



Study Protocol and Mission for the Tohoku Registry of Acute Aortic Dissection (TRAD)

Kota Itagaki, MD; Shintaro Katahira, MD, PhD; Konosuke Sasaki, RN, PhD;
Midori Miyatake, RN, PhD; Koki Ito, MD, PhD; Kiichiro Kumagai, MD, PhD;
Norihiro Kondo, MD, PhD; Shinya Masuda, MD, PhD; Daichi Takagi, MD, PhD;
Azuma Tabayashi, MD; Keisuke Kanda, MD, PhD; Ai Ishizawa, MD;
Atsushi Yamashita, MD; Cholsu Kim, MD; Shunsuke Kawamoto, MD, PhD;
Masaaki Naganuma, MD, PhD; Keiichi Ishida, MD; Kyohei Ueno, MD;
Yoshikatsu Saiki, MD, PhD, FJCS; on behalf of the TRAD Investigators

Background: Acute aortic dissection (AAD) is a life-threatening condition that imposes a significant socioeconomic burden on society. The Tohoku Registry of Acute Aortic Dissection (TRAD) is a collaboration of 13 tertiary referral hospitals in the Tohoku region of Japan designed to investigate all aspects of AAD treatment in this district, and to address significant clinical questions to help understand its dynamic pathology and develop optimal strategies for treating AAD.

Methods and Results: Comprehensive cases developing type A and type B AAD, including those with prehospital cardiopulmonary arrest transported to TRAD centers, over 5 years from 2017 to 2022 are registered. The TRAD dataset encompasses prehospital information, diagnostic imaging findings, treatment modalities, and outcomes for each case. After discharge, patients will be followed up for 10 years for survival, aortic events and inspection data.

Conclusions: We believe that this multicenter registry of AAD analyses will clarify the current short-term outcomes of recent surgical, endovascular, and medical treatments in the Tohoku region, and provide insights into the long-term outcomes of different treatment modalities to achieve extended life expectancy in reasonably good health.

Key Words: Acute aortic dissection; Multicenter; Observational study; Registry; TRAD

Although acute aortic dissection (AAD) is a life-threatening condition and an issue that is unable to be ignored, AAD treatment outcomes have improved substantially.¹ Data from the International Registry of Aortic Dissection (IRAD) and other registries for AAD that have been established worldwide are being used to further improve mortality.² The postoperative in-hospital mortality rate of type A AAD surgery was 15.8% in the latest report from IRAD.³ In the Nordic registry, the Society of Thoracic Surgeons registry, and the German

registry for type A AAD, the 30-day mortality rate after surgery was approximately 17%.⁴⁻⁶

In Japan, there are national database projects such as the Japan Cardiovascular Surgery Database (JCVSD), which have been established to provide information on the in-hospital outcome of all cardiovascular surgeries in Japan. The treatment results for type A AAD in Japan have been reported to be favorable.^{1,7,8} In the JCVSD,⁷ the 30-day mortality rate was 9.2%, which is more favorable than global standards.³⁻⁶ However, these data are averaged

Received July 8, 2024; accepted July 10, 2024; J-STAGE Advance Publication released online September 13, 2024 Time for primary review: 2 days

