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Electrocardiographic analysis in mice (C57BL/6) inoculated with melanoma (B16F10)

[Análise eletrocardiográfica em camundongos (C57BL/6) inoculados com melanoma (B16F10)]

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Abstract: B16F10 cells are a murine melanoma cell line characterized by high metastatic potential and resistance to various treatments. Studies indicate that cancer can cause significant alterations in the heart's electrical conduction system. The aim of this study was to evaluate and compare electrocardiographic tracings in C57BL/6 mice using a non-invasive computerized electrocardiography method, comparing healthy animals and mice inoculated with B16F10 cells. C57BL/6 mice were used and subcutaneously inoculated with B16F10 cells, being divided into a control group and a melanoma group. The animals were monitored over 21 days, with electrocardiographic measurements performed at seven-day intervals. Non-invasive electrodes were used to analyze parameters such as heart rate, amplitude and duration of the P wave, QRS complex, and PR and RR intervals. Changes in heart rate were observed, as well as alterations in PR and RR intervals and in the amplitude and duration of the P and R waves, indicating possible electrical conduction dysfunctions associated with melanoma. These findings suggest that B16F10 inoculation may have a direct impact on the heart's electrical conduction system, possibly due to the release of inflammatory cytokines or tumor-induced alterations in cardiac metabolism. The presence of electrocardiographic alterations in mice with melanoma reinforces the hypothesis that cancer can affect cardiac function. These results may contribute to a better understanding of the relationship between cancer pathophysiology and cardiovascular diseases and may support the development of new therapeutic strategies aimed at protecting cardiac function during melanoma treatment.

Keywords: Skin cancer; electrocardiogram; *Mus musculus*; cardiovascular system.

Resumo: As células B16F10 são uma linhagem de melanoma murino caracterizada por alto potencial metastático e resistência a diversos tratamentos. Estudos indicam que o câncer pode causar alterações significativas no sistema de condução elétrica do coração. O objetivo deste estudo foi avaliar e comparar os traçados eletrocardiográficos em camundongos C57BL/6 utilizando um método de eletrocardiografia computadorizada não invasiva, comparando animais saudáveis e camundongos inoculados com células B16F10. Camundongos C57BL/6 foram utilizados e inoculados subcutaneamente com células B16F10, sendo divididos em um grupo controle e um grupo melanoma. Os animais foram monitorados ao longo de 21 dias, com medições eletrocardiográficas

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realizadas em intervalos de sete dias. Eletrodos não invasivos foram utilizados para analisar parâmetros como frequência cardíaca, amplitude e duração da onda P, complexo QRS e intervalos PR e RR. Foram observadas alterações na frequência cardíaca, bem como nos intervalos PR e RR e na amplitude e duração das ondas P e R, indicando possíveis disfunções na condução elétrica associadas ao melanoma. Esses achados sugerem que a inoculação de B16F10 pode ter impacto direto no sistema de condução elétrica cardíaco, possivelmente devido à liberação de citocinas inflamatórias ou a alterações no metabolismo cardíaco induzidas pelo tumor. A presença de alterações eletrocardiográficas em camundongos com melanoma reforça a hipótese de que o câncer pode afetar a função cardíaca. Esses resultados podem contribuir para uma melhor compreensão da relação entre a fisiopatologia do câncer e as doenças cardiovasculares, além de apoiar o desenvolvimento de novas estratégias terapêuticas voltadas à proteção da função cardíaca durante o tratamento do melanoma.

Palavras-chave: Câncer de pele; eletrocardiograma; *Mus musculus*; sistema cardiovascular.

1. Introduction

Melanoma is a potentially fatal disease and is considered the most aggressive form of skin cancer. It is defined as a cluster of abnormal cells capable of proliferating and spreading throughout the body [1]. Melanoma is characterized by a pathological process occurring at the dermoepidermal junction, where the uncontrolled proliferation of melanocytes leads to their transformation into atypical cells, resulting in malignancy [2].

Unlike infections caused by external agents, cancer originates within the organism itself. In this context, cells may initiate a neoplastic process, transforming into pathological entities capable of uncontrolled proliferation and dissemination. Normally, cells contribute to host homeostasis; however, when regulatory mechanisms fail, they lose the ability to respond to growth signals and begin to proliferate uncontrollably. This pathological behavior confers aggressiveness, enabling metastasis and invasion of multiple organ systems [3].

Metastasis is considered an evolutionary process of cancer. Recent studies describe it as a dynamic progression in which tumor cells proliferate, acquire metastatic potential, and develop new phenotypic characteristics according to their microenvironment. This process involves the dissemination of cancer cells from the primary tumor to distant sites through blood or lymphatic circulation [4].

Tumor progression and metastatic spread are closely associated with systemic physiological alterations, including neuroendocrine responses. Catecholamines, hormones primarily released by the adrenal glands, play a central role in this process. In melanoma and its interaction with the cardiovascular system, catecholamines activate the sympathetic nervous system and regulate key physiological functions such as heart rate, bronchodilation, and energy mobilization, preparing the organism for the fight or flight response. Evidence suggests that these mediators may contribute to cancer progression and induce significant alterations in cardiovascular function [5].

Studies have shown that the tumor microenvironment of melanoma can be affected by catecholamines, which act through adrenergic receptors expressed on tumor cells. The activation of these receptors can promote various intracellular signaling pathways that lead to cell proliferation, angiogenesis (the formation of new blood vessels), and the inhibition of apoptosis (programmed cell death). Additionally, norepinephrine and epinephrine can increase the expression of pro-inflammatory molecules and growth factors, such as vascular endothelial growth factors, which facilitate melanoma cell invasion and metastasis. They also influence the cardiovascular system, impacting heart rate, blood pressure, and vascular tone [6, 7].

The interaction between melanoma and the cardiovascular system is partially modulated by the release of catecholamines. Patients with metastatic melanoma often exhibit elevated stress levels, leading to a sustained increase in the release of these substances. This increase can have direct harmful effects on the cardiovascular system, worsening conditions such as hypertension, arrhythmias, and heart disease [8, 9].

