The Study Design and Rationale of the Registry of Taiwan Transcatheter Therapeutics-Complex and High-risk Indicated Patients (TTT-CHIP)

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Abstract

Objective: This study aimed to evaluate the management strategies and clinical outcomes of complex and high-risk indicated percutaneous coronary intervention procedures (CHIP) in Taiwan, as reported in the TTT-CHIP Registry. This included understanding procedural success and safety profiles in Taiwanese patients with elevated procedural complexity.[1]

Methodology: This multicenter, retrospective cohort study focused on high-risk coronary intervention cases. Data were collected using a standardized online case report form from January 2014 to December 2021 across multiple hospitals in Taiwan. The study included adult patients undergoing complex and high-risk PCI, including those with SYNTAX score > 32, and those with multiple comorbidities, e.g., reduced left ventricular function, acute myocardial infarction, cardiogenic shock, or true left main bifurcation disease. The primary endpoint was the incidence of major adverse cardiovascular events (MACEs) within one year post procedure. MACEs were defined as cardiovascular death, non-fatal myocardial infarction, repeat revascularization, and stroke. Secondary endpoints included all-cause mortality, the incidence of specific procedural complications (e.g., stent thrombosis, vascular complications, need for re-intervention), and acute kidney injury. A total of 452 patients were enrolled to ensure robust statistical power to detect outcome differences among the various intervention techniques and patient risk profiles.

Conclusion: This registry provided insight into the management of complex PCI cases in Taiwan, informing clinicians about the risks and outcomes associated with CHIP procedures in high-risk patients.[2,3] Findings may support the development of localized treatment protocols, improving safety and effectiveness in high-risk PCI interventions.[4]

Keywords: complex and high-risk indicated patient procedure (CHIP), mechanical circulatory support (MCS), clinical outcome

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Introduction

Percutaneous coronary intervention (PCI) has become a cornerstone in the management of coronary artery disease (CAD), particularly for patients presenting with acute coronary syndromes (ACS). However, the growing complexity of cases due to aging populations, increased prevalence of comorbidities, and advances in revascularization techniques have led to a subset of patients needing complex and high-risk indicated procedures (CHIP).[5] These procedures, often involving patients with multivessel disease, left main coronary artery involvement, or reduced ventricular function, present unique clinical challenges due to higher risks of adverse outcomes and procedural complications.[6]

In Taiwan, where cardiovascular diseases are a leading cause of morbidity and mortality, the need to better understand the outcomes and management strategies for CHIP cases is critical.[7] While international guidelines and studies can provide some insight, localized data specific to Taiwanese patients are necessary to tailor treatment approaches effectively. In 2020, The Taiwan Society of Cardiovascular Interventions (TSCI) launched a registry to track these CHIP patients in Taiwan and evaluate the effectiveness and prognosis of PCI treatment in the TTT-CHIP (Taiwan Transcatheter Therapeutics- Complex and High-risk Indicated Procedures/Patients) registry. The registry was established to address the knowledge gap, providing a comprehensive dataset of high-risk PCI cases under management across multiple hospitals in Taiwan.

This study aimed to report on the management strategies, clinical outcomes, and predictors of adverse events in complex PCI cases in Taiwan. By analyzing data collected from 2014 to 2021, the registry sought to inform clinical decision-making, improve patient outcomes, and support the development of guidelines that reflect the unique characteristics and needs of the Taiwanese population undergoing CHIP procedures.

Methods

Patient selection

Patients were included if they met the following inclusion criterion nr. 1 and at least one of the conditions listed in criterion nr. 2:

1. SYNTAX Score > 32, and
2. Left ventricular ejection fraction (LVEF) < 40% or acute myocardial infarction (AMI) or cardiogenic shock or severe left main disease, whereby severe left main disease included true left main bifurcation (Medina 1,1,1 or 0,1,1) or heavy calcification requiring scoring balloon, cutting balloon or debulking techniques.

Data collection

Data were collected retrospectively using a standardized online case report form (Figure 2A, 2B). At each study site, local study coordinators gathered additional information by completing an online electronic data capture form based on patient medical charts. Clinical data were extracted from hospital and outpatient records, including demographic details, underlying comorbidities, lifestyle factors, medication usage, echocardiographic findings, angiographic data and clinical outcomes. The study variables are outlined in Table 1.

