Review Article

Knowledge domain and emerging trends in Takotsubo cardiomyopathy: a scientometric review based on CiteSpace analysis

Xintian Shou[1,2#^], Yumeng Wang[2#], Qiulei Jia[1,2], Jingjing Shi[1], Xuesong Zhang[1], Shuai Shi[1], Shu-Qing Shi[1,2], Guozhen Yuan[1], Ruoning Chai[1], Wenjing Xue[1,2], Yihan Yang[1,2], Chenglin Duan[1,2], Yuanhui Hu[1]

[1]Department of Cardiovascular Medicine, China Academy of Chinese Medical Sciences Guang'anmen Hospital, Beijing, China; [2]Graduate School, Beijing University of Chinese Medicine, Beijing, China

Contributions: (I) Conception and design: X Shou, Y Wang; (II) Administrative support: Y Hu; (III) Provision of study materials or patients: X Shou, Q Jia, J Shi, X Zhang, S Shi; (IV) Collection and assembly of data: Y Wang, SQ Shi, G Yuan, R Chai, W Xue; (V) Data analysis and interpretation: X Shou, Y Wang, Y Yang, C Duan; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Yuanhui Hu. Department of Cardiovascular Medicine, China Academy of Chinese Medical Sciences Guang'anmen Hospital, No. 5, beixiange, Xicheng District, Beijing 100053, China. Email: huiyuhui55@sohu.com.

Abstract: Takotsubo cardiomyopathy (TTC) is often acute with a high mortality rate and is subject to relapse. Meanwhile, its complex pathogenesis has attracted increasing attention. To learn more about TTC, CiteSpace V.5.7 R5W was used in this study to analyze the research status, hot spots, and trends in TTC before 2020. The keywords, co-citation references, as well as country and institution distribution were explored. A total of 2,349 papers were reviewed. The United States, Italy, and Germany were the main countries studying TTC and had good cooperation relationships. The Mayo Clinic topped the institution list, but the rate of inter-institutional cooperation was not high. Research hotspots include disease features, auxiliary diagnostic methods, epidemiology, and pathophysiological mechanisms, and the latest ones are complications related to prognosis, such as cardiovascular abnormalities caused by myocardial infarction and normal or non-obstructive coronary arteries (MINOCA), atrial fibrillation, stroke, cancer, and COVID-19. In conclusion, the research of TTC is in a hot development period. Our research will help clinicians and researchers to better understand TTC and its research status by providing a foundation for research objectives. In doing this, our research will help to provide better scientific management, diagnosis, and treatment for patients with TTC, which will in turn improve the prognosis of this condition.

Keywords: Takotsubo cardiomyopathy (TTC); knowledge domain; emerging trends; CiteSpace; scientometric review

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Introduction

Takotsubo cardiomyopathy (TTC) and associated variants are a form of acute but usually reversible heart failure. TTC was diagnosed in about 0.02% of all hospitalizations in the United States in 2008 (1). However, the total number of TTC cases is underestimated due to insufficient knowledge of the condition (2). Initially, TTC was considered benign,

^ ORCID: 0000-0002-1581-9495.

but studies have shown that it is often acute and patients can easily relapse. The morbidity and mortality of TTC are comparable to those of acute coronary syndrome, which is considered to be a clinical acute condition and has attracted an increasing amount of attention within the medical community (3).

CiteSpace is a bibliometric analysis software developed by Dr. Chaomei Chen. CiteSpace can quantitatively analyze the intrinsic relationship and cross-reference information between knowledge about TTC using mathematical and statistical methods. It enables us to analyze the potential knowledge contained in science or a field of science, and present the structure, law, and distribution of scientific knowledge maps by visual means (4). In this study, CiteSpace visualization was used to review and analyze the current research status and future trends of TTC with the aim of providing some suggestions for the mechanistic study and clinical study of this disease.

Methods

Literature search and collection

A literature search of the Web of Science Core Collection database was conducted (5). The search string was as follows: [TOPIC= (takotsubo OR tako-tsubo OR "tako tsubo" OR "stress cardiomyopathy" OR "apical ballooning syndrome" OR "broken heart syndrome")] AND Indexes= (SCI-EXPANDED OR CCR-EXPANDED) AND IC Timespan= (1985-2020) AND The literature types= (article or review).

The literature was retrieved on June 11, 2021. The following information was recorded from each retrieved article/review: publication date, title, abstract, keywords, author, and institutional affiliations of authors.

Search methods

Full records of the search results with cited references were exported in plain text and named download_*-*.txt to allow for their identification by the CiteSpace software. The data files were imported into CiteSpace, and the following parameter settings were selected: time slicing (2004 to 2020), 1 year per slice; term source (all selected), and node type (one at a time). To perform a visual analysis of the literature, we first selected the top 50 most cited or most frequently occurring items from each slice. Then, network cropping (pathfinder and pruning sliced networks) and visualization (cluster view-static and show merged network) were conducted. The node types selected for this study were the cooperative analysis nodes "institution" and "country", the co-occurrence analysis node "keyword", and the literature co-cited node. GraphPad Prism 7.0.0.159 software was employed to display the number of documents issued per year.

