ORIGINAL ARTICLE

Cavernous Sinus Involvement in Rhino-orbital Cerebral Mucormycosis and Impact of Concurrent COVID-19 on Patient Outcome: A Retrospective Observational Study



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ABSTRACT

Background: Cavernous sinus thrombosis (CST) in rhino-orbital cerebral mucormycosis (ROCM) poses a challenge for clinicians in predicting outcomes and formulating management strategies, particularly with the concurrent coronavirus disease 2019 (COVID-19) infection.

Purpose: This study was done to evaluate cavernous sinus (CS) involvement in ROCM. Additionally, we explored the association between CS thrombosis and COVID-19, exploring its potential impact on patient mortality.

Materials and methods: A retrospective analysis was conducted on 106 ROCM patients, examining their COVID-19 status and reviewing imaging findings from contrast-enhanced computed tomography (CT) and magnetic resonance (MR). The imaging assessment focused on evaluating fungal sinusitis, identifying CS involvement qualitatively, and detecting extension to orbit or other intracranial areas. Findings were correlated with patient mortality.

Results: CS involvement in ROCM was 48.1%, with a higher distribution (clinically insignificant) in COVID-positive patients (51.8%) compared to the COVID-negative group (34.8%). Most participants showed unilateral (78%) and diffuse pattern (71%) of CS involvement. A statistically significant association was observed between CS imaging parameters (filling defect, diffuse involvement pattern, convex shape of the lateral wall, and orbital cellulitis) and patient mortality, according to bivariate analysis (p < 0.05). Among 106 ROCM patients, 9.4% succumbed to the disease, with significantly higher mortality in those with CS thrombosis. However, subgroup analysis for the additional effect of COVID-19 on mortality yielded nonsignificant results.

Conclusion: CS involvement in ROCM does not significantly impact mortality in both COVID-positive and negative patients. Imaging parameters such as filling defects, diffuse CS involvement, convex lateral wall, and orbital cellulitis may suggest the disease severity when observed.

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Introduction

Rhino-orbital cerebral mucormycosis (ROCM) is the most common form of mucormycosis encountered concurrently or after coronavirus disease 2019 (COVID-19). The prevalence of ROCM in India (0.14 cases per 1,000 population) exceeded that of developed nations, constituting 80% of COVID-19-associated ROCM cases during the second pandemic peak. Intracranial dissemination of mucormycosis is associated with increased mortality. The infection advances by infiltrating vascular and neural tissues, permeating the walls of blood vessels. It then extends from one sinus to neighboring sinuses, the orbit, the retro-orbital area, and eventually intracranial spread.

Cavernous sinus thrombosis (CST), first described by Duncan in 1821, is a potentially fatal intracranial complication of mucormycosis. CST is an uncommon condition, typically arising from septic, traumatic, or inflammatory causes. Computed tomography (CT) and magnetic resonance (MR) imaging offer diagnosis through both

direct signs, such as alterations in density/ signal intensity on plain and contrast scans, changes in the size and contour of the CS, and indirect signs, including superior ophthalmic vein dilatation, exophthalmos, and increased dural enhancement along the lateral margin of the CS.⁷ CS involvement in ROCM may arise from drainage *via* ethmoidal, facial, and ophthalmic veins, direct extension from the sphenoid sinus, or perineural spread along neural foramina.^{8–10} CS can be directly involved due to contiguous spread, or there may be septic thrombophlebitis, a condition often regarded as life-threatening.

Numerous research studies have reported that COVID-19 infection can increase the likelihood of thrombotic events like pulmonary embolism, lower limb venous thrombosis, and strokes. The underlying mechanisms driving these occurrences may involve a cytokine storm that triggers the onset of systemic inflammatory response syndrome and subsequent thrombotic processes. Few cases have also been reported in the literature in which patients

developed CST while getting infected with COVID-19, and these cases occurred without concurrent mucormycosis infection.¹² This highlights the significance of recognizing CST as a potential complication of COVID-19, even when mucormycosis is absent.

