

# Loss of engagement in controlling chronic anticoagulation therapy during COVID-19 stringency measures. A single center experience of disproportioned increase of stuck mechanical valves

Olga Vrizz<sup>1,2</sup>, Andrea Rossi Zadra<sup>1</sup>, Abdalla Eltayeb<sup>1</sup>, Fatima Asiri<sup>1</sup>, Claudio Pragliola<sup>3</sup>, Nader Ashraf Fawzy<sup>2</sup>, Domenico Galzerano<sup>1</sup>, Khalid Feras<sup>1</sup>, Zohair Alhalees<sup>1</sup>, Abdulhalim J Kinsara<sup>4</sup>, Fadl Elmula Mohamed Fadl Elmula<sup>1</sup>

<sup>1</sup>Heart Centre Department, King Faisal Specialist Hospital and Research Center, Riyadh; <sup>2</sup>College of Medicine, Alfaisal University, Riyadh; <sup>3</sup>Department of Adult Cardiac Surgery, Prince Sultan Cardiac Center, Riyadh; <sup>4</sup>Ministry of National Guard Health Affair, COM-WR, King Abdullah International Research, Saudi Arabia

## Abstract

Stuck valve is a very rare and severe complication that occurs in mechanical valve replacement patients with ineffective anticoagulation. However, with COVID-19 restriction measures, it became challenging to regularly assess INR to make sure it falls

within the target therapeutic range to prevent this complication. We present a series of 10 patients who either underwent transthoracic echocardiography for a suspected stuck valve or were seen at the outpatient valve clinic with the residual consequences of a stuck valve during the COVID-19 restriction measures in our institute. Stuck prosthetic valves incident has increased significantly during this period, particularly those in the mitral position for which urgent replacement and prolonged hospitalization were necessary. Particularly with the COVID-19 restrictions in place, these cases highlight the need for physicians to be aware of the dramatic increase in the incidence of stuck prosthetic valves in patients on chronic warfarin therapy.

Correspondence: Prof Olga Vrizz, Heart Centre, King Faisal Specialist Hospital and Research Centre, Zahrawi St, Al Maather, Al Maazer, Riyadh 12713, Saudi Arabia.  
Tel. +966.1.1464-7272 extension 32056.  
Fax: +966.1.14427791.  
E-mail: olgavrizz@yahoo.com

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## Introduction

In December 2019, coronavirus disease (COVID-19) emerged in Wuhan, Hubei Province, China, and the WHO raised its classification from 'epidemic' to 'pandemic' on March 11 2020 [1]. In response, hospitals had to both increase their surge capacities in emergency and intensive care departments but also significantly reduce internal medicine, family medicine, routine out-patient clinic and laboratory check-up activities [2,3] As such, several countries prohibited non-essential surgical and oncological elective procedures for an indeterminate period of time [4,5] As yet, it is unclear how the duration, timing and nature of these measures impacted patients, and the long-term consequences of limiting their access to health services, including simple routine coagulation screening, is yet to be seen. During the pandemic, patient access to healthcare was further impeded by quarantine measures and curfews, and compounded by elevated numbers of missed appointments due to nervous patients choosing to avoid hospital settings.

During the COVID-19 pandemic, Saudi Arabia, like most countries worldwide, imposed restrictions on people's movements. As such, regular outpatient follow-ups were performed remotely by telephone, and patients were only occasionally requested to attend clinic in-person where necessary for routine laboratory checks, such as determining international normalized ratio (INR).

Warfarin, a vitamin K inhibitor, is used in patients with mechanical valve prosthesis to prevent thromboembolic events and stuck valves, among other indications. In mechanical valves, a target INR range of 2.5–3.5 is the current recommendation for mechanical

mitral valve replacement. Regular assessment of INR is necessary to maintain its value within the target therapeutic range.

Herein, we describe a case series of patients on warfarin anti-coagulation therapy with stuck mechanical valves during the COVID-19 restriction measures in Saudi Arabia.

