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Asia CMR Registry - A Registry Study of Cardiac MRI in Asia

Study Protocol Ver.2

Principal Investigator
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1. Background

Cardiac MRI is a noninvasive imaging technique for the diagnosis of cardiac disease, without exposure to radiation. Cardiac MRI in combination with other imaging techniques can provide various types of information on the morphology, function, and volume of the heart; the diagnosis of myocardial ischemia; the evaluation of myocardial infarction and fibrosis; and coronary stenosis. The examination cost is less than that of radionuclide studies. Therefore, cardiac MRI is considered very useful for the diagnosis of coronary artery disease and myocardial disease. In Japan and Asia, however, the current usage and safety of cardiac MRI, its role in deciding the treatment policy, and its usefulness for the evaluation of prognosis remain unclear. In Europe, the European Society of Cardiac Magnetic Resonance started the EuroCMR Registry, “a multicenter registry study of cardiac MRI in Europe,” in 2007. To date, several tens of thousands of cardiac MRI case data and images have been compiled. Studies on the status of the clinical use of cardiac MRI, examination safety, the role of cardiac MRI in determining treatment policy, and the usefulness of cardiac MRI for the evaluation of prognosis are ongoing. However, the cardiac disease incidence and healthcare systems differ between Europeans and Asians. Studies on the current usage, safety, and effectiveness of cardiac MRI in Asians, including Japanese, have therefore become more important.

2. Objective

The objective of the present study is to clarify the current usage and safety of cardiac MRI in Asia, the image quality of cardiac MRI, the role of cardiac MRI in the treatment of cardiac disease, and the usefulness of cardiac MRI for the evaluation of prognosis. The study will be mainly conducted by the Asian Society of Cardiovascular Imaging (ASCI). A server will be established in Mie University, the core institution, and case data on cardiac MRI and MR images will be compiled. This is a registry study performed in cooperation with the EuroCMR Registry. The methods for compiling clinical data and images on cardiac MRI will be in accordance with the EuroCMR Registry.

3. Institutions scheduled to participate and names of investigators (as of June 1, 2014)

Tokyo Medical University Hachioji Medical Center (Kunihiko Teraoka), Saitama

International Medical Centre (Fumiko Kimura), Hyogo Brain and Heart Center (Yasuyo Taniguchi), Nippon University Itabashi Hospital (Satoshi Kunimoto), Aoyama Hospital Tokyo Women's Medical University (Eri Watanabe), Keio University Hospital (Shigeo Okuda), Kanagawa Cardiovascuiar and Respiratory Center (Tae Iwasawa), Saitama Prefectural Cardiovascular and Respiratory Disease Center (Takatomo Nakajima), Toyama City Hospital (Hiroaki Kiyokawa), Juntendo University Hospital (Eiryu Sai), Seoul National University Hospital (W Lee), and Seoul National University Bundang Hospital (YE Yoon), etc.

4. Inclusion criteria

4.1 Subjects

The study group will comprise patients who undergo cardiac MRI for diagnosis and treatment in hospitals participating in the Asia CMR Registry and give informed consent to the registration of anonymous data. However, medical institutions participating in the Asia CMR Registry will participate in the study after obtaining approval from the ethics committee of each medical institution. Persons cooperating with this research will receive an adequate explanation of the study from the study investigator and informed consent will be obtained.

4.2 Exclusion criteria

Patients incapable of giving informed consent or those suspected to lack the ability to give informed consent. Nonadult patients for whom informed consent is not obtained from their guardian.

5. Target number of patients and study period

5.1 Target number of patients

10,000 patients.

5.2 Study period

From the date of approval until September 30, 2023

Minimal patient follow-up duration is 12 months. Therefore, the patient registration and follow-up period is from the date of approval until September 30, 2022 and September 30, 2023, respectively.

When the patient number will successfully reach 10,000 before September 30, 2022, patient recruit will be continued until September 30, 2022. When the patients number will not reach 10,000 as of September 30, 2022, Multi-Centre Study Committee of the ASCI will be held and discuss if the study period is extended or not.

