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Review Article

Investigating the effect of cancer medication in the development of Takotsubo cardiomyopathy

On Chen[1], Azad Mojahedi[2]

[1]Divison of Cardiology, Stony Brook University Hospital, Stony Brook, New York, The United States; [2]Department of Internal Medicine, Stony Brook University Hospital, Stony Brook, New York, The United States

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Abstract: Takotsubo cardiomyopathy (TCM) is a cardiac condition that is usually characterized by sudden heart failure (HF) or chest pain that resembles acute coronary syndrome (ACS). It is identified by severe systolic dysfunction of the left ventricle (LV) and can be caused by physical, medical, or emotional stress. The pathophysiological mechanisms leading to TCM have not yet been clearly determined. TCM is a complex condition to diagnose and may go undetected during cancer treatment due to the wide variety of cardiotoxic effects associated with antineoplastic therapies. Consequently, timely identification and effective treatment are critical to enhancing the prognosis. Nevertheless, TCM is a more prevalent condition in oncology than was previously believed; therefore, clinicians who treat cancer patients should consider it in their differential diagnosis. The purpose of this manuscript is to provide physicians with a summary of the available evidence regarding the ramifications of the association between TCM and cancer to aid in improving patient management.

Keywords: Takotsubo cardiomyopathy, malignancy, chemotherapy

Introduction

Patients diagnosed with cancer who are receiving systemic therapy frequently have cardiovascular disease and risk factors concurrently. Cardiovascular events that are not associated with cancer treatment can be complex for physicians to distinguish from cardiotoxicity induced by chemotherapy [1]. It is crucial to identify cardiotoxicity induced by chemotherapy, as a potentially irreversible injury to the heart can result from repeated administration of the offending drug. Conversely, oncologic morbidity and mortality may be increased if an effective anti-neoplastic agent is discontinued prematurely for co-existing cardiac events that are not directly related to therapy. Takotsubo cardiomyopathy (TCM) is a cardiac condition that can arise entirely independently of chemotherapy or as a direct consequence of the drug [2, 3].

TCM, also known as stress cardiomyopathy, is a clinical syndrome that typically manifests as abrupt heart failure (HF) characterized by severe left ventricular (LV) systolic dysfunction or as chest discomfort resembling acute coronary syndrome (ACS) in reaction to psychological, physical, or medicinal stress [4]. In contrast to ACS, where coronary artery scans are typically regular, LV dysfunction surpasses the coronary distribution and usually resolves within days to weeks. Ballooning with hyperdynamic basal segments, or apical akinesis, is the most prevalent type of LV dysfunction. Signs of TCM include dyspnea, chest pain, electrocardiographic alterations indicative of ischemia, a slight elevation in cardiac enzymes, and malfunction of the segmental ventricles [5]. However, TCM can be difficult to identify because the clinical signs are frequently identical to acute myocardial infarction (MI). Consequently, electrocardiogram (ECG) results, cardiac biomarker levels, imaging studies, and clinical presentation are usually used in combination to diagnose TCM.

Although the exact etiology of the condition is unknown, microvascular dysfunction, coronary artery vasospasm, and excess catecholamines

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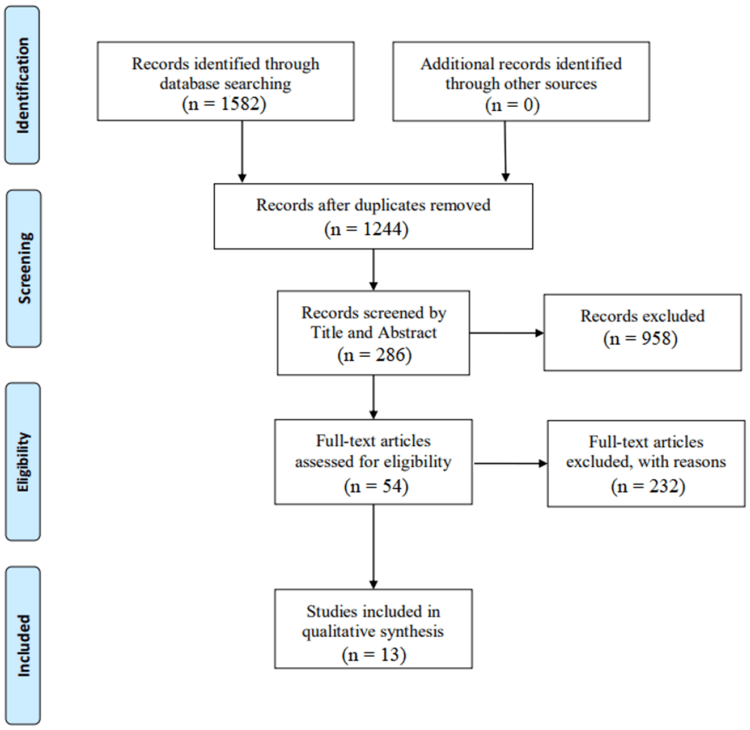

