Added Value of Multi-slice CT Scan (320 Slice) in Evaluation of Cardiac Complications Post COVID-19 Infection

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Original Research Article

ABSTRACT

Background: The COVID-19 pandemic had affected population health throughout the world. Few studies had focused on post-COVID19 complications detection using multi-slice CT scans. Our trial aimed to assess the value of cardiac CT utility during the COVID-19 pandemic for the detection of cardiac complications and correlation with the severity scoring system for chest manifestations. Since the beginning of COVID-19 outbreak, cardiac computed tomography (CT) had a sudden increased value and use with a huge reduction in face-to-face patient care and elective diagnostic testing. This study started from May 2021 to April 2022 in a single cardiac CT centre. This prospective cohort trial was conducted on 40 patients proved to have COVID-19 infection by positive RT-PCR test for COVID-19 and/or CT chest manifestations. CT results were reviewed and compared to echocardiography and/or catheterization data.
Results: In the CT severity score, the more severe score for COVID-19 infection was noted in cases with coronary artery occlusion and pulmonary embolic diseases. Meanwhile, the mild and moderate severity score groups developed myocarditis, pericarditis, and dilated cardiomyopathy, respectively, with statically significant differences with p-value= 0.007 for coronary artery disease (CAD) and 0.026 for pulmonary embolism. The significance of echocardiography examination was noted in cases with pericarditis and dilated cardiomyopathy, with p-value= 0.018 for pericarditis and 0.01 for dilated cardiomyopathy.

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Conclusions: MSCT is a very useful technique to for patients presenting with suspected post-COVID cardiac complications, in addition to severity scoring of chest involvement, also providing its correlation with the occurrence of cardiac complications.

ABBREVIATIONS

CT   : Computed Tomography
COVID-19 : Corona Virus Disease 2019
SARS   : Severe Acute Respiratory Syndrome
CORAD   : COVID-19 Reporting and Data System
MSCT   : Multi-Slice Computer Tomography
PCR   : Polymerase Chain Reaction
CMR   : Cardiac Magnetic Resonance Imaging

1. INTRODUCTION

The novel coronavirus disease (COVID-19) pandemic caused by SARS-CoV-2, represents a public health emergency, causing a significant morbidity and mortality worldwide [1]. It was reported first in Hubei province, Wuhan, China, on 8 December 2019 [2]. COVID-19 essentially affects the lungs resulting in severe acute respiratory distress syndrome and affects other organs as well such as the cardiovascular system [3]. There is much overlap between both primary cardiac symptoms of COVID-19 disease including arrhythmias, myocarditis, and Acute Coronary Syndrome (ACS), and secondary cardiac involvement, which is usually due to systemic inflammatory response as congestive heart failure and acute myocardial injury [4]. The incidence of ACS increases in cases of viral infection with a 3-to-10-fold higher risk, usually due to inflammatory-mediated plaque destabilization [5]. The potential mechanisms of cardiac injury are usually the immune-mediated cytokine release syndrome, direct viral toxicity in host cells, and myocyte injury from hypoxia [6]. Since the beginning of COVID-19 outbreak, cardiac computed tomography (CT) had a sudden increased value and use with a huge reduction in face-to-face patient care and elective diagnostic testing [7,8]. The main objective of our study is a prospective detection of post-COVID-19 infection cardiac complications and correlation with CT chest severity scoring system aiming for more caring and early diagnosis of COVID-19 cardiac complications by CT rather than MRI to decrease time contact in examination and reduced financial burden

2. PATIENTS AND METHODS

2.1 Study Design, Setting

This prospective cohort study was carried out on 40 patients proved to have COVID-19 infection by positive RT-PCR test for SARS-COV2 with suspected cardiac complications clinically as acute angina pain, heart failure, arrhythmia.

Inclusion criteria: The trial included infected cases above 25 years with COVID-19 who referred with echocardiographic changes or suspected cardiac complications clinically.