6. Used equipment and drugs

6.1 MRI

MRI equipment for clinical use that is available in each medical institution participating in the Asia CMR Registry

6.2 Drugs

1) Gadolinium-based contrast agents
2) Adenosine or ATP

7. Methods and Analysis

7.1 Methods

A protocol for cardiac MRI examinations performed for diagnosis and treatment as covered by health insurance in each medical institution participating in the Asia CMR Registry

7.2 Analysis

In Mie University, the core institution (core laboratory) of the Asia CMR Registry, case data and cardiac MR images obtained from the participating medical institutions will be registered and compiled on a dedicated server and transferred to a work station, where image analysis will be performed using a specialized image processing tool. The results of image analysis and clinical data will be statistically analyzed with the use of statistical analysis software.

8. Expected results

In Asia, a prospective multicenter registry study of cardiac MRI has yet to be performed. The results of this study are expected to demonstrate the current usage status and safety of cardiac MRI in routine medical practice in Asia, the significance with regard to the treatment policy for cardiac disease, and the significance for the

evaluation of prognosis and risk stratification for various cardiac diseases, thereby establishing the clinical usefulness of cardiac MRI examinations.

9. Expected advantages and disadvantages for subjects

9.1 Expected advantages for subjects

If this study demonstrates that cardiac MRI is effective for risk stratification and prognosis in patients with cardiac disease, it may contribute to the selection of more appropriate treatment and prophylaxis for the participants.

9.2 Expected risks and disadvantages for subjects

The present study requires registration in a registry of MRI examinations performed for diagnosis and treatment. MRI is a noninvasive examination technique unaccompanied by exposure to radiation, but is associated with the risk of adverse effects caused by contrast agents and administered drugs, similar to conventional cardiac MRI examinations.

9.3 Means to reduce and countermeasures against 9.2

If MRI examinations for diagnosis and treatment may possibly be registered in a registry, each participating institution will be informed about the need to obtain written informed consent after providing an explanation of the risk of adverse effects caused by contrast agents and administered drugs, performed with the use of an examination informed consent form.

12. Ethical matters

12.1 Regulations that should be complied with

All persons involved in this study will be informed to carefully read and understand principles to be followed in all medical research conducted in human subjects, such as “The World Medical Association Declaration of Helsinki” and “Ethical Guidelines for Epidemiologic Studies” (Ministry of Health, Labour and Welfare), and to perform the study in accordance with such guidelines.

12.2 Explanation and informed consent

Participating institutions will be informed that adults willing to cooperate in the study are to receive an explanation with the use of a written form and that informed

consent is to be obtained in writing.

For non-adults willing to cooperate in the study, the participating institutions will be informed to provide potential subjects with a written explanation and to obtain written informed consent in accordance with criteria previously defined by each country or each participating medical institution. In Mie University Hospital, consent from a legal guardian must be obtained for persons willing to cooperative in the study who are younger than 20 years. If persons willing to cooperate in the study are younger than 20 years but 16 years or older, consent must be obtained directly from the subject as well as from a legal guardian.

1) The study objectives and methods for this and the principal investigator
2) The study period (from the date of approval to September 30, 2023) and scheduled numbers of participants
3) Advantages and disadvantages for persons cooperating in the study (me)
4) Consent for participating in the study is given by my own free will and can be withdrawn at any time.
5) Concrete methods for protecting my personal information
6) Matters concerning cost allocation
7) Advantages and disadvantages for persons cooperating in the study (me)
8) The presence of a data manager (name: Takahiro Takada)
9) Complete anonymity will be maintained when the study results are reported at medical congresses or in journals.
10) The results of analysis may be disclosed or may not be disclosed at my request.
11) Intellectual property rights arising from this study will belong to the principal investigator and the study investigators.
12) Even after the completion of the study, the data and specimens will be preserved and used for scientific research under the condition of anonymity.
13) Regardless of participation or nonparticipation in this study, the cardiac MRI examination method will not differ from that covered by health insurance.
14) Patient data and cardiac MR images that have been made completely anonymous or encoded will be registered and stored in a dedicated server.
15) For follow-up after examination, the study staff will review patients' medical records, directly contact patients or their relatives by telephone, or ask patients' current physicians at 12-month intervals after the examination to confirm their cardiac and

health status.

