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Chest Computed Tomography Patterns in Patients with COVID-19 According to Evolution Phases: Multicenter Study with 463 Patients

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Abstract: Chest CT has proven to be a fundamental tool in COVID-19, with variable findings. The aim of this article is to analyze the prevalence of chest CT patterns in COVID-19 according to the evolution time of the pathology, and to define if there are dominant patterns in each phase. CT studies of COVID-19 patients performed in local clinics over a 3-month period were retrospectively reviewed. The studies were classified as: phase 1 (0-4 days), phase 2 (5-8), phase 3 (9-13) and phase 4

(≥14), and CT findings as: normal study, ground glass opacities (GGO), consolidations, crazy paving and architectural distortion. The predominant finding was identified as single or combined pattern. The results included 463 CT studies, 266 men (57.4%), aged 19–96 years. 18.1% of CT scans were normal (n=84), with a predominance in phase 1 ($p<0.001$). In relation to pathological CT, male patients predominated ($p<0.006$), with an age older than in normal CT ($p<0.001$). In all stages, GGO pattern predominated as the single pattern, similar in all phases ($p=0.545$), and always above 65%. In combinations of patterns, GGO with consolidation was the prevalent one, with a peak in phase 3 (63.3%). In conclusion, in all the phases of COVID-19, GGO prevail over other CT patterns. Initial CT phase may also be presented with a normal CT; intermediate stages (phase 2 and 3) with GGO in combination with consolidation; and phase 4 with a combination of GGO and architectural distortion.

Keywords: COVID-19, Tomography, Lung Diseases, Thorax

1. Introduction

The COVID-19 global pandemic has become a challenge for all countries of the world, especially for their health systems, quickly becoming a global health emergency. Until August 2021, more than 220 million cases have been reported worldwide and more than 5 million in Argentina [1].

Diagnosis of COVID-19 is typically realized using polymerase chain reaction (PCR) testing via nasal swab, which detects genetic material of the virus [2]. Chest computed tomography (CT) has proven to be a fundamental tool. Due to its findings, it can be used to diagnose the disease in certain cases, to study its evolution and to monitor the response to treatment [3-5]. However, imaging screening is not routinely recommended in COVID-19 patients, leaving images only for certain well-identified clinical scenarios, although recommendations can vary according to each institution [6, 7].

There is a wide range of tomographic findings that can be observed in patients with COVID-19, depending on the degree of inflammation, the involvement or destruction of the lung parenchyma, the patient's conditions and the time of evolution of the pathology [8].

From the published literature, 4 phases or stages of the disease emerge, considered from the onset of symptoms, with their consequent evolutionary pulmonary tomographic findings [9, 10].

The objective of this study is to describe and analyze the pulmonary manifestations in the chest tomography of patients with COVID-19 according to their evolutionary phase, and define if there are dominant CT patterns in each phase.

2. Materials and Methods

This is a retrospective, observational, analytical multicenter study carried out in the city of La Plata, Buenos Aires, Argentina, which included patients with a diagnosis of COVID-19, in a period of 3 months (June-August 2020). The data collected was anonymized and had the approval of the ethics committee of the main research institution (HSMLP2020 / 0033). Due to the retrospective design of the study, the context of the pandemic situation and because it is of great epidemiological interest, the requirement to obtain informed consent for this retrospective study was waived.

2.1. Patients and Data Collection

Patients older than 15 years with COVID-19 confirmed by PCR test were included, who underwent a chest CT scan in the different participating institutions between June and August 2020. Data were obtained from the review of medical records at Imaging Diagnostic services of the city.

Patients with chest CT and characteristic symptoms of COVID but with a negative PCR test were excluded.

The data of each patient (sex, age, day of onset of symptoms and day of CT) were transcribed from each institution to an anonymous file prepared for the study through the Google Forms platform, where the imaging findings were transferred according to the phase in which the patient was at the time of performing the CT. Information upload into Google Forms was carried out by the main imaging specialist of each institution, guaranteeing the anonymous upload of patient data at all times, without details that would allow their identification.

CT images were sent from each participating center in DICOM format, anonymized, to the main investigators of the coordinating center for classification, review and archiving, through an email address generated for this purpose.

