Early Outcomes of the Surgical Treatment of Non-traumatic Massive Pericardial Effusion in the University of the Philippines -Philippine General Hospital COVID-19 Referral Center

Eduardo R. Bautista, MD, Ace Robert B. Alfabeto, MD, Adrian E. Manapat, MD, Racel Ireneo Luis C. Querol, MD and Carlo Martin H. Garcia, MD

Division of Thoracic, Cardiac and Vascular Surgery, Department of Surgery, College of Medicine and Philippine General Hospital, University of the Philippines Manila

ABSTRACT

Objective. To describe the treatment outcomes of patients who underwent tube pericardiostomy for all etiologies of non-traumatic massive pericardial effusion or tamponade during the COVID-19 pandemic and determine the association between patient profile and treatment outcomes.

Methods. Data were obtained from patients with massive pericardial effusion or cardiac tamponade who underwent surgical drainage from January 1, 2020, to September 1, 2022, in the University of the Philippines – Philippine General Hospital (UP-PGH). These patients' demographic and clinical profiles, and treatment outcomes were evaluated using frequencies and percentages. Chi-squared and Fisher's tests determined the differences between COVID (+) and (-) groups. Odds Ratio was used to assess the risk of complications and mortality.

Results. The study population comprised 90 patients with a mean age of 45 years. 54.4% were females. Fifteen (16.67%) were COVID-19 (+) and 75 (83.33%) were COVID-19 (-). Most of the patients were of O+ blood type (34.4%), with no smoking history (67.8%) and no COVID-19 vaccination (76.7%). Common comorbidities were cancer (70%), tuberculosis infection (32.2%), and hypertension (25.6%). No significant difference was found between the two study groups. The presentation was subacute (one week to three months) (62.2%), with the most common symptoms of dyspnea (81.1%), orthopnea (61.1%), and cough (52.2%). Tachycardia (80%) and tachypnea (57.8%) were the most common presenting signs. Hypotension was found more frequently among COVID-19 (+) patients (46.7% vs. 12.0%, p = 0,003, 95% CI). Most patients had abnormal WBC, coagulopathy, elevated inflammatory markers, and cardiac biomarkers. Sinus tachycardia, regular sinus rhythm, ST-T wave changes, and low voltage QRS were common ECG findings. The most common chest X-ray results were pleural effusion (80%), pneumonia (71.1%), and enlarged cardiac border (42.2%). Majority of echocardiographic findings were large effusion (>2 cm) (97.8%), RV collapse (40%), and RA collapse (23.3%). An average of 628 ml of pericardial effusion was drained, predominantly serous and exudative. One specimen yielded a positive AFB culture. 6.7% showed carcinoma cells on fluid cytology. The pericardium was normal in 78.9%. 10.0% of the pericardial biopsy specimen had carcinoma, with metastatic cancer being the most common etiology. The most common cancers were lymphoma (22.7%), breast (25.8%), and lung (16.7%). Hospital length of stay was 18 days in COVID-19 (+) patients and 12 days in COVID (-). The complication and in-hospital mortality rate in the COVID-19 (+) compared to the (-) group (86.7% vs. 73.3% and 46.7% vs. 41.3%, respectively) were not statistically significant. The most common complications were respiratory failure (60%), shock (53.3%), and nosocomial pneumonia (40%). There was no association between clinical factors and the risk for complications.



elSSN 2094-9278 (Online) Published: August 15, 2024 https://doi.org/10.47895/amp.vi0.7612

Corresponding author: Eduardo R. Bautista, MD Division of Thoracic, Cardiac and Vascular Surgery Department of Surgery Philippine General Hospital, University of the Philippines Manila Email: edbau1818@gmail.com ORCiD: https://orcid.org/0009-0003-9740-7412 Any complication increased the risk for mortality (OR 15.0, 95% CI 3.2-19.7, p=0.002). The presence of hypertension (OR 0.08, 95% CI 0.02 to 0.4, p=0.001) and subacute duration (OR 0.3, 95% CI 0.09 -0.9, p=0.045) decreased the mortality risk.

Conclusions. Profiles were similar in both groups. There was no association between patient profile and complications. Having COVID-19 did not affect patient outcome. The presence of any complication increases the risk of mortality. In-hospital mortality was high at 42.2%.

Keywords: tube pericardiostomy, massive pericardial effusion, COVID-19

INTRODUCTION

Pericardial effusion is the abnormal accumulation of fluid in the pericardial space.

When the rate of fluid formation is too fast, or the volume is large, the heart is compressed, causing a life-threatening cardiac tamponade. Early recognition of this emergency condition and prompt surgical drainage is the key to survival.

Possible causes of non-traumatic pericardial effusion are varied. Viral, bacterial, fungal, or parasitic infections have been shown to produce pericardial effusion with a disease of the pericardial sac. Tumors in the heart or metastasis can damage the pericardium. Immune system conditions or inflammatory disorders, including lupus, rheumatoid arthritis, Sjogren's syndrome, and hormonal diseases such as hypothyroidism, have also been shown to cause pericardial effusion. Myocardial infarction and aortic dissection are also known etiologies. Pericardial effusion can happen after heart surgery, radiation therapy for cancer, or medication side effect. Pericardial effusion can occur with heart failure, chronic kidney disease, liver cirrhosis, or for unknown reasons.¹

On December 31, 2019, the World Health Organization (WHO) Office in China reported a viral disease in Wuhan with flu-like symptoms. This novel coronavirus COVID-19, rapidly spread worldwide, causing a pandemic.^{2,3} Around 586 million COVID-19 cases had been confirmed as of August 12, 2022, and 6.4 million people had perished globally.^{4,5}

SARS-CoV-2 injures the host's pulmonary tree and almost all organ systems.⁶ The cardiovascular system is one of the systems affected by the virus. Some clinical entities are acute coronary syndrome, heart failure, arrhythmias, thromboembolic events, and pericardial diseases, such as pericarditis and pericardial effusion.⁷ While not a usual presentation, pericardial effusion with tamponade is a cardiac emergency requiring urgent surgical drainage.

The University of the Philippines–Philippine General Hospital (UP-PGH) treated a significant number of COVID-19 patients, being one of the largest COVID-19 referral centers in the country. The Division of Thoracic, Cardiac, and Vascular Surgery (TCVS), treated all surgical cases of pericardial effusion and cardiac tamponade, both in COVID-19 and non-COVID-19 patients. This study aimed to review the clinical experience of the Division of TCVS in the surgical drainage of non-traumatic massive pericardial effusion with tamponade during the COVID-19 pandemic.

The objectives of this study were to determine the following:

- 1. The demographic and clinical profile of patients who underwent surgical drainage of massive pericardial effusion or cardiac tamponade.
- 2. The outcomes of surgical treatment, morbidity, and inhospital mortality rates.
- 3. The association between the clinical factors, complications, and in-hospital mortality rate.

METHODS

We included patients 18 years and older with massive pericardial effusion or cardiac tamponade who underwent tube pericardiostomy in the UP-PGH from January 1, 2020, to September 1, 2022. Patients were identified using the Integrated Surgical Information Systems (ISIS) database of the Department of Surgery. The patient's medical data were retrieved from the PGH Records Section and the electronic Registry of Admissions and Discharges (RADISH).

Demographic and clinical data were collected, such as age, gender, blood type, smoking history, vaccination status, comorbidities, clinical presentation (duration of symptoms before consultation, presenting symptoms, presenting signs), laboratory findings including CBC, PT, PTT, inflammatory markers, COVID-19 status (PCR), cardiac biomarkers, 12lead ECG findings, chest x-ray findings, 2-D echocardiographic findings, pericardial fluid analysis, pericardial biopsy results, medications, etiology of pericardial effusion, length of hospital stay, complications during admission, and mortality.

Clinical factors, which included age, gender, smoking history, comorbidities, COVID-19 (+) or (-), vaccination, duration of symptoms, and etiology of pericardial effusion, were analyzed to determine the association with complications and mortality.

The data were evaluated using frequencies and percentages. Chi-squared and Fisher's exact test determined the differences between COVID (+) and (-) groups. Odds Ratio was computed to assess the risk of complications and mortality.