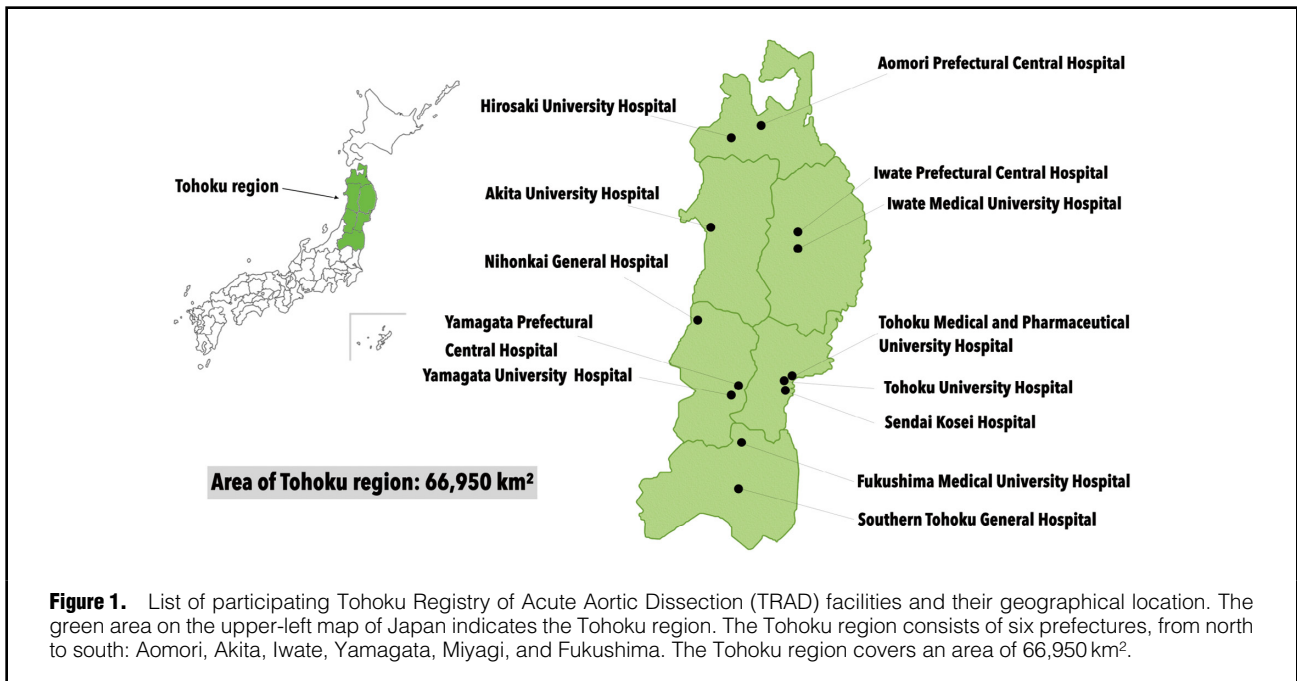
Division of Cardiovascular Surgery, Tohoku University Hospital, Sendai (K. Itagaki, S. Katahira, K.S., M.M., K. Ito, K. Kumagai, Y.S.); Department of Thoracic and Cardiovascular Surgery, Hirosaki University Hospital, Aomori (N.K.); Department of Cardiovascular Surgery, Aomori Prefectural Central Hospital, Aomori (S.M.); Department of Cardiovascular Surgery, Akita University Hospital, Akita (D.T.); Department of Cardiovascular Surgery, Iwate Medical University Hospital, Iwate (A.T.); Department of Cardiovascular Surgery, Iwate Prefectural Central Hospital, Iwate (K. Kanda); Second Department of Surgery, Yamagata University Hospital, Yamagata (A.I.); Department of Cardiovascular Surgery, Yamagata Prefectural Central Hospital, Yamagata (A.Y.); Department of Cardiovascular Surgery, Nihonkai General Hospital, Yamagata (C.K.); Department of Cardiovascular Surgery, Tohoku Medical and Pharmaceutical University Hospital, Sendai (S. Kawamoto); Department of Cardiovascular Surgery, Sendai Kosei Hospital, Sendai (M.N.); Department of Cardiovascular Surgery, Fukushima Medical University Hospital, Fukushima (K. Ishida); and Department of Cardiovascular Surgery, Southern Tohoku General Hospital, Fukushima (K.U.), Japan

Mailing address: Yoshikatsu Saiki, MD, PhD, FAHA, FJCS, Division of Cardiovascular Surgery, Tohoku University Hospital, 1-1 Seiryō-machi, Aoba-ku, Sendai, Miyagi 980-8574, Japan. email: yoshisaiki@med.tohoku.ac.jp