Figure 1. PRISMA flow diagram for enrollment of studies.

are believed to be the main mediating factors. A variety of stressors, including emotional or psychological strain, infection, surgical intervention, medication use, and the worsening of chronic illnesses, have the potential to trigger these mechanisms. In addition, considering the prevalence of familial cases, a genetic predisposition to TCM has been hypothesized [4, 6].

Recent research has linked TCM to the use of anti-neoplastic agents. There is evidence to suggest that specific cancer medications may induce this type of cardiomyopathy. The various cardiac side effects that can result from cancer therapy include ventricular dysfunction, myocarditis, hypertension, ischemia, venous thromboembolism, arrhythmia, accelerated atherosclerosis, and QT prolongation. While there have been many investigations on the cardiotoxic effects of chemotherapeutic agents, there is little information on this type of cardiomyopathy caused by cancer treatment, and there is currently no known association between chemotherapy dose and TCM [3, 7, 8].

Our review investigates the potential etiological relationship between several cancer medications and TCM. Cancer therapy includes conventional chemotherapeutic medicines, newly targeted drugs, and immune checkpoint inhibitors (ICIs) [2]. The purpose of this manuscript is to provide physicians with a summary of the available evidence regarding the ramifications of the association between TCM and cancer to aid in improving patient management.

Material and methods

Search strategy

We have conducted a literature review to evaluate the effect of malignancy on TCM causes. The research was performed in compliance with the PRISMA criteria, Preferred Reporting Items for Systematic Reviews and Meta-Analyses, and the Flow Diagram is shown in **Figure 1**. The research was conducted in the PubMed, Web of Science, Science Direct, and Google Scholar databases between January 2018 and October 2023. It used the Advanced Search Builder, and the keywords were searched in [Title OR Abstract]. We have filtered only research articles published in the English language and using the terms (Takotsubo Cardiomyopathy [Mesh] OR Takotsubo Syndrome [Mesh] OR Apical Ballooning Syndrome [Mesh] OR Broken Heart Syndrome [Mesh] OR Stress Cardiomyopathy [Mesh]) AND (Cancer [Mesh] OR Malignancy [Mesh] OR Neoplasm [Mesh] OR Tumor [Mesh]).

Inclusion and exclusion criteria

Original articles that evaluated the latest advances of the effect of malignancy and anticancer therapy on TCM causes were eligible for inclusion in the systematic review. References in selected research were reviewed for other relevant literature. Retrospective and prospective cohort studies and case-control studies related to anticancer therapy and TCM. Case reports and series involving a limited number of patients, review articles lacking original data, editorials, letters, and conference papers were excluded.

Table 1. The main investigation evaluating the impact of malignancy on Takotsubo cardiomyopathy development

Study	Year	Study type	Study population	Patients with cancer	The most prevalent type of cancer	Duration of follow-up
Tini et al.	2022	Retrospective	318	42 (13%)	Breast cancer	2.7 years
Pogran et al.	2022	Retrospective	147	25 (17%)	-	126 months
Jang et al.	2021	Retrospective	61,553	7,542 (12%)	-	Hospital admission days
Núñez-Gil et al.	2020	Prospective	1,097	129 (12%)	Breast cancer	120 days
Cammann et al.	2019	Prospective	1,604	267 (16.6%)	Breast cancer	5 years
Nguyen et al.	2019	Prospective	346	58 (17%)	Breast cancer	4.1 years
Zaghlol et al.	2019	Retrospective	318	81 (25%)	Breast cancer	Hospital admission days

Data extraction and quality evaluation

Azad Mojahedi reviewed titles and abstracts. After implementing inclusion and exclusion criteria, data from studies were extracted based on the survey's requirements. In the studies that have been reviewed, factors such as ECG abnormalities, troponin level, and the time of occurrence of TCM after chemotherapy have been used as indicators of the role of chemotherapy in the occurrence of TCM.

Any relevant studies were included after scanning the references in previously published review articles. We obtained 17 eligible published research articles in their final version. For some of them, we chose to include only the main findings that fit the purpose of this review (**Figure 1**).

