**The Impact of Obesity on Prostate Cancer Aggressiveness: A Retrospective**

 **Analysis in Kiambu County, Kenya**

# Abstract

**Background**: Obesity is a growing world concern, with one-third of the world’s population estimated to be obese or overweight. Obesity affects all age groups, both genders, and different ethnicities at variable rates with an increase in prevalence since 1980 having doubled.

**Aim:** This study aimed to evaluate obesity as a potential risk factor for the aggressiveness of prostate cancer among male patients in selected hospitals within Kiambu County i.e. Gatundu Level 5 Hospital, Kiambu Level 5 Hospital and Thika Level 5 Hospital.

**Research Methods:** Purposive and convenience sampling methods were employed to select patients from three hospitals: Gatundu Level 5, Kiambu Level 5, and Thika Level 5 Hospital.The study employed a convenience and purposive sampling technique to select the sample for this research. An analytical retrospective research design was used to analyze the retrospective aspect of obesity on PC among patients.

**Results:** This present study involved 256 patients with prostate cancer. The findings, it was revealed that there was a high level of prostate cancer aggression among men in Kiambu County, cumulative of 52.9%. The findings revealed that age (p=0.003), marital status (p=0.042), length of diagnosis (p=0.005), and stage of cancer (p=0.000) of the patients significantly influenced the aggression of prostate cancer (p ¡ 0.05) and more than 40 percent of those with PC were above 45 years. There was a significant association between prostate cancer aggression and obesity with (p ¡ 0.05), i.e. the association between PC aggression with ever being obese

(p=0.018), patient still obese (p=0.0111), obesity contributing to PC symptoms (p=0.003), difficulty managing PC with obesity (p=0.017), and deaths due to obesity (p=0.000).

**Conclusion**: Understanding the implications of high aggression in prostate cancer can help guide clinical decision-making and patient education, emphasizing the importance of personalized approaches in managing this disease.

**Keywords**: Prostate Cancer, Obesity, Gleason Score, risk factor

# Introduction

Obesity is a global concern, with estimates suggesting that one-third of the world’s population is either obese or overweight. Affecting individuals across all age groups, genders, and ethnicities, obesity has seen a dramatic increase since 1980, with prevalence rates doubling (Choi et al., 2019). Numerous studies have investigated the relationship between obesity and cancer, particularly in relation to disease progression and survival outcomes (Ye et al., 2020; Kim & Scherer, 2021; Pappachan, 2021). Obesity is characterized by excessive accumulation of fatty tissue in the body, and Body Mass Index (BMI) serves as a widely used indicator of adiposity (Dal & Ulutas, 2021). According to Slawinski et al. (2020), a BMI between 25 and 29 is categorized as overweight, while a BMI of 30 or higher denotes obesity. Individuals with obesity are at increased risk for a variety of diseases, including type 2 diabetes, hypertension, cardiovascular conditions, respiratory diseases, and various cancers (Apovian, 2016). Brown et al. (2018) emphasize that obesity is the second leading risk factor for cancer, following smoking. Prostate cancer (PC), the second most commonly diagnosed cancer among men worldwide, is a leading cause of cancer-related mortality (GLOBOCAN, 2018; Jenifer et al., 2023). In Kenya, prostate cancer screening rates are low, with only 4.4% of men getting screened (Okyere et al., 2023). The likelihood of screening is higher among men aged 50–54 years and those residing in Eastern, Nyanza, and Nairobi regions (Okyere et al., 2023). Wambalaba et al. (2019) noted that prostate cancer is the second most common cancer among Kenyan men.

# Materials and Method

An analytical retrospective survey was conducted at Thika, Kiambu, and Gatundu Level 5 hospitals to explore the relationship between obesity and prostate cancer aggression among men in Kiambu County. The survey involved several hospital departments: pathology, prostate cancer clinic, nutrition, palliative care, and surgery. Data retrieval was facilitated using the Smart Care electronic system, covering the timeframe from January 2022 to January 2024. Sample size was calculated using the Taro Yamane formula (Yamane, 1967) as shown below;

