ORIGINAL PAPER

Identifying important risk factors for survival of HIV-infected patients using censored quantile regression

Omid Hamidi[1], Saman Maroufizadeh[2], Jalal Poorolajal[3], Tara Azimi[4], Payam Amini[5]

[1]Department of Science, Hamedan University of Technology, Hamedan, 65155, Iran
[2]School of Nursing and Midwifery, Guilan University of Medical Sciences, Rasht, Iran
[3]Research Center for Health Sciences and Department of Epidemiology, School of Public Health, Hamadan University of Medical Sciences, Hamadan, 65175-4171, Iran
[4]School of Public Health, University of Alberta, Edmonton, Alberta, Canada
[5]Department of Biostatistics, School of Public Health, Iran University of Medical Sciences, Tehran, Iran

Abstract

Introduction: This study aimed to estimate the effect of potential risk factors on survival of human immunodeficiency virus/acquired immunodeficiency syndrome (AIDS) patients using censored quintile regression model.

Material and methods: We used a dataset from a (registry-based) retrospective cohort study conducted in Tehran (from April, 2004 to March, 2018). Demographic information, such as age, sex, marital status, and educational level as well as behavioral information, including being-in-prison, drug/alcohol abuse and smoking, antiretroviral therapy, co-infection with tuberculosis (TB), and CD4+ cell count, were investigated as potential risk factors for AIDS progression. Censored quintile regression was used to estimate and investigate these factors for AIDS progression.

Results: Mean age of patients was 33.93 years. Time to progression ranged from 0.01 to 223.17 months, and mean of time to progression was 40.55 months. A total of 1,249 (50.5%) patients experienced an event by end of the study. Impact of age, gender, prison, being addicted, being infected with tuberculosis, and using highly active antiretroviral therapy (HAART) were significant for most of quintiles ($p < 0.05$).

Conclusions: It was shown that age, being prisoned, TB infection, and HAART were significantly associated with a lower time in AIDS progression. Censored quintile regression could be an appropriate choice for considering time-varying effects and easy interpretation of regression coefficients in analyzing AIDS progression data.

HIV AIDS Rev 2023; 22, 1: 19-24
DOI: https://doi.org/10.5114/hivar.2023.125016

Key words: censored quintile regression, HIV/AIDS, survival, cohort studies.

Introduction

According to public health report (PHR), global trend and adverse health impact of communicable diseases, such as human immunodeficiency virus (HIV) remains the major and urgent public health problem across the world [1]. Acquired immunodeficiency syndrome (AIDS) has been recognized as the most advanced and final stage of HIV infection [2, 3]. Based on the World Health Organization (WHO)

Address for correspondence: Payam Amini, Department of Biostatistics and Epidemiology, School of Public Health, IRAN University of Medical Sciences, behind Milad Tower, Hemmat Highway, Tehran, Iran, postal code: 1449614535, phone: +98-21-86704801, e-mail: payam.amini87@gmail.com

Article history:
Received: 24.07.2021
Received in revised form: 11.08.2021
Accepted: 11.08.2021
Available online: 28.01.2023

statistics, since AIDS started to be an epidemic, approximately 75 million people have been infected with this deadly virus, and there was an estimated about 36.7 million people living with HIV at the end of 2016, with 1.8 million people becoming newly infected in this year worldwide [3, 4]. HIV damages people's immune system, and defense system weakens against infection and other types of disease, including cancer. Probability of AIDS development varies among individuals, and depends on age, sex, and other conditions, i.e., being co-infected with other diseases [3].

At present, no functional cure exists for HIV infection; however, the rate of HIV-related mortality can be reduced using highly active antiretroviral therapy (HAART) [3-5]. On the other hand, HIV/AIDS-related treatment can be complicated by multiple prognostic factors, including chronic pathologies associated with immunodeficiency, and chronic viral and bacterial infections [6]. CD4+ T lymphocyte count (CD4+ count) is known as a main biomarker of immune function and HIV disease progression to AIDS [3]. Greatest risk of HIV progression is related to CD4+ counts that falls below 200 cells/mm^3 [7]. Opportunistic infection with HIV is often misdiagnosed because HIV symptoms occurring within first months are extremely infrequent [8]. Tuberculosis (TB) is known as a co-infection for HIV-infected patients, and may lead to a reduction in survival rate among patients [3, 4].

