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## INTRODUCTION

The increasing incidence of colorectal cancer in Brazil has been following the growth on population's level of obesity and sedentary lifestyle, both of which are important risk factors for this type of cancer<sup>1</sup>. Regular practice of aerobic exercise reduces the risk of developing colon cancer and preclinical studies demonstrated that physical exercise promotes antagonistic effects on colon tumorigenesis, reducing the formation of pre-neoplastic lesions and tumors<sup>2,3</sup>.

Physical exercise seems to impact in all stages of tumorigenesis and this anti-tumoral effects it's shown to be involve in most of cancer hallmarks, suggesting that it's implementation in the clinic may have positive impacts on disease control and patients prognostic<sup>3,4,5</sup>. However, first this broad mechanisms need further clarification as well as the optimal timing for exercise program application for a greater impact on colon tumors burden.

## METHODOLOGY

75 Balb/C mice (adult males, 7 weeks of age) were divided in four experimental groups (Figure1). The moderate-intensity swimming protocol was adapted from Frajacomo et al. (2015) and carried out in a polyethylene box with a capacity of 36 liters (dimensions 21 x 39 x 60 cm) filled with preheated water (33°+ 2°). The training intensity was established by the determination of the maximal lactate stade-state in the control group (MLSS).

After tumor counts, performed with fresh colon (Figure 2), part of colon and tumor tissue was paraffinized for histopathological classification and recounting and a other part was frozen at -80° for molecular analyzes.