n = N/(1+Ne2) = 3847*/*(1 + (3847)0*.*052) = 285

The targeted sample size was 285 patients with prostate cancer. However,

256 patient records were successfully obtained and followed up on phone call interview. The inclusion criteria for the present study included male patients aged 18 years and above who underwent treatment for prostate cancer through- out the entire study duration, encompassing both new diagnoses and recurrent cases (Freitas et al., 2024). Infants, toddlers, and adolescents up to the age of 18 years and patients whose MUAC measurement is below 30 were excluded from the study. After obtaining ethical committee approval (Ref no: MKU/ISERC/3762/2024 June) 256 patients who had prostate cancer were selected for the study. Selected participants did not show the presence of any other complications. Patient in- formation was procured via fles obtained from the medical record departments, and these were fled systematically. Variables recorded as part of the study in- cluded name, age, occupation, complaints and duration of illness, past history, personal history, family history, general examination, Gleason scores.

# Statistical Analysis

Data was analyzed using IBM SPSS Statistics for Windows, Version 28.0. (Ar- monk, NY: IBM Corp). To describe the data, frequency and percentage analysis were used for categorical variables. Inferential statistics such as chi-sqaure tests of association, multinomial logistic regression models were also used to deter- mine relationships between variables in this study.

# Results

Of the 256 prostate cancer patients selected for the study, 26.6% were aged above 50 years, 37.6% were aged 41 to 45 years, and 46 to 50 years cumulatively being the majority. Of the patients sampled for this study, 72.3% lived in the urban settlements and had better access to the healthcare systems than 27.7% who were situated in the rural areas. Most of the patients were married according to the findings in this study, 37.9%, those who were single were 34.8%, cohab- iting were 19.9%, and those who were widowed/divorced accounting for 7.4% due to frustrations from their partners as a result of their illness.On the high- est level of education attained by the patients, 28.1% had attained secondary education, 27.7% had attained up to primary education, 27% had achieved a university/college education and only 1.2% had attained post-graduate educa- tion. However, 16% reported to have not attended any formal education forum. Majority of the prostate cancer cases were highly aggressive 39.5%, 13.3% were aggressive, 12.1% were moderately aggressive, 18.8% were slightly aggressive and 16.4% of the cases were not aggressive. The research question on what is the level of prostate cancer aggression among men in selected hospitals in Kiambu County is thus answered. The level of aggression of prostate cancer among men in Kiambu County is high. Majority of of the PC patients 78.5% (Table 4) have ever been declared as obese with 21.5% having no medical history of obesity. Of those who were recorded to have been obese, 59% agreed that

obesity led to the aggression of PC with most experiencing severe symptoms. Some of the symptoms experienced by the PC patients include inflammation which they highly attributed to prostatitis. The inflammation contributed to the sharp pain in their pelvic area, difficulty in urinating, and discomfort. Some PC patients reported experiencing hormonal imbalance, 12.5%, while 12.9% re- ported insulin resistance symptoms. Majority of the PC patients were admitted to the hospital once due to the severity of the symptoms. 42.6% (Table 4). Those who were occasionally admitted to the hospital were 39.5% and 18% were admitted several times to the hospital due to the severity of the symp- toms of the PC. This study revealed that 36.2% of the PC patients were in stage 4 of WHO cancer staging, 25.4% were in stage 1 of cancer, 23.0% were in stage 3 of cancer, and 15.2% were in stage 2 of cancer. Our observations also pointed to the fact that the majority of those with cancer stage 4 of PC were men aged 50 years and above followed closely by those between the age of 40 and 50 years. Chi-sqaure association between PC aggression and being obese and one point in life was found to be statistically significant in the as-

sociation (Table 5) (Chi-square=3.998, p=0.0262 *<* 0.05). A patient’s cancer staging can be influenced by obesity at some point. Obesity has been identified

as a risk factor that can impact the staging of prostate cancer. However, once a patient is no longer obese, then the risk to influence prostate cancer staging is thus eliminated thus there is no association found in this case study scenario of ever being obese based on the patients’ health history. There was a statisti-

cally significant strong association between the stage of cancer and the patient still being obese, (Chi-sqaure = 11.818, p=0.0111 *<* 0.05). Aggression of PC which was also attributed to the staging of PC also had a strong statistically sig- nificant association with obesity contributing to severe symptoms, difficulty in

managing PC for patients with obesity, and mortality due to obesity, (p=0.000

*<* 0.05). The p-values *<* 0.05 hence we reject a null hypothesis that there is no significant association between obesity and PC aggression. This is to say that there was a strong association between obesity and PC aggression. On the confounding factors leading to aggression of PC (Table 6), 46.88% responded

