The Influence of Adjunctive Traditional Chinese Medicine Therapy on Survival in Primary Liver Cancer: A Real-world Study Based on EMRs

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Research

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Abstract

Background

Primary liver cancer is a common clinical malignancy. Traditional Chinese medicine (TCM) is an alternative treatment for primary liver cancer. TCM effectively improves the survival rate and quality of life of patients, but high-level evidence is lacking.

Patients and methods

This study determined whether the combination of TCM and conventional cancer treatment affects the survival of liver cancer patients. Patients were selected from 5 tertiary hospitals in Henan Province. Two thousand and sixty-seven patients with primary liver cancer were included in the study for analysis. Patients who received adjunctive TCM treatment and underwent treatment for more than 1 month were classified as the TCM intervention cohort, i.e., the exposure group. Patients who did not receive adjunctive TCM treatment or who received adjunctive TCM treatment for less than 1 month were classified as the non-TCM intervention cohort, i.e., the non-exposed group. The main outcome indicators were the survival outcome and survival time of primary liver cancer patients. The propensity score inverse probability weighting method was used to balance the differences in the observed characteristics between the groups.

Results

The primary cohort comprised 2,067 patients with primary liver cancer, including 462 patients who received adjunctive TCM treatment and 1,605 patients who did not receive adjunctive TCM treatment. Multiple logistic (binary) regression analysis results showed that adjunctive TCM treatment may reduce the mortality of primary liver cancer patients (regression coefficient = −0.82, P<0.001). The results of the Kaplan-Meier survival analysis indicated that the survival rate and median survival time of the exposure group before and after propensity score weighting were greater than those of the control group (P<0.0001). Multiple Cox regression analysis showed that adjunctive TCM treatment was an independent protective factor for survival in liver cancer patients (regression coefficient = −0.2477, hazard ratio (HR) = 0.7806, 95% confidence interval (CI) [0.6311–0.9655]), and cancer embolus was an independent risk factor (regression coefficient = 1.0546, HR = 0.3483, 95% CI [0.2831–0.4286]).

Conclusion

Adjuvant treatment with TCM has a protective effect on the prognosis of patients with primary liver cancer; it can reduce the mortality of primary liver cancer and prolong the survival time of patients. Cancer embolus is a risk factor that impacts the therapeutic effect of treatment in liver cancer patients.

Introduction

Liver cancer is predicted to be the sixth most commonly diagnosed cancer and was the fourth leading cause of cancer death worldwide in 2018, with approximately 841,000 new cases and 782,000 deaths that year. Primary liver cancer is currently the fourth most common malignant tumor and the second leading cause of death in China, seriously threatening the lives and health of people [1, 2]. Traditional Chinese medicine (TCM) is widely used in Chinese and East Asian societies, and therapy that combines TCM and conventional cancer treatment is already considered acceptable treatment for cancer. TCM treatments have targeted stimulation of the host immune response for cytotoxic activity against liver cancer by inhibiting proliferation and promoting the apoptosis of tumor cells [3–5], thereby alleviating chemoradiotherapy-related or gene therapy-related side effects [6, 7]. However, these studies on TCM treatment for primary liver cancer have only been conducted in laboratories, with only one multicenter randomized control trial having evaluated the effects of TCM use in preventing recurrence after resection of small hepatocellular carcinoma [8]. To date, high-level evidence-based medicine is still lacking.

For a long time, the clinical evaluation of TCM has remained at the empirical level, with related research results and clinical experience mostly presented in the form of case reports, which are considered the lowest level of evidence in evidence-based medicine, so the credibility of TCM is not optimal [9]. The higher the level of evidence is in evidence-based medicine, the more conducive the findings are to guiding clinical practice. High-quality evidence is mostly found in randomized controlled trials, but this type of trial requires strict inclusion and exclusion criteria to eliminate nonspecific factors to the greatest extent possible. Although high-level clinical evidence has laid the foundation for the formulation of clinical practice guidelines for TCM, its extrapolation to actual medical practice has always been questionable [10].

With the rapid development of information technology and the advent of big data, high-tech approaches such as big data, artificial intelligence, Internet+, and cloud computing continue to emerge. The external environment of real-world research has undergone significant changes, and high-quality clinical big data are now easier to obtain. In addition, continuous improvements in research methods have made research results more reliable. Real-world studies have become an important supplement and continuation of randomized controlled trials (RCTs), and they are also a suitable method for evaluating curative effects within the context of the characteristics of TCM diagnosis and treatment [11, 12]. In recent years, hospital information systems at all levels have also been widely used and gradually improved. A patient's complete medical records can be preserved, transmitted, managed and shared through an electronic medical record (EMR) system. EMRs contain personal patient information (name, sex, age, address, medical insurance number); physiological indicators; laboratory test results; nonwritten records (such as computed tomography (CT) and electrocardiogram results and audio recordings); past history; genetic history; and medical expenses. Massive amounts of EMR data have laid a solid data foundation for knowledge discovery in the medical field [13]. Compared with other types of data, EMR data have the characteristics of a large data volume, objectivity, and convenient storage and transmission. Therefore, real-world research based on EMR data have gradually become a popular research topic.