Exclusion criteria: Pregnant females and patients under 25 years old were excluded from this trial due to radiations hazards from CT, as well as cases with an allergy to contrast media, impaired renal functions, previous cardiac disease, or previous cardiac CT or echocardiography changes were excluded.

All patients were subjected to full history taking, complete clinical cardiac assessment, PCR assay using a nasopharyngeal swab, and radiological evaluation by MSCT, specific patients' preparation was performed in the form of fasting 4-6 hr., avoid caffeine products 12 hours before the examination, blood pressure and pulse were measured, all procedure details were explained to the patient before scanning with written informed consent. A cannula was inserted in the right antecubital vein of sufficient size (≥18G) to allow for the needed high flow rate (4–5 mL/sec). To avoid problematic elevated heart rate, we ensured that the patient understood that there would be noise and a warm sensation during the scanning, β-blocker was used if indicated. Metallic items were removed as coins, etc. ECG gated technique was performed on 320 multi-slice CT scanners, Aquilion one, and Canon Medical Systems. Scans were done in the supine position. The field of view was adjusted. Automatic tube current modulation was done. Skin preparation with alcohol, ECG electrodes were placed on the chest wall, and the ECG trace was examined to

confirm that the R wave had a good amplitude. Breath-holding test was performed to avoid respiratory motion artifact. The intravenous (IV) line was placed, and a saline test injection was given to confirm that the IV line was working properly and that there was no extravasation. Following that, a scout was taken, with the scan extending from Carina to below the heart. Scan extent is ideally determined by calcium scoring, just below tracheal bifurcation to below the heart with scan direction cranio-caudal. Bolus tracking with a pre-monitoring scan at the mid-heart level and region of interest (ROI) at descending aorta. Injection of non-ionic contrast medium (Ultravist 370, Schering AG, Germany or Omnipaque 350, Nycomed, Amersham) through the peripherally inserted cannula with a dose of 2ml/kg with a high flow rate 5ml/sec or more. Repetitive low dose monitoring examination with parameters as follows; (120 KV, 50 mAs, 0.5 second scanning time), when the trigger threshold was reached (120HU), the scan started immediately after breath holding command. Scanning CT parameters adjusted to patient's body habitus, using single phase retrospective ECG gated computed tomography angiography (CTA) volume scan with rotation time 0.35s and tube voltage 120kv, which increased to 135kv in obese patients. In patients who referred with suspected to have pulmonary embolism as elevated D Dimer levels of more than 500 ng/ml, a triple rule-out protocol of imaging was done to examine both Coronary Artery Disease (CAD) as well as to assess pulmonary vessels, biphasic injection technique was used; 80 ml of undiluted contrast material was injected (ultravist 370 ml) was injected at 5 ml/s, followed by 25 ml of the same contrast diluted with 25 ml saline at 5 ml/s. Bolus tracking in the first injection phase at coronary arteries while in the second phase at pulmonary arteries, scan acquisition began from the clavicle's head inferior margin to the base of the heart. Images were examined in axial cuts and curved multi-planner reconstruction was performed using of a viewing console. After each examination, disinfection was done with alcohol 70%. The dataset was anonymized and exported to a dedicated segmentation suite. CT images were reviewed on the workstation by senior professional consultants with 10, 14 years of experience each. For disagreement between the primary interpretations, a cardiac imaging professor with 21 years of experience adjudicated a final decision.

Curved MPR were used for curved vasculature and for optimal qualitative and quantitative analysis of coronary stenosis and plaques.

Protective measures for healthcare providers and staff: All healthcare professionals were protected from infection and transmission to other colleagues and cases to maintain continuous medical service to the patients in need.

Personal Protective Equipment (PPE) was mandatory to maintain a safe patient service onsite. PPE included multiple types of masks ranging from simple surgical masks for general staff to highly protective masks for healthcare providers with direct contact with COVID-19 cases, as well as protective gowns and face shields.

Access routes to CT scan unit were highlighted to transport services and clinicians and clearly indicated to non-radiology staff. Normal patient pathways were separated from waiting areas.