## Case series

This is a single-center prospective study of consecutive patients seen in our clinic between January 2000 – January 2021 who either i) underwent transthoracic echocardiography for a suspected stuck valve or ii) were seen at the outpatient valve clinic with the residual consequences of a stuck valve. During this period, 10 patients (mean age  $53.9 \pm 16.2$  years, 80% female) were admitted to the King Faisal Specialist Hospital and Research Center, tertiary referral hospital in Saudi Arabia, for further diagnosis and management of a suspected stuck cardiac valve.

Diagnosis of stuck valve was confirmed in 9/10 patients, and one patient was diagnosed with the residual effects of stroke. For this patient, diagnosis was performed at the local hospital where the patient received medical treatment (Table 1).

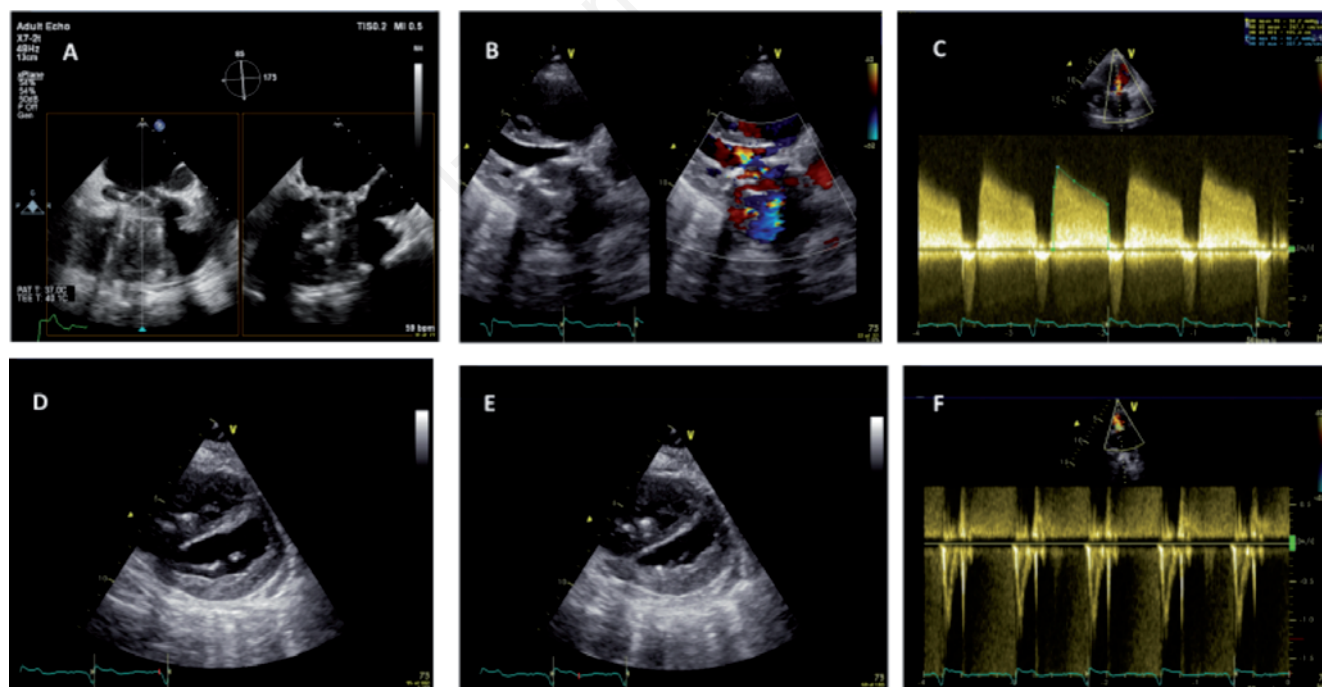
All patients were COVID-19 negative; general characteristics are summarized in Table 1. Five patients (50%) were from outside Riyadh city, four patients were admitted through the emergency department (Figure 1) and two were referred from other hospitals. In two cases, stuck valve was an incidental finding observed during a routine echocardiographic follow-up, and patients did not complain of specific symptoms.