In recent years, HIV-related mortality has been decreased; however, to improve life expectancy of HIV-positive patients, it is important to identify prognostic factors affecting patients' survival [6]. But, in developing countries and in the Eastern Mediterranean region, there are limited studies on survival of patients with HIV infection [4, 9]. In order to design effective intervention plans to increase life expectancy of patients with HIV-infection, valid information of survival times and potential risk factors should be collected and analyzed [4, 6, 9]. Therefore, utilizing appropriate statistical models to identify important prognostic factors to improve patients' survival prediction is a significant issue.

There are several modeling approaches, including Cox proportional hazards mode and accelerated failure time models, which have been widely used for analyzing survival data. Nevertheless, studies have shown that some risk factors may not affect survival of patients with prolonged survival, while they may have a special impact on prognosis of patients with shorter survival. This might imply a dynamic situation in survival analysis that is not taken into account by a proportional hazards model, which only considers static settings. In this situation, quintile regression, as an alternative to the usual survival statistical models, may introduce new aspects of the data, indicating that the impact of risk factors may be time-varying. As time-to-event data are often skewed distribution and marginal distribution of the response variable accompanies with kurtosis, quintile regression technique has received a lot of interest in analyzing in these type of data. This is because of the fact that this model is a powerful and robust technique in detection of skewed distribution of data, such as time-to-event data. Quintile regression is very flexible in evaluating effect of explanatory variables on survival times as well. Therefore, this model can depict a more complete picture of a relationship between risk factors and survival time. Censored quintile regression, like Cox regression model, addresses censored observations. However, the former does not enforce assumptions, i.e., proportionality assumption that might not hold in practice [10, 11].

To our knowledge, there is no study that investigate the impact of risk factors on progressing AIDS in HIV-infected patients using quintile regression; therefore, the present study aimed to estimate the effect of potential risk factors on survival of HIV/AIDS patients using censored quintile regression model. The results of this study can be used by health policy makers to design effective interventions to increase patients' life expectancy, and to provide targeted policies improving survival time of these patients regarding treatment. In order to identify the factors affecting the survival of these patients, the performance of Cox regression and censored quintile regression models were compared.

Material and methods

Data set

In the present study, we used a data set from a (registry-based) retrospective cohort study that was conducted in Tehran (between April, 2004 and March, 2018). The study was approved by the Research Council of Hamadan University of Medical Sciences. Study population consisted of HIV-positive people, with a medical record in one of the two Behavioral Diseases Counseling Centers in Tehran (Imam Khomeini and Zamzam Centers). Information about the services provided by these centers is given in [2].

Medical records data included demographic information on age, sex, marital status, and educational level, and behavioral information, including being in prison, drug/alcohol abuse, and smoking as well as ART, TB co-infection, CD4+ cell count, and AIDS progression [2].

Statistical analysis

Descriptive features of patients were presented as mean (± standard error) and frequency (percentage) for continuous and categorical variables, respectively. Mean time to progression for each variable and its' sub-groups were calculated, and log-rank test was applied to evaluate distribution differences among variables of sub-groups.

Numerous statistical tools exist to study time-to-event data. In the present study, we used censored quintile regression (CQR) to find the overall time to progression of patients, using adjusted effects of variables [12-14]. This model arranges numerous quantiles of survival time based on several risk factors, and estimates p^{th} quantile of survival time (Q_p), in which X is the vector of independent variables and β_p is the vector of coefficient for p^{th} quantile.

$$Q(p|X) = X'\beta_p$$

In the above formula, $Q_{50} = \alpha(days)$ means that a randomly selected person from the sample has a probability of 0.5 to face

the event within α days. The quantile model specifies linear dependence of conditional quantiles of Y_i on x_i. This model uses bootstrap resampling method to estimate coefficients' standard error. The bootstrapping approach can be carried out through three option, such as delete-d jackknife, xy-pair, and weighted resampling method with exponential weights. We used Jackknife, which estimates interquartile range using a random sample of R data sets. Details about this approach and handling the censorship can be found in a study by Portnoy [15]. In the current study, factors with *p*-value less than 0.15 were the predictors in CQR model to assess the amount of adjusted effects of independent factors on the survival of patients [16]. Data analysis was carried out using 'survival' and 'quantreg' packages in statistical programing R language, version 3.3.1. All statistical tests were 2-sided, and a *p*-value < 0.05 was considered statistically significant.