Equipment disinfection: Disinfection of the CT unit after each patient was performed according to local guidelines by a solution of 70% ethanol, 0.5% hydrogen peroxide, or 0.2% sodium hypochlorite within 1 min of contamination.

2.2 Statistical Analysis

This study's statistical analysis was done using SPSS V.28. Chi-square test or Fisher's exact test was used to analyse qualitative data given as numbers and percentages. Quantitative data was provided as mean and standard derivation. A two-tailed P value < 0.05 was deemed statistically significant.

3. RESULTS

A total of 40 patients with COVID-19 infection, above 25 years old, were included in this study, with male to female ratio: of 65% to 35%. The patient's ages ranged from 25-65 years old, with a mean age of 41.650 ± 10.678 SD. Their age was divided into four groups, with the highest numbers was noted at group > 35–45-year-old, represented by 8 cases (40% of the studied cases), while the lowest number was noted in the elder group >55-65 years old that was represented by only 2 cases, as shown in (Table 1).

Table 1. Sociodemographic data of the studied patients (N=40)

Criteria		N=40 (%)
Sex	Male	26 (65%)
	Female	14 (35%)
Age	Mean± SD 41.650 ± 10.678 years	
Occupation	Healthcare provider	18 (45%)
	Teacher	14 (35%)
	Worker	4 (10%)
	Housewife	4 (10%)
Comorbidities	Diabetic	2 (5%)
	Hyperlipidemia	2 (5%)
	Smoking	2 (5%)

Regarding the clinical cardiac findings of the studied cases (as shown in Table 2), 50% of patients had sinus tachycardia as ECG changes, while the lowest number, 5% had a T wave. Out of the studied 40 patients, 4 cases died and 36 survived patients, 80% of them didn't develop any associated non-cardiac complications, but 10% developed cerebral infarctions as well as 10% developed deep venous thrombosis, 75% of survived cases underwent echocardiography, meanwhile 8 cases underwent cardiac catheterization in the cardiology department. Moreover. 5 cases had associated cerebral stroke, and 7 patients had deep venous thrombosis.

Out of 30 patients who underwent echocardiography, (21.4%) of them showed basal wall dyskinesia, and systolic dysfunction with an ejection fraction of less than 50% was noted in 14.2% of patients.

Table 2. Shows clinical, ECG, echocardiographic changes in the studied cases

ECG changes (N=40)	Sinus tachycardia		N (%)
			20 (50%)
	High T wave		2 (5%)
	ST segment elevation		8 (20%)
	Non-ST segment elevation		10 (25%)
Echo (N=30)	Wall motion abnormality	Anterior wall dyskinesia	2 (7.14%)
		inferolateral wall dyskinesia	4 (14.2%)
		Septal dyskinesia	0 (0%)
		Inferior wall dyskinesia	2 (7.14%)
		Basal wall dyskinesia	6 (21.4%)
	Systolic dysfunction	EF >50%,	4 (14.2%)
		EF 40-50%	2 (7.14%)
		EF 30-40	2 (7.14%)
		EF < 30%	0 (0%)
	Pericardial effusion	Rim	6 (21.4%)
		Mild	2 (7.14%)
Complications	Coronary artery disease		10 (25%)
	Pericarditis		6 (15%)
	Myocardial inflammation		6 (15%)
	Pulmonary embolism		10 (25%)
	Dilated Cardiomyopathy		8 (20%)
Other complications		Cerebral infarction	5 (12.5%)
		DVT	7 (17.5%)
Outcome	1)Survived		36 (90%)
	*Echocardiography		30 (75%)
	*Catheter Angiography		8 (20%)
	2)Dead		4 (10%)

Table 3. Correlation between the occupation, risk factors, and occurrence of post-COVID-19 Cardiac complications

