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Risk Factors and Treatments Impacts for the Gene of Two Different Types of Skin Cancer: Survival Analysis

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Abstract. Two distinct types of skin cancer are Cutaneous Melanoma and Melanoma of Uncertain Primary. Their causes may be distinct. Several variables, including genetic mutation, UV exposure, sex, age, and others, will affect the survival months. In this study, the Kaplan-Meier method and the Cox model will be used to compare the two types of skin cancer. For the KM technique, one unique variable will be employed to assess its association with the survival months. Cox model will employ multiple variables to describe the overall association between several variables and the survival months. In conclusion, the difference on sex will have a distinct impact on two different kinds of skin cancer. Genetic expression does not clearly differentiate between them. UV exposure and therapy have a substantial impact on the number of months of survival for Cutaneous Melanoma. The results of the study indicate that additional research and prevention are required. Prevention is almost always more effective than treatment for cancer. For specific patient populations, clinicians should prioritize skin cancer prevention and therapy.

Keywords: Survival Analysis, Genes of Skin Cancer, Cox Model.

1. Introduction

Melanoma is skin cancer. Just 4% of skin cancers are melanomas, but they cause 80% of mortality [1]. Possible genetic mutation. Trauma, UV exposure, and friction can also cause melanoma. Over 97% of melanomas may be traced to the patient's skin. It can also grow on mucous membranes (including visceral membranes), the ocular uvea, and soft meninges. Mucous membranes are everywhere. Melanoma of unknown primary is rare and has no apparent beginning site (MUP). 60% of mucocutaneous urticaria (MUP) cases involve lymph nodes, with the rest affecting distal skins/subcutaneous tissue, the lung, the brain, and the Gastrointestinal tract [2]. Malignant melanoma can't be given from person to person, but it can spread within families [3]. Malignant melanoma is becoming more frequent and has a poor prognosis. As a result, determining the factors that pose a risk has become an essential task.

The factors can be related to survival rate to encourage people to take initial data seriously. The latest study compared gene influence on two cancers using survival analysis. In the dataset,18.4% of 462 patients had MUP. MUP was linked to brain metastases. Cutaneous Melanoma and MUP had insignificant variations in their genetic patterns. There was no statistically significant difference between somatic mutation patterns and survival rates [4]. This study examined skin cancer's genetics. But there are other things besides genes that could change the gene and make it more likely that melanoma or

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MUP will happen. The power law illustrates the incidence–sunlight exposure association for skin malignancies. SCC depends on cumulative UV exposures, whereas BCC and CM rely on exposure patterns, with intermittent exposures being most carcinogenic [5]. These factors may affect MUP and Cutaneous Melanoma survival rates.

Using numerous models, this study will examine the relationship between risk factors, genes, and treatment and skin cancer survival rate. This paper will evaluate each other's usefulness using the KM technique. The Kaplan-Meier method is used to analyze 'time-to-event' data [6]. In skin cancer survival analysis, all-cause death may include drive class, sex, UV exposure, and radiation. Each variable affects a person's longevity. Next, patients will be split by treatments, cancer sites, and UV exposure to see if these factors change genes. This determines if genes are changed. The Cox proportional-hazards model evaluates patient survival and predictor variables in medical research. Cox modeled this. In addition to the KM technique, the cox model will be employed because it can use numerous survival-related variables simultaneously [7].

In this study, these questions will be analyzed to find the relationship between some variables and the survival months, which include some genetic driver class, treatment, sex, and UV exposure. How does this paper determine the nature of the gene's interaction with other factors? This type of treatment also affects the cancer's survival rate. Is there any way to estimate the percentage of people who will still be alive in the future?

2. Data Source

All the data may be found on cBioPortal, which can be accessed at https://www.cbioportal.org/. There are a total of 696 observations in one of the data sets, which covers two distinct kinds of skin cancer and some related variables. 448 observations are included in the second data set was Cutaneous for the radiation treatment. The third data set contains 359 observations related to the UV exposure effects of cutaneous.