Therefore, this study aimed to evaluate and compare electrocardiographic tracing in 44 C57BL/6 mice using a non-invasive computerized electrocardiography method in both healthy and B16F10-bearing mice. It assessed electrical changes, rhythm, and heart rate, as well as the morphological analysis of the amplitude (mV) and duration (ms) of the P wave, PR interval duration, QRS complex duration, R wave amplitude and R-R interval duration in control and melanoma-bearing mice.

2. Material and methods

The study used 44 C57BL/6 mice and was approved by the Ethics Committee on the Use of Animals (CEUA) of the State University of Ponta Grossa (UEPG), under protocol number 23.000041280-0. All procedures complied with international guidelines for animal use. Body weight was measured in all animals using a digital precision scale throughout the experimental period. The animals underwent non-invasive electrocardiography and were divided into two groups: a control group and a melanoma group.

In the melanoma group, mice were subcutaneously inoculated with B16F10 tumor cells, whereas the control group received a placebo. The animals were evaluated at baseline (day 0) and subsequently at 7, 14, and 21 days after inoculation. The mice were evaluated on different days to monitor the progression of the disease and the correlation of melanoma with the heart's electrical conduction system using a veterinary electrocardiograph. Were selected 22 animals to participate in the melanoma group and 22 animals for the control group.

For the experiment, the murine melanoma B16F10 cell line was used, which was provided by the Center for Translational Investigation in Oncology at the Cancer Institute of the State of São Paulo (ICESP), affiliated with the Faculty of Medicine of the University of São Paulo. Conducted under aseptic conditions using a laminar flow hood with an ultraviolet lamp and sterile materials to minimize the risk of cross-contamination, thus controlling the lineage being researched. The cells were cultured in RPMI – 1640 medium, supplemented with 10 % Fetal Bovine Serum (FBS). The cell culture was evaluated daily using an inverted microscope, and the culture medium was replaced every three days and subsequently assessed. The flasks were stored in an incubator at a standard temperature of 37º C, with an atmosphere of 5 % carbon dioxide.

The animals were subjected to subcutaneous (SC) administration of B16F10 cell line cells in the right dorsal region, using a 1 mL syringe and a hypodermic needle (13 x 0.3 mm). Each mouse was inoculated with 0.1 mL containing 5×10^4 tumor cells in the right dorsal region. They were monitored daily and subsequently underwent electrocardiographic evaluation at predetermined intervals (zero, seven, fourteen, and twenty-one days).

The animals were sedated with Midazolam at a concentration of 1 mg/mL and a dose of 5 mg/kg, intraperitoneal (IP) [10], with the aim of reducing the stress of the mice during the acquisition of the electrocardiographic exam. In both groups, electrocardiographic recordings were made in lead DI, DII, DIII, aVR, aVL and, aVF, using a 12-lead digital veterinary electrocardiograph (InPulse®), calibrated to a tracing speed of 50 mm/s and a sensitivity of 10mm/mV (N).

The collection of electrocardiographic data was carried out with the animals positioned in ventral recumbency using alligator clip electrodes placed near the humero-radial joints above the olecranon, with the L electrode (yellow) on the left thoracic limb and the R electrode (red) on the right thoracic limb, and near the femorotibial joints with the F electrode (green) on the left pelvic limb and the N electrode (black) on the right pelvic limb. This setup allowed for the simultaneous capture of six leads (DI, DII, DIII, aVL, aVr e aVF) [11–13].

The electrocardiographic examination was conducted for a continuous period of three minutes for each animal, with the mice positioned in ventral recumbency. The animals were identified and registered in a database of the electrocardiographic equipment's software, which included the identification of the mouse, species, date, and time of the electrocardiographic tracing execution.

Data analysis was conducted using GraphPad Prism software (version 8.0.1). The data were subjected to a normality test, Shapiro-Wilk, followed by an Analysis of Variance (ANOVA), a statistical method suitable for comparing means between experimental groups. Due to statistical differences between the groups, Student's t-test was applied to determine which groups differed significantly from each other. A significance level of 5 % ($P<0.05$) was adopted in all analyses, ensuring rigor in the interpretation of the effects of the B16F10 group on the control group. The research will involve 44 mice, and this sample size was obtained based on the calculation of sample size determination, using the formula:

$$n = \frac{\sigma^2 Z_\gamma^2}{\varepsilon^2}$$

Where "n" corresponds to the sample size, "$\sigma 2$" to the unknown variance of the population, "$z\gamma$" to the critical value associated with the desired confidence level, and "ε" to the maximum sampling error [14].

3. Results

Histopathological analysis of tumor tissue obtained from B16F10-inoculated mice revealed a dense proliferation of neoplastic cells arranged in a disorganized pattern, lacking clear architectural organization (Figure 1). The tumor was composed predominantly of pleomorphic cells with hyperchromatic nuclei, prominent nucleoli, and scant to moderate cytoplasm, consistent with a highly aggressive phenotype. Areas suggestive of tumor necrosis were observed, characterized by regions of reduced cellularity and eosinophilic debris. Additionally, the presence of congested blood vessels and focal hemorrhagic areas was noted within the tumor microenvironment. These findings are consistent with the known histopathological features of murine melanoma induced by B16F10 cells and reinforce the aggressive and infiltrative nature of this tumor model.

