

Transitional Care for Patients with Cirrhosis: a Multidisciplinary Care Model for Prevention Complications Post-TIPS

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Abstract

AIM To evaluate the efficacy of transitional care interventions of multidisciplinary teams for patients with cirrhosis post-TIPS. METHODS 68 patients undergone TIPS were randomly allocated to control or intervention group. Patients in control group received conventional care, patients in the intervention group received conventional care combined with transitional care. The compliance behavior, incidence of HE and shunt dysfunction, Child-Pugh scores and ammonia of two groups were compared at 1,3,6 and 12 month post-TIPS. RESULTS Repeated measures analysis of variance showed significant group effects from 1,3,6 and 12 month post-TIPS for compliance behavior scores of the two groups. Intervention group had significant higher compliance behavior scores than control group 1, 3 and 6 month post-TIPS respectively. The incidences of HE the intervention group were significantly lower than control group 12 months after TIPS. The incidences of shunt dysfunction in the intervention group were significantly lower than control group 12 months after TIPS. The group effects ,time effects and group*time interaction showed no significant difference in Child-Pugh scores and blood ammonia between the two groups. CONCLUSION Post-TIPS transitional care interventions increase the accessibility of patients to scientifically informed nursing, significantly improve patients' compliance behavior and health, decrease the incidence of HE and shunt dysfunction. KEW WORDS Transjugular intrahepatic portosystemic shunt (TIPS); Transitional care; Compliance behaviors; Hepatic function.

Introduction

Transjugular intrahepatic portosystemic shunt (TIPS) is an important option for the management of complications of portal hypertension in patients with cirrhosis caused by various etiologies.^[1] TIPS is an effective emergency treatment for esophageal variceal bleeding in patients who have failed conventional therapy.^[2] Although TIPS can effectively resolve problems associated with portal hypertension, there are two main drawbacks to the procedure: the occurrence of shunt dysfunction and hepatic encephalopathy (HE), which are frequent post-TIPS complications. These two complications have significant implications in terms of quality of life and the long-term success of the procedure.

TIPS dysfunction, defined by a loss of decompression of the portal venous system, an increase in the hepatic venous pressure gradient to more than 12 mm Hg, or a recurrence of complications of portal hypertension,^[3] may occur because of stenosis or blockage of TIPS. ATIPS may be restored to full patency with mechanical unblocking^[4] or the placement of another stent.^[5] The use of polytetrafluoroethylene-covered stents enhances shunt patency.^[6] The incidence of TIPS dysfunction has significantly decreased; however, to maintain long-term shunt efficacy, TIPS patients need regular follow-up visits.

HE is one of the major complications that occurs post-TIPS.^[7] Approximately one-fifth to one-half of patients experience HE after the insertion of a TIPS.^[8-13] Unfortunately, no attempt to reduce the incidence of post-TIPS HE has been successful to date. A randomized controlled trial (RCT) failed to show an effect of the administration of non-absorbable disaccharides or antibiotics on the incidence of HE during the first month post-TIPS,^[14] which is another possible approach that is broadly thought to avoid the excessive diversion of portal blood using stents with smaller diameters, at least in patients at high risk of post-TIPS HE. However, the use of stents with a smaller diameter (8 vs 10 mm) failed to reduce the incidence of post-TIPS HE and was less efficient in controlling the complications of portal hypertension.^[15] Another potential solution is to use adjustable stent systems to modulate the portal pressure gradient (PPG) to reduce the incidence of HE. One of the difficulties associated with this solution is that the value of PPG required to avoid the occurrence of HE is unknown.^[16]

A controlled trial in cirrhosis patients showed that a nearly positive diet intervention improved patient compliance with a low-protein diet and reduced the incidence of HE.^[17] While the exact pathogenesis of post-TIPS HE is complex and unknown, the known risk factors associated with post-TIPS HE in patients with portal hypertension due to cirrhosis are non-alcoholic liver disease, female gender, low albumin levels, older age, hepatic functional status, and the presence of a portosystemic pressure gradient.^[18-20] Patients are expected to be monitored overnight following the procedure for these complications. Thus, a careful and evidence-based efficacious prophylactic treatment to prevent the occurrence of HE is greatly needed.