In a CiteSpace network, the thicker the link between nodes, the stronger the connection between them, and the brighter the color of the link, the more recent the cooperation. Betweenness centrality reflects the key strength of the nodes in a network: the larger the centrality, the more closely the intermediary link is represented by the node. Purple circles in the network represent nodes with a high degree of centrality (centrality >0.1). The keywords in the CiteSpace atlas were extracted from the literature based on the downloaded text content. High-frequency keywords represented hotspots for research in TTC at certain stages. The centrality of a keyword represented its critical degree in the network and the correlation between it and other nodes. CiteSpace uses a log-likelihood ratio algorithm to cluster closely related keywords. Clusters are considered successful with a silhouette coefficient of >0.7. The silhouette coefficient is a measure of whether the clustering is reasonable and effective. The closer the value of the silhouette coefficient is to 1, the more reasonable the sample clustering will be (6). Co-word maps (characteristic words or keywords) can aid in identifying research hotspots, especially when the burst term function is used (7,8). The keyword burst shows the frequency of keywords within a certain period. The time between the beginning and end of a burst indicates the period during which the keyword burst occurred, and the keyword's influence strength.

Results

Annual publication volume

A total of 2,349 relevant articles on TTC were retrieved, the first of which was published in 2004. The h-index of these articles was 62. The average number of citations per item was 31.05; the total citation frequency was 19,496 (excluding self-citations); and 8,581 references were cited (excluding self-citations). The annual number of papers published on TTC increased rapidly between 2004 and 2010, before stabilizing at high numbers in the period from 2010 to 2020, which indicates that TTC research was rapidly developing during this time (*Figure 1*).

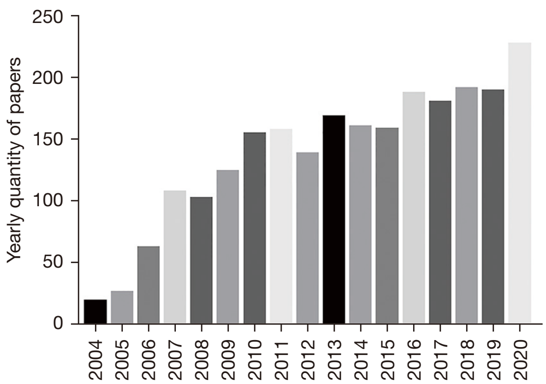

Figure 1 Yearly quantity of papers about TTC from 2004 to 2020. TTC, Takotsubo cardiomyopathy.

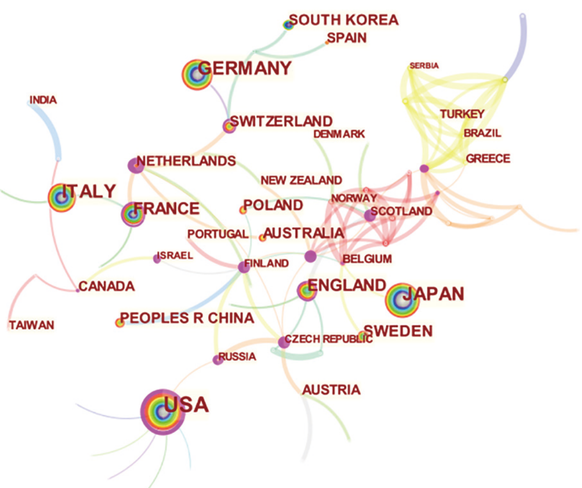

Figure 2 Countries network of publications about TTC. Circle node represents output country of papers; link between nodes represents partnership. TTC, Takotsubo cardiomyopathy.

Cooperation analysis of countries and institutions

Cooperation maps can display social relations between countries or research institutions within a certain research field, thus providing a new perspective for evaluating the academic influence of countries and institutions, and enabling us to identify research works that are deserving of attention (9,10).

After running CiteSpace, we obtained an international cooperation relationship with 77 nodes, each of which represented a country that had contributed to research on TTC, and 104 links (*Figure 2*). The network density was 0.0355. Among the top 10 countries (*Table 1*) ranked by the number of documents published, the United States had the highest publishing frequency (676 times), followed by Italy (314 times), and Germany (293 times). The centrality of the United States was 0.21. France and the United Kingdom were ranked fifth and sixth, respectively, with centralities of 0.13 each (>0.1). According to the network data, the countries above dominated the study of TTC, had good cooperation relationships, and played a positive leading role in the field of TTC research between 2004 and 2020.

Table 1 Top 10 of country co-occurrence analysis

Rank	Count	Centrality	Year	Countries
1	676	0.21	2004	USA
2	314	0.04	2006	Italy
3	293	0.00	2004	Germany
4	267	0.00	2004	Japan
5	140	0.13	2005	France
6	127	0.13	2006	England
7	93	0.00	2011	Sweden
8	90	0.00	2004	Australia
9	79	0.09	2007	Poland
10	75	0.00	2006	China

The institution network (*Figure 3*, *Table 2*) had 1,612 nodes, each of which represented an institution that participated in TCC research, and 3,942 edges. The network density was 0.003. The institutions were mainly universities and their affiliated hospitals. The Mayo Clinic topped the institution list with 91 documents published. Although every institution had published a large number of articles, the rate of inter-institutional cooperation was not high. All the institutions had centrality of <0.1, meaning that the research at each institution was more isolated. This finding suggests that the gap between institutions needs to be eliminated, and the exchange of knowledge and cooperation between institutions needs to be strengthened to achieve more in-depth research in future.