Eight patients were female, two of whom were pregnant at the first trimester and eventually went on to receive an abortion;

six patients received urgent valve replacement cardiac surgery; four patients were managed medically e.g., with heparin; none had thrombolytic therapy. In two patients, surgery was contraindicated by comorbidities and severely compromised left ventricular function (marked by an ejection fraction  $<25\%$ ). Four patients died, including one pregnant woman following surgical valve replacement and maximal support on extracorporeal support (ECMO) over 36 days of hospitalization. In three cases, patients clearly reported that they were afraid to attend the hospital for determination of their INR. The diagnosis of stuck valve was performed by transthoracic echocardiography and transesophageal echocardiography and fluoroscopy was done in 80% of the patients (Figure 2). Mean hospital admission time was  $27.5 \pm 18.5$  days. The cost of treatment, as average estimated reimbursement, was 11,000 USD for medical admission only, and 43,200 USD when surgery was required, up to 64,000 USD when ECMO was part of patient management. As a comparison, from 2015-2019 only one patient per year was admitted to our institute with stuck valve, of whom two died during hospitalization due to complications (Figure 3).

## Discussion

Shortly after the beginning of the COVID-19 pandemic, concerns were raised about the potential negative consequences resulting from limiting elective or non-Covid healthcare services [6], as the number of follow-up and primary care services dramatically decreased due to concerns about virus transmission. These concerns were shared by both patients and healthcare providers, particularly those working in outpatient settings [7].



**Figure 1.** The case of emergency admission of a 36 years old pregnant woman. A) TEE with disks closed in diastole. B) TTE parasternal long axis in diastole. C) CW across the valve, peak and mean gradients 46/26 mmHg at 75bpm. D,F) Short axis with D shape of the left ventricle suggestive of right pressure/volume overload. F) Pulse Doppler on the pulmonary valve with very short acceleration time suggestive of significant increase in pulmonary pressure.

**Table 1. General characteristics of the population.**

N	Age	Sex	Comorbidities	Valve involved	Previous re-do	Symptoms	Therapy	LOS	Complications	Outcome	Mean MV	PASP(mmHg) gradient (mmHg)
1	27	M	No	Mitral	0	Dyspnea	Medical (severe LV dysfunction)	17	None	Alive	10	70
2	70	F	AFib, ischemic stroke, CML	Mitral	0	Headache	Surgical	53	Tamponade, LV free wall rupture	Death	10	32
3	38	F	No	Mitral	0	Dyspnea	Surgical	27	1 <sup>st</sup> trimester abortion	Alive	17	40
4	68	F	Endometrial Ca S/P hysterectomy and bilateral salpingectomy and oophorectomy, GI bleeding, SDH secondary to head trauma	Mitral	2	Headache	Surgical	54	MOF	Death	27	100
5	51	M	SLE and LN, kidney transplant, ischemic stroke, gouty arthritis, atrial flutter	Mitral	2	Dyspnea	Surgical	16	none	Alive	6	28
6	70	F	S/P TAVI, complete heart block with VVI PPM, atrial tachycardia with Wenckebach AV block, DM	Mitral	0	No specific symptoms	Surgical	26	AV Block	Alive	8	30
7	71	F	DM, HTN hypothyroidism, CMP EF 25%, recurrent stroke	Aortic/mitral	0	Stroke	Medical	6	Stroke	Alive	Echo done at local hospital	
8	36	F	S/P AVSD repair, chronic AFib S/P PPM, frequent miscarriage, TIA	Mitral	2	Dyspnea, abdominal pain	Surgical	36	1 <sup>st</sup> trimester abortion, multiple organ failure, DIC, septic shock, ECMO, cardiac tamponade	Death	26	110
9	57	F	CMP EF 15%, S/P ICD insertion, AFib, hypothyroidism	Mitral	2	Dyspnea and severe LV dysfunction	Medical (comorbidities and severe LV dysfunction)	4	Cardiac arrest	Death	19	70
10	50	F	No	Aortic	2	Dyspnea	Medical	35	None	Alive	5 (46*)	33