Patients' data were made anonymous by assigning a code.

This study protocol was approved by the University of the Philippines Manila Research Ethics Board (UPMREB Registration NO. 2022-0517-01).

RESULTS

Ninety patients underwent surgical drainage of massive pericardial effusion or cardiac tamponade. The mean age was 45, and the majority were females (54.4%). The majority had blood type O+ (34.4%). Of the 90 patients, 15 (16.67%) were PCR, COVID-19 (+), and 75 (83.33%) were COVID-19 (-). The majority (76.7%) were not vaccinated. Table 1 shows the demographics and clinical profiles for both study groups. No significant difference was seen between the two groups.

Table 2 shows the comorbidities identified during the initial consult. Cancer (70%), tuberculosis infection (32.2%), and hypertension (25.6%) were the most frequent comorbidities in both study groups. Although proportions differ between both groups, these differences were not significant.

The clinical presentation during the consult is shown in Table 3. Most patients from both groups had subacute symptoms from one week to three months (62.2%). Dyspnea (81.1%), orthopnea (61.1%), and cough (52.2%) were the most common presenting symptoms. Tachycardia (80%) and tachypnea (57.8%) were the most common signs. Hypotension was seen in 17.8% and was found to be significantly higher in COVID-19-positive patients (46.7 vs. 12.0% p=0.003).

The results of laboratory tests are shown in Table 4. The majority of patients from both groups had coagulopathy (82.2%), elevated inflammatory markers (70%), abnormal WBC (57.8%), and cardiac biomarkers (27.8%). No significant difference was shown between the two groups.

Table 5 shows the common electrocardiographic findings in the study population. Among COVID-19 (+) patients,

sinus tachycardia, normal sinus rhythm, and nonspecific ST-T wave changes occurred in the same proportion at 46.7%. In COVID-19 (-) patients, tachycardia (52%) and ST-T wave changes (40%) were more common. These differences were not statistically significant.

Chest x-ray findings are shown in Table 6. Pleural effusion (80%), pneumonia (71.1%), and an enlarged cardiac border (42.2%) were the most common findings in the study group. Differences in the frequency of findings seen are also

Table 1. Demographic Profile of COVIE	ו (+) and (-) Patients who Underwent Surg	ical Drainage for Pericardial Effusion
---------------------------------------	---	--

	T (N	otal =90)	COVID-19 positive (n=15)		COVID-19 negative (n=75)		Chi-squared/ Fisher's test
	f	(%)	f	(%)	f	(%)	and <i>p</i> -value
Age (average)	45:	±15.0	46:	±13.2	45±	15.3	0.754
<20	4	4.44	1	6.67	3	4.00	3.4
20-29	12	13.33	2	13.33	10	13.33	0.641
30-39	17	18.89	4	26.67	13	17.33	
40-49	22	24.44	1	6.67	21	28.00	
50-59	20	22.22	4	26.67	16	21.33	
>60	15	16.67	3	20.00	12	16.00	
Sex							
Male	41	45.60	4	26.70	37	49.30	0.091*
Female	49	54.40	11	73.30	38	50.70	
Blood Type							
A+	17	18.90	1	6.70	16	21.30	6.92
B+	18	20.00	3	20.00	15	20.00	0.140
AB+	3	3.30	2	13.30	1	1.30	
O+	31	34.40	5	33.30	26	34.70	
Unknown	21	23.30	4	26.70	17	22.70	
Smoking							
Never	63	67.80	13	86.70	48	64.00	4.74
Previous	21	23.30	1	6.70	20	26.70	0.093
Current	6	6.70	0	0.00	6	8.00	
Vaccination				0.00	0	0.00	
Fully vaccinated	19	21.10	2	13.30	17	22.70	2.14
Incomplete	2	2.20	1	6.70	1	1.30	0.343
None	69	76.70	12	80.00	57	76.00	

*p-value from Fisher's exact test

Table 2. Comorbidities in Patients who Underwent Surgical Draina	age for Non-traumatic Pericardial Effusion
--	--

Comorbidities	Total (N=90)		COVID-19 positive (n=15)		COVID-19 negative (n=75)		Chi-squared/ Fisher's test
	f	(%)	f	(%)	f	(%)	and <i>p</i> -value
Cancer	63	70.0	11	73.3	52	69.3	0.540/0.338
Hypertension	23	25.6	6	40.0	17	22.7	0.178/0.103
Heart Disease	11	12.2	1	6.7	10	13.3	1.000/0.459
Type II Diabetes	13	14.4	2	13.3	11	14.7	1.000/0.674
Chronic Kidney Disease	8	8.9	1	6.7	7	9.3	1.000*
Tuberculosis	29	32.2	2	13.3	27	36.0	0.211*
Pneumonia	22	24.4	6	40.0	16	21.3	0.097*
Chronic Liver Disease	5	5.6	2	13.3	3	4.0	0.171*
Cerebrovascular Disease	3	3.3	1	6.7	2	2.7	0.402*
Autoimmune	1	1.1	0	0.0	1	1.3	1.000*

*p-value from Fisher's exact test

Table 3. Clinical Presentation of Patients who Underwent Surgical Drainage for Pericardial Effusi	sion
---	------

	Total (N=90)		COVID-1 (n=	COVID-19 positive (n=15)		COVID-19 negative (n=75)	
	f	%	f	%	f	%	and <i>p</i> -value
Duration of symptoms							
Acute (<1 week)	8	8.9	1	6.7	7	9.3	2.458
Subacute (1 week - 3 months)	56	62.2	7	46.7	49	65.3	0.293
Chronic (>3 months)	18	20.0	5	33.3	13	17.3	
Presenting symptoms							
Dyspnea	73	81.1	13	86.7	60	80.0	0.292*
Orthopnea	55	61.1	9	60.0	46	61.3	1.000*
Chest pain	22	24.4	6	40.0	16	21.3	0.097*
Fever	18	20.0	3	20.0	15	20.0	0.877*
Cough	47	52.2	8	53.3	39	52.0	0.092*
Abdominal enlargement	7	7.8	3	20.0	4	5.3	0.073*
Bipedal edema	29	32.2	7	46.7	22	29.3	0.133*
Weakness / Malaise	33	36.7	6	40.0	27	36.0	0.213*
Presenting signs							
Hypotension	16	17.8	7	46.7	9	12.0	0.003*
Tachypnea	52	57.8	10	66.7	42	56.0	0.143*
Tachycardia	72	80.0	11	73.3	61	81.3	0.156*
NVE	20	22.2	3	20.0	17	22.7	0.867*
Muffled heart sounds	21	23.3	3	20.0	18	24.0	0.877*
Friction rub	5	5.6	0	0.0	5	6.7	1.000*
Pulsus paradoxus	3	3.3	1	6.7	2	2.7	0.402*

*p-value from Fisher's exact test

 Table 4. Laboratory Results in Patients who Underwent Surgical Drainage for Pericardial Effusion

Laboratory results	Total (N=90)		COVID-19 positive (n=15)		COVID-19 negative (n=75)		Chi-squared/ Fisher's exact	
	f	%	f	%	f	%	test and <i>p</i> -value	
CBC findings								
Abnormal WBC	52	57.8	12	80.0	40	53.3	1.816	
Abnormal Platelet	26	28.9	3	20.0	23	30.7	0.645*	
Coagulopathy	74	82.2	12	80.0	62	82.7	1.000*	
Inflammatory markers								
Elevated	63	70.0	12	80.0	51	68.0	0.904	
Normal	14	15.6	2	13.3	12	16.0	0.636	
None sent	12	13.3	1	6.7	11	14.7		
Cardiac Biomarkers								
Elevated	25	27.8	8	53.3	17	22.7	5.929	
Normal	7	7.8	1	6.7	6	8.0	0.052	
None sent	58	64.4	6	40.0	52	69.3		

*p-value from Fisher's exact test

described below. No significant difference was seen between the two study groups.

The most common echocardiographic findings were large effusion (>2 cm) (97.8%), RV collapse (40%), and RA collapse (23.3%). Results in both groups are shown in Table 7. No statistical significance was seen between the two groups.

