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RELATIONSHIP BETWEEN COMORBIDITIES AND THORACIC CT SCAN IMAGES IN COVID-19 CONFIRMED PATIENTS

Silvia Suminto[1], Sri Asriyani[1], Nikmatia Latief[1], Andi Alfian[2], Irawaty Djaharuddin[3], Bachtiar Murtala[1]
1Department of Radiology, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia
2Department of Public Health Sciences, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia
3Department of Pulmonology, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia
silviasuminto13@yahoo.com

ABSTRACT

This study aimed to determine the relationship between comorbidities and disease severity based on chest CT scan images in confirmed COVID-19 patients. The research was conducted in Radiological Department of dr. Wahidin Sudirohusodo Hospital, Makassar with a total of 192 confirmed COVID-19 patients. Analysis of the characteristics of the patient's chest CT scan was performed on the lung and mediastinal window to investigate the appearance of Groundglass opacity (GGO), consolidation, crazy paving, halo sign, air bronchogram sign (ABS), fibrosis, nodules, mediastinal lymphadenopathy, and pleural effusion. Differences in the proportion of CT scan images based on comorbidity were analyzed with chi-square test. There were significant correlation between patients with a history of comorbidities with appearance of GGO, consolidation, crazy paving, nodules, fibrosis, and effusion (all $p<0.05$). There was a significant correlation in patients with a history of hypertension with GGO, and crazy paving (both $p<0.05$), history of diabetes mellitus with a consolidation ($p<0.05$), history of chronic kidney disease with pleural effusion ($p<0.05$), history of malignancy with nodules ($p<0.05$), history of CAD with crazy paving ($p<0.05$), and history of tuberculosis with fibrosis, tree in bud and nodules (all $p<0.05$). This study concluded that patient with comorbidities may showed more variable lesion, which may be identified on chest CT scan.

Keywords: COVID-19, Chest CT scan, comorbidities

INTRODUCTION

In December 2019, several cases of respiratory illness of unknown cause appeared in Wuhan, China, with clinical symptoms resembling viral pneumonia. Analysis of respiration samples showed the presence of a novel coronavirus (SARS-CoV-2) and the disease was named by WHO as Coronavirus Disease 2019 (COVID-19).[1] COVID-19 cases are rapidly increasing in China and globally. In March 2020, the World Health Organization (WHO) declared COVID-19 a pandemic.[2]

Symptoms that appear in patients with COVID-19 vary, from mild respiratory infection symptoms to severe respiratory distress and can even cause death. One of the things that affects the severity of symptoms of COVID-19 patients is comorbidity. Comorbidities are thought to cause an increase in Angiotensin-converting-enzyme-2 (ACE-2) receptors, which is where the COVID-19 virus attaches, causing higher virulence. Comorbidities also increase the inflammatory response, which causes greater tissue damage so that patients can show more severe symptoms.3,4 Data from the task force for accelerating the handling of COVID-19 in Indonesia show that the most common comorbid conditions of COVID-19 positive patients are hypertension (50.5%), diabetes mellitus (34.3%), heart disease (19.9%), and chronic obstructive pulmonary disease (10.1%).[5]

Thoracic computed tomography (CT) scans can play an important role in diagnosing COVID-19 and determining the severity of COVID-19 cases, evaluating pulmonary comorbidities, excluding other pulmonary disorders and evaluating treatment results, so that it can help in the management approach of each patient. Typical features found on a CT scan of COVID-19 are bilateral groundglass opacities (GGO) with the most distribution in the posterior and periphery. Other features such as consolidation, reticular pattern, air bronchogram sign, crazy paving, halo sign, nodules and fibrosis lines can also be found. The CT scan features found can also be influenced by the patient's history of comorbidities. [6,7,8] Therefore, this study aims to determine the potential relationship between comorbidities and thoracic CT scan images in COVID-19 patients.

