

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active. *et al.* with the exception of a pre-symptomatic phase.<sup>7</sup> CT findings begin as single or multifocal ground-glass opacities, pulmonary nodules, or air bronchograms, which progress with development of interlobular septal thickening and crazy paving, before regression in both size and density at the end of the second week of infection. Opacities often have extensive distribution, typically bilaterally, but also seen unilaterally, with occasional round morphology or reversed-halo or atoll sign.<sup>5</sup> In the dissipation phase, there may be continued patchy consolidative opacities in addition to reticular "strip-like" opacities, bronchial wall thickening, and interlobular septal thickening.<sup>18</sup>

The characteristic ultrasound findings (bilateral and multilobar B-lines, subpleural consolidates, irregular pleural line, and decreased blood flow<sup>3,4,9</sup>) have been shown to be highly consistent with CT findings<sup>3,4</sup> and can be expected to develop over a similar timeline. During the first few days of symptom presentation, scattered unilateral or bilateral multilobar B-lines can be visualised.<sup>3,9</sup> As the disease progresses from the end of week 1 through week 2, development of alveolar interstitial syndrome with diffuse, bilateral B-lines can occur in addition to an irregular pleural line with punctate defects and formation of subpleural consolidations with visible air bronchograms. Lastly, after the end of week 2 during convalescence, there can be an expected regression of prior findings with re-emergence of A-lines.<sup>9</sup> A summary of findings is listed in Table 1.

Although the literature remains limited, there is still a clear benefit for clinicians to be familiar with ultrasound findings and their progression in COVID-19 patients. It may be particularly useful in helping emergency personnel to triage and diagnose suspected patients,<sup>4</sup> but also for monitoring progression of the disease throughout hospitalisation. Additionally, it offers substantial benefits in comparison to CT imaging, including portability, lower cost, reduced radiation, and ease of sterilisation. Physicians are

#### Table 1

Timeline of common findings of COVID-19 in computed tomography (CT) and ultrasound.  $^{\rm 1,3-9}$ 

Symptom onset	СТ	Ultrasound
(days)		
0-3	Single or multiple scattered and patchy GGO, patchy grid-like thickness of interlobular septa	Unilateral or bilateral focal B-lines
3–7	Fused and large-scale consolidation with internal air bronchograms, crazy-paving pattern, multi-lobe GGO	Bilateral diffuse B-lines with irregular pleural line and punctate defects, subpleural
7–14	Multiple patchy consolidations that are reduced in size and density, crazy-paving pattern	consolidations, air bronchograms
14–21	Reduced patchy consolidations, strip-like opacities, grid-like thickening of interlobular septum, minimal crazy paving	Resolving consolidations, A-lines

GGO, ground-glass opacity.

encouraged to be familiar with and to utilise lung ultrasound in the management of COVID-19 patients.

# **Conflict of interest**

The author declares no conflict of interest.

