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ORIGINAL RESEARCH

Risk of Mortality Associated with Rapid versus Delayed ART Initiation and Associated Factors Among Late-Presenting People with HIV: An 8-Year Retrospective Analysis in China

Lianfeng Lu[1,*], Jiale Xi[1,*], Xiang Zhang[1], Hongjing Guan[2], Jingli Peng[1], Rentian Cai[1], Hongxia Wei[1]

[1]Department of Infectious Diseases, The Second Hospital of Nanjing, Affiliated to Nanjing University of Chinese Medicine, Nanjing, 210003, People's Republic of China; [2]Department of Infectious Diseases, The School of Public Health of Nanjing Medical University, The Second Hospital of Nanjing, Nanjing, 210003, People's Republic of China

*These authors contributed equally to this work

Correspondence: Hongxia Wei, Department of Infectious Diseases, The Second Hospital of Nanjing, Affiliated to Nanjing University of Chinese Medicine, Nanjing, 210003, People's Republic of China, Email wghongxia@sina.com

Objective: To explore the association between the timing of antiretroviral therapy (ART) initiation and all-causes mortality, as well as related risk factors, for late presenters living with HIV (PWH).

Methods: Treatment-naive PWH with CD4+T cell count<350 cells/μL, also called late presenters, who initiated ART at the Nanjing Second Hospital from January 2017 to June 2022 were enrolled in this study and followed for at least 3 year and a maximum of 8 years. Based on the time from diagnosis to ART initiation, subjects were divided into a rapid ART group (ART initiation≤14 days after HIV diagnosis, median 12 days) and a delayed ART group (ART initiation>14 days after HIV diagnosis, median 35 days), with a significant difference in initiation time (p<0.001). The difference in mortality, cause of death and immunological profiles between the two groups were compared, and a Cox proportional hazards model was constructed to analyze death-related risk factors.

Results: A total of 1538 PWH were included in the study, and 68 patients died, with the total case mortality rate of 4.42%. There were 459 (29.8%) patients in the rapid ART initiation group, and the mortality rate was 3.92% (18/459), there was no significant difference in case mortality compared to the delayed initiation group (4.63%, 50/1079). The most common cause of death among these patients was non-AIDS-related cancer. Besides, risk factors for death were being single, divorced or widowed, and having a baseline CD4+T cell count <200 cells/μL.

Conclusion: The all-cause mortality rate of PWH with CD4+T cell counts <350 cells/μL was 4.42%, and the cause of death in China have shifted over time. Rapid initiation of ART was not significantly associated with reduced mortality in this cohort; however, low CD4+T cell counts at baseline and social factors showed a more significant association with mortality.

Keywords: HIV/AIDS, antiretroviral therapy, CD4+T cell count, mortality

Background

With the application of antiretroviral therapy (ART), the global incidence rate and mortality rate of HIV have significantly decreased,[1] and the life expectancy of people living with HIV (PWH) has increased.[1,2] ART has been recommended by the World Health Organization (WHO) since 2015 for PWH regardless of their CD4 T cell levels. In 2017, scientists introduced the idea of "rapid initiation of ART". This approach suggests starting ART immediately after diagnosis, regardless of the CD4 count, instead of waiting for days or weeks.[3] While early ART generally refers to starting treatment soon after HIV diagnosis, rapid ART specifically denotes initiation within a very short timeframe, typically within 7 to 14 days, or even same-day.[4].

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The advancement of this concept has resulted in shortening the time to achieve virological suppression, reducing risk of transmission, controlling and minimizing follow-uploss, and decreasing the morbidity and mortality rates of HIV/acquired immune deficiency syndrome (AIDS).[5–7] Research has shown that rapid initiation of ART maintains higher treatment rates and virological suppression rates at 10–12 months compared to delayed initiation therapy.[6–8] Research data from China also shows that the mortality rate of patients who immediately receive ART (within 30 days after diagnosis)decreased by 63%.[9,] The mortality decreased from 27% to 10% with the early initiation of ART and follow-up lasting 6–18months.[10].

Although early ART initiation is widely supported, the implementation of rapid ART initiation in resource-limited areas is impacted by pretreatment testing coverage and availability. It has been demonstrated by studies that the percentage of newly diagnosed patients receiving ART is less than 75% within 30 days,[11,] and within 7 days it is only 18.7%.[12,] Moreover, 55–70% of newly diagnosed PWH have CD4+T cells<350 cells/μL, and 29–45% have CD4+T cells<200 cells/μL.[13,14,] For late presenters living with HIV,[15,] the risk of opportunistic infections, tumors, and even death is much higher than that of patients with CD4+T cells>500 cells/μL.[16,]

