Letter to the Editor

Cardiac imaging findings of recovered COVID-19 patients with increased myocardial injury biomarkers in acute phase—the role of Multimodal cardiovascular imaging examination

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There is no doubt that COVID-19 could cause cardiac injuries (1-7), and cardiovascular imaging examination including Cardiac Magnetic Resonance Imaging (CMR) and Coronary Computed Tomography Angiography (CCTA) are helpful for detecting cardiovascular injury and exploring pathophysiological mechanisms of multiple cardiovascular disease include COVID-19 (3-7). Chen *et al.* (4) performed CMR in 25 COVID-19 patients with at least one marker of cardiac involvement [cardiac symptoms, abnormal electrocardiograph (ECG), or abnormal cardiac biomarkers] within the first 10 days of the onset of COVID symptoms, and found in patients with early-stage COVID-19, myocardial edema, and functional abnormalities are a frequent finding, while irreversible regional injury such as necrosis may be infrequent. However, considering the risk of infection associated with patient transport and imaging examination, it is not feasible to learn cardiovascular injury by multiple imaging examinations during the acute phase in most hospitals.

To provide imaging evidence and basis for revealing the pathogenesis of myocardial injury of COVID-19, CMR and CCTA were performed on recovered COVID-19 patients whose virus detection turned negative and clinical observation was done in our hospital prospectively. The selection criterions were as follows: (I) patients were previously confirmed of SARS-CoV-2 infection by reverse transcription and polymerase chain reaction (RT-PCR) swab test; (II) patients were considered recovered by the discharging criteria (a. normal temperature lasting longer than 3 days; b. resolved respiratory symptoms; c. substantially improved acute exudative lesions on chest CT images; d. two consecutive negative RT-PCR test results separated by at least 24 hours and was isolated for 14 days; (III) the recovery of respiratory function and being able to tolerate the special respiration requirements of CMR. This study was approved by the institutional review board of the Fifth Affiliated Hospital of Sun Yat-sen university (No.: K214-1).

Seven COVID-19 patients who recently recovered from COVID-19 infection were included. Patient characteristics, blood test results, treatment before discharge and CMR imaging findings are provided in *Table 1*.

Six (85.71%) patients were found of myocardial injury. The final diagnosis are: Case 1: hypertensive cardiomyopathy, coronary artery disease (CAD), coronary artery fistula, ischemic injury of left ventricular basal lateral wall and myocarditis of left ventricular basal inferior and septal wall caused by Acute Respiratory Syndrome

Table 1 Patient Characteristics, blood test results, treatment before discharge and CMR imaging findings

Characteristics		Cases						
		Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Patient characteristics								
Gender		F	F	F	M	F	M	M
Age (years)		75	70	59	38	22	29	36
BMI		23.22	31.25	26.2	22.25	15.6	21.25	24.9
Comorbidities								
Hypertension		Y	Y	N	N	N	N	N
Diabetes mellites		N	N	N	N	N	N	N
Known Coronary artery disease		N	N	N	N	N	N	N
Chronic obstructive pulmonary diseases		N	N	N	N	N	N	N
Cerebrovascular disease		N	Y	N	N	N	N	N
Chronic renal diseases		N	N	N	N	N	N	N
Chronic liver diseases		N	N	N	N	N	N	N
Blood pressure, mmHg								
Systolic		174	130	154	108	108	125	118
Diastolic		86	62	94	76	72	87	79
Heart rate (highest), beats per min		85	71	67	86	70	72	94
Duration between confirming of COVID-19 to CMR examination (day)		54	59	27	48	51	43	54
Clinical types		Critical	Severe	Common	Severe	Common	Mild	Severe
Precordial chest pain	Acute	N	N	N	N	N	N	N
	Convalescents	N	N	N	N	N	N	N
Palpitation	Acute	N	N	N	N	N	N	N
	convalescents	Y	N	Y	N	N	N	N
Chest distress	Acute	Y	N	N	Y	Y	Y	N
	Convalescents	Y	N	Y	N	N	N	N
Blood test results								
Laboratory findings	NRR							
White blood cell count ($\times 10^9$/L)	3.5–9.5	21.24^h	10.25^h	4.43^h	5.91^h	5.14^h	7.45^h	12.2^h
		3.79^L	3.85^L	2.53^L	2.47^L	2.21^L	4.92^L	4.45^L
Lymphocyte count ($\times 10^9$/L)	1.1–3.2	0.97^h	1.56^h	1.14^h	1.56^h	1.48^h	2.46^h	1.71^h
		0.31^L	0.54^L	0.84^L	0.64^L	0.89^L	1.43^L	0.68^L
Platelet count ($\times 10^3$/L)	152–350	345^h	182^h	189^h	274^h	370^h	269^h	373^h
		304^L	117^L	163^L	118^L	201^L	232^L	142^L

