To the patient

ReLatIonship BEtween implementation of evidence-based and suppoRtive ICU cAre and ouTcomes of patIents with acute respiratOry distress syNdrome

～LIBERATION Study～

Study Protocol

Version 2.

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1. Introduction: What is clinical research?

The hospital conducts clinical research to provide patients with the best medical care and to develop better treatment and diagnostic methods. Research in which patients participate to find out whether a treatment or diagnostic method is effective or safe is called clinical research.

This document has been prepared to assist the investigators in charge in explaining and helping patients to understand when they are asked to participate in research. Please read this information document carefully, understand it thoroughly and make a well-considered decision as to whether or not you are willing to participate in the clinical research. If you have any questions or concerns that are difficult to understand, please do not hesitate to ask the investigators in charge.

Please read the following instructions carefully, check with your investigators in charge if you have any questions, and then decide whether or not you agree to participate in this clinical research. If you agree, please sign and date on the consent form and hand it to your investigators in charge. You will not be disadvantaged in any way if you do not participate in this clinical research.

2. Background of this study

To improve the quality of cares in an ICU that patients receive after ICU admission, a variety of academic societies, including the Japanese Society of Intensive Care and the Society of Critical Care Medicine, are currently developing evidence-based guidelines which are supported by abundant evidence that patient outcomes are improved when performed, such as ABCDEF bundles, nutritional therapy and ICU diaries. Guidelines and statements that have been developed and consensus reached have been developed and are being promoted for implementation in hospitals around the world. Acute Respiratory Distress Syndrome (also known as ARDS) is reported as one of the worst diseases that lead to high mortality and poor functional outcomes even after surviving because ARDS frequently require mechanical ventilation support due to severely damaged lung conditions.

However, there is still little evidence on how the quality of these ICU care practices (compliance rates) associate with patient prognosis and outcomes, and there are currently no clear goals or indicators for the ICU care we should aim for.

3. Objective

The aim of this study is to investigate the current epidemiology of patients with ARDS in the ICUs, treatment strategies given to them, the implementation of evidence-based ICU care such as analgesia, sedation, rehabilitation and nutrition, and its association with patient outcomes around the world

4. Methods

4-1. Patient eligibility

We are asking you to participate in this study because there are a number of conditions for participation and your current physical condition is considered suitable for this study.

●Eligible criteria for those who can participate (Inclusion criteria)

1）Patients aged 18 years and more who admitted to our ICU between 1 June 1 2023 and May 31 2024

2）Patients who require non-invasive or invasive mechanical ventilation within 24 hours of ICU admission and are expected to require it for 48 hours after the ICU admission

3）Patients who meet the definition of ARDS within 24 hours of ICU admission.

4）Patients who provide the written consent to participate in this study from themselves or their family members

●Exclusion criteria

1）Patients in terminal condition on ICU admission

2）Patients who have been admitted to the ICU and have been assigned to a terminal care policy or are expected to be assigned to a terminal care policy within 24 hours of ICU admission.

3）Patients who did not provide the written consent or refuse to participate in this study.

There are a number of other criteria, but your investigators in charge will make a decision based on your conditions and results of examinations. Please ask your investigators in charge for more information. Also, depending on the results of your tests, you may not be able to participate in this study.

4-2. Study methods

4-3. Timelines

	ICU admission Day 1	ICU Stay	ICU discharge	Hospital discharge	3-month follow-up
Patient Characteristics※1	●	●	●		
ICU care related data※2	●	●	●		
Respiratory status※3	●	●	●		
Treatments※4	●	●	●		
Outcomes※5			●	●	●
PICS related data※6				●	●
Functional data after hospital discharge※7					●

※1 Patient Characteristics

- Age, Sex, Height, Weight
- Comorbidity、Pre-admission ADL、physical, cognitive, and psychological state、employment status
- Causes of ICU admission/ARDS、Severity score, etc.