Chowdhary et al., in their study on 61 patients of mucormycosis during the COVID pandemic in 2021, concluded that 34.4% of patients developed CST and found no significant increase in the risk of death when patients had both COVID-19 and CST simultaneously.¹³

Given the complexities associated with managing ROCM patients, particularly amid the COVID-19 pandemic, our retrospective observational study aimed to determine the extent of CS involvement in these individuals. We sought to conduct a comprehensive qualitative assessment of CS on imaging, considering potential interactions with COVID-19, an aspect that has not been extensively documented. The correlation between CS involvement and COVID-19 and its impact on patient mortality were key objectives in this study.

MATERIALS AND METHODS

This retrospective observational study was conducted in a tertiary care institute

¹Associate Professor, Department of Radiodiagnosis; ²Associate Professor, Department of Community and Family Medicine, All India Institute of Medical Sciences, Bathinda, Punjab; ³Professor, Department of Orthopedics, Maharishi Markandeshwar Medical College, Solan, Himachal Pradesh; ⁴Additional Professor, Department of Radiodiagnosis; ⁵Additional Professor, Department of Otorhinolaryngology; ⁶Professor, Department of Ophthalmology, All India Institute of Medical Sciences, Bathinda, Punjab, India; *Corresponding Author

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Study Population

The study included patients previously diagnosed with ROCM, either during hospitalization or in outpatient settings within the Department of Otolaryngology or Ophthalmology, and were subsequently referred to the Department of Radiodiagnosis for contrast-enhanced CT/MRI of the paranasal sinus region and brain. Upon retrospective analysis, the patients who were found to have presented with sinusitis and CST on imaging but tested negative for ROCM were excluded. Those who had undergone only a plain scan without administering contrast were also excluded.

Sample Size and Sampling Strategy

The sample size was calculated using an online sample size collection software (https://www.openepi.com/SampleSize/SSPropor.htm). A sample size of 106 was calculated using the population proportion formula after considering the overall prevalence of CST in COVID-associated mucormycosis patients to be around 20%, 13 with an 80% confidence interval and a margin error of 5%.

Scanning Protocol

The data of all such participants was analyzed where ROCM was confirmed through potassium hydroxide (KOH) testing, and

contrast-enhanced CT (CECT) or contrastenhanced MR (CEMR) was conducted based on the requests from the referring clinician. CECT and CEMR were performed on a 256slice scanner (Siemens: Somatom Drive) and a 3 tesla MR scanner (Siemens: Skyra) with a defined scan protocol mentioned in Table 1. The scan acquisition encompassed plain and contrast-enhanced CT or MR imaging of the paranasal sinuses, face, orbits, suprahyoid neck, skull base, and the intracranial compartment in all anatomical planes. The imaging assessment focused on evaluating sinonasal fungal involvement, identifying the filling defect in CS, conducting a thorough qualitative evaluation based on a predefined set of parameters, and detecting any signs of orbital involvement or potential extension into other intracranial areas.

Mucor involvement of the sinonasal region was determined by the presence of mucosal thickening with hyperdense foci on NCCT and hypointense components on T2W MR and nonenhancement of involved mucosa on postcontrast CT or postcontrast MR, in conjunction with the presence of ancillary features (Figs 1 and 2). The presence of CST was defined by observing filling defects in either one or both sinuses on contrast imaging in conjunction with the criteria outlined below in the proposed criteria. COVID-positive status was taken as a positive COVID RT-PCR test conducted within the 3 months preceding the current presentation of ROCM.

Proposed Qualitative Criteria

For the qualitative evaluation of CS involvement/thrombosis, the following variables were examined to assess the nature and characteristics of this entity in our study:

- Signal intensity on plain MR/heterogeneity on NCCT.
- Filling defects on contrast imaging.

