



Coronary Artery Tortuosity in Takotsubo Syndrome: A Closer Look at Coronary Flow and Myocardial Stunning

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Backgrounds: Coronary artery tortuosity (CAT) is often viewed as a benign angiographic finding; however, emerging evidence suggests its potential hemodynamic significance, particularly in non-atherosclerotic cardiomyopathies such as Takotsubo syndrome (TS). This study aimed to investigate the prevalence and hemodynamic implications of CAT in patients diagnosed with Takotsubo cardiomyopathy (TCM) and to evaluate the association between the severity of tortuosity and myocardial injury markers, recovery of ventricular function, and other clinical variables.

Methods: A retrospective review of 100 patients with Takotsubo cardiomyopathy (TCM) from the Baptist Memorial Hospital network (2015–2025) was conducted. Coronary artery tortuosity severity was quantified using angiographic criteria based on the number and degree of vessel curvatures in major epicardial arteries. Associations between coronary artery tortuosity and biochemical or echocardiographic parameters were evaluated using multiple linear regression and non-parametric tests.

Results: CAT was highly prevalent (85.1%) in this TCM cohort, with a mean tortuosity index of 3.26-significantly higher than in general angiography populations. No significant correlations were found between tortuosity severity and peak troponin levels ($P = 0.588$) or ejection fraction (EF) at presentation ($P = 0.820$). Full EF recovery (55–65%) at ≥ 3 months occurred in 70.7% of patients and was not significantly associated with prior cardiomyopathy, coronary artery tortuosity index or baseline troponin levels.

Conclusion: Coronary artery tortuosity was highly prevalent in this cohort of patients with Takotsubo syndrome. However, tortuosity severity was not associated with markers of myocardial injury or recovery of ventricular function. These findings suggest that coronary tortuosity may represent a vascular phenotype frequently observed in Takotsubo syndrome, although its direct pathophysiologic role remains uncertain.

Keywords: Cardiomyopathy; Coronary artery tortuosity; Takotsubo; Heart failure.

Introduction

Coronary artery tortuosity (CAT) is a relatively common finding on angiography and was traditionally considered a benign incidental feature, primarily noted when proximal to a lesion, where it could complicate percutaneous coronary intervention. CAT is typically defined as three or more consecutive 45°–90° curves in a major epicardial artery, and it is considered severe when two or more 180° curves are present.

Recent studies have associated CAT with non-atherosclerotic cardiomyopathy. Estrada et al.^[1] reported a statistically significant association between CAT and myocardial ischemia in a retrospective cohort. Similarly, studies have identified myocardial ischemia in patients without obstructive coronary artery disease^[1], suggesting that unrecognized structural or hemodynamic factors,

such as tortuosity, may contribute to myocardial dysfunction.

Computer simulations have demonstrated that increased tortuosity correlates linearly with decreased perfusion pressure^[2,3]. Takotsubo cardiomyopathy (TCM), which presents as acute coronary syndrome (ACS) with transient LV dysfunction and elevated cardiac biomarkers in the absence of obstructive lesions^[4], may share underlying hemodynamic mechanisms with CAT.

This study aims to determine the association between CAT and Takotsubo cardiomyopathy, examining the relationship between tortuosity severity and myocardial injury, functional recovery, and other clinical variables.

Methods

Study population

This retrospective study included 100 patients from the Baptist Memorial Hospital network (East Arkansas, North Mississippi, and West Tennessee) diagnosed with TCM between 2015 and 2025.

Inclusion criteria required a cardiologist-confirmed diagnosis of TCM with echocardiographic findings within 24 hours of coronary angiography showing no significant atherosclerotic dis-

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ease. Patients with incomplete echocardiographic or angiographic data were excluded.

Collected variables included initial and peak troponin levels, ejection fraction (EF) at diagnosis, Pro-BNP, and follow-up EF (≥ 3 months). Additional data encompassed history of fibromuscular dysplasia, hypertension (with stage), smoking status, and use of guideline-directed medical therapy (GDMT) at discharge (SGLT2 inhibitors, ACE/ARB/ARNI, β -blockers, and aldosterone antagonists). Angiograms were reviewed by investigators and cardiologists who were not blinded to clinical data, which may introduce observer bias in the assessment of tortuosity.

Tortuosity definitions

Following Eleid et al.^[4], CAT was defined as ≥ 3 consecutive curvatures ranging from 90° – 180° in a major epicardial coronary vessel (≥ 2 mm diameter).

Severe: ≥ 2 consecutive curvatures $\geq 180^\circ$ in a ≥ 2 mm vessel.

Moderate: ≥ 3 consecutive 90° – 180° curvatures in ≥ 2 mm vessel (not meeting severe criteria).