※2 ICU care related data

- Implementation of the following ICU care

1) ABCDEF bundle implementation ratio (Attachment file 1)
2) Evaluation of PADIS and its compliance status (Attachment file 2)
3) Nutrition
4) ICU diary
5) The presence or absence of physical restraints, etc.

※3 Respiratory status

- mechanical ventilation settings (mode, respiratory rate, tidal volume, PEEP) and blood gas results

※4 Treatments

- Use of drugs, prone positioning, neuromuscular blockade, dialysis, etc.

※5 Outcomes

- ICU/hospital admission date, ICU/hospital discharge date, length of ICU/hospital stay,

• Destination after hospital discharge, respiratory status at the time of ho spital discharge, mechanical ventilation perios, etc.

※6 PICS related data

• Physical, cognitive, and psychological function, QOL, and ALD at the tim e of hospital discharge, etc.

※7 Functional data after hospital discharge

• Survival, employment status, physical, cognitive, and psychological functi on, QOL, and ALD at the time of 3-month follow up after hospital dischar ge, etc.

●How to evaluate at the time of hospital discharge and 3-month follow u

Examinations and questionnaires are conducted to patients at the time of discharge to evaluate their quality of life and physical, cognitive and mental functions. We also follow up with patients three months after h ospital discharge to assess how their QOL and physical, cognitive and mental functions have changed. At follow up, questionnaires will be per formed by telephone. Patients can refuse or request to discontinue thei r participation in the study at any time.

A telephone questionnaire will be performed to all discharged patients

To note, the telephone questionnaire is expected to take 10-20 min utes to complete and get a detailed picture of your condition

The information obtained at each participating site will be deanony mized with eliminating the patient's personal information, and collected on the online database for the analysis by the research office..

4-4. Study participating period

If you participate in this study, your planned study period will be fro m ICU admission to hospital discharge, and then to a point around t hree months after hospital discharge.

4-5. Expected numbers of enrolled patients

The study will involve approximately 100 sites across the world, and will involve approximately 1000 participants, 10 of whom will be fro m our hospital.

4-6. Storage and disposal of specimens and information

Information obtained in this study will be stored by the chief investigator of the participating site in a responsible and appropriate manner for a period of five years after the completion of this study, or three years after the date on which the final publication of the results of the research is reported, whichever is later. The specimens and information will be stored in an appropriate manner under the responsibility of the chief investigator of the participating site. When specimens or information are disposed of, they will be discarded in an appropriate manner so that individuals cannot be identified.

Specimens and information obtained in this study will not be used for any other purpose other than this research.

5. Benefits and disadvantages of participating in this study

5-1. Expected benefits

During hospital stay, this study will involve the usual diagnosis, treatment and tests, and will collect medical information obtained in the course of these tests. After hospital discharge, with the patient's consent, the patient's ADL, quality of life, physical and mental functions will be measured. Patients will therefore have a more detailed knowledge of their own health status after hospital discharge, which may help them to manage their health in the future. In addition, the data obtained can contribute to the development of better treatments and ICU cares for patients with ARDS by clarifying the relationship/association between patient prognosis/outcomes and treatment or ICU carse such as analgesia, sedation, rehabilitation and nutrition.

5-2. Predictable disadvantages

Any unwelcome symptoms, signs of illness or changes in laboratory values that occur when a study drug is used are referred to as 'adverse events'. An event judged to be 'caused by' or 'suspected to be caused by' a study drug is referred to as an 'adverse effect'. As this study does not involve any study drug or new treatment, there will be no 'adverse events' or 'side effects' in this study.

The study includes blood and urine tests to obtain a more detailed picture of the patient's condition. The testing methods are considered very minimally invasive as they are exactly the same as the procedures and techniques that are usually performed on patients in usual clinical practice. However, although a fine needle is used, symptoms such as blee

ding and pain may occur, as frequent as with normal procedures. We will take measures to minimize the burden on the patient by matching t he timing of the examination to a time of normal examination, or by ha ving a healthcare professional who is familiar with the procedure perfor m the examination.

