HOKKAIDO UNIVERSITY

Title	Oxidative stress markers in dogs : A comparison between intact and gonadectomized individuals
Author(s)	Shono, Saori; Nemoto, Saki; Kikuchi, Yukino et al.
Citation	Japanese Journal of Veterinary Research, 74(1), 13-21 https://doi.org/10.57494/jjvr.74.1_13
Issue Date	2026-03-10
Doc URL	https://hdl.handle.net/2115/99040
Type	departmental bulletin paper
File Information	JJVR74-1_13-21_SaoriShono.pdf

Hokkaido University Collection of Scholarly and Academic Papers : HUSCAP

Japanese Journal of Veterinary Research 74(1): 13–21, 2026

JJVR

REGULAR PAPER Clinical Case Report

Oxidative stress markers in dogs: A comparison between intact and gonadectomized individuals

Saori Shono[1,*], Saki Nemoto[1,2], Yukino Kikuchi[2], Mituho Kikuchi[2] and Mariko Mochizuki[1]

[1] Department of Applied Science, School of Veterinary Nursing and Technology, Nippon Veterinary and Life Science University, Tokyo 180-8602, Japan
[2] Famille animal hospital, Tokyo 192-0033, Japan

Received for publication, July 16, 2025; accepted, November 30, 2025

Abstract

This study measured serum or plasma levels of reactive oxygen metabolites (d-ROMs), biological antioxidant potential (BAP), and oxidative stress index (OSI) in dogs. The subjects were classified into four groups according to sex and gonadal status: intact males, castrated males, intact females, and spayed females, both off-therapy and during therapy. No significant differences were observed in d-ROMs, BAP, or OSI between the off-therapy and during therapy groups. Among off-therapy dogs, intact males showed significantly higher mean d-ROMs and BAP values compared with females and neutered dogs. In contrast, among during therapy dogs, no significant differences were found in d-ROMs among the groups; however, intact males had significantly higher mean BAP values than castrated males, and the OSI was significantly higher in castrated males than in intact males. These results suggest that gonadectomy in male dogs may influence the balance between oxidative and antioxidative processes through factors such as sex hormones. The findings highlight the importance of considering the effects of spaying and neutering when establishing reference values for oxidative stress markers in dogs.

Key Words: BAP; dog; d-ROMs; gonadectomy; oxidative stress marker

Introduction

Oxidative stress is a pathological condition that arises when the generation of reactive oxygen species (ROS) exceeds the capacity of the body's antioxidant defense systems to neutralize them. The oxidative reaction causes DNA damage, cell structure degradation, lysis, and tissue injury when ROS accumulate excessively during metabolic processes[21,42]. It has been long implicated that the multiple oxidation-reduction reactions are associated with aging, cancer, diabetes mellitus and lifestyle-related diseases[23,24]. Some ROS, such as superoxide and hydrogen peroxide, play important roles in immune function, defense mechanism against infection, energy production, and the induction of cell death[9,32]. Therefore, ROS must not be completely removed and decomposed. Antioxidant reactions are important to control excessive ROS and protect the body from oxidation. The excessive amount of ROS is decreased through antioxidative substances and antioxidative enzymes[23]. Thus, maintaining redox homeostasis (the balance between oxidants and antioxidants) is essential for preventing oxidative stress. Factors that generate ROS to the extent that it exceeds the

* Corresponding author: Saori Shono
Department of Applied Science, School of Veterinary Nursing and Technology, Nippon Veterinary and Life Science University, Tokyo 180-8602, Japan
Email: sshono@nvlu.ac.jp
doi: 10.57494/jjvr.74.1_13

antioxidant capacity of the living body are various lifestyle-related habits such as obesity, excessive exercise, smoking, drinking, and ultraviolet rays[10,16,14]. There is a reference value for oxidative stress in humans. Based on this, oxidative stress is evaluated, and it is attracting attention in the field of preventive medicine as an effective index for the early detection of lifestyle-related diseases.

