

COVID-19 pandemic: no increase of takotsubo syndrome occurrence despite high-stress conditions

Clement Delmas¹ , Frédéric Bouisset² and Olivier Lairez^{2,3}

¹Intensive Cardiac Care Unit, Rangueil University Hospital, Toulouse, France; ²Department of Cardiology, Rangueil University Hospital, Toulouse, France; ³Cardiac Imaging Center, Rangueil University Hospital, Toulouse, France

Impact of COVID-19 pandemic: isolation, impairment of well-being, and insecurity

With the current COVID-19 pandemic, unprecedented restrictions have been decided by governmental authorities on social freedoms in order to allow strict social distancing to reduce transmission of SARS-CoV-2 and risk of COVID-19 spread.¹ These measures aim to drastically reduce social interactions (school shutdown and home working), prohibiting visits from relatives and minimizing the use of public transports, and were gradually adopted worldwide. In certain countries, especially in Europe, containment restrictions were severe with the entire population advised to stay at home.

The psychological effects of containment/quarantine have been recently described revealing numerous emotional consequences, including stress and fear, depression and insomnia, anger and irritability, frustration, and boredom with possible persisting sequelae even after the quarantine was lifted. A greater duration of confinement, inadequate supplies, limited access to medical care and medications, and financial losses are aggravating factors.²

Fear, uncertainty on the future, unclear or even contradictory messages from the authorities, and continuous and alarming media reports (daily number of deaths and insecurity) may play an additional impact on the emergence of emotional stress.³

Takotsubo physiopathology and role of stressful event

The pathophysiology of takotsubo syndrome (TTS) is complex and still not fully understood, but the role of stress and its

interaction with the autonomic nervous system seems predominant.

An increase in circulating and intracardiac catecholamines has been frequently described, as well as a modification of the activity of G proteins coupled to B₂ receptors.⁴ Animal TTS models (immobilization stress) have demonstrated a protective effect of beta-blockers and alpha-blockers,⁵ which is also suspected in humans at the acute stage of TTS but does not persist in the long term.⁶ Chronic stress (dependent, cancer and depression) seems to facilitate TTS occurrence.⁷ An acute emotional or physical trigger is found in almost 50% of TTS cases.⁸

Impact of COVID-19 pandemic on TTS occurrence

In this context of pandemic and containment, one could expect a rise in the rate of TTS episodes by an increase of triggering mechanisms such as stress and anxiety, but this remains to be proven. To date, few rare clinical cases report TTS cases during COVID-19.^{9,10}

In our tertiary centre, we observed from 1 March 2020 to 15 April 2020 a relatively stable incidence of TTS in comparison to the same period during the previous years. On the contrary, we observed a drop of approximately 30% of the incidence of ACS cases (*Table 1*). This decline in the number of cases of acute myocardial infarction has been previously highlighted by some authors¹¹; however, to the best of our knowledge, no studies to date have described the evolution of the incidence of TTS during the current COVID-19 outbreak.

Mechanisms of this significant reduction of ACS cases are probably multiple and at least in part common with the absence of a TTS incidence increase during this period. It is likely that a certain number of cases exist but are not visible

Table 1 Incidence of cases of ACS and takotsubo syndrome between 1 March and 15 April

	STEMI ACS			Non-STEMI ACS			ACS (all types)			Takotsubo		
	Count	P	P*	Count	P	P*	Count	P	P*	Count	P	P*
2016	71	Ref	0.016	185	Ref	<0.001	256	Ref	<0.001	4	Ref	0.711
2017	72	0.933		165	0.285		237	0.392		7	0.372	
2018	60	0.337		182	0.876		242	0.53		5	0.739	
2019	67	0.734		144	0.024		211	0.038		8	0.258	
2020	46	0.022		112	<0.001		158	<0.001		5	0.739	

ACS, acute coronary syndrome; non-STEMI ACS, acute coronary syndrome without ST elevation; P*, 2020 vs. 2016–2019; STEMI ACS, acute coronary syndrome with ST elevation.

because (i) patients do not consult for fear of being infected in the hospital or for fear of disturbing the emergency services; (ii) TTS patients are drowned in the middle of calls to emergency and rescue services which are currently overwhelmed; and (iii) minor cases of TTS consulting the emergency department are sent home after a COVID-19 infection has been ruled out with no further diagnostic procedure such as an electrocardiogram and an echocardiogram which allow identification of TTS.

One could also assume that changes in the emotional and socio-professional environment could also play a role in this absence of increase in TTS cases (reduction of professional and societal stress: disappearance of traffic jams, reduction in criminal assaults, less social and professional pressure, etc.).