This study was based on real-world clinical EMRs and used the generalized boosted model (GBM) propensity score weighting method to address the problems of nonrandom and confounding factors, which are found in real-world TCM clinical data. The aims of the study were to observe the efficacy of adjunctive TCM treatment in primary liver cancer patients and to provide a practical basis for future real-world studies.

Methods

Study design

This study used a retrospective cohort study design. Five tertiary hospitals in Henan Province were selected, including 3 hospitals that integrate Chinese and Western medicine and 2 hospitals that use Western medicine. The data are real-world clinical EMR data based mainly on the structured EMR system of the hospital, and they were extracted from the medical record homepage in the medical record system and from the hospitalization information. With the approval of the ethics committee, the patient's written informed consent was not required for this study.

Patients

This study mainly included inpatients with primary liver cancer from 5 tertiary hospitals from 2015 to 2017. A total of 2,067 patients were enrolled. The inclusion criteria were as follows: ① patients diagnosed with primary liver cancer consistent with the "Guidelines for the Standardized Pathological Diagnosis of Primary Liver Cancer (2011 Edition)" [14]; ② patients aged ≥18 years old; ③ patients with complete relevant examination results and hospitalization information; and ④ patients and their families who were willing to cooperate with follow-up visits and follow-up calls, the data from which were included in the information collected. The exclusion criteria were as follows: ① patients with other primary tumors who were receiving treatment; ② patients and their family members were unwilling to follow up or patients whose original data were severely insufficient; and ③ patients who died unexpectedly.

Data source

The data of this study are based mainly on real-world clinical EMRs. Through data mining, the information in the clinical EMRs was extracted, and the data were cleaned and standardized. Finally, a relatively standardized database was established. The patient information collected in the study included the medical records of patients admitted for primary liver cancer at 5 tertiary hospitals from 2015 to 2017, as well as the telephone follow-up information for patients from August 2018 to March 2019. The EMR information mainly included basic demographic information, disease-related information (family history, drinking history, history of illness), indicators related to disease progression (Child-Pugh classification, Barcelona Clinic Liver Cancer (BCLC) staging, Chinese staging, complications, etc.), admission/discharge information, and disease treatment-related information (surgery treatment and Chinese medicine intervention). The patient follow-up information obtained by telephone follow-up mainly included the patient's final outcome, the time of diagnosis, the time of death and information related to the patient's out-of-hospital medication use.

Exposure

In this study, adjunctive TCM treatment was regarded as the exposure factor, and the cohort was divided according to the degree of adjunctive TCM treatment received by primary liver cancer patients. Patients who received adjunctive TCM treatment and had a cumulative treatment time of more than 1 month were classified as the adjunctive TCM intervention cohort, i.e., the exposure group, and patients who have not receive adjunctive TCM treatment or whose cumulative adjunctive TCM treatment time was less than 1 month were classified as the non-Chinese medicine adjuvant intervention cohort, i.e., the non-exposure group [15]. TCM treatment included TCM decoction treatment, Chinese patent medicine treatment, and TCM characteristic therapies (acupuncture, massage, external treatment, etc.).

Outcome variables

The main observation indicators in this study were the survival outcome and survival time of primary liver cancer patients. The survival outcome and survival time of patients during the study period were recorded. The survival time starting point was the time at which primary liver cancer was diagnosed, and the end point was the time when the patient died of liver cancer or the end of the study period.

Statistical analysis

According to the inclusion and exclusion criteria and the TCM exposure criteria, this study analyzed the data of patients exposed and not exposed to TCM. First, we described the baseline conditions of all patients statistically. Quantitative data were described by the mean ± standard deviation or median (upper and lower quartiles), and comparisons between groups were performed using a t test or Wilcoxon rank sum test; qualitative data were analyzed using frequencies or percentages. Comparisons between groups were performed using the Chi-square test or Fisher's exact test.

Screening for confounding factors was mainly based on the results of the comparison between the baseline groups, removing variables with $P<0.05$, and combining the relevant literature and the recommendations of clinicians to choose individual variables. To balance confounding factors, the GBM propensity score weighting method was adopted. The GBM algorithm is achieves equilibrium between the confounding variables of the treatment group and the control group. It does not perform significance tests between the means and standard deviations of the confounding factors of the two groups but uses the best commonly used tools to measure balance or matching: average standardized absolute mean difference (ASAM) and the Kolmogorov-Smirnov test statistic (Kolmogorov-Smirnov test statistic). In this study, the difference in propensity scores before and after weighting is represented by the KS statistic, and a KS statistic <0.05 is regarded as equality between groups [16-18].