	*Occupation				P-value
	Health care Providers (N=18)	**Teachers (N=14)**	**Housewives (N=4)**	**Workers (N=4)**	
Coronary artery disease	6 (33.3%)	0 (0%)	4 (100%)	0 (0%)	0.041*
Pericarditis	0 (0%)	4 (28.6%)	0 (0%)	2 (50%)	0.192
Myocardial inflammation	2 (11.1%)	4 (28.6%)	0 (0%)	0 (0%)	0.77
Pulmonary embolism	8 (44.4%)	2 (14.3%)	0 (0%)	0 (0%)	0.39
Dilated cardiomyopathy	2 (11.1%)	4 (28.6%)	0 (0%)	2 (50%)	0.51
*Risk Factors					
	Diabetes	**Hyperlipidemia**	**Smoking**	**No risk Factors**	
Coronary artery disease	0 (0%)	2 (20%)	2 (20%)	6 (60%)	0.14
Pericarditis	0 (0%)	0 (0%)	0 (0%)	6 (100%)	1
Myocardial inflammation	0 (0%)	0 (0%)	0 (0%)	6 (100%)	1
Pulmonary embolism	2 (20%)	0 (0%)	0 (0%)	8 (80%)	0.6
Dilated cardiomyopathy	0 (0%)	0 (0%)	0 (0%)	8 (100%)	0.51

Significant as P value <0.05

Table 4. Correlation between the occurrence of cardiac complications and vaccination, CT severity score, and echocardiography findings

	*Vaccination			P-value
	More than one month (N=10)	**Less than one month (N=12)**	**Not vaccinated (N=18)**	
Coronary artery disease	0 (0%)	8 (66.7%)	2 (11.1%)	0.027*
Pericarditis	4 (40%)	0 (0%)	2 (11.1%)	0.29
Myocardial inflammation	4(40%)	0 (0%)	2 (11.1%)	0.29
Pulmonary embolism	0 (0%)	0 (0%)	10 (55.6%)	0.018*
Dilated cardiomyopathy	2 (20%)	4 (33.3%)	2 (11.1%)	0.77
	*CT severity score			
	Mild (N=14)	**Moderate (N=8)**	**Severe (N=14)**	
Coronary artery disease	0 (0%)	0 (0%)	10 (71.4%)	0.007*
Pericarditis	4 (28.6%)	0 (0%)	0 (0%)	0.31
Myocardial inflammation	4 (28.6%)	2 (25%)	0 (0%)	0.4
Pulmonary embolism	0 (0%)	6 (75%)	4 (28.6%)	0.026*
Dilated cardiomyopathy	6 (42.9%)	0 (0%)	0 (0%)	0.91
	*Echocardiography (N=30)			
	Pericardial Effusion (N=8)	**Systolic Dysfunction (N=8)**	**Wall motion Abnormality (N=14)**	
Coronary artery disease	0 (0%)	0 (0%)	6 (100%)	0.2
Pericarditis	6 (100%)	0 (0%)	0 (0%)	0.018*
Myocardial inflammation	0 (0%)	0 (0%)	6 (100%)	0.2
Pulmonary embolism	2 (50%)	0 (0%)	2 (50%)	1
Dilated cardiomyopathy	0 (0%)	8 (100%)	0 (0%)	0.01*

*Significant as P value <0.05

Table 3 shows a correlation between patients' occupation and the occurrence of cardiac complications developed; as in healthcare providers and teachers groups who were exposed to a large number of population with high viral load by different viral strains and long-time contact with infected patients, who were liable more to develop coronary artery thrombosis and pulmonary embolism, rather than the other less exposed groups as housewives and workers, with statistically significant difference p-value = 0.041 for CAD. In addition to a correlation between risk factors and developed cardiac complications, with no statistically significant difference.

