

Sociodemographic and Survival Profile of Human Immunodeficiency Virus-Infected Patients Attending a Tertiary Health Facility in India

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Abstract

Our objectives of the study is to assess the sociodemographic profile and survival profile of HIV patients. A retrospective cohort study was conducted among patients enrolled at a single antiretroviral therapy center at North Karnataka. A total of 11099 were recruited during April 2007 to January 2020. The outcome of interest was the time to death in months of HIV patients on ART. R Studio Version 1.3.1093 was used for statistical analysis. Out of 7423 HIV-positive people majority were female (51.4%), heterosexual typology (89.2%), and in the age group 31 to 45 years (45.5%). In the multivariable analysis that hazards of mortality increased by 3.11 times and 2.11 times in patients with baseline CD4 count \leq 50 and baseline CD4 count 51 to 200 respectively as compared to those who had baseline CD4 count $>$ 200. The mortality rate was high in the initial three months after the start of ART and overall survival probabilities among HIV-infected patients declined over follow-up time. This study proved that age, sex, baseline CD4 count, and TB status act as risk factors for mortality among HIV-positive individuals. Prevention strategies, control measures, and program planning should be done based on the sociodemographic determinants of mortality.

Introduction

As per 2020, UNAIDS factsheet,¹ 38 million people are living with HIV globally. In the year 2019, a total of 1.7 million newly infected cases of HIV has occurred, and 690,000 people have died of AIDS related illness globally. Globally, 2.6 million people have access to ART regimens, and 67% of the diagnosed HIV population were accessing ART. India is home to the highest number of people living with HIV (PLHV). Reported HIV prevalence among adult males was 0.24%, and adult females were 0.20% as per National AIDS Control Organisation (NACO) report. In 2019, there were 69.22 thousand new infections, 23.48 lakh people are living with HIV, and an estimated 58.96 AIDS related deaths.² The primary mode of transmission of HIV among adults is insecure heterosexual intercourse. Another significant mode is mother-to-child transmission that can occur during pregnancy in utero, intrapartum during labor and delivery.^{3,4} Combined antiretroviral therapy is one of the successful public health interventions in recent times, with increased survival, individual and societal improvement. The success has been possible because of the simplicity of use, its potency, and low side effect profile.⁵ HIV infection being a long-term chronic disease causes morbidity and mortality. Long-term comorbidities and adverse effects can occur due to the disease or the treatment per se. In this context, accurate data on the causes of death are of great importance and should help to define priorities in the prevention and management of lethal comorbidities. Such evidence has come from previous prospective studies on HIV patients.⁶⁻⁸ These kinds of studies are not available for the Indian subpopulation, and there is a gap in the understanding of factors affecting the long-term mortality among HIV-positive patients in India. Although efforts have been made in reducing mortality and extending the life expectancy in people living with HIV, there is considerable morbidity and mortality caused by the disease.

On 1st April 2004, the government of India launched free ART program for the benefit of all HIV-infected patients. Since then, enrolment and access to ART have improved. HIV/AIDS not only remains a serious public health issue but also has a grave impact on the socioeconomic and development of the nation. This is attributed to the disease occurrence in the young adult working population, which is the economically productive age group (15-44 yrs).² In the year 2015, the World Health Organization (WHO) reported that 11% of the 10.4 million new cases of TB infection globally occurred in HIV-positive individuals.⁹ TB was the leading cause of mortality among people with HIV, and nearly 300,000 people died from HIV-associated TB in the year 2017.¹⁰ Both TB and HIV significantly affect the human's immune system by their ability to evade immune surveillance and clearance, although the mechanism is not fully understood.¹¹ As compared with the general population, the risk of latent TB activation increases 20-fold in HIV-positive patients.¹²

There are few studies on mortality at an early stage among HIV patients soon after initiation of ART which is unlikely to be caused due to drug efficacy.¹³⁻¹⁵ This indicates there are several other factors that can indirectly contribute to mortality among PLHIV, which are often poorly understood.¹⁶ Identification and rectification of these modifiable factors during routine clinical care might help in prolonging survival, thereby preventing more deaths among PLHIV. The literature available on factors influencing the mortality of HIV patients in India is very few. The evidence from that available literature is considerably inadequate due to the less sample size, hence, not covering the diversity of the population of PLHIV. This study was planned to fill in these lacunae by studying a wide population of PLHIV and to study the various factors that have an influence on the long-term mortality of PLHIV.