The impact of the adjunctive TCM intervention on the survival outcome of primary liver cancer patients was analyzed by logistic regression. The Kaplan-Meier method was used to calculate the survival rate and draw a survival curve, and the survival rate was compared between groups by the log-rank test. Multivariate Cox proportional hazard regression analysis was performed to observe the influence of the adjunctive TCM intervention on the survival outcome and survival time of primary liver cancer patients and related risk factors.

Sensitivity analysis of potential confounding recognition: We usually only build models to estimate the propensity scores for the observed variables. The models do not include unobserved confounding factors or potential biases. Therefore, we needed to identify possible potential confounding factors; sensitivity analysis tests whether a model is sensitive to potential confounding bias by sequentially removing confounding variables from the model.

Results

Study population

From 2015 to 2017, approximately 3,114 patients were hospitalized in the 5 tertiary hospitals included in the study. Among them, 3 patients were excluded because they did not meet the diagnostic criteria; 3 patients were excluded because they were less than 18 years of age; 8 patients were excluded for lack of a time of diagnosis; 251 patients were excluded due to a short admission and discharge; and 938 patients were excluded because they did not have disease confirmation. Thus, 2,067 patients were ultimately included in the cohort.

Patient characteristics

Table 1 shows the baseline demographic characteristics and clinical characteristics of the study subjects before and after propensity score weighting. Among the 2,067 study subjects included, according to the exposure standards, 462 patients were treated with adjunctive TCM therapy; they had an average age of 57.51 years (standard deviation, 10.91), with 79% being male and 21% being female. A total of 1,605 patients did not use adjunctive TCM treatments; they had an average age of 56.23 (standard deviation 11.19) years old, with 82% being male and 18% being female. Patients who used adjunctive TCM therapy were more likely to have the following characteristics: family history of liver cancer or viral hepatitis; history of hepatitis C, cirrhosis, or alcoholic liver disease; and complications of hepatic encephalopathy or abdominal infection. Patients treated with TCM assistance may have had higher BCLC staging or Chinese staging.

Figure 2 shows the p-value and uniform distribution value of the confounding variables before and after weighting of the two groups. After propensity score weighting, the difference between the baseline confounding variables between the two groups was close to that expected with random assignment.

Primary Outcomes

1. Survival outcome — probability of death

Table 2 is the result of single-factor logistic regression analysis of the influence of adjunctive TCM treatment on the survival outcome of primary liver cancer patients. The coefficients before and after weighting were less than zero and statistically significant ($P<0.001$); combined with the analysis results from Table 1, after the propensity score adjustment, there were still some confounding factors that were not balanced, such as liver cirrhosis, Child-Pugh grade 1, direct bilirubin (DBIL), cancer thrombus, alpha-fetoprotein (AFP), thymosin α1, and adefovir dipivoxil. Therefore, multivariate logistic regression analysis was performed with the weighted results, and the unbalanced covariates that were screened out and had important effects on the outcome, such as liver cirrhosis, Child-Pugh grade 1, DBIL, cancer thrombus, AFP, and other variables, were reincorporated into the model for adjustment. The results are shown in Table 3. According to the combined results of Table 2 and Table 3, the regression coefficients for adjunctive TCM treatment are all less than 0, and $P<0.001$, which indicates statistical significance. These results suggest that adjunctive TCM treatment has a protective effect on survival in patients with primary liver cancer and, to a certain extent, improves the probability of patient survival.

2. Survival analysis

1) Survival time — Kaplan-Meier survival analysis

Using the median survival time of the total population as an effect indicator, Kaplan-Meier survival analysis was performed on the two groups of populations, and survival curves were drawn before and after propensity scores weighting, as shown in Figure 2. Before and after propensity score weighting, the median survival time of the TCM intervention group was longer than that of the control group, and the difference was statistically significant (P<0.001).

2) Multivariate Cox regression analysis after the GBM trend score increased

Taking into account that unbalanced confounding factors remained after propensity score weighting, as well as clinical experience and the single-factor analysis results, the factors that had an important impact on the outcome were screened out: CT-cancer thrombus and liver cirrhosis. These two covariates were included in the adjusted model, and the results are shown in Table 6. The covariate-adjusted propensity score weighted Cox regression analysis showed that the regression coefficient for adjunctive TCM treatment was less than 0, and the difference was statistically significant (P=0.0224). This suggests that the adjuvant treatment with TCM has a protective effect on the prognosis of primary liver cancer patients; it can prolong the survival time and reduce mortality. In addition, both liver cirrhosis and cancer thrombus are risk factors affecting the therapeutic effect of liver cancer treatment (with regression coefficients of 0.17 and 1.0546, respectively, and p-values of 0.0954 and less than 0.001, respectively).

