DISCUSSION

In the present study, ~~T~~the overall estimated survival time ~~from~~ at CD4+ lymphocyte count 200×10^6/L ~~at 200 x 10^6/L to death~~ was 43.4 months, which was (~~a little~~ Ed-high light: give some statistical or quantifiable comparison) longer ~~than~~ that of ~~from~~ San Francisco Homosexual Cohort Study (SFHCS) (3), as the later observed ~~,~~ a ~~The~~ median survival time of 38 ~~months from CD4+ lymphocyte count at 200 x 10^6/L to death in San Francisco Homosexual Cohort Study was quite similar to the result~~ months under similar experimental conditions. Additionally, the data obtained from SFHCS was similar to a Korean study which followed ~~from the study of~~ 17 Korean homosexual ~~men~~ men with a survival time of ~~(~~39.7 months from their CD4+ lymphocyte count~~)~~ 200×10^6/L (REF). Furthermore, in a multicenter AIDS cohort study, when the CD4+ lymphocytes were in the range of 101–200×10^6/L, at least 71% survival was observed in a 2.5 years period ~~In Multicenter AIDS Cohort Study, 71 % of HIV infected persons with CD4+ lymphocyte count in the range of 101 – 200 x 10^6/L were alive for 2.5 years from 1989 to 1993~~ (4). Also, the above study indicated ~~In this study~~the survival of ~~,~~ 70.6 % ~~–~~of subjects ~~survived~~ for 2 years and 66.6 % of subjects ~~survived~~ for 2.5 years ~~from the date of CD4+ lymphocyte count~~ at the CD4+ lymphocyte count of 200~~×~~ ~~x~~ 10^6/L. Interestingly, ~~to death. t~~~~T~~he median survival ~~time~~ of 19.8 months ~~from the estimated date of~~at CD4+ lymphocyte count ~~at~~ 50~~×~~ ~~x~~ 10^6/L ~~to death was~~ observed in the present study was ~~somewhat~~ longer than that reported by Elizabeth G~~G.~~ (16 months) ~~, >25% at 2 years)~~(12) and ~~, Robert~~ Yarchoan R ~~showed that the median survival time of HIV infected persons with CD4+ lymphocyte count less than 50 x 10^6/L was~~ (12.1 months) ~~(95% confidence interval: 7.2 – 19.4 months)~~ (13). ~~–~~ ~~According to the previous report~~As suggested earlier, the ~~– that~~ AIDS-defining diseases could be unequivocally diagnosed ~~occurred at~~when CD4+ lymphocyte counts are ~~of~~ 50 x 10^6/L ~~for diagnoses~~(REF), hence, we compared our results of survival ~~time from~~at CD4+ lymphocyte count ~~at~~ 50 x 10^6/L ~~to death~~ with other AIDS survival studies. An investigation from France showed survival of 97% for 6 months and 86% of them for 12 months (14). However, ~~Ninety-seven percentages of AIDS patients survived at 6 months and 86% of them at 12 months in France (14)~~ as depicted in Table 6, ~~, t~~~~T~~he median survival time of 16.4 months ~~among~~ in homosexual men of MACS ~~shown in table 6 were shorter than the median survival time of~~were less than that ~~–~~of ~~19.8 months from the date of~~ CD4+ lymphocyte count ~~at~~ 50 x 10^6/L where the survival of 19.8 months was noted~~to death in this study~~. Ed-Highlight: Not very clear. Our ~~result was included in the range of median survival time~~data on the survival ~~(from~~ (8 months ~~through~~ to 28 months) were in accordance with many other ~~) by the~~ studies on AIDS survival time ~~of many countries~~across the globe ~~(Table 6)~~ (15-28). ~~—~~

Our results on the ~~D~~differential~~nce~~ median survival time (23.6 months) between ~~the median survival time from the date of~~ CD4+ lymphocyte count at 200~~×~~ ~~x~~ 10^6/L ~~to death and that from~~and 50×10^6/L ~~50 x 10^6/L to death was about 2 years (23.6 months). Our result was~~were in line with earlier reports ~~supported by the reports that the time from HIV infection to CD4+~~