3. Method

The Kaplan-Meier estimate measures patient survival following treatment accurately. KM could be used to determine which cancer traits affect survival. In a clinical study or community trial, the effect of an intervention is evaluated by counting the number of test participants that live or are saved. Survival time is the time between a point in time and an event, like death; survival analysis analyzes cohort data. This can alter the results if the subjects are recalcitrant and refuse to continue participating; if some of the individuals do not experience the event or die before the study's conclusion, even though they would have if observed; or if it loses communication with them halfway through the study. The Kaplan-Meier estimator is the easiest approach to calculate survival over time. Survival curves form in many situations. Steps in this approach include calculating the likelihood of a certain event at a given time and multiplying each subsequent probability by any previously computed probabilities [8].

In addition, Kaplan-Meier curves and log rank tests are only applicable in situations in which the variable being predicted is categorical, such as two different treatment method, sex different. They are not very useful for quantitative predictors like gene expression or age because of how difficult it is to use them.

The Cox proportional hazards regression analysis is a method that can be used as an alternative. This method is applicable for use with both quantitative predictor variables and categorical variables. In addition, the Cox regression model is an extension of survival analysis methodologies that allows for the simultaneous assessment of the effect of many risk factors on overall survival time [9, 10]. In this study, the purpose of using the cox model was to determine the association between several different variables and the length of survival time and the status.

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4. Results

The strategy and model were utilized to arrive at the conclusions that are presented in this section in Fig. 1 of the overall survival curve shows that the likelihood decreases from 1 to 0.25 with time. After 200 months, the likelihood stabilizes around 0.25. Skin cancer patients have a greater overall survival rate than other cancer patients evaluated in months. In the column below the graph, the number of dangers patients faced is listed. Fewer people are vulnerable or in danger.

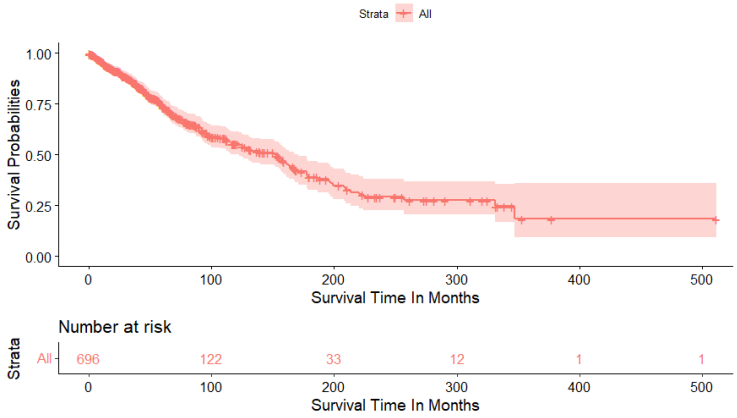

Figure 1. Survival analysis including both kinds of skin cancer.

Skin cancer survival curves are similar for cutaneous melanoma. Skin melanoma is prevalent. Basal epidermis contains melanocytes (the outer layer of the skin). They produce the pigment melanin. Melanin blocks UV rays [11]. MUP survival differs from melanoma. Survival lowers from 100% to 50% in the first 60 days. After 60 months, it's roughly 50%. Although MUP is rarer than Cutaneous Melanomas, its dropping survival rate must be considered.

Sex is a very important factor that affects the survival rate of cancer, and after observing all of the patients who have Cutaneous Melanoma, researchers have found that the p value for sex in patients with Cutaneous Melanoma is approximately 0.0027, which is significantly lower than the target value (0.05). The results can be seen rather plainly in the Fig. 2.