Recently, the average lifespan of companion animals is increasing due to the development of veterinary medicine and the improvement of the quality of pet food in developed countries. We need to extend the healthy life expectancy so that companion animals can live without health problems. Oxidative stress is known to be involved in the onset and progression of various diseases, and oxidative stress markers have been suggested as useful indicators for the early detection of such diseases. The various reports describing the oxidative stress have also been studied in animals. For example, there were studies about oxidative stress associated with atopic dermatitis[28], cancer[29], heart failure[18], infection[33], intestinal disease[36], kidney disease[13,39], diabetes mellitus of animals[12]. Although numerous studies have been conducted, no research has clearly established reference values for oxidative stress markers in dogs regardless of breed. When determining such reference values, it may be necessary to consider the influence of sex, as oxidative stress is affected not only by oxygen consumption and inflammatory responses but also by various physiological factors, including hormonal balance and energy metabolism[4,15,44]. Moreover, in dogs, neutering induces alterations in hormonal balance and metabolism, which have been reported to potentially cause obesity, joint disorders, urinary incontinence, and tumor formation[22,37,40]. Several studies have examined the transient inflammatory response associated with neutering surgery or changes in oxidative stress markers immediately after ovariohysterectomy[2,41]. However, the medium- to long-term effects of neutering on oxidative stress markers remain insufficiently elucidated. Therefore, the present study aimed to clarify the variations in oxidative stress markers according to sex, neutering status, and disease condition in dogs, and to provide fundamental data that may contribute to the establishment of future reference values for canine oxidative stress markers.

Materials and Methods

Animals and sample preparation

The study included 161 dogs that presented to Famille Animal Hospital for routine health checkups or regular follow-up examinations for existing conditions, regardless of health status, disease or medication history, neutering status, age, or breed. Dogs that had undergone any surgical procedure, including neutering or spaying, immediately prior to blood sampling were excluded. The samples were collected from 2017 to 2018. A total of 161 samples were obtained from 25 breeds: Toy poodle (n = 31), Dachshund (n = 28), Mixed breed (n = 18), Chihuahua (n = 16), Pomeranian (n = 10), Shihtzu (n = 6), Yorkshire terrier (n = 6), Maltese (n = 6), Miniature schnauzer (n = 5), Welsh corgi pembroke (n = 4), Papillon (n = 4), Shiba (n = 4), Pekingese (n = 3), Miniature pinscher (n = 3), American cocker spaniel (n = 3), French bulldog (n = 2), Labrador retriever (n = 2), Beagle (n = 2), Border collie (n = 2), Staffordshire Bull Terrier (n = 1), Cavalier king Charles spaniel (n = 1), Bernese mountain dog (n = 1), Japanese spitz (n = 1), Standard poodle (n = 1), Cairn terrier (n = 1). The age of animals ranged from 4 to 201 months.

The dogs were classified into four sex groups: intact male dogs or castrated dogs or intact female dogs or spayed dogs. Additionally, the dogs were classified into two groups: off-therapy or during therapy (status at the time of sample collection). Dogs during therapy were those that had a confirmed diagnosis or were receiving medications or supplements for treatment or health maintenance at the time of sample collection. Dogs with a history of illness were classified as off-therapy if they were completely cured and were not receiving any medications or supplements.

Serum samples were obtained using serum separator tubes, including clot activator and

gel separator (Terumo, Tokyo, Japan). Plasma samples were obtained using heparin blood collection tube, including lithium heparin (Terumo, Tokyo, Japan). The time of blood sampling varied. The serum or plasma samples were immediately stored at −80 °C until further use. And then, the analysis was conducted immediately in our laboratory.

This study was reviewed and endorsed by the Ethics and Animal Welfare Committee of the Nippon Veterinary and Life Science University Animal Research Committee (29K-28, S29K-28).

Measurement

The samples were used to measure the concentration of d-ROMs and BAP using a free radical analyzer (Free Carpe Diem, Diacron International srl., Grosseto, Italy). We used a simple method to measure d-ROMs and BAP concentration[19,34,43].

The d-ROMs (derivatives of reactive oxygen metabolites) test quantifies total hydroperoxides, which are metabolites generated by reactive oxygen species and free radicals. The samples are mixed with an acetate buffer at pH 4.8, and in the presence of iron ions, hydroperoxides are converted to radicals. These radicals react with a chromogenic substrate, producing a colored compound whose concentration is measured spectrophotometrically at 505 nm. Results are expressed in Carratelli units (1 CARR U = 0.08 mg hydrogen peroxide/dl), with higher values indicating greater oxidative burden.

The BAP (biological antioxidant potential) test evaluates the overall reducing capacity of both endogenous antioxidants, such as albumin and reduced glutathione, and exogenous antioxidants, including vitamins C and E and polyphenols. In this assay, the addition of plasma sample to a colored solution, obtained by mixing a ferric chloride solution with a thiocyanate derivative solution, causes a recoloration. This change in color is measured using a spectrophotometer at 505 nm. Results are expressed in micromoles per liter (μmol/L), reflecting the total antioxidant capacity.