Discussion

Adjunctive TCM treatment of primary liver cancer is widely used in China. Inpatients with liver cancer generally use TCM, such as TCM injections, for adjuvant treatment. This study is the first large-scale real-world study based on clinical EMRs to examine the impact of TCM treatment on the survival of primary liver cancer patients. This study adopted a retrospective cohort study design. A total of 2,067 liver cancer patients were included in the exposed group, 462 patients were included in the non-exposure group, and 1605 patients were included in the non-exposed group. The GBM propensity score weighting method was used to balance the influence of confounding factors to achieve the "effect of postmortem randomization" and enhance the credibility of the evidence.

The results of the study show that Chinese medicine interventions are independent protective factors in the survival of patients with primary liver cancer. The median survival time of the Chinese medicine-assisted intervention group was longer than that of the nonintervention group, and the survival rate was also improved. Cancer thrombus is a risk factor affecting the survival of patients with primary liver cancer. Some previous studies used a retrospective cohort study to observe the effect of adjunctive TCM treatment on the survival of patients with advanced primary liver cancer, and the results all suggested that adjunctive TCM treatment can improve the survival rate of patients with primary liver cancer [19,20], but these study did not use appropriate methods to control confounding factors. In contrast with their study, this study adopted the GBM propensity score weighting method, which controlled the confounding factors between the groups well, resulting in stronger evidence. In addition, some studies showed that the use of Chinese medicine compounds in the treatment of primary liver cancer has a good effect [21-23]. A randomized controlled trial of TCM combined with Transarterial Chemoembolization(TACE) in the treatment of patients with unresectable HCC showed that TCM can stimulate the host immune response by causing cytotoxic activity in liver cancer [24].

This study also has some shortcomings. First, detailed patient discharge information, such as the type of medication, dosage, frequency, and duration of use, could not be accurately obtained. Electronic medical record data can only be used to collect information about patient medication use during hospitalization, not after discharge. The researcher's prescribing frequency, the number of patients and the memories of patients or family members were used to infer the patient's medication status at discharge. This causes a certain bias. Second, because the data were collected retrospectively, the patient's disease was classified and staged. The information was stratified by the researchers based on the patient's medical record information, making the results easily affected by the medical records. Finally, in this study, the composition of the Chinese medicine prescriptions that were taken were not recorded in detail, and the medication information could not be analyzed in depth.

Conclusions

This study was based on real-world clinical EMRs and used the GBM propensity score weighting method to effectively control for nonrandom and confounding factors in the data; the effect of adjunctive TCM treatment on the survival of primary liver cancer patients was also explored. This preliminary study found that adjuvant traditional Chinese medicine therapy may improve the survival rate and prolong the survival time of patients with primary liver cancer. However, the specific effect of TCM interventions still needs to be further studied. This study provides a practical basis for future real-world research.

Abbreviations

AFP, alpha-fetoprotein; **ASAM**, average standardized absolute mean difference; **BCLC**, Barcelona Clinic Liver Cancer; **CI**, confidence interval; **CT**, computed tomography; **DBIL**, direct bilirubin; **EMRs**, Electronic Medical Record system; **GBM**, generalized boosted model; **HR**, hazard ratio; **HCC**, Hepatocellular Carcinoma; **KS**, Kolmogorov-Smirnov; **OR**, odds ratio; **P**, Probability; **RCT**, randomised controlled trial; **SD**, standard deviation; **SE**, Standard Error; **TACE**, Transarterial Chemoembolization; **TCM**, Traditional Chinese medicine.

Declarations

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Author Contributions

LLW and RXZ contributed equally;LLW and RXZ conducted data analysis and article writing; MYS carried out the overall research design;YBL, WY and YF contributed to data quality control;QLG, JAF, CPZ, WGJ, YFF and XHX contributed to the case collection.QZ, RRZ, YXZ and FLS contributed to data collection.

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Availability of data and materials

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the First Affiliated Hospital of Henan University of Chinese Medicine.

Consent for publication

Not applicable.

Disclosure

The authors have declared no conflicts of interest.

