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Effect of ovariohysterectomy on queen myocardial function: echocardiographic evidence

Boshra Elyasi, Mohammad Nasarolahzade Masouleh*, Alireza Jahandideh

Department of Clinical Science, Faculty of Specialized Veterinary Sciences, Science and Research Branch, Islamic Azad University, Tehran, Iran.

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Abstract

Ovariohysterectomy (OHE) is one of the most common surgeries in veterinary medicine. Although this surgical method has several advantages, it can alter the function of various organs such as heart. The present study investigated the effect of OHE on cardiac functions using M-mode echocardiography. A total of 10 healthy adult domestic short-haired cats were enrolled in the current study. Fractional shortening (FS) and ejection fraction (EF) percentages along with cardiac output (CO) were measured through the right parasternal approach in papillary muscle level view. Moreover, the levels of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) were measured by enzyme-linked immunosorbent assay before OHE (D0) as well as 10 (D10), 20 (D20) and 30 (D30) days after OHE. The results of this study showed that the mean FS and EF decreased on all days of the study. The FS reduction was significant between D10 and D30 and EF changes were significant between D10 and D20. The means of CO increased significantly on D0 compared to the D10. After D20, CO reduced until the end of the study. Mean concentrations of LH and FSH increased on all research days; but, the changes were significant until D20. Despite the negative effects of OHE on myocardial function, there was no significant correlation between hormonal levels and echocardiographic findings after OHE in this study.

Introduction

Echocardiography is a useful diagnostic tool for measuring various cardiac parameters. Heart diseases can be diagnosed by comparing echocardiographic measurements with normal ranges in each animal.[1] Various physiological changes can affect cardiac function. One of the influential factors is alterations in sex hormone levels which may result from changes in sex hormone levels following ovariohysterectomy (OHE) or menopause in humans.[2-4]

The OHE affects brain function through dysregulating the hypothalamic-pituitary-gonadal (HPG) axis. The release of gonadotropin-releasing hormone (GnRH) by the hypothalamus stimulates the synthesis and secretion of luteinizing hormone (LH) and follicle-stimulating hormone (FSH).[5] In females, LH and FSH cause the ovaries to produce estrogen and progesterone. These hormones exert negative feedback on the production of GnRH. Therefore, if gonads are removed, the ovarian inhibitory influence will be lost and a rapid increase in the plasma concentration of both LH and FSH will be induced by the HPG axis.[6] Ovaries produce and release the two sex hormones progesterone and estrogen. Choijookhuu *et al*., López and Tena-Sempere and Lønning have shown that OHE affects body tissues by diminishing the secretion of progesterone and estrogen.[7-9] However, the scope and type of these effects are still unknown.

The FSH has direct and indirect effects on the cardiovascular system. The FSH receptors on the endothelium[10,11] have signaling effects on the heart and vascular wall.[12,13] In addition, FSH has an indirect impact on the heart with its role in inflammation, atherosclerosis, insulin resistance, reactive oxygen species (ROS) formation and adipocyte rearrangement.[14]

The OHE can change the secretion of steroid hormones. These hormones have direct and indirect effects on the heart. These changes are still unknown in cats. Therefore, this study was conducted to investigate the influence of OHE on feline echocardiographic parameters including fractional shortening (FS) and ejection fraction (EF) percentages as well as cardiac output (CO). Furthermore, the relationship of these parameters with steroid hormones (LH and FSH) was also evaluated.

***Correspondence:**

Mohammad Nasarolahzademasouleh. DVM, DVSc
Department of Clinical Science, Faculty of Specialized Veterinary Sciences, Science and Research Branch, Islamic Azad University, Tehran, Iran
E-mail: mnmasouleh@srbiau.ac.ir

Materials and Methods

Animals. This study was conducted on 10 adult healthy intact female domestic short-haired cats weighing 3.30 - 4.30 kg (mean 3.93 kg) and aged 1 - 4 years. None of the cats had a congenital or acquired myocardial disease before or during the study. The cats were kept by their owners under the same conditions in March 2021. The animals fasted for 12 hr before the surgery.

Surgical procedure. All cats underwent routine elective neutering (OHE using a ventral midline approach). The medications used for analgesia were 5.50 mg kg^{-1} ketamine (Alfasan, Woerden, Netherlands) and 0.28 mg kg^{-1} diazepam (Caspian tamin, Tehran, Iran) intravenously and for maintenance were 0.60 mg kg^{-1} ketamine and diluted in ringer solution at the rate of 8.00 mL kg^{-1} per hr.

