Neuroimaging Features of COVID-19: Retrospective Northern Italy Multicenter Study and a Scoping Review of the Prevalence of COVID-19 Associated Acute Cerebrovascular Diseases

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Research Article

Keywords: COVID-19, Coronavirus, Neuroimaging, Neurological, Cerebrovascular disease

Posted Date: January 29th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-150229/v1>

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Neuroimaging features of COVID-19: retrospective Northern Italy multicenter study and a scoping review of prevalence of COVID-19 associated acute cerebrovascular diseases

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Keywords COVID-19 – Coronavirus - Neuroimaging – Neurological – Cerebrovascular disease

Abbreviations

COVID-19 coronavirus disease 2019

SARS-CoV-2 Severe acute respiratory syndrome coronavirus 2

CVD Cerebrovascular disease

CT Computed tomography

MRI Magnetic resonance imaging

DSA Digital subtraction angiography

PRES Posterior reversible encephalopathy syndrome

AIS Acute ischemic stroke

ICH Intracranial hemorrhages

SAH Subarachnoid hemorrhages

SDH Chronic subdural hematomas

MS Multiple sclerosis

ADEM Acute disseminated encephalomyelitis

GBS Guillain–Barré syndrome

GCS Glasgow coma scale

CNS Central nervous system

Abstract

Background The primary aim of this study was to provide additional data of neuroimaging features of coronavirus disease 2019 (COVID-19) in a large-scale population admitted in several northern Italy institutions. The secondary aim was to analyze acute cerebrovascular disease (CVD) prevalence in COVID-19.

Methods A database of confirmed COVID-19 hospitalized patients who developed acute neurological symptoms and underwent any neuroimaging was retrospectively gathered from twelve institutions based in Lombardy from February 21st to July 10th. To assess the prevalence of CVD we conducted a scoping review following the PRISMA extension guidelines for scoping reviews. We searched PubMed/Medline, SCOPUS and EMBASE databases for peer-reviewed in-press or published studies from December to January 2021 reporting CVD in COVID-19 patients.

Results Out of 90 COVID-19 patients who were referred to neuroimaging, 78 (87%) showed CVD, in particular 65 had acute ischemic strokes (AIS), 8 had intracerebral hemorrhages, 2 subarachnoid hemorrhages (SAH) and 3 showed clinical and imaging findings in keeping with posterior reversible encephalopathy syndrome (PRES); 6 patients (7%) showed clinical and imaging findings highly suggestive of encephalitis; 3 patients (3%) showed demyelinating diseases: 1 case of MS progression, 1 case of newly diagnosed MS and 1 case of acute disseminated encephalomyelitis (ADEM); 2 cases (2%) acuity of chronic subdural hematoma (cSDH); 1 patient (1%) with Guillain Barré syndrome. In addition two patients with CVD developed cauda polyradiculitis and tetraparesis.

In our scoping review out of 3275 studies, 24 satisfied the inclusion criteria: in a pooled total population of 136198 patients, the pooled prevalence of CVD was 0.9%. In particular 0.8% of AIS and 0.1% of ICH and 0.003% of PRES.

Conclusions Our study shows a high prevalence of CVD among patients who developed acute neurological symptoms, which is in line with papers reporting data comparable to ours. The heterogeneity of clinical reports, however, constitutes a limitation when comparing our findings with those of the clinical papers. Nonetheless, CVD could be a frightening association with COVID-19, particularly in critically ill patients. Healthcare policymakers and clinicians should be prepared to a likely increase in workload and to rearrange the strategy of healthcare delivery.

Background

Since the World Health Organization (WHO) declared coronavirus disease 2019 (COVID-19) a pandemic on March 11, [1] worldwide SARS-CoV-2 infections are still dramatically increasing with over 90 million total cases and roughly 2 million deaths on January 13, 2021 [2]. USA has been suffering the highest number of infections and deaths, closely followed by India and Brazil [2]. On February 21, the first Italian COVID-19 case was diagnosed in the northern region of Lombardy. From there the infection rapidly spread in the whole country, which became the second world epicenter of COVID-19 outbreak, after China [2]. Currently Europe is facing a second wave of the pandemics. In Italy a total of 2,3 million infections and almost 80.000 deaths have been reported so far [2]. A growing body of evidences is unveiling the multi-organ involvement [3] by SARS-CoV-2 rather than the sole respiratory and gastrointestinal systems manifestations as initially thought. In particular the nervous system involvement most commonly manifests as anosmia, ageusia and impaired consciousness [4-7], however acute cerebrovascular diseases (CVD), hereinafter comprising ischemic/hemorrhagic stroke and PRES (posterior reversible encephalopathy syndrome), seem to have a high share among other etiologies of acute neurological impairment. As of today few large scale studies on neurological manifestations in COVID-19 and their imaging findings have been published [9, 16, 18, 23–28], thus the vast majority of current literature consists of case series or single case reports and focus on a single neurological manifestation [8-22]