Keyword co-occurrence analysis

Keywords with similar significance were combined by CiteSpace to obtain the keyword co-occurrence atlas (*Figure 4*) and the top 20 keywords (*Table 3*).

The keywords with the top three occurrence frequencies were "Takotsubo cardiomyopathy" (occurring 1,266 times),

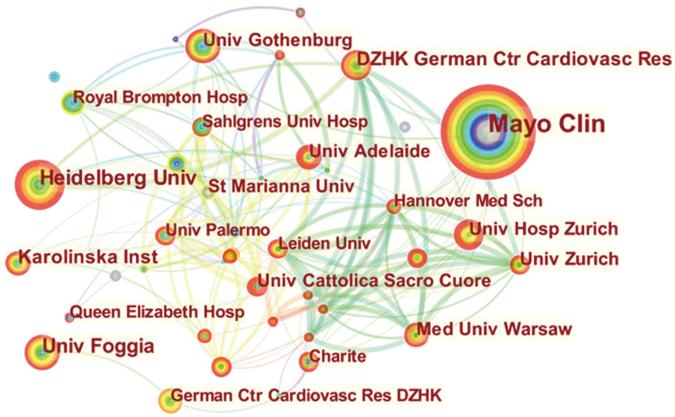

Figure 3 Institution network of publications about TTC. Circle node represents output institution of papers; link between nodes represents partnership. TTC, Takotsubo cardiomyopathy.

Table 2 Top 10 of institution co-occurrence analysis

Rank	Count	Centrality	Year	Institutions
1	91	0.08	2006	Mayo Clin
2	46	0.00	2011	Heidelberg Univ
3	34	0.01	2009	Univ Foggia
4	32	0.01	2011	Karolinska Inst
5	29	0.00	2015	DZHK German Ctr Cardiovasc Res
6	28	0.01	2011	Univ Adelaide
7	27	0.00	2017	Univ Hosp Zurich
8	27	0.01	2009	Univ Cattolica Sacro Cuore
9	26	0.01	2014	Univ Zurich
10	26	0.00	2013	Univ Gothenburg

"myocardial infarction" (occurring 749 times), and "apical ballooning syndrome" (occurring 600 times). Top 20 keywords with centrality >0.1 included "cardiomyopathy" (0.15), "ST-segment elevation" (0.2), and "emotional stress" (0.23), and both "takotsubo" and "heart failure" had a centrality of 0.1. The frequencies of keywords and centrality data suggest that TTC has various names, and that it can present as left-sided heart failure or as a myocardial infarction-like manifestation on the electrocardiogram, such as "ST-segment elevation", which often needs to be distinguished in clinical practice (11). At the same time, "emotional stress" due to various causes is often a predisposing factor for TTC, which explains one of the possible pathophysiological mechanisms of the disease.

Keyword clustering

The algorithm gives each keyword a value, and the keyword with the largest median value in the cluster is chosen as the representative of this class and becomes the class name. The sequence number of the cluster is negatively correlated with the cluster size; for instance, #0 represents the largest cluster.

Sixteen categories were included for analysis (*Figure 5*, *Table 4*). The first three clusters were #0 subarachnoid hemorrhage, #1 apical ballooning syndrome, and #2 myocarditis. In #0, the top 5 keywords were "heart failure", "catecholamine", "clinical features", "subarachnoid hemorrhage", and "infarction". They were associated with the clinical features of catecholamines, arachnoid hemorrhage and heart failure, myocardial infarction, and other diseases, and were related to the neurohumoral mechanism of action. In #1, the top 5 keywords were "stunned myocardium", "myocardial contrast echocardiography", "complication", "magnetic resonance", and "ventricular function", which were all related to functional tests as well as the diagnosis and management of diseases. In #2, the top 5 keywords were "prognosis", "clinical characteristics", "apical ballooning", "patient", and "stress-induced cardiomyopathy", which were all related to clinical characteristics and disease prognosis. These findings suggest that the research on TTC conducted between 2004 and 2020 was focused on the characteristics and the prognosis and complications of the disease, as well as the assessment of its functionality.