Transitional care interventional programs are usually multidisciplinary in nature and aimed at improving health care provider outcomes through improvements in care coordination and continuity for patients in the transition between health care settings.^[21] The theoretical concept underlying transitional care interventions is that readmissions are largely preventable if issues that predispose patients to return to the hospital for treatment can be addressed.^[21] Transitional care interventional programs have been targeted at patients with specific diagnoses^[22,23] or focused on general medical patients at an average risk of readmission.^[24,25] A new model of specialized caregiving, which is based on a series of diagnostic imaging performed in real time and on the integrated activity of consultant

hepatologists in outpatient departments, dedicated nurses, physicians in training, and primary physicians, has reduced the rates of 30-day readmission and 12-month mortality in patients with cirrhosis and ascites.^[26] There have been few well-designed studies supporting the effectiveness of transitional care for patients with cirrhosis post-TIPS, primarily due to the multifaceted nature of these complex portal hypertension complications and the difficulty of performing randomized controlled studies on transitional care interventions.

We conducted a RCT to determine whether multidisciplinary and patient-centered transitional care interventions for patients with cirrhosis post-TIPS would improve compliance behavior and reduce complications post-TIPS. We hypothesized that:

- 1) Patients referred to transitional care interventions would have significantly higher total scores of compliance behavior associated with complications post-TIPS than the control group.
- 2) Patients referred to transitional care interventions would exhibit significantly lower incidence of HE and shunt dysfunction.
- 3) Patients who experienced transitional care interventions would exhibit significantly greater improvement in their Child-Pugh scores and blood ammonia levels post-TIPS than the control group.

Methods

2.1 STUDY DESIGN

The prospective, quasi-experiment was conducted from January 2013 to December 2015 in the Third Affiliated Hospital of Shihezi University (Shihezi City People's Hospital).

The study protocol was approved by the ethical committees for human investigations at the Third Affiliated Hospital of Shihezi University and by the Local Department of Health and Family Planning Commission. The study protocol also fulfilled the guidelines of Good Clinical Practice in clinical trials. The study was registered in an independent clinical trial database (www.clinicaltrials.gov; identifier: NCT02877953)(08/23/2016). The purpose of the study, enrolment, follow-up, and details of the TIPS operation were explained to all the patients, and written informed consent was obtained. All data were recorded on regularly monitored case report forms that were entered into a database by the same investigator. All authors had access to the study data and reviewed and approved the final manuscript.

2.2 PARTICIPANTS

A total of 76 patients who underwent TIPS insertion successfully and had a diagnosis of cirrhosis (ICD-9 code) were included in the study. Cirrhosis was diagnosed by specialized physicians in training and primary physicians based on biopsy, endoscopy, or radiological evidence of portal hypertension or cirrhosis and/or signs of hepatic decompensation (HE, ascites, variceal bleeding, and jaundice).^[27]

Study inclusion criteria:

- clinical diagnosis of cirrhosis
- Child-Pugh score ≥ 10
- informed consent

Study exclusion criteria:

- age < 18 years
- right ventricular failure
- severe systemic infection
- hepatocellular carcinoma (HCC)
- terminal disease
- failure to provide written consent to participate in the study.

We excluded 8 patients from the study, two of whom were diagnosed with HCC, and Child-Pugh scores of the rest of 6 participants were more than 10. Figure 1 shows an illustration of the study design.

2.3. RANDOMIZATION

Patients who underwent TIPS were assigned to the control group or intervention group randomly. Sixty-eight subjects who met the inclusion criteria underwent TIPS insertion and were effectively enrolled and randomized to the transitional care intervention group (n=34) or control group (n=34). All patients were followed for a period of at least 12 months or until death.