Epidemiology

In cancer patients, TCM has been chiefly described as either a side effect of specific cancer treatments or a problem caused by certain tumors, like pheochromocytoma and paraganglioma [9]. TCM's pathophysiology in cancer patients and non-cancer patients is complex and unclear even though oncological patients are frequently underdiagnosed, and cancer and TCM coexist more regularly than was previously assumed. There is evidence that the incidence of TCM is higher among oncological patients than in the general population, with a mean incidence of approximately 53 per 100,000 chemotherapy-related hospitalizations compared to 20.4 in the general population. However, the prevalence of TCM in patients hospitalized with suspicion of ACS was approximately 2% [1, 2].

Also, several studies and registries indicate that patients with TCM have a higher incidence of neoplasms than healthy individuals of the same age and gender who do not have the syndrome. The estimate of the range of malignancy prevalence during follow-up and at the time of diagnosis is 4-29% [7, 10]. Notably, TCM prevalence in cancer patients is comparable in both genders despite a well-documented preference for women in the general population [1, 11].

A substantial cohort study including 4.7 million hospitalized patients with active cancer was published in 2021 by Javaid et al. [12], and it was based on a national inpatient sample in the US. Using propensity-score adjustment and machine learning, the scientists further explored the correlation between primary tumor type and the risk for TCM, and they found that 12% of these patients had TCM. Breast and lung cancer were the only conditions associated with a substantially increased likelihood of TCM, according to their findings. Furthermore, the stage of cancer should be taken into account, as TCM appears to be more prevalent in patients with metastatic or recurrent disease, in addition to tumor type. In 2023, Osawa et al. [13] also performed a meta-analysis investigating cancer incidence in patients with TCM. Fourteen investigations involving 189,210 patients were assessed. The incidence of malignancy among patients with TCM was 8.7% (16,461 cases). Other recent observational studies have shown a higher prevalence of malignancy in TS patients (**Table 1**).

Pathophysiology

At present, the precise pathophysiology causing TCM remains obscure. The reasons for the

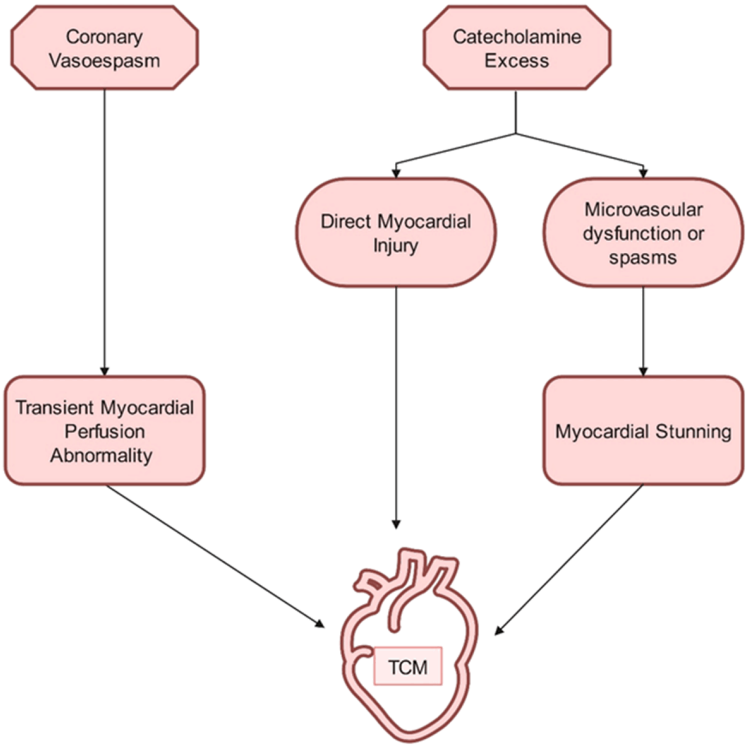

Figure 2. Pathophysiological mechanisms that lead to Takotsubo cardiomyopathy (TCM).

increasing prevalence in postmenopausal women and the preference for the LV apex or mid-cavity remain unknown [14]. Numerous hypothesized mechanisms of TCM include an excess of catecholamines, vasospasm of the coronary artery, microvascular dysfunction, and the upregulation of specific cardiac genes (**Figure 2**) [5, 15].