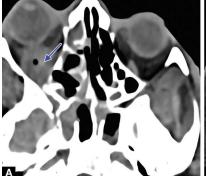
Table 1: The scan protocol followed in the study

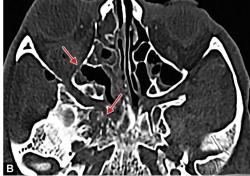
MR protocol followed in the study:

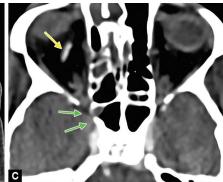
- T1-weighted TSE (turbo spin-echo) [repetition time TR ms/echo time TE ms (617/7)].
- T2-weighted TSE (turbo spin-echo) [repetition time TR ms/echo time TE ms (6780/90)].
- Short-tau inversion recovery sequence or STIR [repetition time TR ms/echo time TE ms (3200/47)].
- IV gadolinium-based macrocyclic contrast [0.1 mmol/kg at a 2–3 mL/second rate using a pressure jet injector].
- Postcontrast T1W in all three planes and one T1W 3D sequence obtained 7–10 minutes after contrast administration.

CT protocol followed in the study:

- Patient position: supine.
- Topogram: perpendicular to the hard palate.
- Tube voltage and tube current: 120 kV and 130–165 mAs.
- Scan extent: from the chin to above the end of the frontal sinuses.
- Scan direction: caudocranial.
- Scan geometry: field of view 140 mm; slice thickness: 0.6–1.0 mm; pitch: 0.8; scan time: 6.0 seconds.
- · Multiplanar reconstruction: coronal and sagittal planes.
- Contrast parameters: performed after injecting 60–80 mL of intravenous iodinated contrast material at a rate of 2–3 mL/second with a delay of at least 45 seconds after contrast material injection.







Figs 1A to C: Rhino-orbital cerebral mucormycosis with right orbital and CS invasion; (A) Axial NCCT image (soft tissue window) shows partial opacification of the right sinonasal region with heterogeneous mucosal thickening containing hyperdense foci extending to the right orbit (blue arrow) and resultant proptosis; (B) Axial NCCT image (bone window) shows erosion (red arrows) of bony septae, lamina papyracea, sinus walls, and sphenoid bone on the right side; (C) Axial CECT image reveals a partial filling defect in the anterior part of the right CS with a bulging convex lateral wall (green arrows). The right superior ophthalmic vein is also prominent (yellow arrow); CECT, contrast-enhanced computed tomography; NCCT, noncontrast computed tomography

- The lateral wall's convexity or flatness.
- The presence of meningeal thickening and enhancement along the CS.
- The presence of proptosis (eye protrusion).
- Superior ophthalmic vein prominence.
- Orbital apex involvement.
- · ICA involvement.

Statistical Analysis

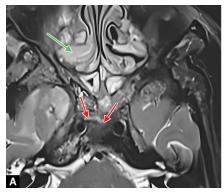
Statistical analysis utilized the Statistical Package for Social Sciences (SPSS for Windows; Version 28.0.1.0, Armonk, NY: IBM Corp).

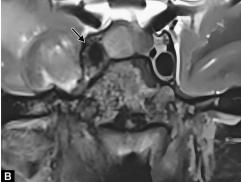
Descriptive statistics were employed to outline the sociodemographic and clinical characteristics of the study participants. Nominal data, including age, gender, sinus involvement, bony destruction, and orbital and intracranial involvement, were presented as frequencies and percentages, while continuous variables were represented using mean and interquartile range (IQR). Associations between dependent and independent variables were illustrated using

Chi-square analysis. Statistical significance was considered for p < 0.05.

RESULTS

We included 106 ROCM patients in our analysis. The mean age of the patients was 52 (range: 9–76; IQR: 41–64) years. Table 2 depicts the distribution of the study participants based on the history of COVID-19 infection as per sociodemographic and clinical characteristics. Most participants with ROCM were COVID-







Figs 2A to C: Rhino-orbital cerebral mucormycosis with CS invasion and right temporal lobe abscess: (A) Axial T2W FS image shows heterogeneous mucosal thickening completely occluding bilateral sinonasal regions (green arrow); clival invasion is seen as altered marrow signal (red arrows); (B) Coronal T2W image shows a bulky right CS with a convex lateral wall and altered hypointense signal (black arrowhead), compared to the normal left CS; (C) Coronal postcontrast T1 MR image reveals a hypointense filling defect in the right CS and meningeal thickening along the sinus (black arrow). The flow void of the right ICA is also attenuated and displaced superiorly (blue arrowhead). A peripherally enhancing right temporal lobe abscess is also evident (white arrow); FS, fat-saturated; ICA, internal cerebral artery; MR, magnetic resonance