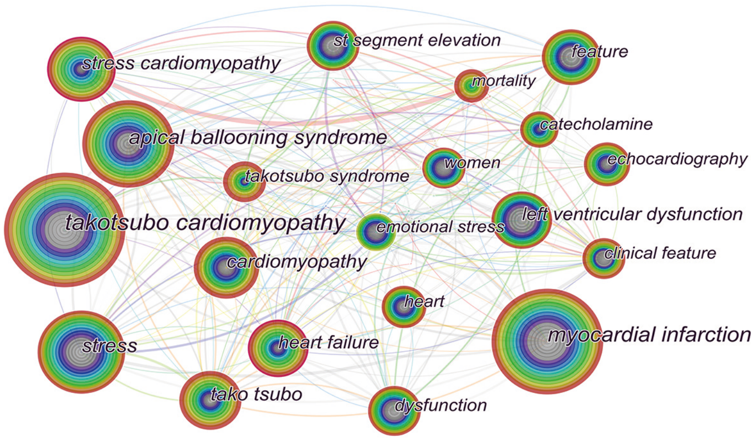

Figure 4 Keyword co-occurrence of publications about TTC. Circle node represents keyword; link between nodes represents that two keywords appear in a study at the same time. TTC, Takotsubo cardiomyopathy.

Table 3 Top 20 of keyword co-occurrence analysis

Rank	Count	Centrality	Year	Keywords
1	1,266	0.07	2004	Takotsubo cardiomyopathy
2	749	0.01	2004	Myocardial infarction
3	600	0.06	2005	Apical ballooning syndrome
4	421	0.00	2005	Stress
5	397	0.08	2005	Stress cardiomyopathy
6	391	0.15	2004	Cardiomyopathy
7	330	0.10	2005	Tako tsubo
8	250	0.00	2004	Left ventricular dysfunction
9	248	0.10	2004	Heart failure
10	244	0.04	2005	Feature
11	215	0.03	2006	Takotsubo syndrome
12	205	0.20	2004	ST segment elevation
13	203	0.07	2004	Dysfunction
14	165	0.00	2005	Heart
15	161	0.23	2004	Emotional stress
16	157	0.04	2005	Women
17	141	0.09	2004	Echocardiography
18	141	0.03	2004	Catecholamine
19	135	0.07	2004	Clinical feature
20	132	0.03	2004	Mortality

Reference co-citation analysis

A literature co-citation map can help to analyze the evolution of a research topic through the use of key nodes on the map (7). Two articles co-cited by the same article form a co-citation relationship. Co-cited references represent the core literature in the field of TTC. The academic influence of literature can, to a certain extent, be quantified by two indicators: co-citation frequency and centrality.

The top 10 citations were listed, six of which assessed clinical features, neurohumoral features, outcomes, clinical spectrum, and cardiovascular magnetic resonance (CMR) findings of TTC, respectively (12-17) (*Table 5*). This suggests that excessive sympathetic stimulation may be the core cause of TTC. For most of the patients included in the literature, TTC was induced by emotional stress, and only a small portion of patients were men or individuals without stress-inducing factors. TTC mainly affects the distal left ventricle. On CMR, TTC presents as left ventricular dysfunction and myocardial edema, but there are no obvious changes related to myocardial necrosis and fibrosis. Four reviews elucidated the pathophysiological mechanism, diagnosis, treatment, complications, and prognosis of TTC. The position statement from the taskforce on TTC of the Heart Failure Association of the ESC (European Society of Cardiology) was a milestone in the systematic study of the disease and inspired an increase in efforts to understand TTC (18-21).

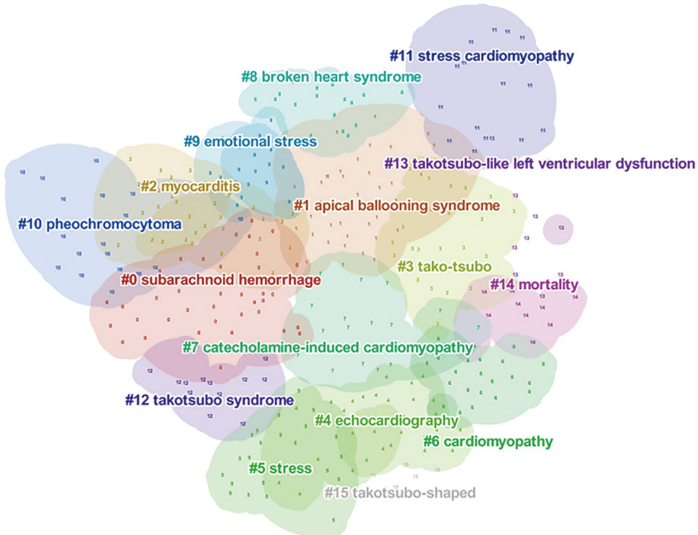

Figure 5 Visualization of keyword clustering.

Table 4 Keyword clustering information

Cluster ID	Size	Silhouette coefficient	Mean (year)	Cluster name
0	42	0.942	2006	Subarachnoid hemorrhage
1	39	0.902	2008	Apical ballooning syndrome
2	34	0.884	2009	Myocarditis
3	32	0.983	2005	Tako-tsubo
4	30	0.879	2007	Echocardiography
5	24	0.942	2011	Stress
6	21	0.960	2005	Cardiomyopathy
7	20	0.942	2006	Catecholamine-induced cardiomyopathy
8	18	0.905	2007	Broken heart syndrome
9	18	0.963	2005	Emotional stress
10	18	0.983	2008	Pheochromocytoma
11	15	0.999	2005	Stress cardiomyopathy
12	15	0.929	2008	Takotsubo syndrome
13	10	1.000	2005	Takotsubo-like left ventricular dysfunction
14	10	0.984	2015	Mortality
15	5	0.992	2005	Takotsubo-shaped

The silhouette coefficient in the table is greater than 0.7.