However, if the vast majority of the population is confined and less exposed to TTS triggers, we can assume that some individuals are exposed to stress in this setting: elderly and/or isolated subjects, people exposed to domestic violence, patients with pre-existing psychiatric conditions or past history of substance abuse, relatives of deceased COVID-19 patients, and healthcare providers.

In addition, a risk of a rebound phenomenon in the number of TTS cases is plausible during or after the current crisis, due to the likely emergence of numerous cases of major depressive disorders, generalized anxiety, or equivalent of post-traumatic stress disorder (PTSD) known to be associated

with TTS.⁷ An increase in PTSD and TTS was noted after terrorist attacks in France in January 2015 and after natural disasters.^{12–14}

Awareness of TTS among physicians is therefore necessary. TTS diagnostic algorithms can be used to improve management and eliminate acute coronary syndrome/myocarditis, or identify dysthyroidism or pheochromocytoma.⁸

Conclusions

We observed a stable rate of TTS during the COVID-19 pandemic in contrast to a decrease in acute coronary syndromes. Late catch up is possible due to the presence of TTS triggers in this setting.

Conflict of interest

None declared.

Funding

None.

References

- Galea S, Merchant RM, Lurie N. The mental health consequences of COVID-19 and physical distancing: the need for prevention and early intervention. *JAMA Intern Med* 2020. Apr 10. <https://orcid.org/10.1001/jamainternmed.2020.1562>
- Brooks SK, Webster RK, Smith LE, Woodland L, Wessely S, Greenberg N, Rubin GJ. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. *Lancet* 2020; **395**: 912–920.
- Pfefferbaum B, North CS. Mental health and the Covid-19 pandemic. *N Engl J Med* 2020. Apr 13. <https://orcid.org/10.1056/NEJMp2008017>
- Wittstein IS, Thieman DR, Lima JAC, Baughman KL, Schulman SP, Gerstenblith G, Wu KC, Rade JJ, Bivalacqua TJ, Champion HC. Neurohumoral features of myocardial stunning due to sudden emotional stress. *N Engl J Med* 2005; **352**: 539–548.
- Ueyama T. Emotional stress-induced Tako-tsubo cardiomyopathy: animal model and molecular mechanism. *Ann N Y Acad Sci* juin 2004; **1018**: 437–444.
- Templin C, Ghadri J, Diekmann J, Napp L, Bataiosu D, Jaguszewski M, Cammann VL, Sarcon A, Geyer V, Neumann CA, Seifert B. Clinical features and outcomes of Takotsubo (stress) cardiomyopathy. *N Engl J Med* 2015; **373**: 929–938.
- Delmas C, Lairez O, Mulin E, Delmas T, Boudou N, Dumonteil N, Biendel-Picquet C, Roncalli J, Elbaz M, Galinier M, Carrié D. Anxiodepressive disorders and chronic psychological stress are

- associated with Tako-Tsubo cardiomyopathy—new physiopathological hypothesis. *Circ J* 2013; **77**: 175–180.
8. Lyon AR, Bossone E, Schneider B, Sechtem U, Citro R, Underwood SR, Sheppard MN, Figtree GA, Parodi G, Akashi YJ, Ruschitzka F, Filippatos G, Mebazaa A, Omerovic E. 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; **18**: 8–27.
 9. Meyer P, Degrauwe S, Van Delden C, Ghadri J-R, Templin C. Typical takotsubo syndrome triggered by SARS-CoV-2 infection. *Eur Heart J* 2020; **41**: 1860.
 10. Minhas AS, Scheel P, Garibaldi B, Liu G, Horton M, Jennings M, Jones SR, Michos ED, Hays AG. Takotsubo syndrome in the setting of COVID-19 infection. *JACC Case Rep* 2020. <https://doi.org/10.1016/j.jaccas.2020.04.023>
 11. Metzler B, Siostrzonek P, Binder RK, Bauer A, Reinstadler SJ. Decline of acute coronary syndrome admissions in Austria since the outbreak of COVID-19: the pandemic response causes cardiac collateral damage. *Eur Heart J* 2020;**41**: 1852–1853. <https://doi.org/10.1093/eurheartj/ehaa314>
 12. Leor J, Poole WK, Kloner RA. Sudden cardiac death triggered by an earthquake. *N Engl J Med* 1996; **334**: 413–419.
 13. Ben-Ezra M, Leshem E, Goodwin R. In the wake of national trauma: psychological reactions following the *Charlie Hebdo* terror attack. *Am J Psychiatry* 2015; **172**: 795–796.
 14. Rosa FD, Van Rothen J, Dongay B, Pathak A. We are CHARLIE: emotional stress from “Charlie Hebdo attack” extensively relayed by media increases the risk of cardiac events. *Clin Res Cardiol Off J Ger Card Soc juill* 2016; **105**: 630–631.