MATERIALS AND METHODS

This study is a cross-sectional study, conducted at the Radiology Installation of Doctor Wahidin Sudirohusodo Hospital Makassar, with retrospective data collection. Medical record data of confirmed COVID-19 patients who underwent thoracic CT scans at the Radiology Installation of Dr. Wahidin Sudirohusodo Hospital Makassar were

collected from April 2020 to September 2020. Inclusion criteria included all patients with confirmed positive SARS-CoV-2 RT-PCR results who underwent thoracic CT scans at Dokter Wahidin Sudirohusodo Hospital Makassar while exclusion criteria were patients with thoracic MSCT scan recordings that could not be assessed due to technical errors. A total of 192 samples were obtained (97 men, 95 women) which were further categorized according to the presence or absence of comorbidities, the number of comorbidities, and the type of comorbidity. The CT scan instrument used was Light speed VCT 64 Slice GE with the technique of taking scans from the tip of the lung to the level of the costophrenic angle, scan thickness 5 mm with a reconstruction thickness of 1.5 mm. Analysis of the characteristics of the patient's thoracic CT scan images was performed on the lung window (width 1500 HU; level -700 HU), and mediastinal window (width 350 HU; level 40 HU). The following imaging characteristics were evaluated: Groundglass opacity (GGO), consolidation, crazy paving, halo sign, air bronchogram sign (ABS), fibrosis, nodules, mediastinal lymphadenopathy, pleural effusion. In addition, the lesion location was also assessed, which was divided into 20 regions: right superior lobe apical segment (segment 1), right superior lobe posterior segment (segment 2), right superior lobe anterior segment (segment 3), right lobe medius lateral segment (segment 4), right lobe medius medial segment (segment 5), right inferior lobe superior segment (segment 6), right inferior lobe basal medial segment (segment 7), right inferior lobe basal anterior segment (segment 8), right inferior lobe basal lateral segment (segment 9), right inferior lobe basal posterior segment (segment 10), left superior lobe apical segment (segment 11), left superior lobe posterior segment (segment 12), left superior lobe anterior segment (segment 13), superior lingula segment (segment 14), inferior lingula segment (segment 15), left inferior lobe superior segment (segment 16), left inferior lobe basal medial segment (segment 17), left inferior lobe basal anterior segment (segment 18), left inferior lobe basal lateral segment (segment 19), left inferior lobe basal posterior segment (segment 20).

Pengolahan data terkait hubungan komorbiditas dengan gambaran CT scan toraks dilakukan menggunakan uji chi-square pada data kategorik. Pengolahan data akan menggunakan software Statistical Programme Social Science (SPSS) versi 23.0 .

RESULT

Table 1: Characteristics of the samples

Characteristics	**Total (n)**	**Proportion (%)**
AGE		
≤50 tahun	111	57,8
>50 tahun	81	42,2
GENDER		
Male	97	50,6
Female	95	49,4
Presence/No Comorbidities		
Presence	92	47,9
NO	100	52,1
Total Comorbidities		
1	49	53,3
>1	42	46,7
Comorbidities		
Hipertensi	51	26,5
Diabetes Melitus	37	19,2
CKD	29	15,1
CANCER	14	7,2
CAD	14	7,2
Tuberkulosis	6	3,1

Thoracic CT scan features

Table 2: Thoracic CT scan features in participants by lesion type

lesion type	Total (n)	Proportion (%)
GGO	115	59,9
Konsolidasi	41	21,4
Crazy Paving	31	16,1
Halo Sign	5	2,6
Nodul	9	4,7
Tree in Bud	2	1
ABS	5	2,6
KGB	6	3,1
Fibrosis	47	24,5
Efusi	17	8,9