Table 1 (*continued*)

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Characteristics		Cases						
		Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Red blood cell count (×10^9/L)	3.8–5.1	3.75^h	3.52^h	4.05^h	5.48^h	4.42^h	5.55^h	4.77^h
		3.04^L	3.05^L	3.65^L	4.53^L	3.43^L	5.08^L	4.17^L
Hemoglobin, g/L	115–150	109^h	112^h	127^h	162^h	138^h	169^h	149^h
		85^L	92^L	117^L	131^L	108^L	154^L	133^L
Procalcitonin, ng/mL	0–0.5	1.24^h	0.26^h	0.11^h	0.17^h	0.48^h	0.13^h	0.16^h
		0.12^L	<0.10^L	<0.10^L	<0.10^L	<0.10^L	<0.10^L	<0.10^L
CRP (highest) (mg/L)	0.068–8.2	127.5^h	45.79^h	0.460^h	19.52^h	5.590^h	0.210^h	46.57^h
		12.9^L	1.22^L	<0.220^L	0.560^L	<0.120^L	>0.03^L	3.19^L
Hs-cTnI (pg/mL)	0–0.0229	0.15^h	0.056^h	<0.010h	0.017^h	<0.010^h	<0.010^h	<0.010^h
		<0.010^L	<0.010^L	<0.010^L	<0.010^L	<0.010^L	<0.010^L	<0.010^L
Creatinine kinase–myocardial band, U/L	0–25	10.7^h	15^h	30.7^h	34.9^h	25.9^h	26.8^h	29.30^h
Glutamic Oxaloacetic Transaminase, U/L	13–35	117^h	80.10^h	21.5^h	29^h	28.2^h	19.3^h	36.8^h
Glyoxylate Aminotransferase, U/L	7–40	55.1^h	100.8^h	14.4^h	25.2^h	32.2^h	13.0^h	63.1^h
Albumin, g/L	40–55	30.2^L	32.3^L	36.5^L	33.6^L	37^L	40.3^L	44.1^L
Myoglobin, μg/L	23–112	/	/	29	/	31	/	/
NT-proBNP, μg/L	0–125	4,480^h	4,710^h	156^h	123^h	53^h	20^h	932^h
		149^L	496^L	80^L	51^L	<20^L	20^L	<20^L
DD-dimer (ng/mL)	0–243	1,087^h	491^h	2,093^h	284^h	109^h	61^h	423^h
		208^L	121^L	40^L	89^L	57^L	23^L	252^L
Arterial oxygen saturation	0.93–0.98	0.622^L	0.89^L	0.981^L	0.952^L	0.982^L	0.92^L	0.959^L
		0.988^h	1.003^h	1.001^h	0.999^h	1.005^h	0.989^h	0.994^h
Revised arterial oxygen partial pressures	83-108	39.6^L	56.7^L	87.1^L	38.6^L	101^L	87.2^L	77.20^L
Creatinine, μmol/L	41-81	89.4^h	75.2^h	71.5^h	105^h	81^h	75.6^h	106^h
Treatment before discharge								
Antiviral therapy		Y	Y	Y	Y	Y	Y	Y
Antibiotic therapy		Y	Y	Y	Y	Y	N	Y
Intensive immunotherapy		Y	Y	Y	Y	Y	Y	Y
Hydroxychloroquine		N	N	Y	Y	Y	N	Y
Use of corticosteroid		Y	N	N	N	N	N	Y
Nasal cannula oxygen		Y	Y	N	Y	Y	N	Y
Non-invasive ventilation or high-flow nasal cannula oxygen		Y	Y	N	N	N	N	N