Hot domains and frontiers

The burst of TTC keywords can roughly be divided into two periods: an early stage and a late stage (*Figure 6A*). In the early stage (2004 to 2013), "ampulla cardiomyopathy", "coronary artery stenosis", and "ST-segment elevation" were first detected and persisted, which was consistent with the keyword co-occurrence analysis. The burst analysis showed that TTC and myocardial infarction share many clinical features and are difficult to distinguish. The diagnosis of TTC requires non-invasive means, such as a cardiac ultrasound and nuclear magnetic resonance, as well as invasive techniques, such as coronary angiography, combined with evaluation of clinical features. The keywords "female" and "emotional stress" also showed that women were more prone to stress clinically, which indicates that the disease is closely related to stress, and this finding is consistent with epidemiological studies (1,22). In the late stage (2013 to 2020), in addition to the pathophysiology characteristics of the disease, the keywords "European Society" and "association" were frequently used, which because of a 2015 position statement from the ESC Heart Failure Association: a comprehensive review of the various clinical and pathophysiological facets of TTC (18).

To find more up-to-date keywords, we used CiteSpace to produce a map of the top 15 burst keywords (*Figure 6B*)

Table 5 Top 10 of reference co-citation analysis

Rank	First author	Article	Journal	Year of publication	Number of citations	Centrality
1	Templin	*Clinical Features and Outcomes of Takotsubo (Stress) Cardiomyopathy*	*New Engl J Med*	2015	393	0.07
2	Wittstein	*Neurohumoral features of myocardial stunning due to sudden emotional stress*	*New Engl J Med*	2005	328	0.04
3	Lyon	*Current state of knowledge on Takotsubo syndrome: a Position Statement from the Taskforce on Takotsubo Syndrome of the Heart Failure Association of the European Society of Cardiology*	*Eur J Heart Fail*	2016	219	0.05
4	Prasad	*Apical ballooning syndrome (Tako-Tsubo or stress cardiomyopathy): a mimic of acute myocardial infarction*	*Am Heart J*	2008	215	0.06
5	Gianni	*Apical ballooning syndrome or takotsubo cardiomyopathy: a systematic review*	*Eur Heart J*	2006	210	0.05
6	Sharkey	*Acute and reversible cardiomyopathy provoked by stress in women from the United States*	*Circulation*	2005	208	0.01
7	Bybee	*Systematic review: transient left ventricular apical ballooning: a syndrome that mimics ST-segment elevation myocardial infarction*	*Ann Intern Med*	2004	194	0.01
8	Sharkey	*Natural history and expansive clinical profile of stress (tako-tsubo) cardiomyopathy*	*J Am Coll Cardiol*	2010	161	0.1
9	Abe	*Assessment of clinical features in transient left ventricular apical ballooning*	*J Am Coll Cardiol*	2003	131	0.01
10	Eitel	*Clinical characteristics and cardiovascular magnetic resonance findings in stress (takotsubo) cardiomyopathy*	*JAMA*	2011	129	0.11

from the 5 years (2015 to 2020) following the publication of the above statement. The burst keywords included "in-hospital mortality", "risk factor", "atmospheric fabric", "stroke", and "epidemiology", among others. In addition to there being a large number of burst keywords, some keywords persisted in literature for a long time, suggesting that research on TTC was in the prototypical stages during the period from 2015 to 2020 and that its popularity will continue to grow. Moreover, many pathophysiological mechanisms of TTC remain unknown, and further examination of TTC is therefore of great research value.

The Timeline view focuses on the relationships between clusters and the historical span of documents within a cluster (7). Analysis of the keyword timeline (*Figure 7*) indicated that some of the keywords in clusters #0 to #5 had a wide connection span and good continuity, suggesting that these clusters (including TTC, inverted TTC, coronary artery stenosis, under-recognized myocardial syndrome, and contrast echocardiography) have current and future research significance. The most recent research hotspots included inflammation, coronavirus disease 2019 (COVID-19), the myocardial infarction and normal or non-obstructive coronary arteries (MINOCA) strain, and cancer. These research hotspots will become new trends in the future.

Discussion

This study employed visualization technology to analyze the TTC-related literature published in the Web of Science database up to 2020. The United States, Italy, Germany, France, and the UK have all conducted a lot of research on TTC, and there has been good cooperation among these