Results

The mean (± standard deviation) age of the patients was 33.93 (± 10.35) years. The time to progression ranged from 0.01 to 223.17 months, and the mean and median of time to progression were 40.55 and 20.01 months, respectively. A total of 1,249 (50.5%) experienced an event by the end of the study. Based on Figure 1, a decreasing trend of time to progression probability was observed and one-, three-, and six-month, and one-, three-, and five-year survival probabilities were 0.71, 0.62, and 0.59, and 0.54, 0.40, and 0.29, respectively. The patients' characteristics are shown in Table 1. The majority of patients were 24-44 years old (73.2%), male (78.3%), single (39.1%), non-academic (79.9%), with an experience of prison (60.9%), smoker (48.5%), addicted (51.4%), without tuberculosis infection (90.0%), without HAART (61.9%), and CD4+ cell count less than 200 (32.6%). The mean (± standard error) survival time for each sub-groups of the variables are shown in Table 1. The log-ranks test results showed that except for marital status, the variables of sub-groups were different in mean time to progression ($p < 0.05$).

Table 2 shows the results of CQR model. In addition to consideration of *p*-values in log-rank tests, collinearity between the predictors was regarded in the procedure of variable selection for the model. Therefore, CD4+ cell count, smoking, and education were excluded from the model. The impact of selected variables in CQR model on the time to progression of the patients were evaluated in every five hundredth from 15th to 95th percentiles. To explain Table 2, we interpret the results for two quartiles. The conditional first quartile and median time to progression can be formulated as follow:

Q (0.25 | *tuberculosis infection*, *age*, *HAART*)
= 2.23 – 0.02 × *age*
– 0.03 (*if a positive tuberculosis infection*)
– 0.49 (*if a positive HAART*)

Q (0.5 | *tuberculosis infection*, *age*, *HAART*)
= 68.12 – 0.77 × *age*
– 10.81 (*if a positive tuberculosis infection*)
– 15.06 (*if a positive HAART*)

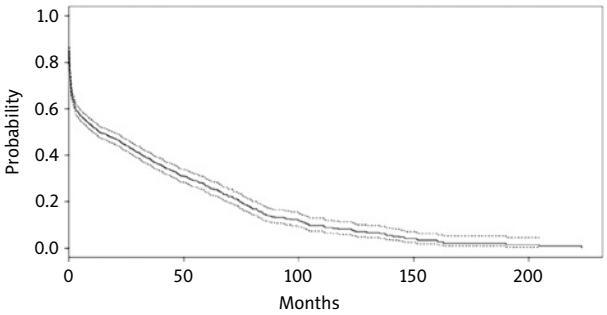

Figure 1. Probability of surviving in months for AIDS progression

According to the above resulted formulas, the 25th percentile of time to progression for a 25-year-old patient with tuberculosis infection and HAART, was 0.94 month. Therefore, the probability of progression to AIDS for that case on 0.94th month was 25%. Moreover, the probability of progression for that case on 23rd month was 50%. In other words, the probability of 50% progression to AIDS for this patient was 23 months. The same interpretation can be used for any other quantiles. As it is shown in Table 2, most of the time to progression quantiles were affected by age, tuberculosis infection, and HAART, and some quantiles of time to progression were affect by the experience of prison, gender, and addiction.

Discussion

The current study assessed the impact of various factors on the duration between the diagnosis of HIV infection and progress to AIDS among patients with HIV/AIDS. In our data, the distribution of time to AIDS progression was considerably skewed. Regarding the skewness of time-to-event data and semi-parametric approaches, censored quantile regression model was used, which resulted in better goodness of fit and more valid estimations as well as easier interpretations [13]. Regardless of the interaction among the predictors, the unadjusted results revealed that patients older than 44, males, non-academics, those with an experience of prison, smokers, and addicted patients, infected with tuberculosis, on HAART, and those with CD4+ count less than 200, were less likely to delay their progression to AIDS. Regarding the association among independent variables, we used a quantile survival regression model, in which age, prison, tuberculosis infection, and HAART predicted status and duration between diagnosis of HIV infection and progress to AIDS significantly.

Our data showed that time between the diagnosis of HIV and AIDS progression was about three years. However, this period can differ based on a number of factors, such as antiretroviral therapy, sexual orientation, and other potential treatments [17]. Chen *et al.* assessed rates and risk factors associated with the progression of HIV to AIDS among HIV-positive patients. They demonstrated that factors, including age, implementing HAART treatment, and early diagnosis and treatment can efficiently increase the time between progression of HIV to its' final and most severe stage, AIDS [18].

