Research Plan

A Study on the Comparison of Success Rate and Side Effects of the Conventional Method and the Method Using a New Fixation Device in Performing Ascites Puncture in Cirrhotic Patients with Ascites

Comparison of success rate and complication between conventional versus new anchoring device using paracentesis for cirrhotic patients with ascites

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1. Title of the research

(Korean) 복수를 가진 간경변증 환자들에서 복수천자 시행 시 고식적인 방법과 새로운 고정장치를 사용한 방법의 성공률 및 부작용 비교에 관한 연구

(English) Comparison of success rate and complication between conventional versus new anchoring device using paracentesis for cirrhotic patients with ascites

2. Name and address of the institution

1) Name of the institution : Soonchunhyang university Bucheon hospital

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2) Support institution: ㈜다림양행

3) Participating institusion

	Institution	Research director
1	Inje University Haeundae Paik Hospital	허내윤
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4. Research Background

When cirrhosis occurs due to various causes, such as chronic hepatitis B and alcohol, intestinal vasodilation occurs due to portal hypertension and effective plasma volume decreases.[1] Ascites is a major complication of cirrhosis and occurs in 50% of cirrhosis patients after 10 years of follow-up.[2] At this time, ascites that is not controlled despite a low-salt diet of 40 mmol/day and high-dose diuretic treatment (spironolactone 400 mg/day + furosemide 160 mg/day) is defined as

refractory ascites, and diuretic-resistant ascites and diuretics Diuretic-intractable ascites can be divided into two types.[2,3]

There are clinical studies showing that albumin administration and repeated therapeutic ascites puncture are relatively safe and effective in cirrhosis patients with large amounts of ascites or refractory ascites.[4,5,6] In cirrhosis patients with refractory ascites, puncture is usually performed using an 18G angiocatheter. However, with conventional methods, the catheter is pulled out during ascites drainage and re-puncture is frequently performed. In many cases, the continuation of the catheter is unstable because it is fixed using tape and gauze without a special fixing device. The carahox set is a medical device created to compensate for the instability of maintaining the catheter. This study aims to suggest a convenient and safe therapeutic ascites method for patients with refractory ascites cirrhosis by comparing the success rate, re-puncture rate and complications of ascites puncture using a traditional method and a new fixation device.

5. Research Hypothesis

In patients with refractory ascites, the ascites puncture method with a new fixation device will have a higher success rate than the existing vascular catheter puncture method.

6. Research Objective

1) Primary Purpose

Comparison of success rates of ascites puncture between palliative ascites and kara-hoc in patients with cirrhosis with refractory ascites2) 이차 목적

a. Surgical complications
b. Patient satisfaction
c. Operator satisfaction
d. Factor of successful puncture
e. Number of re-puncture

7. Research Population

7-1. Target Disease

Liver cirrhosis with ascites

7-2. Inclusion Criteria)

If all of the conditions below are met

1) Adult men and women over the age of 19

2) Patient with pathological or clinical diagnosis of cirrhosis
3) Patients with Grade 2 or higher ascites as a complication due to portal hypertension
4) Patients who are symptomatic and need regular ascites puncture
5) Patients consenting to this study

7-3. Exclusion Criteria

If any of the following conditions apply
1) Patients with ascites due to peritoneal metastasis due to malignant tumor
2) Patients with high bleeding risk (PT INR>3, PLT<30,000/mm3) difficult to perform ascites
3) Hepatic encephalopathy or hepatic nephrotic syndrome
4) Severe cardiovascular disease, lung disease, or DIC
5) Paracentesis refusal
6) Patients with ascites control possible with diuretics
7) Pregnancy

7-4. Target number of cases and calculation basis

In a preliminary study conducted on 20 cirrhotic subjects, 12 cases of successful puncture for ascistes using both Kara-hoc and conventional method were performed, 5 cases of success only with Kara-hoc, and only 1 case of success with conventional method, with a difference of 20%, and a total of 61 cases were required, and 80 cases were required when the drop-out rate of 30% was taken into account.