Outcome measures

The TTT-CHIP registry study's outcome measures included a comprehensive evaluation of procedural success, patient complications, and long-term follow-up data, as shown in Table 2. This extensive outcome dataset enabled a detailed analysis of procedural safety, efficacy, and post-procedural recovery in high-risk PCI patients.[1]

Clinical endpoints

The primary endpoint of the study was the incidence of major adverse cardiovascular events (MACEs) within one year post procedure, defined as cardiovascular death, non-fatal myocardial infarction, repeat revascularization and stroke.

Secondary endpoints included all-cause mortality, the incidence of specific procedural complications such as stent thrombosis, vascular complications, hospitalization due to acute coronary syndrome, and the need for re-intervention.

The distribution of enrolled patients across participating hospitals in the TTT-CHIP registry, along with their respective percentages of the total, was as follows (see also Figure 1):

1. **National Taiwan University Hospital (NTUH):** 32 patients (7.5%)
2. **Taipei Veterans General Hospital (TVGH):** 97 patients (22.7%)
3. **Linkou Chang-Gung Memorial Hospital (CGMH):** 73 patients (17.1%)
4. **Shin Kong Wu Ho-Su Memorial Hospital (SKH):** 95 patients (22.2%)
5. **Cheng Hsin General Hospital (CHGH):** 135 patients (31.6%)
6. **Taichung Veterans General Hospital (TCVGH):** 20 patients (4.7%)

This multi-center collaboration highlighted the geographic diversity of Taiwan's healthcare system and its capacity to manage complex and high-risk PCI cases. The registry provided valuable insights into these hospitals' procedural outcomes and patient management strategies.

The figures illustrate the design and structure of the online registration form used for the TTT-CHIP registry. The form includes fields to capture essential patient information, baseline characteristics, procedural details and outcome measures. It is tailored to ensure consistency in data collection across multiple centers, facilitating accurate and comprehensive documentation for all enrolled patients.

Statistical analysis

Descriptive statistics were used to summarize baseline characteristics and clinical outcomes. Kaplan-Meier survival analysis was used to evaluate event-free survival, visually representing time-to-event data for major adverse cardiovascular events (MACEs) and other adverse outcomes. Multivariate regression models were utilized to identify predictors of adverse outcomes, offering a deeper understanding of risk factors and their influence on clinical results. Sensitivity analyses were performed to test the robustness of the results under different assumptions and data-

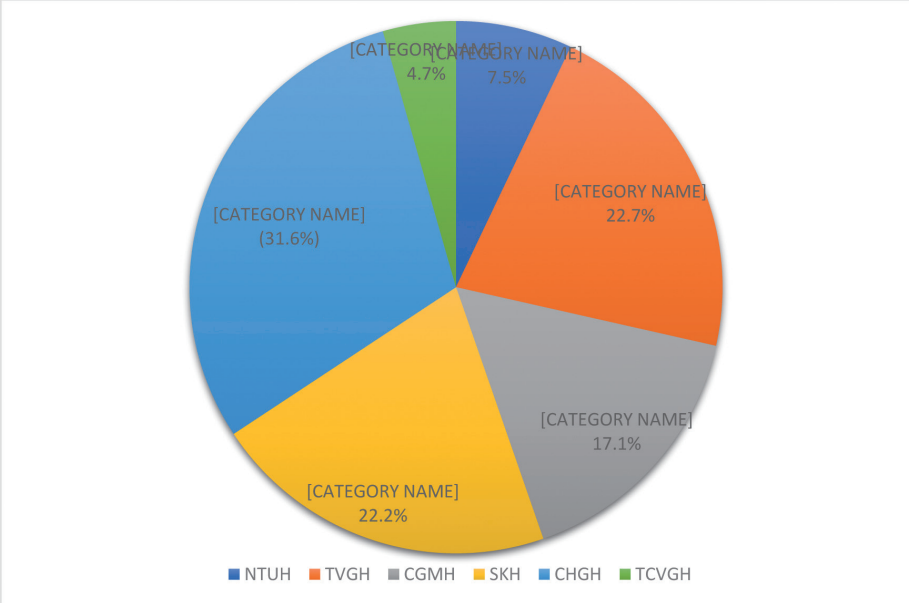

Figure 1. Distribution of enrolled patients across participating hospitals with percentages of the total.

