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## Survival rate: an indicator of the management of acquired immune deficiency syndrome using Traditional Chinese Medicine

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ing Traditional Chinese Medicine (TCM), has been used as therapy against acquired immune deficiency syndrome (AIDS) for almost 30 years. Based on evaluation indicators for AIDS treatment using TCM, we discuss why the survival rate (which has been used widely in Western Medicine) should be adopted as a new important indicator of TCM treatment for AIDS. We advise that further prospective or retrospective cohort studies should be carried out to confirm this hypothesis.

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**Key words:** Acquired immunodeficiency syndrome; Survival rate; Antiretroviral therapy, highly active; Medicine, Chinese traditional

### INTRODUCTION

In China, the first patients with human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) were reported in Beijing in 1985.<sup>1</sup> From 1985 onwards some practitioners of Traditional Chinese Medicine (TCM) began to treat AIDS with the hope of cure, whereas others sought to explore integrative-medicine methods to treat AIDS.

Since 2003, the State Administration of Traditional Chinese Medicine has sponsored a pilot program to treat AIDS patients with TCM in conjunction with anti-retroviral drugs.<sup>2</sup> Some endpoints had been used to evaluate the effects of TCM for the treatment and research of AIDS: symptoms and signs;<sup>3</sup> quality of life (QoL),<sup>4</sup> CD4+ T-cell counts;<sup>5</sup> plasma viral load (PVL) of HIV.<sup>6</sup>

In this review, after analyzing the evaluation methods of HIV/AIDS with combination anti-retroviral therapy (cART) plus TCM, we recommend the survival rate as

### Abstract

Complementary and alternative medicine, includ-

an endpoint for evaluating the effectiveness of TCM treatment against AIDS.

## ADVANCES IN TCM THERAPY FOR AIDS

Since 1996, the prevalence, mortality and morbidity because of HIV/AIDS has been reduced thanks to cART.<sup>7</sup> The latter involves therapy over the lifetime of a patient, so some limitations have been observed: adverse effects of drugs, drug resistance, and the high cost of treatment. Therefore, researchers have been looking for new cART agents, and have investigated complementary and alternative medicine (CAM).<sup>8</sup>

TCM has been used for thousands of years. Some of infectious diseases have been treated successfully by TCM: severe acute respiratory syndromes,<sup>9</sup> influenza A virus subtype H1N1,<sup>10</sup> epidemic encephalitis,<sup>11</sup> and hepatitis.<sup>12</sup>

According to TCM theory, AIDS is an infectious disease. AIDS leads not only to an imbalance in yin and yang but also disharmony of internal pathophysiological functions and the external natural environment. In terms of TCM, the management strategy is to regain a new dynamic balance of yin and yang through pattern identification to recuperate and avoid further damage.

TCM had been used to treat AIDS for nearly 30 years. Some scholars are convinced of its effectiveness against AIDS through: reduction of PVL; increasing CD4 + T-cell counts; promotion of reconstitution of immunity; improving health-related quality of life (HRQOL).<sup>13</sup>

However, there is insufficient evidence to support the use of herbal medicines against HIV. We face some challenges: limited knowledge for using TCM to treat AIDS; lack of well-designed and well-controlled clinical studies.

## EVALUATION INDICATORS OF AIDS TREATMENT USING TCM

According to Western Medicine (WM), AIDS is caused by HIV infection. If the infection is not detected and treated, the immune system is gradually weakened, which leads to the development of AIDS. In the human body, the CD4 + T Cell is the immune cell damaged by HIV. How to eliminate, diminish or suppress the HIV load and to strengthen the immune system are the two most important goals for WM using a cART strategy to restore immune function, prevent opportunistic infections, and reduce the mortality.<sup>14</sup> Thus, CD4+ T-cell counts and HIV loads were initially recommended as primary indicators for evaluation of treatment by the World Health Organization,<sup>15</sup> and have been used widely.

Since 1996, HIV-related mortality and morbidity has been greatly reduced by cART, and the lives of patients

prolonged. However, the prevalence of HIV-related and non-HIV-related diseases and symptoms among those patients has increased. Patients are not merely content with improvement of CD4+ T-cell counts and suppression of PVL, they are motivated by better QoL and fewer side-effects of cART.

Thus, some new indicators have been used to evaluate treatment besides CD4 + T-cell counts and HIV loads in some studies on cART: HRQOL; troublesome symptoms and signs such as fatigue, insomnia, dementia, fever, and diarrhea; and mental and spiritual disorders.<sup>16-18</sup> To some extent, such changes reflect a focus on the demands on the patient rather than HIV and the immune system as the ultimate goal of AIDS treatment.

By contrast, TCM practitioners focus on the symptoms of the patients. They use such symptoms as evaluation indicators if they treat/change their strategy for AIDS patients, and if they research AIDS or AIDS-related diseases.<sup>19-21</sup>

## FEASIBILITY OF USING SURVIVAL RATE FOR EVALUATION OF TCM THERAPY AGAINST AIDS

Besides the evaluation indicators mentioned above, the survival rate of HIV/AIDS patients is an important indicator that can be used to evaluate the treatment effects of TCM against AIDS. However, there have been no reports on this outcome, and there are four main reasons for this knowledge gap.

First, AIDS remains a chronic and potentially fatal disease. The mortality of HIV/AIDS has been reduced owing to cART, and life expectancy among HIV/AIDS patients is increasing. Thus, the survival rate is as important as that mortality. More attention should be paid to improving survival and reducing mortality.