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Tables

Table1. Baseline demographic and clinical characteristics of patients before and after propensity score weighting

Variable	Unweighted			ks.pval	Propensity score weighted			ks.pval
	TCM users	TCM nonusers	ks		TCM users	TCM nonusers	ks	
	(*N*=462)	(*N*=1,605)			(*N*=462)	(*N*=1,605)		
Age, mean (SD)	57.51(10.95)	56.23(11.19)	0.05	0.15	56.62(11.07)	56.35(11.1)	0.03	0.81
Sex, 100%								
Male	0.79	0.82	0.02	0.28	0.8	0.81	0.01	0.56
Female	0.21	0.18	0.02	0.28	0.2	0.19	0.01	0.56
Career, 100%								
Worker	0.02	0.02	0	0.74	0.02	0.02	0	0.86
Farmer	0.46	0.54	0.07	0	0.51	0.53	0.02	0.5
Leader	0.01	0.01	0	0.43	0.01	0.01	0	0.86
Teacher	0.01	0.01	0	0.47	0.01	0.01	0	0.69
Company employee	0.07	0.06	0.01	0.55	0.05	0.06	0.01	0.5
Other	0.29	0.26	0.03	0.23	0.29	0.27	0.02	0.38
Retiree	0.12	0.09	0.03	0.08	0.09	0.09	0	0.91
Missing	0.02	0.01	0	0.43	0.02	0.01	0	0.67
Medical insurance, 100%								
Provincial medical insurance	0.12	0.08	0.04	0.01	0.09	0.08	0.01	0.56
City medical insurance	0.1	0.08	0.02	0.19	0.08	0.08	0	0.89
NCMS[a]	0.56	0.6	0.04	0.17	0.59	0.6	0	1
None	0.2	0.21	0.02	0.38	0.2	0.21	0.01	0.58
Missing	0.03	0.03	0	0.63	0.04	0.03	0.01	0.55
Drinking history, 100%								
Yes	0.32	0.35	0.03	0.27	0.36	0.35	0.01	0.8
No	0.68	0.64	0.04	0.17	0.64	0.65	0	0.98
Missing	0	0.01	0.01	0.08	0	0.01	0.01	0.16
Family history, 100%								
Liver cancer								
Yes	0.12	0.09	0.03	0.05	0.11	0.09	0.02	0.41
No	0.76	0.76	0	0.88	0.77	0.77	0.01	0.77

Cannot confirm	0.12	0.14	0.02	0.19	0.12	0.14	0.02	0.33
Missing	0	0	0	0.15	0	0	0	0.21
Viral hepatitis								
Yes	0.2	0.14	0.06	0.01	0.16	0.15	0.02	0.46
No	0.67	0.73	0.06	0.02	0.71	0.72	0.01	0.71
Cannot confirm	0.13	0.12	0.01	0.6	0.12	0.12	0	0.97
Missing	0	0	0	0.15	0	0	0	0.21
Medical history, 100%								
Hepatitis B								
Yes	0.75	0.76	0.01	0.58	0.75	0.77	0.02	0.44
No	0.25	0.23	0.01	0.5	0.25	0.23	0.02	0.41
Missing	0	0	0	0.29	0	0	0	0.36
Hepatitis C								
Yes	0.09	0.05	0.03	0	0.06	0.05	0.01	0.58
No	0.91	0.94	0.03	0.01	0.94	0.94	0	0.71
Missing	0	0	0	0.29	0	0	0	0.36
Liver cirrhosis								
Yes	0.59	0.35	0.25	0	0.45	0.38	0.07	0.02
No	0.41	0.65	0.24	0	0.55	0.62	0.06	0.02
Missing	0	0	0	0.29	0	0	0	0.36
Alcoholic hepatitis								
Yes	0.02	0.01	0.01	0.01	0.01	0.01	0.01	0.2
No	0.98	0.99	0.01	0.04	0.99	0.99	0	0.44
Missing	0	0	0	0.29	0	0	0	0.36
Complications, 100%								
Hepatic encephalopathy								
Yes	0.06	0.03	0.04	0	0.04	0.03	0.01	0.26
No	0.94	0.97	0.04	0	0.96	0.97	0.01	0.26
Pulmonary infection								
Yes	0.09	0.04	0.04	0	0.07	0.05	0.02	0.15
No	0.91	0.96	0.04	0	0.93	0.95	0.02	0.18
Missing	0	0	0	1	0	0	0	1
Upper gastrointestinal bleeding								

Yes	0.04	0.04	0.01	0.58	0.03	0.04	0	0.61
No	0.96	0.96	0.01	0.58	0.97	0.96	0	0.61
Disease classification, 100%								
Child-Pugh stage								
A	0.56	0.51	0.05	0.09	0.56	0.52	0.05	0.1
B	0.23	0.24	0.01	0.64	0.21	0.25	0.03	0.19
C	0.14	0.17	0.04	0.08	0.13	0.17	0.03	0.15
Missing	0.07	0.07	0	0.98	0.09	0.07	0.02	0.28
BCLC stage								
0	0.02	0.02	0.01	0.32	0.03	0.02	0.01	0.23
A	0.22	0.24	0.01	0.53	0.23	0.24	0	0.83
B	0.29	0.22	0.07	0	0.26	0.22	0.03	0.16
C	0.25	0.32	0.06	0	0.28	0.31	0.03	0.26
D	0.14	0.15	0.01	0.65	0.14	0.14	0.01	0.66
Missing	0.07	0.06	0.01	0.57	0.06	0.06	0	0.85
Liver cancer stage								
[illegible]	0.25	0.27	0.02	0.46	0.27	0.27	0	0.85
[illegible]	0.27	0.19	0.08	0	0.22	0.2	0.02	0.41
[illegible]	0.25	0.29	0.04	0.11	0.29	0.28	0	0.86
[illegible]	0.14	0.18	0.04	0.02	0.13	0.18	0.04	0.06
Missing	0.1	0.07	0.02	0.06	0.09	0.07	0.01	0.38

