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Cohort analysis for the present mutation of NPM1 in bone marrow cancer

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Abstract. DNA is the most important code for deciphering human genetic information. It finally determines proteins through the central dogma. Therefore, gene mutations can cause various diseases. Cancer is one of the most difficult-to-cure diseases caused by mutations. Acute myeloid leukemia is one of the subtypes of bone marrow cancer, this essay will predominantly focus on the study of the mutation gene NPM1 (nucleophosmin 1). In order to understand the differences between the mutated gene NPM1 and other mutated genes, a cohort study analysis of NPM1 is needed. This research helps better understanding of cancer and the variation of NPM1 compared to the others. By researching and analyzing direct clinical data, this essay will contribute to the understanding of cancer and help turn a scientific blank message into a more simple and understandable manner. However, the limitation of this study is insufficient or even missing data. With the development of research and the improvement of data, future studies will be more accurate and effective, providing a more effective reference for exploring targeted therapy of acute myeloid leukemia.

Keywords: Bone marrow cancer, acute myeloid leukemia, mutation gene NPM1.

1. Introduction

Bone marrow cancer: Bone marrow is the soft, spongy tissue in the center of the bones, this bone marrow contains undifferentiated stem cells, which can develop into different types of blood cells as shown in figure 1, like red blood cells, white blood cells, and platelets [1,2]. The human body tends to produce these cells to replace the old blood cells, therefore they can replicate quickly and mutated blood cells will trigger cancer. There are different subtypes of bone marrow cancer, including multiple myeloma, leukemia, and lymphoma [3]. Different subtypes would be caused by mutations in different blood cells. This study will focus on the mutations of red blood cells, which is commonly known as Leukemia. Inside leukemias, acute leukemias is the type of cancer that grows faster compared to chronic leukemias. To be more specific, this study will focus on the Acute myeloid leukemia (AML) cancer subtypes [4].

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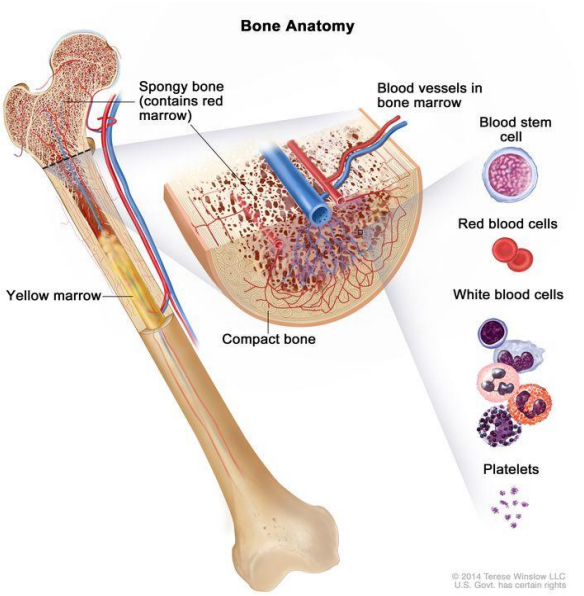

Figure 1. Bone Anatomy [2].

Acute myeloid leukemia: The estimated leukemia in the United States for 2023 is About 20,380 new cases of acute myeloid leukemia and about 11,310 deaths from AML [5]. AML is a disease that targets the elderly and is uncommon before the age of 45. The 5-year relative survival rate for people 20 and older with AML is 28% [6]. In most cases, patients will choose chemotherapy to turn blood cell counts return to within normal limits [7]. On the other hand, stem cell transplant would also be an applicable option for patients. Generally speaking, this is cancer that is based on the development of cancer cells over time, how much is the difference between normal cells and mutated cancer cells This leukemia happens when abnormal leukemia cells produce, it will take over nutrients and rooms from healthy white blood cells, red blood cells, and platelets. Therefore, infection, anemia, or easy bleeding may occur [8].

