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Research paper

Smidt Heart Institute Takotsubo Registry – Study design and baseline characteristics

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ABSTRACT

Background: Takotsubo syndrome (TTS) is an acute form of transient systolic heart failure that occurs predominantly among women and in association with emotional or physical stressors. The Smidt Heart Institute Takotsubo Registry aims to establish a database through an online patient-advocate registry for deep phenotyping of this syndrome.

Methods: The Takotsubo Registry is a retrospective and prospective observational registry of individuals with a prior history of TTS. Participants are sourced through physician referrals, medical records review, peer- and self-referrals using social media. Research Electronic Data Capture (REDCap) and Mitra® microsamplers are used to collect questionnaire data and blood samples to facilitate completely remote study enrollment and participation for most participants.

Results: From January 2019 to May 2021, 125 participants (99% female, mean age: 61.5 ± 9.9 years) enrolled in the registry across 25 US states and 3 international countries, with reported first TTS event a median of 2 years prior to enrollment. Psychosocial characteristics determined by standardized questionnaires at baseline include relatively high anxiety trait (44%), moderate to severe depression severity (19%), moderate to high severity of posttraumatic stress disorder symptoms (58%) and a history of childhood trauma/abuse (50%).

Conclusions: The Smidt Heart Institute Takotsubo Registry will contribute to advancing the management of TTS by deep phenotyping to understand its pathophysiology, and identify treatment targets in a participant base for future clinical trials.

1. Introduction

First described in 1990, Takotsubo Syndrome (TTS) is an acute form of transient systolic heart failure that occurs predominantly in postmenopausal women [1]. It is most often characterized by wall-motion abnormality (WMA) of the apex with preserved basal segment function (apical ballooning syndrome). Mid-ventricular, basal, and focal WMA are other less frequent manifestations of the syndrome. The symptoms, electrocardiographic (ECG) changes, and elevated cardiac biomarkers in TTS mimic acute myocardial infarction thus often leading to misdiagnosis [2]. Also called stress cardiomyopathy, TTS is widely recognized to occur in association with emotional or physical stressors. While the precise etiology remains unclear, factors including multivessel

coronary artery spasm, coronary microvascular dysfunction and catecholamine toxicity have been considered as pathophysiologic pathways [1,3].

Although TTS was initially believed to be benign, there is increasing evidence regarding short- and long-term mortality – comparable to ST-segment elevation myocardial infarction (STEMI) and non-STEMI (NSTEMI) in some cases [4–6]. In-hospital mortality rates between 1 and 5% [5,7,8], as well as long-term mortality rates up to 5.6% per patient-year, have been reported [7,9]. TTS recurrence rates between 5% to 22% and major adverse cardiovascular event (MACE) rates of 9.9% per patient-year have also been documented [8–10]. These figures highlight a significant disease burden that needs to be addressed for the benefit of the affected population.

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The limited knowledge about TTS pathophysiology translates to a lack of standards in clinical management. This has also impacted the development of preventive or mitigating strategies for those at risk. To close this gap, authors have proposed the need for clinical trials to identify evidence-based therapies and prevent recurrence [9]. The Smidt Heart Institute Takotsubo Registry at Cedars-Sinai Medical Center (CSMC) directly addresses this need by collating observational data to understand the history of the disease, its medical impact, pathways to mortality and treatment targets. Analysis of these data will contribute to better estimation of the prevalence of TTS cases, recognition of risk factors, and development of accurate diagnostic, treatment, and prevention strategies. The registry will also contribute to existing literature by studying psychosocial characteristics as well as provide a pool of participants for potential experimental studies in the future.

1.1. Study aims

The Smidt Heart Institute Takotsubo Registry aims to: (1) establish a database for patients with TTS through a convenient and easy to use on-line patient-advocate registry; (2) conduct comprehensive data collection for deep phenotyping including proteomic profiling for further biomedical study of the pathophysiology of TTS. This report presents the study design, methodology, and baseline characteristics of currently enrolled participants. Ultimately, we intend for this database to be leveraged as a platform for patient-centered point-of-care investigation and clinical trials to improve diagnosis, clinical care, and patient outcomes.