Table 1 (*continued*)

Table 1 (*continued*)

Characteristics	Cases						
	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
CMR findings							
LV function							
ED Mass/BSA (g/m^2)	56.19	93.61	52.97	52.46	41.75	60.02	56.34
EDV/BSA (mL/m^2)	42.28	97.61	66.45	88.54	68.24	74.97	61.38
ESV/BSA (mL/m^2)	14.07	48.75	39.1	36.7	25.17	29.19	21.83
SV/BSA (mL/m^2)	28.21	48.86	27.35	51.84	43.08	45.78	39.55
CI (L/min/m^2)	2.48	3.18	1.64	2.64	3.88	3.25	3.01
LVEF, %	75.92	50.05	41.15	58.55	63.12	61.06	64.44
RV function							
EDV/BSA (mL/m^2)	55.66	38.56	60.79	70.44	61.78	81.4	64.51
ESV/BSA (mL/m^2)	17.43	15.8	34.03	33.87	30	41.46	32.14
SV/BSA (mL/m^2)	38.23	22.77	26.77	36.57	31.78	39.94	32.37
RVEF	68.68	59.04	44.03	51.91	51.44	49.06	50.18
CI (L/min/m^2)	3.62	1.48	1.61	1.8	2.86	2.91	2.46
LGE (%)	2.96	8.78	5.23	4.51	0.61	0.84	0
Ischemic	Y	Y	N	N	N	N	/
Nonischemic	Y	N	Y	Y	Y	Y	/
Edema	N	Y	N	N	N	N	N
Pericardial	N	N	N	N	N	N	N
Pericardial effusion	N	N	N	N	N	N	N

Coronavirus-2 (SARS-CoV-2) infection (*Figure 1*); Case 2: CAD, chronic total occlusion (CTO) of LAD and LCX, ischemic cardiomyopathy, left ventricular aneurysm, CAD induced ischemic myocardial injury under the condition of ischemia and hypoxia of COVID-19 (*Figure 2*); Case 3, 4, 5, 6: myocarditis caused by SARS-CoV-2 infection (*Figure 3*); CMR of Case 7 was negative.

Most studies of cardiovascular imaging in recovered COVID-19 patients used CMR only (3,5-7), myocardial edema, fibrosis, and impaired ventricular function are common, however the cause were not discussed by direct imaging evidence. We performed CMR and CCTA on patients 1 and 2 simultaneously, which make it possible to find out the cause. Our results show myocardial injury of COVID-19 patients persistent until early convalescent stage, and maybe caused by multiple factors, including myocarditis, ischemic injury caused by the condition of ischemia and hypoxia of COVID-19, they may occur at the same time and serious injury was more likely to occur in patients with a history of cardiovascular disease. Cardiovascular imaging examination including CMR and CCTA are helpful to confirm it and find out the cause.