The average fluid drained intraoperatively was 702 ml. in COVID-19 (+) and 609 ml. in COVID-19 (-) patients. Analysis of pericardial fluid samples is shown in Table 8. The majority was classified as sanguineous fluid in the COVID-19 (+) group, while the frequencies of serous and serosanguinous were more similar in COVID-19 (-) patients. All specimens sent for bacterial cultures were negative except one sample in the COVID-19 (-) group, which had a positive AFB culture. Only 6.7 % of the fluid specimen yielded findings of carcinoma cells. The rest of the fluid analysis was non-diagnostic. No statistically significant difference was seen between the two groups.

Description of the pericardium was smooth non-thickened (78.9%), thickened (15.5%), and nodular (5.6%).

EKG findings	Tc (N:	Total (N=90)		COVID-19 positive (n=15)		.9 negative =75)	Chi-squared/ Fisher's exact
	f	%	f	%	f	%	test and <i>p</i> -value
Normal sinus rhythm	35	38.9	7	46.7	28	37.3	0.903*
Sinus tachycardia	46	51.1	7	46.7	39	52.0	0.256*
Atrial fibrillation	4	4.4	0	0.0	4	5.3	0.767*
AV block	5	5.6	0	0.0	5	6.7	0.857*
Poor R wave progression	20	22.2	6	40.0	14	18.7	0.102*
Low voltage QRS complexes	31	34.4	6	40.0	25	33.3	0.344*
ST-T wave changes	37	41.1	7	46.7	30	40.0	1.000*
Prolonged QT interval	6	6.7	1	6.7	5	6.7	1.000*

Table 5. Electrocardiographic Findings in Patients who Underwent Surgical Drainage for Pericardial Effusion

*p-value from Fisher's exact test

Table 6. Chest X-ray Findings in COVID (+) and (-) Patients who Underwent Surgical Drainage for Pericardial Effusion

CXR findings	Total (N=90)		COVID-19 positive (n=15)		COVID-19 negative (n=75)		Chi-squared/ Fisher's exact
	f	%	f	%	f	%	test and <i>p</i> -value
Enlarged cardiac border	38	42.2	8	53.3	30	40.0	0.516*
Total opacification of hemithorax	10	11.1	1	6.7	9	12.0	1.000*
Pleural effusion	72	80.0	13	86.7	59	78.7	0.243*
Pulmonary infiltrates	23	25.6	2	13.3	21	28.0	0.505*
Pneumonia	64	71.1	10	66.7	54	72.0	0.179*
Widened mediastinum	4	4.4	1	6.7	3	4.0	0.498*
Lung mass	4	4.4	1	6.7	3	4.0	0.498*
Mediastinal mass	8	8.9	2	13.3	6	8.0	0.235*

*p-value from Fisher's exact test

2D echo findings	Total (N=90)		COVID-1 (n=	9 positive 15)	COVID-1 (n=	Chi-squared/ _ Fisher's exact	
	f	%	f	%	f	%	test and <i>p</i> -value
Large effusion (>2 cm)	88	97.8	15	100	73	97.3	0.796*
Swinging heart	7	7.8	1	6.7	6	8.0	1.000*
Right atrial collapse	21	23.3	4	26.7	17	22.7	1.000*
Right ventricular collapse	36	40.0	5	33.3	31	41.3	0.654*
IVC plethora	13	14.4	2	13.3	11	14.7	1.000*
Alteration in MV or TV flow	9	10.0	0	0.0	9	12.0	0.721*

*p-value from Fisher's exact test

10.0% of specimens had carcinoma findings, with metastatic cancer being the most common finding. Findings suggestive of tuberculosis were seen in 22.2% of patients, all in the COVID (-) group (Table 9). No statistically significant difference was seen between the two groups.

Antibiotics were the most common medications given (91.1%). Remdesivir and Tocilizumab were given only to COVID-19 (+) patients. There was no significant difference between both groups regarding the frequency and type of medications given. (Table 10)

Table 11 shows malignancy as the predominant etiology in both groups (73.3%), with breast (25.8%), lymphoma (22.7%), and lung (16.7%) being the most common cancers. Other etiologies include tuberculous (10%), heart failure (6.7%), uremia (5.6%), iatrogenic (3.3%), and autoimmune (1.1%). No statistically significant difference was seen between the two groups.

The hospital length of stay was 18 days in COVID-19 (+) and 12 days in COVID

-19 (-) patients. The most common complications were respiratory failure (42.2%), nosocomial pneumonia (42.2%), and shock (41.1%). Although complication rates (86.7% vs. 73.3%) and in-hospital mortality rates (46.7% vs. 41.3%) were higher in COVID-19 patients, the difference was not statistically significant (Table 12).

No significant association was found between clinical factors and complication risk. Results are shown in Table 13. COVID-19 infection has an OR of 2.4, which indicates

Table 8. Analysis of Pericardial Fluid in COVID (+) and (-) Patients who Underwent Surgical Drainage for Pericardial Effusion

Pericardial fluid	Total (N=90)		COVID-19 positive (n=15)		COVID-19 negative (n=75)		Chi-squared/ _ Fisher's exact
	f	%	f	%	f	%	test and <i>p</i> -value
Average volume drained	62	8 ml	702	2 ml	60	9 ml	0.525
Quality							
Serous	32	35.6	5	33.3	27	36.0	5.799
Serosanguinous	26	28.9	2	13.3	24	32.0	0.215
Sanguineous	27	30.0	8	53.3	19	25.3	
Chylous	3	3.3	0	0.0	3	4.0	
Purulent	2	2.2	0	0.0	2	2.7	
Classification							
Exudative	60	66.7	11	73.3	49	65.3	0.787
Transudative	3	3.3	0	0.0	3	4.0	0.675
Unknown	27	30.0	4	26.7	23	30.7	
Bacterial culture results							
Positive	0	0.0	0	0.0	0	0.0	0.334
Negative	71	78.9	11	73.3	60	80.0	0.564
None Sent	19	21.1	4	26.7	15	20.0	
AFB culture results							
Positive	1	1.1	0	0.0	1	1.3	0.269
Negative	56	62.2	9	60.0	47	62.7	0.574
None Sent	33	36.7	6	40.0	27	36.0	
Fluid cytology results							
Carcinoma cells present	6	6.7	1	6.7	5	6.7	0.655
Atypical cells suspicious for malignancy	18	20.0	4	26.7	14	18.7	0.364
Inflammatory cells	20	22.2	3	20.0	17	22.7	
Leukocytes and reactive mesothelial cells	22	24.4	4	26.7	18	24.0	
Fibro collagenous tissue	1	1.1	1	6.7	0	0.0	
Negative	13	14.4	1	6.7	12	16.0	
No specimen sent	10	11.1	1	6.7	9	12.0	

*p-value from Fisher's exact test

Table 9. Analysis of Pericardial Tissue in COVID (+) and (-) Patients who Underwent Surgical Drainage for Pericardial Effusion

Pericardium	Total (N=90)		COVID-19 positive (n=15)		COVID-19 negative (n=75)		Chi-squared/ Fisher's exact
	f	%	f	%	f	%	test and <i>p</i> -value
Description							
Normal	71	78.9	13	86.7	58	77.3	1.092
Thickened	14	15.6	1	6.7	13	17.3	0.579
Nodular	5	5.6	1	6.7	4	5.3	
Histopathology and IHC results							
Carcinoma	9	10.0	2	13.3	7	9.3	0.627*
Metastatic	4	44.4	1	50.0	3	42.0	0.498*
Round cell malignancy	2	22.2	0	0.0	2	28.6	0.844
Hematolymphoid	1	11.1	0	0.0	1	14.3	1.000*
Breast	1	11.1	0	0.0	1	14.3	1.000*
Lung	1	11.1	1	50.0	0	0.0	0.525*
Atypical cells	4	44.4	1	50.0	3	42.9	0.498*
Tuberculosis	2	22.2	0	0.0	2	28.6	0.564*
Chronic inflammation	1	11.1	0	0.0	1	14.3	0.102*
Fibro collagenous and adipose tissue	58	64.4	9	60.0	49	65.3	0.427*
No specimen sent	9	10.0	1	6.7	8	10.7	0.798*