McNemar Test Analysis

Numeric Results for Two-Sided Test

Power	N	P10	P01	Difference (P10-P01)	Proportion Discordant	Odds Ratio	Alpha	Beta
0.80516	61	0.250	0.050	0.200	0.300	5.000	0.050	0.19484

References

Schork, M. and Williams, G. 1980. 'Number of Observations Required for the Comparison of Two Correlated Proportions.' Communications in Statistics-Simula. Computa., B9(4), 349-357.
Machin, D., Campbell, M., Fayers, P., and Pinol, A. 1997. Sample Size Tables for Clinical Studies, 2nd Edition. Blackwell Science. Malden, MA.

7-5. Research Subject Recruitment Plan

Registered patients are recruited for patients with cirrhosis who require therapeutic ascites puncture due to intractable ascites among patients with cirrhosis who have visited the gastroenterology department outpatient department, ward, and emergency room.

7-6 . Additional protection measures in case of inclusion of vulnerable research subjects

Vulnerable subjects, such as children, pregnant women, and patients with hepatic encephalopathy, who are likely to have difficulty obtaining informed consent due to cognitive decline, were excluded from the study.

8. Expected study period

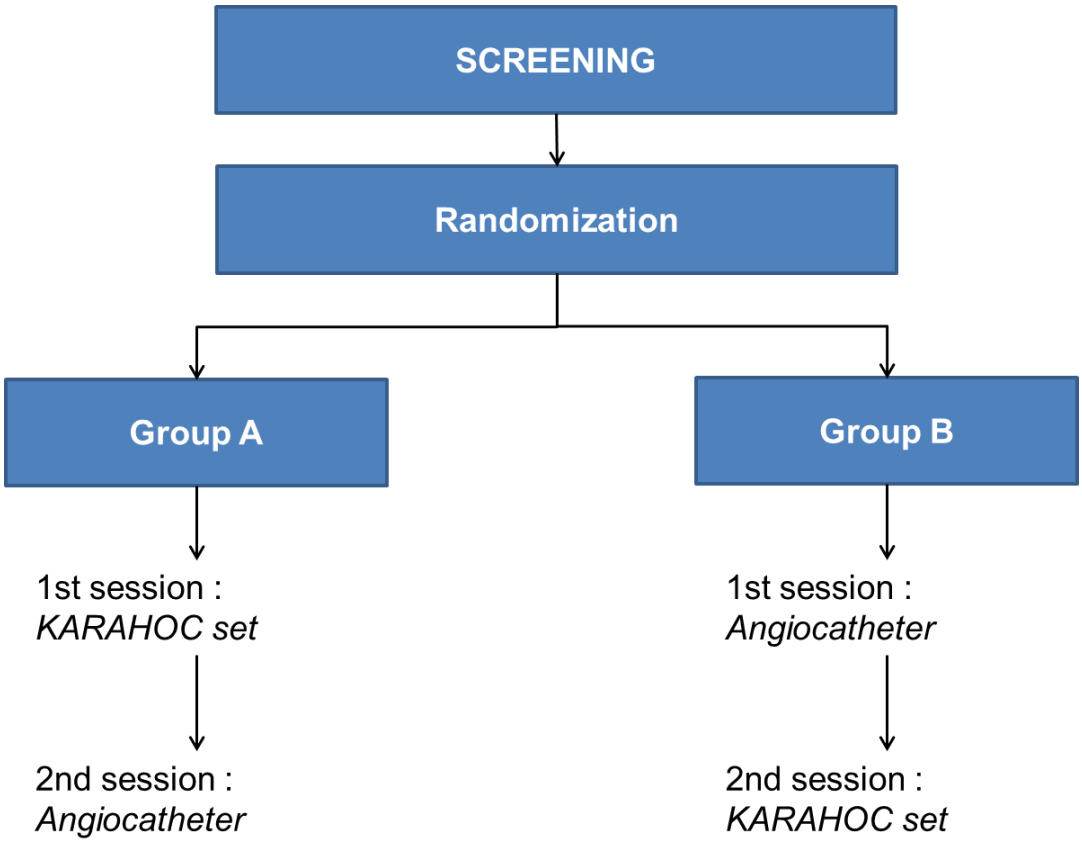
From IRB approval date to December 31, 2022