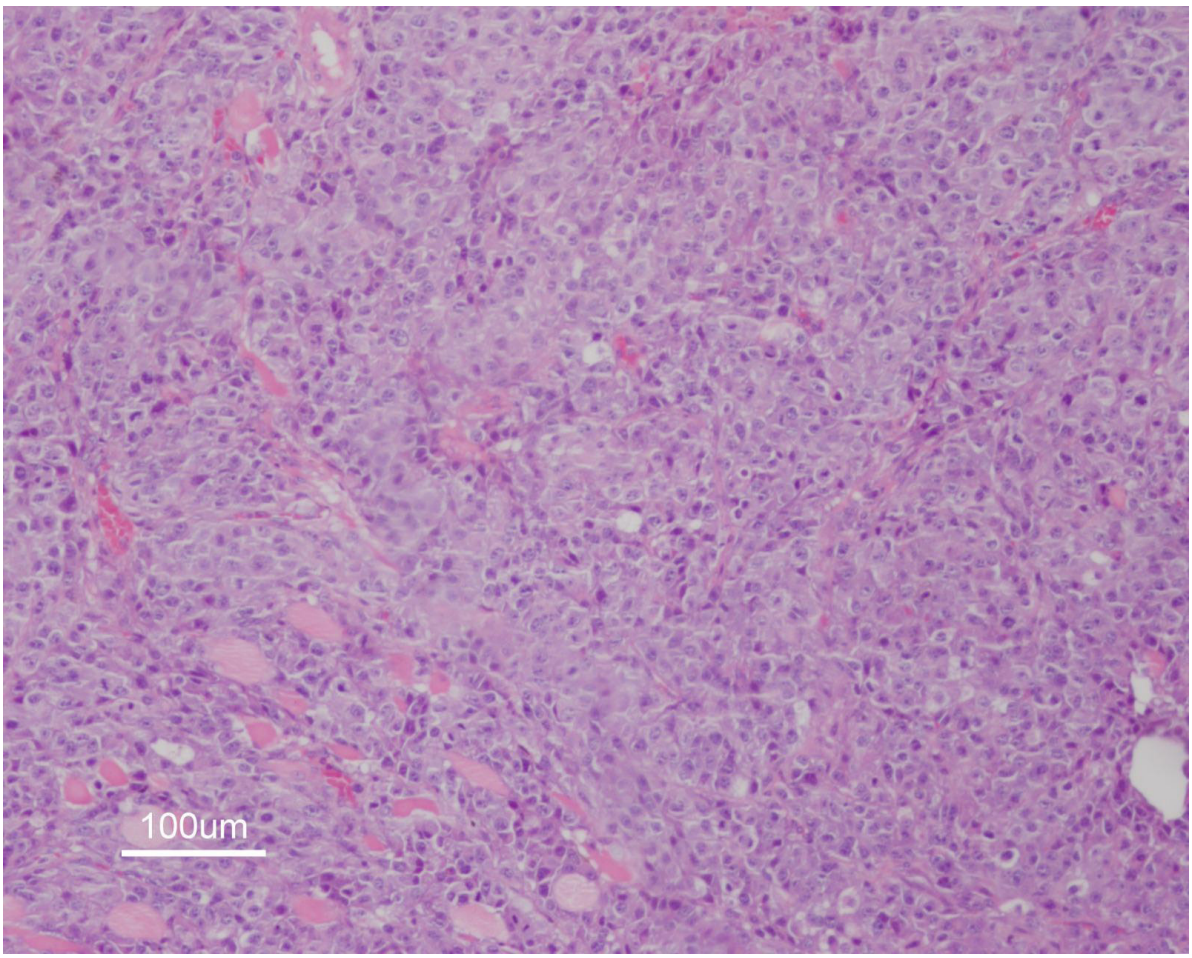

Figure 1. Histopathological features of tumor tissue in C57BL/6 mice inoculated with B16F10 cells. Hematoxylin and eosin (H&E) staining demonstrates a dense proliferation of pleomorphic neoplastic cells with hyperchromatic nuclei and disorganized architecture. Areas suggestive of tumor necrosis and focal hemorrhage can be observed, along with congested blood vessels within the tumor microenvironment.

Electrocardiographic evaluation (ECG) is widely recognized as an essential tool for assessing cardiac electrical activity in both clinical and experimental settings. In the present study, electrocardiographic analysis was performed on leads DI, DII, DIII, aVR, aVL and aVF, providing a detailed characterization of cardiac electrical activity in mice from the control and B16F10 groups. The recordings were free of artifacts, reinforcing the reliability of the non-invasive electrocardiographic method used. In the present study, all mice in the control group exhibited normal sinus rhythm, without evidence of atrioventricular block or arrhythmias (Figure 2). In contrast, mice in the melanoma group also exhibited sinus rhythm; however, they showed a reduction in heart rate, decreased amplitude and duration of the P wave and QRS complex, and an increased RR interval (Figure 3). Electrocardiographic analyses were evaluated in lead DII for analysis of P wave and R wave amplitude and duration, PR interval, QRS complex duration and RR interval (Table 1).