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~~lymphocyte count~~suggesting when the CD4+ lymphocytes are less than 200~~×~~ ~~x~~ 10^6/L, an average of ~~is on average nearly~~ two years or less ~~than~~ to manifest ~~ation of~~ AIDS defining OI Ed-Highlight: Define OI here (3, 29).~~–~~

As ~~mentioned before~~stated above, only 252 (31.1%) of 811 HIV positive~~infected~~ Koreans ~~were infected from foreigner abroad~~contracted the disease from non-Koreans outside of Korea. The statistical analys~~e~~is of survival ~~time from~~at CD4+ lymphocyte counts ~~at~~ 200~~×~~ ~~x~~ 10^6/L or 50 x 10^6/L ~~to death~~ based on the geography of ~~depending on the place of~~ infection indicated ~~showed~~ a significant difference (Figure 1). Moreover, h~~As h~~azard ratios from CD4+ lymphocyte count ~~at~~ 200~~×~~ ~~x~~ 10^6/L and 50~~×~~ ~~x~~ 10^6/L in~~among~~ subjects infected ~~abroad~~ outside of Korea were 2.84 (p=0.0398) and 2.40 (p=0.0444) respectively, ~~which was significant different by~~ with a confidence interval of 95 %. ~~confidence interval. This data showed that~~suggesting the ~~–~~subjects infected in~~side~~ Korea survived longer ~~than those infected abroad~~.

Supporting our present data, ~~According to~~ the molecular epidemiological study of HIV subtypes in Korea (6) found that, the predominance of Subtype B and distinct subclusters with in subtype B in patients infected in Korea. On the contrary ~~the subtype of HIV-1 from whom infected inside Korea was not only subtype B but also the strains grouped into distinct subcluster within subtype B which was different with those from North America and Europe. However, the subtypes of HIV-1 from whom infected abroad~~ the infections outside of Korea identified various subtypes including ~~:~~subtypes A, E, B, C, D, G and ~~,~~H. As suggested by Kanki et al. ~~suggested that~~ HIV-1 subtypes may determine the rates of progression to AIDS (30) ~~), i~~and hence it will be of interest to study whether HIV-1 subtype B found be predominant in Korea may affect the~~o~~ survival ~~and may also be related to the~~ prognosis ~~or not~~of the disease. ~~Based on those results, we need~~The above observations ~~further~~further strengthen the need for investigations ~~studies~~ to identify the factors which may positively influence the survival ~~after~~ at CD4+ lymphocyte count ~~at~~ 200~~×~~ ~~x~~ 10^6/L or 50~~×~~ ~~x~~ 10^6/L. Furthermore, ~~We also need further~~ study which shed light on ~~on whether the infection was acquires in Korea or abroad~~geography of the infection as an important factor to determine and disease ~~is~~progression and ~~an important factor to determine~~ overall survival time from seroconversion ~~to death or not~~. ED-Highlight: This sentence is redundant here as it appears in the last paragraph of the conclusion.

The rate of loss of CD4+ cells ~~loss~~ was significantly associated with survival time at~~from~~ CD4+ lymphocyte counts ~~at~~ 200~~×~~ ~~x~~ 10^6/L or 50 x 10^6/L ~~to death~~. Since, t~~Because t~~he loss of CD4+ cells ~~means the~~leads to dysfunction of immune system, it is understood, there exists a direct correlation of number of CD4+ cells and survival time. ~~we could understand that subjects with the higher rate of CD4+ cell loss survived shorter than other groups.~~

The effective CD8+ cell-mediated immune response has been closely linked to a beneficial host response to infection with retrovirus. Recent studies have suggested that the CD8+ T cell is an important lymphocyte subset in the pathogenesis of HIV infection and is correlated with disease outcome (2-4). Indeed, a~~A~~ strong HIV-specific immune response can prevent the disease progression quantitatively and qualitatively. ~~immune defects of disease progression by HIV~~

