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SEX DIFFERENCES IN HYPERTENSION MANAGEMENT USING KAPLAN-MEIER & LOG-RANK TEST

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Abstract: This study investigated gender differences in hypertensive management by employing Kaplan–Meier Estimator and Log-Rank Test methodologies. Data were collected from 300 hypertensive patients at Specialist Hospital Sokoto between 2015 and 2021. The Kaplan–Meier survival curves demonstrated that the median times to achieve optimal hypertension control were 43.43 months (3.62 years) for men and 37.76 months (3.15 years) for women. Despite these differences, the log-rank test revealed no significant differences in survival curves between genders ($p = 0.259$). These findings suggest that sex did not significantly influence the time to optimal hypertensive management in this cohort. The findings of this study underscore the need for further research with larger sample sizes to explore potential variations in hypertensive management across different demographics. The recommendations include personalized patient care strategies and continued public health efforts to ensure equitable hypertensive management.

Keywords: hypertensive Management, Kaplan–Meier Estimator, Log-Rank Test, Gender Differences, Survival Analysis

1. Introduction

In numerous medical studies, the primary focus is often the time until death (Clark et al., 2003). However, for hypertension, a key measure is the duration required to achieve optimal control of hypertension. Clearly defining the event and observation period is crucial. Hypertension, also known as arterial hypertension, is a chronic condition characterized by elevated blood pressure in the arteries, which forces the heart to exert more effort to circulate blood. Blood pressure is represented by systolic and diastolic values, which reflect the heart's contraction (systole) and relaxation (diastole) phases, respectively. Normal blood pressure ranges from 100 to 140 mmHg systolic and 60 to 90 mmHg diastolic. A diagnosis of high blood pressure is made when the measurements consistently exceed 140/90 mmHg (World Health Organization, 2013). Traditional statistical methods often overlook time factors, focusing only on outcomes at the end of the study period, as outlined in the study protocol (In and Lee, 2018).

Survival analysis is a statistical approach used to assess the influence of predictors on the time until an event occurs, rather than merely the probability of the event. Originating from medical research, this method evaluates the effects of treatments or medications on duration until death (Sheik et al., 2019). Survival data refer to measurements of time until a specific event, such as death, disease occurrence, or response to therapy. An event marks a transition from one state to another, such as moving from being alive to deceased or from health to disease presence (David, 2011). In analyzing survival data, nonparametric methods neither impose assumptions on the distribution of survival times (a specific shape of the survival function or hazard function) nor assume a specific relationship between covariates and survival time. This class includes the Kaplan–Meier estimator and log-rank test (Patrick and Thomas, 2018). Sendek and Hebo (2017) conducted research using the Cox proportional hazards model, Kaplan–Meier estimation, and frailty models. Their Kaplan–Meier estimation revealed that patients with hypertension attained good control of hypertension after an average of 43.6 months (3.63 years), with a median survival time of 48 months (4 years).

GEese (2017) conducted a study that analyzed the major risk factors for cardiovascular disease complications in hypertensive patients using the Cox proportional hazards model. The results revealed that residence, age, baseline systolic blood pressure, baseline diastolic blood pressure, and baseline complication were the major factors that affected the time to cardiovascular complications in patients with hypertension. The Kaplan–Meier method revealed that the mean time from onset to cardiovascular complications was 18.7 months. The incidence rate was 1.2% per month. From the log-rank test result, Patients who had baseline cardiovascular disease significantly differed from patients who had not complication for a shorter time to complications. They concluded that the total number of patients may not be sufficient because of a lack of sufficient data availability in the hospital where they collected the data, and all variables under the study were taken only from baseline.

Bailey et al., (2008) used Kaplan–Meier methods to examine age and sex differences in hypertensive control rates, incorporating treatment intensity scores. They found that hypertension control rates declined with age and varied by sex, with rates decreasing from 80.8% for those aged 15-39 to 42.1% for those aged 80 and older. Their analysis highlights how both efficacy and discontinuation rates influence hypertension control, offering a more nuanced view than previous studies. Joo et al. (2023) compared sex differences in blood pressure control and clinical outcomes among patients with resistant hypertension. The study, involving 4,926 patients from three Korean hospitals, found that men, despite being younger, had higher cardiovascular risks and end-organ damage, including greater incidences of myocardial infarction and dialysis, compared to women. Women showed better target blood pressure achievement rates but higher incidences of stroke and dementia, suggesting that men may require more intensive cardiovascular prevention.

