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Electrocardiographic and Blood Pressure Measurements in Captive African Lions (*Panthera leo*) Immobilized with Xylazine-Ketamine Combination

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Summary: Electrocardiographic and blood pressure measurements are extremely valuable diagnostic tools in the evaluation of the cardiovascular system of living animals. In this study, 6-lead electrocardiograms were recorded from five male captive African lions (*Panthera leo*). Also, blood pressure measurements were recorded and compared from three different sites; fore limb, hind limb and the tail, were recorded. Immobilization was done with a combination of Ketamine Hydrochloride (10mg/kg) and Xylazine (3mg/kg). Measurements were recorded as mean ± standard deviation. ECG readings were analysed using descriptive statistics while blood pressure readings were compared using ANOVA at a 5% level of significance. Heart rate was 66±11.6 beats per minute. The heart rhythm was sinus in all the animals. Mean Electrical Axis (MEA) was between $+81^0$ and $+93^0$ degrees (Mean +89±5). Three animals had their MEA between $+81^0$ and $+89^0$ while two had MEA between $+91^0$ and $+93^0$. Fore limb measurements for Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DAP) and Mean Arterial Pressure (MAP) were 177.6±6.8 mmHg, 157.2±5.9 mmHg and 168.6±5.2 mmHg respectively. Hind limb measurements for the SBP, DBP and MAP were 135.4±9.5 mmHg, 120.6±5.9 mmHg and 123.0±6.8 mmHg respectively while the tail measurements for the SBP, DBP and MAP were 149.6±8.3 mmHg, 132.8±5.9 mmHg and 137.2±5.8 mmHg respectively. There was weak correlation between forelimb vs hindlimb and forelimb vs tail comparisons of SBP, DBP and MAP. However, a strong positive correlation was found between hindlimb and tail comparisons of those parameters. Results from this study should serve as a guide in the cardiovascular monitoring of captive African Lions immobilized with a xylazine-ketamine combination.

Keywords: Electrocardiogram, Blood pressure, African lions

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INTRODUCTION

With less than 30,000 free-ranging individuals left in the wild, the African lion (*Panthera leo*), has been classified as vulnerable, and with an uncertain future (Nowell and Jackson, 1996; Bauer and Van der Merwe, 2004). It has been projected that by the year 2030, the status may change from vulnerable and conservation dependent to endangered (Cardillo *et al*., 2004). Captive breeding has been used tremendously in the prevention of imminent extinction of endangered species (Fraser, 2008). Although cardiac diseases are uncommonly diagnosed in exotic species (Fowler, 1986), reproduction of such animals in a breeding program should be avoided (Larsson *et al*., 2008) thereby making the cardiovascular evaluation of exotic species, including wild felids very important.

The procedure of chemical immobilization of wild and exotic animals is a form of veterinary anaesthesia (Nielsen, 1999). Chemical immobilization is required when animals cannot be safely manipulated into an appropriate holding area with restraint tools. Several drug combinations have been used for the immobilization of wild felids and the choice of drugs to be used is often dictated by factors such as availability, experience with certain drug combinations, cost of drug, size and species of felids, length of time for the procedure and the purpose as well as the health status of the animal (Gunkel and Lafortun, 2007). Several of the routine clinical procedures that are carried out in domestic animals with minimal restraint require the use of anaesthetic agents, not only for the safety of the handlers, but also for the safety of the zoo animals (Vesal and Naeini, 2007; Miller and Fowler, 2012). One of such procedures is the clinical evaluation of the cardiovascular system. Electrocardiography is a useful tool for the clinical evaluation of the heart, and it is important for monitoring veterinary patients with various cardiac diseases (Larsson *et al*., 2008). Cardiac arrhythmias, disturbances of cardiac conduction and cardiac chamber enlargement are also readily diagnosed with ECG. In addition to these, electrolyte

imbalances and response to certain drugs may also be monitored with this tool (Coleman and Robson, 2005). The electrocardiogram also provides critical information on cardiac electrophysiological function especially the effect of test drugs in toxicological studies on various parameters (such as conduction, depolarization and repolarization) which cannot be assessed by other methods and have no morphological correlates that may be visible by histopathology (Hanton and Rabemampianina, 2006).