Mild: ≥ 3 consecutive 45° – 90° curvatures in ≥ 2 mm vessel, or $\geq 390^\circ$ – 180° curvatures in an artery < 2 mm.

Each major epicardial artery (LAD, LCx, RCA) was assigned a score (0–3), producing a composite Tortuosity Severity Index.

Statistical methods

Continuous variables were reported as means $\pm$ SD and categorical variables as frequencies or percentages. The prevalence of CAT was defined as the proportion with a tortuosity index > 0 . Associations between tortuosity and clinical or biochemical parameters were analyzed using multiple linear regression, with independent variables including age, troponin (initial and peak), Pro-BNP, EF, smoking status, hypertension stage, and GDMT. Because biomarker values demonstrated skewed distributions, troponin and Pro-BNP levels were summarized as median (interquartile range) and compared using the Mann-Whitney U test. Statistical significance was defined as $P < 0.05$. Analyses were conducted in Python using pandas and statsmodels.

Limitations

This study has several important limitations. First, its retrospective design introduces inherent risks of selection bias, information bias, and unmeasured confounding. Data completeness and documentation quality may vary across patients and over the study period.

Second, the absence of a contemporaneous control group significantly limits the ability to determine whether the observed prevalence of coronary artery tortuosity differs from that of comparable populations without Takotsubo syndrome. As such, causal inferences regarding the relationship between CAT and Takotsubo syndrome cannot be established.

Third, although tortuosity was assessed using standardized angiographic criteria, the evaluation retains a degree of subjectivity and is susceptible to interobserver variability. This limitation is further compounded by the lack of blinding of angiographic reviewers to clinical data, which may introduce observer bias.

Fourth, the relatively small sample size restricts statistical power, particularly for multivariable analyses, and limits the ability to fully adjust for potential confounding variables such as age, sex, hypertension severity, and medical therapy.

Finally, the study primarily evaluates associations with conventional markers of myocardial injury and systolic function. More sensitive measures of microvascular dysfunction or diastolic function—which may be more relevant to the pathophysiology of coronary tortuosity—were not available in this dataset.

Accordingly, the findings of this study should be interpreted as hypothesis-generating and warrant confirmation in prospective, controlled studies with standardized imaging and blinded assessment.

Results

Prevalence of coronary artery tortuosity

CAT was present in 85.1% of the cohort, with a mean tortuosity index of 3.26. This prevalence appears higher than that reported in general angiographic populations, where rates average 45.2% in women and 19.7% in men^[5]. Among female patients in this study, CAT prevalence reached 85.7%. However, in the absence of a contemporaneous control population, the extent to which this prevalence differs from background rates in similar demographic groups cannot be determined.

Baseline characteristics and association between CAT and clinical variables

Baseline clinical variables stratified by the presence of coronary artery tortuosity are shown in Table 1. Because biomarker distributions were skewed, troponin and Pro-BNP values are presented as median (interquartile range). No statistically significant differences were observed between patients with and without coronary tortuosity across the evaluated clinical variables.

Table 1. Association between CAT index and troponin levels.

Variable	No Tortuosity (n = 14)	Any Tortuosity (n = 87)	P-value
Age, years	69 (IQR 16)	69 (IQR 16)	0.299
Initial Troponin	1.34 (IQR 1.17)	0.33 (IQR 1.17)	0.274
Peak Troponin	4.01 (IQR 3.94)	1.06 (IQR 3.94)	0.300
Pro-BNP	6466 (IQR 13392)	2312 (IQR 13392)	0.357
Hypertension Stage	0.5 (IQR 2)	1.0 (IQR 2)	0.304

No significant association was observed between the tortuosity index and troponin levels (initial: $P = 0.616$; peak: $P = 0.588$).

This finding suggests that no measurable association was identified between tortuosity severity and biomarker elevation in this

cohort. Takotsubo syndrome is generally characterized by transient myocardial stunning rather than extensive myocardial necrosis, which may explain the modest and variable biomarker elevations observed. Accordingly, troponin levels in this setting likely reflect the degree of transient myocardial stress rather than structural coronary features such as tortuosity.

Association between tortuosity index and ejection fraction

Baseline ejection fraction at the time of diagnosis averaged 30.0%, and no significant association was observed between EF and tortuosity severity ($\beta = -0.003$, $P = 0.820$). These findings suggest that the degree of coronary tortuosity was not related to the initial severity of ventricular systolic dysfunction in this cohort. Although Takotsubo syndrome is primarily characterized by transient left ventricular dysfunction, prior studies have demonstrated that right ventricular involvement may also occur in a subset of patients^[6], which may contribute to variability in ejection fraction measurements. These findings are also consistent with prior work suggesting that coronary tortuosity may be associated with alterations in ventricular function, particularly diastolic parameters, rather than systolic impairment^[7].