Echocardiographic evaluation. All cats were prepared with clippings on the right thoracic wall between 4th and 5th ribs. The animals were all positioned laterally recumbent on the right side on the echocardiography table. The timing and conditions of echocardiography for all cats were the same. Echocardiographic parameters including FS, EF and CO were calculated by Teichholz correction using a 9.00 MHz microconvex transducer (Z5; Mindray, Guangzhou, China) via the right parasternal short axis approach in the papillary muscle level view (mushroom appearance; Fig. 1). Interventricular septal thickness, left ventricular internal diameter and left ventricular posterior wall thickness in both diastolic and systolic phases were measured for this purpose.

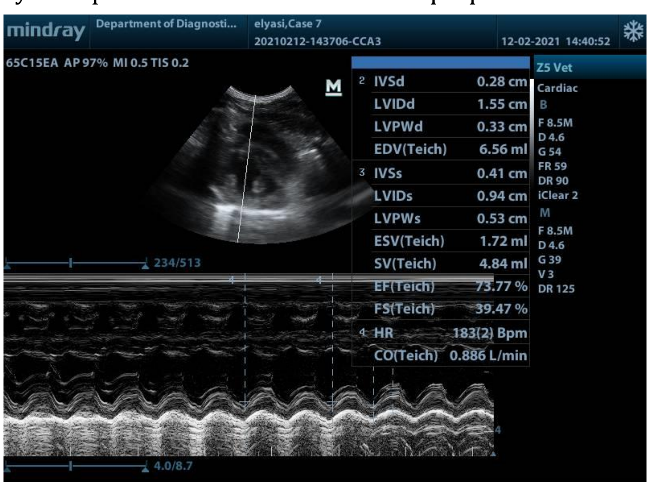

Fig. 1. Echocardiogram (mushroom level). Ejection fraction = 73.77%, fractional shortening = 39.47 % and cardiac output = 0.88 L per min.

Hormone measurements. The concentrations of LH and FSH were measured by enzyme-linked immuno-sorbent assay kits (Pishtazteb, Tehran, Iran).

Sample collection. All animals were sampled every 10 days for 1 month. For this, 2.00 mL of blood was collected from the femoral vein with a 24-G venous catheter into a tube with no anticoagulants. The samples were allowed to clot at room temperature for 40 min, centrifuged for 10 min at 25,000 rpm and stored for hormonal analysis.

Times of hormone measurements and echo-cardiography. The echocardiographic parameters and hormone concentrations were measured before OHE (D0) and 10 (D10), 20 (D20) and 30 days (D30) after OHE.

Statistical analysis. Data were analyzed using SPSS Software (version 21.0; IBM Corp., Armonk, USA). The mean and standard error of the mean of all parameters were calculated. The Kolmogorov-Smirnov test was used to assess the normality of data distribution. One-way repeated measures analysis of variance with Tukey's multiple comparison test was used to compare all pairwise differences between parameter means. Also, Pearson's correlation coefficient was used for assessing the relation-ship between echocardiographic and hormonal parameters. The $p < 0.05$ was considered statistically significant.

Results

All parameters including FS, EF and CO as well as LH and FSH concentrations were normally distributed ($p > 0.05$). As shown in Table 1, FS means decreased from before OHE (47.33%) to D10 (47.07%); but, these changes were not significant. The FS means significantly reduced from D10 to D20 (45.97%; $p = 0.03$) and from D20 to D30 (42.54%; $p = 0.006$, Table 1). The means of EF did not significantly change on D10 (79.23%) compared to D0 (79.56%); while, altered significantly from D10 to D20 (77.67%; $p = 0.02$). The changes were not significant from D20 to D30 (75.23%). A significant reduction was observed in the mean CO on D0 (1.21 L per min) to D10 (1.23 L per min; $p = 0.001$). In addition, the mean CO did not change until D20 (1.23 L per min; $p = 0.82$); while, the mean CO had a statistically significant decrease until the end of the study (1.19 L per min; $p = 0.002$). According to Table 2, the mean LH on D10 (3.89 ng mL^{-1}) significantly increased compared to the D0 (2.33 ng mL^{-1}). Further-more, the mean LH significantly augmented from D10 to D20 (4.75 ng mL^{-1}). The mean LH increased to D30 (5.06 ng mL^{-1}); but, this change was not statistically significant.

Table 1. Mean ± standard error of the mean of fractional shortening (FS), ejection fraction (EF) and cardiac output (CO) at before ovariohysterectomy (OHE; D0), 10th day after OHE (D10), 20th day after OHE (D20) and 30th day after OHE (D30).

Parameters	Day 0	Day 10	Day 20	Day 30
FS (%)	47.33 ± 4.77	47.07 ± 5.17	45.97 ± 5.42*	42.54 ± 4.22*
EF (%)	79.56 ± 3.20	79.23 ± 3.74	77.67 ± 3.83*	75.53 ± 6.09
CO (L per min)	1.21 ± 0.11	1.23 ± 0.12*	1.23 ± 0.12	1.19 ± 0.13*

* indicate significant difference compared to the previous day ($p < 0.05$).