The release of catecholamines due to stress plays a significant role in the development of TCM. Wittstein et al. [16] discovered that patients with LV dysfunction had elevated catecholamine levels as a result of psychological stress. Abraham et al. [17] also emphasize the importance of catecholamines, as they found that TCM can occur after an infusion of norepinephrine and dopamine. It is believed that an increase in intracellular norepinephrine levels due to cAMP stimulation can harm cardiac myocytes. The importance of norepinephrine is further supported by the fact that beta-blockers can significantly reduce damage [18]. Mild myocardial perfusion abnormalities and multifocal coronary vasospasm are additional indicators that coronary artery vasospasm may contribute to the development of TCM. Drugs have also been suggested as a possible cause of TCM in cases where no apparent emotional or other stress stimulus could be identified [18, 19].

Diagnosis

Patients with TCM usually present to the emergency room with symptoms such as acute chest pain, shortness of breath, and palpitations. They may also experience arrhythmia or sinus tachycardia. In severe cases, they may even suffer from presyncope or syncope due to ventricular tachyarrhythmias, acute left ventricular outflow tract obstruction (LVOTO), or cardiogenic shock [15]. Some studies classified TCM as primary or secondary (**Figure 3**) [15, 20, 21]. Primary TCM mainly affects women following an emotional or physical stressor, in the absence of epicardial coronary disease, with minimal troponin release, significantly reduced and promptly reversed LV dysfunction, and a favourable prognosis. Secondary TCM is most common in patients who have been hospitalized for other reasons, such as sepsis, obstetrics, anesthesia or surgery. Secondary TCM affects the sympathetic nervous system, increasing the concentration of circulating catecholamines. Furthermore, TCM is classified clinically depending on the position of the wall motion abnormality (WMA) (**Figure 3**), which divides it into apical, mid-ventricular, basal, focal, and biventricular TCM [20, 22].

The initial clinical presentation of cancer patients is similar to that of the general population, with chest pain and/or dyspnea being the most common symptoms. However, 26.8% of patients may experience cardiogenic shock as the first and potentially fatal manifestation [23, 24]. Baseline characteristics such as race and medical or social history do not differ significantly from patients without cancer. Further complications include respiratory fail-

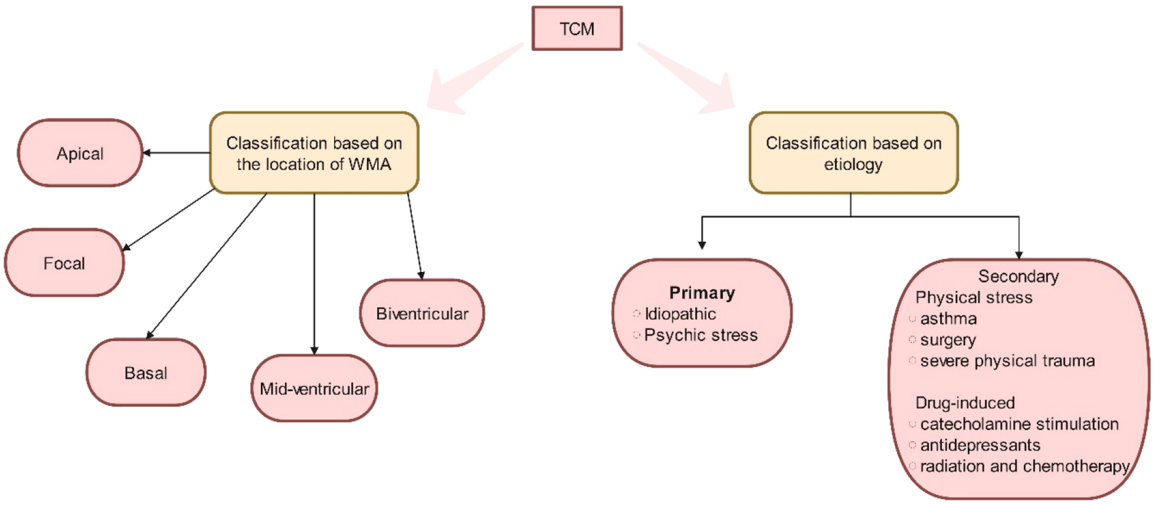

Figure 3. Classification of Takotsubo cardiomyopathy (TCM) based on the etiology and the wall motion abnormality (WMA) location.