The oxidative stress index (OSI), a relative measure of oxidative stress, was calculated using the formula: OSI = (d-ROMs / BAP) × 100. This index integrates both oxidative burden and antioxidant capacity, providing a relative indicator of oxidative stress.

Table 1. Comparison between d-ROMs, BAP levels, and OSI in off-therapy (n = 84) and during therapy (n = 77) dogs. Data are presented as mean ± standard error of the mean.

	n	D-ROMs (U.CARR)	BAP (μmol/L)	OSI
Off-therapy	84	84.64 ± 18.36	2143.35±440.47	4.13 ±1.30
During therapy	77	85.00 ± 18.74	2199.29±372.98	3.96 ±1.01

Statistical methods

All data were presented as the mean ± SD. Significance was determined by the Mann-Whitney U test or Bonferroni test. The significance level was set at $P < 0.05$. IBM SPSS Statistics version 29 (Japanese language version, IBM Japan Co., Ltd, Tokyo Japan) was used for the statistical analysis.

Results

Comparison between Off-therapy and During therapy

The samples were classified as the off-therapy group (n = 84) or the group during therapy (n = 77). The concentrations of d-ROMs and BAP in the serum or plasma of off-therapy and during therapy are shown in Table1. No significant differences were observed in d-ROMs, BAP, and OSI between off-therapy and during therapy dogs.

Comparison between four off-therapy dog groups

The samples of off-therapy dogs were classified as intact male (n = 21), intact female (n = 12), castrated (n = 21) or spayed (n = 30). Values for d-ROMs, BAP and OSI of off- therapy dogs are shown in Figure 1. As shown in Figure1-a, the mean d-ROMs concentrations in intact males was 96.57 U.CARR. This result of intact male was

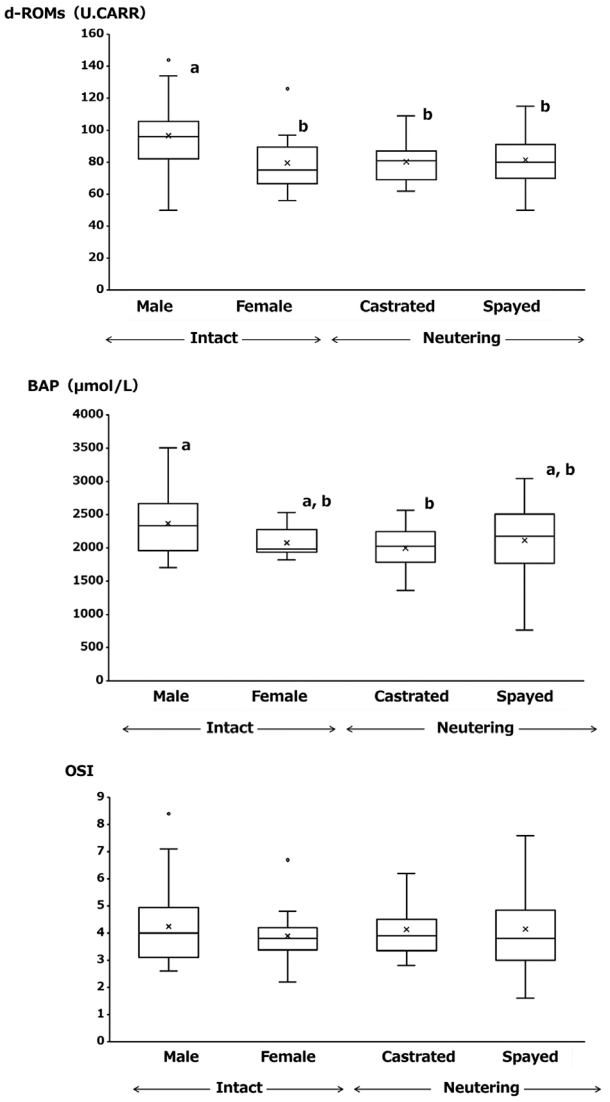

Fig. 1. Comparison between a) d-ROMs, b) BAP, and c) OSI levels in intact male (n = 21), intact female (n = 12), castrated (n = 21) and spayed (n = 30) in off-therapy dogs. Different letters indicate significant differences. (b < a, $P < 0.05$). The asterisk symbol (*) stands for mean values.