All rights are reserved to the Japanese Circulation Society. For permissions, please email: cr@j-circ.or.jp

ISSN-2434-0790





nationwide, and evidence to assess whether a uniformly high standard of emergency aortic care is being provided to the public throughout Japan is scarce. Japan is characterized by its significant extent in latitude, which can generate topographical and climatic variability. The Tohoku district is located in the northern part of Japan and features a relatively cold winter; it covers a large area of land with few inhabitants. These characteristics may or may not affect the prehospital condition of AAD patients and the postoperative outcomes of AAD treatment. Accordingly, the Tohoku Registry of Acute Aortic Dissection (TRAD) might reflect some topographical variations with the data in contrast to the nationwide JCVSD data.

The second unique feature of TRAD is the inclusion of acute Stanford type B aortic dissection. While many studies have examined the management of Stanford type A, few large observational studies have focused on the management of Stanford type B from the acute to the chronic phase, including medical management.^{9,10}

This study presents a protocol of our registry study of AAD care at institutions in the Tohoku region, where emergency treatment for AAD is available and access to care is similar. We are investigating all aspects of AAD treatment in this district and addressing important clinical issues that will help us to understand its dynamic pathology and develop optimal strategies for treating AAD.

Methods

Study Population

We established the TRAD, which encompasses 13 centers in the Tohoku region of Japan that are equipped to perform AAD surgery and agreed to participate in the study. No hospitals disagreed with the TRAD concept. Patients included in the registry must have been diagnosed within 14 days of AAD onset at the participating institution.¹¹ Both Stanford types A and B are documented in the registry, without restrictions on the type of treatment. The registry

also includes cases of aortic dissection and death in patients who were transported to a collaborating institution during resuscitation following cardiopulmonary arrest (CPA). CPA was mainly diagnosed according to the Advanced Cardiovascular Life Support (ACLS) algorithm. The data for CPA patients were input with an affirmative diagnosis made by cardiovascular surgeons based on computed tomography (CT) imaging. Patients with a previous history of aortic dissection were also enrolled in the study.