DesJardin et al. (2024) investigated the "sex paradox" in pulmonary arterial hypertension (PAH) using data from the Pulmonary hypertensive Association Registry. They found that although females with PAH often have less favorable hemodynamic parameters, their survival rates were significantly better compared to males. This paradox was explored through Kaplan–Meier survival analysis and Cox proportional hazard regression. The study also considered potential collider stratification bias and found that adjusting for certain covariates could explain the observed differences in mortality. Waldron et al. (2024) investigated gender and sex disparities in the management and outcomes of patients with severe primary mitral regurgitation using a retrospective cohort study. The study analyzed data from patients diagnosed between 2016 and 2020 and compared the incidence of multidisciplinary evaluation and, 2-year survival rates between men and women. Findings revealed that women were less likely to undergo evaluation and intervention, had a longer delay to intervention, and experienced

higher 2-year mortality rates compared to men. The study concluded that addressing these disparities is essential for improving outcomes and, recommends more equitable intervention practices and tailored cardiovascular prevention strategies.

Lv et al. (2024) investigated sex differences in all-cause and cardiovascular mortality among US adults using NHANES data from 2005 to 2018. The study analyzed 38,924 participants and found that men had higher rates of both types of mortality compared with women, with uric acid levels significantly mediating the association between sex and mortality. The findings suggest that addressing biological and social factors, particularly uric acid levels, can help reduce gender disparities in mortality rates. Despite the wealth of research on hypertension, gaps remain in the understanding of gender-specific management and outcomes. Previous studies have highlighted variations in hypertensive control and cardiovascular risks according to sex but often lack detailed exploration of time-to-event data. This research aimed to fill this gap by evaluating sex differences in hypertensive management using the Kaplan–Meier estimator and log-rank test. These methods were chosen for their ability to handle censored data and provide a detailed comparison of survival distributions, thus providing a clearer picture of how gender impacts the time to optimal blood pressure control and overall management of hypertension.

1. METHODOLOGY

This study was conducted at Specialist Hospital Sokoto in Nigeria from 2015 to 2021. The study included patients with high blood pressure who received hospital treatment. The study followed ethical standards and was approved by the relevant ethics committee, ensuring the protection of patient privacy and rights.

Kaplan–Meier Estimator

The Kaplan–Meier method estimates the unadjusted probability of survival beyond a certain time point (Hosmer, Lemeshow, and May, 2008). Suppose that k patients have events during follow-up at distinct times $t_1 < t_2 < t_3 < t_4 < t_5 < \ldots < t_k$. As events are assumed to occur independently of one another, the probabilities of surviving from one interval to the next may be multiplied together to obtain the cumulative survival probability (Clark *et al.*, 2003). More formally, the probability of being alive at time t_j, $S(t_j)$, is calculated from $S(t_{j\_1})$ the probability of being alive at t_{j_1}, n_j the number of patients alive just before t_j, and d_j the number of events at t_j *as follows:*

$$S(t_j) = S(t_{j-1})\left(1 - \frac{dj}{nj}\right)$$

Eq. (1)

where $t_0 = 0$ and $S(0) = 1$. The value of S(t) is constant between the times of events; therefore, the estimated probability is a step function that changes its value only at the time of each event. This estimator allows each patient to contribute information to the calculations for as long as the patient is known to be event-free. Where every individual experienced an event (i.e. no censoring), this estimator simply reduced to the ratio of the number of events free at time t divided by the number of people who entered the study.

The KM survival curve, a plot of the KM survival probability against time, provides a useful summary of the data that can be used to estimate measures such as median survival time (Clark *et al.*, 2003).

Comparison of the survival of two or more groups

The log-rank test (Peto & Peto 1976) is the most widely used method for comparing two or more survival curves. The groups may be treatment. The method calculates at each event time, for each group, the number of

events one would expect since the previous event if there were no differences between the groups. These values are then summed over all event times to give the total expected number of events in each group (e.g. Ei for group i. The log-rank test compares the observed number of events (for treatment group i, Oi) to the expected number by calculating the test statistic:

$$\chi^2 = \sum_{i}^{g} \frac{(O_i - E_i)^2}{E_i}$$

Eq. (2)

This value is compared to an X^2 distribution with (g_1) degrees of freedom, where g is the number of groups. In this manner, P-values can be calculated to determine the statistical significance of survival curves.

Research Procedure

To begin with, the study analyzed the characteristics of the study patients using basic descriptive statistics. Then, Kaplan–Meier curve was obtained by visualizing the characteristics of the patients during follow-up. Finally, the comparisons of the even experiencing times of two or more groups were performed using the log-rank test.