Table 3: Thoracic CT scan features in participants based on lesion distribution

Location	Total (n)	Proportion (%)
Right Lung		
RUL segmen 1	50	28,2
RUL segmen 2	51	28,8
RUL segmen 3	59	33,3
RML segmen 4	52	29,3
RML segmen 5	60	33,8
RLL segmen 6	86	48,5
RLL segmen 7	57	32,2
RLL segmen 8	52	29,3
RLL segmen 9	80	45,1
RLL segmen 10	88	49,7
Left Lung		
LUL segmen 11	53	29,9
LUL segmen 12	53	9,9
LUL segmen 13	52	29,3
LUL segmen 14	38	21,4
LUL segmen 15	40	22,5
LLL segmen 16	79	44,6
LLL segmen 17	50	28,2
LLL segmen 18	50	28,2
LLL segmen 19	72	40,6
LLL segmen 20	77	43,5

Table 2 shows the features of thoracic CT scans in participants based on the type of lesion. Chest CT scan images found were GGO (59.9%), consolidation (21.4%), crazy paving (16.1%), halo sign (2. 6%), nodule (4.7%), tree in bud (1%), air bronchogram sign (2.6%), Table 3 shows the distribution of lesions, with the most locations in the posterior segment of the right inferior lobe (49.7%), lateral segment of the right inferior lobe (45.1%), posterior segment of the left inferior lobe (43.5%), and lateral segment of the left inferior lobe (40.6%). Relationship between Comorbidities and Thoracic CT Scan Images

The relationship between the history of comorbidities and thoracic CT scan images in patients with COVID-19 can be seen in Table 4. Based on the history of comorbidities, a statistically significant relationship was found in patients with GGO (p = 0.005, OR = 2.407, CI 95% = 1.327-4.368), consolidation (p = <0.001, OR = 3.915, CI 95% = 1.825-8.398), crazy paving (p = 0.002, OR 3.915, CI 95% = 1.617-9.085), nodules (p = 0.015, OR 9.429, CI 95% = 1.156-76.925), fibrosis (p = 0.001, OR = 3.436, CI 95% = 1.693-6.971), and effusion (p = 0.001, OR = 9.545, CI 95% = 2.119-43.007). Further analysis was conducted to assess the

association of each comorbidity history with chest CT scan images. Based on the history of hypertension, a statistically significant association was found in patients with GGO (p = <0.001, OR 3.712, CI 95% = 1.725-7.987), consolidation (p=0.048, OR 2.121, CI 95% = 1.020-4.413), and crazy paving (p = <0.001, OR 4.536, CI 95% = 2.033-10.117). Based on the history of diabetes mellitus, a statistically significant association was found only in patients with a consolidation picture (p = 0.003, OR 3.338 CI 95% = 1.551-7.379). Based on the history of CKD, a statistically significant association was found only in patients with pleural effusion (p = 0.003, OR 5.875, CI 95% = 1.930-17.883). Based on the history of malignancy, a statistically significant association was found only in patients with nodule (p = 0.020, OR 7.818, CI 95% = 1.720-35.534). Based on the history of CAD, a statistically significant association was found only in patients with crazy paving (p = 0.013, OR 4.590, CI 95% = 1.468-14.349). Based on the history of tuberculosis, a statistically significant association was found in patients with nodule (p = 0.027, OR = 12.786, CI 95% = 1.995-81.950), tree in bud (p = <0.001, OR = 92.5, CI 95% = 5.357 - 169.91), and fibrosis (p = 0.018, OR 12, CI 95% = 1.306 - 110.302).