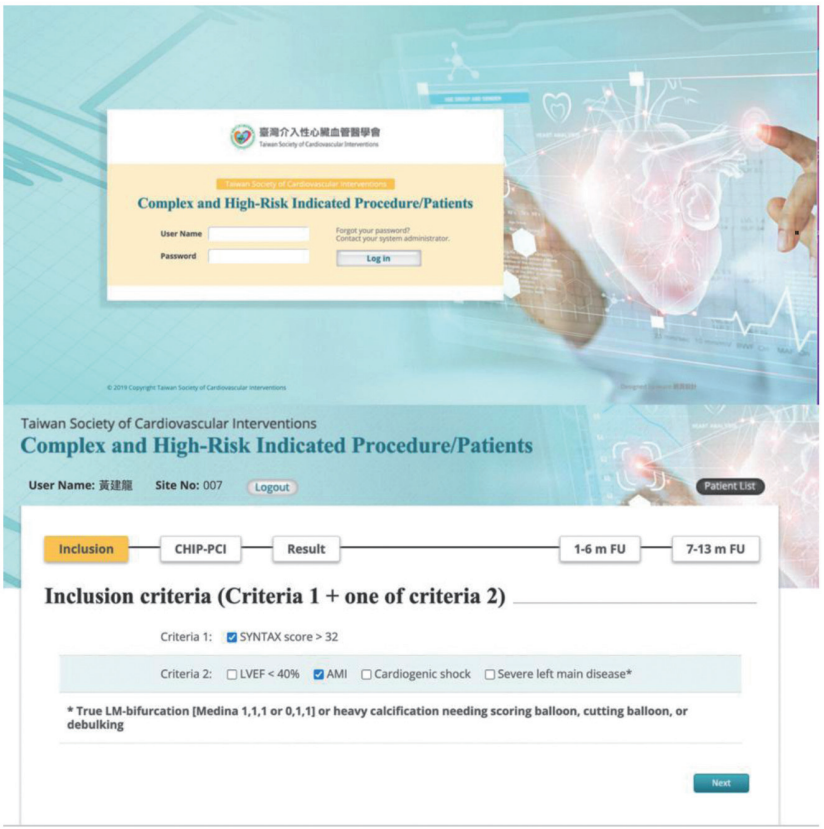

Figure 2A. Screenshot of the online registration form for the TTT-CHIP Registry.

handling strategies.

Subgroup analyses stratified data by overall survival, comparing patients presenting with and without cardiogenic shock and those undergoing elective versus rescue mechanical circulatory support. Additional key patient risk factors such as cardiogenic shock, hypertension, diabetes, atrial fibrillation, chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), the timing of dual antiplatelet therapy (DAPT), and the use of IIb/IIIa inhibitors or thrombus aspiration devices were also evaluated.

Discussion

This study highlighted the importance of CHIP procedures in addressing the needs of high-risk cardiovascular patients, a population with limited therapeutic options in Taiwan.[8] By leveraging data from a multicenter registry, the study was able to provide critical insights into the outcomes of these complex interventions performed within Taiwan's healthcare system.[9] It therefore fills a significant knowledge gap, offering a platform to compare regional results with international benchmarks, fostering global collaboration, and addressing unique challenges such as healthcare accessibility and procedural costs.[10] These insights are pivotal for shaping localized best practices while contributing to the worldwide understanding of CHIP procedures.[11]

The study's retrospective design was a double-edged sword. While its multicenter nature ensured diverse patient representation, limitations such as potential biases in patient selection and missing data must be acknowledged. Incorporating a more precise definition of procedural complexity, such as through SYNTAX