Accurate blood pressure measurement is important and critical to the interpretation of studies of vascular biology, atherosclerosis and cardiovascular diseases (Kurtz *et al*., 2005). This procedure is important in clinical practice and its use is increasing in different branches of veterinary medicine. It is an indicator of an animal's tissue perfusion (Petrič *et al*., 2010) and could give a good insight into the health status of an animal (Sant Cassia *et al*., 2015). There are a few reports of blood pressure measurements in exotic felids using invasive, oscillometric and ultrasonic doppler methods in studies utilizing various anaesthetic drugs (Deem *et al*., 1998; Schumacher *et al*., 1999; Langan *et al*., 2000). This study was designed to evaluate the 6-lead electrocardiogram and blood pressure parameters of apparently healthy captive African lions measured from three different sites, with a view to providing useful physiological and clinical data.

MATERIALS AND METHODS

Electrocardiography

This study was performed on five captive male African lions kept at the Zoological Garden, University of Ibadan, Nigeria. Electrocardiography was carried out using a 6/7 lead computer ECG machine, (EDAN VE-1010, Shanghai, China) Following chemical immobilization with a Xylazine-Ketamine combination, each animal was placed on right lateral recumbency with the limbs positioned perpendicularly to the long axis of the body. Electrocardiographic parameters such as heart rate, P-wave duration, PR-interval, QRS duration, R-amplitude and QT-interval were recorded for each of the leads. For each QT segment recording, the Bazett correction (QTc) was calculated using the formula:

$$QTcB = QT/\sqrt[2]{RR}$$

Where QTcB is the Bazett's QT interval corrected for heart rate, and RR is the interval from the onset of one QRS complex to the onset of the next QRS complex.

Blood Pressure Measurements

Blood pressure measurements were done using an automatic oscillometric blood pressure monitor. For a comparative evaluation of blood pressure measurement from various sites, readings were taken from the fore limb, hind limb and the tail. For each site of blood pressure measurement, five consecutive readings were taken and the average of the Systolic blood pressure (SBP), Diastolic blood pressure (DBP) and Mean arterial pressure (MAP) were recorded.

Statistical Analysis

Electrocardiographic data obtained were summarized using descriptive statistics and values obtained were recorded as mean ± standard deviation. Means of blood pressure measurements obtained were compared using ANOVA. Blood pressure measurements from the different sites were further compared using Pearson's correlation linear regression analysis.

RESULTS

The man heart rate was 66.0±11.6 beats per minute. The heart rhythm was sinus in all the animals. Mean Electrical Axis (MEA) was between $+81.0^0$ and $+93.0^0$ degrees (Mean +89.0±5.0). Average ECG parameters are presented in Table I. The complexes and intervals in lead-I were barely discernible and therefore, were not measured. Every QRS complex had a preceding P-wave. P-wave was positive in leads II, III and aVF while it had negative polarity in leads aVR and aVL. Similarly, R-wave amplitude was positive in leads II, III and aVF while it was negative in leads aVR and aVL. (Fig. I). The lead-II ECG parameters measured in this study were similar to those earlier reported by Larsson *et al*., (2008). The complexes and intervals measured were longer than those earlier recorded for domestic carnivores. In this study, blood pressure was measured from three different sites; the forelimb, the hind limb and the tail. Mean SBP values for the forelimb, hind limb and tail were 177.6±6.8, 135.4±9.5 and 149.6±8.3 respectively. Mean DBP values for the fore limb, hind limb and tail were 157.2±5.9, 120.6±5.9 and 132.8±5.9 respectively. Mean Arterial Pressure

Table 1: ECG parameters of African lions immobilized with Xylazine-Ketamine drug combination