1. Results

Descriptive and Visualization of the Characteristics of Patients with Hypertension During Follow-up

Table 1: Summary Table of some study variables

S/n	Covariates	Mean	Median	Standard deviation	Minimum	Maximum
1	Time (Months)	21.50	19.08	15.96	1	95
2	Age (years)	52.52	53	12.36	21	87
3	SBP (mmHg)	154.64	150	23.04	130	260
4	DBP (mmHg)	93.73	90	13.16	80	140
5	Weight (kg)	68.	67.90	5.19	55	85.70
6	Height (m)	1.64	1.63	0.44	1.51	1.80
7	BMI	25.10	25	1.61	21.10	30.20
8	No. of antihypertensive drugs	2.85	3	0.90	1	6

Table 1 shows that the mean and median follow-up times of the patients were 21.50 months and 19.10 months, respectively, with a standard deviation of 16 months and minimum and maximum of 1 and 95 months, respectively. The mean and median age of the patients were 52.57 and 53 years, respectively, with a standard deviation of 12.36 years and minimum and maximum values of 21 years and 87 years, respectively. The mean value of Systolic Blood Pressure (SBP) is 155.64mmHg and the median was 150 mmHg, with a standard deviation of 23.04 mmHg and minimum and maximum values of 130 mmHg and 260 mmHg, respectively. The mean value of Diastolic Blood Pressure (DBP) was 93.730 mmHg, and the median was 150 mmHg with a standard deviation of 13.160 mmHg and minimum and maximum values of 80 mmHg and 140 mmHg, respectively. The mean and median weight of the patients were 68 kg and 67.90kg, respectively, with a standard deviation of 5.19 kg and a minimum and maximum of 55 kg and 85.70kg. The mean and median height of the patients were 1.72 m and 1.63m, respectively, with a standard deviation of 0.44 m and minimum and maximum of 1.510 m and 1.80m. The mean and median body mass index (BMI) was 25.40 and 25.30, respectively, with a standard deviation of 1.61 and a minimum and maximum of 21.10 and 30.20. The mean and median number of

antihypertensive drugs administered was 2.86 and 3, respectively, with a standard deviation of 0.90 and minimum and maximum values of 1 and 6.

Table 2. Summary Table of Other Study Variables

S/n	Covariates	Group	Frequency	Percentage	Cumulative percentage
1	Gender	Male	111	37	37
		Female	189	63	100
		Total	300	100	
2	Occupation	Civil servant	36	12	12
		House wife	184	61.30	73.30
		Farmer	12	4	77.30
		Business	65	21.70	99.00
		Mechanic	1	0.30	99.30
		Retired	2	0.70	100
		Total	300	100	
3	Educational status	Not formally educated	213	71	71
		Primary school only	21	7	78
		secondary school only	27	9	87
		Tertiary	39	13	100
		Total	300	100	
4	Place of residence	Urban	220	73.30	73.30
		Rural	80	26.70	100
		Total	300	100	
5	No. of antihypertensive drugs	1	16	5.30	5.30
		2	86	28.70	34
		3	134	44.70	78.70
		4	55	18.30	97
		5	8	2.70	99.70
		6	1	0.30	100
			300	100	

From Table 2, from the total number of 300 participants, all hypertensive patients, 186 (63%) were female and 111 (37%) males, with a ratio of 1.7:1. In terms of occupation, 36 (12%) hypertensive patients were civil servants, 184 (61.30%) were housewives, 12 (4%) were farmers, 65 (21.70%) were involved in business, 1 (0.30%) was a mechanic, and 2 (0.70%) were retired. Regarding educational status, 213 (71%) patients were not formally educated, 21 (7%) had only primary school education, 27 (9%) only secondary school education, and 39 (13%) had tertiary education. There were 220 (73%) patients living in urban areas and 80 (26.70%) in rural areas. In the follow-up period, 16 (5.30%) of the patients received only one (1) antihypertensive drug, 86 (28.70%) received a total number of two (2) antihypertensive drugs, 134 (44.70%) received a number of three

(3) antihypertensive drugs, 55 (18.30%) received four (4) antihypertensive drugs, 8 (2.70%) received five (5), and 1 (0.30%) received six (6) antihypertensive drugs.