Second, AIDS is a very complex disease. Many factors affect disease progression and the survival of people living with HIV: age,<sup>22</sup> sex,<sup>23</sup> immune function,<sup>24</sup> nutritional status,<sup>25</sup> risk factors for HIV,<sup>26</sup> disease stage,<sup>27</sup> complications,<sup>28</sup> timing of cART,<sup>29</sup> and geographic location.<sup>30</sup> Multiple effects of TCM on HIV/AIDS have been reported. Some Chinese patients use TCM for the prevention and treatment of disease as well as healthcare because it is convenient, inexpensive and effective. If AIDS/HIV patients also use TCM, it may improve their chance of survival.

Third, use of cART has strict indications and contraindications. Some HIV/AIDS patients have no choice but to use TCM or other methods because they are not suitable for cART, or because they had to stop cART owing to liver disease, kidney disease, or drug resistance. More importantly, the risk of death increases for HIV/AIDS patients who are not being treated. In this situation, TCM therapy against AIDS is particularly important to reduce the risk of mortality and prolong life.

Fourth, from 2004 onwards, the State Administration of Traditional Chinese Medicine of China undertook a pilot program for the use of TCM to treat AIDS patients in conjunction with anti-retroviral drugs. In this way, more than 10 000 HIV/AIDS patients benefited from free TCM treatment in 19 provinces (including autonomous regions and municipalities). By the end of November 2011, different cohorts had been created and considerable data collected. In the same period, some cART-related cohorts in different provinces had been created. Therefore, survival analyses could be used to undertake a retrospective study to explore the effect of TCM on the survival of HIV/AIDS patients. If TCM is shown to improve the survival of AIDS/HIV patients, these results will increase (or eliminate) prejudice against use of TCM against AIDS, and encourage more patients to accept such treatment.

There are some useful evaluation indicators for AIDS treatment, but we recommend survival analysis (which has been used widely in WM) as a new and important indicator for TCM treatment against AIDS. We advise researchers to use survival analysis to evaluate the effect of TCM on prolonging the survival of AIDS patients.

## EVALUATION OF SURVIVAL

Survival rate is defined as the percentage of patients alive with or without treatment after a given period of follow-up (usually 1, 3, or 5 years).<sup>31</sup> Survival rate is important for the prognosis, and can be used to (a) describe the lethality of the disease and (b) evaluate the long-term curative effect. Survival rate is often used in chronic diseases such as cancer,<sup>32</sup> cardiovascular disease,<sup>33</sup> or tuberculosis,<sup>34</sup> but it has also been used to evaluate the effect of cART or other management strategies. Survival of AIDS patients can be prolonged not only by a cART strategy but also by the other methods.<sup>35</sup> Various types of survival rate have been used as endpoints in clinical trials.

"Overall survival" is the time from the diagnosis to the time of death owing to any cause. Researchers often use mean overall survival to estimate the prognosis, and is often expressed over standard time periods (usually 1, 3, 5, or 10 years). If there is a small increase in survival, this can be considered to be clinical evidence of the benefits of a certain type of treatment.

"Net survival" is the time from the diagnosis to the time of death due to the disease, which filters out the effect of mortality from causes other than the disease. There are two main ways to calculate net survival: "relative survival" and "cause-specific survival" ("disease-specific survival"). Relative survival has the advantage of not being dependent upon accurately knowing the cause of death. It is calculated by dividing the overall survival after the diagnosis by the survival as observed in a similar population without the disease. A "similar

population" comprises individuals with at least age and sex similar to those diagnosed with the disease. Cause-specific survival has the advantage that it is not dependent upon finding a similar population of people without the disease. It can be calculated by treating deaths from other causes than the disease as withdrawals from the population that do not lower survival compared with patients who are not being observed any more (e.g. owing to reaching the end of the study period). "Median survival" is also used in regard to survival if the mean survival is relatively short (i.e., the amount of time at which 50% of patients have died and 50% have survived). For example, median survival of six months indicates that, after 6 months, 50% of people with that condition will be alive and 50% will have died.

One-, three-, or five-year survival measures survival at 1, 3 or 5 years, respectively, after the diagnosis. For example, if 5-year survival is 85%, then 85 out of 100 people with a certain disease will be alive after 5 years. Besides HIV/AIDS-related reasons, cause of death is quite complex among patients. Hence, confirming the cause of death is quite difficult. Overall survival is much easier to calculate than net survival, but the latter is much more exact if studying the relationship between survival and the effect of HIV/AIDS. AIDS has a mean duration of 8-10 years from infection to death without timely and effective therapy. Hence, not only the 1-, 3-, or 5-year survival but also median survival is used scarcely. Hence, in studies of the effect of TCM on HIV/AIDS, we recommend overall survival and net survival as evaluation indices.

As mentioned above, many factors simultaneously affect disease progression and the survival of people living with AIDS/HIV, and it is difficult to distinguish which are risk factors and protective factors in different studies. We should take multiple factors into account when employing analyses to ascertain if an intervention increases the survival of AIDS/HIV patients.

## CONCLUSION

AIDS is a worldwide public-health problem. Roles of TCM against AIDS are being accepted by increasing numbers of patients. There are many differences between TCM and WM in terms of philosophy, but we believe that the survival rate of HIV/AIDS patients after TCM treatment could be a new indicator for assessing the efficacy of such treatment.

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