LOS, length of stay; M, male; F, female; S/P, status post; LV, left ventricle; EF, ejection fraction; MOF, multiple organ failure; PPM, permanent pacemaker; ICD, implantable cardioverter defibrillator; GI, gastrointestinal; SDH, subdural hematoma; TIA, transient ischemic attack; CML, chronic myeloid leukemia; Ca, cancer; SLE, systemic lupus erythematosus; LN, lupus nephritis; DM, diabetes; HTN, hypertension; DIC, disseminated intravascular coagulation; ECMO, extracorporeal membrane oxygenation; \*trans aortic valve gradient.

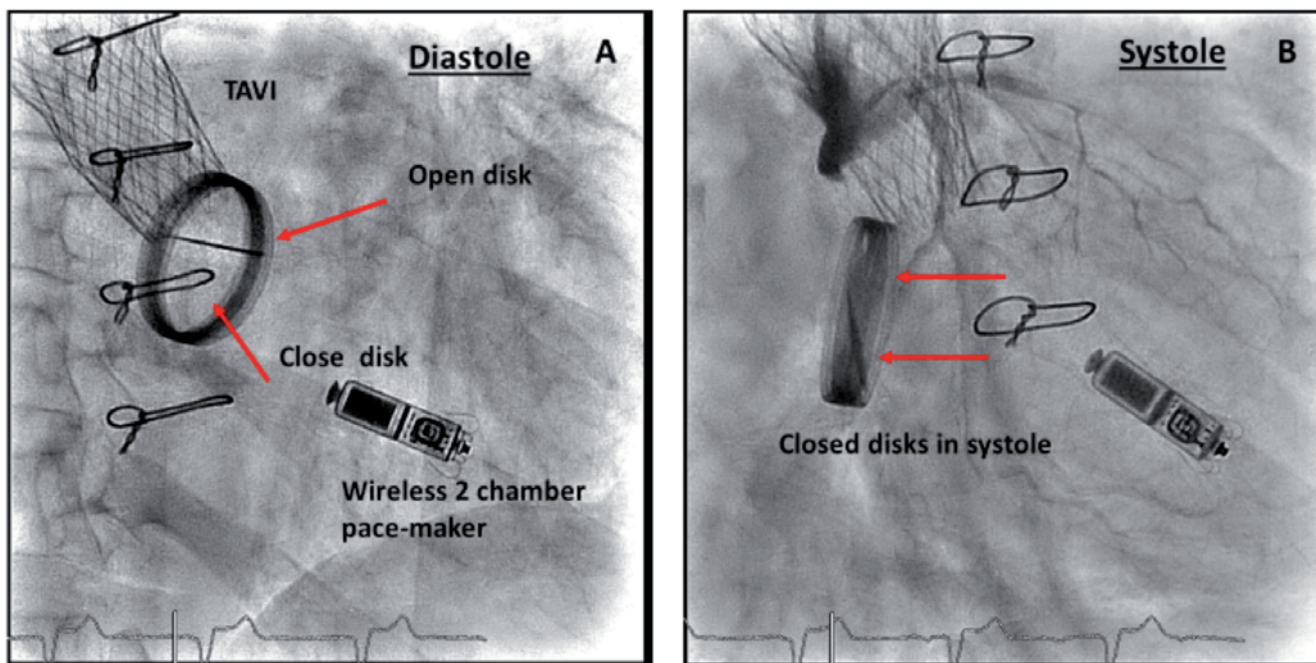


Figure 2. Fluoroscopy in a 70 years old patient. A) Diastole: red arrow address one closed and one open disk. B) Systole: both disks are closed.