2. Methods

2.1. Study design

The Takotsubo Registry is a retrospective with prospective follow-up observational registry of individuals with a prior history of at least one TTS event. Patients are sourced from multiple sources including physician referrals, medical records review, advertisement through a dedicated social media page, and referrals from enrolled participants.

Retrospective data on previous TTS events are obtained at enrollment, and then participants are followed up annually to collect prospective data. Enrollment started in January 2019 and data collection is ongoing with no pre-specified end date.

Informed consent is obtained electronically using an e-link that provides participants access to an online platform for secure e-consent and data collection from remote sites. Study data are collected and managed using Research Electronic Data Capture (REDCap) tools hosted at CSMC [11,12]. REDCap is a secure, web-based software designed to support data capture for research studies, providing 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources. Study questionnaires can be accessed on REDCap only after completion of the e-consent. Subjects who decline consenting are unable to move forward with enrollment. Participants who are less comfortable with accessing the forms online have the option to receive them via mail. Ethical approval for the registry was obtained from CSMC Institutional Review Board. The study is registered on www.clinicaltrials.gov with registration number: NCT03910569 (Fig. 1).

2.2. Inclusion and exclusion criteria

The inclusion criteria for enrollment are 1) previous diagnosis of TTS, and 2) willingness to provide consent and sign a release of information authorization or submit full medical records for event adjudication. Individuals younger than 18 and those unable to give consent are excluded from participation.

2.3. Pre-enrollment

Medical records of patients identified through physician referrals and Deep 6 AI® searches are reviewed for diagnoses of TTS, approved under the "Consent/HIPAA Waiver to Identify & Recruit Subjects Via a Review of Medical Records". Deep 6 AI® is an artificial intelligence software that analyzes structured and unstructured clinical data to