## References

- 1. Jin Y, Cai L, Cheng ZS, *et al.* Zhongnan hospital of Wuhan university novel coronavirus management and research team; evidence-based medicine chapter of China international exchange and promotive association for medical and health care (CPAM). A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). *Mil Med Res* 2020;**7**:4.
- National Health Commission of the people's Republic of China. Diagnosis and treatment of novel coronavirus pneumonia (trial, the fifth version)[EB/ OL]. NHC 2020. Available at: http://www.nhc.gov.cn/yzygj/s7653p/202002/ 3b09b894ac9b4204a79db5b8912d4440.shtml (accessed Feb 28, 2020).
- Huang Y, Wang S, Liu Y, et al. A preliminary study on the ultrasonic manifestations of peripulmonary lesions of non-critical novel coronavirus pneumonia (COVID-19). SSRN 2020:3544750. <u>https://doi.org/10.2139/</u> ssrn.3544750.
- Poggiali E, Dacrema A, Bastoni D, et al. Can lung US help critical care clinicians in the early diagnosis of novel coronavirus (COVID-19) pneumonia? Radiology 2020:200847. <u>https://doi.org/10.1148/</u> radiol.2020200847.
- Bernheim A, Mei X, Huang M, *et al.* Chest CT findings in coronavirus disease-19 (COVID-19): relationship to duration of infection. *Radiology* 2020:200463. https://doi.org/10.1148/radiol.2020200463.
- Kanne J, Little B, Chung J, et al. Essentials for radiologists on COVID-19: an update—radiology scientific expert panel. Radiology 2020:200527. https://doi.org/10.1148/radiol.2020200527.
- Pan F, Ye T, Sun P, et al. Time course of lung changes on chest CT during recovery from 2019 novel coronavirus (COVID-19) pneumonia. Radiology 2020:200370. https://doi.org/10.1148/radiol.2020200370.
- Salehi S, Abedi A, Balakrishnan S, et al. Coronavirus disease 2019 (COVID-19): a systematic review of imaging findings in 919 patients. AJR Am J Roentgenol 2020:23034.
- 9. Peng Q, Wang X, Zhang L. Findings of lung ultrasonography of novel corona virus pneumonia during the 2019–2020 epidemic. *Intensive Care Med* 2020, https://doi.org/10.1007/s00134-020-05996-6.

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# Impact of gender on extent of lung injury in COVID-19



*Sir*—Data from the World Health Organization (WHO) and China indicate significant higher mortality rates in male patients with coronavirus disease 2019 (COVID-19)<sup>1,2</sup>; however, this gender gap is far less noticeable when it comes to the prevalence of COVID-19 infection, indicating that women are as likely as men to contract the virus but are

less likely to die. The goal of the present study was therefore to assess whether male patients with COVID-19 infection show more extensive lung involvement than female patients.

Data were collected from the Imelda Hospital. Bonheiden, Belgium. A total of 216 reverse transcription polymerase chain reaction (RT-PCR)-confirmed COVID-19 patients who underwent chest computed tomography (CT) at admission were retrospectively enrolled from 14 March to 5 April. A semi-quantitative scoring system was used to estimate the extent of pulmonary involvement as reported previously.<sup>3</sup> In short, each lobe was scored from 0 to 5 with a total score ranging from 0 to 25: score 0, 0% involvement; score 1, <5% involvement; score 2, 5-25% involvement; score 3, 26-50% involvement; score 4, 51-75% involvement, score 5, 76-100% involvement. Patients were divided into four groups based on time since symptom onset: early stage (0-4 days), progressive stage (5-8 days), peak stage (10-13 days)days), and absorption stage (>14 days).<sup>3</sup> Data were analysed using R v.3.5.2. (Foundation for Statistical Computing, Vienna, Austria). This study was approved by the institutional review board and informed consent was waived. This study followed the reporting guidelines for cohort studies (STROBE statement). Summary statistics for continuous variables are reported as means  $\pm$  standard deviations (SD) or as medians with interquartile ranges (IQR), as appropriate. Student's t-test for independent samples and the Mann–Whitney U-test were used to compare continuous variables between groups. Categorical variables are reported absolute numbers and percentages, and were compared by using the chi-squared test. A two-tailed pvalue of <0.05 was considered to indicate statistical significance.

Patient demographics and CT findings are summarised in Table 1. There were no significant differences between male and female patients in age or time since symptom onset. Heart disease was more prevalent in men (27.2% versus 13.3%, p=0.02). CT severity score was significantly greater in men (9.2±5 versus 7.0±4.8, p=0.001) with a trend toward more bilateral lung involvement (89.3% versus 78.8%, p=0.06). The differences in lung involvement scores were most pronounced during the progressive and peak stages of disease (Fig 1).