Concerning COVID vaccination, a correlation was done, which revealed that people who were not vaccinated or vaccinated in a period less than one month were more prone to complications than those who were not vaccinated in a period of more than one month, statically significant difference was detected, $p= 0.027^*$ for CAD and 0.018^* for pulmonary embolism. The more severe CT score for COVID-19 infection was noted in cases with coronary artery occlusion and pulmonary embolic diseases. Meanwhile, the mild and moderate severity score groups developed myocarditis, pericarditis, and dilated cardiomyopathy, respectively, with statically significant differences with p-value= 0.007^* for CAD and 0.026^* for pulmonary embolism. The significance of echocardiography examination was noted in cases with pericarditis and dilated cardiomyopathy. Meanwhile no significant difference in patients who developed CAD and pulmonary embolism, as seen in Table 4.
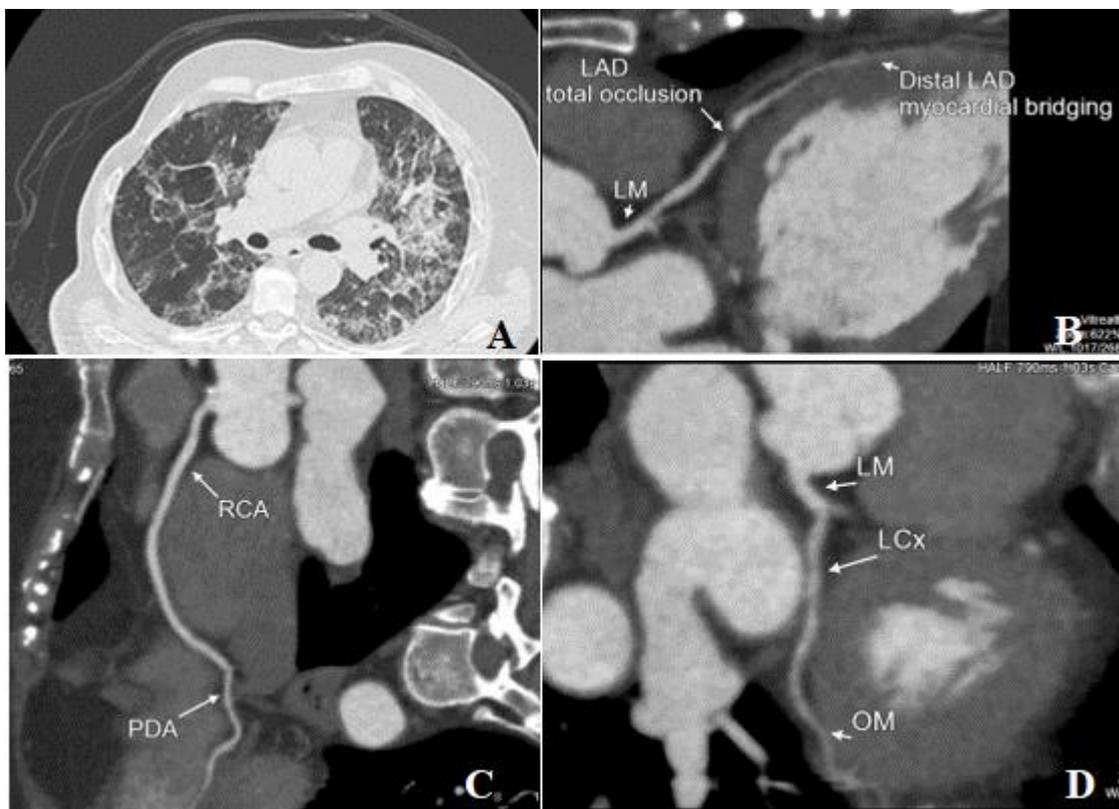
Cases:

Fig. 1. Female patient aged 40 years old, with CT chest findings (CORAD-5) and severity score = 23; a few days later, she developed chest pain and dyspnoea symptoms. A) Axial CT chest (lung window) showing multiple patches of ground glass opacities with subpleural fibrotic bands (B) curved MPR 2D image reveals soft concentric plaque at mid-segment of LAD opposite D2 (the second diagonal branch) take off, exerting total LAD occlusion, (C, D) curved MPR show free RCA, LM & Lcx. The diagnosis was Focal mid-segment LAD total occlusion
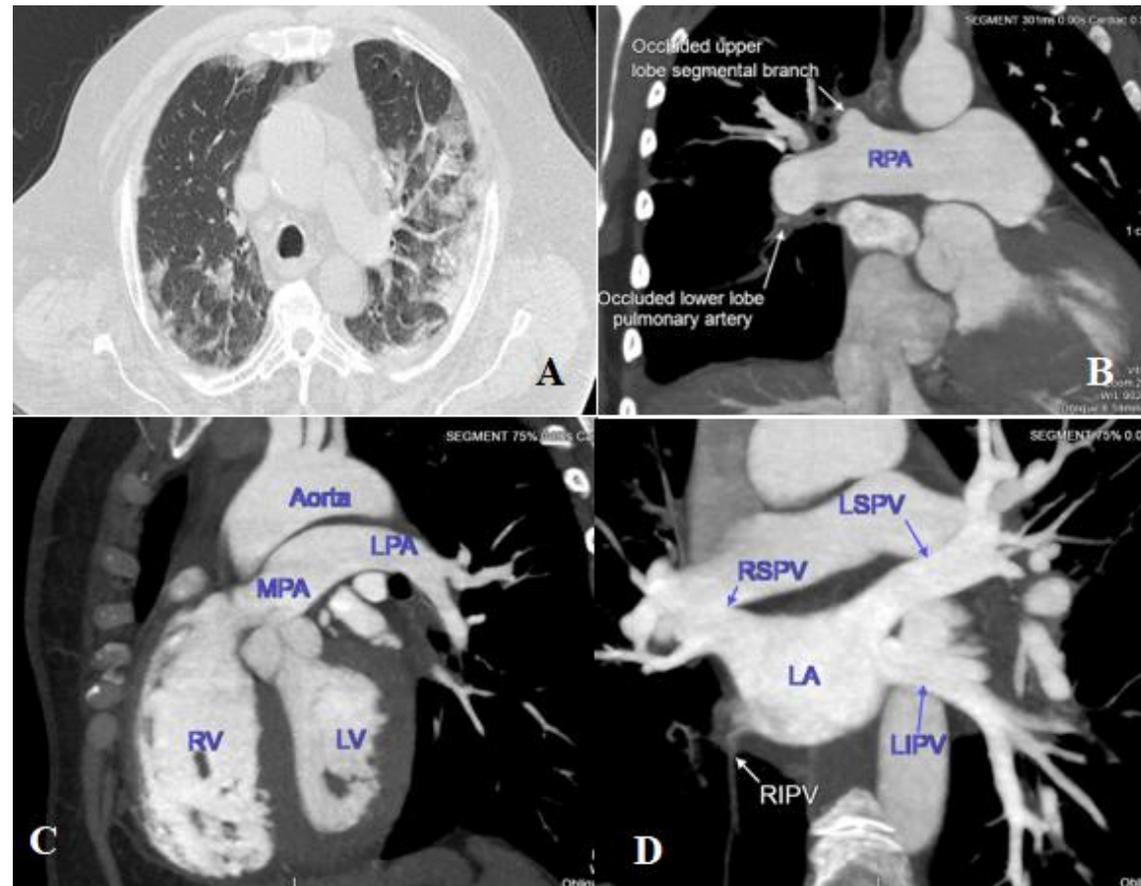
Fig. 2. Female patient aged 35 years with CT chest findings (CORAD 5) and severity score = 22; after 10 days, the patient is complaining from chest pain and dyspnoea. D-dimer test was 700 ng/ml A) CT of the chest shows bilateral peripheral patches of ground glass opacities with bilateral areas of subsegmental consolidation of subpleural distribution, interstitial thickening and fibrotic bands with severity score 22, B) Maximum intensity projection (MIP) image showing occluded lower lobar and upper lobar segmental branches of the right pulmonary artery, C) MIP image showing Totally occluded lateral basal segmental branch of left lower lobe pulmonary artery, D) MIP image showing Occluded right inferior pulmonary vein. Diagnosis: Bilateral pulmonary arterial emboli at lobar, segmental, subsegmental levels and occluded right inferior pulmonary vein