to age being the most-linked non-modifiable factor leading to the aggression of prostate cancer, 31.25% attributed to their diet and lifestyle and thus some were admitting to having a history of obesity and/or were obese. Some of the pa- tients alluded to family history as a confounding factor, 15.63%. Their fathers and close relatives had a history of PC and were suspected to have inherited the genes from them resulting in their woes. Tumor characteristics were not much of a risk factor according to these results and were least reported at 6.25%. In their argument, they asserted that once they had the cancer, it was difficult to attribute the size of the tumor and other characteristics to the aggression of the cancer. The confounding factors were identified and the respondents’ assertions strengthened them as risk factors.

Table 1: Demographic characteristics

|  |  |  |
| --- | --- | --- |
| **Category** | **Frequency** | **Percentage** |
| **Age** |  |  |
| 18-24 yrs | 36 | 14.1 |
| 25-30yrs | 38 | 14.8 |
| 31-35 yrs | 18 | 7.0 |
| 41-45 yrs | 48 | 18.8 |
| 46-50 yrs | 48 | 18.8 |
| above 50 yrs | 68 | 26.6 |
| **Residence** |  |  |
| Urban | 185 | 72.3 |
| Rural | 71 | 27.7 |
| **Availability of means of transport** |  |  |
| Yes | 229 | 89.5 |
| No | 27 | 10.5 |
| **The family member providing HBC.** |  |  |
| Yes | 195 | 76.2 |
| No | 61 | 23.8 |
| **Who provides HBC** |  |  |
| Spouse | 119 | 46.5 |
| Sibling | 60 | 23.4 |
| Parent | 10 | 3.9 |
| Neighbor | 10 | 3.9 |
| **Marital Status** |  |  |
| Married | 97 | 37.9 |
| Single | 89 | 34.8 |
| Cohabiting | 51 | 19.9 |
| Widowed/divorced | 19 | 7.4 |
| **Highest level of education** |  |  |
| None | 41 | 16.0 |
| Primary | 71 | 27.7 |
| Secondary | 72 | 28.1 |
| University/college | 69 | 27.0 |
| Postgraduate | 3 | 1.2 |

Table 2: Multinomial Regression-demographic characteristics & Prostate cancer aggression

## Likelihood Ratio Tests

2\*Effect Model Fitting Criteria Likelihood Ratio Tests

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **-2 Log Likelihood of Reduced Model** | **Chi-Square** | **df** | **Sig.** |
| Intercept | 512.911 | 63.035 | 4 | 0.000 |
| Age | 466.161 | 16.285 | 4 | 0.003 |
| Length of Diagnosis | 464.771 | 14.895 | 4 | 0.005 |
| Residence | 457.610 | 7.734 | 4 | 0.102 |
| Marital Status | 459.791 | 9.915 | 4 | 0.042 |
| Education | 450.216 | .339 | 4 | 0.987 |
| Cancer Stage | 617.171 | 167.294 | 4 | 0.000 |

Table 3: Prostate cancer aggression levels

|  |  |  |
| --- | --- | --- |
| **PC Aggression (based on Gleason score)** | **Frequency** | **Percentage** |
| Not Aggressive | 42 | 16.4 |
| Slightly aggressive | 48 | 18.8 |
| Moderately aggressive | 31 | 12.1 |
| Aggressive | 34 | 13.3 |
| Highly aggressive | 101 | 39.5 |
| **Total** | **256** | **100.0** |

# Discussion

The study findings revealed that there was a high level of prostate cancer aggression among men in Kiambu County and this was due to obesity among the men. Similarly, Vidal et al, (2014) reiterated that obesity is associated with an increased risk of high-grade prostate cancer.

sexual partners can potentially impact various aspects of a person’s health, including their experience with prostate cancer and its aggression. In this study men with sexual partners were either married or cohabiting. The married and those cohabiting with their partners were 37.9% and 19.9% respectively. For instance, being married or in a committed relationship can provide emotional, practical, and social support to individuals facing a cancer diagnosis. Social support has been shown to positively impact psychological well-being, treatment adherence, and overall quality of life in cancer patients. This support network can potentially help individuals cope better with the challenges of a cancer diagnosis and treatment, which may in turn affect the aggression of prostate cancer. Further, Married individuals may be more likely to engage in healthy behaviors such as regular medical check-ups, adherence to treatment plans, and healthy lifestyle choices. These behaviors can contribute to overall better health outcomes and potentially impact the aggressiveness of prostate cancer. Married individuals may have a partner who can assist with scheduling

