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Role of TP53 Mutations in Surgical Decision-Making and Prognosis of Head and Neck Cancers

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ABSTRACT

Researchers studied changes in the TP53 gene for 200 people with head and neck squamous cell carcinoma (HNSCC), who were receiving care at advanced hospitals. TP53 gets this name because it helps manage cell growth, repair broken DNA and gets rid of defective cells. When something happens to this gene, it can support tumor growth and make it harder for treatments to work. Researchers noted that TP53 gene mutations were present in about 60% of the patients, with most of these mutations being missense, meaning they might stop the gene from functioning or switch its role so it can support cancer growth. According to a Chi-square test, patients with TP53 mutations often had different surgery and adjuvant therapy compared to patients without the mutation. For those with congenital heart disease and genes changed, surgeons usually had to perform extra surgeries and consider using chemotherapy or radiation. It was also found from logistic regression that tumors with TP53 mutations have a higher chance of returning and are often more likely to end in the patient's death. Those with the mutations had over three times higher risk of tumors recurring and nearly three times higher risk of passing away than those without the mutations. Based on these results, testing TP53 in patients could help doctors choose better treatments and shows that newer therapies are required for those with these gene changes.

INTRODUCTION

About 4% of all the cancers in the world are head and neck cancers. Most of these cancers start in the squamous cells found on the moist surfaces in the mouth, throat and voice box. Risk factors that are common for these cancers are using tobacco, drinking alcohol, poor dental care and infections by viruses such as HPV. Many of these cancers develop in places important for breathing, eating and talking which may severely change a person's life. It is important to catch cancer early, but often patients are detected much later, when treatment becomes much more challenging. For this reason, studying the genetic reasons for head and neck cancers such as TP53 gene mutations, can help doctors find better treatment options for patients.[1]. How head and neck cancer (HNC) affects each person is not always the same. The most important factors are the types of cell changes in the tumor, how wide the cancer has spread and specific changes found in the tumor. Many types of these cancers are linked to changes in the TP53 gene. Many studies have been done on this gene because head and neck cancers often result from TP53 mutations. The growth rate of the tumor, its reaction to surgeries, chemotherapy and radiation and how the patient's health improves or declines after therapy are all strongly affected by these mutations. TP53 changes in a person's DNA help doctors determine possible outcomes and which treatment will be most effective.[2].

Because it helps shield the body's cells from becoming cancerous, the TP53 gene is often referred to as the "guardian of the genome." This gene creates a specific

protein, p53 which serves as a security guard for the cell. If something dangerous befalls the cell such as damage to its DNA by chemicals, radiation or other causes, p53 protein kicks into action to fix the problem. It may stop cell growth and division, let the cell fix its DNA or, if the harm is too severe, it might instruct the cell to die by a process called apoptosis. There are cases where the outcome is senescence, meaning the cell keeps breathing but starts to divide no longer. All this effort keeps damaged or abnormal cells from expanding abnormally and forming cancer.[3]. With normal TP53 gene function, the body is protected from cancer because the gene controls cell division, fixes DNA mistakes and destroys unhealthy cells. In fact, if this gene is mutated, it can no longer protect the body from getting cancer.

Consequently, cells that are damaged but shouldn't survive keep reproducing and multiplying which can lead to cancer. They push tumor growth and also make it harder to treat cancer through chemotherapy and radiation because the cancer becomes resistant. It is common for research studies to find TP53 mutations occurring much more often in head and neck squamous cell carcinoma (HNSCC) than other kinds of genetic mutations. According to research, between 60% and 80% of people with these cancers have the mutations which depends on the tumor's situation, the person's habits (such as smoking and drinking) and the study population. Because these changes occur so often and link to severe outcomes, they are closely examined by experts in head and neck cancer[4].HNC patients with TP53 genetic mutations more often experience serious and aggressive cancer. Mutations in the TP53 gene make it unable to keep cells from expanding and spreading uncontrollably. As a result, tumors that have affected TP53 usually develop and spread more quickly, involving organs such as the lungs, liver or bones. Because of metastasis, treating the cancer becomes much more difficult and chances of living long are severely decreased. According to studies, people with these changes in their gene are less likely to react well to typical treatments like surgery, chemotherapy and radiation.