Association between tortuosity and hypertension stage

No significant association was observed between coronary artery tortuosity and hypertension stage ($P = 0.304$). Although this finding did not reach statistical significance, it may warrant further investigation with larger cohorts, given the known relationship between hypertension and vascular remodeling.

Observed recovery of left ventricular function

Full LV recovery-defined as EF between 55–65% on follow-up echocardiogram ≥ 3 months was observed in 70.7% of patients. Recovery according to presence or absence of tortuosity is summarized in Table 2.

Table 2. EF recovery vs any tortuosity.

EF Recovery Status	No Tortuosity	Any Tortuosity	P-value
Recovered	5	48	0.2425
Not recovered	5	17	
Total	10	65	

Impact of prior cardiomyopathy on recovery

The impact of prior cardiomyopathy on EF recovery is summarized in Table 3. Prior cardiomyopathy was not significantly associated with reduced likelihood of EF normalization.

Table 3. EF recovery vs prior cardiomyopathy.

EF Recovery Status	No Prior CM	Prior CM	P-value
Recovered	48	5	0.5021
Not recovered	18	4	
Total	66	9	

Multivariable logistic regression for EF recovery

A multivariable logistic regression model including any tortuosity and prior cardiomyopathy as predictors of EF recovery did not identify statistically significant associations. Model coefficients and odds ratios are presented in Table 4.

Table 4. Logistic regression for EF recovery.

Predictor	Coefficient (β)	Odds Ratio (OR)	P-value
Intercept	0.0781	1.08	0.903
Any tortuosity	1.0750	2.93	0.124
Prior cardiomyopathy	-0.8120	0.44	0.271

Discussion

In this retrospective cohort of patients with Takotsubo syndrome undergoing coronary angiography, coronary artery tortuosity (CAT) was highly prevalent, observed in approximately 85% of patients. Despite this high prevalence, no significant associations were identified between tortuosity severity and markers of myocardial injury, presenting ventricular function, or recovery of systolic function. These findings suggest that, while CAT may represent a common anatomical feature in patients with Takotsubo syndrome, it does not appear to directly influence the acute severity or short-term recovery of myocardial dysfunction as assessed by conventional clinical parameters.

Rather than supporting a direct causal relationship, our results raise the possibility that coronary tortuosity represents an underlying vascular phenotype that may coexist with Takotsubo syndrome without independently determining its clinical expression. This interpretation is consistent with the hypothesis that structural coronary features may modulate susceptibility to myocardial dysfunction under stress conditions-potentially through effects on coronary flow dynamics or microvascular function-without being sufficient to drive disease severity on their own.

Catecholamine-induced cardiomyopathy

The association between elevated norepinephrine and epinephrine levels and the development of myocardial ischemia is well established in the literature^[8]. These observations suggest that catecholamine excess may contribute, at least in part, to myocardial dysfunction through direct myocyte injury. However, this mechanism alone does not fully account for the clinical features observed in known catecholamine-mediated cardiomyopathies such as phaeochromocytoma-induced cardiomyopathy^[9]. In Takotsubo syndrome specifically, the absence of late gadolinium enhancement on cardiac magnetic resonance imaging indicates a lack of significant myocardial necrosis, distinguishing TS from classical forms of catecholamine-induced myocardial damage.

Vasospasm

Another proposed mechanism for Takotsubo syndrome involves coronary vasospasm leading to transient myocardial ischemia. This hypothesis was first introduced by Dote et al.^[10], who reported that 4 of the initial 5 patients exhibited vasospasm during angiography. Subsequent studies have similarly described associ-

ations between vasospasm and Takotsubo syndrome^[11,12]. In addition, transient apical ballooning has been reproduced following intracoronary acetylcholine administration in patients undergoing evaluation for Takotsubo cardiomyopathy^[13], further supporting a vasospastic component.

Given the high prevalence of coronary artery tortuosity (CAT) observed in this population, its potential relationship with vasomotor dysfunction has been explored. Jansen et al.^[14] evaluated patients undergoing acetylcholine-provoked angiography and found no significant association between tortuosity and epicardial coronary spasm. In contrast, McChord et al.^[15] reported a higher prevalence of CAT among patients with microvascular spasm compared with those with epicardial spasm or negative testing, suggesting that the relationship between tortuosity and vasomotor dysfunction may be more pronounced at the microvascular level rather than in large epicardial vessels.