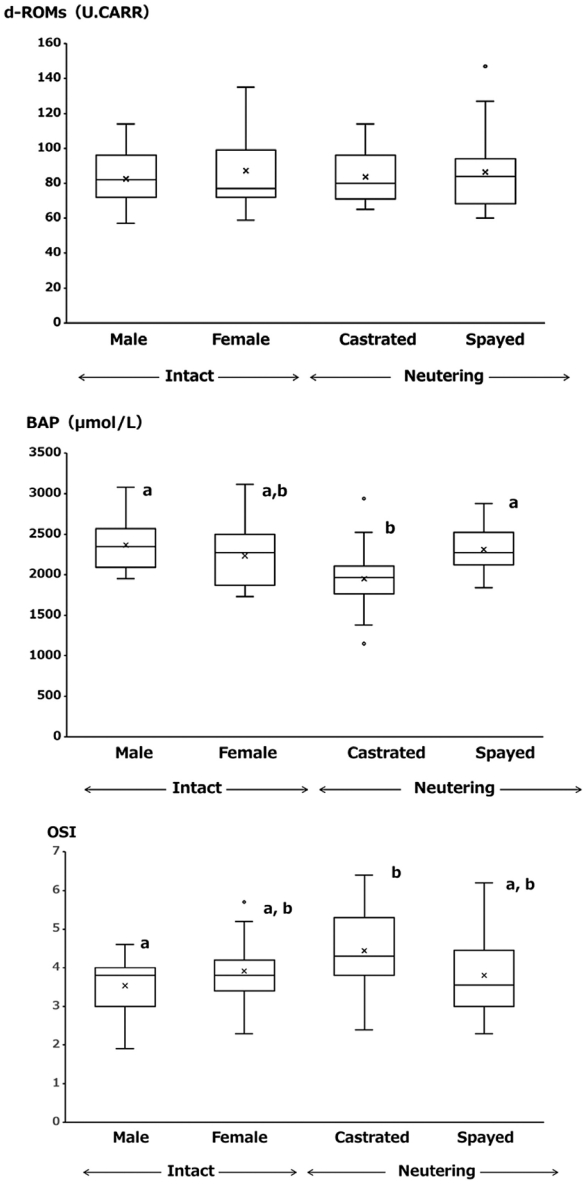

Fig. 2. Comparison between a) d-ROMs, b) BAP, and c) OSI levels in intact male (n = 15), intact female (n = 15), castrated (n = 23) and spayed (n = 24) in during therapy dogs. Different letters indicate significant differences (b < a, $P < 0.05$). The asterisk symbol (*) stands for mean values.

significantly higher ($P < 0.05$) than those in intact female (79.50 U.CARR), castrated (80.24 U.CARR) and spayed (81.43 U.CARR). On the other hand, the mean BAP concentrations of intact males were 2367.02 μmol/L, and the significant difference ($P < 0.05$) was only observed between intact male and castrated (Figure1-b). There was no significant difference between OSI values for four groups, as in shown Figure1-c.

Comparison between four dog groups during therapy

Four groups of dogs during therapy consist of intact male (n = 15), intact female (n = 15), castrated (n = 23) or spayed (n = 24) were compared in the next study as shown in Figure 2. Although the highest mean d-ROMs value was observed on the intact female (87.27 U.CARR), no significant differences observed between d-ROMS values for four groups (Figure2-a). On the other hand,

the mean BAP concentrations of intact male (2366.69 μmol/L), and spayed (2312.22 μmol/L) were significantly higher ($P < 0.05$) than castrated (1949.96 μmol/L) (Figure2-b). As shown in Figure 2-c, the significant difference was observed only between intact male (3.53) and castrated in OSI value (4.44).

Discussion

This study examined oxidative stress markers in dogs in relation to sex, neutering status, and the presence or absence of disease or medical treatment. Although numerous studies have reported on oxidative stress in dogs, fundamental research aimed at establishing reference values remains limited. In particular, little is known about sex-related differences or the impact of gonadectomy. Therefore, clarifying the extent to which sex and medication status influence oxidative stress markers are of considerable importance.

In this study, no significant differences were observed in d-ROMs, BAP, or OSI values between dogs receiving therapy and those off-therapy. The dogs classified as "therapy" were individuals administered medications or supplements for disease treatment or health maintenance. Previous studies have reported that supplementation with antioxidant components improves skin conditions and decreases oxidative stress markers in dogs with atopic dermatitis[35]. Similarly, dogs fed antioxidant enriched diets showed significantly lower oxidative stress indicators compared with their pre-intake levels[6,30,38]. Furthermore, several studies on various diseases have demonstrated that therapeutic interventions or antioxidant administration lead to symptomatic improvement and a reduction in oxidative stress[5,7,20]. Based on these findings, the lack of increased oxidative stress in the therapy group of the present study may be attributed to the compensatory effects of medications or supplements on antioxidant defense mechanisms. In other words, therapeutic interventions may have contributed to the restoration of the redox balance in these dogs.