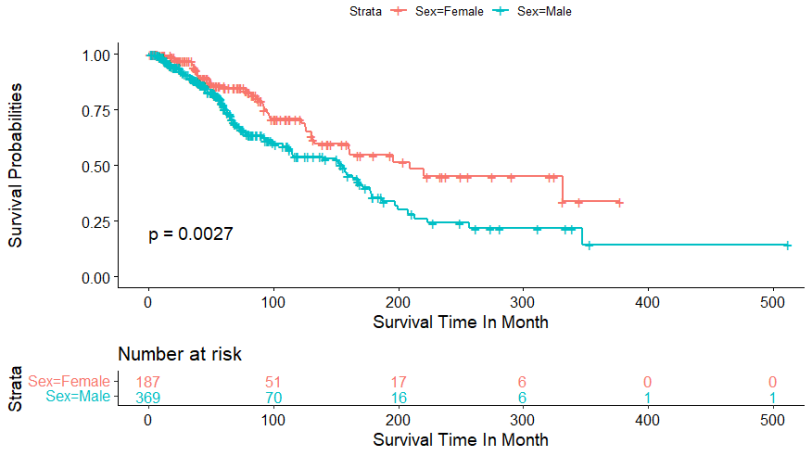

Figure 2. Survival analysis of sex difference on cutaneous melanoma.

Females have a greater survival rate than men. 200 months may bring clarity. At 200 months, female survival is about 50% and male survival is 25%. Male and female medical demands differ greatly. Several studies show that women have a higher melanoma survival rate than men [12 - 14]. Sex is not an obvious feature of MUP, as illustrated in Fig. 3. since 0.4 is more than 0.05 for p. Even though the

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two lines of survival rate data differ slightly, their survival probabilities are similar. All MUP patients have the same survival curve, regardless of sex.

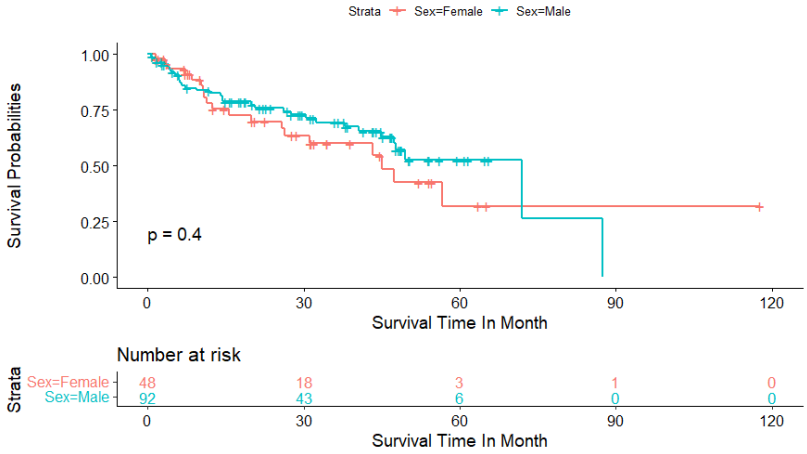

Figure 3. Survival analysis of sex difference on MUP.

According to what is known about cutaneous melanoma, ultraviolet (UV) signature is the most important component that will contribute to mutations in the DNA found in melanocytes. The association between mutation of driver class and the amount of UV is represented by the Fig. 4.

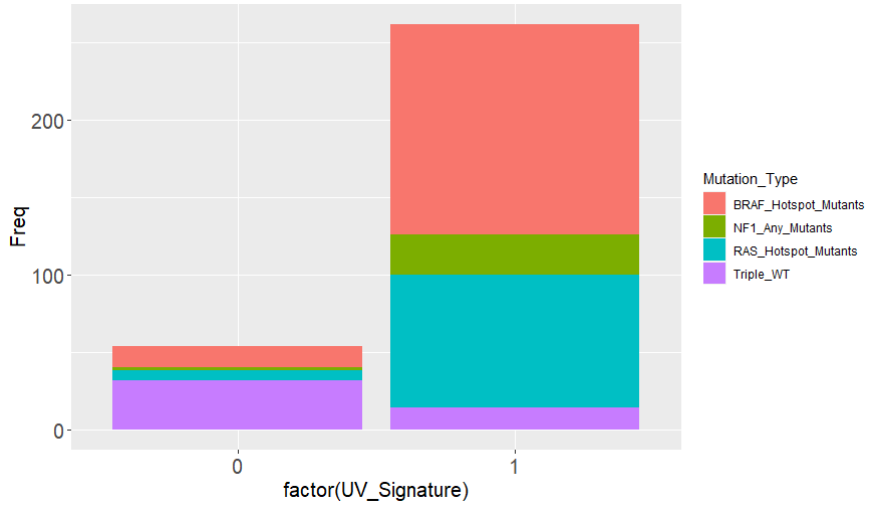

Figure 4. Relationship between mutation of driver class and the amount of UV.