Table 1. Patients' characteristics and results of log-rank test

Variable	*n* (%)	Death, *N* = 1,249 (50.5), *n* (%)	Mean survival time (month), mean (SE)	Log-rank test	
				χ^2 test	*p*-value
Age					
< 24	286 (11.6)	104 (36.4)	72.51 (± 8.12)	75.66	< 0.001
24-44	1,810 (73.2)	911 (50.3)	38.68 (± 1.77)		
> 44	376 (15.2)	234 (62.2)	25.65 (± 3.81)		
Gender					
Male	1,936 (78.3)	1,010 (52.2)	38.71 (± 1.87)	8.548	0.003
Female	536 (21.7)	239 (44.6)	47.13 (± 4.09)		
Marital status					
Single	967 (39.1)	480 (49.6)	42.56 (± 2.83)	4.618	0.202
Married	908 (36.7)	474 (52.2)	40.69 (± 3.18)		
Divorced	359 (14.5)	191 (53.2)	37.98 (± 3.47)		
Widow	117 (4.7)	68 (58.1)	36.46 (± 8.24)		
Education					
Academic	155 (6.3)	71 (45.8)	52.95 (± 6.65)	7.404	0.007
Non-academic	1,975 (79.9)	1,048 (53.1)	39.78 (± 1.89)		
Prison					
Yes	1,506 (60.9)	804 (53.4)	32.91 (± 1.56)	23.091	< 0.001
No	966 (39.1)	445 (46.1)	52.53 (± 3.55)		
Smoke					
Yes	1,198 (48.5)	628 (52.4)	32.80 (± 1.74)	19.789	< 0.001
No	997 (40.3)	469 (47.6)	52.03 (± 3.29)		
Addiction					
Yes	1,271 (51.4)	647 (53.0)	34.56 (± 1.68)	4.422	0.035
No	1,201 (48.6)	575 (47.9)	48.11 (± 3.21)		
Tuberculosis					
Yes	247 (10.0)	181 (73.3)	20.51 (± 2.51)	45.746	< 0.001
No	2,225 (90.0)	1,068 (48.0)	43.34 (± 1.96)		
HAART					
Yes	943 (38.1)	639 (67.8)	29.89 (± 2.01)	74.288	< 0.001
No	1,529 (61.9)	610 (39.9)	46.78 (± 2.45)		
CD4+					
> 500	423 (17.1)	87 (20.6)	86.10 (± 5.81)	1305.56	< 0.001
350-500	302 (12.2)	93 (30.8)	62.23 (± 5.03)		
200-350	434 (17.6)	171 (39.4)	41.17 (± 3.96)		
< 200	807 (32.6)	807 (100.0)	5.99 (± 0.66)		

We found that older patients were more prone to earlier progression to AIDS. Prejean et al. evaluated an estimated HIV incidence in the United States, and found that increase in age among young people arises the risk of AIDS [19]. Numerous risk factors and adverse outcomes are associated with HIV disease, and healthy ageing might be strongly affected [20]. Older age is associated with lower CD4+ cell counts, lower thymic volumes, decline in production of naïve T cells, diminished T cell functionality, reduced memory T cell populations, and fewer numbers of properly functioning CD8+ cytotoxic T cells, and it has been shown that the decrease continuous over time [21]. Therefore, these factors explain the reason for more infections among older patients and non-efficient response to immunizations [20].

This study also showed that male were less prone to have a longer time between the diagnosis and AIDS progression.

Table 2. Results of censored quantile regression (estimated coefficient: standard error) assessing the effect of gender, age, prison, addiction, tuberculosis infection, and HAART on survival time quantiles