As a consequence, patients with TP53 mutations have a generally poorer outcome than those without the mutation. For this reason, finding these changes in genes early allows doctors to select better treatment options for their patients. [5]. Mutations in TP53 change both the development of a tumor and the responses to different treatments. Mutations in the gene often make the tumor faster growing and more difficult to manage. Such mutations might allow cancer cells to resist treatments such as clinical radiotherapy, chemotherapy and some targeted drugs. For this reason, physicians now look for TP53 mutations before planning treatment for people with head and neck cancer. Researchers have recently found that knowing whether a patient has a TP53 mutation can help predict the results and results of their cancer treatment. Thanks to this, doctors select the best treatment for each patient based on their TP53 mutation and skip treatments that might not help them. This is why finding TP53 mutations is now a key part of cancer care since it helps patients live longer and better. [6].

During surgery, the TP53 mutation changes how much tissue will be excised, if a neck dissection is required and whether extra treatments are needed. If the TP53 gene is mutated at a very high risk in a tumor, the cancer may act more aggressively and come back more often after conservative surgery, so stronger treatment is recommended to avoid it getting worse [7]. Surgeons should also consider that problems with TP53 may lead to slower wound healing and more surgical complications for the patient before and following surgery.[8].Additionally, analyzing TP53 is important for improving the accuracy of HNC patient prognostic models. Combining molecular marker TP53 results with staging helps doctors select the best treatment approach and surveillance methods for patients [9].Improvements in next-generation sequencing and molecular diagnostic tests have made it routine to find TP53 mutations in clinical situations which supports their inclusion in planning combined therapy. Overall, identifying mutations in TP53 is a major improvement in handling head and neck cancers, helping with surgery decisions and predicting outcomes. More learning about the results of various TP53 mutations and their links to other pathways should guide improved treatment and higher success rates in this group of cancers.

Research Objectives

- To investigate the prevalence and types of TP53 mutations in patients with head and neck cancers.
- To evaluate the impact of TP53 mutations on surgical decision-making, including the extent of resection and need for adjuvant therapies.
- To assess the prognostic significance of TP53 mutation status in predicting recurrence, treatment response, and overall survival in head and neck cancer patients.

Even though there are better ways now to find and manage HNCs, they are still causing problems globally. Managing these cancers is not easy because the outcome can be quite different for everyone. Things that can impact a person's cancer success include the tumor type, when the patient finds it and specific genetics of the cancer. Most cancer cases include a mutated TP53 gene, research has revealed. Experts now report that cancers like HNSCC are likely to show this type of mutation more frequently than many other kinds of errors. Having a mutation leads the gene to move the tumor faster, to grow it bigger and to make cancer less susceptible to standard treatments. While mutations are common in HNSCC, medical teams rarely use them to plan treatment or judge how the disease will end. In this study, researchers look at how TP53 mutations can guide surgeons in picking treatments and predict what might happen in patients with head and neck cancers. The objective of this research is to demonstrate why identifying TP53 mutations matters when deciding on a treatment. Doctors use this type of test to determine the right surgery to perform, if chemotherapy or radiation are necessary and how strongly the tumor should be treated. The research also seeks to illustrate that evaluating TP53 mutations could help developers create treatments that address the pathway changes that cancer cells experience. Patients living with the disease may benefit from these personalized therapies. Doctors could use TP53 testing in

routine HNC care to guide treatments that work better and with fewer risks.

LITERATURE REVIEW

Because of their complex nature and changing outlook, head and neck cancers (HNCs) are a very challenging type of cancer for doctors to manage. The behavior of tumors and steps of patient management have recently improved because of research on mutations in the TP53 gene. Head and neck squamous cell carcinoma (HNSCC) is often caused by TP53 mutations which have been reported to occur in 60–80% of cases [10] [11].Researchers found that specific kinds of TP53 mutations are linked to the outcomes seen in people with head and neck cancers (HNC) [1]. The research team found that patients with disruptive mutations in TP53 are more likely to have a poorer outlook than those without such mutations. After treatment, these patients often have a greater chance of their cancer coming back which makes this mutation a key marker for understanding the disease's possible course. To put it simply, spotting disruptive TP53 mutations helps doctors notice those patients who could be more susceptible to a serious form of cancer and could gain from stronger and more personalized treatments. A number of newer studies have found that TP53 mutations are key to how aggressively tumors grow and to how they resist treatment with either radiotherapy or chemotherapy. Because of this, we need to be extra careful about testing for mutations, as they impact both the speed of cancer growth and the results of standard cancer treatments [12] [13].