Lead	P-wave duration (ms)	PR-interval (ms)	QRS duration (ms)	R-amplitude (mV)	QT interval (ms)	QTc (Bazett)
II	110.2±25.9	192.8±28.4	77.8±19.4	1.0±0.4	319.8±34.7	331.8±19.4
III	107.0±23.9	187.0±27.6	77.2±19.5	0.9±0.3	317.6±33.0	329.8±19.2
aVR	91.8±20.5	175.2±12.3	71.0±15.4	0.5±0.0	315.2±32.7	327.0±11.8
aVL	92.4±15.3	177.2±17.5	69.4±14.3	0.3±0.0	316.6±30.6	328.4±7.0
aVF	98.4±18.8	186.2±12.9	72.4±25.7	0.9±0.3	311.4±37.6	322.8±15.7

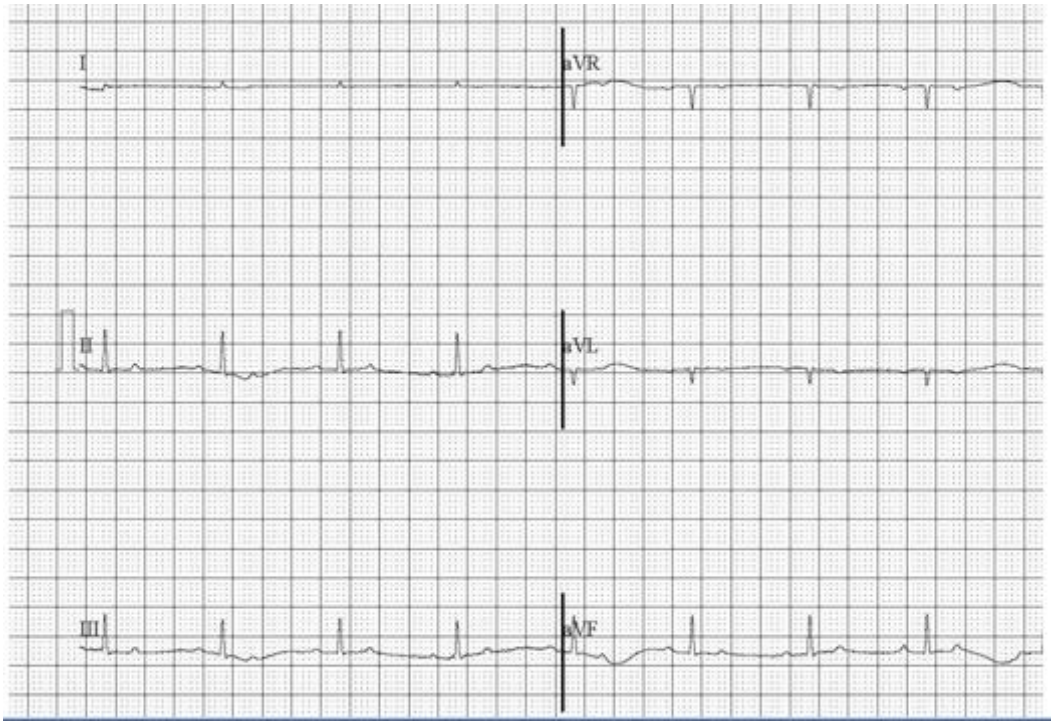

Fig I: Representative six –lead ECG in African lions immobilized with xylazine-ketamine combination (10mm/mV, 50mm/s)

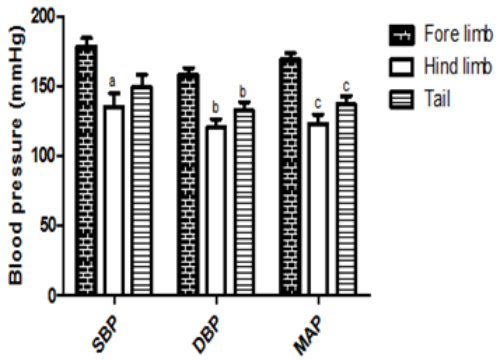

Figure II. Blood pressure measurement from various sites in African lions. Superscript (a,b and c) indicate statistically significant ($p<0.05$) difference for SBP, DBP and MAP respectively.