Methods

Study design and population:

A retrospective descriptive cohort study was conducted in a single antiretroviral therapy centre (ART). The study population was the HIV-infected patients receiving ART from the study setting. The study was conducted April 2007 to January 2020. After ethical approval for the study and waiver of written informed consent from the institutional human ethical committee, Koppal Institute of medical sciences, data was retrieved from the ART centre's database. Waiver of consent was approved by the ethics committee. The ethical review committee of Koppal Institute of Medical Sciences had approved the study experiment (data collection) which was in accordance with institutional ethical guidelines in the purview of declaration of Helsinki. The data retrieved were regarding the sociodemographic profile, HIV diagnosis, treatment status, lab parameters, and survival status.

Procedures:

The data of all the enrolled patients during April 2007 to January 2020 were retrieved from the database. A total of 11099 were included in the study. The inclusion criteria was those patients registered at the study ART centre during the study period. A total of 3676 were excluded from the study due to non-availability of complete data, mismatch between the date of registration and date of death. Data anonymity and confidentiality were maintained throughout the study.

Statistical Analysis

The outcome of interest was the time to death in months of HIV patients on ART. The demographic and clinical variables were analyzed as risk factors for survival analysis. Descriptive statistics were used to present demographic and clinical characteristics of HIV patients on ART. Both univariate and multivariable Cox regression was used to explore the determinants of mortality of patients on ART. Hazard ratio (HR) along with 95% CI and p-values are presented. Kaplan Maier survival curve was used to visualize intergroup differences of the risk factors of the survival analysis, and its significance was tested by log-rank test. Survival probabilities were also calculated according to risk factors at different points in time. P value <0.05 was considered statistically significant. RStudio Version 1.3.1093 was used for statistical analysis. R Studio Version 1.3.1093 was used for statistical analysis.¹⁷

Results

There were 11099 HIV patients registered initially to receive pre ART care. Due to non-compliance of patients and due to invalid follow-up information, 3676 patients were excluded from the analysis.

A total of 7423 HIV patients were included in the study. Table 1 displays demographic and clinical characteristics of HIV patients on ART. The majority of the patients were female (51.4%), heterosexual typology (89.2%), and in the age group 31 to 45 years (45.5%). The baseline CD4 counts and latest CD4 counts of most of the patients were greater than 200. Only 1538 (20.7%) patients were diagnosed with TB. Among 1538 TB patients, the majority (41.2%) had pulmonary TB (MC), 40.2% had extrapulmonary TB (CD), 18.6% had pulmonary TB (CD), and there was only one case of extrapulmonary TB (MC). The majority of the patients spent 2 to 5 years for ART until death/censoring (34.0%).

Table 1
Demographic and clinical characteristics of HIV patients on ART (N = 7423)

Characteristics	Number of patients (%)
Sex	
Female	3813 (51.4%)
Male	3577 (48.2%)
TS/TG	33 (0.4%)
Age Group	
<= 30 years	2925 (39.4%)
31–45 years	3378 (45.5%)
> 45 years	1120 (15.1%)
Baseline CD4Count	
<= 50	421 (5.7%)
51–200	2775 (37.4%)
> 200	4227 (56.9%)
Latest CD4Count	
<= 50	348 (4.7%)
51–200	1937 (26.1%)
> 200	5138 (69.2%)
Typology	
Blood Transfusion	4 (0.1%)
FSW	37 (0.5%)
Heterosexual	6621 (89.2%)
IDU	1 (0.0%)
Mother to Child	711 (9.6%)
MSM	34 (0.5%)
Probable Unsafe Injection	13 (0.2%)
Trucker	2 (0.0%)
TB Diagnosis	
No	5885 (79.3%)
Yes	1538 (20.7%)
Time from Start of ART to death/censoring	
0–3 months	862 (11.6%)
4–6 months	549 (7.4%)
7 months – 1 year	812 (10.9%)
1–2 years	1175 (15.8%)
2–5 years	2527 (34.0%)
> 5 years	1498 (20.2%)