If the value is 0, the patient hasn't experienced any UV exposure; if it's 1, they have. UV exposure affects driving class, study finds. Triple WT driver class is the most common 0 column driver class. After UV exposure, the BRAF driver class had the highest frequency. Every other driver class raised, except Trip WT. A compromised immune system is a predisposing factor in UV-induced skin cancer, which triggers some genes alterations [15]. Extensive sun exposure during childhood increases the risk of melanoma in adulthood. Sun exposure during childhood and adulthood may influence melanoma risk [16].

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Mutation also affects survival rate. Mutations are changes in a cell's DNA sequence. Cell division mistakes and DNA-damaging substances in the environment can induce mutations. Mutations can be dangerous, useful, or have no impact. Various mutations in a cancer driver gene have different effects [17]. According to Fig. 5 and 6, genetic mutation's impact on either type of skin cancer is unclear. NARS Q61, like BRAF V600E, shows a rapidly falling survival rate.

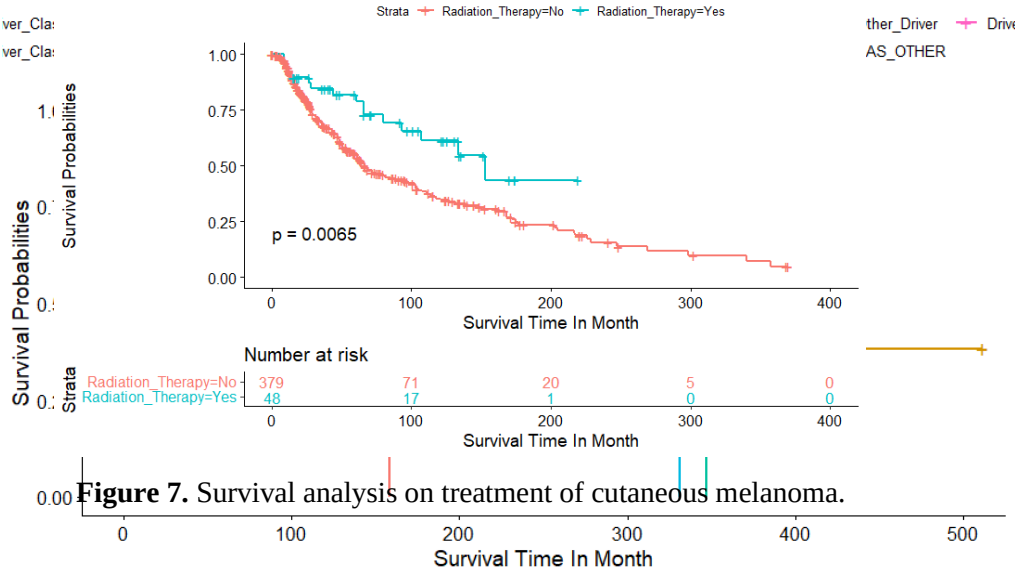

Figure 7. Survival analysis on treatment of cutaneous melanoma.

Figure 5. Survival analysis on genetic driver class of cutaneous melanoma.