This study is the first to use CT to demonstrate more extensive lung disease in male patients with COVID-19, despite similar age and time from symptom onset for both gender groups. Male vulnerability to COVID-19 may, in part, be explained by a gender disparity in behaviour with men more likely than women to engage in unhealthy habits such as smoking and their poorer and less timely use of medical advice.<sup>4</sup> Additionally, biological differences in the immune response may result in differential susceptibility of males and females to infectious diseases (e.g., animal studies have suggested a protective effect of oestrogen against severe acute respiratory syndrome coronavirus [SARS-CoV], a virus closely related to SARS-CoV 2).<sup>5,6</sup> These results may advance

#### Table 1

Patient characteristics and CT findings.

Physical examination and demographics	All ( <i>n</i> =216)	Male ( <i>n</i> =103)	Female (n=113)	p-Value
Age (years) <sup>a</sup>	65.4±17.1	67.6±14.6	63.3±19.0	0.09
BMI (kg/m <sup>2</sup> ) <sup>a</sup>	$28.7 \pm 3.7$	29.1±3.6	$28.3 \pm 4.3$	0.80
Time since symptom	7 (4–10)	7 (5–9)	6 (3–10)	0.22
onset (days) <sup>b</sup>				
Clinical symptoms				
Fever	117 (54.2)	62 (60.2)	55 (48.7)	0.12
Cough	118 (54.6)	58 (56.3)	60 (53.1)	0.74
Dyspnoea	105 (48.6)	47 (45.6)	58 (51.3)	0.48
Chest pain	22 (10.2)	9 (8.7)	13 (11.5)	0.66
Current smoker	19 (8.8)	11 (10.7)	8 (7.1)	0.49
Arterial hypertension	70 (32.4)	31 (30.1)	39 (34.5)	0.58
Diabetes mellitus	36 (16.7)	21 (20.4)	15 (13.3)	0.22
Heart disease	43 (19.9)	28 (27.2)	15 (13.3)	0.02
Chest CT findings				
Ground-glass opacities	188 (87.0)	94 (91.3)	94 (83.2)	0.12
Consolidation	109 (50.5)	47 (45.6)	62 (54.9)	0.22
Bilateral involvement	181 (83.8)	92 (89.3)	89 (78.8)	0.06
Lymphadenopathy	34 (15.7)	13 (12.6)	21 (18.6)	0.31
Pleural effusion	14 (6.5)	6 (5.8)	8 (7.1)	0.92
CT severity score <sup>a</sup>	8.0±5.0	9.2±5.0	7.0±4.8	0.001

Unless otherwise specified, data are numbers of patients, with percentages in parentheses.

CT, computed tomography.

 $^{\rm a}$  Data are means  $\pm$  SD.

<sup>b</sup> Data are medians, with interquartile ranges in parentheses.

our understanding of the epidemiological differences in patient outcome.

This study was limited by a lack of information on whether this more extensive lung involvement on chest CT correlated with a more adverse clinical outcome during follow-up.



**Figure 1** CT severity scores for male and female patients. Patients were grouped based on time from symptom onset. \*p<0.05 between male and female patients.

# **Conflicts of interest**

The authors declare no conflict of interest

# References

- World Health Organization. Coronavirus disease (COVID-19) outbreak. 2020. Available at: https://www.who.int/emergencies/diseases/novelcoronavirus-2019 [accessed 15 April 2020].
- 2. Jin JM, Bai P, He W, *et al.* Gender differences in patients with COVID-19: focus on severity and mortality. *medRxiv* 2020:20026864.
- 3. Dangis A, Gieraerts C, Bruecker YD, *et al.* Accuracy and reproducibility of low-dose submillisievert chest CT for the diagnosis of COVID-19. *Radiol: Cardiothorac Imaging* Apr 21 2020, <u>https://doi.org/10.1148/</u>ryct.2020200196.
- **4.** Yousaf O, Grunfeld EA, Hunter MS. A systematic review of the factors associated with delays in medical and psychological help-seeking among men. *Health Psychol Rev* 2015;**9**:264–76.
- Klein SL, Flanagan KL. Sex differences in immune responses. Nat Rev Immunol 2016;16:626–38.
- Channappanavar R, Fett C, Mack M, *et al.* Sex-based differences in susceptibility to severe acute respiratory syndrome coronavirus infection. *J Immunol* 2017;**198**:4046–53.