All PWH should receive rapid ART initiation as recommended by the WHO, which refers to the prompt commencement of ART within 7 days, or as soon as feasible.[17,] The implementation of rapid antiretroviral therapy (rapid ART) for individuals who have recently been diagnosed with HIV is influenced by their specific conditions and available resources.[18,] A study in Africa showed that rapid initiation within 7 days resulted in a 6-month survival rate of 87.4%.[19,] Besides, the AIDS progression and fatality rate of PWH who begin ART within 14 days are lower than those who start ART after anti-opportunistic infection treatment.[20,] Studies in different countries and regions have adopted different standards, including starting treatment 5 days, 7 days, or 14 days after the diagnosis.[20,21,] A recent meta-analysis showed that in comparison to standard/delayed treatment, rapid ART can reduce the incidence of tuberculosis and severe bacterial infections in HIV patients, but reduce less in mortality or the incidence of adverse events.[22] Overall, there is competitive conclusions into the rapid initiation of ART in PWH with CD4+T<350 cells/μL, as well as significant study populations and mortality data in the low-income countries.

Therefore, we collected and analyzed clinical data of treatment-naïve PWH who were diagnosed with and initiated ART at Nanjing Second Hospital from 2017 to 2022 and followed up until 2025. This study aims to provide real-world comparative data on rapid initiation in PWH with CD4+T<350 cells/μL, especially data on mortality and cause of death.

Methods

Study Design

This was a retrospective, observational study involving the patients who initiated ART at Nanjing Second Hospital between January 1, 2017, and June 30, 2022, and followed by next 3 years until October 2025. The inclusion criteria were as follows: adult HIV-1–infected patients who initial CD4+T cell count<350 cells/μL; initiation of ART at the Nanjing Second Hospital ; patients with baseline records and at least 1 complete antiretroviral follow-up data. Exclusion criteria: patients with combined tuberculous meningitis, cryptococcal meningitis, or Kaposi's sarcoma who should initiate ART after control of opportunistic infection; patients withdraw during follow-up period.

The study subjects were divided into two groups based on the time from HIV diagnosis to initiation of ART. The group that initiated ART ≤ 14 days after diagnosis was referred to as the rapid treatment initiation group (rapid ART, RIG). The group that started ART 14 days after diagnosis was referred to as the delayed treatment initiation group (delayed ART, DIG).

Data Collection

Baseline demographic and clinical characteristics, including age, sex, marital status, route of infection, CD4+T cell count, HIV-RNA viral load (VL) and education were extracted from electronic medical records and laboratory databases. Data was collected from the medical records of the enrolled patients during the treatment and follow-up period, including the database of the National AIDS Basic Prevention and Control Information System, the electronic medical record system

of Nanjing Second Hospital, the laboratory information system and the outpatient follow-up files. This study was approved by the Medical Ethics Committee of Nanjing Second Hospital (No. 2024-LS-ky043).

Outcomes of Interest

The primary endpoint is the all-cause mortality rate. But we also pay attention to their immunological recovery. Follow-up time was defined as the duration from the date of ART initiation to the date of death, loss to follow-up, or the end of the observation period. Patients who did not experience the event of interest (death) by the end of the study or who were lost to follow-up were censored. These data were extracted from electronic medical records and laboratory databases as described above. According to the cause of death filled in the follow-up record, the cause of death belongs to AIDS opportunistic infection, AIDS related tumors, AIDS related symptoms and signs, and is classified as "AIDS related death"The cause of death belongs to cardiovascular and cerebrovascular diseases, malignant tumors other than AIDS related tumors, respiratory system diseases (excluding opportunistic infections), endocrine, nutritional and metabolic diseases, digestive system diseases and other non-AIDSrelated diseases, which are classified as "AIDS unrelated death"If the cause of death is not filled in or cannot be classified into the above two categories, it is classified as "undetermined".

Statistical Analysis

Statistical analysis was performed via SPSS software (version 25.0; IBM Corp, Chicago, IL, USA). Categorical data are expressed as frequencies (percentages) and compared via the χ 2 test and Fisher's exact test. Normally distributed data are expressed as the mean ± standard deviation and were compared via independent samples t-tests. Skewed distribution data are expressed as medians (P25, P75) and compared via non-parametric tests. A *P*-value <0.05 was considered to indicate statistical significance. To analyze the differences in causes of death between the Rapid ART and Delayed ART, and cox regression was applied to analyze the influencing factors of death and evaluated the hazard ratio (HR) of the study variables ART status, demographic variables, and HIV related clinical variables. Candidate variables included age, sex, education level, marital status, time from HIV diagnosis to ART initiation, baseline CD4+T cell count, and baseline viral load . Variables with a P-value <0.1 in univariate analysis were considered for inclusion in the multivariable model. All selected variables were entered simultaneously using the Enter method. Results are presented as HR with 95% confidence intervals (CI). A two-tailed P <0.05 was considered statistically significant. The Kaplan-Meier survival curve compared the survival status of patients in the rapid ART group and delayed ART group.