*p-value from Fisher's exact test

Medications	Total (N=90)		COVID-19 positive (n=15)		COVID-19 negative (n=75)		Chi-squared/ Fisher's exact
	f	%	f	%	f	%	test and <i>p</i> -value
Antibiotics	82	91.1	14	93.3	68	90.7	0.243*
Aspirin, NSAIDs	34	37.8	7	46.7	27	36.0	0.166*
Steroids	47	52.2	12	80.0	35	46.7	0.467*
Heparin	59	65.6	12	80.0	47	62.7	0.777*
Remdesivir	5	5.6	5	33.3	0	0.0	NA
Tocilizumab	3	3.3	3	20.0	0	0.0	NA

Table 10. Medications Given in COVID (+) and (-) Patients who Underwent Surgical Drainage for Pericardial Effusion

*p-value from Fisher's exact test

Table 11.	Diagnosis	of Patients w	vho Underwen	t Surgical	Drainage
-----------	-----------	---------------	--------------	------------	----------

Etiology	Total	(N=90)	COVID-19 positive (n=15)		COVID-19 negative (n=75)		Chi-squared/ Fisher's exact
	f	%	f	%	f	%	test and <i>p</i> -value
Malignancy	66	73.3	12	80.0	54	72.0	0.337*
Lymphoma	15	22.7	1	8.3	14	25.9	0.450*
Leukemia	2	3.0	0	0.0	1	1.9	1.000*
Anterior mediastinal	7	10.6	1	8.3	6	11.1	0.341*
Breast	17	25.8	5	41.7	12	22.2	0.256*
Gynecologic	4	6.1	1	8.3	3	5.6	0.467*
Chest wall	2	3.0	1	8.3	1	1.9	0.877*
Esophageal	1	1.5	0	0.0	1	1.9	1.000*
Laryngeal	1	1.5	0	0.0	1	1.9	1.000*
Liver	1	1.5	0	0.0	1	1.9	1.000*/ 0.844
Lung	11	16.7	3	25.0	8	14.8	0.157*
Prostate	1	1.5	0	0.0	1	1.9	1.000*
Rectal	1	1.5	0	0.0	1	1.9	1.000*
Suprarenal	1	1.5	0	0.0	1	1.9	1.000*
Unknown	2	3.0	1	8.3	1	1.9	0.288*
Tuberculous	9	10.0	1	6.7	8	10.7	0.844*
Uremic	5	5.6	1	6.7	4	5.3	0.278*
Heart failure	6	6.7	1	6.7	5	6.7	0.385*
latrogenic	3	3.3	0	0.0	3	4.0	0.272*
Autoimmune	1	1.1	0	0.0	1	1.3	1.000*

*p-value from Fisher's exact test

an increased risk for complications but is not statistically significant.

Table 14 shows that any complications increase the risk of mortality (OR 15.0, 95% CI 3.2-19.7, p=0.002). The presence of hypertension (OR 0.08, 95% CI 0.02 to 0.4, p=0.001) and subacute duration (OR 0.3, 95% CI 0.09 -0.9, p=0.045) decreased the mortality risk.

DISCUSSION

Demographics

We present an extensive series of patients with massive pericardial effusion requiring surgical drainage in the local setting during the COVID-19 pandemic. Patients treated were either COVID-19 (+) or (-).

Age and Gender

Numerous studies describe cardiac tamponade as more common in males, but the pathophysiology or significant correlation of this gender finding is uncertain. No age group has been identified to be more predisposed to tamponade, but advanced age is a risk factor for severe disease.

Al-Ogaili reported over 100,000 patients of different race groups with cardiac tamponade. The majority (53.5%) were males, and the mean age was 61.9 years, much higher than the average age reported in our study.⁸ Sánchez-Enrique reported on 136 patients with cardiac tamponade and found a predominantly male population (55%) with a median age of 65 \pm 17 years.⁹ In a local study done in UP-PGH by Aleta, 59% of the population were males, and the mean age was 36.47 years, similar to the younger age group in our study.¹⁰ Majidi described COVID-19 patients with

 Table 12. Clinical Outcomes and Complications in COVID (+) and (-) Patients who Underwent Surgical Drainage for Pericardial Effusion

	Total (N=90)		COVID-19 positive (n=15)		COVID-19 negative (N=75)		Chi-squared/ fisher's exact
	f	%	f	%	f	%	test and <i>p</i> -value
Outcomes/Complications							
Shock	37	41.1	8	53.3	29	38.7	0.240*
Respiratory failure	38	42.2	9	60.0	29	38.7	0.083*
Sepsis from non-respiratory causes	20	22.2	5	33.3	15	20.0	0.291*
Nosocomial pneumonia	38	42.2	6	40.0	32	42.7	0.236*
Arrythmias	4	4.4	0	0.0	4	5.3	0.347*
Deep vein thrombosis	9	10.0	3	20.0	6	8.0	0.143*
Pulmonary embolism	10	11.1	4	26.7	6	8.0	0.045*
Urinary tract infection	5	5.6	1	6.7	4	5.3	0.151*
Catheter related infections	2	2.2	1	6.7	1	1.3	0.288*
Myocardial Infarction	1	1.1	0	0.0	1	1.3	1.000*
Hospital LOS	13	days	18	days	12	days	0.082
Complication Rate	75	5.6%	86	5.7%	73	8.3%	1.000*
Mortality Rate	42	.2%	46.	67%	41	.3%	0.778*

*p-value from Fisher's exact test

Table 13. Odds Ratio for Risk of Complications

	Clincal Factors	Odds Ratio	95% Cl	p-value
COVID	Positive	2.4	0.5 to 11.4	0.284
Age	Age	1.0	1.0 to 1.1	0.316
Sex	Male	Reference	n/a	n/a
	Female	2.1	0.8 to 5.5	0.146
Smoker	Never	Reference	n/a	n/a
	Current	1.3	0.2 to 8.5	0.783
	Previous	0.7	0.4 to 1.2	0.212
Presence of Comorbidities	Cancer	1.1	0.4 to 3.2	0.831
	Heart disease	0.8	0.2 to 3.5	0.816
	Hypertension	0.9	0.3 to 2.6	0.832
	Diabetes mellitus	0.7	0.2 to 2.5	0.568
	Chronic kidney disease	0.5	0.1 to 2.3	0.375
	Pulmonary tuberculosis	0.8	0.3 to 2.1	0.633
	Chronic liver disease	n/a	n/a	n/a*
	CVD	0.8	0.2 to 2.7	0.431
Duration of symptoms	<1 week	Reference	n/a	n/a
	1 week – 1 month	0.2	0.02 to 1.4	0.095
	>1 month	0.2	0.01 to 1.7	0.131
Vaccination status	Unvaccinated	Reference	n/a	n/a
	Partial Vaccination	n/a	n/a	n/a*
	Full Vaccination	0.9	0.5 to 1.6	0.725
Etiology of effusion	Malignancy	1.4	0.5 to 4.0	0.531
	Tuberculous	n/a	n/a	n/a*
	Uremia	n/a	n/a	n/a*

*too few cases

pericardial effusion, with the majority being males (62.2%) in the 50-70 age group (54%).¹¹

Large-scale studies of COVID-19 (+) patients with cardiac tamponade in the literature are scarce. In COVID-19 infection, male sex and increasing age have been associated with poorer outcomes. Biswas reported that males had an increased mortality risk compared to females. They also found that age \geq 50 was associated with 15.4 fold increased mortality risk.¹² Henkens also showed the same findings, as male patients over 70 had poor outcomes.¹³ Momtazmanesh