In dogs in the off-therapy group, a sex-related difference was observed in d-ROMs values, with intact males showing a tendency toward higher levels. This finding is likely attributable to the influence of testosterone, which promotes muscle growth and metabolic activation and enhances the production of ROS through increased NADPH oxidase activity[27]. In addition, intact males typically display higher levels of activity and aggression, which may further increase ROS generation through heightened sympathetic nervous system activity and metabolic rate[17,31]. Psychological stress associated with social competition may also induce oxidative stress via cortisol secretion[3,26,31]. Collectively, these findings suggest that elevated d-ROMs levels observed in intact male dogs may result from a combination of metabolic factors related to sex hormones and behavioral or stress-related influences. Furthermore, the mean BAP concentration in intact off-therapy males was significantly higher than that in castrated males. The level of antioxidants generally increases in response to elevated production of ROS, reflecting a compensatory reaction to oxidative stimuli. Conversely, antioxidant concentrations tend to decrease when ROS levels decline, as there is less need to neutralize oxidative reactions[34]. Given that intact off-therapy males exhibited higher d-ROMs concentrations, their elevated BAP values were likely a compensatory response to increased ROS production. No significant differences in OSI values were observed among the off-therapy groups. OSI represents the balance between d-ROMs and BAP, with higher values indicating greater oxidative stress. Even when d-ROMs levels are elevated, an upregulation of the antioxidant defense system that increases BAP can result in lower OSI values. In the present study, both d-ROMs and BAP levels were elevated in intact off-therapy males, suggesting that antioxidant activity effectively neutralized ROS, thereby maintaining the oxidative-antioxidative balance within a physiological range.

No significant differences were observed in d-ROMs levels among any of the groups in therapy dogs. In contrast, BAP levels were

significantly higher in intact therapy males and spayed therapy females compared to castrated therapy males. Furthermore, OSI in castrated therapy males was significantly higher than that in intact therapy males. Intact males are known to have inherently higher basal metabolism, which facilitates the production of reactive oxygen species (ROS)[25,27]. Consequently, their antioxidant capacity tends to be maintained at a higher level. In spayed females, the loss of estrogen is generally associated with a reduction in antioxidant defense. Estrogen acts as an antioxidant by scavenging free radicals due to the presence of a phenolic hydroxyl group[4,27]. However, because no significant differences were observed in d-ROMs, the increase in BAP is likely not a compensatory response to ROM production, but rather a secondary effect induced by therapy or supplementation, leading to enhanced antioxidant capacity. In both the off-therapy and therapy groups, differences in oxidative stress markers were observed between intact and castrated males, suggesting that gonadectomy may influence the balance between oxidative stress and antioxidant capacity in males. In contrast, no significant differences in oxidative stress markers were observed between spayed and intact females, regardless of therapy status. Estrogen is known to exert strong antioxidant effects, and females generally exhibit higher antioxidant capacity than males[4,11,8]. Typically, ovariectomy leads to decreased estrogen levels, resulting in increased d-ROMs, decreased BAP, and elevated OSI; however, such trends were not observed in this study. One possible explanation is that estrogen concentrations fluctuate markedly in intact females across the estrous cycle, causing periodic changes in antioxidant capacity, which may have averaged out individual differences within the group. Additionally, although ovariectomy is expected to reduce antioxidant capacity[1], compensatory antioxidant responses to metabolic changes or mild lipid peroxidation have also been reported[41]. These findings suggest that the impact of gonadectomy on oxidative stress may be less pronounced in females than in males.

This study has several limitations. First, serum concentrations of sex hormones such as testosterone and estrogen were not measured. As these hormones are known to influence both oxidative stress and antioxidant capacity, future studies should include their quantitative assessment to better elucidate their contribution to redox regulation. Second, behavioral parameters and physiological stress indicators were not evaluated. Because stress can significantly modulate oxidative balance, incorporating these factors will allow for a more comprehensive interpretation of oxidative stress dynamics in dogs. Third, the dogs' diets were not standardized. The commercial foods provided may have contained naturally occurring antioxidants such as polyphenols, which could have influenced the measured redox status. Additionally, age is known to affect oxidative stress levels; however, accurate age information was not available for all dogs and was therefore not included in the analysis. Therefore, future studies should incorporate these factors to clarify the physiological background underlying sex-related differences in oxidative stress.