Fig. 3. Male patient aged 47 years old presented with cough and fever, CT chest findings (CORAD-5) with severity score =21; five days later, the patient experienced a severe attack of retrosternal chest pain and palpitation, Cardiac troponin level=24μg/L. A) Axial CT of the chest demonstrating bilateral peripheral patches of ground glass opacities with tree in bud appearance, more in the left side, mild bronchial dilatation B) Hypodense myocardial edema (yellow arrows) is shown on CT scan, C) late image acquisition after 5 minutes with no areas of appreciable enhancement, D,E) Curved MPR image demonstrating patent RCA, PDA, LM, and LCx. F) Curved MPR image demonstrating patent LAD with myocardial bridging, G) Complementary cardiac MRI image showing late gadolinium contrast enhancement. The diagnosis was myocarditis

4. DISCUSSION

The current study evaluated different cardiac complications post-COVID-19 infection by doing CT coronary protocol and triple rule-out protocol in cases with suspected pulmonary embolism to assess the patency of pulmonary vessels side by side with CAD and also to assess other complications like myocarditis, pericarditis and cardiomyopathy in the absence of ischemic coronary disease this is in agreement with Catapano F et al. [9] who described cardiovascular complications among COVID-19 cases such as myocarditis, ACS, arrythmia, pericarditis, and venous thromboembolic events.

In this study, the impact of patient's occupation on the development of complications that was more pronounced in healthcare providers and teachers groups who were exposed to high viral load by different viral strains and long-time contact with infected patients, who were liable more to develop coronary artery thrombosis and pulmonary embolism, rather than the other less exposed patients with statistically significant difference p-value= 0.041* for CAD, this matches the findings of Temel S et al. and Wang D et al.

[10,11] who described a large number of inpatients and healthcare workers were exposed to COVID-19 in hospitals.

As regards previous cardiac diseases in the current study, only 5% of cases described previous attacks of chest pain prior to COVID-19 infection. This doesn't go with Catapano et al. [9], who described the overall percentage of pre-existing cardiovascular disease in COVID-19 cases was 24–48% and this may be due to a limited number of patients included in the current study.

Regarding the laboratory investigations; D-Dimer evaluation ranged from 303-1175 ng/ml and mean 838.800 ± 219.73 with higher levels were detected in between patients with pulmonary arterial occlusion and coronary ischemia, which is in line with Zhou F et al. [12] who reported that elevated coagulation activity, expressed by higher levels of D-dimer, could induce thrombosis and ischemia.

Cardiac troponin levels ranged from 0.01-24 with mean ± SD= 3.217±6.769, with the highest group number was ⩾1 ug/L. This goes with Huang et al. [13], who reported Evidence of myocardial injury, such as an increase in high-sensitivity cardiac troponin I levels (>28 pg/mL) was detected in 5 of the first 41 patients diagnosed with COVID-19 in Wuhan.

Findings of Echocardiography among the patient who did the examination, wall motion abnormality, systolic dysfunction, pericardial effusion were noted in 49.94%, 28.4% and 28.54%, respectively, as reported by the European society of cardiology (ESC) [14] which described the echocardiographic findings in-between cases with cardiac injury post-COVID-19 as global or regional myocardial systolic dysfunction with or without a pericardial effusion and vice versa.

Findings of ECG were variable including 50% of them had sinus tachycardia and 5% had high T wave, those with ST-segment elevation of 20% and non-segment elevation of 25% in agreement with ESC [14] which reported ECG In MERS-CoV, the 12-lead ECG generally shows diffuse T wave inversion where there is myocardial involvement and other dynamic changes.

The complications detected in the current study post-COVID-19 infection as follows; CAD 25%, pulmonary embolism 25%, Dilated cardiomyopathy 20%, and the least number developed myocarditis, pericarditis, each one= 15% of patients, this is consistent with the findings that were described by Catapano F et al. [9].