	Clinical Factors	Odds Ratio	95% Cl	p-value
COVID	Positive	2.4	0.5 to 11.4	0.284
Complications	Presence of any complications	15.0	3.2 to 19.7	0.002
Age	Age	1.0	1.0 to 1.02	0.896
Sex	Male	Reference	n/a	n/a
	Female	1.5	0.6 to 3.6	0.323
Smoker	Never	Reference	n/a	n/a
	Current	1.5	0.4 to 5.6	0.545
	Previous	0.9	0.2 to 4.1	0.891
Presence of Comorbidities	Cancer	1.1	0.4 to 2.7	0.852
	Hypertension	0.08	0.02 to 0.4	0.001
	Heart disease	0.8	0.2 to 2.8	0.675
	Type II Diabetes	0.4	0.1 to 1.4	0.143
	CKD	0.4	0.1 to 2.2	0.313
	Tuberculosis infection	1.4	0.6 to 3.5	0.424
	Pneumonia	1.9	0.7 to 5.1	0.182
	CLD	n/a	n/a	n/a*
	CVD	0.7	0.06 to 7.7	0.753
Duration of symptoms	<1 week	Reference	n/a	n/a
	1 week - 3 months	0.3	0.09 to 0.9	0.045
	>3 months	0.6	0.1 to 2.4	0.465
Vaccination status	Unvaccinated	Reference	n/a	n/a
	Partial Vaccination	n/a	n/a	n/a*
	Full Vaccination	0.9	0.4 to 2.0	0.799
Etiology of effusion	Malignancy	1.0	0.4 to 2.6	0.949
	Tuberculous	n/a	n/a	n/a*
	Uremia	n/a	n/a	n/a*

Table 14. Odds Ratio for Risk of Mortality

*too few cases

showed that elderly patients with chronic comorbid disease are more susceptible to severe COVID due to dysfunction of the renin-angiotensin-aldosterone system that occurs with aging.¹⁴

Our study population had more females than males. This study also had younger patients in both groups (third and fourth decades of life in COVID-19-positive patients and fourth and fifth decades in the COVID-19-negative group).

Blood Type

O+ is the predominant blood type among both of our study groups. It has not been proven that certain blood types are predisposed to developing massive pericardial effusion and cardiac tamponade. On the other hand, several studies have shown an association between blood type and COVID-19 infection, disease severity, and mortality. Kim compiled nine extensive population database studies to determine the relationship between blood type and COVID-19 infection. Four out of nine studies found a significant association between the two factors. However, five studies showed no association between the ABO blood group and COVID-19 disease and severity. They also reported an increased risk of disease and mortality among blood type A patients.¹⁵

Smoking

There was a higher proportion of non-smokers and previous smokers who stopped in this study. This high proportion could indicate better health awareness among the study popu-lation on the risks of smoking, as the majority had already been admitted or consulted for a previous comorbid disease. Extensive studies have not shown a direct association between smoking and the progression of pericardial effusion to cardiac tamponade. However, smoking is known to influence cardiovascular and lung diseases negatively. COVID-19 infection and its association with smoking have been documented, but the exact relationship is not yet established. He reported a significantly higher proportion of current smokers with severe COVID-19 disease, suggesting that active smoking increases the risk of progression to severe COVID-19 disease.¹⁶ With the small number of patients who are current smokers in our study, this correlation could not be assessed.

Comorbidities and COVID-19 Vaccination Status

Pericardial effusion or cardiac tamponade is a complication of systemic disease. All patients in our study had at least one comorbidity, cancer being the most common. However, most patients had multiple comorbidities during the diagnosis of pericardial effusion. All can influence the progression of pericardial effusion to cardiac tamponade. Cancer can directly obstruct the lymphatic drainage in the mediastinum and cause massive pericardial effusion. Tuberculosis is shown to involve the lungs and mediastinal lymph nodes directly and can cause systemic disease, TB pericarditis, and pericardial effusion. Any deterioration in normal heart function can lead to hemodynamic changes leading to pericardial effusion. Hypertension, Type II diabetes, and previous heart disease, although not directly shown to cause pericardial effusion, can cause derangements in multiple organ systems. Systemic infection, autoimmune diseases, and any entity producing an inflammatory reaction can directly affect the pericardium, causing pericardial effusion.

The Centers for Disease Control (CDC) has classified multiple comorbidities as associated with an increased risk for severe COVID. Some of the factors included in the extensive list are age \geq 65 years, asthma, cancer, cerebrovascular disease, chronic kidney disease, chronic lung disease, chronic liver disease, cystic fibrosis, diabetes mellitus, type 1 and type 2, heart diseases, HIV, physical inactivity, pregnancy, smoking, substance use disorders, and tuberculosis infection. A number of these have been identified in the initial history of patients included in our study.¹⁷

Vaccination has decreased the risk of COVID-19 infection, symptomatic disease, severe illness, and mortality. The latest guidelines recommend a bivalent COVID-19 vaccine booster dose specifically in patients at increased risk.¹⁸

Only nineteen (21%) patients had been vaccinated in our study. It was only in mid-2021 that vaccines became more accessible to the general population.

Clinical Presentation

Most patients in this study presented with tamponade in the subacute (>one week to 3 months) course. This presentation is similar to that of Adler's series.¹⁹

Pericardial fluid accumulation was slow and presented with non-specific symptoms like dyspnea, orthopnea, cough, weakness, bipedal edema, and chest pains. The classical Beck's triad findings in cardiac tamponade, namely, hypotension, increased neck vein engorgement, and muffled heart sounds, were found in a subset of the population with acute presentations.

The results of our study were comparable to the UP-PGH study of Aleta. They reported the most common signs to be tachypnea (28.4%), bipedal edema (22.7%), and neck vein engorgement (20.4%). Dyspnea on exertion (31%), fever (24%), and cough (12%) were the most common presenting symptoms.¹⁰

In our study population, there was no significant difference in the clinical presentation of both COVID (+) and (-) study groups.

Laboratory Tests

Blood Tests

The majority of patients in this study had abnormal WBC counts with high percentages of neutrophils. This percentage was higher in the COVID-19 positive group. In recent studies in COVID-19 patients, increased WBC (neutrophil count) and lower platelet count were associated with severe COVID-19 cases and increased mortality risk. It was also correlated to myocardial injury. A higher percentage of neutrophils was associated with ICU admission.²⁰⁻²² However, in this study, outcomes were similar for both groups.

Most of the patients in our study had coagulopathy, 80.0% in the COVID (+) group and 82.7% in the COVID (-) group. No significant bleeding occurred despite prolonged PT and PTT results. Lin showed an association between coagulation indicators to the severity of COVID-19. Platelet, D-dimer, and fibrinogen were found to be correlated with the severity of the disease. Low values were suggested to be used as risk indicators upon admission to guide the treatment of COVID-19 disease.²³

Inflammatory markers investigated in this study were ESR, CRP, procalcitonin, serum ferritin, and interleukin 6. The majority of patients in both study groups had elevated inflammatory markers. Elevated inflammatory markers are present in cases of pericarditis and myocarditis. However, these numbers characterize pericardial effusion alone, as they may also be elevated in infection and autoinflammatory conditions. Due to active pneumonia in most patients, elevated markers are probably caused by infection. Momtazmanesh demonstrated that biomarkers were significantly higher in COVID-19 patients who died. The inflammatory markers described were ESR, CRP, IL-6, and serum ferritin, while cardiac biomarkers were Troponin I and T, LDH, PRO BNP, CK, and myoglobin. They also found that CK levels were higher in patients with severe disease and those needing ICU admission. IL-6 was also found to be 2.9 times higher in patients with complicated COVID-19.14 In our study population, biomarkers did not affect complication and mortality rates.

EKG

Twelve-lead ECG findings have been defined as part of the spectrum of COVID-19 infection or indicate starting pericardial disease. Fabio extensively described common ECG findings in COVID-19, reflecting the range of systems affected by the viral infection. Common ECG patterns in his study of 756 COVID-19-positive patients were: nonspecific repolarization abnormalities (29.0%), T-wave inversion (10.5%), atrial premature beats (7.7%), right bundle branch block (7.8%), atrial fibrillation (5.6%), ventricular premature beats (3.4%), and left bundle branch block (1.5%). Sinus tachycardia was also described as the most common ECG finding in COVID 19, reflecting the hyperinflammatory state and increased adrenergic tone in systemic disease. Pericardial involvement was described as widespread concave ST elevation and PR depression throughout most limbs (I, II, III, aVL, aVF) and precordial (V2-V6) leads, reciprocal ST depression and PR elevation in aVR ST segment/T wave ratio > 0.25.²⁴ This specific finding has yet to be described in our study. 12-lead ECG findings found in our study population were nonspecific.