Result

Baseline Characteristics of Research Subjects

In Nanjing Second Hospital, there were 2999 PWH who initiated ART from January 1, 2017, to June 30, 2022, with 1717 of them being CD4+T cell count≤350 cells/μL, accounting for 57.29%. This study excluded a total of 179 individuals, including 58 with unknown baseline VL, 16 with cryptococcal meningitis or tuberculous meningitis or Kaposi's sarcoma, and 105 pre-treated PWH. Finally, 1538 people were included, divided into 459 people (rapid ART group) and 1079 people (delayed ART group) (see Supplementary Figure S1 for details).

The median age of the population included in this study was 38 years old (IQR, 30–54 years old), and most of them were male (92.3%). The majority of 989 cases (64.3%) were individuals who were single, divorced, or widowed, with men who have sex with men being the main route of transmission (65.3%). 53.7% of PWH had baseline CD4+T cell levels below 200/μL, while baseline viral load was mostly between 50–100000 copies/mL (64.2%). The median time from HIV diagnosis to ART initiation for the entire cohort was 26 days (IQR 13–54). As per the grouping criteria, the rapid ART group initiated treatment at a median of 12 days (IQR 7–12), significantly earlier than the delayed ART group [median 35 days (IQR 22–107); p<0.001]. When comparing the baseline clinical characteristics of rapid ART group and delayed ART group, we found that both groups were predominantly male, and there was no significant difference in the gender ratio between the two groups (91.5% vs. 92.6%, p=0.467). Additionally, there were no significant differences in education level, baseline CD4+T cells, baseline CD4/CD8 ratio, and baseline VL between the two groups (shown in Table 1). However, the

Table 1 Clinical and Immunological Characteristics of Enrolled Subjects

Characteristics	Total (n=1538)	RIG (n=459)	DIG (n=1079)	*p*-value
Age, years				
Median (IQR)	38 (30–54)	38 (30–55)	38 (30–53)	0.958
Gender				
Male, No.(%)	1419 (92.3)	420 (91.5)	999 (92.6)	0.467
Education				0.338
Primary, No.(%)	88 (5.7)	30 (6.5)	58 (5.4)	
Junior middle, No.(%)	189 (12.3)	51 (11.1)	138 (12.8)	
Senior or higher, No.(%)	959 (62.4)	278 (60.7)	681 (63.1)	
Unknown, No.(%)	302 (19.6)	100 (21.8)	202 (18.7)	
Marriage				
Single, divorced or widowed	989 (64.3)	284 (61.9)	705 (65.3)	0.194
Married or cohabitating	549 (35.7)	175 (38.1)	374 (34.7)	
Transmission route	1004 (65.3)	292 (63.6)	712 (66.0)	0.004
MSM, No.(%)				
Heterosexual, No.(%)	423 (27.5)	146 (31.9)	277 (25.6)	
Other/unknown, No.(%)	111 (7.2)	21 (4.6)	90 (8.3)	
Baseline VL, copies/mL				
<50, No.(%)	2 (0.1)	0 (0.0)	2 (0.2)	0.436
50–100000, No.(%)	988 (64.2)	287 (62.5)	701 (65.0)	
>100000, No.(%)	548 (35.6)	172 (37.5)	376 (34.8)	
Baseline CD4+T cell count, cells/μL				
<50, No.(%)	310 (20.2)	106 (23.1)	204 (18.9)	0.273
50–99, No.(%)	186 (12.1)	57 (12.4)	129 (12.0)	
100–199, No.(%)	330 (21.5)	93 (20.3)	237 (22.0)	
200 -349, No.(%)	712 (46.3)	203 (44.2)	509 (47.2)	
Baseline CD4/CD8	0.17 (0.08, 0.29)	0.17 (0.08, 0.29)	0.17 (0.08, 0.28)	0.751
Time from diagnosis to ART initiation	26 (13–54)	12 (7–12)	35 (22–107)	<0.001

Note: The *p*-values are the comparison of the baseline variables between the RIG versus the DIG.
Abbreviations: IQR, interquartile Range; MSM, men who have sex with men; ART, antiretroviral therapy; RIG, rapid ART initiation group; DIG, delayed ART initiation group.

rapid ART group and delayed ART group saw significant differences in transmission routes, with men who have sex with men accounting for 63.5% and 66.0%, respectively.

Analysis of All-Cause Mortality and Causes of Death

In this study, a total of 68 patients died during the 8-year follow-up period of 1538 patients, with an all-cause mortality rate of 4.42% (68/1538). Among them, there were 18 deaths in the rapid ART group, with a mortality rate of 3.92% (18/459); There were 50 deaths in the delayed group, with a mortality rate of (4.63%, 50/1079). Although the mortality rate in the delayed ART group was slightly higher than that in the rapid ART group, there was no significant difference in the all-cause mortality rate between the two groups (p=0.668).

As shown in Table 2, among the 68 death cases, 39 cases were mainly caused by non-AIDS related diseases (39/68, 57.4%), among which non-AIDS related tumors were the most common (14/68, 20.6%), followed by cardiovascular and cerebrovascular diseases (13/68, 19.1%). 20 patients died from AIDS related diseases (20/68, 29.4%), with HIV related tumors being the most common (7/68, 10.3%).