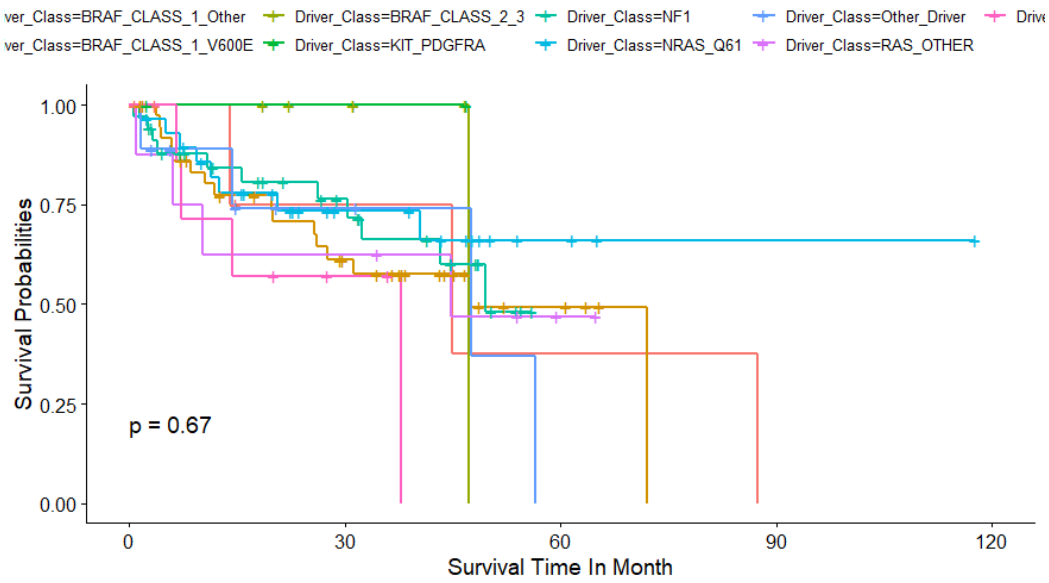

Figure 6. Survival analysis on genetic driver class of MUP.

Radiation is one of the strategies to control Cutaneous Melanoma. The data set is relevant for the treatment of Cutaneous Melanoma. In Fig. 7, patients who receive radiation therapy have a significantly higher survival rate than those who do not. The radiation cannot cure cancer, but it can enhance the quality of life of cancer patients by reducing the size of the cancer site, because in certain cases Cutaneous Melanoma has migrated to other regions of the body via the lymph nodes.

This section examines the relationship between numerous factors and survival. Like the KM approach, each BRAF CLASS V600E variation should be heavily weighted. Despite having the most

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mutations in our data set, NF1 has much less influence on survival than other driver classes. Even though upper extremities are the most prevalent site for cutaneous melanoma, it does not affect survival rate. Upper extremities are the most common site for cutaneous melanoma. Age is one of the most important determinants in a patient's prognosis after being diagnosed with Cutaneous Melanoma, according to previous studies. The incidence of cutaneous melanoma is highest in those aged 60, according to Fig. 8. The risk of cutaneous melanoma peaks at age 60, however it begins to develop at about 50 and rises gradually until 60.

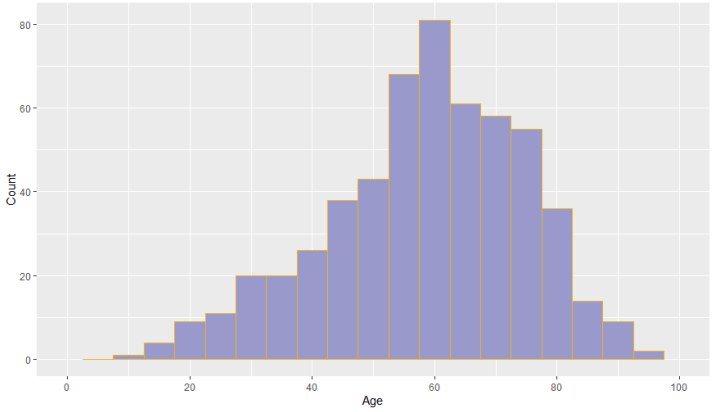

Figure 8. Age distribution of cutaneous melanoma.

The results of the Cox model's survival analysis, on the other hand, show that age does not have a particularly significant influence on the outcome, which can be seen in Fig. 9 and Table 1. This was discovered through the study of survivors. According to the findings of the cox model, the number of mutations, the BRAF class, and the gender of the patient are key variables in the progression of skin cancer.