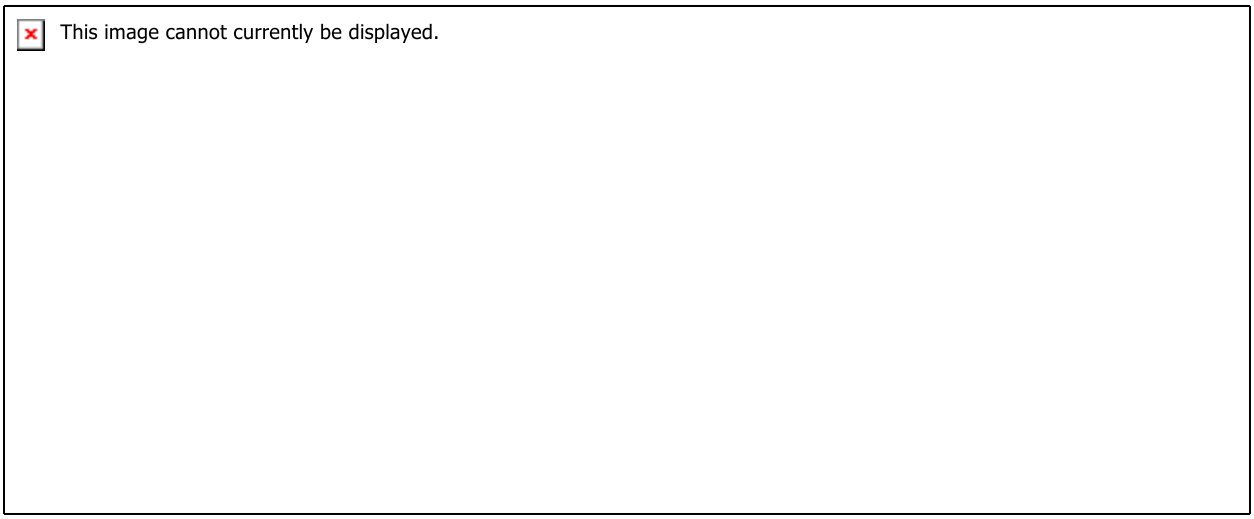

Figure1: Kaplan–Meier (K-M) Curve for Sex

Figure1 reveals that the median survival time for Gender is 43.43 (CI: 30.85-56.01) months (3.62 years) for males and 37.76 (CI: 30.17-45.35) months (3.15 years) for females. This indicates that 50% of the hypertensive patients who were males attained optimal control of hypertension in 43.43 (CI: 30.85-56.01) months (3.62 years), whereas hypertensive patients who were females attained optimal control of hypertension in 37.76 (CI: 30.17-45.35) months (3.15 years). The overall median was 40.43 (CI: 33.67, 47.19) months (3.37 years).

Log-Rank Test

Ho: There was no significant difference in survival curves between males and females at a 5% significance level

Table 3: Log-rank test for gender in hypertensive patients

Sex	**N**	**Observed**	**Expected**	**Chisq. Cont.**
Male	11	42	47.80	0.69
Female	19	9	8.34	0.54

χ^2 = 1.27 on 1 degree of freedom, p = 0.259

From table 4 above, the p-value (0.259) is greater than the typical significance level of 0.05, indicating that the difference in survival curves between males and females is not statistically significant. at 5% level of significance.

Summary

This study evaluated gender differences in hypertensive management using Kaplan–Meier Estimator and Log-Rank Test methodologies. Data from 300 hypertensive patients at Specialist Hospital Sokoto between 2015 and 2021 were analyzed. The Kaplan–Meier survival curves indicated that males achieved optimal hypertension control at a median time of 43.43 months (3.62 years) and females attained it at 37.76 months (3.15 years). The Log-Rank Test showed no significant difference in survival curves between male and female patients (p = 0.259), suggesting that sex did not significantly impact the time to optimal hypertension control.

Conclusion

The analysis using Kaplan–Meier and Log-Rank Test revealed that although males and females showed different median times to optimal hypertension control, these differences were not statistically significant. Both genders achieved similar outcomes in hypertensive management during the study period. The results indicate that sex did not significantly affect the time to achieve optimal hypertension control in the studied population.

Recommendations

1. Further Research: Conduct longitudinal studies with larger sample sizes to explore potential differences in hypertensive management across different populations and settings.
2. Tailored Interventions: Although sex differences were not statistically significant in this study, health care providers should consider individual patient factors and treatment responses when managing hypertension.
3. Public Health Strategies: We will continue to promote awareness and early intervention strategies for hypertension management, ensuring that all patients, regardless of gender, have access to appropriate care and resources.

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