NPM1 is a protein that encodes a multifunctional phosphoprotein that functions in protein trafficking, pre ribosomal assembly, and ARF- TP53 pathway regulations. Acute promyelocytic leukemia which is a type of AML, is known by a specific translocation between chromosomes 15 and 17, which results in fusion protein promyelocytic leukemia - retinoic acid receptor. This mutation causes loss of nucleolar localization with accumulation of nucleophosmin in the cytoplasm. This is a mutation that occurs in 25% to 35% of cases for adults and 7%- 8% of pediatric cases. Which is a cancer that has an incidence increase over age development [9] (Table 1).

Purpose: The aim of this study is to compare and analyze the clinical case study of patients diagnosed with AML from mutation DPM1 gene will better understand the differences between this specific gene mutation and others, hence that bone marrow cancer has such massive subtypes of cancer, this helps recognize and diagnose cancer better and quicker. There are many available resources or data online provided directly by scientists or researchers, this essay focuses on one specific gene and provides a detailed explanation to fill in the research black of the data. This helps better understanding for the reader and the public.

Table 1. Relationship between gamma radiation dose and myocardial damage [3].

Dose	n	ECG or cTnI abnormalities	Myocardial injury rate(%)
<30Gy	26	0	0
30~50Gy	16	2	12.5
50~60Gy	12	2	16.7
>60Gy	10	4	40

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2. Methodology

In order to get clinical data from patients, this study will be using the Genomic Data Commons Data Portal (CGD data portal) [10], This website provides cases of different patients who have been diagnosed with cancer. Which also provides data analysis functions.

So, in order to build a cohort study for NPM1, first research and limit the cases under Bone marrow cancer, acute myeloid leukemia, NPM1 gene. As shown in figure 2, this creates data sets that contain 47 mutated NPM1 cases in one data set (S1), The other hand creates another data set (S2) which is the collection of all the bone marrow, AML cancer but without NPM1 mutation cases, which has 4261 cases in total. Both of the data will have no cases that share the same gene mutations. In order to present clear contrast and demonstrations. After creating the 2 sets of data, plug them into the cohort comparison and the data will show the following analysis of different criteria: survival rate, sex, age at diagnosis, and vital status. These criteria indicate the full range of basic variables that contribute to the prevalence of cancer.

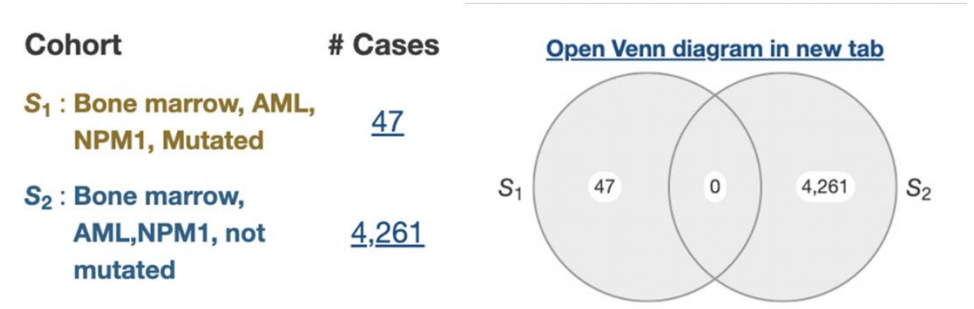

Figure 2. GDC data portal cohort data sets.

3. Results

3.1. Survival rate

The survival rate for both data sets across 8 years is shown in figure 3. Both data sets present an overall trend of decrease in the survival rate. Both data sets have a sharp decrease in survival rate from the first 2 years of diagnosis, which decreased from 1.0 to ~ 0.3 survival rate. Hence the limited case for the mutated NPM1 data set, the trend for S1 stops from year 2. Then S1's survival rate slowly stagnated after year 5, which almost presents a near 0.0 survival rate. Therefore the overall survival rate for S1 is 26% and 21% of the survival rate for S2.