Out of the 7423 patients included to receive the ART care, 2414 (32.5%) died, and 5009 (67.5%) were censored. The death rate was high among transgender (39.4%) and males (39.0%) as compared to females (26.4%). In patients with an age of more than 45, the death rate was high as compared to other age groups. Baseline and latest CD4 count was less among patients who died. It was observed that the death rate was high in FSWs, MSMs, and heterosexuals with 40.5%, 38.2%, and 34.3%, respectively. Death was high among patients with TB (43.2%) as compared to

patients without TB (29.7%). The mortality rate was high in the initial three months after the start of ART (73.3%), and it decreased over the follow-up period. The median age of HIV patients at the start of ART was 35 years with an interquartile range of 27–42 years. The overall median follow-up time for the patients who died was 11 months (IQR 3–30 months), while it was 36 months for the censored patients (IQR 18–61 months). (Table 2)

Table 2
Comparison of demographic and clinical characteristics according to deaths and censored patients

Characteristics	Number of deaths (%)	Number of censored patients (%)
Sex		
Female	1005 (26.4%)	2808 (73.6%)
Male	1396 (39.0%)	2181 (61.0%)
TS/TG	13 (39.4%)	20 (60.6%)
Age Group		
<= 30	704 (24.1%)	2221 (75.9%)
31–45	1231 (36.4%)	2147 (63.6%)
> 45	479 (42.8%)	641 (57.2%)
Baseline CD4Count		
<= 50	242 (57.5%)	179 (42.5%)
51–200	1246 (44.9%)	1529 (55.1%)
> 200	926 (21.9%)	3301 (78.1%)
Latest CD4Count		
<= 50	217 (62.4%)	131 (37.6%)
51–200	1015 (52.4%)	922 (47.6%)
> 200	1182 (23.0%)	3956 (77.0%)
Typology		
Blood Transfusion	1 (25.0%)	3 (75.0%)
FSW	15 (40.5%)	22 (59.5%)
Heterosexual	2268 (34.3%)	4353 (65.7%)
IDU	0 (0.0%)	1 (100.0%)
Mother to Child	117 (16.5%)	594 (83.5%)
MSM	13 (38.2%)	21 (61.8%)
Probable Unsafe Injection	0 (0.0%)	13 (100.0%)
Trucker	0 (0.0%)	2 (100.0%)
TB Diagnosis		
No	1750 (29.7%)	4135 (70.3%)
Yes	664 (43.2%)	874 (56.8%)
Time from Start of ART to death/censoring		
0–3 months	632 (73.3%)	230 (26.7%)
4–6 months	348 (63.4%)	201 (36.6%)
7 months – 1 year	335 (41.3%)	477 (58.7%)
1–2 years	378 (32.2%)	797 (67.8%)
2–5 years	489 (19.4%)	2038 (80.6%)
> 5 years	232 (15.5%)	1266 (84.5%)
Total	2414 (32.5%)	5009 (67.5%)