Conclusion

The present findings suggest that intact males tend to exhibit higher levels of oxidative stress markers compared with intact females, castrated males, and spayed females. Although the underlying mechanisms remain to be fully elucidated, these results underscore the importance of considering the influence of sex hormones when establishing reference values for oxidative stress in dogs. While the current dataset is not sufficient to draw definitive conclusions about the association between oxidative stress and sex differences in canine patients, the study provides valuable preliminary insights. Further large-scale investigations involving broader canine populations are warranted to elucidate the mechanisms linking oxidative stress and sex, thereby contributing to a deeper understanding of redox physiology in dogs.

Conflicts of Interest

The authors declare no conflicts of interest associated with this manuscript.

References

1) Acar BD, Demirel MA, Dizakar SÖA, Birdane KM. The evaluation of the oxidative stress index of reproductive tissues and serum thiol/disulphide homeostasis during estrous cycle in bitches. Ankara Üniversitesi Veteriner Fakültesi Dergisi 67, 87–94, 2020. doi: 10.33988/auvfd.604496.
2) Aengwanich W, Sakundech K, Chompoosan C, Tuchpramuk P, Boonsorn T. Physiological changes, pain stress, oxi-dative stress, and total antioxidant capacity before, during, and after castration in male dogs. Journal of Veterinary Behavior 32, 76–79, 2019. doi: 10.1016/j.jveb.2019.04.004.
3) Aschbacher K, O'Donovan A, Wolkowitz OM, Dhabhar FS, Su Y, Epel E. Good stress, bad stress and oxidative stress: Insights from anticipatory cortisol reactivity. Psychoneuroendocrinology 38, 1698–1708, 2013. doi: 10.1016/j.psyneuen.2013.02.004.
4) Barp J, Araújo AS, Fernandes TR, Rigatto KV, Llesuy S, Belló-Klein A, Singal P. Myocardial antioxidant and oxidative stress changes due to sex hormones. Braz J Med Biol Res 35, 1075–1081, 2002. doi: 10.1590/s0100-879x2002000900008.
5) Barrouin-Melo SM, Anturaniemi J, Sankari S, Griinari M, Atroshi F, Ounjaijean S, Hielm-Björkman AK. Evaluating oxidative stress, serological- and haematological status of dogs suffering from osteoarthritis, after supplementing their diet with fish or corn oil. Lipids Health Dis 15, 139, 2016. doi: 10.1186/s12944-016-0304-6.
6) Baskin CR, Hinchcliff KW, DiSilvestro RA, Reinhart GA, Hayek MG, Chew BP, Burr JR, Swenson RA. Effects of dietary antioxidant supplementation on oxidative damage and resistance to oxidative damage during prolonged exercise in sled dogs. Am J Vet Res 61, 886–891, 2000. doi: 10.2460/ajvr.2000.61.886.
7) Behera SK, Dimri U, Singh SK, Mohanta RK. The curative and antioxidative efficiency of ivermectin and ivermectin + vitamin E-selenium treatment on canine Sarcoptes scabiei infestation. Vet Res Commun 35, 237–244, 2011. doi: 10.1007/s11259-011-9468-8.
8) Bellanti F, Matteo M, Rollo T, De Rosario F, Greco P, Vendemiale G, Serviddio G. Sex hormones modulate circulating antioxidant enzymes: impact on oxidative stress in aging. Redox Biol 1, 340–346, 2013. doi: 10.1016/j.redox.2013.05.003.
9) Bhattacharyya A, Chattopadhyay R, Mitra S, Crowe SE. Oxidative stress: an essential factor in the pathogenesis of gastrointestinal mucosal diseases. Physiol Rev 94, 329–354, 2014. doi: 10.1152/physrev.00040.2012.
10) Bickers DR, Athar M. Oxidative stress in the pathogenesis of skin disease. J Invest Dermatol 126, 2565–2575, 2006. doi: 10.1038/sj.jid.5700340.
11) Brunelli E, Domanico F, La Russa D, Pellegrino D. Sex differences in oxidative stress biomarkers. Curr Drug Targets 15, 811–815, 2014. doi: 10.2174/1389450115666140624112317.
12) Chansaisakorn W, Sriphavatsarakorn P, Sopakdittapong P, Trisiriroj M, Pondeenana S, Buranakarl C. Oxi-dative stress and intraerythrocytic concentrations of sodium and potassium in diabetic dogs. Vet Res Commun 33, 67–75, 2009. doi: 10.1007/s11259-008-9073-7.
13) Chen H, Segev G. Evaluation of oxidative stress in dogs and cats with chronic kidney disease. J Vet Intern Med 38, 3105–3110, 2024. doi: 10.1111/jvim.17230.
14) de Jager TL, Cockrell AE, Du Plessis SS. Ultraviolet light induced generation of reactive oxygen species. Adv Exp Med Biol 996, 15–23, 2017. doi: 10.1007/978-3-319-56017-5_2.
15) Dennis KK, Go YM, Jones DP. Redox systems biology of nutrition and oxidative stress. J