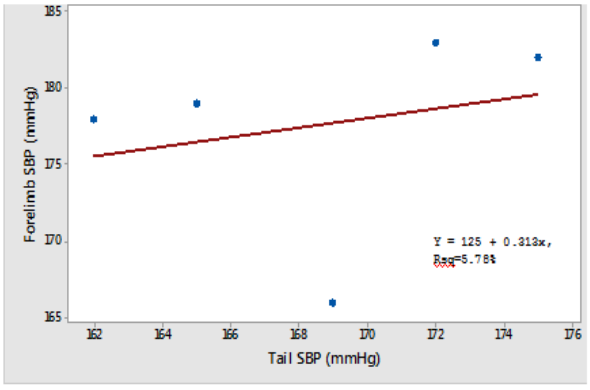

Fig IV. Scatterplot and linear regression of forelimb and tail systolic blood pressure (SBP) obtained from 5 healthy lions. Forelimb and tail systolic blood pressure were weakly correlated.

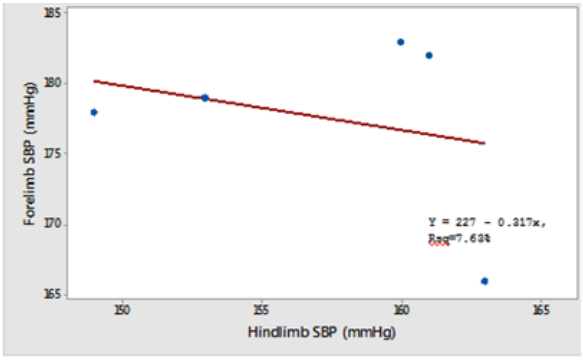

Figure III. scatter plot and linear regression of forelimb and hindlimb systolic blood pressure (SBP) obtained from 5 healthy lions. Forelimb and hindlimb systolic blood pressure were weakly correlated.

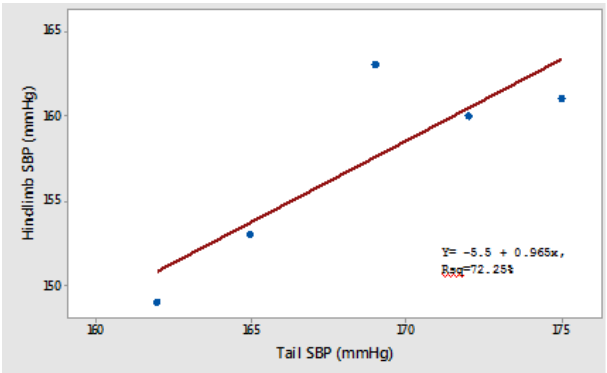

Fig V. Scatterplot and linear regression of hindlimb and tail systolic blood pressure (SBP) obtained from 5 healthy lions. Forelimb and hindlimb systolic blood pressure were well correlated.

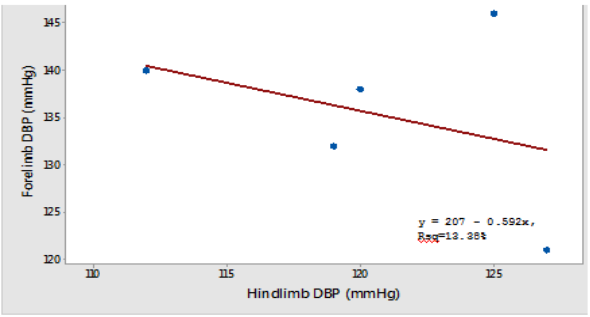

Fig VI. Scatterplot and linear regression of forelimb and hindlimb diastolic blood pressure (DBP) obtained from 5 healthy lions. Forelimb and hindlimb diastolic blood pressure were weakly correlated.