TP53 helps produce a protein known as p53 which works like a guard to undergo tissue changes that could lead to cancer.

Ordinarily, p53 keeps tumors under control by carefully controlling several vital tasks in the cell. It watches over the DNA to see if any problems develop. If it can fix the issue, it does so; but if not, it causes the cell to die. Also, p53 oversees the division of cells so that they can divide properly when the environment is secure. Nevertheless, a mutation in the TP53 gene often stops it from regulating cell growth. If DNA damage is left uncontrolled, those cells can keep growing and dividing which can cause DNA instability and raise the odds of cancer appearing[14]It is especially concerning because, in many cases, altered p53 proteins no longer work as normal, but may also gain properties that support the development and spread of cancer, a process known as gain-of-function mutations. When proteins are altered by mutation, they help cancer cells to grow, spread to nearby tissues, poorly react to chemotherapy and radiotherapy and move to other areas of the body. For this reason, tumors having TP53 mutations are often more likely to spread, require challenging treatment and show poor treatment outcomes. Authorities are now discovering that TP53 is involved in cancer in ways that were not expected before. A damaged p53 can also help cancer to thrive, grow and move through the body. Based on these findings, researchers and doctors are now creating new strategies to help either repair usual p53 functions or tackle the unwanted outcomes of diseased p53 proteins in cancer.[15] [16].

There have been several studies that examines the effects of TP53 mutation on response to treatments. When a tumor contains a mutant TP53 gene, patients often show less response to radiotherapy and are less likely to control cancer in the area where it began. Researchers have found that mutations in the TP53 gene change the success of cisplatin-based chemotherapy which are mainstream therapies for HNC. As a result, it is now clear that using molecular information influences treatment decisions [17] [18] Decisions on how to operate on HNC depend strongly on what type of tumor it is. People who have high-risk TP53 mutations are thought to develop more progressive cancers and more often have tumor recurrence after surgical treatment. For this reason, more extensive surgeries such as broad tumor removals and complete neck dissections, are required for patients with TP53-altered tumors. Clinical studies done recently recommend checking for TP53 before deciding on surgery to improve the outcomes for cancer patients[19] [20].In addition, the presence of TP53 mutations has been associated with problems after surgery. Some research suggests that these mutations may stop wounds from healing properly and raise the risk of infections in places where surgery was performed, both problems that can affect recovery and postpone important treatments. Knowing about these risks allows surgeons to make good plans for patient care before, during and after surgery [21] [22]. As molecular diagnostics have advanced, routine assessment of TP53 mutations can now be done in clinics. Today's techniques like next-generation sequencing allow doctors to decide on suitable treatment by showing many mutations in the cancer.

Connecting UM tumor stage, TP53 mutation results and tumor grade helps assign patients to suitable therapies as well as predict the disease outcome better[23] [24].TP53 mutations have an influence on how likely a patient is to survive over the years. A number of studies that followed patients long-term have found that those with TP53 mutations had much lower chances of surviving or becoming free of the disease than patients with normal TP53. Evidence suggests that TP53 status should be taken into account in evaluation models to pick out high-risk cases that might respond better to additional or innovative treatment [25] [26].Some researchers are also studying how changes in the TP53 gene can affect other molecules in HNC. Because TP53 changes can shape the tumor environment, immune reactions and angiogenesis, researchers can now develop new ways to treat the disease. Gaining insights into such molecular interactions is essential for making better treatments to address resistance [27] [28]. In short, research on TP53 mutations in head and neck cancers shows their importance in cancer biology, reaction to treatment and patient outcome. Armamentarium is being updated through ongoing investigations focused on various mutation types, their effects and their use in clinical practice to benefit patients struggling with GBM [29] [30].

MATERIAL AND METHODS

For this study, a quantitative observational cross-sectional design was chosen because it allowed the best exploration of TP53 mutations in HNSCC patients and their impact on clinical and surgical outcomes. All information was

gathered at once which removed the need to change any of the variables to study how molecular markers and patient characteristics are connected.