Table 2. Single-factor logistic regression before and after GBM propensity score weighting

	Unweighted			Propensity score weighted		
Variable	**Beta (SE)**	**OR (95% CI)**	***P***	**Beta (SE)**	**OR (95% CI)**	***P***
Intercept	-0.03 (0.06)	-	0.58	-0.06 (0.06)	-	0.35
TCM users	-0.73 (0.12)	0.48 (0.38, 0.60)	<0.001	-0.61 (0.13)	0.54 (0.42, 0.70)	<0.001

Table 3. Multivariate logistic regression with GBM propensity score weighted variables

Propensity score weighted			
Variable	**Beta (SE)**	**OR (95% CI)**	***P***
Intercept	0.79 (0.30)	-	0.009
Adjunctive TCM therapy	-0.82 (0.19)	0.44 (0.31, 0.63)	<0.001
Liver cirrhosis			
\ \ \ Yes (ref)	-	-	-
\ \ \ No	0.29 (0.18)	1.34 (0.93, 1.91)	0.11
Child-Pugh stage 1			
\ \ \ No (ref)	-	-	-
\ \ \ Yes	-1.27 (0.20)	0.28 (0.19, 0.42)	<0.001
DBIL	0.03 (0.01)	1.03 (1.01, 1.05)	0.01
Cancer embolus			
\ \ \ Yes (ref)	-	-	-
\ \ \ No	-0.85 (0.21)	0.43 (0.28, 0.64)	<0.001
AFP	0.00 (0.00)	1.00 (1.00, 1.00)	0.10

Table 4. Cox regression with GBM propensity score weighted variables

Variable	Beta	HR (95% CI)	*P*
Adjunctive TCM therapy	-0.2477	0.7806 (0.6311-0.9655)	0.0224
Liver cirrhosis	0.17	0.8437 (0.6909-1.0303)	0.0954
Cancer embolus	1.0546	0.3483 (0.2831-0.4286)	<0.001