The aims of this study were to collect further data on neuroimaging features of COVID-19 patients and to estimate the prevalence of cerebrovascular disease in SARS-CoV-2 infection using, respectively, a multicenter retrospective study design and a scoping review of the literature.

Material and Methods

Multicenter retrospective study

Study design

We retrospectively collected imaging and clinical data from eleven major Lombard institutions: **BLINDED** in the time frame between February to July, including hospitalized patients with: 1) symptoms of SARS-CoV-2 infection and positive rRT-PCR; 2) concurrent or subsequent acute neurological symptoms; 3) receiving neuroimaging scans of the brain and/or spine.

Data collection

Demographic data, comorbidities, neurological findings were retrieved from electronic medical records for each patient by each participating institution (Table 1).

Table 1

Demographic data		Total subset n=90	
Mean age (SD)	69 ±15		
Male	50	55%	
Neurological findings			
Paresis	38	42.7%	
Altered level of consciousness	19	21.1%	
Aphasia	14	15.5%	
Dysarthria	10	11.1%	
Asthenia	8	8.9%	
Seizures	6	6.7%	
Visual field impairment	5	5.6%	
Headache	4	4.4%	
Drowsiness	1	1.1%	
Tetraparesis	2	2.2%	
Other	18	20.2%	
Comorbidities and pre-existing conditions			
Hypertension	33	36.6%	
Diabetes	16	17.9%	
Malignancy	15	16.6%	
Dyslipidemia	12	13.3%	
AF	11	12.2%	
Cardiovascular intervention	10	11.1%	
CAD	9	10%	
Previous stroke	8	8.9%	
COPD	6	6.7%	
CKD	6	6.7%	
Obesity	5	5.6%	
Other	31	34.4%	
None	19	21.1%	
Deaths			
Total	10/90	11%	
<i>Ischemic stroke</i>	5/65	8%	
<i>ICH</i>	3/8	38%	
<i>SAH</i>	0/2	0	
<i>PRES</i>	0/3	0	
<i>Acute on chronic SDH</i>	0/2	0	
<i>Encephalitis</i>	2/6	33%	
<i>Demyelinating diseases</i>	0/4	0	

Image acquisition and analysis

All imaging scans were performed using standard of care protocols. Head computed tomography (CT) with or without contrast scans was employed as the first imaging modality. Brain and spine magnetic resonance imaging (MRI) with or without contrast were acquired either on 1.5T or 3T scanners. Digital subtraction angiography (DSA) was performed on neuroangiography suites with the aim to perform endovascular thrombectomy. Scans were initially read by neuroradiologists at their own Institution and then reviewed by coauthors by each Institutions.

Scoping review

The scoping review was carried out according to the Preferred Reporting Items for Systematic Reviews and Metanalyses extension for scoping reviews (PRISMA-ScR) guidelines. Eligibility criteria were: 1) peer-reviewed original research studies, editorials, review studies published or in-

press, 2) population with confirmed diagnosis of COVID-19, 3) reported data on cerebrovascular diseases. Studies published in any language were considered eligible. Unpublished or ongoing studies and case reports were not included. Boolean logic was employed to search MEDLINE/Pubmed, SCOPUS and EMBASE databases from December 2019 to January 12, 2021 using the following terms: COVID-19 AND stroke, COVID-19 AND “hemorrhage*”, COVID-19 AND “cereb*”, COVID-19 AND cns, COVID-19 AND pres. Two authors independently searched and screened all results first by title and abstract to assess whether the studies fulfilled the inclusion criteria; included studies were further full text reviewed to retrieve data and pooled prevalence of CVD.