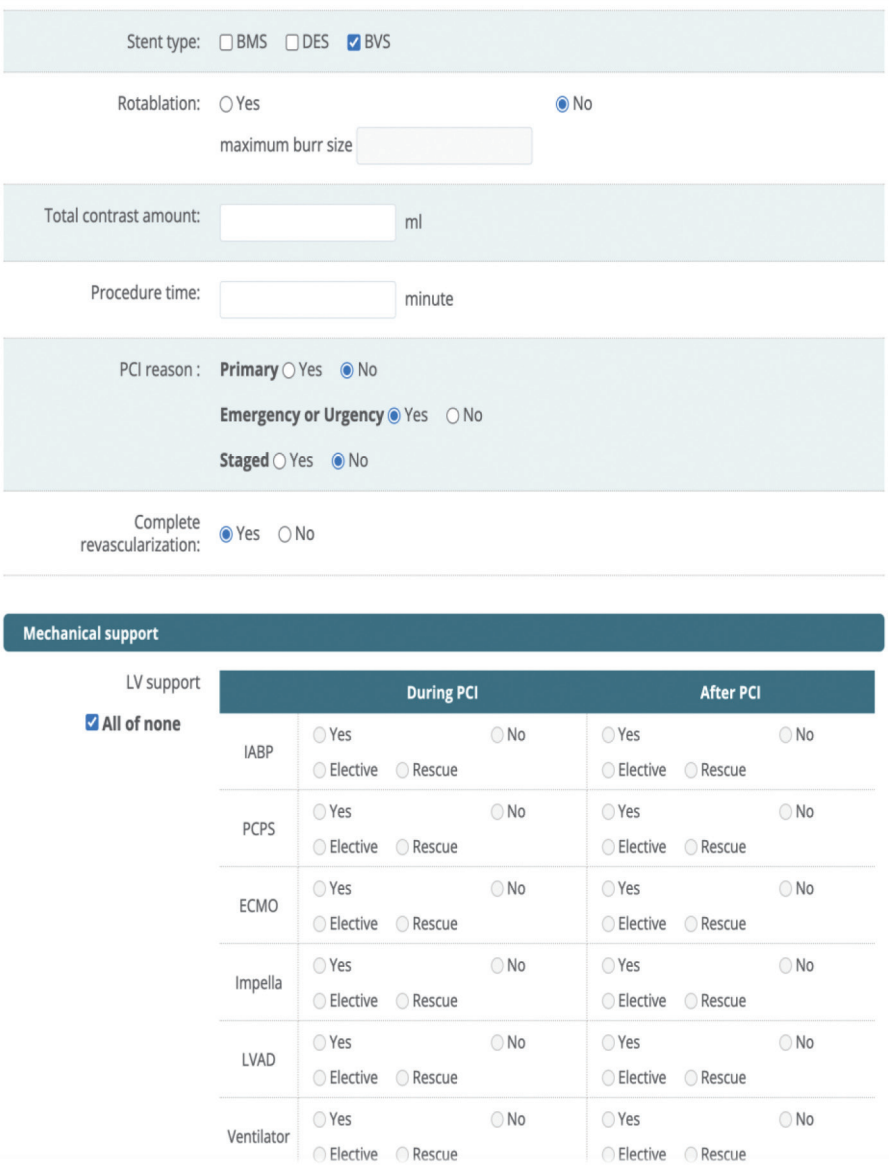

Figure 2B. Sample screenshot of the online registration form used for the TTT-CHIP registry.

scores or other validated metrics, would have enhanced methodological rigor and enabled more standardized comparisons.[12] Additionally, details on how MACEs were adjudicated, such as through independent committees or algorithms, would have further strengthened the reliability of the findings.[13]

Mechanical circulation support (MCS) in high-risk CHIP patients can help stabilize their condition, potentially improving procedural success.[1] While intra-aortic balloon pumps (IABPs) have traditionally been used, newer devices like Impella and ECMO may offer more potent hemodynamic support, contributing to better patient outcomes in appropriate cases.[14] The registry evaluated the application (elective or rescue) and the benefits and risks of MCS for CHIP patients in Taiwan.

The use of high-potency P2Y12 inhibitors enables faster and more effective platelet

Table 1. Study variables collected in the TTT-CHIP Registry

Category	Variables
1. Demographics and admission details	Age, gender, BMI Blood pressure (BP) Admission and discharge dates Admission status: stable angina, unstable angina, NSTEMI or STEMI
2. Medical history	Smoking history Hypertension Atrial fibrillation (with/without anticoagulants: warfarin or DOAC) Pacemaker implantation Hypercholesterolemia, hypertriglyceridemia with low HDL Diabetes mellitus (DM) CKD (with/without regular HD) COPD Asthma
3. Laboratory data	Pre- and post-procedure: BUN and creatinine Troponin I/T Hemoglobin Platelets Glucose HbA1c Bilirubin-T
4. Target coronary lesion characteristics	Diseased vessels: one, two, three, or left main involvement Moderate or severe calcification Bifurcation lesions Chronic total occlusion (CTO) Long lesions (>38 mm) Lesions with angulation (>45 degrees)
5. Concomitant cardiac disease	Structural/valvular heart disease (e.g., AS, AR, MS, MR, post-op status) Previous CABG LV function/dysfunction: LVEF, LVEDD, IVS, LVPW, TRPG, RVSP CVS consultation
6. Interventional procedures	Date of intervention Access site and sheath size (radial, femoral, brachial, or other) Imaging devices Balloon-only procedures Total stent length and stent size Stent type: BMS, DES, or BVS Rotablation (with maximum burr size) Total contrast volume Procedure time PCI indication: primary, emergency, urgent, staged Complete revascularization Mechanical support: IABP, PCPS, ECMO, Impella, LVAD Elective or rescue ventilator use
7. Medications	DAPT at admission and/or during the procedure: including aspirin, ticagrelor, prasugrel, bivalirudin Statin use at admission and/or discharge IIb/IIIa inhibitor administration Thrombus aspiration catheter Intravenous medications during PCI: dobutamine, dopamine, norepinephrine, adrenaline, atropine, diuretics