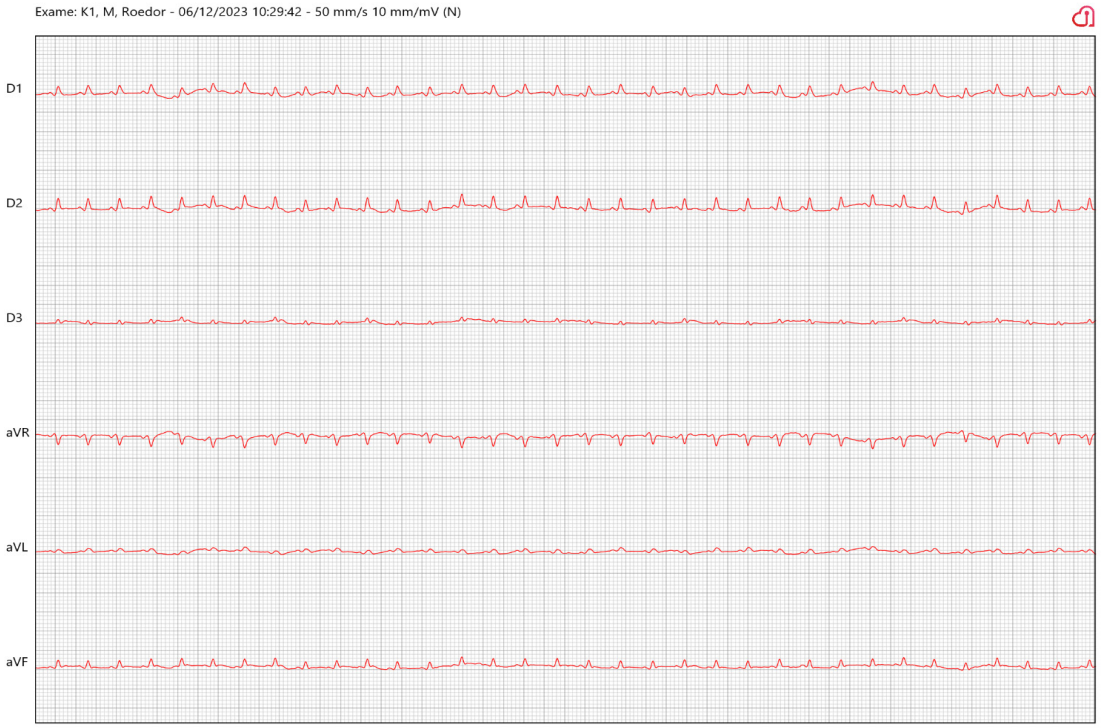

Figure 2. Recordings obtained in leads DI, DII, DIII, aVR, aVL, and aVF show a regular sinus rhythm, consistent with normal cardiac electrical activity in healthy animals. No atrioventricular blocks or arrhythmic events were observed. The tracing was recorded at a paper speed of 50 mm/s and a sensitivity of 10 mm/mV.

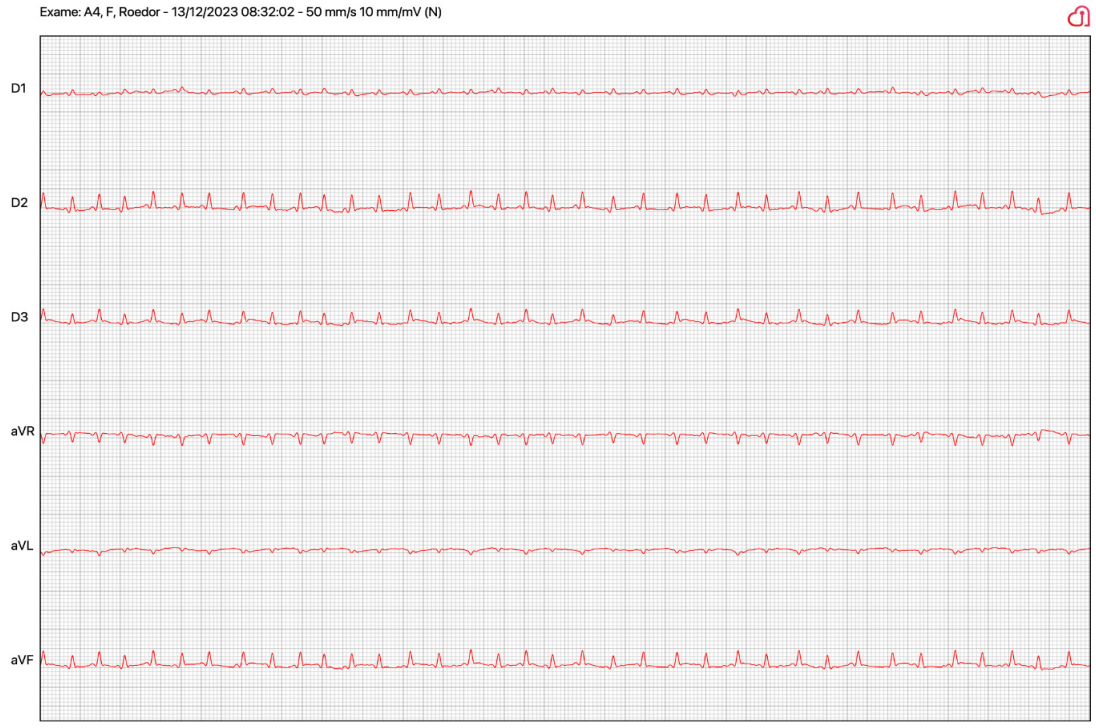

Figure 3. Recordings obtained in leads DI, DII, DIII, aVR, aVL, and aVF show sinus rhythm with alterations in cardiac electrical activity, consistent with the electrocardiographic changes observed in melanoma-bearing animals. The tracing was recorded at a paper speed of 50 mm/s and a sensitivity of 10 mm/mV.

Table 1. Eletrocardiographic data in mice C57BL/6.

ELECTROCARDIOGRAPHIC PARAMETERS									
	CONTROL				B16F10				P value
Day	**0**	**7**	**14**	**21**	**0**	**7**	**14**	**21**	
WEIGHT (g)	19.46 ± 4.55 b	21.11± 3.66 ab	23.07 ± 2.80 a	23.07 ± 2.42 a	19.30 ± 3.82 a	17.64 ± 1.91 a	18.14 ± 1.60 a	18.63 ± 1.76 a	<0.05
HEART RATE (bpm)	505 ± 43 a	512.5 ± 47 a	506.7 ± 40 a	501.2 ± 43 a	473.4 ± 56 a	482.5 ± 50 a	470.6 ± 36 a	482.8 ± 47 a	<0.05
P WAVE DURATION (ms)	24 ± 3 a	24 ± 3 a	25 ± 2 a	25 ± 1 a	24 ± 2.89 a	24 ± 3.12 a	22 ± 2.87 a	23 ± 2.43 a	<0.05
P WAVE AMPLITUDE (mv)	0.06 ± 0.02 b	0.08 ± 0.02 a	0.07 ± 0.02 ab	0.08 ± 0.01 a	0.05 ± 0.02 a	0.06 ± 0.0 a	0.06 ± 0.02 a	0.05 ± 0.01 a	<0.05
PR INTERVAL (ms)	37.3 ± 5.52 a	35.4 ± 1.60 a	36.5 ± 1.70 a	37.1 ± 2.38 a	37.7 ± 4 a	40.7 ± 6 a	38.6 ± 7 a	38.3 ± 6 a	<0.05
QRS COMPLEX (ms)	27.3 ± 3 b	28.4 ± 2 ab	28.3 ± 1 ab	29 ± 1 a	31.6 ± 3 a	29.9 ± 4 ab	28.2 ± 3 b	28.8 ± 3 b	>0.05
R WAVE (mv)	0.20 ± 0.04 b	0.21 ± 0.04 ab	0.22 ±0.04 ab	0.24 ± 0.06 a	0.22 ± 0.08 a	0.21 ± 0.06 a	0.26 ± 0.08 a	0.25± 0.08 a	>0.05
R-R INTERVAL (ms)	122.7 ± 22.75 a	123.9 ± 21.51 a	125.6 ± 20.46 a	131.9 ± 19.65 a	144.8 ± 33.13 a	136.1 ± 28.23 a	152.7 ± 28.47 a	152.7 ± 31.39 a	<0.05