Table 3 shows the hazard ratios from the univariate and multivariable analysis of the association between the possible determinants of mortality and risk of death. The latest CD4 count was not included in the analysis since the baseline CD4 count and latest CD4 count was correlated. Typology was not included in the analysis because many categories had less frequencies and zero/less deaths. Sex, age group, baseline CD4 count, and TB diagnosis showed a statistically significant relationship with the mortality in HIV-infected patients in both univariate and multivariable analysis. It was observed in the multivariable analysis that hazards of mortality increased by 3.11 times (95% CI: 1.19–1.44) and 2.11 times (95% CI: 1.94–2.30) in patients with baseline CD4 count \leq 50 and baseline CD4 count 51 to 200 respectively as compared to those who had baseline CD4 count $>$ 200. The risk of death in males was 1.41 times (95% CI: 1.30–1.54) higher as compared to females. Patients in the age group $>$ 45 years and age group 31 to 45 years were 1.69 times (95% CI: 1.50–1.91) and 1.31 times (95% CI: 1.19–1.44) respectively more likely to die as compared to patients in the age group \leq 30. Tuberculosis was found to be one of the risk factors for mortality in HIV-infected patients. The risk of death in patients who were diagnosed with TB was 1.23 times (95% CI: 1.12–1.35) than those who were not diagnosed with TB.

Table 3
Cox Regression Model to explore determinants of mortality [Hazard Ratio (HR)] of patients on ART

Determinants	Univariate Analysis		Multivariable Analysis	
	HR (95% C.I)	P-Value	HR (95% C.I)	P-Value
Sex				
Female (Reference)	1		1	
Male	1.64 (1.52–1.78)	$<$ 0.001	1.41 (1.30–1.54)	$<$ 0.001
TS/TG	1.76 (1.02–3.04)	0.044	1.72 (1.00–2.98)	0.051
Age Groups (in years)				
\leq 30 years (Reference)	1		1	
31–45 years	1.61 (1.47–1.77)	$<$ 0.001	1.31 (1.19–1.44)	$<$ 0.001
$>$ 45 years	2.13 (1.90–2.40)	$<$ 0.001	1.69 (1.50–1.91)	$<$ 0.001
Baseline CD4 Count				
$>$ 200 (Reference)	1		1	
\leq 50	3.48 (3.02–4.00)	$<$ 0.001	3.11 (2.70–3.59)	$<$ 0.001
51–200	2.31 (2.12–2.52)	$<$ 0.001	2.11 (1.94–2.30)	$<$ 0.001
TB Diagnosis				
No (Reference)	1		1	
Yes	1.39 (1.27–1.52)	$<$ 0.001	1.23 (1.12–1.35)	$<$ 0.001

The median survival time was higher in female patients in the age group \leq 30 years, patients with baseline CD4 count $>$ 200, and patients who were not diagnosed with TB. The median survival of female, male and transgender patients was approximately 99 months, 71 months, and 66 months respectively. The log-rank test for difference in survival gives a p-value $<$ 0.0001, indicating that the sex groups differed significantly in survival. The median survival time of patients in the age group \leq 30 years, 31 to 45 years, and $>$ 45 years was approximately 100 months, 82 months, and 59 months respectively. The log-rank test for difference in survival gives a p-value $<$ 0.0001, indicating that the age groups differed significantly in survival. The median survival of patients with baseline CD4 count \leq 50, 51 to 200, and $>$ 200 was approximately 26 months, 60 months, 101 months, respectively. The log-rank test for difference in survival gives a p-value $<$ 0.0001, indicating that there was a significant difference of survival pattern observed in patients with different baseline CD4 count. The median survival of patients who were diagnosed with TB and who were not diagnosed with TB was 69 months and 98 months, respectively. The log-rank test for difference in survival gives a p-value $<$ 0.0001, indicating that there was a significant difference of survival pattern observed in patients who were diagnosed with TB and those who were not diagnosed with TB. (Fig. 1)

The overall survival probabilities among HIV-infected patients declined over follow-up time. The survival probabilities of male patients at three months, six months, one year, two years, and at five years was 89%, 84%, 78%, 70%, and 54%, respectively. The survival probability of female patients at three months, six months, one year, two years, and five years was 93%, 89%, 85%, 80%, and 70%, respectively. The survival probability of male patients at three months, six months, one year, two years, and at five years was 87%, 81%, 77%, 65%, and 43%, respectively.