Table 2. Mean ± standard error of the mean of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) at before ovariohysterectomy (OHE; D0), 10th day after OHE (D10), 20th day after OHE (D20) and 30th day after OHE (D30).

Parameters	Day 0	Day 10	Day 20	Day 30
LH (ng mL^{-1})	2.33 ± 0.13	3.89 ± 0.51*	4.75 ± 0.85*	5.06 ± 0.36
FSH (ng mL^{-1})	2.36 ± 0.13	3.92 ± 0.48*	4.82 ± 0.84*	5.08 ± 0.36

* Significant difference compared to the previous day ($p < 0.05$).

There was statistically significant increase in FSH from D0 (2.36 ng mL^{-1}) to D10 (3.92 ng mL^{-1}) and D10 to D20 (4.82 ng mL^{-1}). Then, the mean FSH augmented to D30 (5.08 ng mL^{-1}); but, it was not significant. The results of assessing the relationships between echocardiographic and hormonal parameters in the four stages are summarized in Table 3. There were negative correlations (not significant) between FS and LH (r = – 0.75), FS and FSH (r = – 0.74), EF and LH (r = – 0.83) and EF and FSH (r = – 0.82). This means that FS and EF decreased with an increase in LH and FSH. Because of the small changes in CO mean during the study (0.02 L per min), its correlation with LH and FSH cannot be accurately evaluated (despite the same amount of changes, it had not significant correlation with hormones).

Discussion

The results of this study showed that the expected and statistically significant changes in hormone concentrations did not correlate with relatively small significant changes in the echocardiographic measurements (FS, EF and CO reductions were not lower than normal echocardiographic values in the reference books.[15,16] According to the literature, no study examined the effects of hormones on heart changes in domestic animals, especially cats.

Barp *et al*. suggested that changes in the estrogen level following OHE have a role in heart abnormalities.[17] Vitale *et al*. examined the effect of sex hormones (i.e., estrogen and testosterone) on the risk of cardiovascular diseases.[18] The results of their study showed that changes in the levels of estrogen in women increased the risk of cardiovascular diseases. Zhao *et al*. studied the relationship between sex hormone levels and cardiovascular diseases in affected patients. They measured the hormone levels of 2,834 postmenopausal women for 12.10 years. Their findings revealed that the risk of cardiovascular diseases increased in the last years of life with a reduction in hormone levels after menopause.[19] Another study on 72 postmenopausal women found that menopause negatively affected myocardial function and velocity.[4] Similar findings have been reported in humans Sickinghe *et al*., Zhu *et al*., El Khoudary *et al*., and Nappi and Simoncini.[20-26]

There is a hypothesis about the relationship between changes in hormonal levels and cardiac function. Grohé *et al*., have shown that estrogen directly affects heart receptors as the α estrogen receptor in the heart has protective effects on the heart through different mechanisms. Therefore, changes in the concentration of FSH and LH followed by changes in estrogen undermine the protective mechanisms of the heart and inevitably lead to heart malfunction.[27] In this study, negative changes in cardiac functions were also seen; but, probably due to the relatively short time of the study, echocardiographic measurements were still within the normal range.

On the other hand, when the LH and FSH levels increased, the plasma concentration of estrogen reduced, consequently, the anti-oxidant activity decreased, which raised the possibility of changes in the heart. Estrogen levels are associated with plasma anti-oxidant capacity and oxidative enzymes expression during the menstrual cycle.[28-30] Anti-oxidants protect the body against the adverse effects of ROS and thus, prevent the occurrence of vascular diseases such as heart disease.[31]

The results of the present study confirmed that OHE in cats is associated with significant negative changes in myocardial function in short-time, despite the fact that these changes are still within their normal range. However, these are not due to the changes in LH and FSH hormones, suggesting other reasons for cardiac function alterations after OHE. Changes in blood pressure, metabolism, lifestyle and anti-oxidant activity may have led to these alterations. Also, although the heart in cats, similar to other organs, may intelligently adapt to changes in the long run and function normally, but in order to draw more complete conclusion, echocardiography is necessary in a long-time follow-up (at least one year after the start of the study).

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Conflict of interest

The authors declare no financial or personal relationship that would lead to undue bias or influence the findings of this study.

Table 3. Relationship between echocardiographic and hormonal parameters using Pearson correlation.

Parameters	Statistics	Fractional shortening	Ejection fraction	Cardiac output
Luteinizing hormone	Pearson correlation	– 0.75	– 0.83	0.59
	Significance	0.24	0.17	0.40
Follicle-stimulating hormone	Pearson correlation	– 0.74	– 0.82	0.58
	Significance	0.25	0.17	0.41

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