Table 2. Outcome measures of the TTT-CHIP registry study

Category	Outcome measures
1. Intra-procedural complications	Severe hypotension requiring hemodynamic support or CPCR Angiographic results (TIMI score) Procedural success: Emergency CABG, open heart surgery, CPCR, death or medical control only
2. Acute kidney injury (AKI)	Defined by: Serum creatinine >1.5x at baseline or increase by >0.3 mg/dL within 48 hours; urine output <0.5 mg/kg/hour over 6 hours
3. Bleeding events	Categorized by BARC definitions (type 0; no bleeding to type 5; fatal bleeding)
4. Re-hospitalization	Incidence and frequency of rehospitalization due to ACS or heart failure
5. Major adverse events	All-cause mortality Cardiovascular (CV) death Acute stroke or TIA Repeat revascularization
6. Stent thrombosis	Defined by ARC definitions (definite or probable) Treatments: CABG, balloon angioplasty, DEB, DES, or medical control only
7. Cardiac function	Left ventricular parameters: LVEF, LVEDD, IVS, LVPW, and TRPG
8. Laboratory data	Lipid profile: TG, TC, HDL-C, LDL-C Biomarkers: BNP, NT-pro BNP

inhibition, which is particularly beneficial for high-risk patients undergoing PCI.[15] However, the associated increased bleeding risks underscore the need for a personalized approach to antiplatelet therapy.[16] The registry also clarified the optimal strategies for balancing ischemic and bleeding risks in the CHIP population in Taiwan.[17]

This study is distinguished by its inclusion of complications, offering a more comprehensive perspective on procedural results. These insights are critical for the understanding of the broader impact of CHIP interventions on patient well-being. Furthermore, the data generated can guide clinicians in refining patient selection and tailoring procedural strategies, such as determining the best use of adjunctive technologies like rotational atherectomy.[18] Identifying predictors of success or complications can help optimize outcomes and inform risk-reduction strategies.

The findings have far-reaching implications for clinical practice, policy development, and research. The study provides practitioners in Taiwan with actionable insights to enhance decision-making in high-risk interventions. On a policy level, the data can support the creation of localized treatment guidelines tailored to Taiwan's healthcare environment. From a research perspective, the study highlights areas for further exploration, such as comparative analyses of PCI and CABG in high-risk populations, the role of drug-coated balloons, and long-term outcomes of CHIP procedures.[19]

Challenges in performing CHIP procedures, such as operator expertise requirements, resource limitations, and procedural costs, underscore the need for systemic improvements. Building multidisciplinary heart teams, expanding access to advanced technologies and investing in operator training are crucial for addressing these barriers. Future research should include prospective studies to validate the current findings, evaluate the long-term durability of revascularization, and explore novel approaches in order to improve patient outcomes in Taiwan.

Limitations

This study had several limitations that warrant consideration. First, its retrospective design needed the rigor of prospective and randomized methodologies, and potentially introduced bias. Second, the study was confined to six medical centers in Taiwan, excluding centers from the southern and eastern regions of the country, which may limit the generalizability of the findings. Additionally, the non-consecutive inclusion of patients in the registry introduced selection bias.

The TTT-CHIP registry focused on specific conditions, including a SYNTAX score greater than 32, together with one of the following: LVEF less than 40%, acute myocardial infarction (AMI), cardiogenic shock, or severe left main disease. It did not comprehensively address other high-risk conditions, such as coronary artery disease (CAD) combined with severe aortic stenosis or PCI for the last remaining vessel or chronic total occlusion, etc.

Despite these limitations, this registry represents Taiwan's first dataset regarding complex and high-risk percutaneous coronary intervention (CHIP). This highlights the potential value of the registry in understanding and managing CHIP cases in Taiwan.

Conclusion

This study demonstrated that performing PCI in CHIP patients was feasible with proper planning and execution by a skilled and experienced multidisciplinary heart team.[20] Successful outcomes in this high-risk population required tailored strategies, including careful patient selection, advanced procedural techniques, and optimal use of mechanical circulatory support devices.[21]

The TTT-CHIP registry provided insight into the management of complex PCI cases in Taiwan, informing clinicians about the risks and outcomes associated with CHIP procedures in high-risk patients. Findings may support the development of localized treatment protocols, improving safety and effectiveness in high-risk PCI interventions.

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