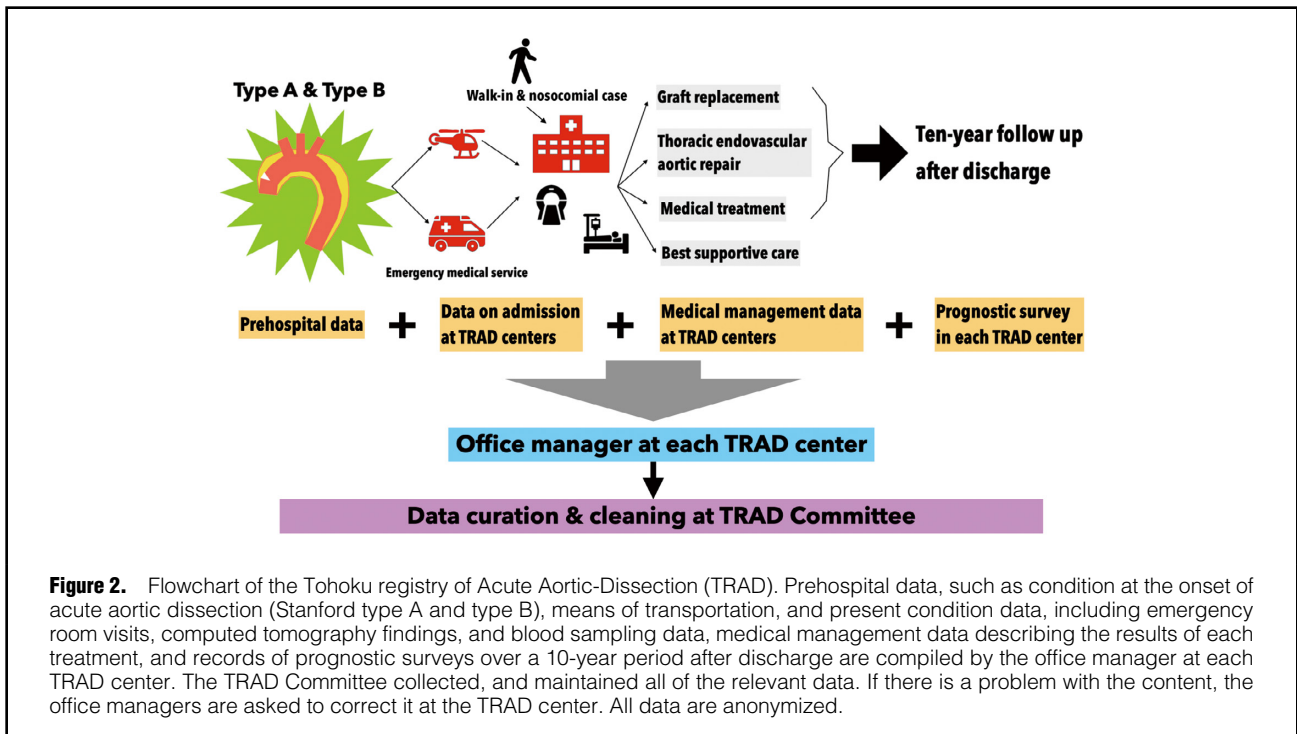
Participating Institutions

The institutions that agreed to participate in the TRAD regularly perform a large number of cardiovascular procedures in the Tohoku region (Figure 1). They must be able to provide emergency aortic care, and both open and endovascular repair.

Data Acquisition and Analysis

The registry was established by cardiovascular surgeons in the Tohoku region. Data on patients with AAD treated at collaborating institutions are collected prospectively by extracting the necessary data from medical information terminals onto a data sheet created using FileMaker (Clarisc International Inc., Cupertino, CA, USA). These sheets are added to a password-protected folder. The primary input was mainly from the cardiovascular surgeons' review of medical records (Supplementary Table 1). The medical management of patients with uncomplicated type B dissection was left to cardiologists at 2 institutions out of 13 TRAD centers. In those institutions, the information on uncomplicated type B cases was closely shared between cardiologists and cardiovascular surgeons. Cardiovascular surgeons, not cardiologists or emergency doctors, were in charge of all data input for the patients.

Data were collected on 150 variables (Supplementary Table 2). In addition to prehospital information, such as time of onset, symptoms at onset, and mode of transportation to the hospital, the following information was collected



after arrival at the hospital. Treatment details were categorized, and were evaluated in terms of the time to starting surgery, the surgical procedure, operative time, and in-hospital complications. The patients' conditions at discharge were also recorded. Patients who are unable to return to their TRAD center hospital after discharge will be followed up periodically by telephone and postcard survey.

The research topics are studied in response to the clinical questions developed at the collaborating institutions, and the items to be discussed are reviewed at a plenary meeting by the representatives from the collaborating institutions before publication. TRAD forms completed by each institution were reviewed for data cleaning. Confirmation of illogical data was requested for each institution. External validation, site monitoring visits, random field selection of 2% in all registered AAD cases in each TRAD center, and an error audit were led by the TRAD committee.

Study Schedule

The study enrollment period was from July 2017 to August 2022. Patients with AAD, including those with cardiopulmonary arrest, who were transported to the study site, were enrolled. Each patient will be followed up for 10 years after hospital discharge to evaluate survival, post-treatment complications, and the frequency of surgical intervention for enlargement of the dissecting aortic aneurysm. In addition, as new clinical questions arise over time, additional information might be collected with the consent of the collaborating institutions (Figure 2).

Ethics

This study has been registered with the University Hospital Medical Information Network (UMIN) Clinical Trial Registry (ID: UMIN000027653), and the protocol has been approved by the Ethics Committee of Tohoku Graduate School of Medicine (No. 2017-1-243). An opt-out approach

will be used, in which participants will be included in the research unless they categorically state that they wish to be excluded.