CXR

The top chest X-ray findings reported in our study population were pleural effusion (80%), enlarged cardiac border/cardiomegaly (42.2%), and pneumonia (71.1%). Although nonspecific for pericardial effusion, CXR findings complicated by pulmonary involvement in most cases indicate severe disease. The pleural effusion diagnosed by radiographic findings did not all require pulmonary drainage. Of 72 patients with pleural effusion on chest X-ray, 37 (51.4%) were evaluated to have significant effusion requiring concomitant pleural drainage. Enlarged cardiac shadow was only reported in 42.2%. This low yield was due to pleural effusion, which could obscure the cardiac border, especially on the left side. In the study by Aleta, common CXR findings in this study were similar to the present study: enlargement of cardiac silhouette (64.3%), pleural effusion (17%), right upper lobe infiltrates 8.6%, lung mass (7.1%) and mediastinal mass (1.4%).10

Echocardiogram

Echocardiographic findings reported in our study were from point-of-care ultrasonography (POCUS). In almost all cases, the diagnosis of pericardial effusion was already considered, and specific findings from the 2-D echocardiogram were only confirmatory. These findings were large pericardial effusion (> 20 mm) or massive effusion (97.8%), the diastolic collapse of the right ventricle (40%), the diastolic collapse of the right atrium (23.3%), swinging heart (7.8%), duration of RA inversion (10%) by the RA inversion time index (duration of inversion/cardiac cycle length for values > 0.34, variations in E velocities during respiration across the MV, TV, and pulmonary outflow tract that are greater than 25, 50 and 30%, and IVC Plethora (14.4%) (defined as dilatation > 20 mm and < 50% reduction in the diameter of IVC with respiratory phases). The above findings warranted an emergency tube pericardiostomy for drainage.

Pericardial Fluid Characteristics

The average fluid drained in our study population was 628 ml. Pericardial fluid was described as serous, serosanguinous, sanguineous, chylous, and purulent.

Sánchez-Enrique described effusion drainage in the general population before the pandemic; the median volume removed was 811 ± 552 ml. Similar to our study, the etiology was predominantly from malignancy. They documented increased fluid drained in the neoplastic group compared to other causes (986.45 ml ± 673 vs712.39 ± 446 ml). Fluid was primarily hemorrhagic (43%).⁹ Aleta drained an average of 543.8 ml, the majority with sanguineous character.¹⁰

Data on pericardial fluid characteristics for COVID-19 (+) patients is limited. For culture results, Sánchez-Enrique isolated bacteria in five patients (4%) and late HIV in another two patients. Tuberculosis was diagnosed via pericardial fluid Adenosine Deaminase (ADA) levels in two patients.⁹

In our study, pericardial fluid analysis alone did not provide a definitive diagnosis in most patients. Most of the fluid did not have any bacterial growth, including AFB. Cancer cells seen in the cytology analysis were deficient (6.7%). In contrast, Aleta reported 12 patients having bacterial growth on fluid cultures (16.7% of the population). The reported bacteria were *Staphylococcus aureus*, *S. epidermidis*, *S. pneumonia*, *Acinetobacter*, *E. coli*, and *Klebsiella* spp. AFB smear was positive for two out of 75 patients.¹⁰ An explanation for this difference would probably be the better accessibility and widespread use of broad-spectrum antibiotics at present compared to what was available almost 20 years ago. Most patients in our study were already treated for community-acquired pneumonia before being transferred to UP-PGH for further treatment.

Pericardial Biopsy Results

The pericardium in our study population was predominantly normal and without implants. The yield for positive cancer cells in the biopsy specimen was very low at 10%, similar to fluid cytology, which was only 6.7%. TB diagnosis was better for tissue biopsy (22.2%) compared to AFB (+) culture, which was only 1.1%. Fluid cytology and tissue biopsy have limited diagnostic value and should be correlated with other clinical data.

Extensive studies on pericardial biopsy results in COVID-19 (+) population are rare. Amoozgar reported a patient with COVID-19 wherein the pericardium was grossly thickened, with myocardium adhesions. Cultures were negative. Pathology analysis revealed pericarditis with acute and chronic inflammation. Immunohistochemical stains (IHCS) were positive for CK AE1/AE2, CK7, and calretinin, and negative for CK20 and TTF-1, indicative of pericarditis.²⁵

Boldes analyzed the diagnostic utility of pericardial biopsy in patients with idiopathic pericarditis, constrictive pericarditis, malignant pericarditis, and inflammatory postcardiac injury syndrome. They reported that the diagnostic value of pericardial biopsy in metastatic neoplasms of the pericardium had an overall sensitivity of 57.69%, a specificity of 100%, a positive predictive value of 100%, and a negative predictive value of 87.06%. Findings suggested that pericardial biopsy had no diagnostic value in patients with an already established etiology via imaging, laboratory, and clinical findings. None of the 100 patients included had their etiologies modified based on a pericardial biopsy result.²⁶

These findings are similar to the results of our study. Few patients with positive fluid cytology or pericardial tissue biopsy were already diagnosed with malignancy. Etiology was still based on previous history, imaging, and other noninvasive diagnostic tools. Pericardial biopsy, in our setting, was used as a confirmatory tool or to prove metastasis from an already known primary. More patients had positive findings on pericardial biopsy (10%) compared to fluid cytology (6.7%), although the overall yield was low, in contrast to the findings in the literature.

Etiology of Pericardial Effusion

The etiology of pericardial effusion varies between geographic and sociopolitical settings. In developed countries, more common etiologies would be malignancy (10-25%), infections (15-30%), iatrogenic causes (15-20%), and connective tissue diseases (5-15%), but up to 50% remain idiopathic. Sagrista'-Sauleda reported 342 patients with pericardial effusion, and the most frequent etiologic diagnoses were acute idiopathic pericarditis (20%), iatrogenic effusions (16%), cancer (13%), and chronic idiopathic pericardial (9%). In 60% of the patients, the etiology of the effusion was a known systemic condition: acute myocardial infarction (8%), ESRD (6%), heart failure (5%), and collagen vascular disease (5%). Tuberculous etiology represented 4% of the entire series. In a subset analysis, cardiac tamponade was more common in patients with malignant pericarditis than in other etiologies.²⁷ Sánchez-Enrique reported the main etiologies to be malignancy (32%), infection (24%), idiopathic (16%), iatrogenic (15%), post-myocardial infarction (7%), and uremic (4%). The most common cancer types were lung tumors (14 adenocarcinomas, two large cell carcinomas, three squamous cells, and one small cell lung cancer). Other cancers identified were breast, cervical, thyroid, melanoma, bladder, and ovarian tumors. Tuberculosis represented 4% of the total sample and 16% of the group classified under infection.9

In contrast, a study by Pradhan in India investigated 55 patients with moderate to large pericardial effusion who eventually underwent pericardiocentesis. Cardiac tamponade was present in 94.54%. Tuberculosis was the most common etiology (63.64%), followed by hypothyroidism (10.9%). Malignancy was only 7.27%.²⁸

In our local setting, Aleta reported that the most common etiology in UP-PGH was tuberculosis (59%), followed by malignancy (19%). Most fluid specimens showed chronic inflammation. For a pericardial biopsy, 29.4% had malignant results, while granulomatous tissue with Langhans' giant cell formation indicative of tuberculosis was 13.1%. For malignancy, they found that lung cancer and metastatic cancer were the most common findings detected (11.5%), followed by adenocarcinoma, non-small cell lung cancer, squamous cell lung cancer, and malignant cells of unknown primary.¹⁰

Our study determined etiology by the entire clinical picture, fluid cytology and pericardial specimen, the demographic profile, history, presentation on admission, laboratory results, and imaging studies, including 2D echo. Malignancy was the predominant etiology in both COVID-19 (+) and COVID-19 (-) groups. Tuberculous was the second most common etiology, with 6.7% in COVID positive and 10.7% in all COVID-negative patients. No significant difference was found between the etiologies of the two groups. Lymphoma, and breast and lung tumors were the most common malignancies among patients. All these tumors directly involve or invade thoracic lymph nodes, causing deranged drainage of pericardial and pleural fluid. Most of these cancer cases presented with advanced disease.