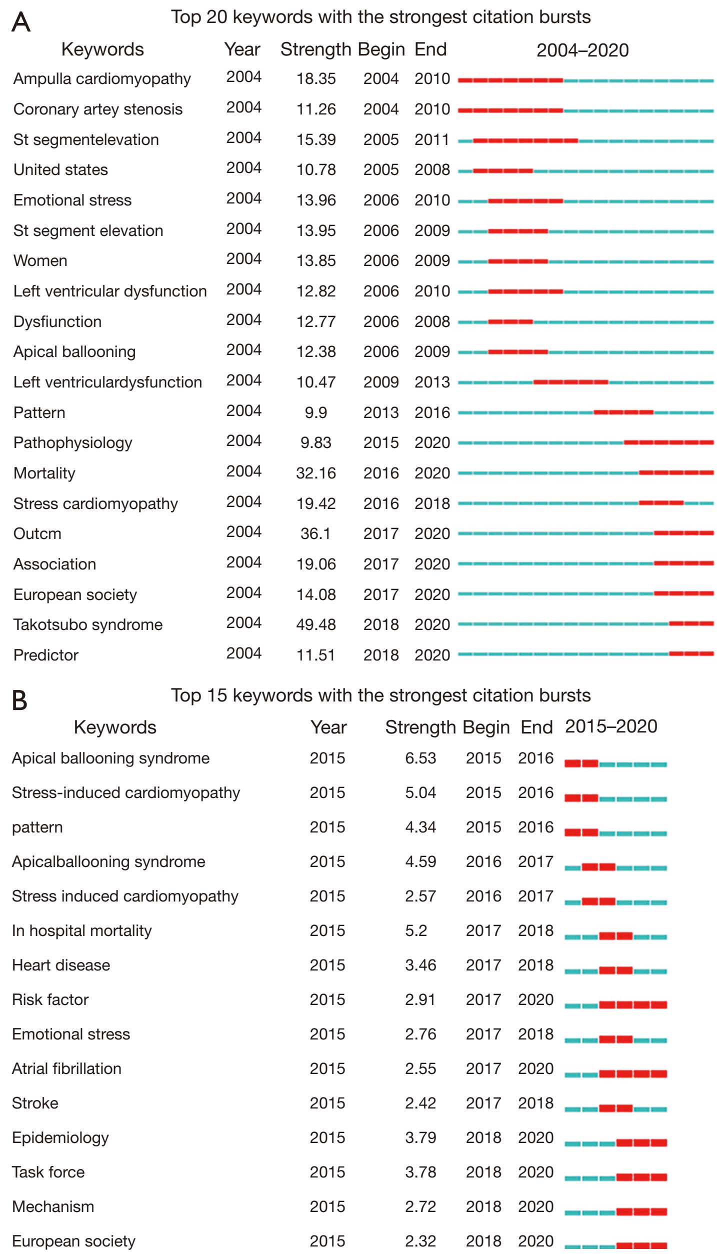

Figure 6 The burst of TTC keywords. (A) Top 20 TTC keywords with the strongest citation bursts from 2004 to 2020; (B) top 15 TTC keywords with the strongest citation bursts from 2015 to 2020. TTC, Takotsubo cardiomyopathy.

countries. However, in developing countries, research has been limited. Despite the publication of many articles by institutions across various countries, there has been little inter-institutional cooperation between them, and research was isolated. Disease characteristics, diagnostic approaches, epidemiology, and pathophysiological mechanisms have always been hot topics in TTC research. Emerging topics are focused on the prognosis and complications of TTC, such as MINOCA, atrial fibrillation (AF), stroke, cancer, and COVID-19-related cardiovascular abnormalities.

The expert consensus of the ESC on TTC in 2015 was the dividing line for the study of the condition. Less attention was paid to research about TTC before the demarcation line, as TTC was generally considered a relatively benign condition with a rapid recovery rate of left ventricular function. At the same time, there was a