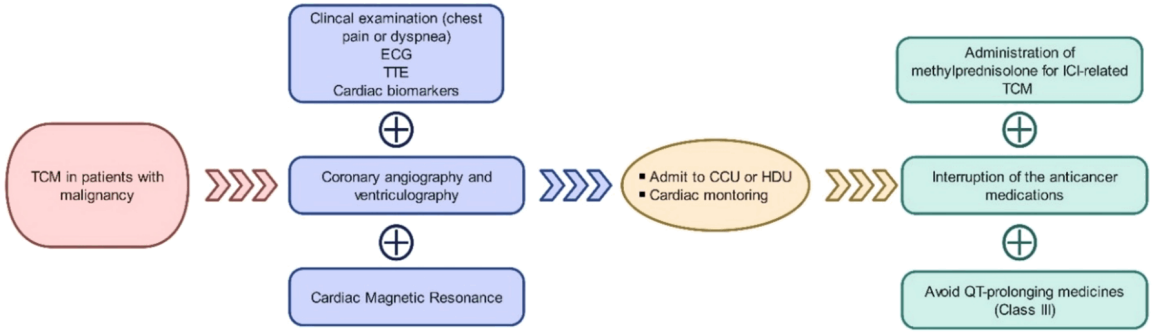

Figure 4. Diagnosis and management of cancer-related Takotsubo cardiomyopathy (TCM). ECG: electrocardiogram, TTE: transthoracic echocardiography, CCU: coronary care unit, HDU: high-dependency unit, CMR: cardiac magnetic resonance, ICI: immune checkpoint inhibitor.

ure, arrhythmias, pulmonary edema, cardiac thrombus, and cardiac arrest. The median time of TCM onset is about two days (1-150) after the starting of treatment, and diagnosis using available TCM criteria has been suggested [23]. For cancer patients with a presumed TCM diagnosis, investigations should include clinical examination, transthoracic echocardiography, ECG, cardiac biomarkers, and cardiac magnetic resonance (CMR) imaging (**Figure 4**) [25].

The diagnostic criteria for TCM are summarized in **Table 2** [26]. Notably, in 2018, the ESC updated this classification with two crucial changes: including pheochromocytoma as a cause of TCM and removing coronary artery disease as an exclusion criterion, provided that the change in contractility extends beyond the affected coronary territory [27]. Additionally, the acute coronary event itself can trigger TCM [28]. Most patients require invasive coronary angiography to exclude acute MI. For patients with advanced malignancy or significant thrombocytopenia that contraindicated to invasive coronary angiography, a coronary computed tomography angiography is advised. Cardiac imaging studies should be conducted as early as possible when the diagnosis is presumed, as LV dysfunction can be transient. If substantial LVD is observed, repeat imaging is recommended to confirm recovery [28, 29]. Nuclear magnetic resonance is an important diagnostic tool, especially in cases where myocarditis needs to be ruled out as a differential diagnosis or in focal TCM concerning the coronary territory, to assess whether the pattern of delayed

Table 2. Diagnostic criteria for takotsubo cardiomyopathy

1	The presence of transitory LV dysfunction. RV dysfunction may occur. A contractility anomaly can extend beyond the boundaries of an epicardial coronary artery. In rare instances, TCM may be conflicted with a single territory.
2	A physical or emotional stress or combination trigger may precede the TCM event, but this is not mandatory.
3	Neurological diseases and pheochromocytoma may be triggers for TCM.
4	Acute ECG changes are frequently observed, but the ECG may be normal in rare cases.
5	Cardiac biomarkers (CK and troponin), and BNP are frequently moderately increased.
6	TCM has the potential to coexist with significant coronary artery disease.
7	No signs of acute myocarditis can exist.