The reason for performing the CT or the symptoms of each patient at the time of the scan was not analyzed because, as this was a multicenter study, there were different protocols in each center.

2.2. Image Acquisition

Chest CT scans were performed with different equipment according to each participating institution, and all included images from the apexes to the lung bases, in the supine position and in the inspiratory phase, with other technical parameters which differed slightly according to each center and the patient's conditions.

High resolution and soft tissue filters were used to assess the mediastinum and lung parenchyma, respectively.

The images were stored in DICOM format for later analysis.

2.3. CT Image Interpretation

Chest CT scans were reviewed and evaluated by 2 experienced radiologists with 13 and 15 years of experience (II and JM respectively), who used Toshiba Vítrea workstation, model Z 600.

CT were first classified according to the time of their performance in terms of the evolutionary phase of the COVID-19 disease, considering day 0 to be the one with the onset of symptoms that determined the application of the PCR test. The evolutionary phases of the pathology were divided as follows: phase 1 (0-4 days), phase 2 (5-8 days), phase 3 (9-13 days) and phase 4 (more than 14 days).

Five possible patterns or findings of lung involvement were defined, based on the terms of the Fleischner Society [11]:

1. Normal CT.
2. Ground glass opacity (GGO): area of greatest attenuation in the parenchyma with preservation and observation of the underlying vascular network.
3. Consolidation: homogeneous opacity that does not allow the observation of the underlying vasculature.
4. Crazy Paving: ground glass opacity with overlapping interlobular septal thickening.
5. Architectural distortion: increased density with retraction of pleural structures, subpleural bands, bronchial or vascular retraction.

It was evaluated whether a single tomographic pattern was observed, or in the case of combined patterns, which of them predominated over the other, considering the one that involved the greatest number of lobes to be dominant. The distribution of pulmonary alterations was not evaluated.

Examples of each pattern can be observed in Figure 1.

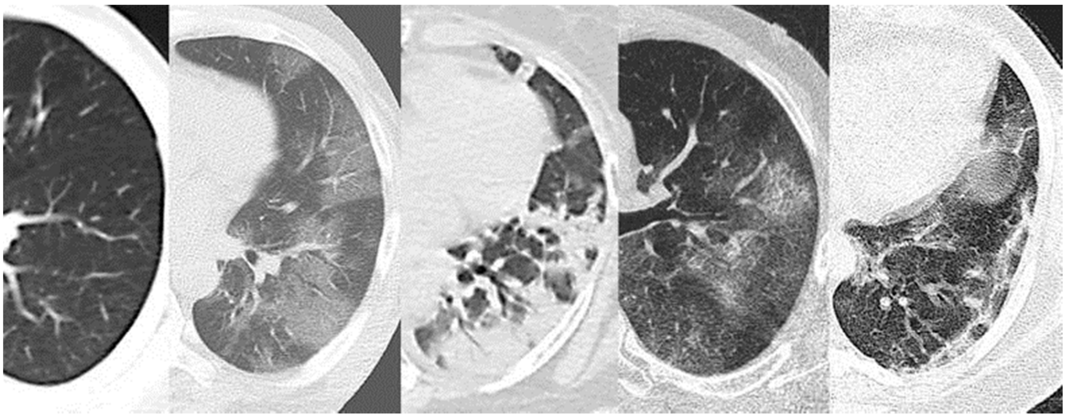

Figure 1. *CT with examples of different tomographic patterns. From left to right: normal CT, ground glass opacities, consolidations, crazy paving and architectural distortion.*

2.4. Statistical Analysis

Patient data was transferred from Google Forms to an Excel 2016 spreadsheet where the different variables were analyzed.

Categorical variables were expressed as percentages, and were compared with X^2 tests. Quantitative variables were expressed as mean ± standard deviation or as median and interquartile range (IQR), and compared using the Student's T test or Mann Whitney's U-test, according to the presence or absence of normal distribution, respectively.

Statistical analysis was performed using the IBM SPSS program, version 2017.

A value of $p<0.05$ was considered statistically significant.