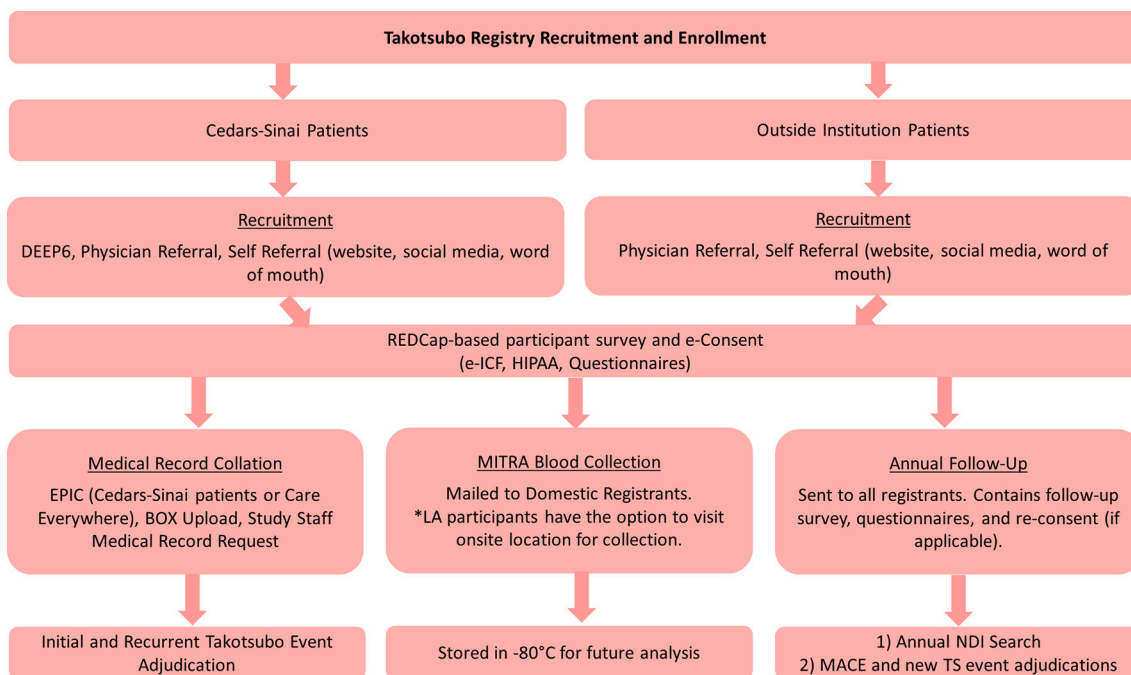


Fig. 1. Smidt Heart Institute Takotsubo Registry recruitment and enrollment flowchart. Pictorial representation of the workflow from recruitment till enrollment and long-term follow up.

identify patients that match complex clinical trial criteria [13]. Permission is obtained from treating physicians before direct contact is made with patients identified through Deep 6 searches. Other prospective participants who contact the study team via self- or peer-referral but do not have records in the CSMC system can enroll in the registry if they have a prior history of TTS diagnosed by a physician. These participants are asked to sign a Release of Information Authorization form that allows the study team to request their medical records from non-CSMC facilities.

All medical records related to prior TTS events (singular and recurrent) are reviewed by Smidt Heart Institute investigators to adjudicate the diagnosis of TTS. This allows for comparison and verification of self-reported TTS information using standard criteria. Adjudications are based on the International Takotsubo (InterTAK) Diagnostic Criteria shown in Fig. 2 [14].

Records required for adjudication include:

- Troponin levels & ECGs at time of event
- Echocardiograms/Ventriculograms (index event & follow-up)
- Coronary angiography
- Hospitalization summary

Events are adjudicated as definite TTS, probable TTS, probable not TTS, and definite not TTS based on medical records review. Subjects are notified of the adjudication results. When diagnosis is uncertain, cases are reviewed by the core team of investigators (cardiologists) to reach consensus. REDCap forms are used to collect patient data extracted from medical records, including baseline medical history, triggering factors, initial vital signs and laboratory values, treatment history, results on electrocardiography, echocardiography, and coronary angiography. TTS is classified as apical ballooning, midventricular, basal, or focal type.

2.4. Baseline data

An e-survey queue on REDCap is used to collect data about participants' demographics and general health with a focus on prior heart disease and potential emotional and mental stressors. This is accomplished by the use of standardized questionnaires including Spielberger State-Trait Anxiety Inventory (STAI) Form Y-2, Cardiac Anxiety questionnaire (CAQ), Post-Traumatic Stress Disorder (PTSD) Checklist-Civilian Form (PCL-C), Perceived Stress Scale (PSS), Patient Health Questionnaire 9 (PHQ-9), Early Trauma Inventory Self Report – Short

form (ETISR-SF), Seattle Angina questionnaire (SAQ), Duke Activity Status Inventory (DASI), and General Health questionnaire (SF-12). SAQ scores range from 0 to 100, with higher scores indicating better function e.g., less physical limitation, higher quality of life. DASI metabolic equivalents (DASI METs) range from 0 to 16.7, higher scores also indicate better functional capacity. The psychosocial characteristics we assess include: Trait-Anxiety measured by the STAI, Heart Focused Anxiety (HFA) measured by the CAQ, PTSD symptom severity measured by the PCL-C, perceived stress levels measured by the PSS, depression severity measured by the PHQ-9, and childhood trauma measured by the ETISR-SF. HFA is a fear of cardiac-related stimuli and sensations because of their perceived negative consequences while Trait-anxiety is a measure of individuals' relatively long-term susceptibility to anxiety [15,16]. STAI Trait-A scale value ≥ 40 is considered as the cut-off for high anxiety trait [15], PHQ-9 ≥ 10 for moderate to severe levels of depressive symptoms [17], PCL-C score ≥ 30 for moderate to high severity of PTSD symptoms [18], Total ETI score ≥ 7 for a significant history of childhood trauma/abuse, and ETI sexual abuse score ≥ 1 for a significant history of childhood sexual abuse [19]. A dedicated questionnaire also collects information about prior TTS events based on participants' recollection. In addition, an integrated questionnaire that focuses on medical and reproductive history as well as past hospitalizations is used to collect baseline data, and a shorter version is used subsequently for follow ups. Participants are required to complete the demographics questionnaire; however, all other questionnaires are optional. Our system also flags psychosocial questionnaire responses that are indicative of suicide risk (e.g., question 9 from the PHQ-9) which allows us to provide immediate support when necessary.

