp	-1,5851	0,5674	0,07024
RAP	0,2573	0,1009	0,05848
SV	-1,11747	0,4934	0,04617
CPBV	0,5195	0,2820	0,03054
Interception constant for regression coefficient			-0,02658

genesis and cause of the 3rd heart sound the following hypothesis emerged from a study of the literature:

1. Abnormal rapid ventricular filling
2. Vibrations caused by direct impact of the heart against the thorax wall
3. Stretching of the mitral valve apparatus because of cardiac dilation
4. Change in ventricular wall motion because of structural or functional changes

Although this study yields no direct evidence against or in favour of the above hypothesis, the results obtained in 2 sheep where 300 ml of blood was withdrawn in an attempt to relieve the congestion, show, however, that the filling pressures decreased in both sheep. The intensity of the gallop sound decreased from 6 to 1 in 1 sheep and from 5 to 2 on the criterium scale in the other sheep. It is further evident from our results that with the smaller pressure gradient (high filling pressure and lesser elevated PAP) for flow to the left ventricle, that the flow to the left ventricle is impeded, and this factor, including the changes in ventricular wall motion as a cause of structural or functional changes in wall properties as a result of the development of the cardiomyopathy, are in favour of the theory proposed by Van de Werf *et al.* (1981), that the left ventricular wall is the major cardiac structure which is set into vibration during deceleration of flow and causing the  $S_3$  heart sound. The hypothesis that gallop sounds are produced as a result of changes in the equilibrium between ventricular wall characteristics (structural and functional) and filling factors (preload, venous return) is hereby proposed for the genesis of gallop sounds.

The measurement of the amplitudes of the gallop sounds and the quantitative presentation of the intensities to a 6 point criterium scale will be valuable in determining the prognosis of at least experimental animals suffering from heart failure, because no animals with gallop sound intensities of 5 or 6 survived.

This dilation cardiomyopathy, as induced after dosing sheep through rumen fistulas with dried plant material from the Rubiaceae family, resulted in gallop sounds associated with heart failure. This experimental model of heart failure in sheep, is useful however, to study heart sounds as well as the progression of pathological  $S_3$  sounds. Because the same factors are probably responsible for the genesis of pathological and physiological  $S_3$  sounds, this model may be valuable in the study of the genesis of the gallop sound.

In brief, this study shows that certain haemodynamic parameters correlate with the intensity of the gallop

sound and some of these haemodynamic factors predispose  $S_3$ , especially in the low intensity range before any treatment has commenced.

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