3. Results

3.1. Patient Characteristics

463 patients with chest CT in different evolutionary phases of the disease were included, aged between 19 and 96 years, of which 266 were men (57.4%) and 197 women (42.6%). No CT studies were performed in patients aged 16-18.

13 diagnostic imaging services participated in the study, 3 belonging to public institutions and 10 to private institutions. The collaboration of each center can be seen as a graphic in the appendix.

Of the total of patients analyzed, the majority were found in phase 1, corresponding to 45.1% (n=209) of the cases; 23.5% (n=109) were in phase 2; 15.9% (n=74) in phase 3 and 15.5% in phase 4 (n=71), as summarized in Figure 2.

Of the 463 scans included, 84 were normal (18.1%) and 379 pathological (81.9%). In the group with pathological CT, male patients predominated, with an older age than in the group with normal CT, yielding statistically significant differences (Table 1).

Table 1. *Poblation characteristics.*

	NORMAL CT (n=84)	PATHOLOGICAL CT (n=379)	p
MALE	44%	60,4%	0,006
AGE (years)	47 +/- 17	55 +/- 16	0,001

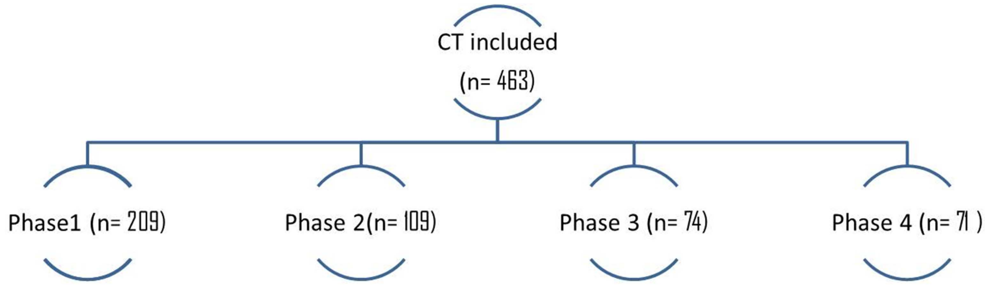

Figure 2. *CT evaluated according to the stage of the disease.*

3.2. General Findings

Of the 84 normal CT scans, the majority (n=56) were seen in phase 1 of the disease; 12 normal cases were observed in phase 2; only 5 cases in phase 3; and 11 in phase 4. The detail of each phase with normal CT scans is summarized in Table 2. A statistically significant predominance of normal CT scans was found in phase 1 (p<0.001).

Regarding pathological CT (n=379), it was observed that in 54.4% of the cases, a single pathological tomographic pattern prevailed (n=252), compared to those in which 2 patterns were identified (n=127).

Overall, the predominant pathological pattern was GGO, observed in 65.2% of the CT, followed by consolidation (26.6%), crazy paving (9.1%) and architectural distortion (8,6%).

Table 2. *Distribution of normal CT according to phase (n=84).*

NORMAL CT	PHASE 1	PHASE 2	PHASE 3	PHASE 4	p
	26,8%	11%	6,8%	1,5%	<0,001

3.3. CT Findings According to Phases

3.3.1. Phase 1

The total number of patients evaluated in phase 1 was 209. Of these, 26.8% (n=56) were normal as previously mentioned. Regarding the 153 pathological CT, in 108 a single tomographic pattern was observed, with 76.9% corresponding to GGO (Figure 3), followed by consolidation (13.9%), crazy paving (8.3%) and architectural distortion (0.9%). Within the combined tomographic patterns (n=45), GGO and consolidation was the most frequent in this phase, reaching 60%, compared to the remaining combinations that did not exceed 20%.

The predominance of GGO in the cases of two patterns reached 77.8%, above the consolidation with 15.6% and followed by the crazy paving pattern with 6.7%. No patterns with predominance of architectural distortion were found in this phase.