This distinction is particularly relevant in Takotsubo syndrome, where microvascular dysfunction is thought to play a central role. As highlighted by Vitale et al.^[16], impairment of the coronary microcirculation may contribute to transient myocardial stunning in the absence of obstructive coronary disease. In this context, coronary tortuosity may not directly induce epicardial vasospasm but could contribute to altered coronary flow dynamics or increased susceptibility to catecholamine-mediated microvascular dysfunction.

One potential interpretation is that coronary tortuosity influences distal perfusion by altering vessel geometry, thereby reducing effective perfusion pressure or impairing coronary flow reserve, particularly under conditions of increased physiological stress. This may help explain why, despite its high prevalence, tortuosity severity was not associated with markers of myocardial injury or ventricular dysfunction in our cohort. If present, its effect is likely indirect and not captured by conventional biomarkers or global systolic function measures. However, this hypothesis cannot be directly tested in the present study and would require prospective evaluation using dedicated assessments of coronary microvascular function.

Spontaneous coronary artery dissection

The association between spontaneous coronary artery dissection (SCAD) and coronary artery tortuosity has been previously established^[4], raising the question of whether SCAD and Takotsubo syndrome (TS) may share overlapping pathophysiologic mechanisms. Early reports noted that several cases initially diagnosed as Takotsubo were later reclassified as SCAD^[17], as SCAD can produce a clinical and imaging presentation-including apical ballooning that closely mimics TS. While this overlap suggests a potential unifying mechanism for a subset of cases, the relationship between SCAD and other characteristic features of TS, such as catecholamine excess, remains incompletely understood.

Gurgoglione et al.^[18] observed a strong association between SCAD and emotional stressors in women, implying a possible link to catecholamine surges similar to those implicated in TS. Notably, patients with pure SCAD tend to be younger and have fewer traditional cardiovascular risk factors compared with typical TS cohorts^[4,17], including the population in our study (mean age 45.3 ± 8.9 vs 65.7 ; Table 2). It is also relevant to note that SCAD was not documented in our patient population. Although

no cases of SCAD were identified in our study population, prior studies have described an association between SCAD and coronary artery tortuosity. The potential overlap between these vascular phenotypes and Takotsubo syndrome has been discussed in the literature, although this relationship cannot be evaluated directly in the present cohort.

Conclusion

The characteristic findings of Takotsubo syndrome are likely driven by a combination of hemodynamic alterations affecting the coronary circulation during episodes of significant catecholamine release. Although direct catecholamine-induced myocardial injury has not been consistently demonstrated, the surge in circulating catecholamines appears to create a vulnerable microcirculatory environment that predisposes susceptible individuals to myocardial stunning. In our study, biomarker levels and presenting ejection fraction were evenly distributed across tortuosity categories, suggesting that tortuosity alone by this definition does not determine the initial severity of myocardial dysfunction. Nevertheless, a more comprehensive assessment of coronary tortuosity-paired with detailed evaluation of both left and right ventricular function in TS may yield important mechanistic insights.

Several factors that predispose individuals to SCAD may also increase susceptibility to TS. As demonstrated by Mughal et al.^[19], patients diagnosed with SCAD were more than seven times more likely to also be diagnosed with TS. However, not all individuals with SCAD develop the classic apical ballooning pattern, highlighting the heterogeneity of this syndrome. Notably, we propose that the microvascular abnormalities associated with coronary artery tortuosity may further amplify the risk of TS, particularly in older patients and in those with traditional cardiovascular risk factors-most notably hypertension.

Future studies are needed to evaluate therapeutic strategies that target the hemodynamic and microvascular disturbances observed in this population. Such approaches have the potential not only to improve outcomes in Takotsubo syndrome but also to benefit patients with non-obstructive coronary artery disease more broadly.

Abbreviations

CAT, coronary artery tortuosity; EF, ejection fraction; GDMT, guideline-directed medical therapy; LAD, left anterior descending artery; LCx, left circumflex artery; Pro-BNP, pro-B-type natriuretic peptide; RCA, right coronary artery; SCAD, spontaneous coronary artery dissection, TCM, Takotsubo cardiomyopathy; TS, Takotsubo syndrome.

Ethical approval and consent to participate

This retrospective study was conducted in accordance with institutional and national ethical standards. Ethical approval was obtained from the appropriate Institutional Review Board of the Baptist Memorial Hospital system. Given the retrospective nature of the study and use of de-identified data, the requirement for in-

formed consent was waived.

Conflicts of interest

The authors declare that they have no competing interests.

Authors' contributions

AA conceptualized the study, participated in data collection and interpretation, and drafted the manuscript. JS contributed to data collection and manuscript preparation. SO assisted with data analysis and interpretation. CR contributed to clinical interpretation and manuscript revision. BB provided senior oversight, contributed to study design, and critically revised the manuscript. All authors reviewed and approved the final version of the manuscript.

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