Results

Multicenter retrospective study

Out of a total of 7937 consecutive patients, 253 (3%) patients had an abnormal neurological examination and underwent neuroimaging (Fig. 1).

Fig 1

Of these, 90 (36%) patients (55% male predominance, mean age 69) showed acute neuroimaging findings. Eighty-eight (98%) patients underwent brain CT, 41 (46%) head and neck CT angiography (CTA), 32 (36%) brain MRI, 5 (6%) spinal MRI, 12 (13%) had DSA (Table 2).

Table 2

	Head CT	Head and Neck CTA	Brain MRI	Spine MRI	DSA
	88/90 (98%)	41/90 (46%)	32/90 (36%)	5/90 (6%)	12/90 (13%)
Ischemic stroke	65/65 (100%)	35/65 (54%)	19/65 (29%)	-	12/65 (18%)
ICH	8/8 (100%)	3/8 (37%)	3/8 (37%)	1/8 (12%)	-
SAH	2/2 (100%)	0/2 (0%)	0/2 (0%)	1/2 (50%)	-
PRES	3/3 (100%)	2/3 (67%)	3/3 (100%)	-	-
a/c SDH	2/2 (100%)	-	-	-	-
Encephalitis	6/6 (100%)	1/6 (17%)	5/6 (83%)	-	-
Demyelinating diseases	2/4 (50%)	0/4 (0%)	2/4 (50%)	3/4 (75%)	-

Eighty patients (89%) had imaging findings of acute cerebrovascular diseases (Table 3), in particular, 65 patients suffered ischemic strokes, 12 patients had intracranial hemorrhages and 3 patients showed typical findings of posterior reversible encephalopathy syndrome (PRES), that was primarily hemorrhagic in 2 cases (66%).

Table 3

Neuroimaging findings	Notes
Ischemic stroke	65% involved anterior circulation, 23% posterior circulation, 11% multifocal lesions, 1 venous stroke; 11% developed hemorrhagic transformation; 18% eligible for endovascular treatment.
ICH	50% supra and infratentorial, 50% supratentorial, 12.5% basal nuclei; 1 patient developed transient flaccid tetraparesis.
SAH	100% non traumatic and without underlying vascular malformations; 1 patient developed transient flaccid tetraparesis.
PRES	2 cases showed multiple hemorrhagic foci.
a/c SDH	100% non traumatic.
Encephalitis	100% involved the temporal lobes; 1 cerebellar peduncles involved, 1 meningeal enhancement
Demyelinating diseases	1 MS exacerbation, 1 new onset MS, 1 ADEM, 1 GBS

Among the 65 cases of acute ischemic stroke (AIS), 42 (65%) involved the anterior circulation (fig. 2), 15 (23%) posterior circulation, 7 (11%) were multifocal and 1 (2%) was a venous stroke (fig. 3).

Fig 3

Of all intracranial hemorrhages (ICH), 8 were intraparenchymal (fig 4), 2 non-aneurysmal and non-traumatic subarachnoid hemorrhages (SAH) and 2 acute on chronic subdural hematomas (SDH).

Fig 4

All 6 patients presenting with acute encephalopathy, showed temporal lobe lesions in keeping with encephalitis (Table 3). We also observed 4 (4%) inflammatory demyelinating disorders, in particular 1 case of multiple sclerosis (MS) exacerbation, 1 case of newly diagnosed MS with supra-tentorial lesions, 1 case of acute disseminated encephalomyelitis (ADEM) with bilateral, multifocal lesions and 1 case of Guillain–Barré Syndrome (GBS). Three patients had spinal involvement: the above described GBS, 1 patient with SAH that developed polyradiculitis and transient flaccid tetraparesis, and 1 patient with a frontal hemorrhage that developed transient flaccid tetraparesis. The most frequent reported neurological symptoms were those related to acute stroke, followed by altered level of consciousness that was reported in 19 patients, of which, 16 had a Glasgow Coma Scale (GCS) score less than 7.

The highest mortality rate was related to ICH (38%) followed by the encephalitis subgroup (33%) (Table 1). Hypertension (36.6%), diabetes (17.9%) were the most frequent comorbidities, followed

by previous or current history of malignancy (16.6%). The most relevant comorbidities, neurological findings are summarized in Table 1. Prevalence data of our cohort are shown in Table 4.