9. Research method (including observation/inspection items)

This study is a multi-center, prospective, interventional study, in which subjects who meet the selection criteria are enrolled at each institution during the study period from the date of research approval. The diagnosis of liver cirrhosis of the subject is made when there is a clear liver surface nodule in the performed imaging test and the liver biopsy is F4 or the liver elasticity measurement method is 11 kPa or more. is based on Subjects should perform multiple puncture at least twice during the outpatient or hospitalization period, and perform Karahoc puncture and vascular catheter puncture once each, and the order is set at random. The standard for successful ascites puncture is set as 3L or more of drainage when performing one puncture, and re-puncture is judged when ascites does not drain from the beginning after catheter insertion or when it is drained to less than 1L due to lumen obstruction or catheter dislocation. do. HR and BP measurements (immediately before and after multiple puncture and drainage are completed) before and after ascites are performed to compare the incidence of complications that may occur in each of the multiple puncture methods.

1) Primary evaluation item: success of multiple puncture
2) Secondary evaluation items: Occurrence of surgical complications, patient satisfaction, operator satisfaction, number of re-punctures

[Figure 1] Study flow chart



10. Evaluation Criteria and Evaluation Method

- Multiple puncture success : Drainage of 3L or more per puncture
- Complications : Bleeding, hematoma, intestinal perforation, hypotension, etc.
- Patients satisfaction : Assessment with Visual Analogue Scale

- Operator satisfaction : Assessment with Visual Analogue Scale
- Re-puncture : When ascites does not drain from the beginning after catheter insertion, or when it drains less than 1 L due to lumen obstruction or catheter dislocation and requires re-puncture

11. Differences from conventional treatment and this study (standard treatment guideline description of the target disease)

Patients with intractable ascites who have severe abdominal distension and dyspnea are referred to in the medical guidelines to perform a mass ascites puncture. Ascites puncture using the Kara-hoc set is also different in that it uses an improved puncture device with an abdominal wall fixation device according to the general indications for mass ascites puncture.

12. Result Variable

Whether the plural puncture was successful

13. Safety Assessment

Measure the pulse rate and blood pressure before and after multiple puncture, and check the properties of the liquid drained immediately after puncture to check for bleeding or intestinal perforation.

14. Data and Statistical Analysis

Comparison of the success rate of ascites puncture using the conventional method and the Karahoc device is a procedure that is repeated once in the same patient, so the influence of other confounding variables can be excluded and analyzed using the McNemar test. Multivariate analysis is performed using logistic regression for factors involved in treatment success in the entire patient group. Patient and operator satisfaction is quantitatively measured using Visual Analogue Scale, and then the average value of satisfaction is compared through t-test.

15. Secruing research ethics

The procedures stipulated in this protocol will ensure that researchers comply with the fundamental spirit of the GCP and the Declaration of Helsinki in conducting, evaluating and recording the results of this study, and will be implemented in accordance with the KGCP, the Law on Bioethics and Safety and related regulations.

This research protocol and its changes, (subject written consent and) related to information provided to the subject, are submitted to the IRB of the conducting institution to obtain formal approval for the conduct of the study in accordance with domestic regulations, and the IRB for conducting the study The study will not be conducted prior to receipt of the documentation relevant to the decision.

16. Matters concerning the protection of personal information of research subjects

In order to protect the information of the research subjects, unnecessary personal identifiers of the collected data are removed. In particular, in the case record, the patient's name, resident registration number, Chart No. etc. should not be recorded, and the identifier code linked to personal information is managed separately. In addition, when presenting research results, make sure to present them in a form that cannot confirm the identity of the individual.