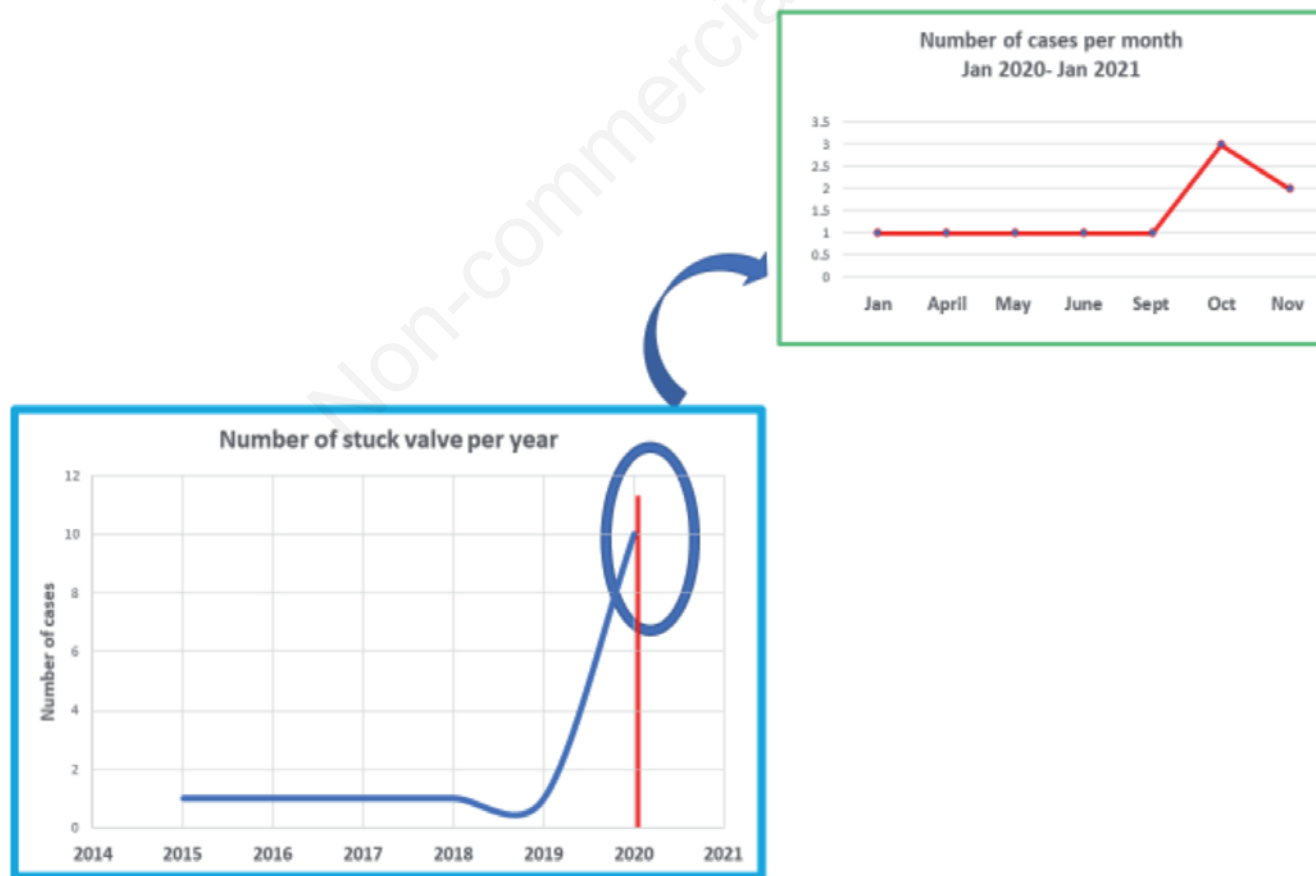


Figure 3. The average number of patients with a mechanical stuck valve is constant over the timeframe 2015-2019, with an increase in the last half of 2020.