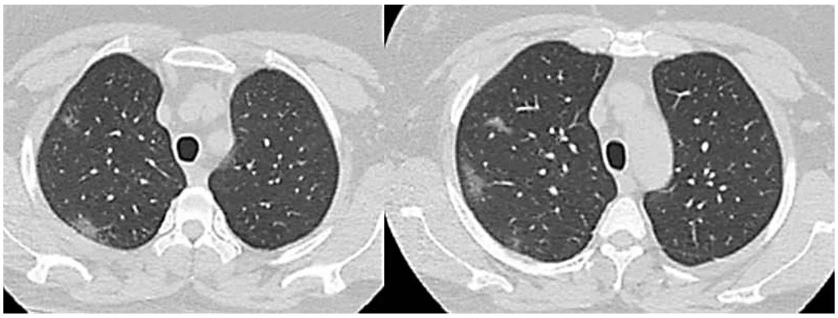

Figure 3. *54-year-old female patient with COVID-19. The CT was performed on day 3 of COVID (phase 1), observing ground glass opacities as the only pattern.*

3.3.2. Phase 2

The total number of patients evaluated in phase 2 was 109. Of these, 12 were normal (11%) as previously mentioned. Regarding the 97 pathological CT, in 65 (67%) a single tomographic pattern was identified. In this group, GGO predominated, reaching 67.7% (n=44) with a great difference compared to consolidation which follows with 18.5%, crazy paving with 10.8% and distortion with only 3.1%.

Within the combined patterns (n=32), GGO with consolidation prevailed (Figure 4), reaching 43.8% in this phase, followed by the combination of GGO with architectural distortion, which reached 37.5%.

GGO continued to be the most frequent pattern with 71.9%, followed by consolidation (15.6%).

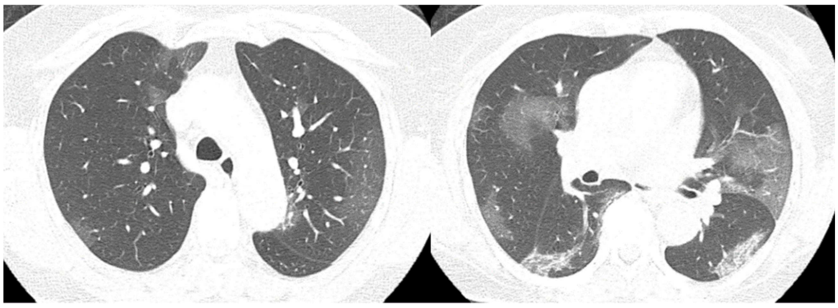

Figure 4. *47-year-old male patient with COVID-19. The CT was performed on day 7 of COVID (phase 2), observing a combination of patterns, with the presence of ground glass opacities and consolidations.*

3.3.3. Phase 3

The total number of patients evaluated in phase 3 was 74. Of these, only 5 cases were normal (6.8%). Regarding the 69 pathological CT, in 36 studies (52.2%) a single tomographic pattern was identified, with a marked predominance of ground glass opacities that reached 77.8% (n=28) followed by consolidation in 16.7% being the values of crazy paving and architectural distortion equal, with 2.8% each.

Within the combined patterns (n=33), GGO and consolidation prevailed, reaching 63.6% in this phase (Figure 5), followed by the combination of GGO with architectural distortion (18.2%).

In this phase, the prevalence of GGO persisted with 63.6% as the dominant pattern, followed by consolidation with 21.2%.

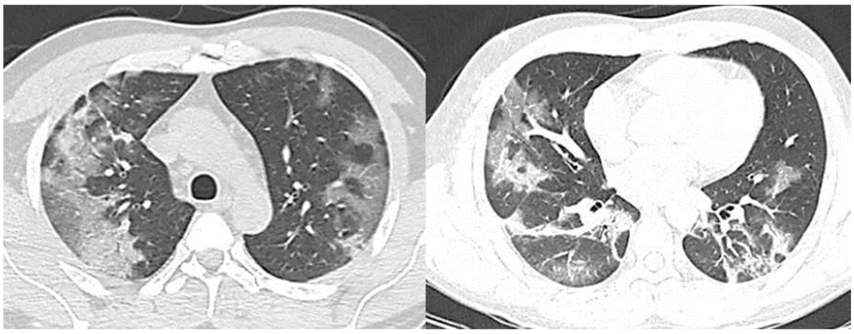

Figure 5. *54-year-old male patient with COVID-19. The CT was performed on day 11 of COVID (phase 3), observing a combination of patterns, with the presence of ground glass opacities and consolidations.*