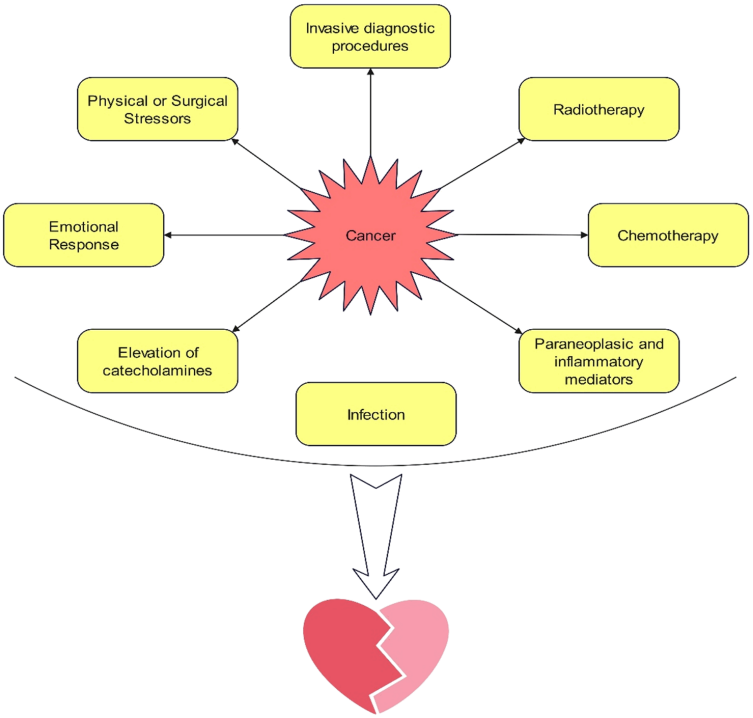

Figure 5. The most common triggers in Takotsubo cardiomyopathy.

enhancement is typical of ischemic disease [30]. Enhancement may be present in a minority of patients - fragmented and not typical for coronary artery disease but absent in most cases. Additionally, it accurately quantifies LV and right ventricular function and detects complications such as thrombi, pleural and pericardial effusion. It is recommended to interrupt anticancer drug treatment in patients with TCM, and QT-prolonging drugs should be avoided [29].

In cases of ICI-related TCM, the role of immunosuppression remains unknown. However, if myocardial inflammation is present in a TCM pattern on CMR, intravenous methylprednisolone is recommended due to the overlap between ICI-induced TCM and ICI-induced myocarditis [31]. Limited information exists regarding the feasibility of ICI rechallenge following TCM and after recovery of left ventricular function. A multidisciplinary team discussion is recommended after recovery from the acute phase of TCM. If restarting the cancer drug is necessary from an oncology point of perspective, cardiac follow-up is recommended [31, 32].

Cancer-induced Takotsubo cardiomyopathy

The chronic nature of cancer causes substantial physical and emotional strain, thereby elevating the susceptibility to stress cardiomyopathy. Anxiety surrounding the cancer diagnosis, the inflammatory condition of the disease, and the physical strain associated with chemotherapy and other cancer treatments are all probable triggers for TCM in cancer patients (**Figure 5**) [2, 33]. Additionally, there is a theory that circulating paraneoplastic mediators might change the adrenoreceptors in cardiac tissue, leading to problems with contractility [1].

In 2019, Brunetti et al. [10] conducted a meta-analysis to examine clinical outcomes in cancer patients who develop TCM. This study reveals that, compared to patients with TCM and no cancer, those who present with both TCM and cancer have a greater likelihood of requiring mechanical ventilation, a longer stay in intensive care, and a threefold increase in the rela-

tive risk of clinical events. Therefore, they found that cancer patients who develop TCM have a poorer prognosis. Núñez-Gil et al. [8] investigated to determine the prevalence of malignancy in patients with TCM. This registry was developed between 2002 and 2019 in 38 hospitals, including patients with a history of any malignancy or tumor, even benign, that received chemotherapy, radiotherapy, or specific surgery, current or in the past. Any neoplasm was described in 129 (11.8%) in a cohort of 1,097 patients with TCM. The most common neoplasm was breast cancer. The results showed that, during a hospital stay, cancer patients suffered more complications, highlighting HF/shock, acute renal failure, and a trend towards combined infections. On follow-up, they presented higher mortality and more combined major adverse cardiovascular events (MACE), with a non-significant trend in cardiovascular recurrences or readmissions.

Although anticancer treatment is thought to be the primary cause of TCM development, Javaid and colleagues [12] did not account for the effect of antineoplastic therapy in their artificial intelligence analysis that concentrated on the initial malignancy type. Multiple registries and case reports have linked various systemic anticancer treatments, including targeted treatments and chemotherapy. The medications that have been most frequently related to TCM include 5-fluorouracil capecitabine, anthracyclines, trastuzumab, and ICIs, whether used alone or in combination with concurrent radiotherapy [33, 34]. Those cancer patients who are exposed to these therapies and have additional risk factors are at a greater likelihood of developing TCM. Several risk factors have been identified by Javaid et al. and prior researchers, including advanced age (greater than 45 years), female gender, and both cardiovascular and non-cardiovascular comorbidities (e.g., hypertension, neurologic disease, anemia, pulmonary disease, and dyslipidemia) [2, 12].