Averages followed by the same letters, within each group (control and melanoma), correspond to inoculation days (0, 7, 14 and 21 days) that did not present a significant difference, according to the Tukey test ($p > 0.05$).

Through the analysis of variance, no significant changes were observed within each group, however, through the variance test comparing the Control and Melanoma groups, changes were observed in some parameters (Table 1). Throughout the experiment, the control group showed a gradual increase in body weight at different measurement times (Figure 4), unlike the B16F10 group, which experienced a decline in body weight as the disease progressed. Through Analysis of Variance (ANOVA), it was observed that there were significant weight changes between the control group of B16F10 group at a significance level of P<0.05. Regarding heart rate, it was observed that the control group had higher values compared to the B16F10 group, with average values of 506 ± 4.57 beats per minute (bpm) and 479 ± 6,95 bpm in the B16F10 group. We observed that the mice in the melanoma group presented a heart rate below the reference values for the species, classified as bradycardia. Thus, through the analysis of variance over the entire period, it was seen that the control group and melanoma group have a significance level of P<0.05.

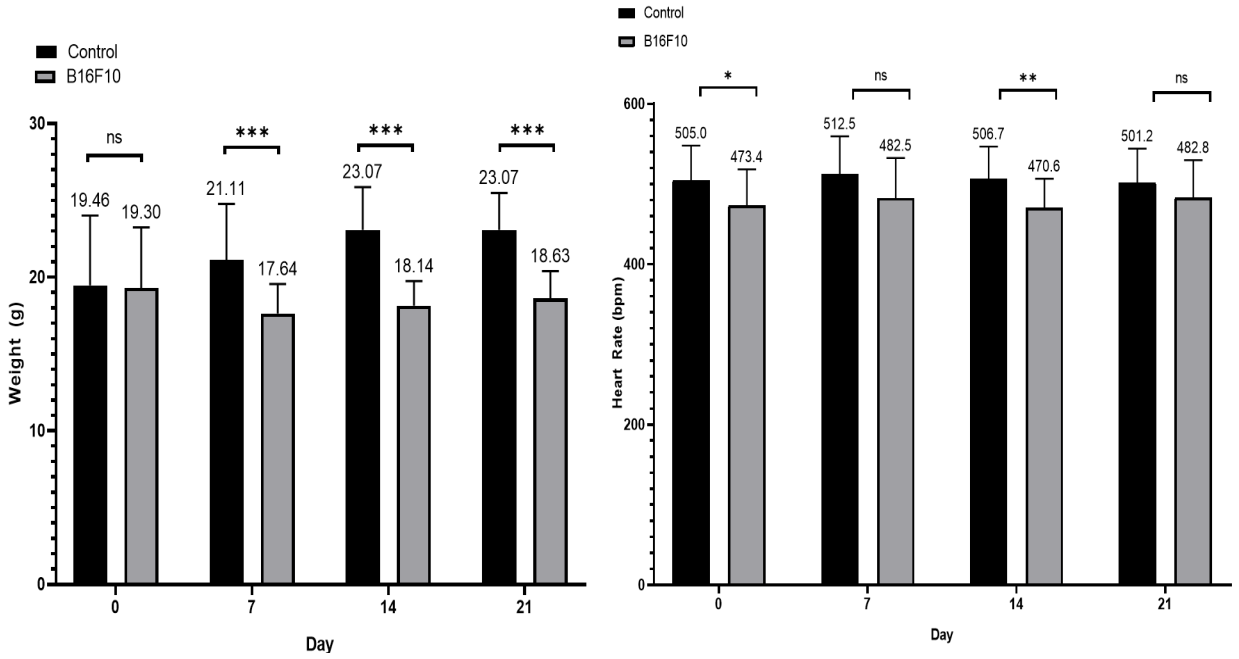

Figure 4. Demonstrative graph of weight and heart rate for the control group and melanoma group. Data are presented as mean ± standard deviation. Statistical differences between groups at each time point were evaluated by Student's t-test. Significance levels are indicated as follows: p < 0.05 (*), p < 0.01 (**), and p < 0.001 (***); ns = not significant.

There were no significant changes in the duration of the P wave between the control group and the B16F10 group. However, significant changes were observed in the amplitude of the P wave and the PR interval, showing a significance level of P<0.05 in the analysis between groups (Figure 5).

There were no changes in the amplitude of the QRS complex and R wave amplitude between the control group and the B16F10 group. The R wave amplitude showed a peak on the fourteenth day in relation to the control group (Figure 4), but overall, it did not achieve a significance level of P<0.05 between the groups. Regarding the R-R interval, differences were observed from the first analysis and a significant increase over the course experiment, demonstrating changes between the control group and the B16F10 group in relation to the periods analyzed according to the variance (ANOVA) performed with a significance level of P< 0.05 (Figure 6).