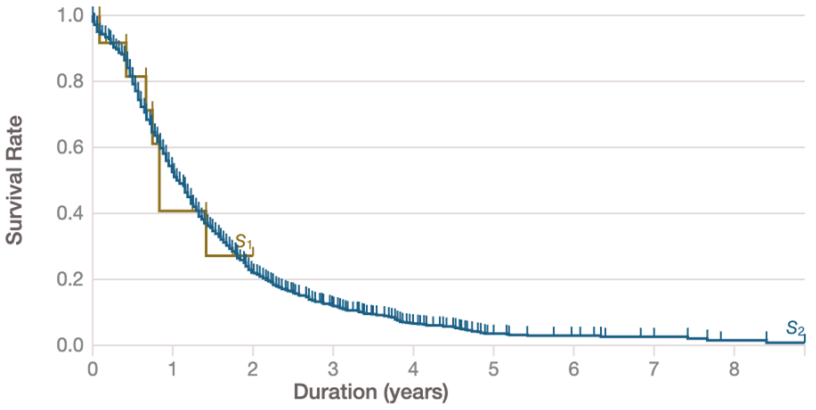

Figure 3. Survival rate of S1 and S2.

The overall survival rate plots communicate certain information, this might indicate that there is not much difference between the incidence rate from the mutated NPM1 and others, As long as it is AML

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the survival rate for this cancer will be shown in the high incidence rate and most of them would not be able to survive longer than 5 years. The overall survival rate would be around 20-30%. Therefore there is not much difference between the incidence rate of AML cancer.

3.2. Gender

Figure 4 shows the percentage of cases contribution from males and females. Based on the observatory, there is an overall decrease or less percentage of cases for females compared to males, no matter data sets S1 or S2. In the S1 data set, there is 59.57% of male and 40% of female, in the S2 data set, there is 53.81% of male group and 45.04% of female group.

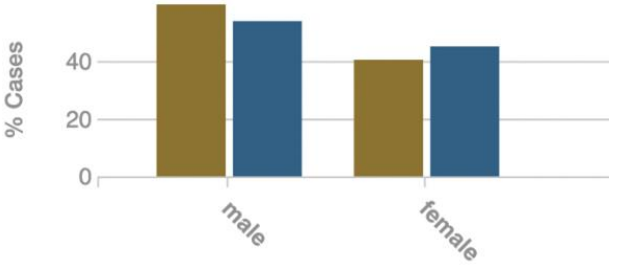

Figure 4. Sex distributions.

Therefore, it also indicates that the prevalence of cancer is generally similar from the two data sets, which shows there is no big variation between genes with NPM1 mutations and other gene mutations. But this chart shows the possible target group of people, which is a male community, and the percentage of cases for both datasets, both have around 10% more cases in males than females. This draws the conclusion that males might have a higher risk of having AML cancer.

3.3. Age at diagnosis

Figure 5 presents the percentage of cases across different ages. In this criteria, the difference between the two data sets is becoming obvious, Data set 2 without the NPM1 mutation gene, most of the percentage of cases around the age of 0 to 20 years old, on the other hand, on S1, most of the percentage of diagnosis is around of the age between 40 to 70 years old.

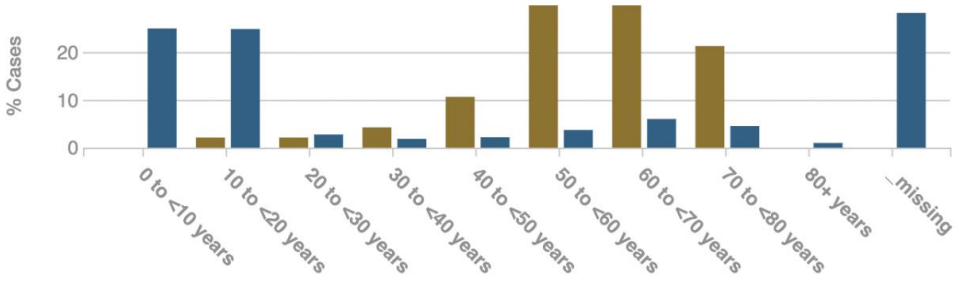

Figure 5. Age at diagnosis for S1 &S2.