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~~infection.~~ CD8+ T cells ~~can~~ are shown to suppress HIV replication in peripheral blood mononuclear cells (PBMCs) (REF). The antiviral effect of CD8+ T cells is mediated by HIV suppressor factors secreted from CD8+ T cells such as stromal cell-~~dried~~derived factors (SDF-1), eotaxin, monocyte chemotactic proteins (MCP-1), macrophage-derived chemokine (MDC), CD8+ cell antiviral factor (CAF)~~,~~ and interleukin 16 (IL-16) ~~et al~~ among others (REF). Recent studies also suggested that beta-chemokines (RANTES, MIP-1~~1 α~~ α and MIP-1β~~β~~) produced by CD8+ T cells ~~showed~~ exhibited a synergistic effect leading to the suppression of HIV replication *in vitro* (REF). $CD8^+$ T cells with anti-HIV activity, especially CTLs, limit the disease progression after HIV infection~~decreases as an HIV infected person progresses from a healthy state to an AIDS condition~~. Thus~~erefore~~, the ~~high rate~~higher loss of CD8+ cells ~~loss~~ inversely affect~~ed~~ the survival at~~from~~ CD4+ lymphocyte count ~~at~~ 200~~×~~ ~~x~~ 10^6/L, however, ~~. But the rate of~~the exact ~~–~~role of CD8+ was not evident on survival ~~cell loss did not affect the survival from~~after ~~–~~CD4+ lymphocyte counts reached ~~at~~ 50~~–×x~~ 10^6/L. Further studies are warranted to underscore the insights of CD8+ cells at ~~We need to study the characterization of CD8+ T cells in detail to explain our result that the rate CD8+ cell loss was lower affect in survival from CD4+ lymphocyte count at~~ 50~~×~~ ~~x~~ 10^6/L ~~than at 200 x 10^6/L~~.~~—~~

Gender, age, route of infection ~~route~~ and AZT treatment did not ~~affected~~ statistically affect the ~~on the~~ survival time at~~from~~ CD4+ lymphocyte count ~~at~~ 200~~×~~ ~~x~~ 10^6/L or 50~~×~~ ~~x~~ 10^6/L ~~to death~~.~~–~~

~~_~~Age was identified as a cofactor of HIV progression~~,~~ and the effect of age was subsequently confirmed in many studies (31, 32). Interestingly, at the CD4+ lymphocyte count 200×10^6/L, ~~T~~the median survival time was shorter in subjects older than 34 years compared to their young counterparts ~~from CD4+ lymphocyte count at 200 x 10^6/L, to death was slightly shorter among group over age 34 than under age 34.~~ Similarly, the ~~H~~hazard ratio of subjects older than 34 years was ~~for over age 34 was~~ found to be 0.82 (p=0.6332) ~~on survival after~~ at CD4+ lymphocyte count ~~at~~ 200~~×~~ ~~x~~ 10^6/L and that for ~~over age~~ subjects older than 38 ~~–~~was 1.12 (p=0.7560) ~~on survival after~~at CD4+ lymphocyte count ~~–at~~of 50 x 10^6/L, after adjustment for other factors. ~~However, we could not find a statistically significant difference by age in our study. The interpretation of these results was that age did not affect on survival time from CD4+ lymphocyte count at 200 x 10^6/L or 50 x 10^6/L to death, T~~though ~~the differences of age between younger and older groups was about 10 years~~survival difference between the older and younger groups were approximately 10 years, the data did not yield statistically significant difference. It is noteworthy to mention here that ~~.—~~

~~L~~longer survival time and lower hazard ratio ~~from~~ at CD4+ lymphocyte count at 200~~×~~ ~~x~~ 10^6/L or 50~~×~~ ~~x~~ 10^6/L were demonstrated among subjects infected through transfusion ~~or blood product~~ than those infected by sexual contacts ~~ly~~(Ed-Highlight: is this from the current study or from a literature?).