The main cause of death for PWH in both rapid ART group and delayed ART group was non-AIDS related diseases (12/18, 66.7% vs 27/50, 54.0%). Besides, there was no significant difference in the proportion of non-AIDS related causes of death between the two groups (p=0.538). The highest number of deaths were caused by non-AIDS-related tumors, with 5 cases (5/18, 27.8%) in rapid ART group and 9 cases (9/50, 18.0%) in delayed ART group. Among the deaths caused by AIDS related diseases, there were 5 cases in the rapid ART group (5/18, 27.8%) and 9 cases in the

Table 2 Analysis of Cases of Death in This Study

Causes of Death	Total Cases of Death, n (%)	RIG, n (%)	DIG, n (%)	*p*-value*
Total	68 (100)	18 (100)	50 (100)	0.668
AIDS-related disease	20 (29.4)	5 (27.8)	15 (30.0)	0.538
HIV-related tumor	7 (10.3)	3 (16.7)	4 (8.0)	0.371
Opportunistic infection	6 (8.8)	2 (11.1)	4 (8.0)	0.652
Other (HIV-related)	7 (10.3)	0 (0.0)	7 (14.0)	0.177
Non-AIDS-related disease	39 (57.4)	12 (66.7)	27 (54.0)	
Non-AIDS-related cancer	14 (20.6)	5 (27.8)	9 (18.0)	0.498
CVD disease	13 (19.1)	3 (16.7)	10 (20.0)	1.000
Respiratory disease	5 (7.4)	3 (16.7)	2 (4.0)	0.111
Other disease (HIV-unrelated)	7 (10.3)	1 (5.6)	6 (12.0)	0.666
Unknown	9 (13.2)	1 (5.6)	8 (16.0)	

Notes: The *p*-value is the comparison of variables between the RIG and DIG; * shows the proportion of causes of death (AIDS-related disease and non-AIDS-related disease) between the RIG and DIG. CVD: cardiovascular disease.
Abbreviations: RIG, rapid ART initiation group; DIG, delayed ART initiation group.

delayed ART group (9/50, 18.0%). Overall, the distribution of causes of death in RIG and DIG group have no significant difference.

We collected and analyzed whether CD4+T cell and CD4+/CD8+ ratio have significant effect on death. As shown in Figure 1a and b, there was no significant difference in CD4+T cell counts between the rapid ART group and the delayed ART group (p=0.21), but there was significant difference in CD4/CD8 ratio between the two groups (p=0.046).

Analysis of Survival Curve and Related Risk Factors

In this study, we followed 1538 PWH receiving ART for a maximum 8-year period. The estimated overall survival time for PWH was 66.27 months. Furthermore, the estimated survival times for PWH who initiated ART within 14 days (RIG), and more than 14 days (DIG) after diagnosis were 61.16 months and 68.44 months, respectively. The overall mortality rate in the cohort during the 101923 person-months of observation was 6.67 per 1000 person-months of follow-up. Cumulatively, 68 PWH died, accounting for 3.92% of the total PWH population over 8 years.

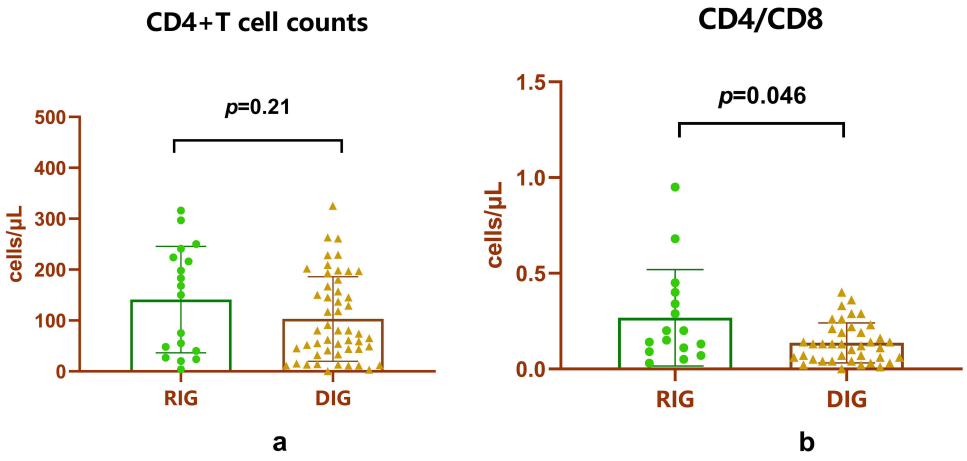

Figure 1 The differences of CD4+T cell counts and CD4/CD8 between death cases with antiretroviral therapy initiation time. (**a**) Comparison of CD4+T cell counts between the rapid ART initiation group (RIG) and delayed ART initiation group (DIG). (**b**) Comparison of the CD4/CD8 ratio between the RIG and DIG.
Abbreviations: RIG, rapid ART initiation group; DIG, delayed ART initiation group.