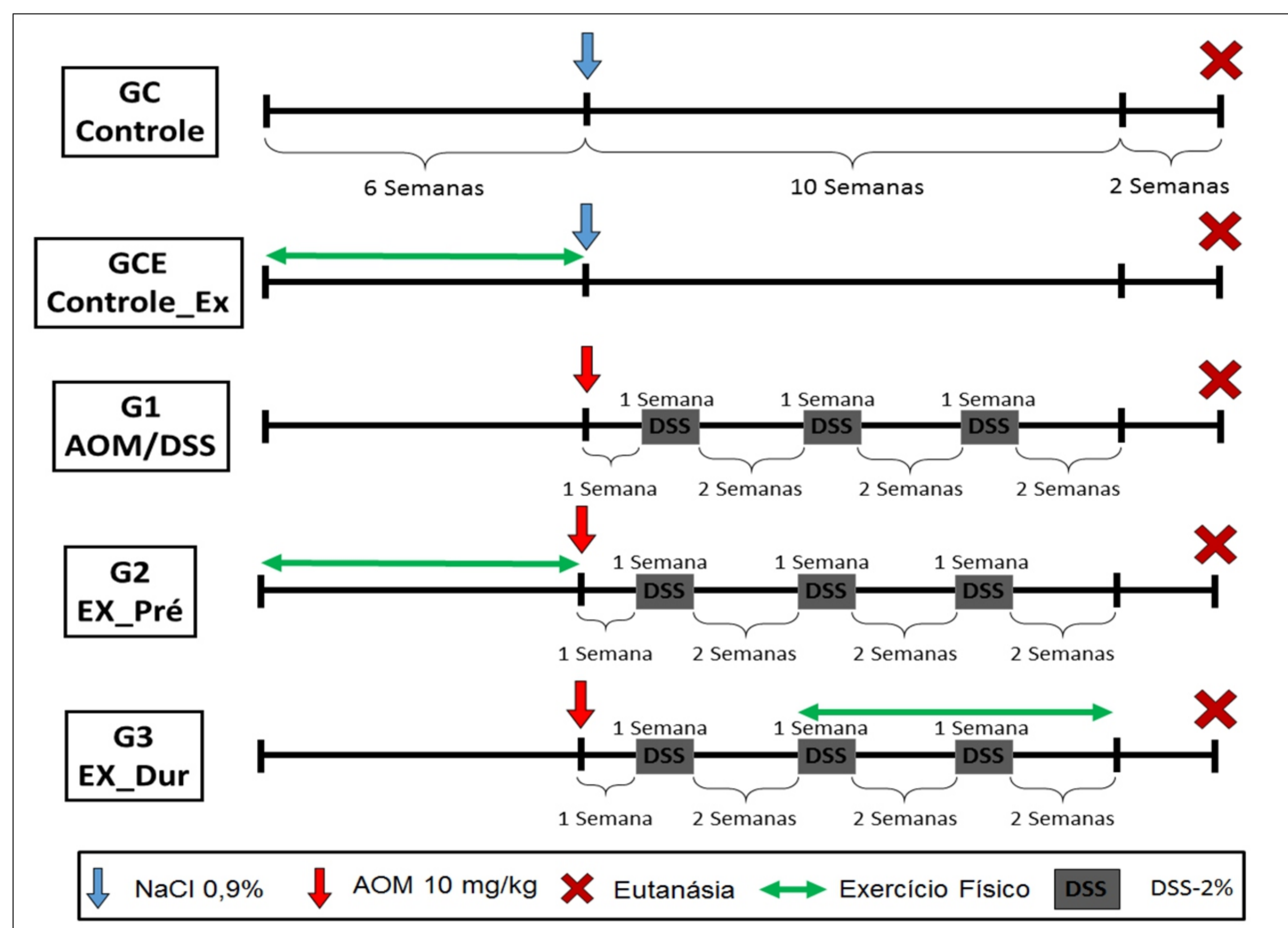


Figure 1. Experimental design. Blue arrow: application of saline solution; Red arrow: application of AOM (10mg/kg); Red X: euthanasia; Green double arrow: Exercise protocol. Gray box: DSS at 2, 1 and 0.5% in water ad libitum; Keys indicate the intervals between activities.