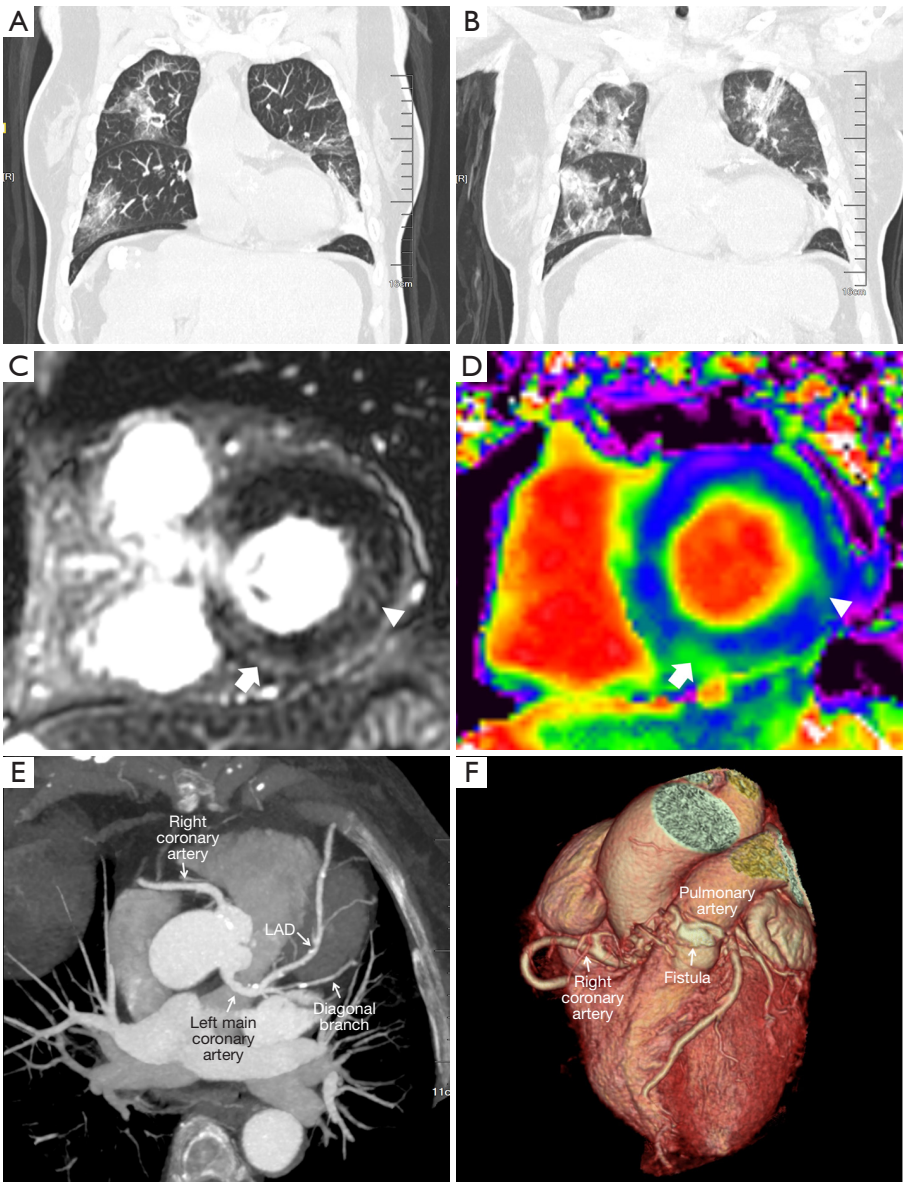

Figure 1 Images of Case 1: she was a 75-year-old female with a history of hypertension for 30 years and exposure to SARS-CoV-2 presented with one week of headache and 4 hours of fever to the infection department. A chest CT obtained on the day of admission showed bilateral lung consolidation with relative peripheral sparing (A), and showed rapid expansion 4 days later (B). C-reactive protein (CRP) got the peak on day 5 (127.5 mg/L, normal value 0.068–8.2 mg/L),with high-sensitivity cardiac troponin I (TnI) serum level increasing (0.15 μg/L, normal value <0.0229 μg/L) and brain natriuretic peptide (BNP) getting 1,930 pg/mL meantime (normal value <125 pg/mL), patient's blood pressure was 150/75 mmHg, heart rate was 85 bpm on the day, creatine kinase isoenzyme (CK-MB) was always normal while hospitalized, bedside echocardiography on day 6 demonstrated left atrium dilated with diastolic and systolic dysfunction (left ventricular ejection fraction, LVEF is 57%). The initial ECG on day 33 showed sinus tachycardia at 101 bpm, T wave inverted or flat was shown in III, aVF, V7-V9. CMR on day 61 demonstrated: (i) hypertrophy of left ventricular wall (C), with history of hypertension, suggested hypertensive cardiomyopathy. (ii) endocardial enhancement of left ventricular basal lateral wall (C, white triangle) without edema and thinning, whereas ECV was a little bit higher (35.2%) (D, white triangle) than other segments (23.1%) D, suggested subacute myocardial infarction, and (iii) epicardial enhancement of left ventricular basal inferior wall (C, white arrow) whereas ECV was a little bit higher (36.4%) (D, white arrow) than other segments (23.1%) (D), suggested myocarditis. CCTA on day 83 demonstrated showed multiple atherosclerotic plaque on LAD and diagonal branch (E), and a fistula between RCA and pulmonary artery (F).