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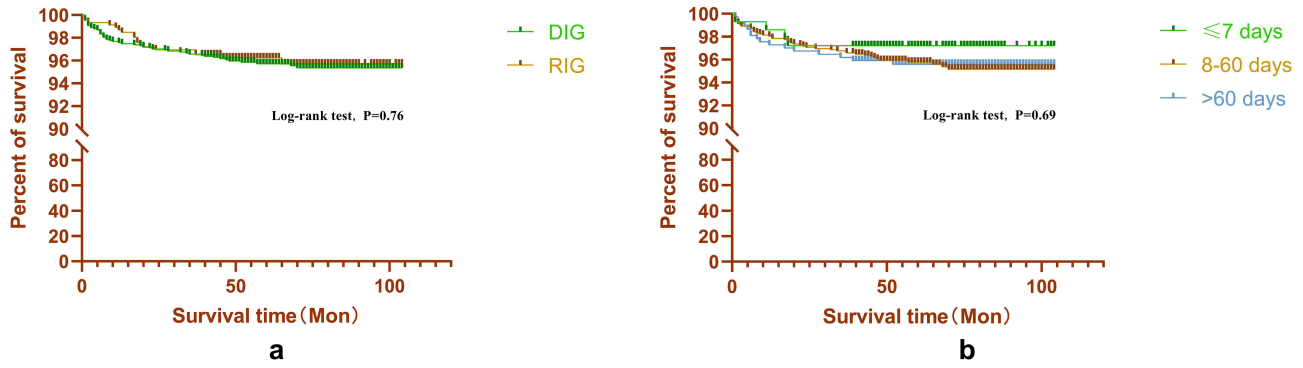

Figure 2 Kaplan–Meier survival curves for patients with different antiretroviral therapy initiation time over the eight-year follow-up period. (**a**) Survival comparison between the rapid ART initiation group (≤14 days) and the delayed ART initiation group (>14 days). (**b**) Sensitivity analysis of survival comparing ART initiation within 7 days, 8–60 days, and after 60 days.
Abbreviations: RIG, rapid ART initiation group; DIG, delayed ART initiation group; Mon, month.

Figure 2 illustrates the Kaplan–Meier survival function for the entire study population over the 8 years following ART initiation. The median time of survival among respondents who initiated ART within 14 days of diagnosis was 100.6 months (95% CI, 99.0 to 102.1). However, the survival time decreased to 99.9 months (95% CI, 98.8 to 101.0) for those who initiated ART after 14 days. However, there were no differences between two groups (Log rank test, p=0.76, shown in Figure 2a). Besides, we did sensitive analysis for initiation time. The results showed that there were no differences between patients starting ART within 7 days, 8–60days, and after 60days (Log rank test, p=0.69, shown in Figure 2b).

Univariate and multivariate cox regression analysis was conducted to examine potential factors associated with mortality among PWH, as shown in Table 3. Variables including sex, age, education, marital status, CD4 count before initiating ART, CD4/CD8 ratio, and time to ART initiation, viral load—were included in the analysis. In the multivariable analysis, the time to ART after diagnosis was not significantly associated with mortality among PWH, which is consistent with result in K-M analysis. As shown in Table 3, Single, divorced or widowed individuals (HR: 1.851, 95% CI: 1.040–3.295, p=0.036) or baseline CD4+T cell counts between 50–100 (HR: 4.441, 95% CI: 1.691–11.659, p=0.002) or below 50 cells/μL (HR: 2.747, 95% CI: 1.170–6.450, p=0.020) had a higher risk of mortality.

Discussion

The application of ART has significantly reduced AIDS-related opportunistic infections and diseases, transforming AIDS from a lethal disease to a manageable chronic condition. Early and effective ART reduces the risk of HIV transmission, treatment interruption, and virologic failure but does not increase adverse events.[21,22], Rapid ART initiation is aimed at PWH and should be initiated regardless of CD4 levels.[5], However, the clinical benefits and mortality risks of rapid initiation of ART with CD4+T cells<350 cells/μL are still unclear.

Studies have found that the mortality rate in China decreased from 10.9% to 4.3% from 2007 to 2019.[23,] A long-term follow-up study from East Africa showed that patients who initiated ART within 14 days after the first follow-up (regardless of CD4+T cell count) had a lower long-term mortality rate (11.7/1000 person years compared to 17.1/1000 person years).[24], In addition, the Rainbow study included 30 late presenting PWH who rapidly initiated ART within 7 days, with a virological suppression rate of 90% at week 48. And their average CD4+T cell count increased from 133 to 309 cells/μL, and the average CD4/CD8 cell ratio increased from 0.18 to 0.44.[25], Different from others, our study found that rapid initiation of ART was not significantly associated with the mortality rate of newly diagnosed PWH with CD4+T cell count<350 cells/μL. Although the mortality rate of the rapid initiation group was slightly lower than that of the delayed group, there was no significant difference between the two groups. Also, when we compared the immunological indicators of the death subjects in the rapid ART and delayed groups, there was no significant difference in CD4+T cell counts, but the CD4/CD8 was significant different. Although not entirely consistent with other research findings, this may be related to our inclusion criteria excluding patients with delayed treatment due to opportunistic infections, and a relatively balanced baseline immunological status, virus levels, and other cofounding factors. Previous studies have

