

An Evaluation of Treatment Strategies for Head and Neck Cancer in an African American Population

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ABSTRACT

Objective: This study evaluated treatment strategies for head and neck cancers in a predominantly African American population.

Methods: Data were collected utilizing medical records and the tumour registry at the Howard University Hospital. Kaplan-Meier method was used for survival analysis and Cox proportional hazards regression analysis predicted the hazard of death.

Results: Analysis revealed that the main treatment strategy was radiation combined with platinum for all stages except stage I. Cetuximab was employed in only 1% of cases. Kaplan-Meier analysis revealed stage II patients had poorer outcome than stage IV while Cox proportional hazard regression analysis ($p = 0.4662$) showed that stage I had a significantly lower hazard of death than stage IV ($HR = 0.314$; $p = 0.0272$). Contributory factors included tobacco and alcohol but body mass index (BMI) was inversely related to hazard of death.

Conclusions: There was no difference in survival using any treatment modality for African Americans.

Keywords: African American, cetuximab, combination-therapy, head and neck cancer, survival

Evaluación de las Estrategias del Tratamiento para el Cáncer de Cabeza y Cuello en una Población Afroamericana

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RESUMEN

Objetivo: Este estudio evaluó las estrategias del tratamiento para los cánceres de cabeza y cuello en una población predominantemente afroamericana.

Métodos: Se recopilaron datos utilizando historias clínicas y el registro de tumores del Hospital Universitario Howard. Se utilizó el método de Kaplan-Meier para el análisis de supervivencia, y el análisis de regresión de riesgos proporcionales de Cox para predecir los riesgos de muerte.

Resultados: El análisis reveló que la estrategia principal para el tratamiento fue la radiación combinada con platino para todas las etapas, excepto la etapa I. Se empleó cetuximab en sólo 1% de los casos. El análisis de Kaplan-Meier reveló que los pacientes de etapa II tuvieron resultados más pobres que los de la etapa IV, mientras que el análisis de regresión de riesgos proporcionales de Cox ($p = 0.4662$) mostró que la etapa I tenía un riesgo de muerte significativamente menor que la etapa IV ($HR = 0.314$; $p = 0.0272$). Los factores contribuyentes incluyeron el tabaco y el alcohol, pero el índice de masa (IMC) fue inversamente proporcional al riesgo de muerte.

Conclusiones: No hubo diferencias en la supervivencia con ninguna de las modalidades de tratamiento para los afroamericanos.

Palabras claves: Afroamericano, cetuximab, terapia de combinación, cáncer de cabeza y cuello, supervivencia

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INTRODUCTION

Head and neck squamous cell carcinomas (HNSCCs) refer to those cancers occurring in the oral cavity, oropharynx and larynx (1). The American Cancer Society estimated 52 140 new head and neck cancer diagnoses and 11 460 deaths attributable to these cancers in the United States of America (USA) in 2011 (2). Globally HNSCCs represent approximately 3% of all cancers diagnosed in men, and 2% diagnosed in women (1).

The incidence and related mortality of HNSCC has increased over the past decades, despite advances in diagnostic and therapeutic techniques (3, 4). Its incidence is three times higher among men, and more common in African American populations than Caucasian populations (5, 6). It is reported that African Americans present at younger ages with a higher incidence of advanced stages and often inoperable disease which is associated with poor survival outcomes even after treatment (1, 6–8). Within the USA, the estimated five-year survival rate for patients with oral cancer is approximately 60% depending on the tumour site (9), however, it is only 45% for blacks and 65% for whites (10); the five-year survival rate for the Caribbean is undocumented.

Several risk factors have been found to be associated with HNSCCs. The relationship between alcohol consumption, tobacco use and HNSCCs has been clear for many years, and remains one of the main risk factors (3, 7–14). Research results have found that the consumption of alcohol coupled with the use of tobacco produces a synergistic effect increasing the likelihood of developing HNSCC (4, 15). Other known aetiological factors include poor oral hygiene, genetic susceptibility, chronic exposure to certain industrial agents and infection with specific subtypes of human papillomavirus [HPV] (1, 4, 8, 14).