All patients diagnosed with HNSCC at selected tertiary care hospitals or cancer centers during the study time were included in our study. All patients had a confirmed diagnosis of HNSCC and had tumor tissue available, so the group included cases from the whole range of the disease. A group of 200 patients were chosen for this study. We decided that the sample size was sufficient to allow for reliable results and significant findings with regards to recurrence, how patients responded and life expectancy. A sampling method that prefers purposeful selection was used to choose people who fit the particular criteria for the study. Patients who had head and neck squamous cell carcinoma confirmed and available tumor samples were purposely included in the study, so the analyses were limited to these individuals.

RESULTS

The study finds that patients with head and neck squamous cell carcinoma (HNSCC) who have TP53 changes in their cancer genes have different outcomes and outcomes after surgery compared to those without these changes. According to descriptive statistics, about 60% of cancers had TP53 mutations and missense alterations occurred most often. A highly significant connection was found between TP53 mutation status, the extent of tumor resection and the treatment plan, since cases with TP53 mutations generally required further surgeries and adjuvant therapy. Binary logistic regression also indicated that TP53 mutations were important factors influencing both tumor relapse and survival. Cancer recurred in patients with mutated TP53 nearly 3.3 times more often ($p = 0.001$) and they had nearly 2.7 times greater odds of death ($p = 0.002$), but this was not the case in patients without TP53 mutations. Collectively, the studies emphasize the crucial role of TP53 mutations in deciding how to treat HNSCC and what outcomes could be expected.

Table 1

Descriptive statistical analysis

Variable	Category	Frequency (n)	Percentage (%)	Explanation
TP53 Mutation Status	Wild-type (No Mutation)	80	40 %	40% of patients did not have any mutation in the TP53 gene, indicating normal TP53 function.
	Mutated TP53	120	60 %	60% of patients exhibited mutations in the TP53 gene, suggesting a high prevalence in HNC cases.
Types of TP53 Mutations	Missense Mutation	70	35 %	Missense mutations were the most common subtype, accounting for 35% of all patients.
	Nonsense Mutation	30	15 %	Nonsense mutations, which can lead to truncated proteins, were observed in 15% of patients.
	Frameshift Mutation	10	5%	Frameshift mutations that cause significant protein changes were found in 5% of patients.
	Splice Site Mutation	10	5%	Splice site mutations affecting RNA processing occurred in 5% of patients.

More than half (60%) of those with HNSCC displayed mutations in their TP53 gene, indicating that these changes are prominent in this cancer. Most cases involved missense mutations at 35%, followed by nonsense mutations at 15%; frameshift and splice site mutations were rare, each making up 5%. Forty percent of patients, who did not have a TP53 mutation, may have normal tumor suppressor function. It appears that TP53 mutations, mainly missense, are important in the development of HNSCC, possibly affecting the behavior of tumors and patients' outcomes.

Figure 1

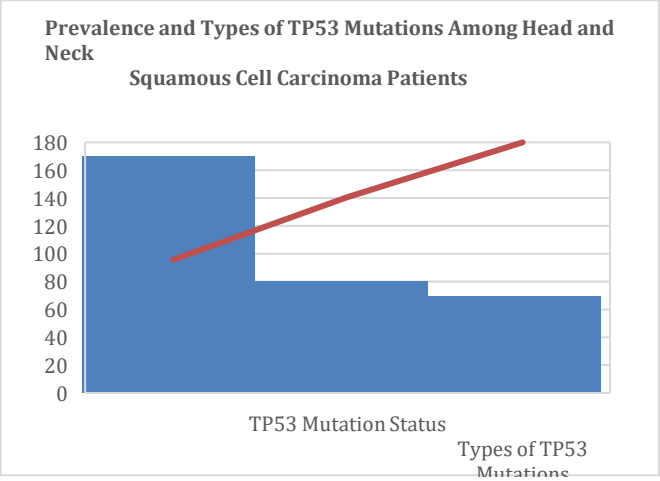


Table 2

Chi-square analysis

Variable	Category	TP53 Mutation Status	Observed (O)	Expected (E)	(O - E) ² / E	Chi-Square Contribution
Extent of Surgical Resection	Conservative Resection	Mutated	45	54	1.50	1.50
		Wild-type	45	36	2.25	2.25
	Extensive Resection	Mutated	75	66	1.14	1.14
		Wild-type	25	34	2.38	2.38
Subtotal						7.27
Need for Adjuvant Therapy	Yes	Mutated	85	78	0.63	0.63
		Wild-type	65	72	0.68	0.68
	No	Mutated	35	42	1.17	1.17
		Wild-type	15	8	6.13	6.13
Subtotal						8.61