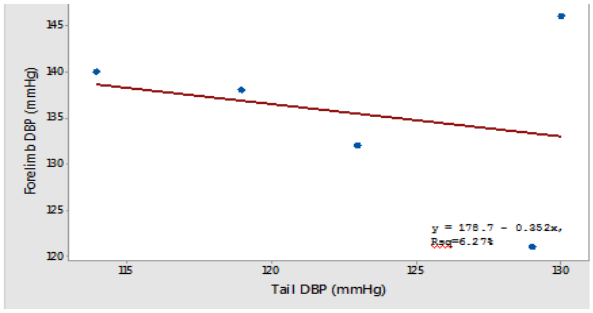

Fig VII. Scatter plot and linear regression of forelimb and tail diastolic blood pressure (DBP) obtained from 5 healthy lions. Forelimb and tail diastolic blood pressure were weakly correlated

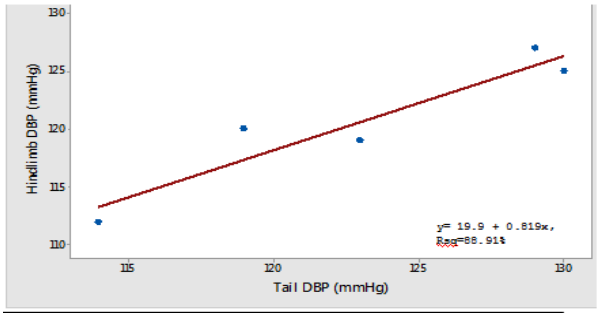

Fig VIII. Scatterplot and linear regression of hindlimb and tail diastolic blood pressure (DBP) obtained from 5 healthy lions. Hindlimb and tail systolic blood pressure were well correlated

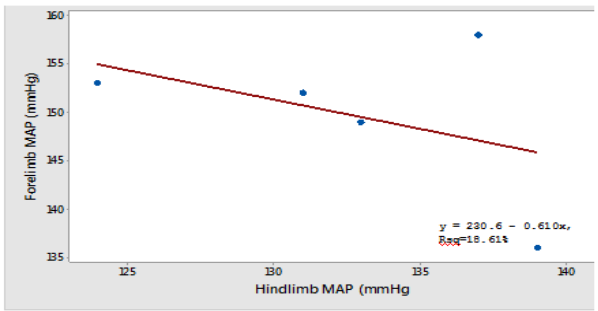

Fig IX. Scatterplot and linear regression of forelimb and hindlimb mean arterial pressure (MAP) obtained from 5 healthy lions. Forelimb and hindlimb MAP were weakly correlated

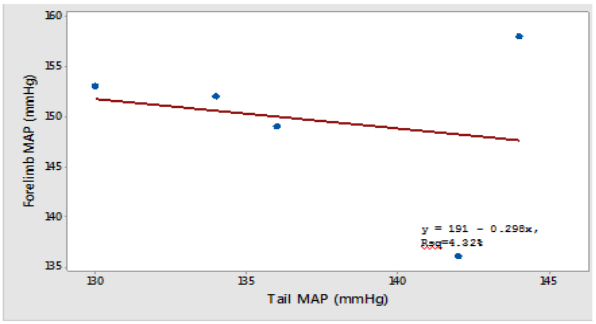

Fig X. Scatterplot and linear regression of forelimb and tail mean arterial pressure (MAP) obtained from 5 healthy lions. Forelimb and tail MAP were weakly correlated

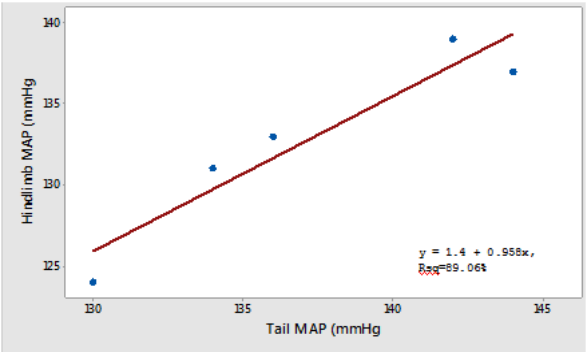

Fig XI. Scatterplot and linear regression of hindlimb and tail mean arterial pressure (MAP) obtained from 5 healthy lions Hindlimb and tail MAP were well correlated.

values for the forelimb, hind limb and tail were; 168.6±5.2, 123.0±6.8 and 137.2±5.7 respectively. Statistically significant $p<0.05$ differences were found between the mean SBP, DBP and MAP readings from the 3 sites (Fig II).