Outcomes and Complications

Complications of shock, respiratory failure, sepsis, and pneumonia were noted in both study groups. The high complication rate reflects the severity of the disease condition, mainly in the far advanced stage of malignancy. Pericardial effusion is already a complication of uncontrolled comorbidities or a manifestation of decompensated disease. We report the other complications that developed during the patient's course in the hospital. The pericardial effusion could have affected the patient's overall outcome, regardless of the etiology. In both COVID-19 (+) and (-) study groups, shock requiring inotropic support, respiratory failure, and nosocomial pneumonia were the most common complications that eventually led to poor treatment outcomes.

COVID-19 infection is known to be a systemic disease. The presence of pericardial effusion and cardiac tamponade is one of the complications of COVID-19. It has been shown that SARS-CoV-2 affects not only the pulmonary system but almost all organ systems. Among the reported extrapulmonary complications are myocardial dysfunction and arrhythmia, thrombo-inflammation, renal complications, gastrointestinal dysfunctions, endocrine system disorders, neurological dysfunctions, dermatological symptoms, and hematologic, musculoskeletal, and reproductive systems problems.⁶ In this study, having COVID-19 did not make a difference in the overall poor treatment outcome.

Mortality

Al-Ogaili reported an overall in-hospital mortality rate of 14.3% for cardiac tamponade. He found that concomitant sepsis, metastatic cancer, chest trauma, and acute kidney injury were independent predictors of mortality.⁸

Sanchez-Enrique reported cardiac tamponade with a 16% in-hospital mortality and a 48% overall mortality over a 125-month follow-up. They also found that mortality is associated with a malignant etiology, with lung cancer having the worst prognosis. Uremic and iatrogenic etiologies of cardiac tamponade were also associated with poor prognosis. On multivariate statistical analysis, the etiology was the most vital risk factor for death, recurrence, or both. The malignancy group showed the worst prognosis among all etiologies.⁹

In recent literature, cardiac involvement in COVID-19 is associated with higher mortality. The exact mechanism is unclear, with some studies attributing to cardiac causes, biventricular failure, myocarditis, pericarditis, or overwhelming systemic inflammation.^{29,30} In a report by Lazar, pericardial effusion was seen in a higher prevalence among patients with severe COVID-19 infection and was associated with higher mortality. One hundred patients were enrolled in the study and classified as those with and without pericardial effusion. They reported the prevalence of pericardial effusion at 27% among COVID-19 patients. The overall mortality among all participants was 24%, 33.3% in those with pericardial effusion, and 20.8% in those without effusion.²⁹ In another study comparing COVID-19 patients with and without pericardial effusion, Ghantous reported that all-cause mortality was

higher in COVID-19 patients with pericardial effusion.³⁰ This study's mortality rate was remarkably high, with 42.2% in the total population, 46.7% in COVID-19 (+), and 41.3% in COVID-19 (-) patients. The presence of COVID-19 did not affect the poor outcomes considering that the majority of the patients were unvaccinated. Several factors could explain this high figure. In contrast to the above studies cited, our study population had typically presented with more advanced and complicated systemic disease. The majority of them already had advanced cancer or multisystem disease. A multi-organ dysfunction syndrome brings about eventual mortalities in most cases. Secondly, suboptimal health-seeking behavior and access to health care brought about by lockdowns during the COVID surge also contributed to the delays in the consultation. Lastly, in addition to multiple comorbidities, most patients also developed further complications during their stay in the hospital.

No significant relationship was found between the patient's clinical factors and the risk of developing complications. Although COVID-19 infection shows an increased odds ratio for complications and mortality, it was insignificant. No studies have shown the protective effect of hypertension. Subacute onset of symptoms may give patients time to adjust to the slow accumulation of pericardial effusion. The lower odds ratio of the subacute duration of symptoms compared to acute (< one week) or chronic (> three months) can probably be explained by the natural history of the etiologies. Chronic effusions allow for a more gradual buildup of fluid, allowing accumulation of very large effusions up to one liter or more. Also, the long duration before consultation could mean other unchecked comorbidities, leading to more complications. On the other hand, the rapidity of fluid accumulation in less than a week causes a sudden increase in pressure in the pericardial space. Presentation is clinically more dramatic: occurring with classical Beck's triad of hypotension, engorged neck veins, and muffled heart sounds.

Consequently, the complication and mortality rates here are much higher than in similar cases reported in the literature.

No significant difference was seen in this study between the COVID-19 (+) and (-) groups, aside from the higher occurrence of hypotension and pulmonary embolism in COVID-19 (+) patients. The results suggest that COVID -19, even with its involvement of multiple organ systems, does not significantly affect the presentation, course, and outcomes of patients undergoing drainage of significant pericardial effusion. The complication rate was very high (75.6%), reflecting how far advanced the disease condition was when admitted to the hospital. Whether they were COVID-19 (+) or (-) did not make a difference. These complications then translated into a high mortality rate (42.2%).

Limitations of the Study

The study was limited by the small sample size and retrospective design.

CONCLUSION

The demographic and clinical profiles of both COVID (+) and (-) patients were similar, with more hypotensive patients seen in the COVID (+) group. Most were middle-aged females, blood type O+, non-smokers, and unvaccinated for COVID-19. The majority presented with the subacute form with non-specific symptoms. The majority had coagulopathy and elevated inflammatory markers. The majority of the fluid cytology and pericardial biopsy was inconclusive.

There was no difference in morbidity (complication rate) and mortality rate for COVID (+) and (-) patients. Overall complication (76.6%) and mortality (42.2%) rates were very high, reflecting a very sick patient population.

There is no relationship between profile and outcomes. Having COVID-19 did not affect outcomes. However, there is a relationship between complication rate and mortality. Therefore, the attending physician should strive to prevent complications resulting in bad outcomes.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

All authors declared no conflicts of interest.

Funding Source

There was no external funding for this paper.

REFERENCES

- Cleveland Clinic, Pericardial effusion: Symptoms, causes and treatment [Internet]. 2022 [cited 2023 Feb]. Available from: https:// my.clevelandclinic.org/health/diseases/17351-pericardial-effusion
- World Health Organization, Coronavirus (COVID-19) outbreak [Internet]. 2022 [cited 2022 Aug]. Available from: https://www.who. int/westernpacific/emergencies/covid-19
- World Health Organization Maldives, Novel Corona Virus Update [Internet]. 2020 [cited 2022 Aug]. Available from https://www. who.int/docs/default-source/maldives/novel-corona-virus-updatemav-30jan.pdf?sfvrsn=a10dfb7b_2.
- 4. World Health Organization. Coronavirus disease (COVID-19) pandemic [Internet]. 2022 [cited 2022 Jun]. Available from: https:// www.who.int/emergencies/diseases/novel-coronavirus-2019?adgr oupsurvey={adgroupsurvey}&gclid=Cj0KCQjwzLCVBhD3ARIs APKYTcRaZPnTzMVSRdiZGan-gsxyd_A9Qbt_eUkIHvYtTawq6iAx5mXNP8aAIBmEALw_wcB.