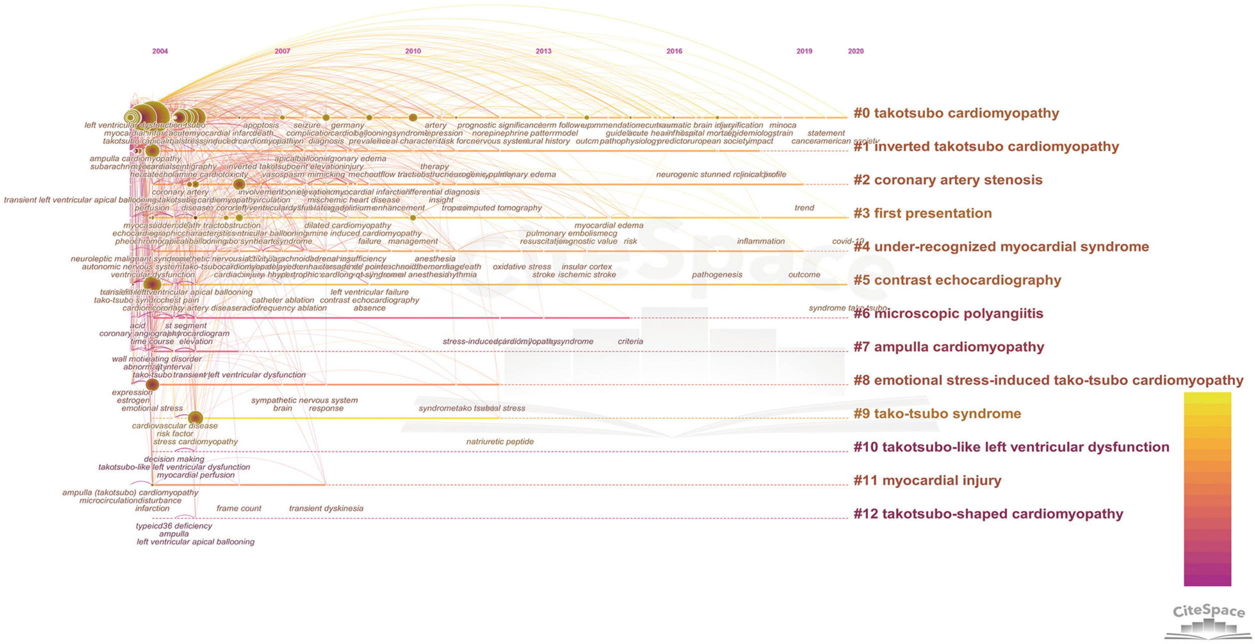

Figure 7 Visualization of keyword timeline. Each horizontal line represents a cluster. The circular nodes on the line represent high-frequency keywords in this time slice. The timeline is shown at the top of the figure, and the year corresponding to the node is its publication time. Link between nodes represents that two keywords appear in a study at the same time.

lack of awareness of TTC among clinicians. Common nomenclature for TTC included stress or stress-induced cardiomyopathy, apical ballooning syndrome, ampullary-shaped cardiomyopathy, and broken heart syndrome. There were also numerous diagnostic criteria, a lack of clarity about clinical manifestations, and auxiliary examinations that contributed to the uncertainty in the diagnosis and treatment of TTC.

However, in 2015, due to the increasing awareness of TTC as an acute heart disease with multiple complications, the ESC issued a statement that highlighted the importance of research about TTC, and the condition has gained increasing attention. It is not only the proposal of seven new diagnostic criteria, but also focus on differentiation of TTC from acute infectious myocarditis and acute coronary syndrome, and auxiliary diagnostic techniques, such as a diagnostic coronary angiography, 12-lead electrocardiogram, coronary computed tomography angiography, echocardiography, and late-stage gadolinium-enhanced CMR imaging to provide guidance for the diagnosis of TTC. Literature in our review hypothesized that the pathophysiology of TTC had three main aspects: separate vascular, myocardial, vascular combined myocardial. The literature recognized that responses of the cognitive centers in the brain, the hypothalamic-pituitary-adrenal (HPA) axis, and the cardiovascular system to catecholamines play a key role in the development of TTC.

Although reports on TTC-related pathophysiology, epidemiology, and auxiliary examination methods exist, comprehensive studies have yet to be performed. For instance, the bursting keyword “risk factor” included “diabetes mellitus” and “cannabis use disorder” (23). Diabetes is present in 10% to 25% of patients from the international, multicenter GEIST registry and may be associated with increased susceptibility to TTC due to autonomic remodeling (24). Subarachnoid hemorrhage and ischemic stroke induce the production of a large number of endogenous cannabinoids, resulting in neurogenic myocardial stunning, which is also highlighted on our keyword timeline (25). There are also other risk factors for TTC to be further studied.

Epidemiology was a prominent keyword. The first Nationwide Inpatient Sample (NIS-USA), a large cohort study, found that most (90%) of patients with TTC were postmenopausal older women (66 to 80 years old) (1). Another study reported that 98% of patients underwent

CMR assessment diagnosed with TTC were women (22). These observations raise the question of why women are prone to TTC. Firstly, women's estrogen levels may play a role in TTC. In studies of rats with their ovaries removed, those supplemented with estrogen had a lower rate of cardiac dysfunction, with estrogen reducing the heart rate and blood pressure associated with emotional stress (26). Some studies have also indicated that estrogen supplementation can also reduce catecholamine concentrations in plasma, therefore protecting the heart from stress-induced cardiomyopathy (26,27). However, in contrast to the catecholamine surge theory described above, research also suggests that coronary artery spasm is the initial pathophysiological factor (28). Acetylcholine testing of endothelial dysfunction may credibly identify the cause of stunning in patients with TTC in specific circumstances (29). Estrogen helps to preserve endothelial function, and a lack of it may lead to coronary microvascular dysfunction. Compared to those of women with acute myocardial infarction or with normal coronary arteries, the E2 concentrations of postmenopausal patients with TTC were found to be elevated during acute events, which resulted in a stress response that diverted myocardial infarction to TTC as opposed to myocardial infarction (30). Therefore, estrogen may play a role in the two kinds of mechanisms of TCC, but the specific mechanism still needs further clarification.

The results of keyword clustering and keyword burst analysis indicated that TTC has a wide variety of complications and a complex prognosis. The following studies partially explained the possible mechanisms or effects of TTC. Studies on the burst keyword "stroke" showed that the catecholamine surge hypothesis was the most widely accepted brain-heart interaction mechanism (31). Myocardial injury is caused by direct catecholamine toxicity, adrenergic receptor-mediated injury, epicardial and microvascular coronary artery constriction and/or spasm, and an increase in cardiac load (32). Human emotions and physical states are regulated by the HPA axis, which is activated after stroke, leading not only to stress but also a significant increase in catecholamine secretion (33-36). Catecholamines act on the heart via β-receptors to increase the intensity and rate of contraction, and β-receptors coupled to G proteins increase cytoplasmic cyclic adenosine monophosphate, trigger calcium overload, and induce cardiomyocyte death (37,38). At the same time, after a stroke, the literature showed that emotions are often altered by stress, and stress also acts on the heart and pressure receptors, which are integrated by the paraventricular nucleus of the hypothalamus and exported by the sympathetic nerves of the heart to induce cardiac injury (31,39). One study also found that pre-existing neurological or psychiatric illness predisposes individuals and contributes to TTC development (40). Therefore, after a stroke, activation of the HPA axis accompanied by pressure changes causes the release of a large amount of catecholamines, which results in abnormal echocardiograms, arrhythmia, myocardial damage, and TTC (41).