Table 4: Obesity & PC Aggression Frequency distribution

|  |  |  |
| --- | --- | --- |
| **Category** | **Frequency** | **Percentage** |
| **Ever been declared obese.** |  |  |
| Yes | 201 | 78.5 |
| No | 55 | 21.5 |
| **Did it lead to aggression** |  |  |
| Yes | 151 | 59.0 |
| No | 50 | 16.4 |
| **PC symptoms** |  |  |
| Inflammation | 114 | 44.5 |
| Hormonal imbalance | 32 | 12.5 |
| Insulin resistance | 33 | 12.9 |
| Difficulty in treatments | 77 | 30.1 |
| **Times admitted to hospital due to severity of symptoms.** |  |  |
| Once | 109 | 42.6 |
| Occasionally | 101 | 39.5 |
| Severally | 46 | 18.0 |
| **Still Obese** |  |  |
| Yes | 146 | 57.0 |
| No | 110 | 43.0 |
| **Ever been enrolled in palliative care for PC** |  |  |
| Yes | 214 | 83.6 |
| No | 42 | 16.4 |
| **WHO Cancer staging** |  |  |
| Stage 1 | 65 | 25.4 |
| Stage 2 | 39 | 15.2 |
| Stage 3 | 59 | 23.0 |
| Stage 4 | 93 | 36.3 |

Table 5: Chi-square- obesity & prostate cancer aggression

## Association Chi-square value P-value Phi &Cramer’s V

|  |  |  |  |
| --- | --- | --- | --- |
| PC aggression \* Ever Been obese | 11.889 | 0.018 | 0.216 |
| PC aggression \* Still Obese | 11.818 | 0.0111 | 0.841 |
| PC aggression \* Obesity contributing to severe PC symptoms | 15.579 | 0.003 | 0.609 |
| PC aggression \* Difficult to manage PC with obesity | 30.238 | 0.017 | 0.344 |
| PC aggression \* Mortality due to obesity | 39.182 | 0.000 | 0.451 |

Table 6: Confounding Factors Affecting Aggression of Prostate Cancer

|  |  |  |
| --- | --- | --- |
| **Confounding Factor** | **Frequency** | **Percentage** |
| Family History | 40 | 15.63 |
| Diet & Lifestyle | 80 | 31.25 |
| Tumor Characteristics | 16 | 6.25 |
| **Total** | **256** | **100** |

appointments, transportation to medical facilities, and navigating the health- care system. This support can help ensure timely access to medical care and potentially impact the management of prostate cancer, including decisions on treatment aggressiveness. A similar study (Rosenblatt et al, 2012) reiterated that there is a direct positive relation between the number of lifetime female sexual partners and the risk of prostate cancer. Another study that supported our finding (Khan et al, 2024) revealed that not being married (vs. married) was associated with increased odds of high-aggressive tumors in the overall study population (adjusted Odds Ratio (aOR): 1.56; 95% Confidence Interval (CI) when in turn increases the aggression of PC. Studies such as Walsh et al, (2023) have suggested that married individuals may experience lower levels of stress and anxiety compared to those who are single or divorced. On education level, 56.2% attained secondary, undergraduate, and postgraduate studies cumulatively sug- gesting that they received a basic education foundation and are knowledgeable about prostate cancer. Higher levels of education are often associated with bet- ter health literacy and awareness of healthcare options. Education level can also influence psychological factors such as coping mechanisms, stress manage- ment, and emotional well-being. Individuals with higher education levels may have more resources and strategies to cope with the emotional aspects of a can- cer diagnosis, potentially reducing the impact of stress on disease progression. A study done by Larsen et al, (2020) suggested that education level may be associated with prostate cancer outcomes, including survival rates and disease progression, and is consistent with the findings of our study. Higher education levels have been linked to improved survival outcomes in some studies, though the exact mechanisms driving this association are complex and multifactorial. The findings of this study are supported by the findings of Larsen et al, (2020). The majority of the patients with PC were aged between 41 years to above 50 years (64.2%). Prostate cancer is primarily a disease of older men, with the like- lihood of diagnosis increasing significantly with age. Similarly, Rawla, (2019) emphasized that prostate cancer incidence and mortality rates are strongly re- lated to age with the highest incidence being seen in elderly men. Older men are more likely to develop aggressive forms of the disease according to this study. Age-related changes in hormone levels and cellular processes can also influence the aggressiveness of prostate cancer. In another similar study (Seibert, et al, 2020) there was found to be a strong association between age and PC risk and Gleason score.