A relationship between inflammation, cytokine synthesis in responses to catecholamines, and various cancer stressors might explain variations in the presentation of TCM among cancer patients. Additional oncologic therapies have been associated with TCM [35]. Arterial thromboembolism is one of the specific cardiovascular adverse effects associated with bevacizumab. An investigation demonstrated that inhibiting the vascular endothelial growth factor (VEGF) signaling pathway resulted in myocardial infarction, contractile dysfunction, and dilation of the ventricles [36]. Infrequent occurrences of MI and deleterious cardiac events, such as arrhythmia, have been associated with rituximab. Acute ventricular dysfunction following a rituximab infusion has been documented. This suggests that alterations in growth factor-β levels may have contributed to the formation of reticulin fibers, which are diffusely distributed in cardiac muscles. Consequently, myocardial contractility and conduction were diminished. Trastuzumab was found to be associated with the putative cardiotoxic and pro-inflammatory effects of pembrolizumab in the context of monoclonal antibodies and immunotherapy agents. These effects may potentially be mediated through the upregulation of inflammatory-related signaling pathways [29, 37].

Review of studies conducted about the effect of cancer treatment on the cause of Takotsubo cardiomyopathy

A recent meta-analysis of 41 case reports of TCM following various anticancer therapies revealed that 5-fluorouracil was the most frequently reported medication in over a third of the cases. A median of two days after receiving the anticancer treatment, patients typically develop TCM. TCM caused cardiogenic shock in 25% of cases; upon follow-up, 89% showed a complete LV function restoration [23]. It is still not entirely clear what causes pyrimidine-related cardiotoxicity or what causes pyrimidine-related TCM. Researchers have postulated microvascular dysfunction and coronary vasospasm as potential mechanisms that contribute to the pathogenesis of TCM [38, 39]. Nevertheless, there is a shortage of case reports that detail acute episodes of TCM or pyrimidine-related angina without overt or provoked vasospasm [39, 40]. In some cases, the existence of non-hemodynamically significant coronary artery disease was documented, or a history of past coronary artery disease served as a predictor of cardiotoxicity development. In certain situations, it may not be possible to rule out plaque instability or vasospasm that narrows the coronary lumen over an already-existing plaque [41, 42]. According to recent research, direct endothelial and myocardial

injuries appear to be the primary mechanisms underlying pyrimidine-associated cardiotoxicity. In conclusion, it is impossible to rule out pure coronary events definitively; therefore, the link between pyrimidines and TCM remains hypothetical despite numerous reports to the contrary [32, 38, 40].

Over the past several years, the indications for ICI therapy have been broadening. Concurrently, there has been an exponential increase in the number of reports of cardiotoxicity linked to ICI [43]. ICIs exemplify the potential of immunotherapy and translational tumor immunology. These medications comprise human antibodies that target programmed death-1 (PD-1) and cytotoxic T lymphocyte antigen-4 (CTLA-4). Despite the significant therapeutic benefits of ICI, it is associated with a distinct range of side effects known as immune-related adverse events. There is a broad spectrum of potential adverse effects, including dermatological, gastrointestinal, hepatic, and endocrine, as well as other inflammatory problems that are less common. Reported instances of immune-mediated myocarditis necessitate advanced therapies for HF. Aside from the well-known issue of myocarditis, various cardiac adverse effects related to ICI have been recorded, including atrial fibrillation, MI, pericardial effusion, and TCM [43, 44].

Regarding pyrimidines, it is unknown what precise mechanism causes TCM in individuals with ICI. There have been multiple reports of an intriguing overlap between myocarditis and TCM. Fourteen percent of thirty cases of ICI-associated myocarditis exhibited a TCM-like syndrome. Given the established recognition of myocarditis as a potential differential diagnosis for TCM, definitive confirmation regarding the association between ICI and TCM remains challenging [45, 46].

In the event of cardiovascular complications, ICIs are typically stopped, and retesting is not advised. However, although we firmly recommend this methodology for myocarditis, its applicability to other forms of cardiotoxicity remains unclear. Although re-evaluations of ICI following cardiotoxicity have been suggested, there is a lack of data on this particular subject [28, 47, 48].

Anticancer therapy-induced TCM is an uncommon occurrence. Nevertheless, it could lead to significant consequences. Given the lack of explicit guidelines, its incidence could potentially lead to the end of oncologic treatment or even a complete cessation. Nevertheless, finding the precise correlation between a specific anticancer treatment and the occurrence of TCM can be difficult due to the possibility that the oncologic status is the cause of TCM or that it is difficult to diagnose with certainty. There is often no apparent association between anticancer drugs and TCM, and recovery of LV systolic function is not always reported in some case reports. These diagnostic and oncological concerns appear to be challenging to resolve. However, the most crucial factor in clinical practice is still providing the best possible care for the patient. Cardiologists and oncologists must collaborate closely to offer appropriate cardiovascular treatment during the acute phase and safely and aggressively transition to oncologic care once the acute HF has resolved [49-51].