As a consequence, hospitals deferred elective and preventive consultations, such as annual physicals, and implemented telemedicine services where possible. Moreover, many patients cancelled their scheduled appointments to limit their risk exposure by staying at home. These behaviors were reinforced by local and government recommendations restricting travel and nonessential services statewide.

In our institution, between March and August 2020, outpatient clinics were run by telephone assessment, and the echocardiography laboratory was available for emergencies only. As such, direct face-to-face interaction was not possible, limiting the normal exchange of information between doctor and patient typically expected from a full consultation. Similarly, many patients on warfarin medication did not regularly attend the anticoagulation clinics -despite these services remaining open- likely resulting in a high rate of patients missing their INR target ranges.

We report a dramatic increase in stuck prosthetic valves during this period, particularly those in the mitral position, which in most cases required urgent replacement and prolonged hospitalization, including intensive care admission, with high in-hospital mortality rates and high costs. Some patients were referred from other hospitals, while others were admitted directly from the emergency department with compromised hemodynamics. Two were identified during regular echocardiographic follow-ups when the outpatient clinics were reopened, corresponding with the increased incidence observed in October-December. While repeat heart valve surgery is generally a high-risk intervention [8], poor outcomes have been reported in patients with severe valvular disease whose valve replacement was deferred for replacement/repair until after pandemic restrictions were lifted [9]. In the particular case of stuck valves, the reported mortality is very high: from 69% in reports back to 1980-1990 [10] to 35% in more recent reports [11]. We were unable to find any data concerning the consequences of curfews associated with the COVID-19 pandemic and routine regular assessment of INR in anticoagulation therapy in patients with mechanical heart valves. In general, as a consequence of the COVID-19 restrictions, substantial reductions have been reported in primary care for acute physical and mental conditions [12].

Of particular note, in a survey of 388 patients from the Cardiology Out-Patient Department of a single center in Saudi Arabia, Samargandy *et al.* [13] reported that 36.3% of patients did not seek help due to fear of infection. Of these patients, 15.7% were concerned about violating curfew, 3.9% were concerned about travelling / public transportation while 44.1% were neutral. Of particular note, 69% of these patients reported that they would not have made the same decision had the pandemic not occurred. Most likely our patients - were unable to receive regular INR assessments – fell into similar categories. From a health systems perspective, consistent resources are necessary to provide high-technology healthcare to patients with highly predictable complications. The direct cost of avoidable complications that require either medical or surgical intervention vastly exceeds the cost of routine assessment of INR value. An unmeasured consequence of avoidable prolonged admissions is the limitation of the number of available beds for emergency or elective admissions, which will further negatively impact health outcomes in a given population [14], especially during the COVID-19 pandemic.

Also, social factors cannot be excluded. Interestingly, 80% of patients from our sample were women, and some speculation may be needed to explain this interesting finding. The most common reason for valve replacement in Saudi Arabia is rheumatic disease; while this affects females more than males, social factors cannot be excluded. Health disparities between genders is a well-described,

worldwide phenomenon that leads to gender inequalities in terms of education, job opportunities, income, family engagement, and may well also affect outcomes during the COVID-19 pandemic. One could speculate that the overwhelming demands and commitments of family during this time of profound uncertainty has led many women to heed less attention to their own personal health.

## Conclusions

Despite government efforts to implement telemedicine and virtual clinics, COVID-19 restrictions and health-messaging affected the routine follow-up of non-COVID-19 patients. Clinics were missed for multifactorial reasons, with personal and social factors at play. We report dramatic consequences to this drastic change in healthcare: clinical complications, lost lives and inflated health-care costs in patients with a prosthetic valve. We believe that non-COVID-19 patients have paid, and will continue to pay in the future, a price that is much greater than those patients who have suffered from COVID-19. Active engagement of patients should be implemented in a time of emergencies, and further studies should address the efficacy and cost-effectiveness of public policies aimed to decrease the burden of avoidable complications and missed diagnoses.

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