Once a patient is diagnosed, the lesion is staged using the American Joint Commission on Cancer (AJCC) tumour/node/metastasis (TNM) system (1). The TNM system combines information concerning the extent of anatomic tumour, and the spread of disease into staging that provides estimates of survival, although according to some (16), this approach has limited prognostic value. The comprehensive histopathologic staging is considered by others (3, 4) as a more important determinant of postoperative management and prognosis prediction. Ultimately, the prognosis of head and neck cancers depends on the characteristic of the tumour, as well as on multiple host factors (17, 18).

The management of HNSCCs during the 1960s and up to the 1980s consisted primarily of surgery and radiation therapy, but with the advances in therapeutic regimens, the treatment of choice of localized, advanced HNSCC is chemoradiation [CRT] (1, 19–21). The introduction of the anti-epidermal growth factor receptor monoclonal antibody cetuximab recently showed the potential of improving the results of CRT. This drug was demonstrated to increase overall survival when combined with radiotherapy alone (22), or when used in combination with fluorouracil (23–26).

Although previous studies have shown that compared to Caucasians, African Americans have a lower survival rate (15, 27–29), few if any have investigated whether the new advances in treatment, and in particular the new combination chemotherapy altered this situation. Howard University Hospital (HUH) services a large urban African American population and thus provides an excellent opportunity to evaluate HNSCC treatment strategies in African Americans. This preliminary study considered the demographics of patients diagnosed with HNSCC, who attended the HUH for the four-year period January 2004 through December 2007. This study aims to retrospectively report the management of HNC in a single oncology centre in a predominantly African American population.

SUBJECTS AND METHODS

This retrospective study evaluated the treatment experience of patients aged 18 years and older, diagnosed with HNSCCs at HUH between January 2004 and December 2007. Relevant approval from the Howard University Institutional Review Board was obtained. Data were collected utilizing medical records and information from the tumour registry at HUH. Study variables defined for analysis included: race, gender, primary site of tumour, TNM staging, histological grade, date of diagnosis, age at diagnosis, history of comorbid disease, tobacco and alcohol use, treatment received and date of death or last follow-up. Treatment groups included radiation only, combined radiation and chemotherapy, no treatment and other. Chemotherapy was considered as treatment using a platinum-based regimen, either cisplatin or carboplatin with or without fluorouracil and/or cetuximab. Patients without date of diagnosis or tumour stage were excluded from analysis.

Statistical analysis

Descriptive statistics including means and frequencies were used to describe all variables. To test associations between nominal study variables, Chi-square and Fisher exact tests were utilized. In cases where multiple comparisons were analysed, Bonferroni's adjustment was used to correct for a Type I Error. To graphically and statistically ascertain the differences in survival between the study groups (treatments, gender, race/ethnicity, tumour site, *etc*), Kaplan-Meier curves and log-rank analyses were performed. Cox proportional hazards regression analysis was also conducted to further assist in predicting the hazard of death. Data were analysed using the SAS statistical package (version 9.2, SAS Institute, Cary, NC). Statistical significance was considered at $p < 0.05$.

RESULTS

Social and clinical characteristics of the patients are listed in Table 1. The most common primary location of HNSCC was the pharynx (35%) followed by larynx (32%) with the tongue, oral cavity, parotid and multiple locations making up

the remainder (33%) [Fig. 1A]. Of those diagnosed, the vast majority, 92%, exhibited squamous cell carcinoma; adenocarcinoma accounted for 3% and sarcoma for 1% (Fig. 1B).

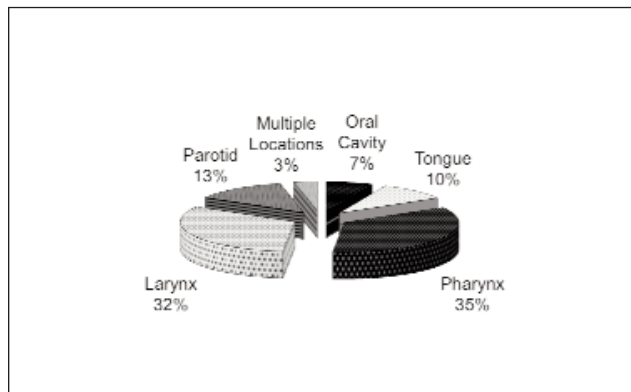


Fig. 1A: Primary site of cancer at diagnosis.