2.4. CONTROL GROUP

During each patient's hospital stay, the transition nurses created a transitional care file that included information on the patient (inpatient medical and nurse care plan and medications) and the discharge plan, which included information on how to prevent gastrointestinal bleeding, infection, and constipation, how to eat a quality low-protein diet, how to recognize minimal HE, how to monitor blood ammonia levels, how to deal with the adverse drug reactions of anticoagulants, and scheduled regular return visits (1, 3, 6, and 12 months post-TIPS). An evidence-based transitional care handbook with all these details was given to the participants post-TIPS.

On the day of discharge of the patient from the hospital, a transition nurse met with the patient to review the follow-up recommendations. The transition nurse verified that the medications were prescribed in accordance with the discharge plan and that the patient and his/her caregiver understood the anticoagulant, liver-protective agent, and lactulose prescriptions and were informed of the planned appointments and the blood biochemistry monitoring.

12 months after hospital discharge, a transition nurse followed-up with the patient once a month by telephone.

2.5. INTERVENTIONS

In addition to receiving the same care as the control group, the patients in the intervention group received transitional care interventions provided by a multidisciplinary team composed of dedicated nurses, transition nurses, physicians in training, and primary physicians by telephone follow-up, family visits, and WeChat guided online sessions. Before discharge, the transition nurses provided the patients with kitchen pan scales to facilitate the maintenance of a high-quality low-protein diet.

2.5.1. Telephone follow-up:

Each telephone follow-up lasted approximately 10-15 minutes and was implemented within 72 hours after the patient was discharged. Follow-up phone calls occurred at 2, 4, 6, and 8 weeks, followed by once a month thereafter. Dedicated nurses were informed of the symptoms of patients, the presence of complications, and the psychological state of patients, and they provided specific guidance for complications and consulted primary care physicians when necessary. Participants with serious complications were admitted to the hospital. Meanwhile, the frequency of telephone follow-ups increased as appropriate.

2.5.2. Family visit:

Family visits were carried out for the patients who did not return regularly for visits 1, 3, 6 and 12 months after discharge. Each visit lasted between 30 and 45 minutes. Dedicated nurses assessed the patient's health status, including vital signs, monitored blood ammonia through a portable blood ammonia detector, and helped patients master simple nursing procedures, such as white vinegar (The main composition of white vinegar is acetic acid which could reduce the absorption of blood ammonia) clysis.

2.5.3. Network communication platform

The QQ and WeChat Internet platforms were used to strengthen communication between the subjects and the multidisciplinary team. Timely online guidance for patients could also be provided. In addition, the latest scientific knowledge regarding cirrhosis and TIPS could be uploaded to the Internet. Transition nurses and physicians were available online to guide patients every Tuesday and Friday night from 20:30 to 21:30.

2.5.4. Intervention content

(1) The prevention of risk factors for HE

Diet cards were custom-made to prevent gastrointestinal bleeding based on the evaluation for

esophageal gastric varices. Patients were guided on how to prevent infection of the upper respiratory tract, the digestive tract, and wounds and how to eat a high-quality low-protein diet. Minimal HE was evaluated by symptom recognition, a digital symbols experiment, and a digital connection test A-1. The multidisciplinary team focused on identifying the cause of infection and took appropriate and timely measures, such as medication by oral or local application, diet adjustment, and white vinegar clysis, to prevent and treat constipation. It was important for the participants to make regular return visits to monitor their blood ammonia levels.

(2) The prevention of shunt stenosis and occlusion

We urged patients to accept regularly doppler ultrasound, so that we can early found shunt

stenosis and take measures timely. During the short-term of postoperative anticoagulation, another

effort were also made to prevent adverse drug reactions associated with anticoagulation medication.