Table 4: Relationship between comorbidities and thoracic CT scan images

Lesions on CT scan	Comorbidities (OR; CI 95%)	Hipertensi (OR; CI 95%)	Diabetes Mellitus (OR; CI 95%)	CKD (OR; CI 95%)	Cancer (OR; CI 95%)	CAD (OR; CI 95%)	Tuberkulosis (OR; CI 95%)
GGO	**2,407; 1,327-4,368***	**3,712; 1,725-7,987***	1,298; 0,615-2,740	1,685; 0,697-4,075	1,738; 0,525-5,756	0,648; 0,218-1,928	-
Konsolidasi	**3,915; 1,825-8,398***	**2,121; 1,020-4,413***	**3,338; 1,551-7,379***	1,232; 0,456-3,331	2,191; 0,692-6,940	3,064; 0,999-9,403	-
Crazy paving	3,833; 1,617-9,085*	**4,536; 2,033-10,117***	2,363; 1,001-5,580	0,348; 0,078-1,554	3,248; 1,008-10,461	**4,590; 1,468-14,349***	2,707; 0,474-15,468
Halo sign	0,719; 0,117-4,399	1,878; 0,305-11,572	1,049; 0,114-9,667	1,343; 0,144-12,479	-	-	-
Nodule	**9,429; 1,156-76,925***	2,122; 0,597-8,983	0,510; 0,062-4,212	2,860; 0,671-12,187	**7,818; 1,720-35,534***	-	**12,786; 1,995-81,950***
Tree in bud	1,088; 0,067-17,648	-	4,278; 0,261-70,028	-	13,615; 0,805-230,36	-	**92,5; 5,357-169,91***
Air Bronchogram Sign	1,652; 0,27-10,113	1,878; 0,305-11,572	2,895; 0,466-17,986	1,343; 0,144-12,479	3,346; 0,348-32,15	3,346; 0,348-32,15	-
Lymphadeno-pathy	2,227; 0,398-12,458	2,638; 0,561-14,727	2,157; 0,380-12,250	1,067; 0,120-9,493	7,250; 1,204-43,65	2,662; 0,289-24,5	-
Fibrosis	**3,436; 1,693-6,971***	1,850; 0,911-3,756	1,399; 0,030-3,105	2,031; 0,871-4,733	1,256; 0,375-4,208	1,799; 0,572-5,662	**12,00; 1,306-110,302***
Efusi	**9,545; 2,119-43,007***	1,168; 0,390-3,497	2,534; 0,873-7,370	**5,875; 1,930-17,883***	3,195; 0,797-12,806	1,811; 0,37-8,86	2,821; 0,295-26,996

DISCUSSION

The most prevalent comorbidities found in our study were hypertension, diabetes mellitus, CKD, malignancy, CAD, tuberculosis. There are some similarities related to the types of comorbidities most commonly found with the data reported by the task force for accelerating the handling of COVID-19 in Indonesia, namely hypertension, diabetes mellitus, and heart disease.[5] The most common thoracic CT scan features found in our study were GGO, consolidation, crazy paving, and fibrosis with a dominant distribution on the periphery. [9] Zhao et al suggested that the pathology features that appear in patients infected with SARS-CoV-2 are local or diffuse alveolitis accompanied by interstitial inflammation, which is consistent with the finding of diffuse alveolar damage (DAD). There is serous exudate, fibrin and hyaline membrane in the alveolar cavity, with exudate cells containing monocytes and macrophages. This exudation will appear as GGO (if only part of the alveolar cavity is filled with exudate) and consolidation (if the entire alveolar cavity is filled with exudate).

In addition, hyperemia, edema, and infiltration of monocytes and lymphocytes in the septa are also seen, which when accompanied by GGO will give a crazy paving picture on a thoracic CT scan. Another finding in COVID-

19 pneumonia is the proliferation of fibrotic tissue in type II alveolar epithelium which gives a picture of pulmonary fibrosis. In this observational study, it was also found that the proliferation of fibrous tissue in the alveolar septa and alveolar destruction in the peripheral part was more severe than in the central part. his can be attributed to SARS-CoV-2 infection initially occurring in the periphery, resulting in more prolonged damage.[10] Several previous studies have found a similar picture in patients with confirmed COVID-19. Zhu et al stated that the most common finding on thoracic CT scans of confirmed COVID-19 patients was GGO (68.1%), followed by air bronchogram (44.7%), crazy paving (35.6%) and consolidation (32%). Less frequent findings were pleural thickening (27.1%), lymphadenopathy and pleural effusion.[1]