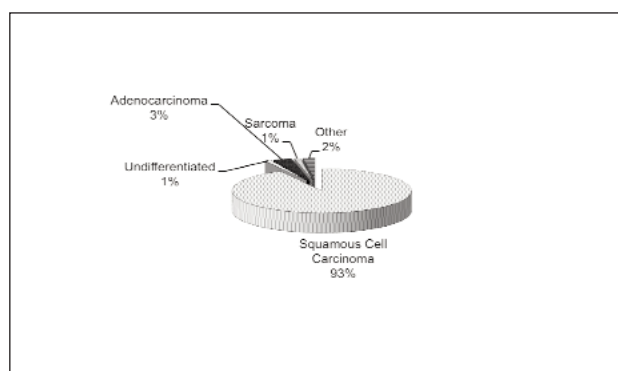


Fig. 1B: Distribution of carcinomas according to the tumour type.

Histological analysis of the biopsy specimen showed 44% as poorly differentiated tumours and another 40% as moderately differentiated tumours. At the time of diagnosis, the majority of patients, 62%, were classified as stage IV; 15% were at stage I and another 14% at stage III (Fig. 2A).

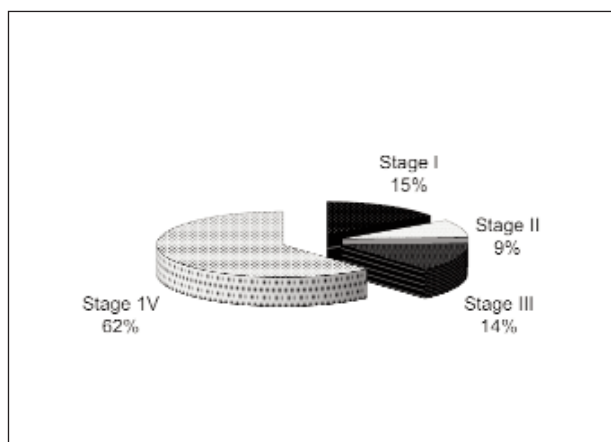


Fig. 2A: Cancer staging at diagnosis.

Overall, the primary treatment modality was radiation therapy only which accounted for 37%. Radiation used in conjunction with combination chemotherapy which included platinum based drugs was received by 23% of patients while 22% of patients received no treatment (Fig. 2B). Only 1% of

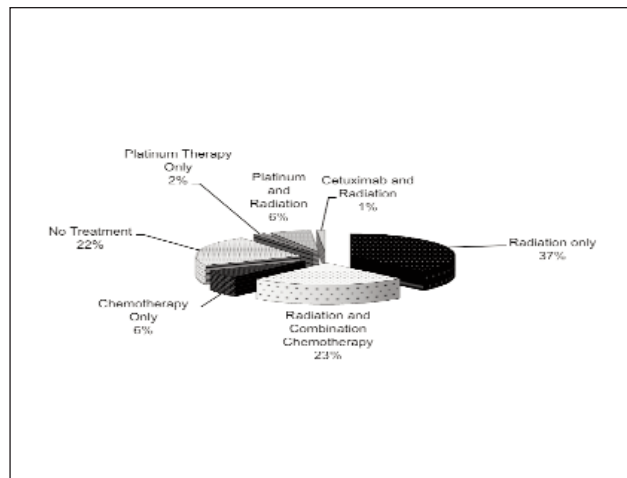


Fig. 2B: Modes of cancer treatment.

patients received cetuximab. In the evaluation of staging and treatment (Table 2), 50% of stage I patients received no treatment and the remaining 50% had radiation only. About 44% of stage II patients received radiation treatment only, 14% had combination therapy and 29% had no treatment. Stages III and IV patients had the most variation in treatment modalities. In the Stage III group, 27% had radiation only, 36% combination therapy, 18% no treatment and the remaining 19% received other therapy (Table 2). For the stage IV, the majority, (35%), received radiation only, 27% had combination therapy, 10% received platinum therapy and 15% received no treatment (Table 2).