Quantiles	Intercept	Age	Gender (male)	Prison (yes)	Addiction (yes)	Tuberculosis (yes)	HAART (yes)
15	0.38 (0.21)	–0.01 (0.001)	–0.10 (0.11)	–0.10 (0.10)	0.10 (0.10)	–0.07 (0.01)	–0.07 (0.02)
20	1.27 (0.29)	–0.01 (0.004)	–0.18 (0.13)	–0.07 (0.11)	0.07 (0.11)	–0.21 (0.05)	–0.24 (0.11)
25	2.23 (0.27)	–0.02 (0.01)	–0.26 (0.23)	–0.21 (0.22)	0.16 (0.14)	–0.3 (0.08)	–0.49 (0.11)
30	4.84 (1.28)	–0.04 (0.01)	–0.52 (0.49)	–0.63 (0.34)	0.29 (0.49)	–0.6 (0.25)	–1.22 (0.48)
35	12.53 (3.83)	–0.12 (0.06)	–1.40 (1.58)	–1.51 (0.89)	0.40 (1.28)	–1.48 (0.72)	–3.13 (0.80)
40	26.82 (6.06)	–0.28 (0.07)	–3.29 (1.81)	–3.65 (1.64)	1.33 (2.00)	–3.39 (1.31)	–6.65 (1.72)
45	44.81 (9.01)	–0.52 (0.07)	–5.28 (4.17)	–4.36 (3.90)	0.72 (3.05)	–6.32 (2.89)	–10.37 (2.73)
50	68.12 (8.45)	–0.77 (0.11)	–9.29 (4.93)	–2.77 (2.79)	–2.15 (5.52)	–10.81 (2.54)	–15.06 (3.16)
55	83.57 (6.15)	–1.01 (0.16)	–9.50 (6.63)	–6.41 (5.43)	–0.07 (1.15)	–15.71 (2.21)	–18.08 (4.37)
60	103.85 (14.62)	–1.25 (0.19)	–4.98 (13.00)	–13.69 (7.44)	0.18 (1.06)	–17.37 (3.56)	–24.58 (4.58)
65	129.23 (10.50)	–1.30 (0.27)	–8.07 (12.99)	–14.04 (5.51)	0.29 (2.61)	–18.96 (6.29)	–29.74 (4.69)
70	146.85 (11.75)	–1.38 (0.17)	–11.31 (13.53)	–14.14 (12.16)	1.32 (2.73)	–14.30 (7.35)	–32.23 (5.98)
75	157.27 (12.48)	–1.47 (0.15)	–3.64 (12.23)	–23.12 (0.14)	5.86 (6.77)	–8.30 (10.12)	–32.91 (5.54)
80	180.34 (13.36)	–1.67 (0.28)	3.75 (12.73)	–31.27 (7.99)	0.90 (4.99)	–10.43 (1.98)	–30.89 (9.69)
85	201.20 (13.76)	–1.83 (0.46)	8.99 (14.20)	–35.70 (9.90)	2.14 (10.91)	–16.30 (6.53)	–36.34 (15.03)
90	226.33 (29.35)	–1.72 (0.34)	17.60 (8.83)	–51.96 (16.03)	3.55 (8.75)	–27.00 (8.94)	–36.09 (13.02)
95	244.02 (20.73)	–1.51 (1.22)	–9.03 (79.62)	–77.57 (78.53)	22.57 (9.82)	–28.01 (8.73)	–37.93 (8.08)

**Bold cells indicate significance*

Abioye *et al.* conducted a meta-analysis to address this question if there are differences in disease progression and mortality among male and female HIV-positive patients. They found that males were more likely of higher risk of progression to AIDS, all-cause mortality, HIV-related disease progression, and survival outcomes compared to females [22]. The difference in gender is not well-known; however, factors, such as genetic and environmental features, healthier lifestyles even after positive diagnosis of HIV, and biologic causes might be responsible [23]. Jarrin *et al.* investigated gender differences in HIV progression to AIDS. They revealed that women responded better to HAART intervention, had a healthier behaviors, presented more conscious health-seeking patterns, and higher adherence rates to other medication [23].

Our study showed that those with low education, smokers and addictions, and experience of prison have more likelihood of lower time between HIV diagnosis and progress to AIDS. It is not unlikely that an experience of prison is associated with low education and negative characteristics of lifestyle, such as smoking habits, addiction, depression and psychological problems [24]. It has been argued that a poor medical adherence after positive HIV diagnosis is strongly associated with addiction, depression, and other psychological factors [25]. This might be the reason for the lower time to AIDS progression among HIV patients with addiction.