Table 4

	Cases (n=90)	Mean age (Range)	Male	COVID-19 (n=7937)	COVID-19 with neurological symptoms (n=253)
CVD	80	71 (21-90)	59%	1.01%	31.6%
<i>AIS</i>	65	72 (47-88)	65%	0.82%	25.7%
<i>ICH</i>	8	60 (21-84)	50%	0.10%	3.2%
<i>SAH</i>	2	84 (78-90)	100%	0.03%	0.8%
<i>PRES</i>	3	70 (63-84)	100%	0.04%	1.2%
<i>a/c SDH</i>	2	67 (49-85)	50%	0.03%	0.8%
Encephalitis	6	69 (40-90)	83%	0.08%	2.4%
Demyelinating diseases	4	43 (9-65)	50%	0.05%	1.6%
Total	90	69 (9-90)	55%	1.13%	35.6%

CVD was the commonest finding in patients who underwent neuroimaging (32%, 80/253), followed by encephalitis (2.4%, 6/253). Among CVD, AIS occurred more frequently (26%, 65/253). In the total COVID-19 population, CVD prevalence was 1% (Table 4).

Scoping review

Titles and abstracts of 1643 studies were reviewed after excluding n=1632 duplicates out of a total 3275 records: 726 studies met the inclusion criteria (Fig. 5) and were full text screened.

Fig 5

Of these, 24 studies [4, 27, 29–50] showed appropriate data to derive prevalence: thirteen retrospective multicentric studies, and eleven retrospective single center studies (Table 5), from the North America, Europe, Asia and Oceania.