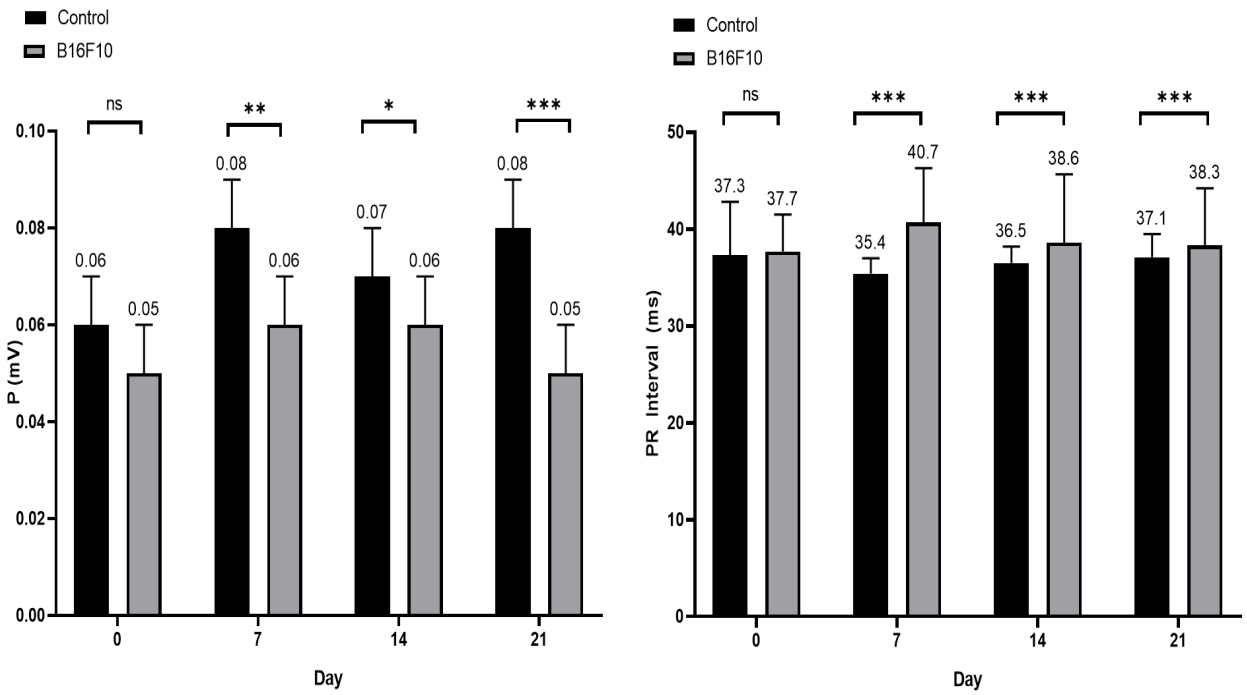

Figure 5. Demonstrative graph of P wave amplitude and PR interval duration for the control group and melanoma group. Data are presented as mean ± standard deviation. Statistical differences between groups at each time point were evaluated by Student's t-test. Significance levels are indicated as follows: $p < 0.05$ (*), $p < 0.01$ (**), and $p < 0.001$ (***); ns = not significant.

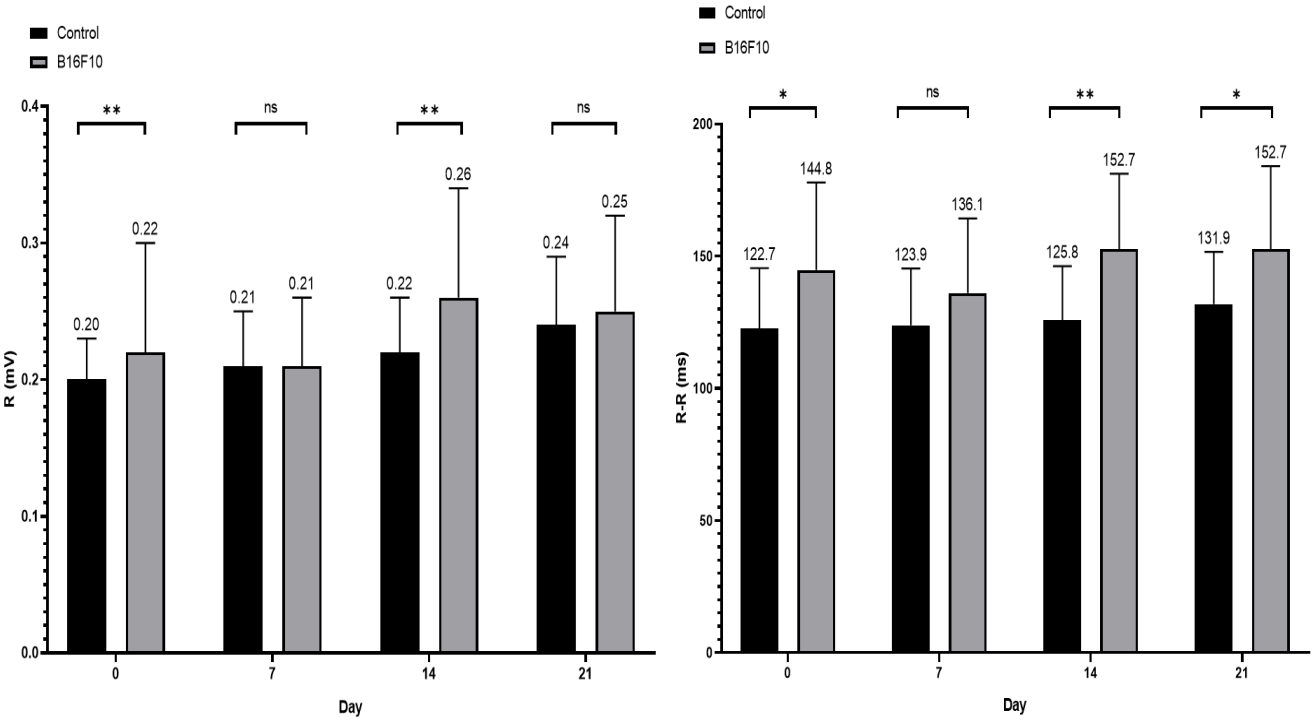

Figure 6. Demonstrative graph of R wave amplitude and RR interval for the control group and melanoma group. Data are presented as mean ± standard deviation. Statistical differences between groups at each time point were evaluated by Student's t-test. Significance levels are indicated as follows: $p < 0.05$ (*), $p < 0.01$ (**), and $p < 0.001$ (***); ns = not significant.