2.5. Proteomic profiling

A simple blood sampling device is used to collect finger-stick blood from patients in the convenience of their homes for discovery proteomic analysis. The Mitra® Microsampler (Neoteryx, Torrance, CA) is an FDA approved class 1 medical device based on Volumetric Absorptive Microsampling (VAMS®) technology [20]. It is beneficial for collecting a fixed volume of blood for transport, extraction, and analysis without need for cold chain logistics. The device wicks up to 20 μ l of blood from a finger prick and is air dried for 2 h before shipping. Samples are stored for future proteomics analysis which will employ Multiple Reaction Monitoring (MRM) mass spectrometry technique. Mitra kits are only distributed to domestic participants.

International Takotsubo Diagnostic Criteria (InterTAK Diagnostic Criteria)

¹ Transient^a left ventricular dysfunction (hypokinesia, akinesia or dyskinesia) presenting as apical ballooning or midventricular, basal or focal wall motion abnormalities. Right ventricular involvement can be present. Besides these regional wall motion patterns, transitions between all types can exist. The regional wall motion abnormality usually extends beyond a single epicardial vascular distribution; however, rare cases can exist where the regional wall motion abnormality is present in the subtended myocardial territory of a single coronary artery (focal TTS).^b

² An emotional, physical or combined trigger can precede the Takotsubo syndrome event, but this is not obligatory.

³ Neurologic disorders (e.g., subarachnoid hemorrhage, stroke/transient ischemic attack, or seizures) as well as pheochromocytoma may serve as triggers for takotsubo syndrome.

⁴ New ECG abnormalities are present (ST-segment elevation, ST-segment depression, T-wave inversion, and QTc prolongation); however, rare cases exist without any ECG changes.

⁵ Levels of cardiac biomarkers (troponin and creatine kinase) are moderately elevated in most cases; significant elevation of brain natriuretic peptide is common.

⁶ Significant coronary artery disease is not a contradiction in takotsubo syndrome.

⁷ Patients have no evidence of infectious myocarditis.

⁸ Post-menopausal women are predominantly affected.

^a Wall motion abnormalities may remain for a prolonged period or documentation of recovery may not be possible. For example, death before evidence of recovery is captured.

^b Cardiac magnetic resonance imaging is recommended to exclude infectious myocarditis and diagnosis confirmation of takotsubo syndrome.

Fig. 2. International Takotsubo diagnostic criteria. Reprinted with permission from Ghadri et al. [14].

2.6. Prospective follow-up

Annual follow up data is collected via e-surveys sent to participants similar to baseline data collection. Surveys collect data about new cardiac events and emerging health issues in the previous year as well as information related to anxiety, PTSD, stress, depression, angina, and health status. In addition, an annual National Death Index (NDI) search is completed for subjects who fail to complete surveys for each follow up period to determine if they are deceased. If death is due to cardiac causes, details are included in the registry database for affected subjects.

2.7. Statistical analysis

Baseline characteristics are presented as frequencies (percentages) of categorical variables, median (IQR) of physical activity variables and mean (SD) of all other continuous variables. All analyses were performed using SAS, version 9.4 (SAS Institute Inc.).