Table 5

Authors	Date of Publication	Study design	Country	Population of COVID-19	Age*		Male	Cohort of COVID-19 with neurological symptoms	CVD in COVID-19			CVD in COVID-19 with neurological symptoms		
									AIS	ICH	PRES	AIS	ICH	PRES
Mao et al ⁴	10-Apr	Retrospective multicentric	China, Wuhan	214	52.7	15.5	41%	78 (36.4%)	5 (2.3%)	1 (0.5%)	—	6.4%	1.3%	—
(1) Lodigiani et al ²⁹	23-Apr	Retrospective single center	Italy, Milan	388	66	(55-75)	68%	Not specified	9 (2.4%)	—	—	—	—	—
Giorgianni et al ²⁷	15-May	Retrospective single center	Italy, Varese	1000	71***	(21-88)***	46%***	26 (2.6%)	4 (0.4%)	5 (0.5%)	—	15.4%	19.2%	—
Jain et al ³⁰	19-May	Retrospective single center	USA, New York	3218	64***	(weeks-105 year)***	60.7%***	454 (14.1%)	26 (0.8%)	9 (0.2%)	—	5.7%	1.9%	—
Mahammedi et al ³¹	21-May	Retrospective multicentric	Italy, Brescia, Novara, Sassari	725	69**	15**	64%**	108(14.9%)	34 (4.6%)	6 (0.8%)	1 (0.1%)	31.5%	5.5%	0.9%
(2) Dogra et al ³²	23-May	Retrospective multicentric	USA, New York	3824	62**	(37-83)**	79%**	755 (19.7%)	—	33 (0.9%)	—	—	4.4%	—
(1) Yaghi et al ³³	26-May	Retrospective multicentric	USA, New York	3556	62.5**	17**	72%**	Not specified	32 (0.9%)	—	—	—	—	—
(1) Cantador et al ³⁴	9-Jun	Retrospective single center	Spain, Madrid	1419	76**	7**	77%**	Not specified	8 (0.5%)	—	—	—	—	—
Pons-Esconda ³⁵	11-Jun	Retrospective single center	Spain, Barcellona	2249	74***	(50.2-90)***	61%***	103 (4.6%)	13 (0.6%)	7 (0.3%)	—	12.6%	6.8%	—
Li et al ³⁶	12-Jun	Retrospective single center	China, Huazhong	219	75.7**	10.8**	56%**	83 (37.8%)	10 (4.6%)	1 (0.5%)	—	12%	1.2%	—
Naliballe et al ³⁷	17-Jun	Retrospective multicentric	Global clinical research platform	40469	not specified	not specified	45%	9086 (22.5%)	406 (1%)	—	—	4.5%	—	—
(1) Merkle et al ³⁸	2-Jul	Retrospective multicentric	USA, New York	1916	69**	(66-78)**	58%**	Not specified	31 (1.6%)	—	—	—	—	—
Rothstein et al ³⁹	20-Jul	Retrospective multicentric	USA, Philadelphia	844	59	18	48%	209 (24.8%)	20 (2.4%)	8 (0.9%)	—	9.6%	3.8%	—
(1) Altschul et al ⁴⁰	26-Jul	Retrospective single center	USA, New York	5227	67**	15.5**	60%**	Not specified	—	16 (0.3%)	—	—	—	—
Requena et al ⁴¹	5-Aug	Retrospective single center	Spain, Barcellona	2050	66.5**	15.2**	56%**	Not specified	18 (0.9%)	4 (0.2%)	3 (0.1%)	—	—	—
Katz et al ⁴²	6-Aug	Retrospective multicentric	USA, New York	10596	67.9**	(25-94)**	55.8%**	Not specified	72 (0.7%)	14 (0.1%)	—	—	—	—
Shahjouei et al ⁴³	17-Aug	Retrospective multicentric	USA, Brazil, Greece, Italy, Finland, Turkey, Lebanon, Iran, India, New Zealand	17799	66**	15**	58%**	Not specified	123 (0.7%)	25 (0.1%)	—	—	—	—
Iltaf et al ⁴⁴	18-Aug	Retrospective single center	Pakistan, Karachi	350	49.5	17.4	70%	68 (19.4%)	2 (0.6%)	—	—	3.9%	—	—
Romero-Sanchez et al ⁴⁵	25-Aug	Retrospective multicentric	Spain, Albacete	841	66.4	14.96	56.2%	Not specified	11 (1.3%)	3 (0.4%)	—	—	—	—
Xiong et al ⁴⁶	15-Sep	Retrospective multicentric	China, Wuhan, Chongqing, Sichuan	917	48.7	17.1	55%	39 (4.3%)	10 (1.1%)	—	—	25.6%	—	—
Siegler et al ⁴⁷	30-Sep	Retrospective multicentric	USA, Spain, Egypt, Romania	14483	not specified	not specified	not specified	Not specified	156 (1.1%)	28 (0.2%)	—	—	—	—
Rifino et al ⁴⁸	07-Oct	Retrospective single center	Italy, Bergamo	1760	64.9***	14.0***	66%***	137 (7.8%)	37 (2.1%)	11 (0.6%)	—	27%	8%	—
Sabayan et al ⁴⁹	6-Nov	Retrospective multicentric	Iran	18407	65**	(38-93)**	79%**	Not specified	14 (0.1%)	—	—	—	—	—
(2) Lee et al ⁵⁰	11-Jan 2021	Retrospective single center	USA, Hartford	3727	62	(52-74)	54%	Not specified	6 (0.2%)	—	—	—	—	—
Total				136198	64.8	—	60.2%	11146 (8.2%)	n: 1222 (0.9%, 0.1 - 5.7%)			11%		
									1047 (0.8%)	171 (0.1%)	4 (0.003%)	9.4%	1.5%	0.03%
									range: 0.1 - 4.6% 0.1 - 0.9%					

(1) study cohort of ischemic strokes
(2) study cohort of intracranial hemorrhage
* mean age (standard deviation or range)
** referring to CVD population
*** referring to population with neurological symptoms

A total population of 136198 COVID-19 patients was included (60.2% of males, mean age 64.8). Pooled prevalence of CVD was 0.9% (range 0.1 – 5.7%), and ischemic stroke was the most common

manifestation (1047/1222, 86%). The prevalence of CVD in the cohort of patients with neurological symptoms (n=11146) was 11%, based on twelve of the total nine studies since in the remainder that cohort was not specified [29, 33, 34, 38, 40-43, 47, 49, 50].