Figures III-XI showed weak correlation with paired forelimb/hindlimb SBP, DBP and MAP (R^2=7.63%, 13.38% and 18.61% respectively) as well as forelimb/tail SBP, DBP and MAP (R^2=5.78%, 6.27% and 4.32%). Hindlimb/tail SBP, DBP and MAP however showed very strong positive correlation (R^2=72.25%, 88.91% and 89.06% respectively).

DISCUSSION

In non-domestic felids, ketamine hydrochloride is one of the most commonly used drugs for immobilization having being found to be safe and effective (Ramsay, 2014). In this study, we evaluated the 6-lead electrocardiogram as well as the blood pressure values of African lions immobilized with xylazine-ketamine combination. The heart rate findings in this study are similar to previous reports on large felids that were immobilized with a xylazine-ketamine combination and it is also in consonance with an earlier reported allometric scaling for the assessment of vital signs (Sedgwick, 1991, Larsson *et al*., 2008). Segdwick (1991) had calculated a heart rate of

approximately 60 to 80 beats per minute for large mammals weighing 100 to 250 kg. In this study, heart rate was 66±11.6 beats per minute. Ketamine is known to increase cardiac output, mean aortic pressure, pulmonary arterial pressure, central venous pressure, and heart rate. In addition to this, it exhibits a central vagolitic property and exerts selective positive inotrope influence in the heart muscle. Ketamine also has antiarrhythmic action, and it elevates myocardial oxygen consumption (Wright, 1982; Booth, 1988). In many animal species, xylazine produces a short-lived arterial pressor effect followed by a longer period of hypotension and bradycardia after intramuscular or subcutaneous injection. It may cause first, second, and third degree atrioventricular blocks probably by increased vagal activity. Xylazine also seems to sensitize the heart to epinephrine, and it may induce ventricular arrhythmias. It also acts as a direct depressant the myocardium and reduces cardiac output (Booth, 1988). There is lack of information regarding the expected rhythm and other electrocardiographic parameters of wild felids however when compared with domestic carnivores, the rhythms recorded in this study are normal (Tilley, 1992; Larsson *et al*., 2008). The higher values of wave durations and intervals may be due to a greater muscle mass which large felids possess (Larsson, *et al*., 2008)

In this study, we determined the blood pressure measurements (SBP, DBP and MAP) of apparently healthy lions from 3 different site; forelimb, hind limb and tail. Blood pressure measurement of wild felids and other domestic carnivores showed a range of values which were quite high (Seal *et al*., 1987; Deem *et al*., 1998; Langan *et al*., 2000; Curro *et al*., 2004; Selmi *et al*., 2004; Brown, 2005). The relatively high values of the SBP, DBP and MAP recorded in this study might have been due to the effect of ketamine on the cardiovascular system. In human patients, ketamine increased arterial blood pressure, systemic vascular resistance, pulmonary capillary wedge pressure and pulmonary arterial wedge pressure by 14-38% (Christ *et al*., 1997). Forelimb measurements were significantly higher than those measured from the tail and the hind limbs. Hind limb measurements were the lowest. An earlier study conducted in greyhounds reported higher values for SBP in the forelimb when compared with the tail (Marino et al., 2011). Although the reason for this variation is not clear, these differences are probably due to factors such as relative distances from the heart and anatomic differences between the 3 sites. There was weak correlation between forelimb vs hindlimb and forelimb vs tail comparisons. However, a strong correlation was found between hindlimb and tail comparisons of the parameters measured. This finding agrees with the work of Haberman et al., (2006) who reported a strong correlation between hindlimb and tail BP measurements. Similar to our findings, Scansen *et al*., (2014) also reported a poor correlation between forelimb and hindlimb SBP measurements in Shetland sheepdogs.

From this study, we have been able to establish electrocardiographic and blood pressure values to serve as a guide in the monitoring of African lions. We found significant differences between blood pressure values taken from the forelimb and those from other sites. Weak correlation was also observed between forelimb vs hindlimb and forelimb vs tail comparisons while a strong correlation was found between hindlimb and tail comparisons. The findings from this study suggest that hind limb and tail blood pressure measurements in captive African lions were comparable with each other. In the cardiovascular monitoring of African lions, either of the 2 sites may be used interchangeably.

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