3. Results

From January 2019 to May 2021, 125 participants enrolled in the registry. Demographic and clinical characteristics at baseline are shown in [Tables 1 and 2](#). Among the enrolled participants, one was excluded due to self-withdrawal. About 89% completed baseline questionnaires and 77% returned Mitra kits with blood samples. Median number of years between first self-reported TTS event and enrollment was 2 (0,5) years. A greater proportion of participants were post-menopausal,

Table 1
Baseline demographic characteristics.

N = 124	n (%) or mean ± SD
Age ^a	61.5 ± 9.9
Sex	
Female	123 (99.2)
Male	1 (0.8)
Race/ethnicity	
Asian or Pacific Islander	2 (1.6)
Black or African American	1 (0.8)
Hispanic/Latino	3 (2.4)
White	112 (90.3)
Other	2 (1.6)
Multiple	4 (3.2)
Marital status	
Never married	9 (7.3)
Widowed/divorced/separated	27 (21.8)
Presently married	84 (67.7)
Living in a marriage-like relationship	4 (3.2)
Educational status	
Some high school	3 (2.4)
High school diploma or G.E.D.	11 (8.9)
Some college education but no degree	22 (17.9)
Associate degree, vocational, or other after high school training school certificate	12 (12.2)
College graduate or baccalaureate degree	26 (21.1)
Master's degree	30 (24.4)
Doctoral degree	16 (13.0)
Income	
Less than \$20,000	5 (4.1)
\$20,000 to 49,999	21 (17.1)
\$50,000 to 99,000	33 (26.8)
\$100,000 or more	57 (46.3)
Don't know	7 (5.7)
Insurance	
Public	52 (41.9)
Private	62 (50.0)
Other	9 (7.3)
None	1 (0.8)
Participants' location	
US-based	104 (83.9)
International	20 (16.1)

^a Mean (SD).

Table 2
Baseline clinical characteristics.

N = 124	n (%) or mean ± SD
Identifiable trigger	79 (68.1%)
Identifiable trigger types	
Emotional trigger only	34 (43.0%)
Physical trigger only	19 (24.1%)
Emotional and physical triggers	25 (31.6%)
Unspecified	1 (1.3%)
No reported trigger	37 (31.9%)
Number of self-reported Takotsubo events ^a	
1	90 (72.6%)
2	22 (17.7%)
3	7 (5.6%)
>4	5 (4.0%)
Mean per participant number of Takotsubo events	1.6 ± 1.1
History of cigarette smoking	40 (34.2%)
History of coronary artery disease	54 (46.2%)
History of hypertension	50 (42.7%)
History of dyslipidemia	39 (33.3%)
History of diabetes	12 (10.3%)
Post-menopausal	105 (91.3%)
Prior use of hormone replacement therapy	46 (40.0%)

^a Participants who did not answer this question were assumed to have 1 self-reported event.

Caucasian females. About a quarter of participants reported more than one TTS event. Commonly reported triggers include emotionally unpleasant events, physical activity, and acute physical medical conditions. Two participants reported emotionally pleasant events as triggers. SAQ-7 scores indicate moderate angina burden, while scores from psychosocial questionnaires show a significant number of participants with relatively high anxiety trait, moderate to high severity of PTSD symptoms and history of childhood trauma ([Tables 3 and 4](#)).

4. Discussion

To the best of our knowledge, the Smidt Heart Institute Takotsubo Registry is the first that employs a community-based recruitment strategy in addition to hospital-based recruitment. Other large Takotsubo registries include the InterTAK Registry [21], GEIST (German Italian Stress Cardiomyopathy) Registry [22], and Spanish RETAKO (Registry for Takotsubo Cardiomyopathy) National Registry [23]. These registries have enrolled subjects either based on medical records review or new diagnoses following presentation at a participating hospital. Our digital marketing approach presents an opportunity for participants to enroll regardless of when they had their TTS event or where they receive care. This helps us to cast a wide net, thereby increasing the chances of obtaining deeper phenotyping that would further contribute to scientific knowledge. The success of this approach is evidenced by the 38% of our enrollees who are self- or peer-referrals; most of them learned about the registry through adverts on a Facebook-based support group for TTS. We also have participants spread across 25 US states and 3 international countries, many of whom may not have had the opportunity to participate otherwise ([Fig. 3](#)).