As it was expected, patients who received HAART had better survival prediction and lower risk of AIDS progression. This is in concordance with results of other studies [26]. Even though HIV/AIDS diagnosis had been considered as a fatal outcome in the early 1980s, the advent of antiretroviral drugs have prolonged survival time of patients with HIV/AIDS after their diagnosis. Observational studies have confirm that HAART reduces mortality rates significantly with a range of 54-92% [27]. Moreover, there are evidences from randomized clinical trials indicating that early initiation of HAART in antituberculosis treatment reduces mortality rates [27].

According to the results of the present study, decreased levels of CD4+ cell counts had a great impact on progression to AIDS, and patients with lower levels of CD4+ had higher risk of AIDS progression, which was also in agreement with results of other studies [2, 28]. Results obtained from epidemiological studies have indicated that an increase in CD4+ cell count level leads to an increase in risk of HIV/TB co-infection [28]. This implies that CD4+ cell count may play a substantial role in the HIV/TB co-infection incidence, and a CD4+ cell count greater than 500 cells/mm^3 leads to a reduction of TB-related mortality among HIV-positive patients [29].

There was an important limitation in the present study. Reliable results can be achieved based on dependable sources of data using prospective cohort studies. However, data used in the present study was obtained from registry centers by a retrospective design that can affect the accuracy of estimations as the associations depended on quality of the recorded data. At this point, validation of the accuracy of the data was not possible. This issue can introduce information bias. In spite of this limitation, the data used

in the study included a large sample obtained from Tehran (comprising about 20% of the Iranian population). This implies that the results of the present study could be applied to the Iranian patients with HIV infection. Furthermore, the effect of several predictive factors on AIDS progression among HIV-infected patients was elucidated using a strong statistical method (censored quintile regression) in a high- and middle-income countries. Our results can be beneficial for institution of intervention measures to conquer the progression of HIV to AIDS as well as to reduce the risk of death amongst HIV-infected people.

To address the effect of variables on time to diagnosis of HIV infection and progress to AIDS, censored quantile regression was utilized. The main advantage of quantile regression is invariance under monotonically increasing transformations, which can be widely operational in the context of survival analysis. The main benefit of the censored quantile regression is that we were able to enter different covariates into the model at each quantile point of the outcome. This was done while the linear parametric structure of the model was still the same [30].

Conclusions

We used censored quantile regression to find the probability of survival in any desired quantile. It was shown that age, an experience of prison, TB co-infection, and HAART were significantly associated with a lower time to AIDS progression after HIV diagnosis.

Conflict of interest

The authors declare no conflict of interest.