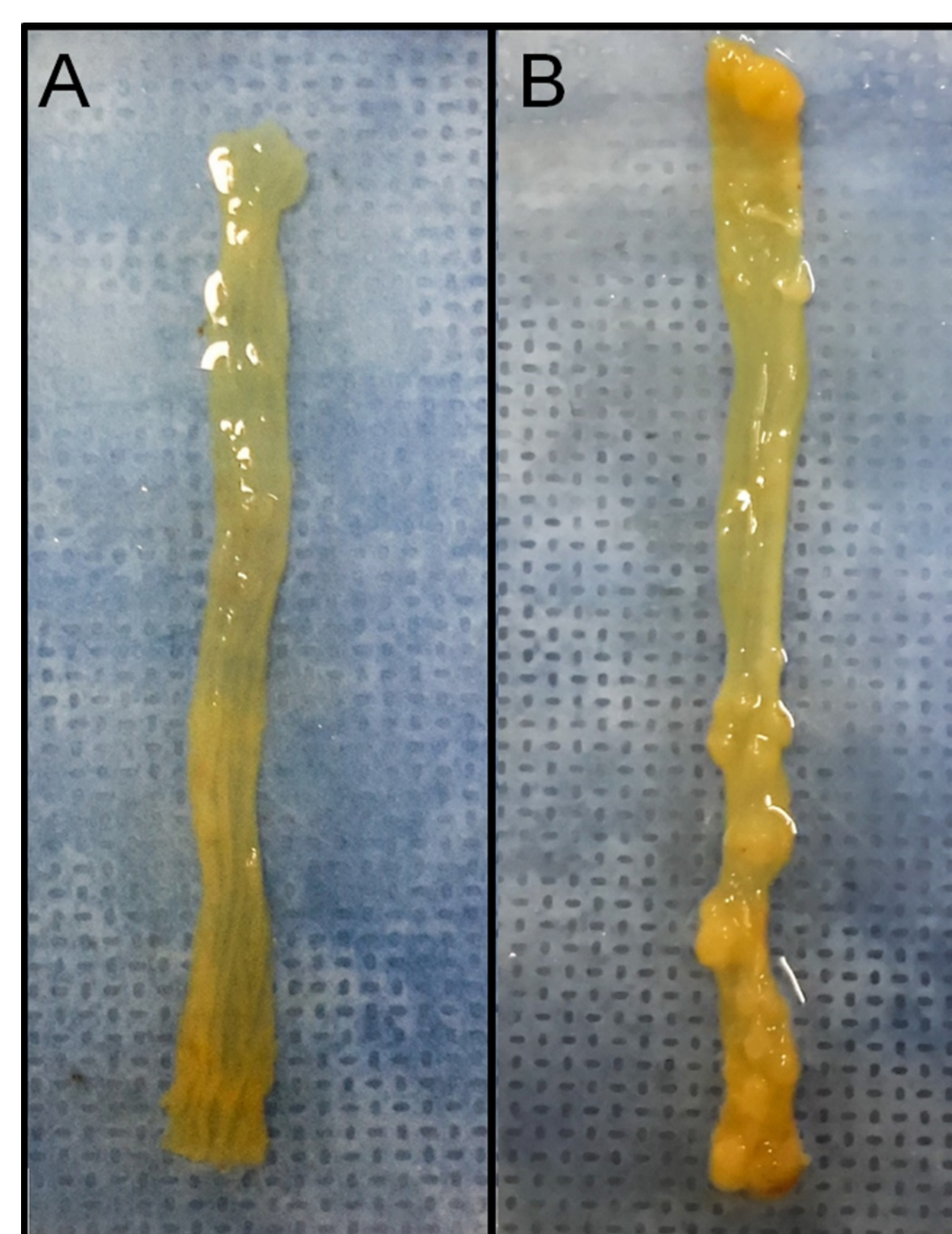


Figure 2. (a) colon without visible tumors; (b) colon with

## OBJECTIVES

The primary endpoint of this project was to investigate the effects of moderate aerobic exercise on the formation, multiplicity and size of colon tumors in Balb/c mice treated with colonotropic carcinogenic inducer azoxymethane (AOM) and inflammatory promoter dextran sodium sulfate (DSS).

The secondary endpoints included: molecular analysis on genetic and epigenetic regulation related to classic altered pathways in colon cancer; Quantification of inflammatory markers as NF-kB, PGE-2, iNOS; Investigate whether the moment of exercise application changes its impact on the neoplastic process.

## PRIMARY RESULTS

Table 1. Tumor incidence among experimental groups.