Table 3 Bivariate and Multivariate Cox Proportional Hazards Regression Analysis for Factors Associated with Mortality Among PWH

Characteristics	Cases of Death (N=68)	Univariate Analysis		Multivariate Analysis	
		RR (95% CI)	*P*-value	RR (95% CI)	*P*-value
Age, n (%)			0.491		0.283
>60	36 (53)	1.00			
18–35	5 (7)	0.920 (0.359–2.359)	0.862	0.479 (0.142–1.612)	0.234
35–60	27 (40)	1.331 (0.802–2.207)	0.268	1.171 (0.645–2.127)	0.604
Gender, n (%)			0.005		0.003
Female	4 (6)	1.00			
Male	64 (94)	0.225 (0.079–0.638)		0.157 (0.047–0.526)	
Education level, n (%)			0.841		0.955
Unknown	36 (53)	1.00			
Primary school or less	6 (9)	0.912 (0.381–2.188)	0.837	0.923 (0.347–2.456)	0.872
Junior middle school	9 (13)	0.809 (0.379–1.727)	0.583	0.797 (0.330–1.924)	0.614
Senior high school or higher	17 (25)	0.778 (0.433–1.397)	0.401	0.879 (0.449–1.723)	0.708
Marital status, n (%)			0.349		0.036
Married or cohabiting	32 (47)	1.00			
Single, divorced or widowed	36 (53)	1.262 (0.775–2.054)		1.851 (1.040–3.295)	
Time of diagnosis to treatment, n (%)			0.825		0.710
>14 days	50 (74)	1.00			
≤14 days	18 (26)	0.940 (0.544–1.623)		1.130 (0.594–2.149)	
Baseline CD4+T cell count, cells/μL, n (%)			0.055		0.011
201–349	13 (19)	1.00			
<50	24 (35)	1.934 (0.962–3.887)	0.064	2.747 (1.170–6.450)	0.020
50-100	14 (21)	2.969 (1.326–6.648)	0.008	4.441 (1.691–11.659)	0.002
101–200	17 (25)	1.530 (0.721–3.429)	0.268	1.603 (0.710–3.617)	0.256
Baseline VL, copies/mL, n (%)			0.245		0.378
>100,000	30 (44)	1.00			
<1000	1 (1)	0.784 (0.106–5.802)	0.811	0.249 (0.028–2.260)	0.217
1000–10,000	7 (10)	0.597 (0.260–1.372)	0.224	0.597 (0.239–1.493)	0.270
10,000–100,000	30 (44)	0.592 (0.348–1.006)	0.053	0.753 (0.412–1.378)	0.358

Notes: Univariate analysis: Examining the association between a single variable and the outcome; Multivariate analysis: Examining the association between multiple variables and the outcome.
Abbreviations: HR, Hazard Ratio; VL, viral load.

shown that the level of CD4+T cells in late-presenting PWH is closely related to mortality.[9],However, in our study, there was no significant difference in CD4+T cell levels between the two groups, which partially explains why the timing of ART initiation in this study had no significant effect on mortality in PWH with CD4+T cell count<350 cells/μL.

On the other hand, we analyzed the causes of death in two groups. Despite the low number of death cases, our data indicate a shift in the causes of death for PWH with CD4+T cell count<350 cells/μL over the past years. In this study, 66.7% of deaths in the early ART group and 54.0% of deaths in the delayed ART group were classified as non-AIDS related deaths. Data analysis in the United States and the developed countries have found that non-AIDS related deaths account for 43.6–62.3%, significantly higher than AIDS related deaths.[26,27] In 2016, PWH in China still died mainly from AIDS related causes.[28], In 2021, Chinese data reported that 51.7% of PWH died from non-AIDS related diseases, which is consistent with the proportion of deaths reported in this article. However, the non-AIDS related tumor deaths reported in this article rank higher.[23], In the past five years of Chinese data, there were less reports on the follow-up causes of mortality for late-presenting PWH and delayed initiation of ART. Finally, our study found that PWH with baseline CD4+T cells<200 cells/μL, as well as being single, divorced, or widowed, are independent risk factors for late-presenting PWH death. Consistent with previous reports, CD4+T cell levels are closely related to mortality, especially in late presenters.[9,29,] In addition, family companionship, care, and emotional support for late presenters have a certain

positive effect on improving mortality rates. A study in the United States shows that single or unmarried individuals are 13 times more likely to die from HIV than married individuals.[30], This highlights the critical public health implication that social determinants and family support systems play a vital role in long-term HIV care and survival.