Results

More than 2,500 cases of Stanford A and B AAD have been reported over a 5-year period. By excluding unclassified cases during the process of data curation, we expect to register approximately 1,500 cases of type A dissection and approximately 1,000 cases of type B dissection. Patients diagnosed with AAD at the time of data collection and cleaning were included in the study.

Discussion

The Japanese region of Tohoku, which covers an area of 66,950 km², is located north of Honshu, Japan, and consists of 6 prefectures, with the northernmost prefecture at 41°N (Aomori Prefecture) and the southernmost at 36°N (Fukushima Prefecture). The population is estimated at approximately 8.42 million according to the Ministry of Internal Affairs and Communications Report, 2022, Japan, with the highest proportion of the population over 65 years old in Japan.¹² Tohoku is geographically characterized by heavy snowfall in winter, which makes travel difficult. It is expected that evaluation of the transportation situation during the increase in winter snowfall, which is a problematic characteristic of the region, will clarify the issues to be addressed according to the season.

In Japan, national databases and large registries related to acute aortic syndrome have been established.^{7,8,10} However, they have the following limitations: difficulty in understanding regional characteristics; limited information on non-surgical, medical-only cases, lack of available data on prehospital information and CT evaluation performed

at presentation for each case; and insufficient information on remote study periods.^{7,8,10}

At present, studies on a range of outcomes for type A AAD, including region-specific prehospital information, are increasing in Japan. In the TRAD, most of the detailed data from pretreatment to post-discharge were evaluated. This information will facilitate comparison of the outcomes with those of surgical treatment for AAD in Japan, which is considered to be relatively favorable, and evaluation of the prognosis after medical treatment of type B dissection at operating centers, the prognosis of patients undergoing thoracic endovascular aortic repair (TEVAR), and the status of emergency transport for AAD in the Tohoku region in recent years based on prehospitalization information.

We believe that this registry is an important record of the current status of AAD in the Tohoku region of Japan in recent years. We hope to accumulate follow-up data and leave room for planning a repeat survey as new clinical issues are identified, which will help save lives and elucidate the pathophysiology of more patients with AAD.

Study Limitations

AAAD cases with cardiopulmonary arrest on arrival at each TRAD center were registered, but not all cases were able to be curated because a part of the cases was not directly reported to cardiovascular surgeons and it was difficult to find the missing data, especially for those where AAD was found later.

The treatment strategy for each case of AAD was determined by the participating institution. In the case of graft replacement, the decision regarding the extent of replacement and the choice of applying the frozen elephant trunk technique depends on the institution's policy; however, most TRAD centers generally performed tear-oriented surgery when the graft replacement was performed for type A AAD cases. Cases of pre-emptive TEVAR for type B aortic dissection were also included in the study, but the criteria for this procedure varied from center to center. However, interviews with office managers at all TRAD centers were conducted to ensure that the indication for preemptive TEVAR was determined according to the positive predictive factors for chronic-phase enlargement in the acute/subacute phase of Stanford type B aortic dissection as documented in the Japanese national guideline.¹³

Conclusions

A registry of AAD in the Tohoku region has been established. We hope that this registry will not only report the recent outcomes of AAD treatment but also help revamp the local emergency medical care system to improve the efficiency and standard of care, and formulate new clinical questions for more sophisticated medical management of AAD. We hope that this registry will provide insight into pathological conditions, thereby increasing the number of lives that can be saved.

Acknowledgments

We appreciate all of the staff who participated in the medical management of AAD in the Tohoku region of Japan. We thank Editage (www.editage.jp) for English language editing.

Sources of Funding

Not applicable.

Disclosures

The authors declare that there are no conflicts of interest.

IRB Information

The present study was approved by the Ethics Committee of Tohoku Graduate School of Medicine (No. 2017-1-243).

Data Availability

The deidentified participant data will not be shared. The curated data will not be publicly available because patient consent in each TRAD center does not allow for such publication. The corresponding author will respond to inquiries regarding analyses.