The study does not use any specific equipment and only observes t he diagnosis, treatment and tests that are carried out as part of norma l medical practice. It is unlikely that there will be any adverse events. H owever, follow-up after hospital discharge may require patients' time an d may cause psychological strain due to the administration of several q uestionnaires. Patients can refuse or decline to participate in the study at any time. Personal information will be managed with standard securit y in a specific location and will be secured with the utmost effort and i ngenuity.

6. Treatment strategy in case of non-participation

This research involves the usual diagnosis, treatment and examinations. Failure to participate in the research will not change the way in which they are treated.

7. Participation based on your will

It is completely your decision based on your will on whether or not to p articipate in this study. If you agree to participate, you will be asked to sign a consent form. You can also refuse to participate in this study. E ven if you have agreed to participate, you can withdraw your consent at any time during your participation in the study. In particular, you can refuse any additional blood or urine tests that involve minor invasive pr ocedures, especially if they are performed at a different time from your regular medical examinations. This will not cause any awkwardness wit h your doctors and will not be detrimental to your future treatment. Yo u will be provided with the treatment that we think is best for you eve n when you are not participating in this study.

8. Withdrawal from this study

To note, even after you have given your consent to participate in the r esearch, you may not be able to participate in the research or the rese arch may be discontinued in the following situations.

- When the test results show that your condition does not meet the criteria for participation in the study
- When your doctor decides that you should stop the study participation due to your conditions or for any other reason during the course of your participation.
- When the situations make it difficult to continue the study.

9. What you need to do during this study

The person in charge may visit the patient at the time of hospital discharge to collect questionnaires and other forms. In addition, a face-to-face questionnaire may also be performed. Please complete the questionnaire.

10. New findings of this study

During the course of your participation in this study, we might receive any new information that may affect your willingness to participate in the study. In that case, we will inform you of this information as soon as possible. It is completely your decision whether or not you wish to continue participating in the study.

11. Treatment and Compensation in case of adverse events

This is a study to collect medical information obtained during the diagnosis, treatment, procedures, tests and evaluations that are usually carried out in medical practice, and it is extremely unlikely that any adverse events or other health problems will occur to you as a direct result of your participation in this study. Therefore, the costs related to the treatment for the adverse events will be covered by your health insurance.

12. Protection of your personal information

When the information obtained in this study is submitted outside the hospital, information that can immediately identify you, such as your name and address, will be deleted and a specific research number, not the hospital ID, will be assigned. A corresponding table/list linking the specific research number to your name/hospital ID will be created by the chief investigator at the participating site and used for purposes such as checking against your medical information. The c

orresponding table will be managed appropriately with the responsibility of the chief investigator at the participating site.

The results of the research will be presented at conferences and published in scientific journals, but even then information that can immediately identify you as an individual will not be included nor used.

In addition, if you participate in this study, other people involved in the study (including people from other organizations) and other hospital staff may have direct access to your medical records and test results, in addition to the doctors and nurses at your hospital, to ensure that the tests and consultations are carried out correctly and in accordance with the study schedule. However, these parties are obliged to maintain confidentiality and your personal information will not be disclosed to outside parties.

To note, by signing the consent form for this study, you are giving your consent for us to obtain your medical information (e.g. details of your treatment) and for the people involved in the study to see your medical records and test results.

13. Attribution of the results / Secondary analysis

The results obtained may generate intellectual property such as patent rights. In that case, the patent rights will belong to the researcher or the research group/committee/organization. In addition, as the data obtained is very large and may contribute widely to the treatment of acute respiratory distress syndrome, secondary analysis (explaining the same data from different angles) may be performed. The data obtained will belong to the research group/committee/organization.

14. Research group and fundings

The study is led by the LIBERATION Study Steering Committee under the support of the Japanese Society of Early Mobilization. The Study group is composed of multi-disciplinary teams whose aim is to promote standardized ICU care in ICUs.

The funding required to carry out this study is provided by the Steering Committee from its own research funding.