2.6. DATA COLLECTION

Subjects were followed for 12 months or more post-discharge to monitor clinical symptoms. Collected data included the following: (1) demographic characteristics; (2) compliance behavior; and (3) clinical data including cirrhosis etiology, routine blood tests, coagulation tests, hepatic function tests (Child-Pugh score), blood ammonia levels, color ultrasound, CT scans, and/or gastroscopy. Ultrasonography was repeated monthly to exclude shunt dysfunction. Adverse events, such as HE, TIPS dysfunction, readmission details, and death, were recorded in a new database. HE often occurs in cirrhosis patients within 3 months after the TIPS procedure.^[28]

2.6.1. Primary Outcome Measures: Compliance Behavior

Time Period: 1, 3, 6 and 12 month after discharge

The compliance behaviors of post-TIPS patients with cirrhosis were surveyed using a self-designed questionnaire.^[29] The questionnaire included reminders to take medicine on time, eat a high-quality and low-protein diet, go to sleep at a regular time, engage in moderate exercise, regulate emotions, and attend regular follow-ups. Item responses were documented on a 4-point scale (0 = never to 3 = always). Total scores ranged from 0 to 18, with higher scores indicating better compliance. Data were collected by face-to-face interviews with trained transition nurses.

2.6.2. Secondary Outcome Measures:

(1) Incidence of adverse events: shunt dysfunction and HE. The evaluation of the degree of HE was based on the alteration of the patient's mental state using modifications of the West Haven Criteria (Connett et al. 1977).

Time Period: 12 months after discharge

(2) Child-Pugh scores and blood ammonia levels

Time Period: Baseline, 1, 3, 6 and 12 month after discharge

2.7. SAMPLE SIZE

Approximately one-fifth to one-half of patients experience HE after TIPS insertion. To decrease the incidence of HE by 20%, with an alpha of 0.05 and a beta of 0.10, the study should have included 66 patients (33 per arm). Sixty-eight subjects were enrolled in our study.

2.8. STATISTICAL ANALYSES

Statistical analyses were conducted using SPSS version 17.0 (Chicago, IL, United States). Summary statistics for continuous variables are presented as the means with standard deviations or standard errors of the mean for comparison tests and as proportions for categorical variables.

The chi-square test was used to determine the differences in proportions. Continuous variables were compared with the unpaired Student's t test (or the nonparametric Mann-Whitney rank-sum test, when required) and repeated measures analysis of variance. Patients were considered lost to follow-up if they did not attend two consecutive 12-month clinical examinations. Statistical significance was established at a P value <0.05.

Results

3.1 Baseline Characteristics

Between 2013 and 2015, 68patients who had previously undergone TIPS were identified and enrolled in the study.Demographic and procedural data for the entire population and a comparison based on Child-Pugh scores are summarized in Table 1.Both groups were comparable with respect to age; gender; education (highest qualification); occupation;disease etiology; and severity of liver disease, including Child-Pugh scores.7 participants died and 7were lost to follow-up in the control group. 4 participants died and 1were lost to follow-up in the control group.

3.2 Primary Outcome Analysis

As shown in Tables3, repeated measures analysis of variance showed significant group effects from 1 month,3 month,6 month to 12 month post-TIPS for compliance behavior scores of the two groups ($F=6.768, P=0.016$). To clarify the difference in compliance behavior scores between the two groups at different time points, multivariate analysis of variance was used to compare differences between the two groups at each time point. The results showed that intervention group had significant higher compliance behavior scores than control group 1month ($F=7.067, P=0.014$), 3 month ($F=5.388, P=0.029$) and 6 month ($F=5.531, P=0.027$) post-TIPS respectively (Table 4). Fig.2 showed changing trend of compliance behavior scores between the two groups, both were down before they rise. While, the compliance behavior scores of the intervention group were higher than the control group in the diagram.The data further showed that the intervention group had bettercompliance behaviors thanthe control group.

3.3 Secondary Outcome Measures

As expected, the incidence of HE, was significantly lower in the intervention group than the control group 12 months after TIPS[23.53% (8/34) in the intervention group versus 32.35%(11/34) in the control group, $Z=-2.62, P<0.01$] (Table 2).The incidences of shunt dysfunction in the intervention group(8.82%,3/34) were significantly lower than those in the control group

(29.41%,10/34)12 months after TIPS ($=4.66, P<0.031$). The group effects,time effects and group*time interaction assessed by repeated measures analysis of variance showed no significant difference in Child-Pugh scores and blood ammonia levels between the two groups($P>0.05$).