We must address two critical aspects. Firstly, cardiologists should provide a supportive viewpoint, given that oncologists are responsible for determining whether, when, and how to recommence an anticancer treatment. Even when a purported relationship between TCM recurrence and anticancer treatment exists, it is unreasonable to stop anticancer therapy due to this rare occurrence permanently. Secondly, rather than comparing the existence and absence of other cardiovascular risk factors or prior occurrences, examine whether a condition is stable and well-treated and the clinical history of its development. This is especially essential in cardio-oncology, where specific cardiovascular comorbidities can have a significant impact on cancer treatment. After the acute TCM period, the cardiologic perspective should be one of reassurance and cooperation with the oncologist and oncologic therapy [49, 51].

Follow-up of malignant patients with high risk for developing Takotsubo cardiomyopathy

It is recommended that cancer patients who have a higher risk of developing TCM should receive more careful clinical follow-up. The cardio-oncology guidelines in Brazil suggest that baseline testing should include an ECG, labora-

tory tests (such as a complete blood count, thyroid function tests, type B natriuretic peptide, liver and kidney function tests, and cardiac troponin), and, if possible, follow-up appointments at 3, 6, and 12 months [52]. Apart from these general cardiac follow-up recommendations for cancer patients, additional tests should be carried out whenever new diagnostic or therapeutic methods are used during cancer treatment that could cause the development of TCM.

Clinicians must identify cancer as an indicator of poor prognosis in TCM patients, which significantly increases the risk of adverse long-term outcomes. Although this concept appears simple, it is difficult to use in clinical practice and has significant consequences. When the acute phase of TCM is over, the focus moves from just one cardiologist to a team of experts from several fields working together to provide the best care possible. Although integrated therapy for each condition appears essential, it may be difficult to implement in everyday clinical practice. It is worth mentioning that the high occurrence of malignancy in TCM has led some writers to advocate for oncologic screening of these individuals. However, no precise data has been presented in this regard, and there is currently no clear signal for carrying out such a screening. The objective of management following the acute cardiovascular phase in patients with actively treated malignancies who develop TCM should be to enable a secure resumption of oncologic therapy [53, 54].

It is recommended to do a regular follow-up for the first 3 to 6 months after the acute event, during which LV systolic function and ECG recover entirely in most cases. Tailored heart failure therapy should be delivered according to patients' tolerability. During this period, it is essential to maintain strict interaction with the oncologist to allow the initiation or re-initiation of the anticancer treatment [55]. Since there is a lack of data about the clear-cut association of specific anticancer treatments with TCM occurrence, we suggest discussing the re-initiation of oncologic therapy case-by-case in a multidisciplinary setting. This means that not only aspects related to the TCM events should be considered, but also those related to the oncologic treatment. In most cases, after three months from the TCM event, the oncologic therapy can be started or restarted if the anticancer treatment can be safely paused. With careful management, the anticancer treatment used before the TCM event can be re-challenged. However, if there is an incomplete recovery of LV systolic function, which is unusual in TCM, suspicion of myocardial injury rather than TCM should be considered. In such cases, it is more reasonable to modify the oncologic treatment.

Conclusion

There is an increased risk of TCM in cancer patients. Patients with cancer have a far poorer prognosis than those without the disease when this happens because, in addition to the morbidity, their cancer treatment is frequently interrupted or altered, which can exacerbate their clinical condition even more. Patients with an increased risk of developing TCM may be subject to strict clinical follow-up strategies to facilitate early identification and appropriate treatment. Finding the cancer patients most likely to have TCM may be possible with a risk model approach that uses contemporary data tools like artificial intelligence and machine learning. Translational research has the potential to shed light on the mechanism of action of TCM, identify preventative and therapeutic targets, and determine the safety and feasibility of re-exposing patients to the same or similar anticancer medicines.

Disclosure of conflict of interest

None.

Address correspondence to: Azad Mojahedi, Department of Internal Medicine, Stony Brook University Hospital, Stony Brook, New York, The United States. Tel: 818-519-195; +98-9112774-184; Fax: +98-3137265007; E-mail: Azad.mojahedi@stonybrookmedicine.edu

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