Discussion

In this study we showed neurological and imaging findings in consecutive COVID-19 patients admitted in eleven centers in Lombardy region, which was the first in Europe to bear the burden of the outbreak of COVID-19 epidemic. Acute CVD had the highest prevalence among the COVID-19 related acute neurological diseases. The association between acute cerebrovascular events and SARS-CoV-2 infection has been reported in several studies, with ischemic events outnumbering the primarily hemorrhagic. This evidence has been ascribed to the neurotrophic and neuroinvasive tendency of SARS-CoV-2, specifically, to its interaction with ACE-2 host receptors expressed on neurons and nervous system endothelial cells membranes [51] which results in endothelial damage. [51-52]. Once it reaches the central nervous system (CNS), SARS-CoV-2 can determine the activation of self-reinforcing inflammatory response through a 'cytokine storm', causing irreversible neuronal damage [53]. In addition, the endothelial ruptures in cerebral capillaries, due to the inflammatory process, can contribute to the pathophysiology of SARS-CoV-2 brain damage [51]. Ischemic stroke, cerebral venous thrombosis included, could be related both to the development of endotheliitis and hypercoagulability status. In this regard, Spiezia et al. [54] described a severe hypercoagulability status related to the inflammatory response and Zhang et al. [55] found the presence of antiphospholipid antibodies in few patients. In addition, SARS-CoV-2 infection can lead to cardiovascular complications including incident atrial fibrillation [56-58], which in turn is a risk factor of to cardio-embolic cerebral infarction. In our cohort, the majority of CVD occurred in older patients (mean age: 71 year old) with typical risk factors for CVD, in accordance to other reports [38]. In addition, acute viral infections may increase the risk of ischemic stroke as noted by some authors [59]. It could therefore be speculated that SARS-Cov2 could possibly play a role as a precipitating factor in the development of CVD through diverse mechanisms. CVD has also been reported in other Coronavirus infections, as in MERS and SARS, even if most of the paper published were case series [60]. It is suggested that Coronavirus infections, and other respiratory infections, is an independent risk factor for acute cerebrovascular disease [61].

We had severe PRES cases, some of which were primarily hemorrhagic. The occurrence of PRES in COVID-19 has been reported by some [14, 21, 62-65] and, notably, a number cases were complicated by intracranial hemorrhages [21, 62, 64, 65]. This evidence may support that endothelium

inflammation and the resulting abnormal vasoconstriction has a role in the pathophysiology of PRES in COVID-19 patients [66]. Many studies have shown that COVID-19 effects on CNS and peripheral nervous system most often become apparent [4–7, 67] as anosmia, ageusia, impaired consciousness, dizziness and headache, on the other hand, acute CVD syndromes are less frequent but bear potentially permanent CNS dysfunction hence worse prognosis. Notably, compared to influenza virus, COVID-19 patients have higher prevalence of AIS, highlighting how COVID-19 may be a risk factor for AIS [38]. Furthermore Merkler et al. found that initial plasma D-dimer levels were higher in COVID-19 ischemic stroke versus patients with influenza [38]. The prevalence of acute CVD in COVID-19 population was 1.0% and on COVID-19 with neurological symptoms was 36%, the highest among other neurological syndromes, which is comparable to the results in the pooled population from the scoping review (1% vs 0.9%). Compared to the Italian population, where the most recent prevalence data of CVD in the general population is 6.5% [68], according to our results, CVD was lower in COVID-19 patients. This could be due to the clinical setting, i.e. intensive care unit patients with multiorgan failure and to the difficulty to obtain a complete neurological examination (intubated patients) which may have led to an underestimation of the true prevalence. Central nervous system damage associated with SARS-CoV-2 invasive potential may underly the development of encephalitis and myelitis. This evidence confirms the neurotrophic and neuroinvasive tendency of SARS-CoV-2 ACE-2 host receptor mediated expressed on brain and spinal cord neurons [51, 69, 70]. Only few case reports recently described the association of COVID-19 with demyelinating diseases [71]. However a clear causative correlation between SARS-CoV-2 and the new onset or exacerbation of demyelinating diseases is yet to be determined [72]. It has been speculated that SARS-CoV-2 may activate lymphocytes and induce an inflammatory response leading to exacerbation or new onset of demyelinating disorders [73, 74]. Although our study has one of the largest populations of COVID-19 patients with neurological manifestations and positive neuroimaging, further data and larger samples could widen further the multifaceted nervous system involvement in COVID-19. Our scoping review is limited by the heterogeneity of study designs of the included works, their retrospective nature, fragmentary data reported and relatively small samples.