12.3 Protection of personal information

Persons involved in the study at each participating institution will be informed to comply with applicable laws and regulations to protect the personal information of subjects. The related persons will be informed to make maximal efforts to protect the personal information and privacy of subjects and not to disclose personal information obtained by performing the study, without an appropriate reason. The same shall apply after the related person retires.

In this study, personal information on patients who undergo cardiac MRI for diagnosis and treatment at a medical institution participating in the ASA CMR Registry is registered in a Website, and DICOM images of cardiac MRI examinations are uploaded to a dedicated server. These information and data, including the DICOM header, are made completely anonymous. (Unlinkable anonymization is performed to make identification of the individual impossible.) At the time of Web input and image uploading, personal information is not transferred to the server via the Internet, and there is no risk of the personal information of patients being leaked from the server at Mie University.

At each participating medical institution including Mie University, unique 64-digit registration numbers are automatically and randomly assigned as patient IDs at the time of registration in the Registry server. However, because these numbers are not transferred to or stored in the Registry server, a list linking the patient ID with the Registry server registration numbers will be prepared at each participating medical institution, and the person responsible for the management of personal information will preserve the list in the hospital. No other linkage lists will be prepared. Information linking the patients IDs and the Registry server registration numbers are handled in an adequate manner to ensure the protection of personal information, as stated in the ethical review application.

13. Completion of clinical research

On the completion of research, the principal investigator will promptly submit a study completion report form to the Dean of Mie University Graduate of School of Medicine and the Director of Mie University Hospital.

14. Handing of material related to epidemiologic research

In Mie University, documentation related to the execution of research (such as copies of various application forms and reports, subject identification code lists, copies of informed consent forms, and documents or records required to ensure data reliability) will be preserved in the Department of Diagnostic Radiology, Mie University Hospital for a designated period (10 years after completion of the study period) and then be discarded. Medical institutions other than Mie University that participate in the Asia CMR Registry will be informed to preserve documentation related to performance of the study in each hospital and then to discard such documentation after a designated period (10 years after completion of the study period).

15. Public announcement of the results

The results of the study will be reported at medical congresses and in journals.

Interim analysis will be performed every 3 years from the date of approval. Then, “interim analysis report” will be documented as soon as possible. Within 6 months after completion of the study period, September 30, 2023, “Research result report” will be documented. Those results will be considered to go for the publication in English peer-reviewed medical journals.

16. Study organization

16.1 Participating medical institutions

1. Hiroshi Takeda, Director, Mie University Hospital,
2-174 Edobashi, Tsu City, Mie 514-8507 Japan

2. Institutions participating in this study in Asian countries that were approved by the ASCI Multi-Centre Research Committee

16.2 Principal investigator

Hajime Sakuma, Professor, Department of Diagnostic Radiology, Mie University Graduate of School of Medicine, and director in charge of the Multi-Centre Research Committee, Asian Society of Cardiovascular Imaging (ASCI)

16.3 Persons in charge of the study

1. Hajime Sakuma, Professor, partment of Diagnostic Radiology, Mie University Graduate of School of Medicine, and director in charge of the Multi-Centre Research Committee, ASCI

2. Representatives of institutions participating in this study in Asian countries that were approved by the ASCI Multi-Centre Research Committee

17. References

1. The World Medical Association Declaration of Helsinki
   http://www.med.or.jp/wma/helsinki08_j.html
2. Ethical Guidelines for Epidemiologic Studies
   http://www.mhlw.go.jp/general/seido/kousei/i-kenkyu/ekigaku/0504sisin.html