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From ground-glass opacities to pulmonary emboli. A snapshot of the evolving role of a radiology unit facing the COVID-19 outbreak



Sir—The aim of this letter is to report what is currently happening in our Radiology Department at a tertiary infectious disease hospital in Milan, a hotspot for COVID-19, 2 months after the outbreak of the epidemic.

The early phase was highly critical, and we had to find ways to manage both suspected and confirmed cases, which involved separating them from patients undergoing imaging tests for other reasons such as oncological staging or follow-up. At the time, promptness of action was favoured amongst clinicians, and in agreement with the most recent consensus statements<sup>1,2</sup>, computed tomography (CT) was not used as a screening test, but reserved for selected symptomatic patients. As a result, most suspected or confirmed COVID-19 patients were examined using chest

radiography, thus minimising patient radiation exposure and infection transmission to the radiology staff and uninfected patients.

In the course of time, about a month after the epidemic outbreak, we noticed a sudden rise in requests for CT, mostly related to CT angiography (CTA) studies to exclude acute pulmonary embolism (PE).<sup>3</sup> Based on our experience of 30 consecutive CTA examinations performed in confirmed COVID-19 patients, the prevalence of PE is approximately 35%, with peripheral branch preponderance. Preliminary data indicate that approximately 5–10% of COVID-19 patients who require mechanical ventilation suffer from acute PE or deep venous thromboembolism (DVT). The probability is higher in those with signs of DVT, inexplicable hypotension or tachycardia, worsening respiratory status, or risk factors for thrombosis. The rate of micro-PE is probably even higher, as suggested by unreleased autopsy results.

As undiagnosed or untreated PE may negatively affect patient outcome, empirical therapeutic anticoagulation has been recommended; however, considering the lack of evidence regarding improvement and the risk of major bleeding, CTA should be used to confirm this diagnosis and to support any decision to start therapeutic anticoagulation.<sup>4</sup>

Another clinical scenario that is progressively causing an increase in CT requests is pulmonary fibrosis. In fact, COVID-19 patients, particularly those recovering from a period in the intensive care unit, are at risk of developing fibrosis.<sup>5</sup>

In conclusion, after having faced preparedness and diagnostic procedures, radiology departments should also be prepared to deal with these two clinical issues.

# **Conflict of interest**

The authors declare no conflict of interest.

## References

- Rubin GD, Ryerson CJ, Haramati LB, *et al.* The role of chest imaging in patient management during the COVID-19 pandemic: a multinational consensus statement from the Fleischner Society. *Radiology* 2020 Apr 7:201365. https://doi.org/10.1148/radiol.2020201365.
- Rodrigues JCL, Hare SS, Edey A, *et al.* An update on COVID-19 for the radiologist. A British society of Thoracic Imaging statement. *Clin Radiol* 2020 May;**75**(5):323–5. <u>https://doi.org/10.1016/j.crad.2020.03.</u> 003.
- Chen J, Wang X, Zhang S, *et al.* Findings of acute pulmonary embolism in COVID-19 patients. *Lancet Infect Dis* 2020, <u>https://doi.org/10.2139/</u> <u>ssrn.3548771.</u>
- Marietta M, Ageno W, Artoni A, et al. COVID-19 and haemostasis: a position paper from Italian Society on Thrombosis and Haemostasis (SISET). Blood Transfus 2020, https://doi.org/10.2450/2020.0083-20.
- Kligerman SJ, Franks TJ, Galvin JR. From the radiologic pathology archives: organization and fibrosis as a response to lung injury in diffuse alveolar damage, organizing pneumonia, and acute fibrinous and organizing pneumonia. *RadioGraphics* 2013;33:1951–75. <u>https://doi.org/</u> 10.1148/rg.337130057.