3.3.4. Phase 4

The total number of patients evaluated in phase 4 was 71. Of these, 11 cases were normal (15.5%). Regarding the 60 pathological CT, in 43 (71.7%) a single tomographic pattern was identified, continuing the predominance of GGO that reached 72.1% (n=31), followed by consolidation with 27.9%. No CT with crazy paving or architectural distortion was observed. Within the combined patterns (n=17), GGO and architectural distortion prevailed, reaching 41.2% (Figure 6) over the combination between GGO and consolidation, which reached 35,3%. In this last phase, GGO also presented as the prevailing pattern with 70.6%.

The detail by phase of the single tomographic patterns is summarized in Table 3 and the detail of the combined patterns according to phase in Table 4.

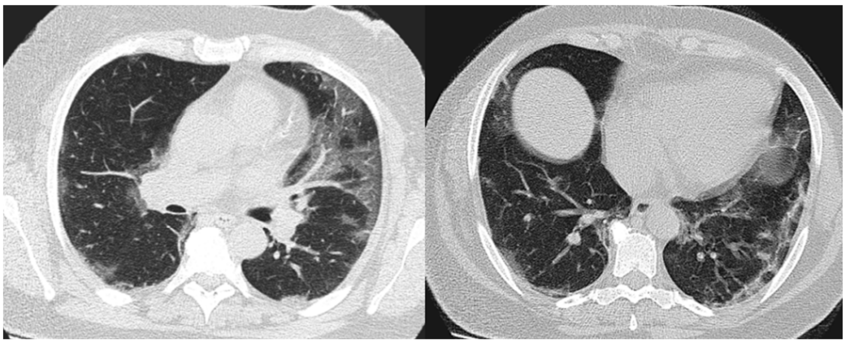

Figure 6. *47-year-old female patient with COVID-19. The CT was performed on day 14 of COVID (phase 4), showing a combination of patterns, with the presence of ground glass opacities and architectural distortion.*

Table 3. *Patients with a single tomographic pattern according to phase (n=252).*

PATTERN	PHASE 1 (n=108)	PHASE 2 (n=65)	PHASE 3 (n=36)	PHASE 4 (n=43)	p
GGO	76,9%	67,7%	77,8%	72,1%	0,545
Consolidation	13,9%	18,5%	16,7%	27,9%	0,244
Crazy Paving	8,3%	10,8%	2,8%	0%	0,106
Architectural Distortion	0,9%	3,1%	2,8%	0%	0,523

Table 4. *Most frequent combinations of tomographic patterns.*

PATTERNS	PHASE 1 (n=45)	PHASE 2 (n=32)	PHASE 3 (n=33)	PHASE 4 (n=17)	p
GGO and Consolidation	60%	43,8%	63,6%	35,3%	0,132
GGO and Crazy Paving	20%	12,5%	9,1%	5,9%	0,239
GGO and Architectural Distortion	13,3%	37,5%	18,2%	41,2%	0,026*

*The statistically significant difference was found between phases 2 and 1 (p 0.01) and phases 4 and 1 (0.02).

3.4. General Findings of Patterns

Regarding the CT with a single pattern, GGO remained at values higher than 70% in phase 1, 3 and 4, reaching 67% in phase 2. These percentages were higher than those obtained by consolidation, which had its highest prevalence in phase 4, but not exceeding 28%.

The crazy paving single pattern was rare in all phases, although it prevailed in phase 2 (10.8%), compared to phases 1 and 3, with no cases in phase 4. Similar findings were obtained with architectural distortion, which reached its maximum value of 3.1% in phase 2, decreasing in phase 1 and 3 respectively, with no cases in phase 4.

Regarding the combinations of patterns, GGO with consolidation was the prevalent one, reaching its maximum percentage in phase 3 (63.3%), very close to the value in phase 1 (60%).

No statistically significant differences were found regarding the predominance of GGO according to disease stages (p=0.545). Likewise, within the remaining isolated patterns, no statistically significant differences were found in their prevalence according to disease phases.

Within the combined patterns, although the combined pattern of GGO and consolidation prevailed, its distribution was similar in all phases, with no statistically significant difference between them (p=0.13).