3.4. Secondary Outcome Measures

The group effects,time effects and group*time interaction assessed by repeated measures analysis of variance showed no significant difference in Child-Pugh scoresbetween the two groups 1,3,6 and 12 month post-TIPS , $P>0.05$. (Table 3)

The measured blood ammonia levels were not normally distributed.The data were normally distributedafter square root transformation. Repeated measures analysis of variance was used to compare differencesin the blood ammonia levels between the two groups at each time point. However, the time effects and group-time interaction assessed byrepeated measures (RM) ANOVA showed no difference between the two groups at different time points($P>0.05$) (Table 3).

Discussion

TIPS insertion is an effective method for resolving the symptoms of portal hypertension.^[30]After TIPS insertion, the portal vein blood flow to the liver is reduced, and the hepatic artery bloodflow is increased to compensate for this reduction,^[31,32]based on the interdependence of the portal vein and hepatic artery. However,increases in the symptom recurrence rate and the incidence of HE after TIPS, which may adversely affect quality of life and accelerate liver function deterioration, are the main cause of death.^[33]In fact, HE is very frequent post-TIPS insertion and may be persistent and refractory to medical treatment in a minority of patients, thus significantlyaffecting quality of life.^[34] Therefore, efforts at discharge must focus on this high-risk group of patients to decrease the incidence rate of complications post-TIPS.

Transitional care has been demonstrated to greatly reduce the risk of readmissions of patients with conditions such as congestive heart failure and could be an option for patients with cirrhosis.^[35]A recent single-center study in patients with cirrhosis and ascites showed that this multidisciplinary transitional care approach that included managing cirrhosis complications and ensuring optimal follow-up and prompt communication with outpatient teams, not only reduced readmissions but also improved overall mortality.^[26]Consistent with this report, the results of the present study suggest that transitional careinterventions provided by a multidisciplinary team could improve

compliance behavior and decrease the incidence of HE and shunt dysfunction 12 month post-TIPS. In this study, patients who received transitional careinterventions from a multidisciplinary team reported significantly higher compliance behavior scores. The intervention group had better compliance with the items of maintaining a high-quality low-protein diet, taking medicine on time, going to sleep at a regular time, engaging in moderate exercise, regulating emotions and attending regular follow-up at three time points post-TIPS.

Because patients are vulnerable soon after leaving the hospital, post-discharge telephone calls, which is an important part of transitions of care, may improve clinical outcomes.^[36] Some studies in this review showed improvement in outcomes, such as knowledge, adherence, satisfaction, emergency department (ED) visits, and readmissions.^[37,38] Luo et al. showed that early positive dietary intervention can significantly improve the compliance of cirrhosis patients with maintaining a low-protein diet and reduce the incidence of HE.^[17] According to these studies, increasing compliance scores were associated with a decreased risk of adverse events. Consistent with these reports, the results of the present study also showed that transitional careinterventions can dramatically decrease the incidence of HE and shunt dysfunction. To improve clinical outcomes post-TIPS, transitional careinterventions may be an important initiative worth considering.

TIPS insertion results in the portosystemic shunting of blood, which markedly reduces first-passhepatic clearance of intestinally derived neurotoxins such as ammonia. Furthermore, there is also an upregulation of intestinal glutaminase activity, which results in increased ammonia production in the intestine.^[39,40] As a result, blood ammonia levels play an important role in monitoring/

preventing HE post-TIPS. The present results showed that the time effects and group-time interaction determined by RM ANOVA showed no differences in the blood ammonia levels between the two groups at different time points. Nonetheless, the study results showed that the two groups had a different incidence of HE. The sharp rise in blood ammonia levels may still predict the possible recurrence of HE post-TIPS. Therefore, continuous monitoring of blood ammonia levels in post-TIPS patients is recommended.

Limitations

Our data should be interpreted in light of several limitations, which are common to most prospective analyses. First, potential bias may be present in the selection of samples. Subsequent transitional carestudies should be stratified according to risk factors of complications post-TIPS. Second, the trial could not be blinded; however, it is unlikely that this had any effect on our findings, as the outcomes were objective. Third, the follow-up periods were relatively short, so the long-term effects of transitional careintervention on the prevention of complications post-TIPS are still not clear.