Table 3
Patient-reported characteristics.

N = 108	Median (IQR)
Seattle Angina Questionnaire (SAQ) Scores	
Physical limitation	86.1 (61.1, 97.2)
Angina stability	50.0 (50.0, 50.0)
Angina frequency	90.0 (70.0, 100.0)
Treatment satisfaction	81.3 (50.0, 100.0)
Quality of life	66.7 (41.7, 83.3)
Overall SAQ-7 score	85.3 (60.8, 95.8)
Duke Activity Status Inventory (DASI)	
DASI METs	7.1 (3.1, 13.0)

Table 4
Psychosocial characteristics.

N = 108	Mean ± SD
Cardiac Anxiety Questionnaire (CAQ)	
Total score	1.6 ± 0.7
Subscale 1: Fear Scale	1.7 ± 0.8
Subscale 2: Avoidance Scale	1.5 ± 1.0
Subscale 3: Heart Focused Attention Scale	1.5 ± 0.8
Spielberger State-Trait Anxiety Inventory T-Anxiety Scale	39.1 ± 12.6
Perceived Stress Scale (PSS)	
PSS total score	22.2 ± 10.8
PTSD Checklist-Civilian Form (PCL-C)	
PCL-C total score	34.5 ± 14.0
Patient Health Questionnaire – 9 (PHQ-9)	
PHQ-9 total score	6.2 ± 5.5
Early Trauma Inventory Self-Report – Short Form (ETISR-SF)	
General trauma	3.2 ± 2.4
Physical abuse	1.2 ± 1.3
Emotional abuse	1.7 ± 1.8
Sexual abuse	1.2 ± 1.7
Total ETI score	7.3 ± 5.0

Initial design and results demonstrate feasibility of a patient-support TTS Registry with virtual enrollment driven by remote data capture tools and a mobile blood collection kit. This approach is advantageous because it eliminates complexities related to scheduling visits and transportation reimbursements which are typical for clinical research studies. However, it could be associated with higher risk of missing data since participants may be less motivated to complete multiple questionnaires when they are unsupervised. Although sample collection with a micro-sampler provides lesser blood volumes than usual, given that this method has proven to be useful for our purposes of phenotyping, it is equally effective and likely more efficient than traditional sample collection methods [25]. However, a disadvantage of this approach is the challenge of coordinating shipping logistics across international borders for participants outside the US. This has led us to put a hold on

obtaining blood samples from international registrants. There have also been a few participants who were uncomfortable with pricking themselves. Retrieving medical records from facilities where participants have previously received care has been relatively easy for domestic participants but could be challenging for international registrants. So far, having international participants request and upload their medical records to our secure Box platform has been a good work-around, although it adds an extra layer of effort on their part.

Younger patients with TTS are generally more likely to survive, thus being at risk for recurrence, longer-term morbidity, and mortality. Successfully enrolling a substantial number of younger participants presents an opportunity to design further studies that focus on facilitating prompt identification and optimal clinical management in this group as well as developing secondary prevention measures to prevent recurrence. Accordingly, our population is slightly younger (mean age: 61.5 ± 9.9 years) and has a lower proportion of males (1%) compared to prior studies. Mean age reported by others range from 66 to 69 years while the proportion of female participants in these studies range between 87 and 92% [7,10,26–28]. Using the incidence of more than one TTS event as a proxy for recurrence, our participants have a higher self-reported recurrence rate (27%) than other study populations which range from 5% to 22% [6,9,10]. A higher prevalence of acute neurologic and psychiatric disorders has been identified among younger patients as well as higher rates of TTS recurrence specifically in younger women, however these data are limited by medical diagnostic coding considerations [29,30]. There are also concerns that younger patients with TTS require more aggressive and vigilant clinical support during their initial presentation due to higher levels of sympathetic stimulation [31], suggesting that a focus on younger TTS survivors is warranted.