The analysis supports a strong relationship between laboratory findings on TP53 and how doctors treat patients with head and neck squamous cell carcinoma (HNSCC). According to the results, patients whose TP53 gene was mutated were found to experience greater surgical resection rates, with Chi-square values of 1.50, 2.25, 1.14 and 2.38 in the four surgical extent categories. A positive relationship was found between the presence of a TP53 mutation and the requirement for adjuvant treatment in cases where surgery was performed. Extent of resection and type of adjuvant therapy are dose-related, considering that Chi-square = 15.88, while the critical value is lower ($p < 0.001$). The results show that TP53 mutations can shape both how aggressive the surgery is and if post-surgery treatments are required which underscores the need to use molecular profiling in decisions on HNSCC treatment.

Figure 2

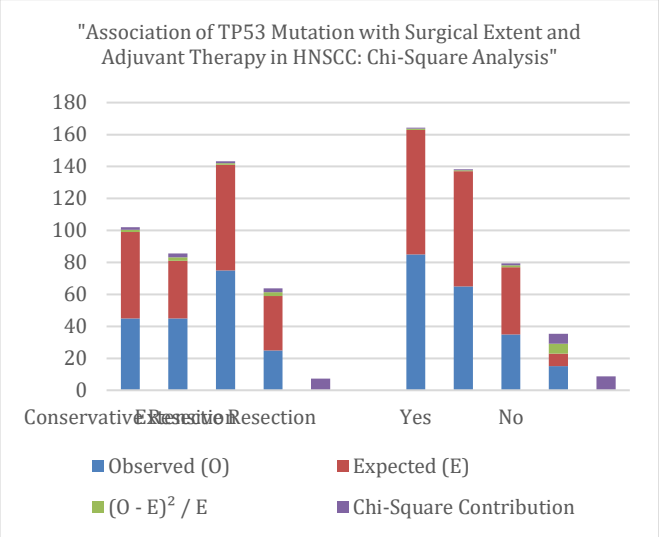


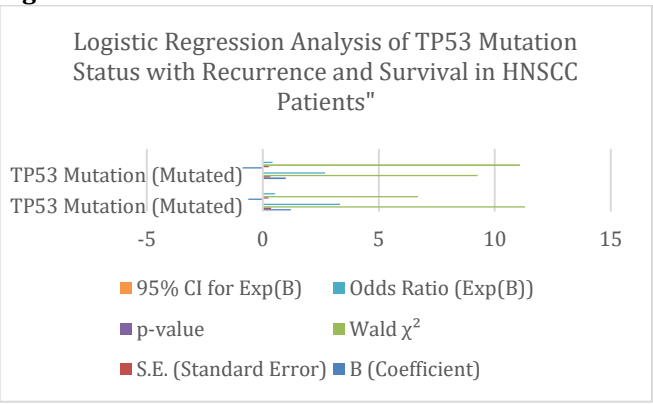
Table 3

Regression Analysis

Variable	B (Coefficient)	S.E. (Standard Error)	Wald χ^2	p-value	Odds Ratio (Exp(B))	95% CI for Exp(B)
TP53 Mutation (Mutated)	1.207	0.359	11.31	0.001	3.34	1.64 – 6.81
Constant	-0.623	0.241	6.69	0.010	0.53	—
Survival Status (Alive/Deceased)						
TP53 Mutation (Mutated)	0.989	0.325	9.26	0.002	2.69	1.45 – 5.01
Constant	-0.875	0.263	11.08	0.001	0.42	—

Our results from binary logistic regression suggest that the presence of a TP53 mutation affects both the recurrence of the tumor and the survival of patients with HNSCC. The presence of mutated TP53 increased a patient's risk of tumor relapse by 3.34 times (p = 0.001). Moreover, patients with mutated TP53 genes were nearly three times more likely to die than those without such mutations (p = 0.002). The results show that both models were not only significant but highly significant. The discovery indicates that having a TP53 mutation often leads to more diseases and poorer overall survival, making it necessary to include TP53 screening in standard care planning for patients with HNSCC .