Table 1. Cox model result for Cutaneous Melanoma.

Variable	Beta (SE)	HR (95% CI)	P Value
Sex			
Female	-	-	-
Male	0.54 (0.19)	1.71 (1.18, 2.47)	0.004
Driver_Class			
BRAF_CLASS_1_Other	-	-	-
BRAF_CLASS_1_V600E	-0.41 (0.36)	0.66 (0.32, 1.35)	0.26
BRAF_CLASS_2_3	-0.72 (0.47)	0.49 (0.19, 1.24)	0.13
KIT_PDGFRA	-16.23 (2295.47)	0.00 (0.00, inf)	0.99
NF1	-0.22 (0.37)	0.80 (0.39, 1.64)	0.54
NRAS_Q61	0.16 (0.35)	1.18 (0.59, 2.33)	0.64
Other_Driver	-0.74 (0.47)	0.48 (0.19, 1.20)	0.12
RAS_OTHER	-0.34 (0.56)	0.71 (0.24, 2.15)	0.55
Unknow_Driver	-0.11 (0.53)	0.90 (0.32, 2.51)	0.83
Mutation_Count	-0.01 (0.00)	0.99 (0.98, 1.00)	0.004
Primary_Site			
Head	-	-	-
Lower Extremity	-0.24 (0.27)	0.78 (0.46, 1.33)	0.37
Truck	-0.19 (0.23)	0.82 (0.53, 1.28)	0.39
Upper Extremity	-0.43 (0.27)	0.65 (0.38, 1.11)	0.11
Fraction_Genome_Altered	0.10 (0.44)	1.10 (0.47, 2.59)	0.83
Age	0.03 (0.01)	1.03 (1.01, 1.04)	<0.001

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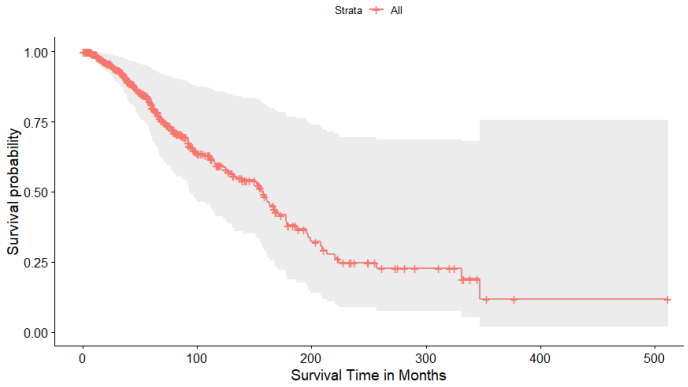

Figure 9. Cox model of cutaneous melanoma.

The results of a MUP test are quite distinct from those of a cutaneous melanoma test in Fig. 10 and the Table 2. There is a substantial association between the modified section of the genome and the survival rate, but only that portion. When opposed to the development of Cutaneous Melanoma, both BRAF and sexual activity play a less significant effect in the development of MUP. A p value of 0.006 is assigned to FGA. (The term "Fraction of Genome Altered" refers to the fraction of the genome that has been changed because of gains or losses in copy number.

Table 2. Cox model result for MUP.

Variable	Beta (SE)	HR (95% CI)	P Value
Sex			
Female	-	-	-
Male	-0.18 (0.33)	0.84(0.44, 1.61)	0.60
Driver_Class			
BRAF_CLASS_1_Other	-	-	-
BRAF_CLASS_1_V600E	0.68 (0.77)	0.66 (0.44, 8.88)	0.38
BRAF_CLASS_2_3	-0.99 (1.26)	0.49 (0.08, 10.71)	0.94
KIT_PDGFRA	-15.75 (4337.43)	0.00 (0.00, inf)	1.00
NF1	0.29 (0.78)	0.80 (0.29, 6.12)	0.71
NRAS_Q61	0.25 (0.79)	1.18 (0.27, 6.07)	0.76
Other_Driver	1.01 (0.90)	0.48 (0.47, 16.16)	0.26
RAS_OTHER	0.84 (0.90)	0.71 (0.39, 13.59)	0.36
Unknow_Driver	1.13 (0.93)	0.90 (0.51, 19.06)	0.22
Mutation_Count	0.00 (0.01)	0.99 (0.99, 1.02)	0.70
Fraction_Genome_Altered	1.83 (0.73)	6.22 (1.52, 25.54)	0.01
Age	0.22 (0.01)	1.02 (0.99, 1.04)	0.23