The survival probabilities of patients in the age group \leq 30 years at three months, six months, one year, two years, and at five years was 94%, 91%, 87%, 83%, and 72%, respectively. The survival probabilities of patients in the age group 31 to 45 years at three months, six months, one year, two

years, and at five years was 90%, 85%, 79%, 72%, and 59%, respectively. The survival probabilities of patients in the age group > 45 years at three months, six months, one year, two years, and at five years were 87%, 79%, 74%, 65%, and 49%, respectively.

The survival probabilities of patients with baseline CD4 count ≤ 50 at three months, six months, one year, two years, and at five years was 77%, 68%, 61%, 52%, and 38%, respectively. The survival probabilities of patients with baseline CD4 count 51 to 200 at three months, six months, one year, two years, and at five years was 86%, 80%, 72%, 65%, and 50%, respectively. The survival probabilities of patients with baseline CD4 count > 200 at three months, six months, one year, two years, and at five years was 96%, 93%, 90%, 85%, and 74%, respectively. The survival probabilities of patients who were not diagnosed with TB at three months, six months, one year, two years, and at five years were 92%, 87%, 82%, 77%, and 65%, respectively. The survival probabilities of patients who were diagnosed with TB at three months, six months, one year, two years, and at five years were 91%, 85%, 79%, 70%, and 54%, respectively. (Table 4)

Table 4
Survival probabilities according to risk factors at a different point in time

Characteristics		Time in months				
		3	6	12	24	60
Sex	Male	89%	84%	78%	70%	54%
	Female	93%	89%	85%	80%	70%
	TS/TG	87%	81%	77%	65%	43%
Age group	≤30 years	94%	91%	87%	83%	72%
	31 to 45 years	90%	85%	79%	72%	59%
	> 45 years	87%	79%	74%	65%	49%
Baseline CD4	≤50	77%	68%	61%	52%	38%
	51 to 200	86%	80%	72%	65%	50%
	>200	96%	93%	90%	85%	74%
TB diagnosis	No	92%	87%	82%	77%	65%
	Yes	91%	85%	79%	70%	54%

Discussion

This retrospective descriptive cohort study was conducted considering the data of patients during April 2007 to January 2020. The aim of this study was to assess the sociodemographic profile and survival profile of HIV patients attending a single antiretroviral therapy center and to find the sociodemographic determinants that influence the survival of HIV-positive patients on ART. The study's findings showed that the most commonly affected age group was 31 to 45 years, and females were most commonly affected. The heterosexual route was the commonest mode of transmission among study participants. Sex, age group, baseline CD4 count, and TB diagnosis have a significant relationship to the mortality of HIV-positive patients. Among the study population, 51.4% were females. The most commonly affected age group was 31 to 45 years. These findings were similar to the study by Sunita Kumawat et al.,¹⁸ where the most commonly affected age group was 15 to 49 years, and in contrast to the current study, males were most commonly affected. This difference may be due to the low sample size of 300 in their study. Hence, reducing the representativeness of the HIV-positive population. Stigma and discrimination, poor health-seeking behavior all remain as main obstacles in the prevention, care, and treatment of HIV and AIDS.¹⁹ Transmission through heterosexual contact was most common (89.2%) among the study participants, followed by mother-to-child transmission. Similar findings were observed in previous studies by Sunita Kumawat et al.¹⁸ (87.67%), Umesh S. Joge et al. (94.39%),²⁰ Jha AK et al. (72.2%).²¹ Among the study participants, 20.7% had tuberculosis also. A previous study has shown 10.66% of the 300 participants had tuberculosis.¹⁸ Co-existing TB infection causes an increase in HIV replication.²² The cytokines induced by immune responses caused by TB infection enhance the replication of HIV and quicken AIDS progression.²³ Due to this mechanism, superadded TB infection is one of the most common reasons for mortality in HIV-infected patients, accounting for 26% of AIDS related deaths,²⁴ the majority (99%) of which occurred in developing countries.¹¹ TB/HIV co-infection is the reason for high mortality, low survival, and it is therefore handled together in a comprehensive manner by articulated control programs.²⁵ Development of co-infections control strategies, by early diagnosis of both diseases and adequate, timely treatment has been done.²⁶ According to a 2015 report, the risk of a person with HIV/AIDS developing active TB is 26 times higher compared to the general population.²⁷ Sex, age group, baseline CD4 count, and TB diagnosis showed a statistically significant relationship with mortality in HIV-infected patients. It was observed in the multivariable analysis that hazards of mortality increased by 3.11 times (95% CI: 1.19–1.44) and 2.11 times (95% CI: 1.94–2.30) in patients with baseline CD4 count ≤ 50 and baseline CD4 count 51 to 200 respectively as compared to those who had baseline CD4 count > 200. Suppression of viral load plays an important role in delaying the progression of the disease and mortality. In order to achieve viral suppression, routine HIV viral load (VL) monitoring is recommended by The World Health Organization (WHO).²⁸ This is due to the