In this study, 4 out of 40 cases developed severe chest pain, with abnormal ECG findings and elevated levels of cardiac troponin after infection with CT coronary showed pleural effusion and haziness of underlying myocardium and absence of obstructive coronary lesions, with the final diagnosis of myopericarditis based on the clinical and echocardiographic correlation with CT findings. On the other side, Inciardi et al. [15] used cardiovascular magnetic resonance imaging (CMR) which showed marked biventricular myocardial interstitial edema and diffuse transmural late gadolinium enhancement with circumferential pericardial effusion in addition to urgent invasive coronary angiography with no evidence of obstructive coronary disease.

with whom reported that late gadolinium contrast enhancement seems to be less-frequently observed in cases with post-COVID-19 myocarditis, reflecting a limited myocyte necrosis at least in the acute phase, and highlighting the key role of the new Lake Louise Criteria in the diagnosis of myocarditis.

In the current study, 25% of cases were presented by high D-Dimer levels with severe dyspnea and chest pain, with CT findings consistent with PE. Which in line with Sauer F et al. [16], Cundari G et al. [17], who reported that thromboembolic disease represents another piece in the mosaic of SARS-CoV-2 infection, which is commonly seen in COVID-19 along with elevated D-dimer levels.

In this study, 20% of patients were diagnosed as dilated cardiomyopathy on the basis of echocardiographic findings of systolic dysfunction and left ventricular dilation in the absence of CAD. This goes with Chen N et al. [18], Beitzke D et al. [19] findings that non-gated low-dose CT can also be helpful in cardiac abnormalities detection. While GUO T et al. [20] reported that coronary CTA provides insights into lung structure and pathologies in COVID-19 cases, which is more relevant in cases with moderate to severe respiratory symptoms or to scan for complications, but does not include all lung fields, the current study added that severity scoring for patients with mild severity = 38.88%, and those consistent with moderate severity =

22.22%, while the percentage consistent with severe scoring= 38.88% of the studied cases.

Moreover, the correlation between the severity scoring system and the development of complications was detected. A more severe score for COVID-19 infection was noted in cases with coronary artery occlusion and pulmonary embolic diseases. Meanwhile, the mild and moderate severity score groups developed myocarditis, pericarditis, and dilated cardiomyopathy, respectively, statically significant differences and in agreement with Shi s et al. [21], who reported a more severe respiratory disease in cases with cardiac injury.

5. LIMITATIONS

This is a prospective trial, so some cases did perform additional comparative tests to verify the result of most coronary CTA, and we were able to verify the result of severe cases only compared to cardiac catheterization results and patients with myocarditis we were able to do CMR to a limited number of them to confirm the diagnosis due to the fact that MRI examination carries more risk infection than CT examination due to long time needed, unavailability in some of the quarantine centres, more financial burden, as well as the limited number of patients included in our study. Also, inability to perform late iodine contrast sequences for the majority of patients due to the risk of more radiation overdose in immunocompromised patients, and overuse of x-ray tubes in the era of COVID-19.

6. RECOMMENDATIONS

For future research, we recommend including a larger sample size, over longer periods of time and multi-centric to compare different viral strains globally, and financial support to include CMR for all patients as a comparative imaging modality.

7. CONCLUSION

Multi-slice CT is a very valuable and mandatory modality in patients with suspected post-COVID cardiac complications. In addition to severity scoring of chest involvement, it also provides their correlation to their occurrence with less time of patient contact and less financial burden than CMR, as well as more superior than echocardiography in the assessment of coronary artery thrombosis and pulmonary embolism as complications for COVID-19 which is also a

bedside modality with more patient contact and is operator dependent.

ETHICAL APPROVAL AND CONSENT

The trial was done after approval from the Ethical Committee (Approval code: 34478/2/21). An informed written consent was obtained from the cases. The study started from May 2021 to April 2022

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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