Conclusion

In conclusion, transitional careintervention by a multidisciplinary team for 12 month post-TIPS can significantly improve the compliance behavior of cirrhosis patients, reduce the incidence of complications post-TIPS, and improve patient health status.

Declarations

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Author Contributions

H.W., X.Y., W.Q. contributed equally to this work. H.W. and W.Q. conceived the study and developed the contents of the evidenced-based transitional care handbook post-TIPS. X.Y., Y.R., F.X. and L.J. carried out the patient recruitment and coordinated the study. X.Y., Y.R., F.X. participated in the transitional care intervention follow-ups. H.W., C.J. and W.C. completed the statistical analyses and wrote the manuscript. W.Z. participated in the design of the study and assisted in drafting the manuscript. All authors read and approved the final manuscript.

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Institutional review board statement

The study protocol was approved by the ethical committees for human investigations at the Third Affiliated Hospital Shihezi University and by the Local Department of Health and Family Planning Commission.

Clinical trial registration statement

The study protocol also fulfilled the guidelines of Good Clinical Practice in clinical trials. The study was registered in an independent clinical trial database (www.clinicaltrials.gov; identifier: NCT02877953) (08/23/2016).

Imformed consent statement

All authors had access to the study data and reviewed and approved the final manuscript.

Conflicts of Interest

There are no conflicts of interest.

Data sharing statement

No additional data are available.

Consort 2010 Statement

The authors have read the CONSORT 2010 Statement, and the manuscript was prepared and revised according to the CONSORT 2010 Statement

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Tables

Table 1. Comparison of the baseline characteristics of the post-TIPS patients between the control and intervention groups.

Variable	Control group (n=34)	Intervention group (n=34)	t/ value	P value
Age(y)	55.26±11.12	51.58±11.58	1.34	0.186
Gender			1.72	0.294
Male	21	26		
Female	13	8		
Etiology			4.27	0.233
HBV	28	21		
HCV	3	8		
Cholestasis	2	2		
Budd-Chiari syndrome	1	3		
Education (highest qualification)			1.03	0.795
Primary school	2	2		
Junior high school	8	10		
Senior high school or technical secondary school	19	15		
University or above	5	7		
Occupation			8.03	0.236
Farmers	6	6		
Workers	5	9		
Professional and technical personnel	7	4		
Civil servants	3	5		
individual	10	4		
Medical staff	1	0		
other	2	6		
Child-Pugh score post-TIPS	8.5±0.76	8.75±1.48	0.191	0.667
Blood ammonia	9.93±3.36	9.22±2.20	0.715	0.480

Table 2. The incidence of hepatic encephalopathy between the control and intervention groups 12 months post-TIPS

Groups	Stage of hepatic encephalopathy				
	0	1	2	3	4
Control group(n=34)	1	1	0	4	5
Intervention group(n=34)	2	3	1	1	1

Table 3. Repeated measures analysis of variance of compliance behavior scores,

Child-Pugh scores and blood ammonia levels in the control and intervention groups

Items	Groups	1 month post-TIPS	3 months post-TIPS	6 months post-TIPS	12 months post-TIPS	F values of group effect	P values	F values of time effect	P values	F values of group*time interaction	P values
scores of compliance behavior	Control group	11.92±1.98	11.77±2.20	11.46±2.11	11.84±1.86	6.768	0.016	0.538	0.583	0.022	0.976
	Intervention group	13.76±1.54	13.69±2.02	13.38±2.06	13.62±2.98						
Child-Pugh scores	Control group	8.50±2.64	8.25±2.50	8.01±2.58	7.52±2.51	0.287	0.600	1.655	0.191	0.117	0.950
	Intervention group	8.17±1.58	7.42±1.67	7.67±1.87	7.00±1.65						
Blood ammonia levels	Control group	10.04±1.67	9.45±1.89	9.25±1.72	9.38±1.36	0.041	0.842	1.135	0.324	0.153	0.804
	Intervention group	10.28±1.98	9.26±1.38	8.85±1.16	8.71±1.59						