fact that a decrease in CD4 count, which is a marker of immunological failure, occurs as a result of viral replication, which can thus be considered as an endpoint.²⁹ In this current study, the median survival time was higher in females, patients in the age group ≤ 30 years, patients with baseline CD4 count > 200 , and patients who were not diagnosed with TB. The overall survival probabilities among HIV-infected patients declined over follow-up time. A similar survival analysis of HIV-positive patients during the year 1996 to 2013 was done by ART cohort collaboration. The study findings compared the ART regimens and survival. The study concluded that in the late ART era, the survival during the first three years of ART initiation improved, which can be attributed to the transition to less toxic antiretroviral drugs in the early 2000s.³⁰ The strength of this current study being it was done on a relatively large sample; long-term survival analysis was done. The limitation being it a single-center experience; diversity in the population remains a query. Prospective, multicentric studies involving a large population are recommended in the future.

Conclusion

Baseline CD 4 count below 50 and 51 to 200 has high hazards of mortality compared to CD4 count more than 200. Hence, baseline CD4 count has a role in the long-term survival of the patients. Tuberculosis was found to be one of the risk factors for mortality in HIV-infected patients. The median survival time was higher in female patients in the age group ≤ 30 years, patients with baseline CD4 count > 200 , and patients who were not diagnosed with TB. This study has created evidence on the role of age, sex, baseline CD4 count, and TB status as risk factors for the deaths among HIV-positive individuals. Prevention strategies, control measures, and program planning should be done based on the sociodemographic determinants of mortality. Continued efforts are required to address the delay in diagnosis, poor adherence to treatment and monitoring in order to decrease the mortality caused due to the disease. These minor targeted measures can result in prolonged survival of the patients.

Declarations

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Conflict of interests: The authors declare no conflicts of interest.

Data availability statement: The datasets used and/or analysed during the current study available from the corresponding author and is also uploaded as Supplementary File.

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Contributors: Author R.A.S has conceptualized the study and played primary role in compiling, analysis and interpretation of the data. All the drafts were prepared, reviewed and final draft was approved by M S A, SKH, M.M.V, MM. R.A.K has contributed by data cleaning and data analysis. B.A.A, R.A.S have contributed in fine tuning of the proposal, contributed in data collection and entry. R.A.S, M S A, reviewed the results and contributed to preparation and review of drafts. All the authors have read and approved final version of the manuscript. All the authors take complete responsibility for the content of the manuscript.