Frequencies of identifiable triggers in prior studies range from 58 to 76% similar to our finding of 68% [7,10,24,32]. Our participants have a higher prevalence of emotional triggers (emotional only – 43% v. physical only – 24%; Both – 32%) in contrast with other studies that report a higher prevalence of physical triggers [1,7]. Emotional triggers have been reported to occur more commonly in women [27], which may explain the higher prevalence in our study population. We extend prior observations in smaller sample sizes that among participants who filled

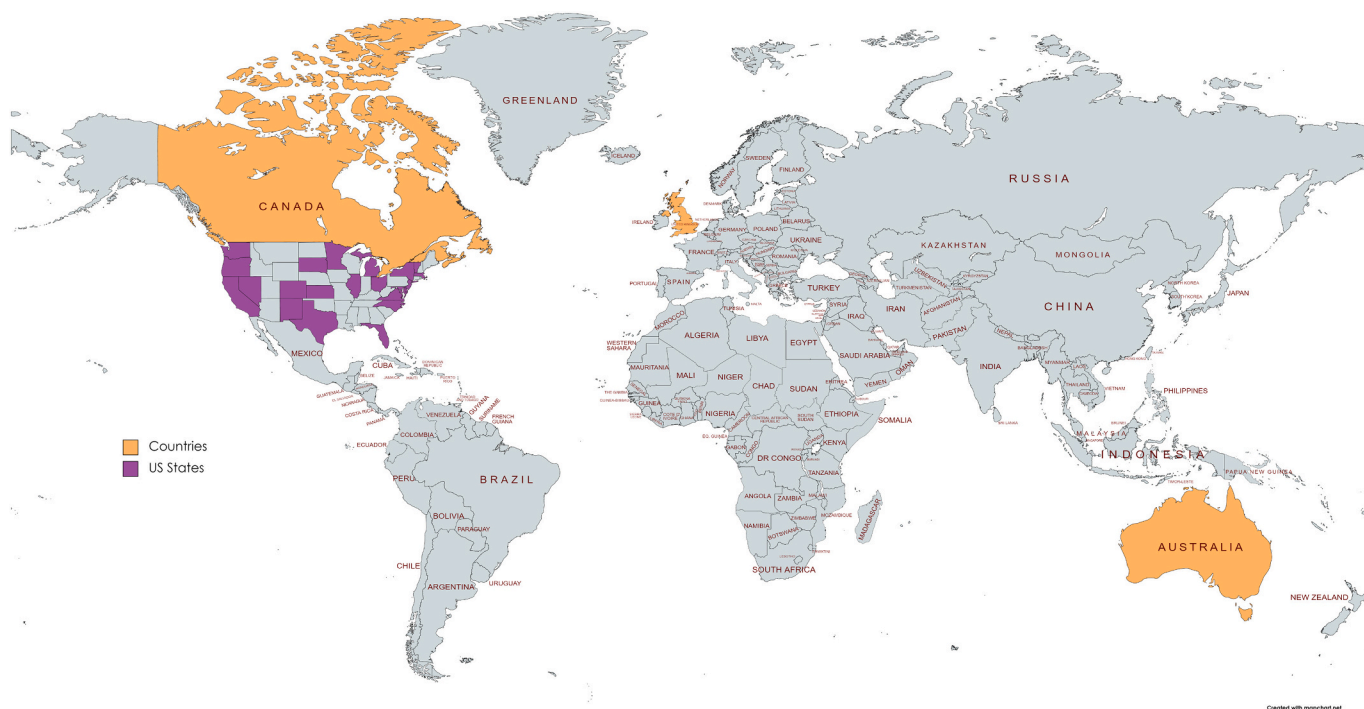


Fig. 3. Geographical distribution of Smidt Heart Institute Takotsubo Registry participants.

out the psychosocial questionnaires, 44% had high anxiety trait, 19% had moderate to severe levels of depressive symptoms and 58% had moderate to high severity of PTSD symptoms [15,17]. We report for the first time, ETISR-SF scores which indicate a history of childhood trauma/abuse among 50% of this subset, with 47% reporting a history of sexual abuse specifically. Although few studies have focused on comprehensive assessments of psychological measures apart from anxiety and depression, the common association between TTS and stress makes this exploration important to identify more specific correlations [17,33]. In addition, these assessments highlight an area of focus for comprehensive clinical care that improves the quality of life for this population.