Nutr 149, 553–565, 2019. doi: 10.1093/jn/nxy306.
16) Dursun E, Akalin FA, Genc T, Cinar N, Erel O, Yildiz BO. Oxidative stress and periodontal disease in Obesity. Medicine (Baltimore) 95, e3136, 2016. doi: 10.1097/MD.0000000000003136.
17) Farhoody P, Mallawaarachchi I, Tarwater PM, Serpell JA, Duffy DL, Zink C. Aggression toward Familiar People, Strangers, and Conspecifics in Gonadectomized and Intact Dogs. Front Vet Sci 5, 18, 2018. doi: 10.3389/fvets.2018.00018.
18) Freeman LM, Rush JE, Milbury PE, Blumberg JB. Antioxidant status and biomarkers of oxidative stress in dogs with congestive heart failure. J Vet Intern Med 19, 537–541, 2005. doi: 10.1892/0891-6640(2005)19[537:asaboo]2.0.co;2.
19) Fukui T, Yamauchi K, Maruyama M, Yasuda T, Kohno M, Abe Y. Significance of measuring oxidative stress in lifestyle-related diseases from the viewpoint of correlation between d-ROMs and BAP in Japanese subjects. Hypertens Res 34, 1041-1045, 2011. doi: 10.1038/hr.2011.76.
20) Halfen DP, Caragelasco DS, Nogueira JPS, Jeremias JT, Pedrinelli V, Oba PM, Ruberti B, Pontieri CFF, Kogika MM, Brunetto MA. Evaluation of electrolyte concentration and pro-inflammatory and oxidative status in dogs with advanced chronic kidney disease under dietary treatment. Toxins(Basel) 12, 3, 2019. doi: 10.3390/toxins12010003.
21) Halliwell B. Reactive species and antioxidants. Redox biology is a fundamental theme of aerobic life. Plant Physiol 141, 312–322, 2006. doi: 10.1104/pp.106.077073.
22) Hart BL, Hart LA, Thigpen AP, Willits NH. Neutering of German shepherd dogs: associated joint disorders, cancers and urinary incontinence. Vet Med Sci 2, 191-199, 2016. doi: 10.1002/vms3.34.
23) He L, He T, Farrar S, Ji L, Liu T, Ma X. Antioxidants maintain cellular redox homeostasis by elimination of reactive oxygen species. Cell Physiol Biochem 44, 532–553, 2017. doi: 10.1159/000485089.
24) Hur J, Sullivan KA, Schuyler AD, Hong Y, Pande M, States DJ, Jagadish HV, Feldman EL. Literature-based discovery of diabetes- and ROS-related targets. BMC Med Genomics 3, 49, 2010. doi: 10.1186/1755-8794-3-49.
25) Ide T, Tsutsui H, Ohashi N, Hayashidani S, Suematsu N, Tsuchihashi M, Tamai H, Takeshita A. Greater oxidative stress in healthy young men compared with premenopausal women. Arterioscler Thromb Vasc Biol 22, 438–442, 2002. doi: 10.1161/hq0302.104515.
26) Juodžentė D, Karvelienė B, Riškevičienė V. The influence of the duration of the preoperative time spent in the veterinary clinic without the owner on the psychogenic and oxidative stress in dog. J Vet Med Sci 80, 1129–1133, 2018. doi: 10.1292/jvms.18-0066.
27) Kander MC, Cui Y, Liu Z. Gender difference in oxidative stress: a new look at the mechanisms for cardiovascular diseases. J Cell Mol Med 21, 1024–1032, 2016. doi: 10.1111/jcmm.13038.
28) Kapun AP, Salobir J, Levart A, Kotnik T, Svete AN. Oxidative stress markers in canine atopic dermatitis. Res Vet Sci 92, 469–470, 2012. doi: 10.1016/j.rvsc.2011.04.014.
29) Macotpet A, Suksawat F, Sukon P, Pimpakdee K, Pattarapanwichien E, Tangrassameeprasert R, Boonsiri P. Oxidative stress in cancer-bearing dogs assessed by measuring serum malondialdehyde. BMC Vet Res 9, 101, 2013. doi: 10.1186/1746-6148-9-101.
30) Minieri S, Altomonte I, Bellini V, Casini L, Gazzano A. A diet supplemented with oil-free olive pulp flour (MOP-ManniOlivePowder®) improves the oxidative status of dogs. Animals (Basel) 14, 2568, 2024. doi: 10.3390/ani14172568.
31) Motlagh DA, Asadpour R, Jarolmasjed SH, Ansari MHK, Darabadi SK. Comparative Analysis of Oxidative Stress Induced by Chemical and Surgical Castration in Male Dogs. Veterinary and Comparative Biomedical Research 2, 28–35, 2025. doi: 10.22103/