Table 1: Social and clinical characteristics of the patients

Patient variables	Mean (SD) (n = 91)
Age at diagnosis – mean year (SD)	59.8 (12.11)
Gender – n (%)	
Male	63 (69.2)
Female	28 (30.8)
Race – n (%)	
African American	86 (95.4)
Other	5 (5.5)
Body mass index (BMI) - n (%)	22.21 (5.5)
Tobacco use	73 (80.2)
Alcohol use	64 (70.3)
Histologic type	
Poorly differentiated	38 (43.7)
Moderately differentiated	35 (40.2)
Well differentiated	2 (2.3)
Not specified or other	12 (13.8)

Table 2: Treatment of head and cancer by stage

Treatment approach	Stage I (%)	Stage II (%)	Stage III (%)	Stage IV (%)
No treatment	50	29	18	15
Radiation only	50	44	27	35
Combination	—	14	36	27
Platinum	—	—	—	10

Multivariate analyses

Poorly differentiated histology was found to be associated with the use of alcohol ($p = 0.00040$) and tobacco ($p = 0.0017$). Similarly, moderate histological grade was found to be associated with the use of alcohol ($p = 0.0011$) and tobacco ($p = 0.0037$). Both tobacco and alcohol use were associated with an increased risk of death ($HR = 2.123$) but the unadjusted Cox proportional hazard models detected an inverse relationship for body mass index (BMI) [$HR = 0.921$, $p = 0.0095$].

Comparison of the survival curves of treatment modalities (Fig. 3A) showed that survival was not significantly influenced by differences in the treatment regimens. The multivariate Cox proportional hazard regression analysis (log-rank test $p = 0.4662$) showed that individuals diagnosed with stage I had a significantly lower hazard of death than individuals diagnosed with stage IV ($HR = 0.314$; $p = 0.0272$). In assessing the overall survival, stage I ($n = 14$) had the highest median survival whereas stage IV had the lowest outcome. By way of contrast, the Kaplan-Meier curves suggest that stage II patients had a poorer outcome than stage IV (Figs. 3A and B).

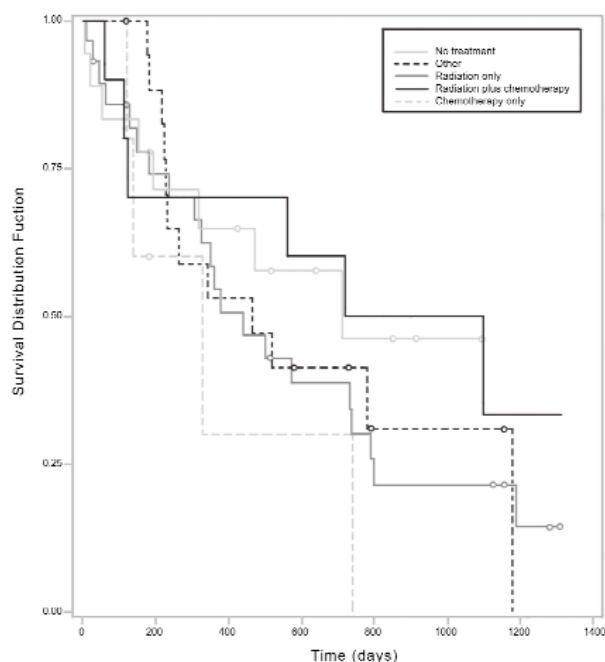


Fig. 3A: Kaplan-Meier plots for survival in patients according to treatment category.

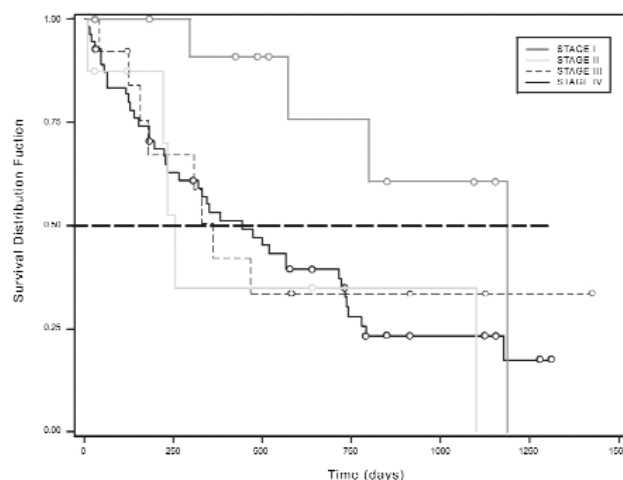


Fig. 3B: Kaplan-Meier plots for survival in patients stratified by stage at diagnosis.