Conclusions

Our multicenter retrospective observational data confirm the high variability of neuroimaging features of COVID-19, additionally, CVD has the highest prevalence among other acute neurological manifestations in our cohort as well as in the current literature. This evidence demands awareness

among clinician and healthcare policy maker to hone the daily practice and healthcare delivery strategy towards a more efficient response to the pandemic.

Declaration

Ethics approval and consent to participate

Ethical approval for this study was waived by the ethics committee of the Di Circolo e Fondazione Macchi Hospital, ASST Settelaghi, Varese, Italy because the emergency setting and the retrospective nature of the study.

All methods were carried out in accordance with ethical committee guidelines and regulations.

Consent for publication

Written informed consent was obtained from all subjects before the study

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

Not applicable

Funding

KARDIA SRL sustained the submission fee, but KARDIA SRL had no role in the design of the study, neither in the collection, analysis, and interpretation of data nor in writing of the manuscript.

Authors' contributions

GA, DAF, VG, AE, PLS, DVA, PA, VL, TM, NL, SC, BS, MA, TAV, TF, CS, NNP, AF, GV, LE, BE, BP, C-TE, LL, BF and BF collected patients data. DAF, VG, AE and GA analyzed and interpreted the patient data. DAF and VG wrote the manuscript. DAF, VG, GA and LP review the manuscript. All authors read and approved the final manuscript

Acknowledgements

Not applicable.

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Table 1

Demographic and clinical data

AF = atrial fibrillation, CAD = coronary artery disease, COPD = chronic obstructive pulmonary disease CKD = chronic kidney disease, ICH = intracerebral hemorrhage, SAH = subarachnoid hemorrhage, PRES = posterior reversible encephalopathy syndrome, SDH = subdural hematoma.

Table 2

Neuroimaging studies

ICH = intracerebral hemorrhage, SAH = subarachnoid hemorrhage, PRES = posterior reversible encephalopathy syndrome, a/c SDH = acute on chronic subdural hemorrhage

Table 3

Neuroimaging findings

ICH = intracerebral hemorrhage, SAH = subarachnoid hemorrhage, PRES = posterior reversible encephalopathy syndrome, a/c SDH = acute on chronic subdural hemorrhage, MS = multiple sclerosis, ADEM = acute disseminated encephalomyelitis, GBS = Guillain-Barré Syndrome

Table 4

Diseases prevalence and demographic data in the study cohort.

CVD = cerebrovascular disease, AIS = acute ischemic stroke, ICH = intracerebral hemorrhage, SAH = subarachnoid hemorrhage, PRES = posterior reversible encephalopathy syndrome, a/c SDH = acute on chronic subdural hemorrhage.

Table 5

Prevalence and demographic data of cerebrovascular diseases in COVID-19 patients.

AIS = acute ischemic stroke, ICH = intracranial hemorrhage, PRES = posterior reversible encephalopathy syndrome

Figure 1

Flowchart of the multicenter study.

Figure 2

Anterior circulation stroke. A 85 year-old woman with history of hypertension presenting with sudden onset of left hemiparesis. (A) CT without contrast shows an ill-defined cortical-subcortical hypoattenuating area in the right lateral posterior frontal lobe. (B) CTA VR reformat shows thrombotic occlusion of the (right) middle cerebral artery M2 segment. (C-D) b1000 and ADC map: the lesion shows restricted diffusion and (E) T2-FLAIR hyperintensity consistent with acute ischemia.

Figure 3

Dural sinus thrombosis and venous ischemia. A 61 year-old woman with history of hypertension presenting with altered consciousness and headache. CT without contrast shows hyperattenuating right transverse sinus (a) straight sinus, vein of Galen and internal cerebral veins (b) and focal mesial parietal ischemic changes (c). Venous CT angiography MIP reformats show filling defects at the level of the right transverse sinus and torcula Herophilii (d), jugular bulb and superior sagittal sinus (e) sinus and right internal cerebral vein (f). A somewhat generalized superficial venous engorgement is also noted.

Figure 4

Hemorrhagic stroke. A 79 year-old male with history of hypertension with loss of consciousness and coma. Upon admission CT without contrast (A and B) shows right frontal-parietal hematoma with massive intraventricular extension.

Figure 5

PRISMA-ScR Extension flow diagram.

Figures

Figure 1

Flowchart of the multicenter study.

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