To further explore the relationships among electrocardiographic variables, a principal component analysis (PCA) was performed, as shown in Figure 7, the first two components explained a substantial proportion of the total variance (77.33 %). The analysis demonstrated a clear separation between control and melanoma groups, with healthy animals associated with higher heart rate values, while melanoma-bearing mice were associated with increased RR intervals, particularly at later time points. In addition, strong correlations were observed among variables, including a positive association between heart rate and P-wave amplitude, as well as between QRS complex and PR interval, whereas RR interval showed a strong negative correlation with P-wave duration. These findings reinforce the notion that melanoma progression is accompanied by coordinated changes in cardiac electrophysiological parameters rather than isolated alterations. Moreover, the temporal distribution observed in the PCA suggests a progressive shift in autonomic and electrophysiological regulation as the disease advances, particularly after 14 days of tumor development. Taken together, this multivariate approach strengthens the evidence that melanoma exerts a systemic effect on cardiac function, supporting the hypothesis of an integrated tumor–cardiovascular interaction.

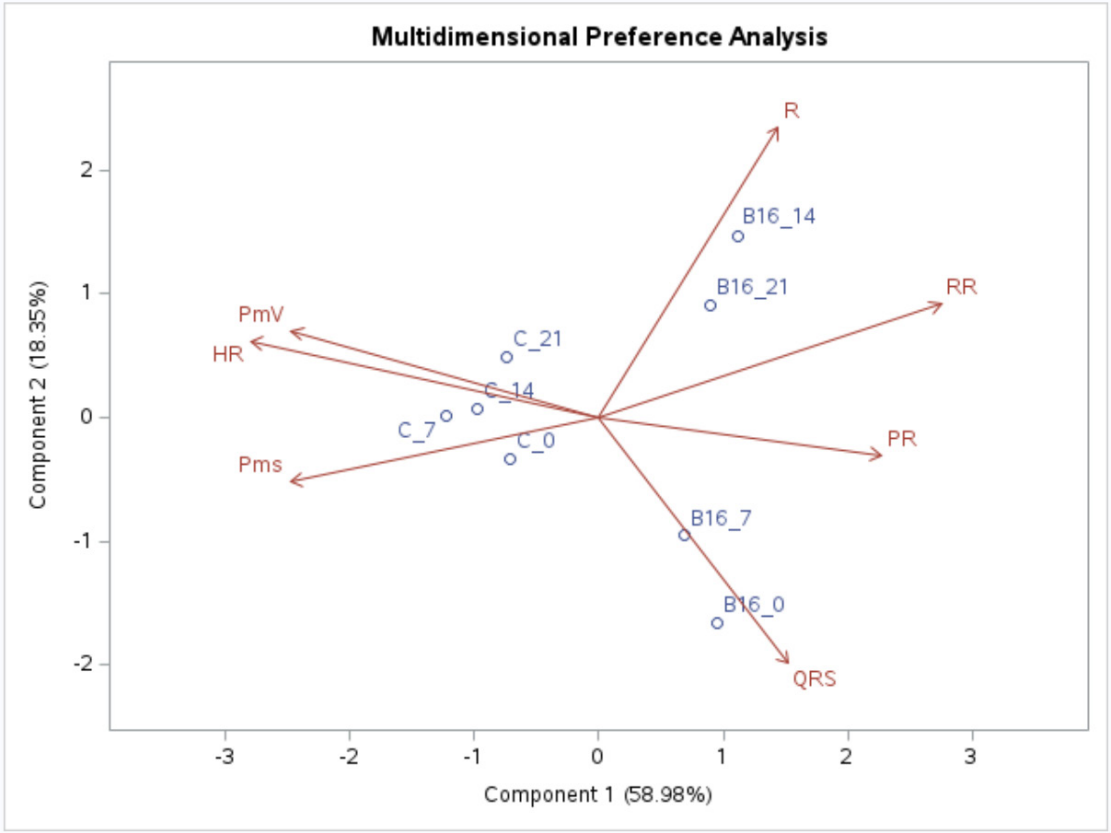

Figure 7. Principal component analysis (PCA) of electrocardiographic parameters in B16F10 mice, either inoculated with 4T1 melanoma cells (B16) or non-inoculated (control, C). The variables included heart rate (HR), P wave duration (P, ms), P wave amplitude (P, mV), PR interval, QRS complex duration, R wave amplitude, and RR interval. The first two principal components (PC1 and PC2) explained 77.33 % of the total variance. PC1 was mainly associated with heart rate, while PC2 was associated with RR interval. The animals were evaluated at 0, 7, 14 and 21 days.

4. Discussion

Muscle atrophy is recognized as a significant phenomenon in cancer-associated cachexia syndrome, characterized by a progressive loss of skeletal muscle mass that substantially contributes to the functional debilitation of patients. Although early-stage melanomas often are not associated with significant weight loss, metastatic spread or solid tumor growth in melanoma can trigger a

state of cachexia [15]. In the early stages of melanoma, progressive weight loss can be observed, however, by day 21, the animals did not reach a state of cachexia, stabilizing their weight. This early weight loss may be related to the pro-inflammatory response and the consequent release of inflammatory interleukins in elevated amounts, causing the initial stages of the disease to progress with a decrease in the weight of the animal. In other words, these cytokines can trigger a cascade of systemic inflammatory events that contribute to muscle degradation, appetite suppression, and dysregulation of energy metabolism, resulting in weight loss [16].