References

1. Abe T, Yamamoto H, Miyata H, Motomura N, Tokuda Y, Tanemoto K, et al. Patient trends and outcomes of surgery for type A acute aortic dissection in Japan: An analysis of more than 10 000 patients from the Japan Cardiovascular Surgery Database. *Eur J Cardiothorac Surg* 2020; **57**: 660–667.
2. Hagan PG, Nienaber CA, Isselbacher EM, Bruckman D, Karavite DJ, Russman PL, et al. The International Registry of Acute Aortic Dissection (IRAD): New insights into an old disease. *JAMA* 2000; **283**: 897–903.
3. Wolfe SB, Sundt TM 3rd, Isselbacher EM, Cameron DE, Trimarchi S, Bekeredjian R, et al. Survival after operative repair of acute type A aortic dissection varies according to the presence and type of preoperative malperfusion. *J Thorac Cardiovasc Surg* 2022; S0022-5223(22)01024-8.
4. Olsson C, Ahlsson A, Fuglsang S, Geirsson A, Gunn J, Hansson EC, et al. Medium-term survival after surgery for acute Type A aortic dissection is improving. *Eur J Cardiothorac Surg* 2017; **52**: 852–857.
5. Lee TC, Kon Z, Cheema FH, Grau-Sepulveda MV, Englum B, Kim S, et al. Contemporary management and outcomes of acute type A aortic dissection: An analysis of the STS adult cardiac surgery database. *J Card Surg* 2018; **33**: 7–18.
6. Conzelmann LO, Weigang E, Mehlhorn U, Abugameh A, Hoffmann I, Blettner M, et al. Mortality in patients with acute aortic dissection type A: Analysis of pre- and intraoperative risk factors from the German Registry for Acute Aortic Dissection Type A (GERAADA). *Eur J Cardiothorac Surg* 2016; **49**: e44–e52.
7. Okita Y, Kumamaru H, Motomura N, Miyata H, Takamoto S. Current status of open surgery for acute type A aortic dissection in Japan. *J Thorac Cardiovasc Surg* 2022; **164**: 785–794.e1.
8. Inoue Y, Matsuda H, Uchida K, Komiya T, Koyama T, Yoshino H, et al. Analysis of acute type A aortic dissection in Japan Registry of Aortic Dissection (JRAD). *Ann Thorac Surg* 2020; **110**: 790–798.
9. Tolenaar JL, Froehlich W, Jonker FH, Upchurch GR Jr, Rampoldi V, Tsai TT, et al. Predicting in-hospital mortality in acute type B aortic dissection: Evidence from International Registry of Acute Aortic Dissection. *Circulation* 2014; **130**(Suppl 1): S45–S50.
10. Yamaguchi T, Nakai M, Sumita Y, Miyamoto Y, Matsuda H, Inoue Y, et al. Current status of the management and outcomes of acute aortic dissection in Japan: Analyses of nationwide Japanese Registry of All Cardiac and Vascular Diseases-Diagnostic Procedure Combination data. *Eur Heart J Acute Cardiovasc Care* 2020; **9**(Suppl): S21–S31.
11. Hirst AE Jr, Johns VJ Jr, Kime SW Jr. Dissecting aneurysm of the aorta: A review of 505 cases. *Medicine (Baltimore)* 1958; **37**: 217–279.
12. Statistics Bureau, Ministry of Internal Affairs and Communications, “Computation of Population by Sex for Prefectures”, 2023-04-12, <https://www.e-stat.go.jp/en/stat-search/file-download?statInfId=000040045505&fileKind=4> (accessed August 13, 2024).
13. Ogino H, Iida O, Akutsu K, Chiba Y, Hayashi H, Ishibashi-Ueda H, et al. JCS/JSCVS/JATS/JSVS 2020 guideline on diagnosis and treatment of aortic aneurysm and aortic dissection. *Circ J* 2023; **87**: 1410–1621.

Supplementary Files

Please find supplementary file(s); <https://doi.org/10.1253/circrep.CR-24-0079>