DISCUSSION

Head and neck squamous cell carcinomas of the oral cavity, which include the oropharynx and larynx, are the sixth most common cancers worldwide with an estimated annual burden of 633 000 cases and 355 000 deaths (30). Within the USA, the American Cancer Society estimated that for 2011, there would have been 52 140 new cases and 11 460 deaths attributable to these cancers (2). In particular, the disease has proven to be a death sentence for persons of African descent, as patients in this group respond poorly to treatment (1, 27). Several studies have shown that radiation when combined with platinum-based chemotherapy improves survival of HNSCC patients (1, 20–22). In recent years, it has been shown that cetuximab, a monoclonal antibody which inhibits binding to epidermal growth factor, increases overall survival when combined with radiotherapy alone (24) or when used with the platinum-fluorouracil (23).

In light of the forgoing, the study uncovered two surprising findings. Analysis of the HUH records revealed that between 2004 and 2007, less than 50% of the HNSCC patients received chemotherapy, 22% had no treatment at all and a mere 1% of patients received cetuximab (Fig. 2B). It could be that cost may have been a major factor in deciding the treatment regimen, as the combination of chemotherapy and radiation is more expensive than radiation alone. Both the 1989 American Cancer Society Report (31) and a study conducted by Molina *et al* (27) reported that low socioeconomic status among the poor and African Americans impacts negatively on the survival of cancer patients in these two groups. For both groups, a lack of adequate insurance and a lack of affordability of the most appropriate treatment, whether it be chemotherapy or surgery, lead to poorer survival rates. In addition to the cost factor, it has been reported that poor patients, when diagnosed with cancer, often adopt an attitude of resignation to imminent death, and do not always seek medical attention (27, 31). In this study, the

Kaplan-Meier curves (Figs. 3A and B) indicated that persons diagnosed with stage II had a poorer survival than those diagnosed with stage IV. This is not consistent with normal cancer prognosis where stage IV is expected to have the worst of all outcomes (6, 17). This finding could be attributed to the poor attitude adopted by blacks in the USA when diagnosed with cancer as previously mentioned (27, 31). Indeed, one in five patients in this study received no treatment. The question now arises, how can these trends and attitudes be changed for the better?

Consistent with the findings of many other studies (3, 7–9, 11, 13–15), our study revealed that both tobacco use and regular consumption of alcohol increased the risk of death, however, we were unable to say definitively whether there was a synergistic effect as previously reported (4, 9, 11). Interestingly, our study revealed that there was an inverse relationship between BMI and hazard of death. This finding is in keeping with that of Liu *et al* (30) who evaluated oral cancer, Dray *et al* (33) who evaluated colorectal cancer and others (32).

There may be two possible explanations for the inverse relationship between BMI and hazard of death. In the first instance, HNSCC patients usually experienced difficulty eating and swallowing and therefore nutritional intake decreases dramatically. In such circumstances, those patients with BMIs that are above the accepted norm would have a better prognosis as they could make use of their body's abundant stores of energy. In a similar vein, it has been established that treatment of cancer, whether by surgery, radiation or chemotherapy, involves the destruction of large numbers of normal cells. Following treatment, individuals may recover if regeneration of the destroyed cells occurs. Here again, for HNSCC sufferers where the practicality of maintaining good nutrition is difficult, those with above normal BMIs would be at an advantage as they could use their excess fat stores to meet energy and carbon needs.

In conclusion, our study points to the need for earlier diagnosis, more education and use of a wider range of treatment modalities in order to improve overall outcomes for African Americans and blacks in general suffering with HNSCC. It also suggests that before the commencement of cancer therapy, a period of over-nutrition might be beneficial for HNC patients with normal and below normal BMIs.

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