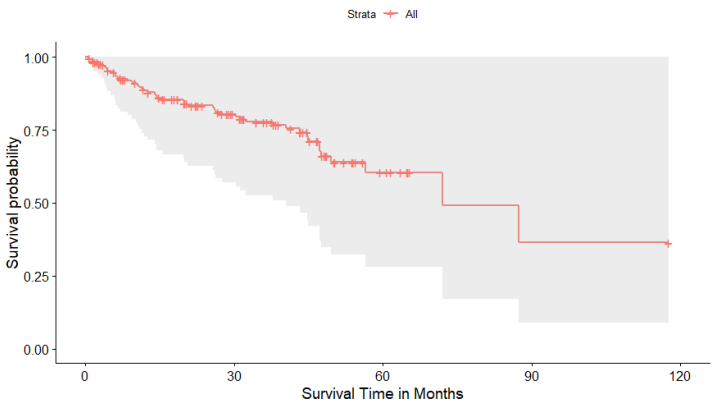

Figure 10. Cox model of MUP.

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"Total Mutations" refers to all mutations in the tumor genome [18]. The distribution shifts are discreet. MUP, like Cutaneous Melanoma, appears at about 60, but it's most common at age 70. S This is because of the increased risk of sun exposure at that age. Between 40 and 70, there is a significant spike in the number of occurrences of the event.

5. Discussion

In this study, survival variables for cutaneous melanoma and MUP are compared. These include genetic expression, age, gender, mutations, and changed genome fraction. The findings indicate that further investigation and prevention is necessary. Prevention is always better than treatment for cancer. Physicians should emphasize skin cancer prevention and treatment for some patients. Males should engage in protected activities to lower their risk of cutaneous melanoma. Some vacations need long hours in the sun. If someone has one of these jobs, they must keep a watchful check on their body and get regular screenings to lower the chance of late-stage cancer. According to this research, characteristics strongly correlated with survival months were used to determine high risk. The study's results will allow CNN [19] to make better forecasts. This project's findings can help researchers and doctors determine if patients are at risk.

Due to the paucity of available research, there is more than one type of radiation that might cause skin cancer. Some treatments, such as surgical removal of affected lymph nodes, immunotherapy, and targeted therapy, have also proven the ability to produce a visible effect for patients with cutaneous melanoma [20]. The results of various therapies for Cutaneous Melanoma are not included in the data set, however. In the case of MUP, the data set in question does not include the treatments or the UV effect. As a result, the researchers were unable to compare the differences between these two parameters in their study. In addition, the magnitude of the data is insufficient for describing this cancer. The percentage of patients who have the MUP only takes 20% of the total number of patients. The absence of baseline clinical features in the data sets that are currently available impedes the ability to conduct an exhaustive investigation of clinical impact. For instance, the fact that the survival analysis does not include the prior treatment and the clinical appearance of all of the patients and the clinical will also lead to a decline in the accuracy of the study.

6. Conclusion

Age and genetic driver class did not reach statistical significance between the two types of skin cancer according to the KM technique and cox model. Compared to MUP, sex has a significant impact on the months of survival for Cutaneous Melanoma. In addition, when more information regarding cutaneous melanoma becomes available, radiation and UV exposure will impact the total number of months of survival. Due to the incomplete treatment data for MUP and cutaneous melanoma, this study does not assess the effectiveness of treatments for these two kinds of skin cancer. In addition, the proportion of patients with MUP in our data set is extremely low, thus it may not be representative of all patients. This study examines risk factors for skin cancer patients and the effect of treatment on months of survival. Survival analysis will become more comprehensive in the future as additional data and clinical characteristics of individuals receiving certain medications become available.