Li et al also found similar thoracic CT scan patterns, which included GGO (97.6%), linear opacity (65.1%), consolidation (63.9%), interobular septal thickening (62.7%) and crazy paving pattern (36.1%). Patients with severe symptoms showed a higher incidence of consolidation, linear opacity, crazy paving pattern and bronchial wall thickening than patients with mild symptoms.[11] Based on the distribution of lesions, the most lesions were found in the posterobasal segment of the inferior lobe, followed by the laterobasal segment of the inferior lobe. This imaging picture is also in accordance with previous studies by Yang et al, namely posterior involvement and predominance in the lower lobe when compared to the upper and middle lobes. There was no significant difference between the right or left lung involved.[12,13]

Based on chi square analysis between the history of comorbidities and thoracic CT scan images, there were statistically significant results in patients with a history of comorbidities for GGO, consolidation, crazy paving, nodules, fibrosis, effusion. This finding may be attributed to the higher expression of ACE-2 receptors in patients with comorbidities so that more viruses reach alveolar type II cells, and cause an inflammatory response, which can be seen on CT scans.[14,15]

In the analysis of each comorbidity on thoracic CT scan images, statistically significant results were found in patients with a history of hypertension with GGO images, and crazy paving. Hypertension is known to cause overactivation of the RAAS, and an increase in angiotensin II. In high angiotensin II conditions, ACE-2 receptors cannot bind to angiotensin 1 receptors so that more free ACE-2 can bind to the SARS-CoV-2 virus. Angiotensin II also causes vasoconstriction and increased permeability which may explain the crazy paving images that are more commonly found on thoracic CT scans of patients with comorbid hypertension.[16,17] Baeis et al. suggested the association of crazy paving with the cytokine storm induced by viral invasion, and is a sign of the progress or peak of COVID-19. Patients with crazy paving patterns are also associated with symptoms of hypoxemia (SpO2 < 90% on room air).[18] In this study, there were statistically significant results in patients with a history of diabetes mellitus with a picture of consolidation. Diabetics are more susceptible to infectious diseases due to the release of enzymes related to tissue damage, uncontrolled inflammatory response, and hypercoagulable state due to dysregulation of glucose metabolism. Consolidation is also associated with more fluid exudation in the alveoli suggesting that diabetic patients are prone to more extensive lung damage. This finding is consistent with previous research conducted by Lu et al, where a wider consolidation volume was obtained in patients with diabetes mellitus compared to normal patients, indicating that COVID-19 patients with diabetes mellitus have a higher inflammatory status and a decreased ability of the body to kill the virus, resulting in faster progress.[19,20] For other findings, this study found statistically significant results in patients with a history of CKD with a picture of pleural effusion; Patients with a history of malignancy with a picture of nodules; Patients with a history of CAD with a crazy paving picture; patients with a history of tuberculosis with a picture of fibrosis, tree in bud and nodules. However, the thoracic CT scan images found can overlap with the picture of the accompanying disease, because patients with CKD without COVID-19 can also find pleural effusion. In patients with malignancy without COVID-19, nodules can also be found, and in patients with a history of tuberculosis without COVID-19, fibrosis, tree in bud and nodules can be found. In addition, no significant relationship was found in the other variables studied. This retrospective study has several limitations, namely, the analysis of thoracic CT scans was carried out on the first CT scan taken at the time of hospitalization, so this study was not controlled by the number of days of symptom onset, which could affect the thoracic CT scan images found. This study also did not distinguish between patients with comorbidities who received routine treatment and those who did not, which may affect the extent and findings of thoracic CT scan images.

With the increase in new and severe cases of COVID-19, patient management has become a challenging issue during this COVID-19 pandemic. Proper identification of patients at risk of developing acute respiratory distress syndrome can help determine treatment plans, thereby optimizing the use of hospital facilities and preventing worsening. Based on the results of this study, thoracic CT scans can provide images of lesions in the lungs, especially in patients with comorbidities, which can help stratify patients and determine treatment plans for patients with confirmed COVID-19.

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