Obesity is known to have important roles in driving prostate cancer ag- gressiveness and increased mortality. In a similar study, (Zhang et al, 2020), prostatitis or BPH could lead to escalating risks of PC are very much consis- tent with our study findings. Another study (Haugnes et al, 2024), asserted that weight gain among obese men was associated with a higher risk of PC, and obesity was associated with higher PC -specific mortality, especially among nonsmokers which concurs with our study findings. Obesity can impact the aggression of prostate cancer by promoting tumor growth, complicating treat- ment, increasing the risk of recurrence and progression, exacerbating symptoms through comorbidities, and creating a pro-inflammatory environment in the

body (Rivera-Izquierdo et al, 2021). Also, Zhu et al, (2022) emphasized that obesity increases the risk of aggressive PC. In contrary, Slawinski et al, (2020) found that being overweight or obese is associated with improved survival.

In the findings family history of prostate cancer, especially in close relatives like a father or brother, was found to increase the risk of developing aggressive prostate cancer. Similar findings by Beebe-Dimmer et al, (2020) that indicate that a family history of PC among close relatives is an established risk factor support our findings in this study. This is attributable to the genetic factors and inherited mutations in certain genes which contribute to the aggressive- ness of the disease. Factors such as a diet high in saturated fats, low intake of fruits and vegetables, smoking, and a sedentary lifestyle may contribute to the aggressiveness of prostate cancer. Such a diet is not considered healthy. These lifestyle choices can impact inflammation, hormonal balance, and overall health, potentially influencing the course of the disease. According to Plym et al, (2023), maintaining a healthy lifestyle provides a way to offset the genetic risk of lethal prostate cancer which concurs with the results of our study. The specific biological features of the tumor, such as Gleason score, tumor stage, and presence of metastasis, were also found to directly impact the aggressiveness of prostate cancer as provided in the patient’s clinical records. These tumor char- acteristics were critical in determining the prognosis and treatment strategies for individuals with the disease. Based on the size and condition of the tumor the healthcare professional could determine how aggressive the PC was and in what stage they could categorize the cancer.

# Conclusion

There is a significant correlation between obesity and an elevated risk of prostate cancer among men, highlighting a crucial public health concern. The evidence suggests that the mechanisms linking excess body weight to prostate cancer pathogenesis may involve hormonal, inflammatory, and metabolic factors that warrant further investigation. The complex interplay between sociodemographic variables and disease progression highlights the importance of considering in- dividual characteristics in the assessment and management of prostate cancer aggression. The compelling evidence linking obesity to an increased risk of prostate cancer among men, reinforces the notion that excessive body weight contributes significantly to the prognosis of the disease. The observed associa- tion highlights the need for increased awareness and preventive measures target- ing obesity as a modifiable risk factor, particularly in populations at higher risk for prostate cancer. By fostering healthier lifestyles and promoting weight man- agement programs, healthcare practitioners may play a vital role in reducing the incidence of prostate cancer. Additionally, diet, lifestyle, metabolic health, and psychosocial factors play a crucial role in disease progression and patient out- comes. These insights underscore the necessity for a comprehensive approach to prostate cancer prevention and management that encompasses not only medical interventions but also lifestyle modifications and psychosocial support.