Table 4. Compliance behavior scores of the participants in the control and intervention groups at different time points post-TIPS

Groups	1 month post-TIPS	3 months post-TIPS	6 months post-TIPS	12 months post-TIPS
Control group	11.92±1.98	11.77±2.20	11.46±2.11	11.84±1.86
Intervention group	13.76±1.54	13.69±2.02	13.38±2.06	13.62±2.98
F values	7.067	5.388	5.531	3.282
P values	0.014	0.029	0.027	0.083

Figures

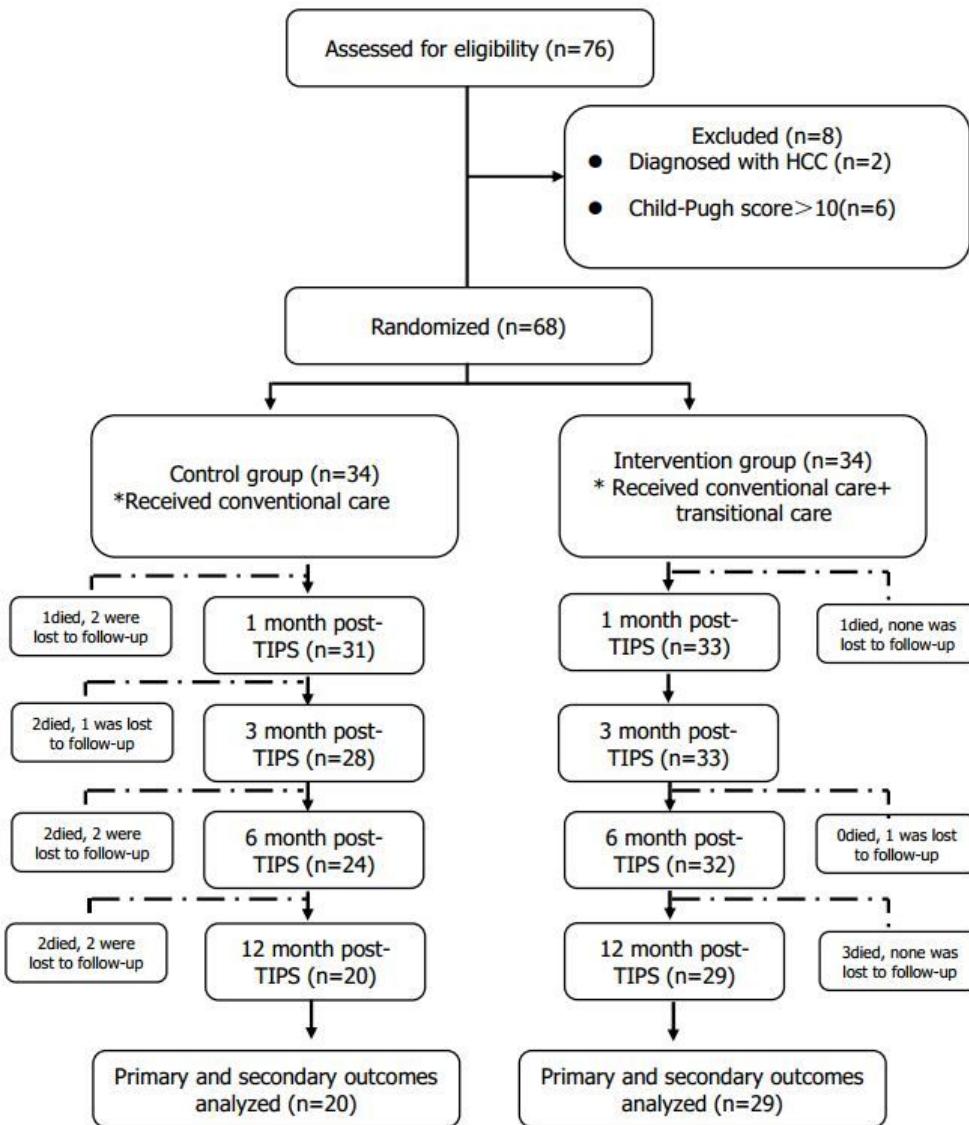


Figure 1

Study design

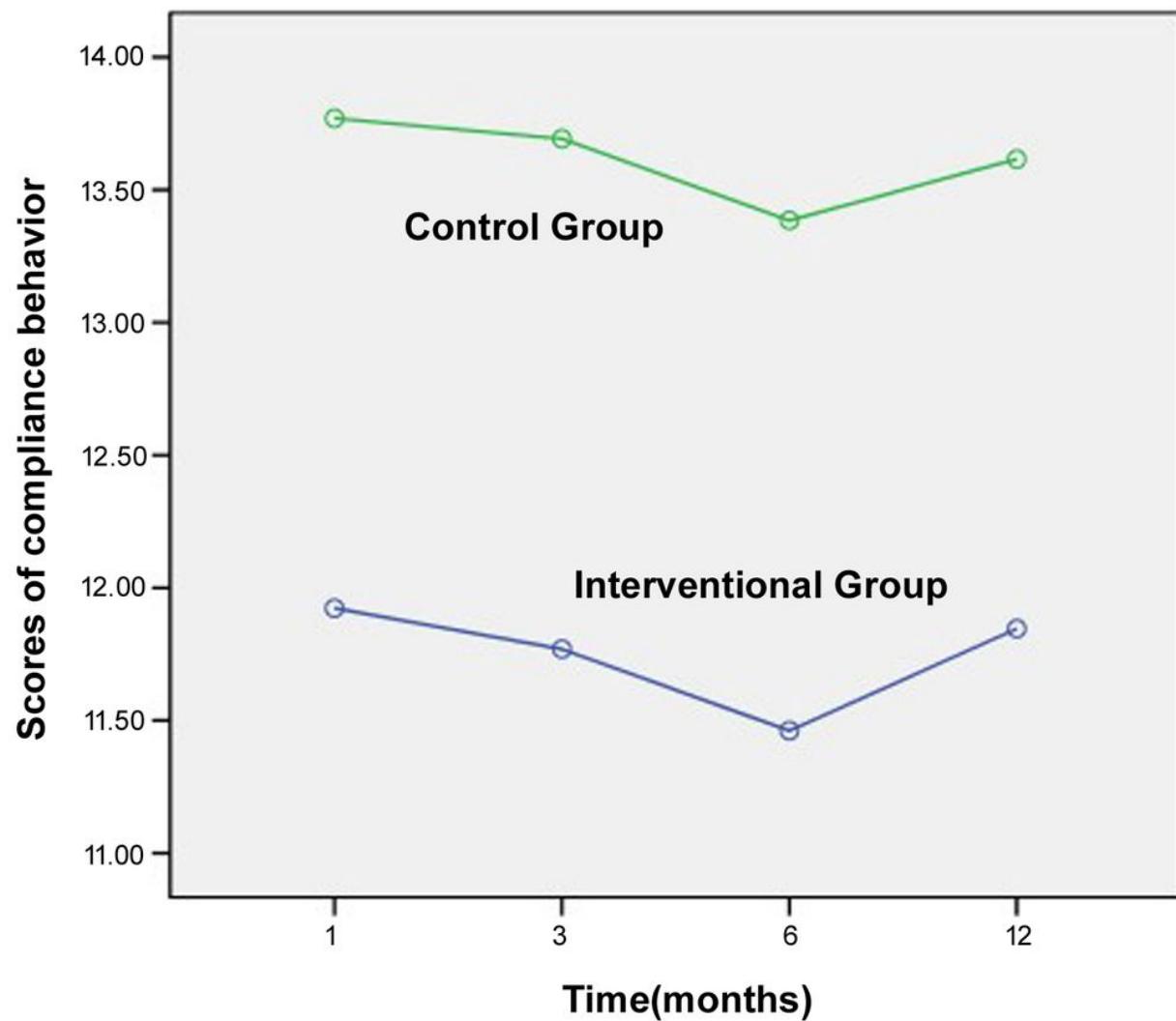


Figure 2

Scores of compliance behavior