17. Research subject information and consent form

This study is for patients with refractory ascites, and the names of all subjects are kept confidential and the subjects are identified during recording and evaluation by the number assigned in the study. Inform the study subjects that all research data will be stored on a computer and treated in strict confidentiality. The subject consent form that has been signed is kept by the research director. By signing this protocol, the principal investigator agrees to obtain informed consent from the research subjects participating in the study, and also to receive due diligence upon request.

18. 연구자료 관리 및 보관

Electronic document files will be stored by installing an appropriate firewall and setting a password, and the password should be changed periodically. In addition, the person who can access the research file should be limited to those who are registered in the research and have the right to access. Relevant records should be stored in a secure space with controlled access or in a file storage with a lock. The data collected in the clinical trial will be stored for 3 years from the study end date and then destroyed, and after the end date, these documents will be transferred to a designated place such as a document storage room to prevent damage or loss due to accidents.

19. Benefit and risk of study subjects

Based on this study, we aim to improve patients' symptoms and improve the quality of medical care by enabling a more practical and safe method of ascites puncture for patients in need of therapeutic ascites.

20. Compensation plan for research subjects (if there is no compensation, the relevant reason)

This study will comply with relevant laws and regulations and strictly conduct clinical trials in accordance with related literature, recommendations, and suggestions, and immediate medical management will be made for complications that occurred during the course of this study. However, since the puncture needle of the Karahox set uses the same formulation as the vascular catheter, general complications that may occur during the puncture process will be treated in the daily treatment area, so there is no separate compensation provision for this.

21. Confidentiality (including protection of personal information of research subjects) and record keeping

The personal information to be collected is gender, date of birth, height, weight, disease name, past medical history, and blood test findings, and sensitive information is not included in the personal information to be collected. The purpose of collecting and using the above items is for the academic purpose of analyzing all patients to find out what factors cause a significant difference during ascites puncture, and it is not used for any other purpose.

Clinical trial schedule

Observation and inspection items	Screening	Intervention	
Session number	Session 0[1)]	Session 1[1)]	Session 2
Subject consent	●		
Basic information	●		
Physical Exam/Vital Signs	●	●	●
Laboratory test [7)]			
Hematology test	●	●	●
Blood coagulation test	●	●	●

Serum biochemical test	●	●	●
Radiologic examination	●		
Inclusion/Exclusion criteria	●		
Randomization[2)]		●	
Therapeutic ascites puncture		●	●
Confirmation of puncture success		●	●
Confirmation of stability (adverse reaction)		●	●

1) Session 0 and session1 can be identical

2) Randomization is performed if the selection/exclusion criteria are met after confirming the screening test results. If randomization is a kara-hoc set, session 1 uses a kara-hoc set, session 2 uses a vascular catheter, and if randomization is a vascular catheter, session 1 uses a vascular catheter and seesion 2 uses a kara-hoc set.

22. References

1. Iwakiri Y Pathophysiology of portal hypertension. Clin Liver Dis. 2014;18:281-291

2. Moore KP, Aithal GP. Guidelines on the management of ascites in cirrhosis. Gut. 2006 Oct; 55(Suppl 6): vi1–vi12.

3. Gentilini P, Laffi G, La Villa G, Romanelli RG, et al. Albumin improves the response to diuretics in patients with cirrhosis and ascites: results of a randomized, controlled trial. J Hepatol 1999;31:1088-1097

4. Gines P, Arroyo V, Quintero E.et al Comparison of paracentesis and diuretics in the treatment of cirrhotics with tense ascites: results of a randomized study. Gastroenterology 1987;93:234–241

5. Quintero E, Gines P, Arroyo V.et al Paracentesis versus diuretics in the treatment of cirrhotics with tense ascites. Lancet 1985;16:611–612

6. Salerno F, Badalamenti S, Incerti P.et al Repeated paracentesis and i.v. albumin infusion to treat 'tense' ascites in cirrhotic patients: a safe alternative therapy, J Hepatol 1987;5;102–108