Groups	Incidence	%
AOM / DSS	5 / 15	35
EX_PRE	3 / 14	20
EX_DUR	5 / 14	35

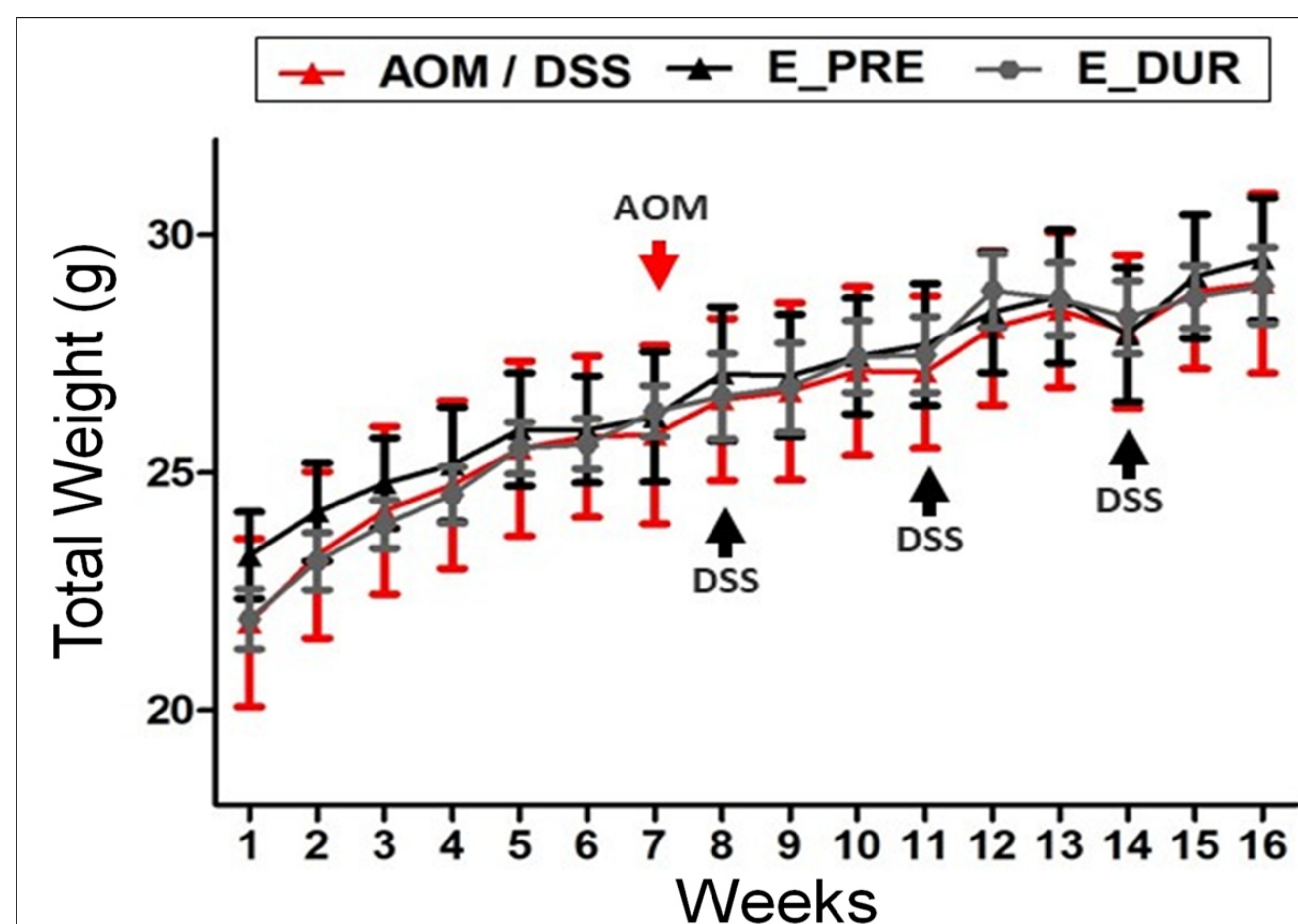


Figure 3. Weekly total weight gain in animals among aom/dss treated groups.

## CONCLUSION

The histological counting revealed that the previous exercise practice had lowed the tumor incidence while exercise performed along with tumor development did not impact on tumor burden. Histopathology analysis in paraffinized tissue will add more information about exercise mechanisms upon tumors size and grade.

## REFERENCES

1. WOLIN, K.Y. et al. Physical activity and colon cancer prevention: a meta-analysis. *British journal of cancer*, v.100, n. 4, p. 611-616, 2009.
2. INSTITUTO NACIONAL DO CÂNCER. Estimativa 2016: incidência de câncer no Brasil. Instituto Nacional de Câncer José Alencar Gomes da Silva, Rio de Janeiro, INCA, (2015).
3. ASHCRAFT, K.A. et al. Efficacy and mechanisms of aerobic exercise on cancer initiation, progression, and metastasis: a critical systematic review of in vivo preclinical data. *Cancer research*, 2016.
4. RUIZ-CASADO, A. et al. Exercise and the Hallmarks of Cancer. *Trends in Cancer*, 2017.
5. BROWN, J. C.; HARHAY, M. O.; HARHAY, M. N. Physical function as a prognostic biomarker among cancer survivors. *British journal of cancer*, v. 112, n. 1, p. 194, 2015.
6. FRAJACOMO, Fernando Tadeu et al. Aerobic training activates interleukin 10 for colon anticarcinogenic effects. *Med Sci Sports Exerc*, v. 47, p. 1806-1813, 2015.