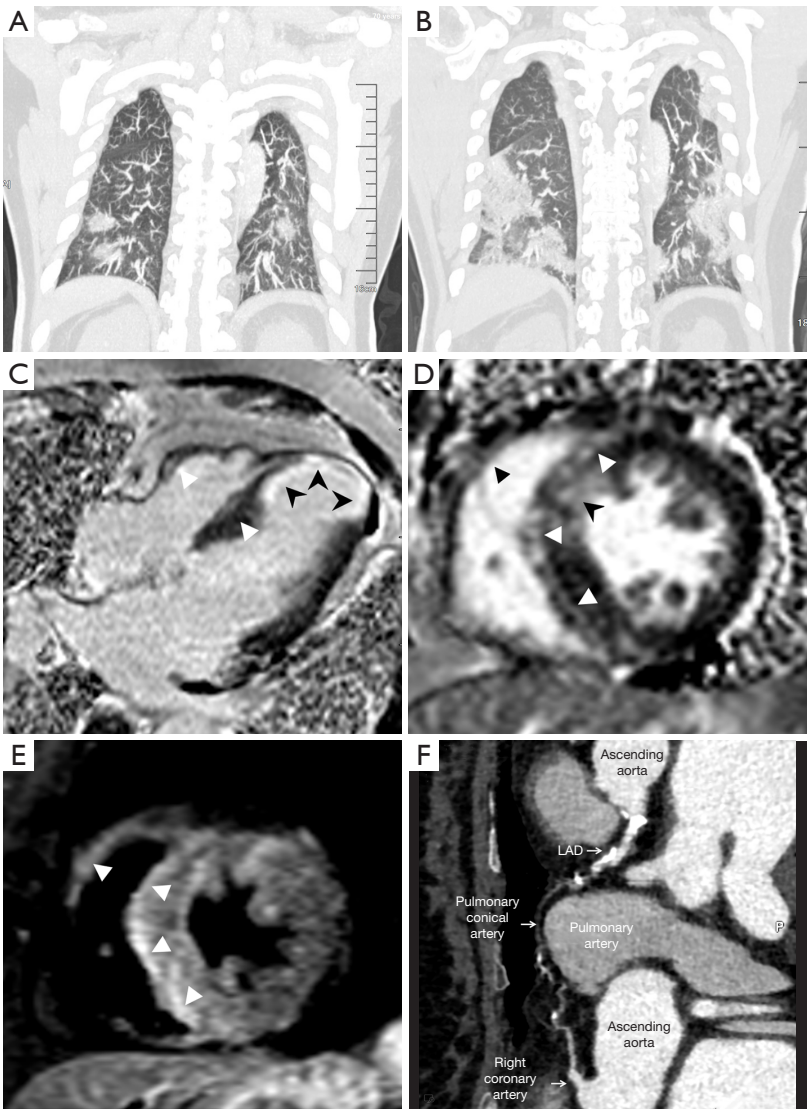

Figure 2 Images of Case 2: she was a 70-year-old female with a history of hypertension, hyperlipidemia, stent implantation of basilar artery, and exposure to SARS-CoV-2 presented with 4 days of fever to the infection department. High-sensitivity cardiac TnI serum level increased the admission day (0.056 μg/L, normal value <0.0229 μg/L), and decreased to normal 3 days later, while BNP was always abnormal (value on day 1 was 496 pg/mL, maximum value 4,710 pg/mL, normal value <125 pg/mL). Chest CT obtained on the day of admission showed bilateral lung consolidation with relative peripheral sparing (A), and showed rapid expansion on day 5 (B), and oxygenation index decreased sharply on the day as 85.6 mmHg with BNP sharp increasing to 3,900 pg/mL. CRP increased repeatedly (value on day 1 was 10.90 mg/L, maximum value 45.79 mg/L, normal value 0.068–8.2 mg/L), CK-MB and BP were always normal while hospitalized. She denied chest pain, tightness, palpitation for symptom and history. Bedside echocardiography on day 10 demonstrated LV dilated with motion reduced of apical wall, calcification of posterior sub valvular, mild reflux of mitral valve, and diastolic dysfunction (LVEF, 65%, M-mode). CMR on day 58 demonstrated decreased LVEF (50.05%), focal thinning, obvious enhancement and reverse motion of apical anterior, septal and lateral wall of LV (C, black arrowheads), suggested chronic myocardial infarction and ventricular aneurysm formed. Images of short TI inversion recovery sequence showed widely high signal of right ventricle wall and septum (E, white triangles), and there was linear enhancement of septum besides right ventricle and right ventricle wall (C,D, triangles), suggested latest myocardial injury include necrosis and edema. Enhancement of septal wall besides left ventricle without edema (D, black arrowheads) suggest chronic myocardial necrosis. CCTA on day 76 showed chronic total occlusion of proximal LAD and mid LCX, and collateral circulation were formed between LAD and RCA through pulmonary conical artery (F).