15. Conflict of interests

A conflict of interest is a situation in which a third party may be concerned that the research is not being conducted fairly and appropriately, such as falsification of research data or preferential treatment of a particular company, due to financial interests with external parties.

This researchwill not alter your treatment plan or compromise the fairness of the research by favoring the interests of a particular company.

Conflicts of interest of the involved researchers in this study are reviewed and properly managed by the Steering Committee/ the local Ethic Committee. In addition, the conflicts of interest of all involved investigators and other researchers associated with the research organization are reviewed by the conflict-of-interest committees of the respective organizations to which they belong and are managed appropriately.

16. Costs and rewards during the study

As this study includes usual diagnosis, treatments, and cares under the usual insurance, you will pay for the cost of the hospital admission, using your health insurance to cover your own costs. To note, you need to pay for the cost regardless your participation. In addition, there is no honorarium for participating in this study and you will participate as a volunteer.

17. Treatments after the completion of this study

After the end of the study, even after the withdrawal, you will still receive the usual medical care appropriately according to your condition.

18. Registration of this study

This study will be registered in the open access clinical research registration bank: University Hospital Medical Information Network Research Centre Clinical Trials Registration System (UMIN-CTR: http://www.umin.ac.jp/ctr/index-j.htm) or ClinicalTrials.gov (https://www.clinicaltrials.gov/) before the study begins. The registration will be updated according to the progress of the study. When a study is completed, the results of the study are registered on the system. If you would like to know more about the research plan or research methods in more

detail, please contact your investigators in charge. We will provide you with access to the research protocol and explanations to the extent that it does not interfere with the personal information of other participants in the study, or with the intellectual property of the study.

19. The ethics committee

The appropriateness and methods of this study have been thoroughly reviewed by a number of experts. This hospital has also established the Ethics Committee consisting of doctors, non-physician staff and external persons who have no vested interest in the hospital as an advisory body to the Director, which examines whether there are any scientific or ethical problems. This study has receives official approval from the Director and the Ethics Committee after the intensive review and assessment.

The name of the Ethics Committee :

The location of the Ethics Committee :

Documents relating to the ethical process, the members of the Ethics Committee, and the summary of ethical review records can be reviewed. These documents are available on the website below and can be viewed by anyone. It is also possible to review the documents in person. Please inform your investigators in charge if you wish to do so. (HP address :)

20. Contact information of the chief investigator at the hospital

If you have any questions or concerns about this study or anything else that you do not understand after reading the instructions given by your investigators in charge or this information sheet, please do not hesitate to ask your investigators or the research office at the hospital whatever and whenever. It is also a good idea to talk to your family and friends about whether or not you want to participate in this study. Also, if you are undergoing other treatment for an illness or injury, please contact your doctor listed below.

OO Hospital

●*Department of OO*

The name of chief investigator: _____

Tel : ( ) Email:

●The clinical research office at this hospital

The name of representative: _____

Tel：（ ） Email:

21. Organization related to this study and the principal investigator

This study will be conducted in collaboration with other facilities. Please contact us if you would like to know the names of other facilities and the chief investigator and other investigators at each participating site.

21.1. Principal Investigator
LIBERATION Study Steering Committee
Principal Investigators: Keibun Liu and Kensuke Nakamura

21.2. Research Office
The Japanese Society for Early Mobilization (JSEM)
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21.3. Co-Investigator
(Domestic)
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Hajime Katsukawa, Physical Therapist, Japanese Society for Early mobilization
Tadahiro Goto, Chief Scientific Officer, TXP Medical Corporation; Visiting Scholar, Department of Clinical Epidemiology and Health Economics, School of Public Health, The University of Tokyo
Yohei Okada, Researcher, Department of Preventive Services, Graduat

e School of Medicine, Kyoto University
Shunsuke Taito, Physical Therapist, Department of Rehabilitation, Hiro shima University Hospital
Hideaki Sakuramoto, Nurse, Department of Critical care and Disaster Nursing, Japanese Red Cross Kyushu International College of Nursing
Keibun Liu, Physician, Intensive Care Collaboration Network