In summary, compared to initiating ART with high CD4+T cell counts,[31], this study focuses on the impact of the timing of initiation of late-presenting PWH on mortality outcomes and immune changes, revealing the changing causes of death in late-presenting PWH. However, our research has several limitations. Firstly, this is a single-center retrospective study, which may limit the generalizability of the findings, and some potential confounding factors affecting mortality were missing at baseline and could not be included. Secondly, the exclusion of patients with severe opportunistic infections who required delayed ART might introduce selection bias, limiting our ability to detect mortality differences related to ART timing among the most critically ill. Thirdly, the relatively low number of mortality events (68 deaths) limits our statistical power. Finally, due to the observational nature of the study, our findings should be interpreted cautiously as associative rather than causal.

Conclusion

The all-cause mortality rate of late-onset PWH is 4.42%, and the timing of ART initiation showed no significant association with the mortality rate and immune changes of late presenters living with HIV. Non-AIDS related deaths have become the leading cause of mortality for PWH with CD4+T cell counts <350 cells/μL. Low baseline CD4+T cell count and lack of social support (being single, divorced, or widowed) are the most important risk factors for late-presenting PWH death. Clinical and public health strategies should prioritize comprehensive care, regular monitoring for non-AIDS comorbidities, and social support interventions for HIV patients presenting with advanced disease.

Abbreviations

ART, Antiretroviral therapy; PWH, People/Presenters living with HIV; WHO, World Health Organization; AIDS, acquired immune deficiency syndrome; RIG, rapid treatment initiation group; DIG, delayed treatment initiation group; VL, viral load; HR, hazard ratio; IQR, interquartile Range; MSM,men who have sex with men.

Ethical Approval and Consent to Participate

All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the Helsinki declaration. Informed consent was obtained from patients included in the study. This study was approved by the Medical Ethics Committee of Nanjing Second Hospital (No. 2024-LS-ky043).

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors have no conflicts of interest to disclosure.