Within the past 5 years Between 2015 and 2020, another term whose burst that lasted for 4 years was AF, which is a complication of TTC. Inflammation and oxidative stress are key factors in the development of AF, and anxiety may increase catecholamine load, resulting in the production of reactive oxygen species and inflammation (42,43). Furthermore, one study reported that anxiety also activates the renin angiotensin aldosterone system, and promotes AF occurrence and progression (44). As mentioned above, elevated serum catecholamine levels can trigger TTC through microvascular endothelial injury and catecholamine cardiotoxicity. Because AF and TTC share the same inducing mechanism, the development of TTC is likely to be accompanied by AF. Compared to those TTC alone, patients with comorbid TTC and AF experience significantly more in-hospital events, such as cardiogenic shock, and have increased short- and long-term mortality (45-48). Furthermore, a meta-analysis also showed that the presence of AF was associated with all-cause mortality (pooled odds ratio =2.19; 95% confidence interval) (49). AF can therefore affect the prognosis of TTC. However, no study to date has explored the effects of TTC on the prognosis of AF. Consequently, it is unknown whether the poor prognosis of TTC with AF is caused by the AF itself, and further research is required to understand this relationship.

The complications mentioned in the keyword timeline included cancer, COVID-19, and MINOCA. One study showed that patients with TTC had a high incidence of malignant tumors, and that specific malignant tumor-related factors (tumor type, metabolic and neurohumoral alteration, and treatment measures) influence the development and outcome of TTC (50). The TTC group of chemotherapy patients had almost two-fold greater odds (OR =2.17) of experiencing in-hospital mortality. The risk was also increased for patients who were older, Asian, or treated in an urban teaching hospital, and for those who experienced complications such as septicemia, fluid-electrolyte disorders, or cardiogenic shock. A history of respiratory failure independently raised the odds of mortality for patients in the TTC group who were receiving chemotherapy (51). A meta-analysis revealed that, compared to controls, patients with cancer showed an increased risk for clinical events (RR 3.24; 95% CI: 3.04–3.45; P<0.01). The risk of in-hospital events was also significantly higher in the cancer group (RR 2.08; 95% CI: 1.50–2.87; P<0.01), which was mainly because of the higher need for respiratory support (RR 1.67; 95% CI: 1.58–1.77; P<0.01) (52). In studies of TTC in patients with COVID-19 or MINOCA, a variety of auxiliary examinations were performed to assist in the diagnosis and evaluation of TTC. A Journal of the American College of Cardiology scientific expert panel proposed using multimodal imaging to evaluate cardiovascular complications in patients with the COVID-19 infection. Furthermore, for patients with a clinical manifestation of acute MINOCA, such as TTC, CMR can assist in confirming myocardial infarction or provide alternative diagnoses (53). In a prospective international survey of 1,216 patients from 69 countries across 6 continents, echocardiography detected TTC in 2% of patients diagnosed with COVID-19 (54). Further, MINOCA and TTC can be predicted by measuring the coronary fat attenuation index (pFAI), which is a marker of coronary inflammation, through standard CCTA. Therefore, the application of CMR, CCTA, and echocardiography is helpful in the diagnosis of TTC in patients infected with COVID-19, and can reveal the possible inflammatory mechanism of TTC.

Our literature search showed that there are still some limitations. First, the study tended to organize the research in terms of bibliometrics, which is a majority view and may fail to summarize all TTC knowledge. Second, our paper's data scope was limited to the Web of Science, which was sufficient to meet our objectives but may not contain all available published research about TTC.

Conclusions

We used CiteSpace mapping of literature about TTC during the period from 2004 to 2020 to identify the main countries and institutions that have contributed to the study of TTC and their cooperative relations. Our analysis of keywords has revealed emerging trends, hot spots, and prospects in TTC research. Research on TTC is dominated by developed countries, and there is close cooperation between countries but not between institutions. Pathogenic factors identified in the literature are related to abnormal levels of estrogen, cortisol, and catecholamines. Research shows that diseases such as AF, cancers, COVID-19, and MINOCA can trigger TTC. Our literature review has also shown that multimodal imaging, CMR, echocardiography, and CCTA can aid in the diagnosis of TTC. Our research will help clinicians and researchers to better understand TTC and its research status by providing a foundation for research objectives. In doing this, our research will help to provide better scientific management, diagnosis, and treatment for patients with TTC, which will in turn improve the prognosis of this condition.

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Footnote

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