Our univariate estimate showing longer survival among subjects infected through transfusion ~~or blood product~~ was~~ere~~ different from other studies in which survival trends of hemophiliacs were similar to those of homosexual men and intravenous drugs users ~~with AIDS~~ (17, 33, ~~,~~ 34). ~~But~~

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However, the route of infection ~~route~~ did not significantly affect ~~significantly on survival from~~the survival at the CD4+ lymphocyte counts ~~at~~ 200×~~ x~~ 10^6/L or 50×~~ x~~ 10^6/L ~~to death since the~~possibility due to the low power of the study~~. number of subjects through transfusion or blood product was small.~~

~~After AZT was licensed,~~As AZT has come into use, number of reports indicated that treatment of AZT increased the survival by at least 10 months in AIDS patients ~~. many studies was reported that AIDS cases treated with AZT had a median survival of more than 20 months, compared with about 10 months for AIDS cases not treated~~ (35-38), however, ~~. But some studies reported tha~~literature also argue that ~~t~~ early initiation of antiretroviral therapy might have little effect on overall survival time (39, 40). Our results ~~showed~~ suggest that AZT treatment did not affect the median survival ~~after~~ at the CD4+ lymphocyte counts ~~at~~ 200×~~ x~~ 10^6/L or 50×~~ x~~ 10^6/L, which was ~~. However~~contrary to some reports which showed~~, some studies suggested that~~ AZT treatment could affect~~ed~~ the rate of CD4+ cell loss (41, 42) and increase survival time. One explanation to this conundrum could be ~~It is~~ the possible extension of ~~that~~ AIDS incubation period ~~was extended because the rate of CD4+ cell loss was lower before AIDS onset~~low rate of CD4+ cell loss at the onset stage.~~s. Since 1997 in Korea, the~~

In Korea, since 1997, there has been a rapid increase in the use of combination antiretroviral therapy including protease inhibitors in HIV positive individuals. Many studies ~~ percentage of HIV infected persons who receive the combination therapy including protease inhibitor has increased rapidly. It has been reported that the~~support that the combination therapy ~~had a significant effect on lengthening survival time~~ significantly improved survival time in HIV patients (43, 44), ~~but~~ however, it is still uncertain is the extent ~~of effect of combination~~this ~~therapy on~~ survival in these patients ~~ED-Highlight~~ ~~–Not very clear of this sentence!!is still uncertain.~~ Although AZT treatment did not show any positive effect on survival ~~after~~ at the CD4+ lymphocyte counts ~~at~~ 200×~~ x~~ 10^6/L or 50×~~ x~~ 10^6/L, ~~we need~~ a longitudinal study may be necessary unravel ~~to investigate t~~the effects of the combination therapy, apart from ~~including~~the AZT mono therapy, on survival ~~among~~ in HIV ~~infected persons~~positive individuals.~~——~~

The present investigation is the ~~This study is the~~ first to report ~~on the~~ the survival time and survival rate from HIV positive individuals of Korean origin. ~~AIDS indicated level to death in Korean.~~ The median survival time after AIDS indicated level is ~~similar with results of~~corroborating to the data obtained in studies across the globe ~~in other countries~~. Though, ~~While we had the limitation that~~low power as well ~~–~~the number of subjects enrolled ~~included~~ in survival study are the limitations of the present manuscript.~~dy was small, we found interesting characteristic that~~an interesting finding in our study is that ~~–~~individuals who contracted the disease ~~HIV infection~~ inside Korea had significantly longer survival time ~~from~~ at the CD4+ lymphocyte counts ~~at~~ 200×~~ x~~ 10^6/L or 50×~~ x~~ 10^6/L ~~to death~~. Further studies are warranted ~~We need further~~ to ~~study~~ identify ~~which~~ the factors influence ~~affect~~ the natural history of HIV infection from seroconversion to death.

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