Figures

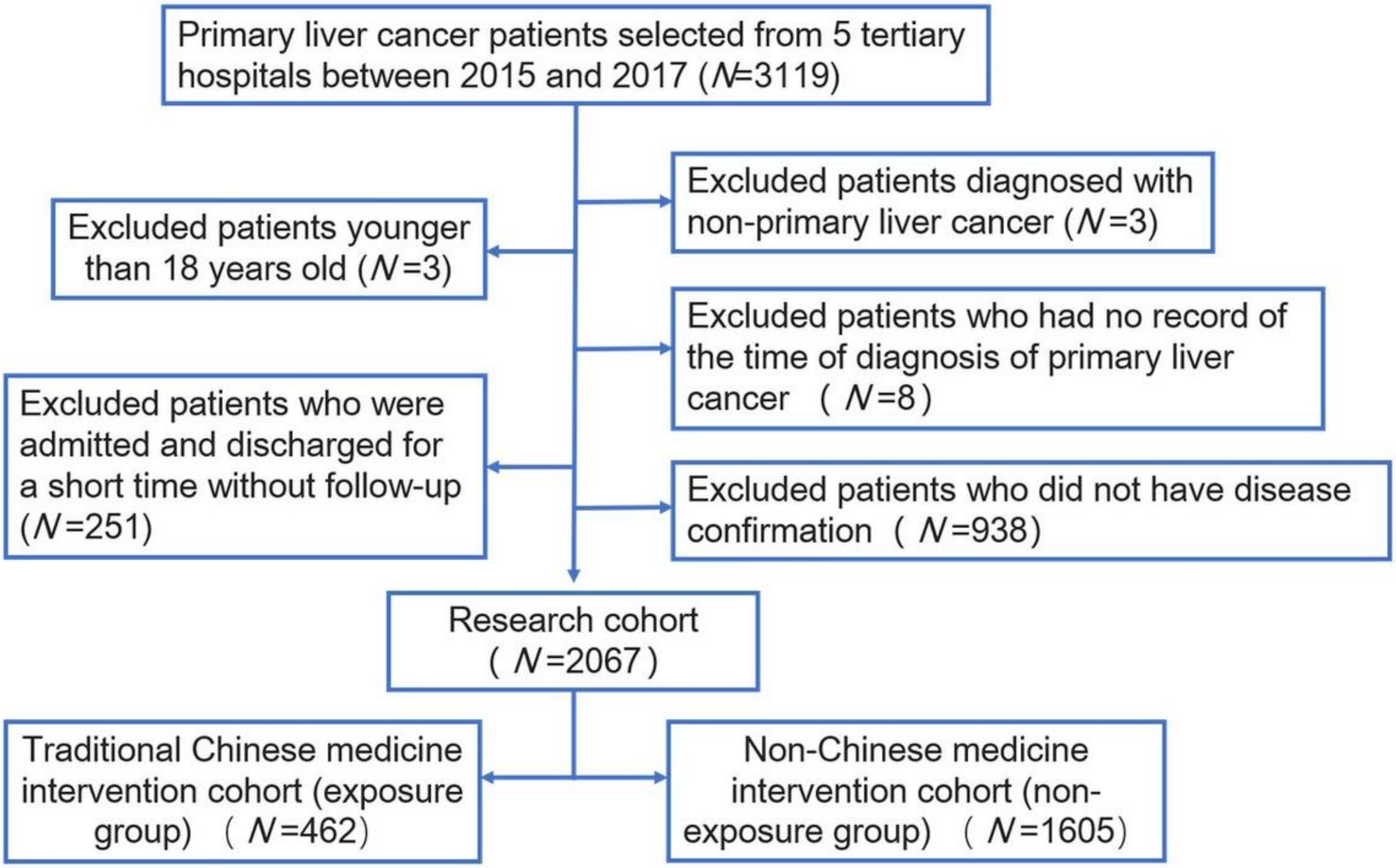

Figure 1

Chart of research cohort creation

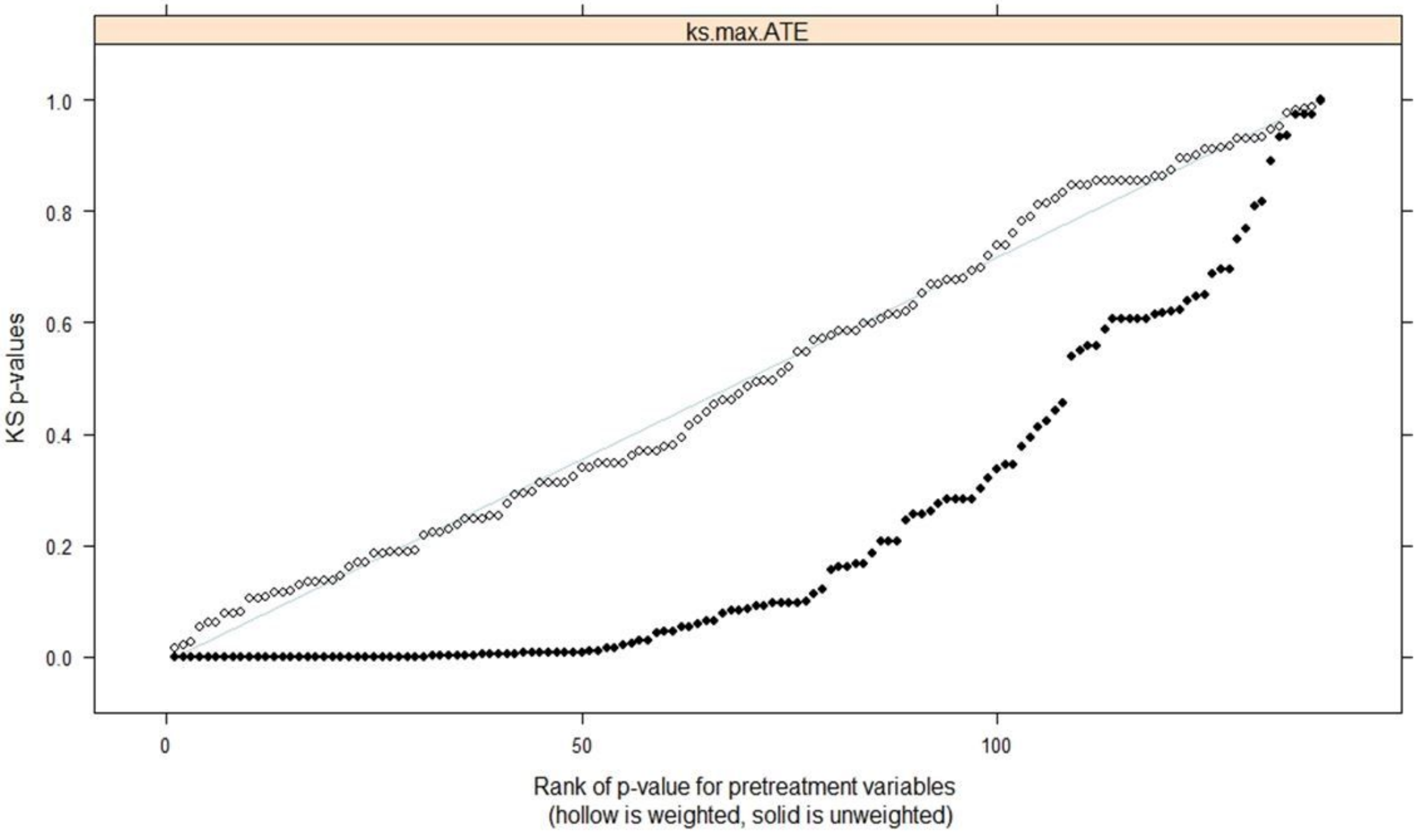

Figure 2

Comparison of the p-value and the uniform distribution value of the difference test between