# References

* 1. Amling, C. L. (2005). Relationship between obesity and prostate cancer. Current Opinion in Urology, 15(3), 167-171.
	2. Arain, M., Campbell, M. J., Cooper, C. L., & Lancaster, G. A. (2010). What is a pilot or Feasibility study? A review of current practice and editorial policy. BMC Medical Research Methodology, 10, 67. https://doi.org/10.1186/1471- 2288/10/67
	3. Bandini, M., Gandaglia, G., & Briganti, A. (2017). Obesity and prostate cancer. Current Opinion in Urology, 27(5), 415-421.
	4. Bechis, S. K., Carroll, P. R., & Cooperberg, M. R. (2011). Impact of age at diagnosis on prostate Cancer treatment and survival. Journal of Clinical Oncology, 29(2), 235.
	5. Khan, S., Fuzzell, L., Langston, M., Han, Y., Moore, J. X., Gilbert, K., & Lewis-Thames, M. W. (2024). The impact of marital status on tumor aggressiveness, treatment, and screening among black and white men diagnosed with prostate cancer. Cancer Causes & Control, 35(3), 531-539.
	6. Mao, W., Huang, X., Kong, M., Fan, J., & Geng, J. (2019). More lymph node dissection improves survival in patients with newly diagnosed lymph node- positive penile cancer. International Urology and Nephrology, 51, 641-654.
	7. Mbugua, R. G., Oluchina, S., & Karanja, S. (2021). Prostate cancer awareness and screening among men in a rural community in Kenya: A cross- sectional study. African Journal of Urology, 27(1), 1-10.
	8. Mbugua, R. G., Oluchina, S., Karanja, S., & Cheboi, S. (2020). Uptake of Prostate Cancer Screening and Associated Intra-Personal Factors among Men Aged 40-69 Years: A cross-sectional study in a rural community in Kenya. African Journal of Health Sciences, 33(3), 73-82.
	9. Okyere, J., Ayebeng, C., Owusu, B. A., Ankomahene, B., & Dickson,

K. S. (2023). Prostate cancer screening uptake in Kenya: an analysis of the demographic and health survey. Journal of Cancer Policy, 100427.

* 1. Tyson, M. D., Andrews, P. E., Etzioni, D. A., Ferrigni, R. G., Humphreys,

M. R., Swanson, S.K., & Castle, E. K. (2013). Marital status and prostate can- cer outcomes. The Canadian journal of urology, 20(2), 6702–6706.

* 1. Tzenios, N., Tazanios, M. E., & Chahine, M. (2022). The impact of body mass index on prostate cancer: An updated systematic review and meta- analysis. Medicine, 101(45).
	2. Wambalaba, F. W., Son, B., Wambalaba, A. E., Nyong’o, D., & Nyong’o,

A. (2019). Prevalence and capacity of cancer diagnostics and treatment: a demand and supply survey of health-care facilities in Kenya. Cancer Control, 26(1), 1073274819886930.

* 1. Wilson, R. L., Taaffe, D. R., Newton, R. U., Hart, N. H., Lyons-Wall, P., & Galv˜ao, D. A. (2022). Obesity and prostate cancer: A narrative review. Critical Reviews in Oncology/Hematology, 169, 103543.
	2. Albertsen, P. C. (2020). Prostate cancer screening and treatment: where have we come from and Where are we going?. BJU international, 126(2), 218- 224.
	3. Bernard, B., Burnett, C., Sweeney, C. J., Rider, J. R., & Sridhar, S.

S. (2020). Impact of age at diagnosis of de novo metastatic prostate cancer on survival. Cancer, 126(5), 986-993.

* 1. Bleyer, A., Spreafico, F., & Barr, R. (2020). Prostate cancer in young men: An emerging young adult and older adolescent challenge. Cancer, 126(1), 46-57.
	2. Dal, M. B., & Ulutas, K. T. (2021). Assessment of visceral and subcuta- neous obesity to understand the efficiency of adipose tissue in acute pancreatitis. Nigerian Journal of Clinical Practice, 24(7), 993-996.
	3. Freitas , Carla Simone Moreira de, Amanda Damasceno de Souza, Fabiana Rocha-Silva, Thaís Almeida Marques-Silva, and Aleida Nazareth Soares. 2024. “Determinants of Survival and Prognostic Factors in Patients With Prostate Cancer: A Retrospective Analysis (2009-2018)”. Journal of Advances in Medicine and Medical Research 36 (5):245-57. <https://doi.org/10.9734/jammr/2024/v36i55433>.
	4. Jenifer, S.E. , Nancy, Evelyn Rainy, J.W, and Janaki Velmurugan. 2023. “Role of Nanotrace Element in Prostate Cancer an Update”. Journal of Cancer and Tumor International 13 (4):33-54. <https://doi.org/10.9734/jcti/2023/v13i4246>.