vcbr.2025.25128.1062.
32) Nagai H, Noguchi T, Homma K, Katagiri K, Takeda K, Matsuzawa A, Ichijo H. Ubiquitin-like sequence in ASK1 plays critical roles in the recognition and stabilization by USP9X and oxidative stress-induced cell death. Mol Cell 36, 805–818, 2009. doi: 10.1016/j.molcel.2009.10.016.
33) Panda D, Patra RC, Nandi S, Swarup D. Oxidative stress indices in gastroenteritis in dogs with canine parvoviral infection. Res Vet Sci 86, 36–42, 2009. doi: 10.1016/j.rvsc.2008.05.008.
34) Pasquini A, Luchetti E, Marchetti V, Cardini G, Iorio EL. Analytical performances of d-ROMs test and BAP test in canine plasma. Definition of the normal range in healthy Labrador dogs. Vet Res Commun 32, 137–143, 2008. doi: 10.1007/s11259-007-9014-x.
35) Plevnik Kapun A, Salobir J, Levart A, Tavčar Kalcher G, Nemec Svete A, Kotnik T. Vitamin E supplementation in canine atopic dermatitis: improvement of clinical signs and effects on oxidative stress markers. Vet Rec 175, 560, 2014. doi: https://doi.org/ 10.1136/vr.102547.
36) Rubio CP, Martínez-Subiela S, Hernández-Ruiz J, Tvarijonaviciute A, Cerón JJ, Allenspach K. Serum bi-omarkers of oxidative stress in dogs with idiopathic inflammatory bowel disease. Vet J 221, 56–61, 2017. doi: 10.1016/j.tvjl.2017.02.003.
37) Salt C, Morris PJ, Wilson D, Lund EM, German JA. Association between life span and body condition in neutered client-owned dogs. J Vet Intern Med 33, 89–99, 2019. doi: 10.1111/jvim.15367.
38) Sechi S, Fiore F, Chiavolelli F, Dimauro C, Nudda A, Cocco R. Oxidative stress and food supplementation with antioxidants in therapy dogs. Can J Vet Res 81, 206–216, 2017.
39) Silva AC, de Almeida BF, Soeiro CS, Ferreira WL, de Lima VM, Ciarlini PC. Oxidative stress, superoxide production, and apoptosis of neutrophils in dogs with chronic kidney disease. Can J Vet Res 77, 136–141, 2013.
40) Spain CV, Scarlett JM, Houpt KA. Long-term risks and benefits of early-age gonadectomy in dogs. J Am Vet Med Assoc 224, 380–387, 2004. doi: 10.2460/javma.2004.224.380.
41) Szczubial M, Kankofer M, Bochniarz M, Dąbrowski R. Effects of ovariohysterectomy on oxidative stress markers in female dogs. Reprod Domest Anim 50, 393–399, 2015. doi: 10.1111/rda.12501.
42) Toyokuni S. Reactive oxygen species-induced molecular damage and its application in pathology. Pathol Int 49, 91–102, 1999. doi: 10.1046/j.1440-1827.1999.00829.x.
43) Trotti R, Carratelli M, Barbieri M. Performance and clinical application of a new, fast method for the detection of hydroperoxides in serum. Panminerva Med 44, 37–40, 2002.
44) Villegas-Aguilar MdC, Fernández-Ochoa Á, Cádiz-Gurrea, MdlL, Pimentel-Moral S, Lozano-Sánchez J, Arráez-Román D, Segura-Carretero A. Pleiotropic biological effects of dietary phenolic compounds and their metabolites on energy metabolism, inflammation and aging. Molecules 25, 596, 2020. doi: 10.3390/molecules25030596.