The group of mice carrying the B16F10 murine melanoma showed lower heart rate (HR) values compared to the control group. This decrease in heart rate may be related to factors associated with physical and emotional stress as the disease progresses. Research indicates that an increased heart rate not only raises the risk of cardiovascular diseases but also plays a significant role in the prognosis of cancer patients [17,18]. On the other hand, a reduction in heart rate has been identified as a protective factor, increasing survival [19]. Melanoma can trigger paraneoplastic syndromes, which are indirect effects of cancer due to the release of cytokines such as interleukins (IL-1 and IL-6), as well as the release of catecholamines or abnormal immune responses. These syndromes can affect the autonomic nervous system, leading to a predominance of vagal tone (parasympathetic activity), thereby reducing heart rate [20]. In experimental melanoma models, tumor growth is frequently associated with inflammatory processes and areas of tumor necrosis, which may stimulate the release of pro-inflammatory mediators such as IL-6 and TNF-α. These systemic inflammatory alterations may influence cardiovascular function and cardiac electrophysiology. In addition, tumor-induced physiological stress may promote increased catecholamine release, which can contribute to changes in heart rate and electrical conduction [9,10].

Left atrial depolarization is initiated by the propagation of electrical impulses from the sinoatrial node, generating an electrical potential that induces the contraction of its atria. In healthy mice, depolarization occurs physiologically, while mice affected with B16F10 show changes in the electrical conduction system of the left atrium from the fourteenth day, generating impulses that compromise the contraction and ejection of blood from the atrium. No studies provide information about the duration of the P wave in patients affected by skin cancer.

There are few studies showing that melanoma has an impact on the amplitude of the P wave; however, it is believed that there are factors that can trigger changes in the heart's electrical conduction system. These changes may be related to the release of catecholamines, as well as the release of interleukins, melanoma metastases, presenting important clinical characteristics, affecting the sinoatrial node and generating electrical changes that can cause anything from bradyarrhythmia to tachycardias. This electrical factor can be associated with the invasion of cancer cells into the right atrium causing overload and providing an increase in the amplitude of the same wave [20].

In the current study, there were changes in the PR interval. Studies report that the changes in the PR interval are associated with serious electrical conduction issues, such as atrioventricular blocks, atrial fibrillation, and an increased incidence of acute myocardial infarction [21]. No findings were reported regarding an increase in the PR interval in patients with melanoma. However, in patients with malignant pericardial disease in humans, changes related to the PR interval has been observed. This alteration is described as a possible direct invasion of the pericardium through hematogenous or lymphangitic spread, which presents characteristics that affect the atrial

repolarization system. Additionally, factors described in relation to changes in the same segment are associated with therapy, including the use of chemotherapy and radiation methods that can alter the conduction system [22].

In a broad context, there have been no findings that demonstrate that melanoma causes significant changes in the duration of the QRS complex. However, the evaluation of the amplitude of the R wave shows an increase in its amplitude. The relationship between increase in the R wave in humans with melanoma can be multifactorial, and there is no single or definitive explanation. However, some theories and observations suggest that right ventricular hypertrophy may be correlated with human patients with melanoma. This could occur as a compensatory response to pulmonary hypertension caused by pulmonary metastases from melanoma [23]. Melanoma metastases can cause structural changes in the heart, affecting the ECG pattern, including an increase in the R wave [24]. Studies indicate that paraneoplastic effects can influence the electrical activity of the heart due to the chemical release of substances produced by melanoma, as well as changes in the nervous system and granulomatous cardiomyopathy, which can consequently lead to changes in the amplitude of R wave [25]. However, it is important to note that the increase in the R wave in mice and humans with melanoma is not a characteristic universally observed in all cases, but it was evidenced in this study.

The relationship of RR interval with patients affected by melanoma is not well-documented. In studies involving breast cancer patients, a decrease in the RR interval was observed compared to the control group of the same disease. The parasympathetic nervous system (PNS) plays a crucial role in regulating the cardiovascular system, promoting a decrease in heart rate and an increase in the RR interval (26). The activity of the parasympathetic nervous system (PNS) may be related to an increase in the sympathetic nervous system activity recurrent in cancer, and cancer-related stress triggering autonomic responses, which can influence heart rate. It is possible that in situations of chronic or pathological stress, such as in the case of cancer, an increase in sympathetic nervous system activity could lead to compensatory adaptations in the parasympathetic nervous system, acting to reduce heart rate in individuals with cancer [27, 28].

5. Conclusion

This study demonstrates that melanoma progression in C57BL/6 mice is associated with significant electrocardiographic alterations, including changes in heart rate and cardiac electrical conduction. These findings reinforce the interaction between cancer and cardiovascular function and highlight the importance of cardiac monitoring in experimental oncology. Understanding these alterations may contribute to improved strategies to minimize cardiovascular risks during cancer progression and treatment.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

Data availability statement

Data will be provided upon request to the corresponding author.

Author contributions

Conceptualization: Almeida, P.R.C.; Campos, E.C.R. and Favero, G.M. Data curation: Almeida, P.R.C. and Bosetto, L. Formal analysis: Bosetto, L. and Almeida, P.R.C. Methodology: Almeida, P.R.C.; Campos, E.C.R. and Favero, G.M. Supervision: Campos, E.C.R. and Favero, G.M. Validation: Almeida, P.R.C.; Bosetto, L. and Paludo, K.S. Investigation: Almeida, P.R.C.; Fagundes, G.R. and Paludo, K.S. Writing (original draft): Almeida, P.R.C. and Janz, F.L. Writing (review and editing): Janz, F.L.; Cancela, A.E.; Campos, E.C.R. and Favero, G.M. Translation: Cancela, A.E.

Generative AI use statement

The authors did not use generative artificial intelligence tools or technologies in creating or editing any part of this manuscript.

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