References

1. GBD 2021 HIV Collaborators. Global, regional, and national burden of HIV/AIDS, 1990-2021, and forecasts to 2050, for 204 countries and territories: the global burden of disease study 2021. *Lancet HIV*. 2024;11(12):e807–e822. doi:10.1016/S2352-3018(24)00212-1
2. World Health Organization. Consolidated Guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach. 2021.
3. Ford N, Meintjes G, Calmy A, et al. Managing advanced HIV disease in a public health approach. *Clin Infect Dis*. 2018;66(suppl_2):S106–SS110. doi:10.1093/cid/cix1139
4. Jin J, Pan S, Jing X, et al. Effect of rapid antiretroviral therapy initiation on loss to follow-up, mortality, and virologic failure among people with human immunodeficiency virus under the treat-all policy in China: analysis of routine data. *Front Cell Infect Microbiol*. 2026;15:1736328. doi:10.3389/fcimb.2025.1736328
5. Lundgren JD, Babiker AG; INSIGHT START Study Group. Initiation of antiretroviral therapy in early asymptomatic HIV infection. *N Engl J Med*. 2015;373(9):795–807. doi:10.1056/NEJMoa1506816
6. Koenig SP, Dorvil N, Devieux JG, et al. Same-day HIV testing with initiation of antiretroviral therapy versus standard care for persons living with HIV: a randomized unblinded trial. *PLoS Med*. 2017;14(7):e1002357. doi:10.1371/journal.pmed.1002357
7. Rosen S, Maskew M, Fox MP, et al. Initiating antiretroviral therapy for HIV at a patient's first clinic visit: the rapit randomized controlled trial. *PLoS Med*. 2016;13(5):e1002015. doi:10.1371/journal.pmed.1002015
8. Labhardt ND, Ringera I, Lejone TI, et al. Effect of offering same-day ART vs usual health facility referral during home-based HIV testing on linkage to care and viral suppression among adults with HIV in Lesotho: the CASCADE randomized clinical trial. *JAMA*. 2018;319(11):1103–1112. doi:10.1001/jama.2018.1818
9. Zhao Y, Wu Z, McGoogan JM, et al. Immediate antiretroviral therapy decreases mortality among patients with high CD4 counts in China: a nationwide, retrospective cohort study. *Clin Infect Dis*. 2018;66(5):727–734. doi:10.1093/cid/cix878
10. Wu Z, Zhao Y, Ge X, et al. Simplified HIV testing and treatment in China: analysis of mortality rates before and after a structural intervention. *PLoS Med*. 2015;12(9):e1001874. doi:10.1371/journal.pmed.1001874
11. Wu X, Wu G, Ma P, et al. Immediate and long-term outcomes after treat-all among people living with HIV in China: an interrupted time series analysis. *Infect Dis Poverty*. 2023;12(1):73. doi:10.1186/s40249-023-01119-7
12. Wei L, Zhan Y, Gan XM, et al. Analysis of the timeliness of antiviral treatment for HIV infected individuals in China (2011—2020). *Int J Epidemiol Infect Dis*. 2022;49(6):365–370. doi:10.3760/cma.j.cn331340-20220928-00196
13. Hu X, Liang B, Zhou C, et al. HIV late presentation and advanced HIV disease among patients with newly diagnosed HIV/AIDS in Southwestern China: a large-scale cross-sectional study. *AIDS Res Ther*. 2019;16(1):6. doi:10.1186/s12981-019-0221-7
14. Antinori A, Coenen T, Costagiola D, et al. Late presentation of HIV infection: a consensus definition. *HIV Med*. 2011;12(1):61–64. doi:10.1111/j.1468-1293.2010.00857.x
15. Shi L, Tang W, Liu X, et al. Trends of late HIV presentation and advance HIV disease among newly diagnosed HIV cases in Jiangsu, China: a serial cross-sectional study from 2008 to 2020. *Front Public Health*. 2022;10:1054765. doi:10.3389/fpubh.2022.1054765
16. Xie B, Huang W, Hu Y, et al. Anemia and opportunistic infections in hospitalized people living with HIV: a retrospective study. *BMC Infect Dis*. 2022;22(1):912. doi:10.1186/s12879-022-07910-5
17. World Health Organization. *Guidelines for Managing Advanced HIV Disease and Rapid Initiation of Antiretroviral Therapy*. Geneva: World Health Organization; 2017.
18. Bigna JJ, Plottel CS, Koulla-Shiro S. Challenges in initiating antiretroviral therapy for all HIV-infected people regardless of CD4 cell count. *Infect Dis Poverty*. 2016;5(1):85. doi:10.1186/s40249-016-0179-9
19. Tiam A, Paulin H, Machekano R, et al. Rapid antiretroviral therapy initiation in patients with advanced HIV disease: 6-month outcomes of an observational cohort evaluation in Lesotho. *PLoS One*. 2023;18(10):e0292660. doi:10.1371/journal.pone.0292660
20. Zolopa A, Andersen J, Powderly W, et al. Early antiretroviral therapy reduces AIDS progression/death in individuals with acute opportunistic infections: a multicenter randomized strategy trial. *PLoS One*. 2009;4(5):e5575. doi:10.1371/journal.pone.0005575
21. Bai R, Du J, Lv S, Hua W, Dai L, Wu H. Benefits and risks of rapid initiation of antiretroviral therapy: a systematic review and meta-analysis. *Front Pharmacol*. 2022;13:898449. doi:10.3389/fphar.2022.898449
22. Jiao J, Dai LL, Chen XH, et al. Research progress of rapid antiviral treatment strategies for AIDS. *AIDS & STD China*. 2020;26(06):660–663. doi:10.13419/j.cnki.aids.2020.06.27
23. Cai CH, Tang HL, Li DM, Lyu P. Analysis of death trend and related risk factors of AIDS patients in China. *Chin J Epidemiol*. 2021;42(1):121–125. doi:10.3760/cma.j.cn112338-20200918-01169
24. Baisley K, Orne-Gliemann J, Larmarange J, et al. Early HIV treatment and survival over six years of observation in the ANRS 12249 treatment as prevention trial. *HIV Med*. 2022;23(8):922–928. doi:10.1111/hiv.13263
25. Camici M, Gagliardini R, Lanini S, et al. Rapid ART initiation with bictegravir/emtricitabine/tenofovir alafenamide in individuals presenting with advanced HIV disease (Rainbow study). *Int J Antimicrob Agents*. 2024;63(1):107049. doi:10.1016/j.ijantimicag.2023.107049
26. Chiao EY, Coghill A, Kizub D, et al. The effect of non-AIDS-defining cancers on people living with HIV. *Lancet Oncol*. 2021;22(6):e240–e253. doi:10.1016/S1470-2045(21)00137-6
27. Farahani M, Mulinder H, Farahani A, et al. Prevalence and distribution of non-AIDS causes of death among HIV-infected individuals receiving antiretroviral therapy: a systematic review and meta-analysis. *Int J STD AIDS*. 2017;28(7):636–650. doi:10.1177/0956462416632428
28. Qiao YC, Xu Y, Jiang DX, et al. Epidemiological analyses of regional and age differences of HIV/AIDS prevalence in China, 2004-2016. *Int J Infect Dis*. 2019;81:215–220. doi:10.1016/j.ijid.2019.02.016
29. Lelisho ME, Wotale TW, Tareke SA, et al. Survival rate and predictors of mortality among TB/HIV co-infected adult patients: retrospective cohort study. *Sci Rep*. 2022;12(1):18360. doi:10.1038/s41598-022-23316-4

30. Kposowa AJ. Marital status and HIV/AIDS mortality: evidence from the US national longitudinal mortality study. *Int J Infect Dis*. 2013;17(10): e868–874. doi:10.1016/j.ijid.2013.02.018
31. Lima VD, Reuter A, Harrigan PR, et al. Initiation of antiretroviral therapy at high CD4+ cell counts is associated with positive treatment outcomes. *AIDS*. 2015;29(14):1871–1882. doi:10.1097/QAD.0000000000000790