Conversely, the combination of GGO and architectural distortion was most prevalent in phases 2 and 4 compared to phase 1 and 3, which was statistically significant (p<0,026).

4. Discussion

Due to the involvement of the respiratory system by COVID-19, pulmonary images play a fundamental role in the evaluation and follow-up of this entity, as well as in the adequate management and treatment of the patient [12]. The present study was carried out in order to describe and analyze chest CT findings in patients with COVID-19 disease according to the time of evolution of the pathology.

Ground glass opacities represent the most frequent CT pattern observed throughout the entire evolution of COVID-19, that is, in all its evolutionary phases, reaching approximately 70% of pathological cases. These findings match those of Soriano Aguadero I. et al [13], with 60%, and those of Xu Xi et al [14], with 72%, confirming that GGO constitute a highly prevalent finding in COVID-19. Moreover, some authors such as Guan CS. et al [15] and Cheng Z. et al [16] found GGO in all pathological CT with COVID-19.

In our study, GGO remains highly prevalent in all evolutionary phases of COVID-19, unlike the findings of Lei P. et al [17] and Saleshi [12], who mention that GGO decrease as the disease progresses. A theory for this is presented by Pan et al [9], who explain that the high percentage of GGO in the final phase is due to the resorption of the consolidations in the intermediate phases, with the consequent passage through the GGO before returning to lung normality. However, considering that consolidations never reach the same percentage as GGO in the intermediate phases, Pan's theory may either not really apply, or it may not be the only reason for the predominance of GGO even in the final stages of COVID-19.

Although some authors such as Parekh M. et al [18] point out that there are other conditions that occur with a predominance of GGO, in the current epidemiological context and due the notorious prevalence obtained in the present study of this pattern over the rest, any CT with GGO should be considered COVID-19 infection until proven otherwise.

According to Revzin V, et al [3], there are 2 types of GGO, the pure and the mixed pattern, where GGO is combined with consolidations. Salehi S, et al [12] mention as infrequent the association of GGO and consolidation at the onset of the disease. In discrepancy with this author, this combination was the most frequent at the onset of the disease in our study, with a prevalence of 60% in phase 1, with values similar to those obtained by Kanne J. [19]. The prevalence of this combination in phases 2 and 3 is similar to that previously mentioned by various authors [20-21], highlighting the clear predominance of ground glass opacities, with or without consolidation, as mentioned by Yu M, et al. [22].

The crazy paving pattern deserves a different analysis. It has not shown significant prevalence in our study, in discrepancy with Shi H, et al [23] and others [9, 24], who obtained high prevalence of this pattern in the second disease stage. This could be due to the difficulty of identifying crazy paving as a pattern to begin with. Despite having a clear definition in the Fleischner society glossary [11], its identification is difficult and controversial since there is a tendency to include it in GGO and /or in the consolidation pattern instead.

Architectural distortion in combination with GGO has a high prevalence in phase 4 of COVID-19, in agreement with that reported by Kwee TC, et al [25].

Regarding normal CT scans in patients with COVID-19, our study reveals a percentage of normal CT higher than that published by other authors such as Adams et al [26], who obtained 10.6% of normal CT scans. Likewise, our percentages of normality are higher in the detailed analysis of phase 1, being 26.8% with respect to the total of patients in this phase, higher values than those described by Wang Y. et al [24] and Ling Z. et al [27], who obtained 14% and 17% normality in phase 1, respectively. However, our results were similar to those obtained by Ding X. et al [28], who found 21.2% of normal CT scans in phase 1. In contrast to this, some authors have obtained a higher percentage of normality in phase 1 such as Bernheim A. et al [29], who obtained 56% of normal CT scans in the initial stage. To account for these discrepancies, it is worth noting that our study covers a greater number of patients than other studies. Another factor could be that because our study was multicenter, each institution presents its own protocol to perform CT scans on patients with COVID-19.

To date, no studies have been published to evaluate the tomographic phases of COVID-19 with such a large number of patients as ours, therefore our conclusions regarding each phase can be considered relevant and useful for the evaluation of images within such a unique pandemic.