There are now reports of residual reduction in functional capacity after TTS events which warrant further investigation [34]. SAQ and DASI measures provide a basis for characterizing physical function and will be useful to understand these residual effects of TTS as well as the possibility of compounded impairment for those who have comorbid cardiovascular diseases. Our proactive recruitment strategy allows us to obtain robust historical data about each event as well as other aspects of their health from the patients' perspective rather than relying solely on medical records. Complementing this information with medical records will be beneficial to compare findings with other studies that have used mainly clinical data. Annual follow up data will also contribute to understanding the intersections of TTS with other areas of cardiovascular health. The ease of filling out questionnaires through our online platform is expected to increase the chances of follow up visit completion.

The Smidt Heart Institute Takotsubo Registry is a foundation to advance the understanding and management of TTS. While the current paper explores clinical characteristics based solely on patient reports, future publications will discuss findings from clinical adjudication based on medical records. Other aspects to be explored include metabolomic predictions of adverse outcomes, rehospitalization, recurrent TTS events, mortality, and other MACE rates. As we recruit more participants, there will be further data analysis to identify risk factors including physical and emotional health states that predispose to the development of TTS. Together, these will provide insight into the natural history of TTS and effectiveness of current management techniques across various healthcare settings. We believe this information will be useful for developing future guidelines.

4.1. Limitations

Currently, our population has limited diversity with respect to gender and race. While this may be representative of the groups with higher biological risk, it could also be related to the potential for peer-referral to occur among groups with similar demographics. Studies have shown racial/ethnic differences in TTS outcomes including higher rates of in-hospital mortality and complications among African American and Japanese patients [35–37]. Medical and demographic factors (e.g. Higher prevalence of physical triggers, male gender, and other comorbidities) have been posited as drivers of these variations. Targeting our recruitment efforts to include participants from diverse groups will help us to further explore these differences.

5. Conclusions

The Smidt Heart Institute Takotsubo Registry aims to improve scientific knowledge and clinical management of TTS. Our innovative approach towards recruitment increases the potential to reach a large participant base and capture a wide variety of participant experiences. This will be used for deep phenotyping including proteomic profiling to understand TTS pathophysiology and identify treatment targets for future clinical trials.

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Disclosure

Dr. Bairey Merz has disclosures from Sanofi, Abbott Diagnostics, and iRhythm. Dr. Wei has disclosures from Abbott Vascular.

CRedit authorship contribution statement

Okezi Obrutu: Writing – original draft, Formal analysis, Data curation, Visualization. **Jenna Maughan:** Writing – review & editing, Formal analysis, Software, Data curation, Visualization, Project administration. **Benita Tjoe:** Writing – review & editing, Investigation. **Romana Herscovici:** Methodology, Investigation. **Prizzi Moy:** Project administration, Investigation. **Natalie Rojas:** Investigation, Visualization. **Janet Wei:** Conceptualization, Writing – review & editing, Validation. **Chrisandra Shufelt:** Conceptualization, Writing – review & editing. **Thomas Rutledge:** Writing – review & editing, Validation. **C. Noel Bairey Merz:** Conceptualization, Funding acquisition, Writing – review & editing, Supervision.

Declaration of competing interest

Dr. C. Noel Bairey Merz, serves as Board of Director for iRhythm, fees paid through CSMC from Abbott Diagnostics and Sanofi. Dr. Janet Wei served on an advisory board for Abbott Vascular.

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