the two groups of confounding variables before and after weighting

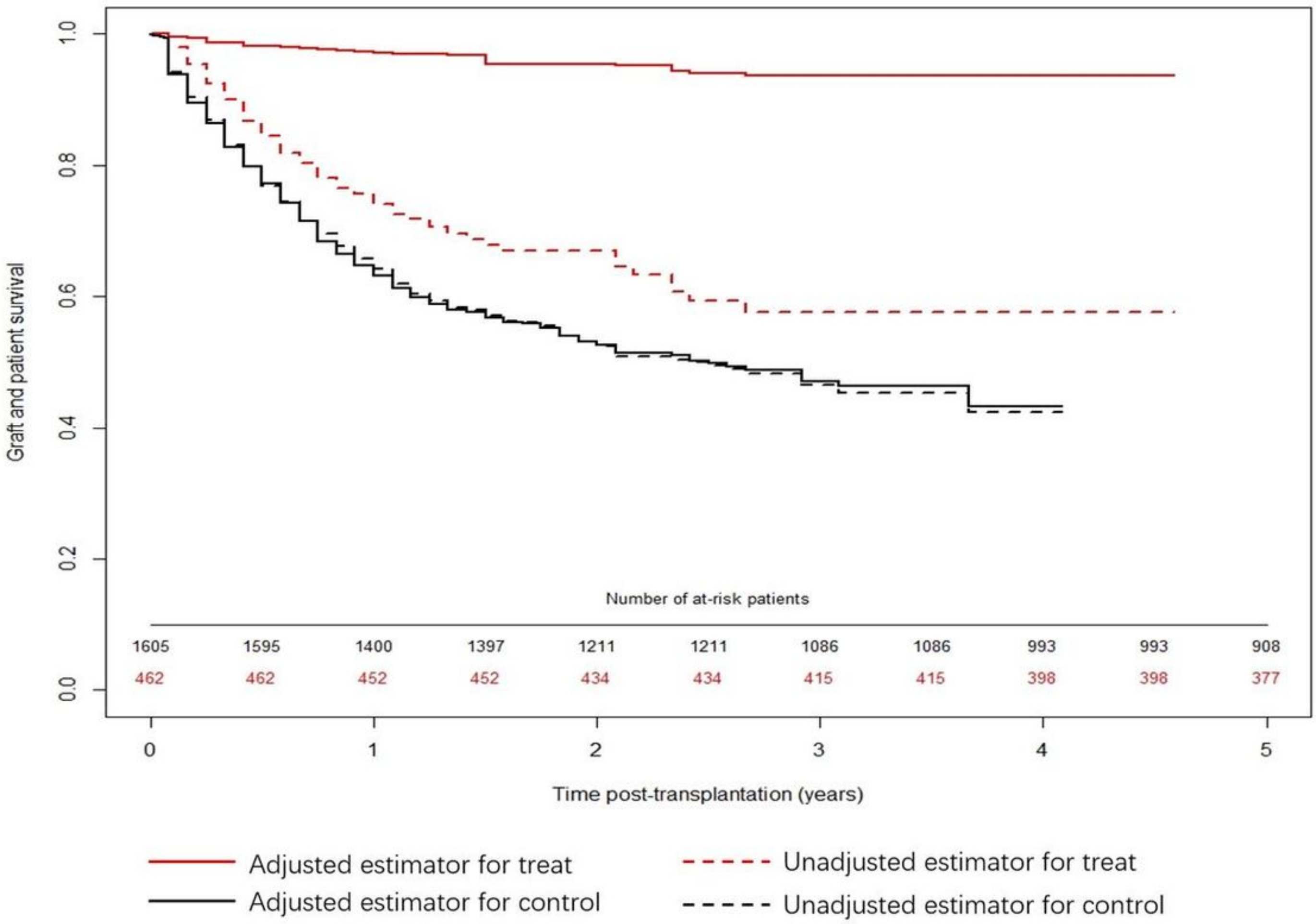

Figure 3

Distribution of the survival curves of the exposure group and control group before and after propensity score weighting