The limitations of our study include the lack of evaluation of the distribution of the patterns (central or peripheral; or uni- or bilateral), and the correlation of the findings with the clinical manifestations of each patient.

5. Conclusion

In all the evolutionary phases of the COVID-19 disease, ground glass opacities prevail over the other CT patterns, without significant variations in their prevalence regarding time elapsed since the onset of symptoms. Beyond this clear predominance of ground glass opacities, the initial CT phase of the COVID-19 disease may also appear with a normal tomography; phase 2 and phase 3 with ground glass opacities in combination with consolidation; and phase 4 with a combination of GGO and architectural distortion, although ground glass opacities always prevail over other possible CT patterns.

In the current epidemiological context, any ground glass opacities in a chest CT should be considered as possible COVID-19. In contrast, in the absence of ground glass opacities in a pathological chest CT, another entity should be considered rather than COVID-19.

Knowledge of CT evolution of COVID-19 is extremely useful for radiologists, in order to know its dynamics and eventually distinguish this process from other entities, to facilitate the management and timely treatment of these patients.

Appendix

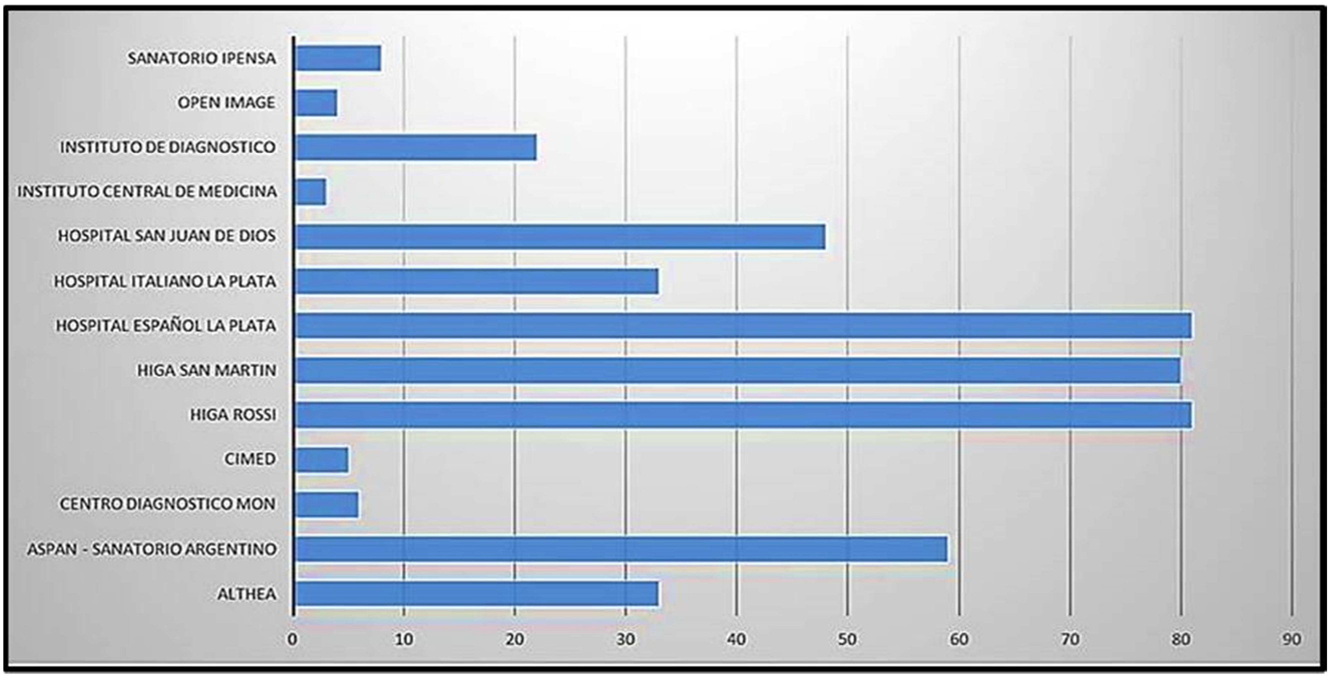

Figure 7. *Number of CT scans provided by each center for the study.*

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