- Department of Health, Updates on Novel Coronavirus Disease 2019 (COVID-19) [Internet]. 2022 [cited 2022 Aug]. Available from: https://doh.gov.ph/2019-nCoV?gclid=Cj0KCQjwzLCVBhD3AR IsAPKYTcQWhjtMdb4V0FMkJ_gCrXX818PYCf-SMnNJawuk8FgwCbtqybTDWYaAtC7EALw_wcB.
- Li N, Zhu L, Sun L, Shao G. The effects of novel coronavirus (SARS-CoV-2) infection on cardiovascular diseases and cardiopulmonary injuries. Stem Cell Res. 2021 Mar;51:102168. doi: 10.1016/j. scr.2021.102168. Epub 2021 Jan 12. PMID: 33485182; PMCID: PMC7801189.
- Sarkesh A, Daei Sorkhabi A, Sheykhsaran E, Alinezhad F, Mohammadzadeh N, Hemmat N, et al. Extrapulmonary clinical manifestations in COVID-19 patients. Am J Trop Med Hyg. 2020 Nov;103(5):1783-96. doi: 10.4269/ajtmh.20-0986. PMID: 32940201; PMCID: PMC7646754.
- Al-Ogaili A, Ayoub A, Fugar S, Kolkailah A, Rios LP, Fuentes, H. Cardiac tamponade incidence, demographics and in-hospital outcomes: analysis of the national inpatient sample database. J Am Coll Cardiol. 2018 Mar, 71 (11_Supplement) A1155. doi: 10.1016/S0735-1097(18)31696-6.
- Sánchez-Enrique C, Nuñez-Gil IJ, Viana-Tejedor A, De Agustín A, Vivas D, Palacios-Rubio J, et al. Cause and long-term outcome of cardiac tamponade. Am J Cardiol. 2016 Feb;117(4):664-9. doi: 10.1016/j.amjcard.2015.11.023. PMID: 26718232.
- Aleta KNR, Bautista ER, Catalan GT, Danguilan JLJ, Esquivel JF, Gonzales JC, et al. Massive pericardial effusion in the Philippine General Hospital: Clinical profile of patients over a five-year experience. Philipp J Thorac Cardiovasc Surg. 2004 Dec;11(1):30-7.
- Majidi F, Faraji, M, Zamanifard S, Nikdoust F. Assessment of clinical characteristics and outcomes of COVID-19 patients with pericardial effusion, Trauma Monthly. 2022 Jan-Feb; 27(Especial Issue (COVID-19 and Emergency Medicine)):34-40. doi: 10.30491/ tm.2021.310322.1385.
- Biswas M, Rahaman S, Biswas TK, Haque Z, Ibrahim B. Association of sex, age, and comorbidities with mortality in COVID-19 patients: A systematic review and meta-analysis. Intervirology. 2021;64(1): 36–47. doi: 10.1159/000512592.
- Henkens MTHM, Raafs AG, Verdonschot JAJ, Linschoten M, van Smeden M, Wang P, et al. CAPACITY-COVID collaborative consortium. Age is the main determinant of COVID-19 related inhospital mortality with minimal impact of pre-existing comorbidities, a retrospective cohort study. BMC Geriatr. 2022 Mar;22(1):184. doi: 10.1186/s12877-021-02673-1. PMID: 35247983; PMCID: PMC8897728.
- Momtazmanesh S, Shobeiri P, Hanaei S, Mahmoud-Elsayed H, Dalvi B, Malakan Rad E. Cardiovascular disease in COVID-19: a systematic review and meta-analysis of 10,898 patients and proposal of a triage risk stratification tool. Egypt Heart J. 2020 Jul;72(1):41. doi: 10.1186/ s43044-020-00075-z. PMID: 32661796; PMCID: PMC7356124.
- Kim Y, Latz CA, DeCarlo CS, Lee S, Png CYM, Kibrik P, et al. Relationship between blood type and outcomes following COVID-19 infection. Semin Vasc Surg. 2021 Sep;34(3):125-31. doi: 10.1053/j. semvascsurg.2021.05.005. PMID: 34642032; PMCID: PMC8286549.
- He Y, He Y, Hu Q, Yang S, Li J, Liu Y, et al. Association between smoking and COVID-19 severity: A multicentre retrospective observational study. Medicine (Baltimore). 2022 Jul;101(29):e29438. doi: 10.1097/MD.00000000029438. PMID: 35866793; PMCID: PMC9302364.
- Kompaniyets L, Pennington AF, Goodman AB, Rosenblum HG, Belay B, Ko JY, et al. Underlying medical conditions and severe illness among 540,667 adults hospitalized with COVID-19, March 2020-March 2021. Prev Chronic Dis. 2021 Jul;18:E66. doi: 10.5888/pcd18.210123. PMID: 34197283; PMCID: PMC8269743.

- Rosenblum HG, Wallace M, Godfrey M, Roper LE, Hall E, Fleming-Dutra KE, et al. Interim recommendations from the Advisory Committee on Immunization Practices for the use of bivalent booster doses of COVID-19 vaccines — United States, October 2022. MMWR Morb Mortal Wkly Rep 2022 Nov;71(45):1436–41. doi: 10. 15585/mmwr.mm7145a2. PMID: 36355612; PMCID: PMC9707353.
- Adler Y, Charron P, Imazio M, Badano L, Barón-Esquivias G, Bogaert J, et al. ESC Scientific Document Group. 2015 ESC Guidelines for the diagnosis and management of pericardial diseases: The Task Force for the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology (ESC)Endorsed by: The European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J. 2015 Nov;36(42):2921-64. doi: 10.1093/eurheartj/ehv318. PMID: 26320112; PMCID: PMC7539677.
- Wu X, Liu L, Jiao J, Yang L, Zhu B, Li X. Characterization of clinical, laboratory and imaging factors related to mild vs. severe COVID-19 infection: a systematic review and meta-analysis. Ann Med. 2020 Nov;52(7):334-44. doi: 10.1080/07853890.2020.1802061. PMID: 32755287; PMCID: PMC7877997.
- Alnor A, Sandberg MB, Gils C, Vinholt PJ. Laboratory tests and outcome for patients with coronavirus disease 2019: a systematic review and meta-analysis. J Appl Lab Med. 2020 Sep;5(5):1038-49. doi: 10.1093/jalm/jfaa098.
- Henry BM, de Oliveira MHS, Benoit S, Plebani M, Lippi G. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis. Clin Chem Lab Med. 2020 Jun;58(7):1021-8. doi: 10.1515/cclm-2020-0369. PMID: 32286245.
- Lin J, Yan H, Chen H, He C, Lin C, He H, et al. COVID-19 and coagulation dysfunction in adults: A systematic review and metaanalysis. J Med Virol. 2021 Feb;93(2):934–44. doi: 10.1002/jmv.26346. PMID: 32706426; PMCID: PMC7405098.
- Angeli F, Reboldi G, Spanevello A, De Ponti R, Visca D, Marazzato J, et al. Electrocardiographic features of patients with COVID-19: One year of unexpected manifestations. Eur J Intern Med. 2022 Jan;95:7-12. doi: 10.1016/j.ejim.2021.10.006. PMID: 34670682; PMCID: PMC8514650.
- Amoozgar B, Kaushal V, Mubashar U, Sen S, Yousaf S, Yotsuya M. Symptomatic pericardial effusion in the setting of asymptomatic COVID-19 infection: a case report. Medicine (Baltimore). 2020 Sep;99(37):e22093. doi: 10.1097/MD.00000000022093. PMID: 32925751; PMCID: PMC7489591.
- Fallek Boldes O, Dahan S, Segal Y, Ben-Ami Shor D, Huber RK, Barshack I, et al. Characteristics of pericardial biopsy: 100 cases in a single center. Isr Med Assoc J. 2019 Mar;21(3):183-8. PMID: 30905104.
- Sagristà-Sauleda J, Merce J, Permanyer-Miralda G, Soler-Soler J. Clinical clues to the causes of large pericardial effusions, Am J Med. 2000 Aug;109(2):95–101. doi:10.1016/s0002-9343(00)00459-9. PMID: 10967149.
- Pradhan A, Vishwakarma P, Bhandari M, Sethi R, Snigdha B, Narain VS, et al. Demographic, clinical and etiological profile of pericardial effusion in India: A single centre experience. Indian J Tuberc. 2022 Apr;69(2):220-6. doi: 10.1016/j.ijtb.2021.08.023. PMID: 35379405.
- Lazar M, Barbu EC, Chitu CE, Anghel AMJ, Niculae CM, Manea ED, et al. Pericardial involvement in severe COVID-19 patients. Medicina (Kaunas). 2022 Aug;58(8):1093. doi: 10.3390/ medicina58081093. PMID: 36013560; PMCID: PMC9415465.
- Ghantous E, Szekely Y, Lichter Y, Levi E, Taieb P, Banai A, et al. Pericardial involvement in patients hospitalized with COVID-19: prevalence, associates, and clinical implications. J Am Heart Assoc. 2022 Apr;11(7):e024363. doi: 10.1161/jaha.121.024363. PMID: 35311354; PMCID: PMC9075494.