Reference

1. Dean HD, Fenton KA. Addressing social determinants of health in the prevention and control of HIV/AIDS, viral hepatitis, sexually transmitted infections, and tuberculosis. Los Angeles: SAGE Publications Sage CA; 2010.
2. Poorolajal J, Molaeipoor L, Mohraz M, et al. Predictors of progression to AIDS and mortality post-HIV infection: a long-term retrospective cohort study. AIDS Care 2015; 27: 1205-1212.
3. World Health Organization. HIV/AIDS. 2017. Available from: http://www.who.int/mediacentre/factsheets/fs360/en/ (Accessed: 17.02.2017).
4. Hamidi O, Tapak M, Poorolajal J, Amini P, Tapak L. Application of random survival forest for competing risks in prediction of cumulative incidence function for progression to AIDS. Epidemiology, Biostatistics and Public Health 2017; 14: e12663-1-e12663-10. doi: 10.2427/12663.
5. Poorolajal J, Hooshmand E, Mahjub H, Esmailnasab N, Jenabi E. Survival rate of AIDS disease and mortality in HIV-infected patients: a meta-analysis. Public Health 2016; 139: 3-12.
6. Hamidi O, Tapak L, Poorolajal J, Amini P. Identifying risk factors for progression to AIDS and mortality post-HIV infection using illness-death multistate model. Clin Epidemiol Global Health 2017; 5: 163-168.
7. Langford SE, Ananworanich J, Cooper DA. Predictors of disease progression in HIV infection: a review. AIDS Res Ther 2007; 4: 11. doi: 10.1186/1742-6405-4-11.
8. de Oliveira Silva M, Bastos M, Martins Netto E, de Lima Gouvea NA, Leite Torres AJ, Kallas E, Watkins DI, et al. Acute HIV infection with rapid progression to AIDS. Braz J Infect Dis 2010; 14: 291-293.
9. Hamidi O, Poorolajal J, Tapak L. Identifying predictors of progression to AIDS and mortality post-HIV infection using parametric multistate model. Epidemiology, Biostatistics and Public Health 2017; 14: e12438-1-e12438-9. doi: 10.2427/12438.
10. Koenker R, Geling O. Reappraising medfly longevity: a quantile regression survival analysis. J Am Stat Assoc 2001; 96: 458-468.
11. Peng L, Huang Y. Survival analysis with quantile regression models. J Am Stat Assoc 2008; 103: 637-649.
12. Fitzenberger B. 15 A guide to censored quantile regressions. Handbook of Statistics 1997; 15: 405-437.
13. Portnoy S. Censored regression quantiles. J Am Stat Assoc 2003; 98: 1001-1012.
14. Wang HJ, Wang L. Locally weighted censored quantile regression. J Am Stat Assoc 2009; 104: 1117-1128.
15. Portnoy S. The jackknife's edge: Inference for censored regression quantiles. Comput Stat Data Analysis 2014; 72: 273-281.
16. Graham MH. Confronting multicollinearity in ecological multiple regression. Ecology 2003; 84: 2809-2815.
17. Antiretroviral Therapy Cohort Collaboration Survival of HIV-positive patients starting antiretroviral therapy between 1996 and 2013: a collaborative analysis of cohort studies. Lancet HIV 2017; 4: e349-e356. doi: 10.1016/S2352-3018(17)30066-8.
18. Chen L, Yang J, Zhang R, et al. Rates and risk factors associated with the progression of HIV to AIDS among HIV patients from Zhejiang, China between 2008 and 2012. AIDS Res Ther 2015; 12: 32. doi: 10.1186/s12981-015-0074-7
19. Prejean J, Song R, Hernandez A, et al. Estimated HIV incidence in the United States, 2006-2009. PLoS One 2011; 6: e17502. doi: 10.1371/journal.pone.0017502.
20. Deeks SG, Lewin SR, Havlir DV. The end of AIDS: HIV infection as a chronic disease. Lancet 2013; 382: 1525-1533.
21. Althoff KN, Gebo KA, Gange SJ, et al. CD4 count at presentation for HIV care in the United States and Canada: are those over 50 years more likely to have a delayed presentation? AIDS Res Ther 2010; 7: 45. doi: 10.1186/1742-6405-7-45.
22. Abioye AI, Soipe AI, Salako AA, et al. Are there differences in disease progression and mortality among male and female HIV patients on antiretroviral therapy? A meta-analysis of observational cohorts. AIDS Care 2015; 27: 1468-1486.
23. Jarrin I, Geskus R, Bhaskaran K, et al.; CASCADE Collaboration. Gender differences in HIV progression to AIDS and death in industrialized countries: slower disease progression following HIV seroconversion in women. Am J Epidemiol 2008; 168: 532-540.
24. Djachenko A, St John W, Mitchell C. Smoking cessation in male prisoners: a literature review. Int J Prisoner Health 2015; 11: 39-48.
25. Nijhawan A, Kim S, Rich JD. Management of HIV infection in patients with substance use problems. Curr Infect Dis Rep 2008; 10: 432-438.
26. Socio-economic Inequalities and HIV Writing Group for Collaboration of Observational HIV Epidemiological Research in Europe (COHERE) in EuroCoord; Lodi S, Dray-Spira R, Touloumi G, et al. Delayed HIV diagnosis and initiation of antiretroviral therapy: inequalities by educational level, COHERE in EuroCoord. AIDS 2014; 28: 2297-2306.
27. Blanc FX, Sok T, Laureillard D, et al. Earlier versus later start of antiretroviral therapy in HIV-infected adults with tuberculosis. N Engl J Med 2011; 365: 1471-1481.
28. Hwang JH, Choe PG, Kim NH, et al. Incidence and risk factors of tuberculosis in patients with human immunodeficiency virus infection. J Korean Med Sci 2013; 28: 374-377.
29. Opportunistic Infections Project Team of the Collaboration of Observational HIV Epidemiological Research in Europe (COHERE); Mocroft A, Reiss P, Kirk O, et al. Is it safe to discontinue primary Pneumocystis jiroveci pneumonia prophylaxis in patients with virologically suppressed HIV infection and a CD4 cell count < 200 cells/μL? Clin Infect Dis 2010; 51: 611-619.
30. Wey A, Wang L, Rudser K. Censored quantile regression with recursive partitioning-based weights. Biostatistics 2014; 15: 170-181.