References

[1] Miller A J, Mihm Jr M C. “Melanoma[J].” New England Journal of Medicine, 2006, 355(1): 51-65.

[2] J.M. Bae, Y.Y. Choi, et al. “Metastatic melanomas of Unknow primary show better prognosis than those of unknow primary: A systematic and meta-analysis of observational stidies.” Journal of the American Academy of Dermatology. (2015), pp.59-70.

[3] J. F. Scott, and M. R. Gerstenblith. "Melanoma of unknown primary." Exon Publications (2018): 99-116.

[4] E. Rassy, S. Boussios, A. Chebly, "Comparative genomic characterization of melanoma of known and unknown primary." Clinical and Translational Oncology 23.11 (2021): 2302-2308.

[5] Moan J, Grigalavicius M, Baturaite Z, et al. “The relationship between UV exposure and incidence of skin cancer[J].” Photodermatology, photoimmunology & photomedicine, 2015, 31(1): 26-35.
[6] Jenkins S P. “Survival analysis[J].” Unpublished manuscript, Institute for Social and Economic Research, University of Essex, Colchester, UK, 2005, 42: 54-56.
[7] Madhur Modi, Chaitanya Sagar, Vishnu Reddy, Saneesh Veetil, "Steps to Perform Survival Analysis in R | R-Bloggers,"(2018).
[8] M. K. Goel, P. Khanna, and J. Kishore. "Understanding survival analysis: Kaplan-Meier estimate." International journal of Ayurveda research 1.4 (2010): 274.
[9] C. R. David, "Regression models and life tables (with discussion)." Journal of the Royal Statistical Society 34.2 (1972): 187-220.
[10] M. J. Bradburn, T. G. Clark, S. B. Love, and D. G, "Survival analysis part II: multivariate data analysis–an introduction to concepts and methods." British journal of cancer 89.3 (2003): 431-436.
[11] Jonathan Meddings, Melanoma – Health, BMedLabSc, (22 September 2014).
[12] J. S. Muliken, J. E. Russak, D. S. Rigel, “The effect of sunscreen on melanoma risk.” Dermatol. Clin, 30 (3) (2012), pp.369-376.
[13] V.Nikolaou, A.J. Stratigos, “Emerging trends in the epidemiology of melanoma.” Br. J. Dermatol, 170 (1) (2014), pp.11-19.
[14] M.A. Weinstock, “Cutaneous melanoma: public health approach to early detection.” Dermatol. Ther, 19 (1) (2006), pp. 26-31.
[15] Lucio Andreassi, (2011) “UV exposure as a risk factor for skin cancer, Expert Review of Dermatology,” 6:5, 445-454.
[16] Autier P, Doré for Epimel and Eortc Melanoma Cooperative Group J F. “Influence of sun exposures during childhood and during adulthood on melanoma risk[J].” International journal of cancer, 1998, 77(4): 533-537.
[17] Y. Mossé, M. Laudenslager, L. Longo, "Identification of ALK as a major familial neuroblastoma predisposition gene." Nature 455.7215 (2008): 930-935.
[18] Natives, Digital. "Fraction Of Genome Altered and Total Mutations Added to Cbioportal Plots Tab - The Hyve,"(2022).
[19] X. Dai, I. Spasić, B. Meyer, S. Chapman and F. Andres, "Machine Learning on Mobile: An On-device Inference App for Skin Cancer Detection," 2019 Fourth International Conference on Fog and Mobile Edge Computing (FMEC), 2019, pp. 301-305.
[20] M.C.F. Simoes, J. J. S. Sousa, A.A.C.C Pais, “Skin Cancer and new treatment perspectives: A review Cancer Letters.” Volume 357, Issue 1, (2015), pp. 8-42.