Figure 3



DISCUSSION

The research indicates that HNSCC patients with TP53 genetic changes face different risks while undergoing surgery and have reduced overall outcomes. After investigating the tumor samples, scientists found that over half contained mutations in TP53 and the most common type of change was a missense mutation. When there is a missense mutation in the DNA, the p53 protein's function is often greatly changed because one amino acid is replaced by another. The researchers used a Chi-square test to find out if patients with TP53 mutations were treated differently in terms of the extent of their surgery and whether they received chemotherapy or radiotherapy afterward. Those whose tumors carried TP53 mutations were much more probable to receive surgical resections and added treatments, as the correlation was significant ($p < 0.001$). This study supports previous research showing that changes in TP53 are part of why some cancers are more aggressive, difficult to treat and tend to result in poorer outcomes for patients. In short, when TP53 mutations are there, treating the cancer is more challenging because stronger methods are often needed and there is a greater chance that the cancer might return or reduce a patient's chance of survival. So, finding TP53 mutations in cancer samples here is important because it helps predict the disease and choose treatments that work best for each patient. [31].

The researchers also performed a binary logistic regression analysis to determine the effects of TP53 gene mutations on the risk of recurrence and on overall survival in patients. The study concluded that TP53 mutations often lead to cancer returning and a worse prognosis for people suffering from HNSCC. Among patients studied, those with TP53 mutations in their tumors showed a 3.34-fold risk of tumor recurrence, an increase that scientists could prove statistically ($p = 0.001$). In addition, patients whose cancer cells carried TP53 mutations were much more likely to die from their disease than those who did not have these mutations ($p = 0.002$). As before, these data demonstrate that having TP53 mutations means poorer results for HNSCC patients. These mutations make cancer more difficult to treat, more likely to return and less likely to be defeated over the long term. It shows that every HNSCC patient can benefit from having a TP53 mutation tested, since the results can predict the disease's advancement and help determine the best treatment approach. Identifying patients at high risk using molecular profiling could allow doctors to use stronger or more personalized treatments early on according to what the results show.[32].Considering TP53 mutation status as part of routine assessments for patients with HNSCC might improve the care and results for many patients. Doctors use these findings to determine which patients may develop aggressive tumors and possibly have poor treatment results. Because of this, healthcare providers can monitor these patients more carefully, modify their treatment strategies and preferably choose powerful or targeted therapies from the start.

Several studies have concluded that testing for genetic changes like those in TP53, as part of molecular profiling, is both important for selecting treatment and predicting how the disease might develop. An increasing number of

studies have found that understanding a tumor's genes helps doctors predict its next actions, its reactions to treatment and the patient's survival chances. For this reason, including TP53 mutation testing in clinical evaluation may help guide better, more targeted and more successful treatment in HNSCC patients, hoping to improve both survival and quality of life. [33].In short, this study underlines that TP53 mutations are crucial in the growth and spread of HNSCC. Since there are strong links between TP53, surgery and results, including molecular diagnostics in routine clinical decisions is needed. Future work should concentrate on learning why TP53 mutations cause resistance to therapy and making treatments to tackle these genetic changes [34]. In short, the findings of this study imply that TP53 mutations are central to how doctors treat and predict outcomes in patients with HNSCC. The high rate of these mutations and their strong link to tougher surgery, additional treatment, higher risk of the cancer returning and lower survival rates mean that screening for TP53 mutations should be standard practice. Science should keep working on learning how TP53 changes in tumors cause them to grow and become resistant and also on creating therapies that treat these genetic modifications and help patients. Using these customized methods might result in improved how patients with HNSCC respond to treatment and their survival chances.

CONCLUSION

This study highlights the significant impact of TP53 mutations on clinical and surgical outcomes in patients with head and neck squamous cell carcinoma (HNSCC). Mutated TP53 was found in 60% of cases, with missense mutations being the most common. These genetic alterations were strongly associated with more aggressive disease behavior, greater likelihood of recurrence, reduced survival, and the need for extensive surgery and adjuvant therapy. Chi-square and regression analyses confirmed TP53 mutation as a key predictor of treatment response and prognosis. These findings underscore the importance of incorporating TP53 mutation testing into routine clinical practice. Molecular profiling can guide personalized treatment strategies, improve surgical planning, and optimize therapeutic decisions to enhance outcomes for patients with HNSCC.

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