From these observations, it is likely to understand the difference between the NPM1 gene and other mutated genes. In the target community of S2 which is another mutation gene, children are at higher risk of being diagnosed with AML that contain other mutated gene, but for S1, which is NPM1, it is more specific down to the community of age between 40-70 years old populations, therefore adult and middle age people are in a higher risk of getting AML with NPM1 mutation gene.

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3.4. Vital status

Figure 6 shows the vital status of patients who are diagnosed with AML cancer. However, there are variations between the group with NPM1 mutations and without NPM1 mutations. In S1, There is a higher percentage of cases shown dead than alive, which is 55.32% and 36.17% respectively. But, there is a higher percentage of alive for S2 than dead, which shows 39.99% and 31.47% respectively.

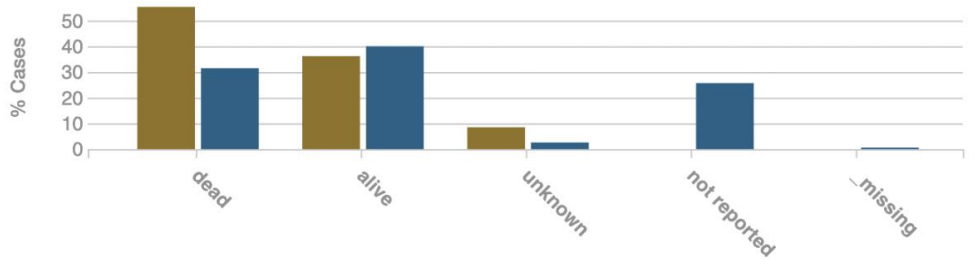

Figure 6. Vital status for S1&S2.

Therefore, It is shown that the variation between the NPM1 gene and others. People who are diagnosed with NPM1 would risk a higher and lesser possibility of survival, but people who are diagnosed with other gene mutations might have a higher rate of cure or survival. This indicates the level of development of the cure method for both gene mutation and the incidence rate for different gene mutations.

4. Discussion

Based on the observations of different categories, the general pattern is shown. In the survival rate, both data sets show a sharp decrease in survival rate access times. For the target community, the chart shows, that in both data sets, males are at higher risk of AML compared to females. For age at diagnosis, normal AML tends to have patients spread around the age of 0 to 20 and middle ages. However, NPM1 showed a greater proportion of elderly in the target community. For vital status, NPM1 mutations tend to have more death compared to others.

5. Conclusion

In conclusion, combine the observation pattern and background knowledge. Acute myeloid leukemia is a cancer that has a high mortality rate. Therefore this is a serious and crude disease. The elderly and male populations should pay more attention to cancer because they have a higher prevalence of diseases. On the other hand, inside AML elderly and middle-aged people tend to become the high prevalence populations, but particularly NPM1 elderly are more affected by this mutation. This pattern might help with quicker diagnosis of the diseases. Lastly, NPM1 mutations show a higher mortality rate compared to other AML mutations, this might indicate the detrimental effect of the cancer. This might draw more attention to these specific mutation genes and develop more treatments or preventions.

Therefore, this observed data and conclusions could be used for further analysis and purpose for the research of NPM1 gene mutations, Proper and reliable observatory experiments would help increase the change of lab experiments and decrease the risk of failure. For this research study, there are also many limitations, like the cases from the CGD data portal are not enough to represent the entire NPM1 cancer research, and only 47 cases would not be enough and viable for the research. Also, there is not enough data for all the criteria, for instance, the NPM1 survival rate plot is not enough which decreases the reliability of the graph and hypothesis. In different charts, there are many “not reported” “missing” and “unknown” data. This is also a limitation of data, which is not accurate and even missing. There are also very big limitations for clinical data analysis, the maintenance of valid and reliable data from patients, the ethical problem of security and protections, and the problem of getting large amounts of data would all be considered as the limitations of this research.

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