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Figures

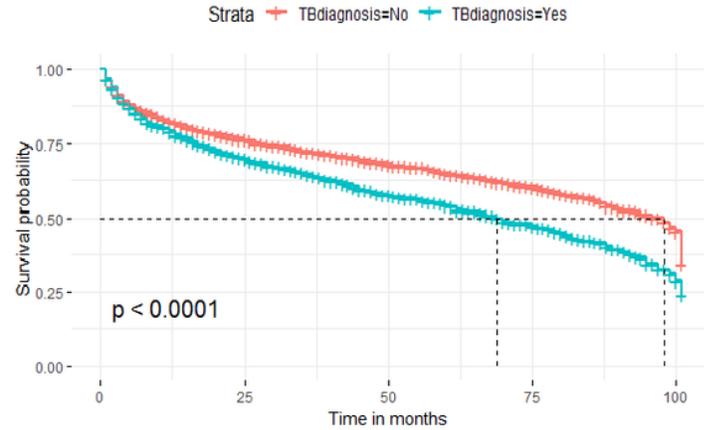
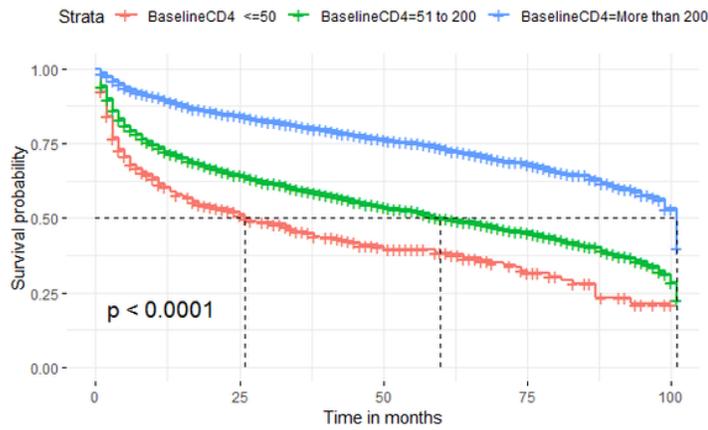
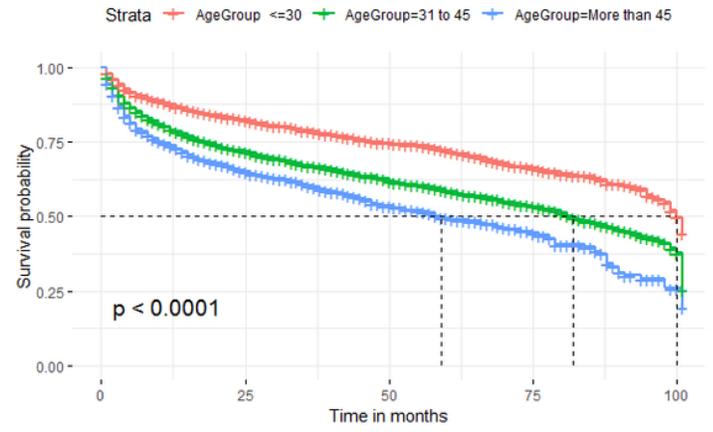
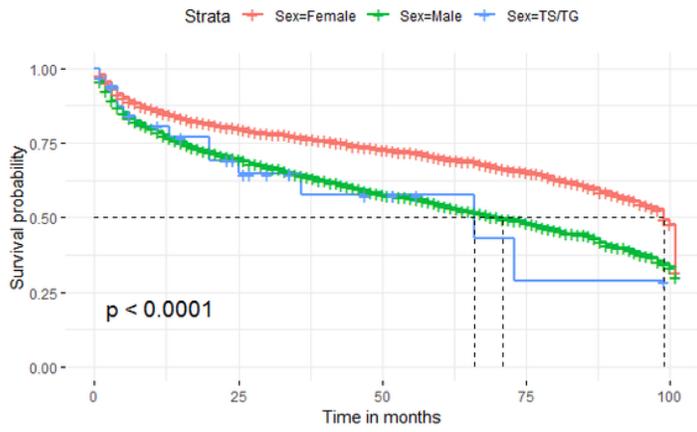


Figure 1

Kaplan-Maier survival curves showing intergroup differences of the risk factors

Supplementary Files

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