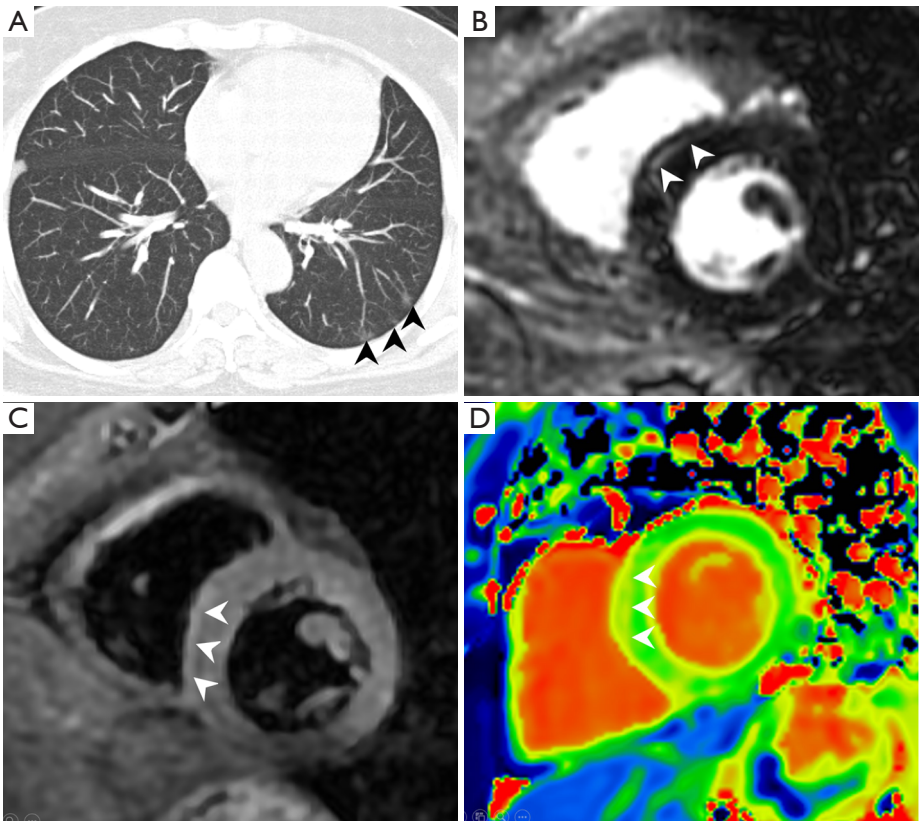

Figure 3 Images of Case 3 She was a 59-year-old female with exposure to SARS-CoV-2 and positive of virus nucleic acid test presented with slight cough three days before to the infection department. A chest CT obtained on the next day of admission showed slightly exudation on the posterior and lateral basal segments of left lower lobe (A, black arrowheads), which absorbed obviously after 5 days. CK-MB transitorily increased on day 4. BNP increased slightly twice on days 2 and 6 (156 and 140 pg/mL, normal value <125 pg/mL). TnI, CRP, OS and BP were always normal while hospitalized. The ECG on day 7 showed normal sinus rhythm at 67 bpm. She felt palpitation and chest tightness after discharge. CMR on day 27 demonstrated decreased LVEF (41.15%), linear enhancement (B, white arrowheads) and edema (C, white arrowheads) of septum besides right ventricle, whereas T1 value increased (D, white arrowheads) suggest latest myocardial injure include necrosis and edema.

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Footnote

Provenance and Peer Review: This article was a standard submission to the journal. The article has undergone external peer review.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/jxym-21-23). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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