Table 2: Characteristics of ROCM patients based on the status of COVID-19 infection

	Present/past h/o COVID-19 infection				
	Negative	Positive	Total	p-value	
	No. of participants (%)	No. of participants (%)	No. of participants (%)		
Total	23 (100)	83 (100)	106 (100)		
Age (completed years)				0.592	
<50	8 (34.8)	34 (41)	42 (39.6)		
>50	15 (65.2)	49 (59)	64 (60.4)		
Sex				0.877	
Female	6 (26.1)	23 (27.7)	29 (27.4)		
Male	17 (73.9)	60 (72.3)	77 (72.6)		
Comorbidities				0.086	
Nil	0 (0)	6 (7.2)	6 (5.7)		
Single	22 (95.7)	62 (74.7)	84 (79.2)		
Multiple	1 (4.3)	15 (18.1)	16 (15.1)		
Paranasal sinus involvement					
Frontal	12 (52.2)	50 (60.2)	62 (58.5)	0.487	
Maxillary	22 (95.7)	81 (97.6)	103 (97.2)	0.620	
Ethmoid	15 (65.2)	73 (88)	88 (83)	0.010	
Sphenoid	19 (82.6)	66 (79.5)	85 (80.2)	0.742	
Palate	15 (65.2)	43 (51.8)	58 (54.7)	0.253	
Nasal cavity	17 (73.9)	79 (95.2)	96 (90.6)	0.002	
CS involvement					
Yes	8 (34.8)	43 (51.8)	51 (48.1)	0.148	

Table 3: Proportion of CS involvement in ROCM as per demographics

	CS involvement				
	Present	Absent	Total	p-value	
	No. of participants (%)	No. of participants (%)	No. of participants (%)		
Total	51 (48.1)	55 (51.9)	106 (100)		
Status of COVID-19 infection				0.148	
Negative	8 (34.8)	15 (65.2)	23 (100)		
Positive	43 (51.8)	40 (48.2)	83 (100)		
Age (completed years)					
<50	17 (40.5)	25 (59.5)	42 (100)	0.202	
>50	34 (53.1)	30 (46.9)	64 (100)		
Sex					
Female	16 (55.2)	13 (44.8)	29 (100)	0.372	
Male	35 (45.5)	42 (54.5)	77 (100)		
Laterality					
Bilateral	11 (100)	0 (0)	11 (100)	0.000*	
Unilateral	40 (100)	0 (0)	40 (100)		
NA	0 (0)	55 (100)	55 (100)		
Pattern of involvement					
Diffuse	36 (100)	0 (0)	36 (100)	0.000*	
Partial	15 (100)	0 (0)	15 (100)		
NA	0 (0)	55 (100)	55 (100)		

^{*}Indicates statistically significant value

positive, with a higher prevalence in those over 50 years of age and males. However, the distribution lacked statistical significance. More than three-fourths of the participants had at least a single comorbidity, and the proportion was higher in COVID-negative patients.

In overall ROCM patients, the majority showed involvement of the maxillary sinus at 97.2%, followed by the ethmoid sinus at 83% and the sphenoid sinus at 80%. In total, the proportion of CS involvement in ROCM was found to be 48.1%, with a higher distribution in COVIDpositive patients at 51.8% compared to the COVID-negative group at 34.8% (Table 3). However, the involvement did not depict statistically significant distribution based on age, history of COVID-19, or gender. Among cases with CS involvement, the distribution of paranasal sinus involvement was as follows: 100% had maxillary sinusitis, 92.2% exhibited ethmoid sinusitis, 86.3% presented with sphenoid sinusitis, and 75.4% displayed frontal sinusitis. The majority of the study participants showed unilateral (78%) and diffuse patterns (71%) of CS involvement.

By considering mortality as the prognostic marker, we further gathered insights into the outcomes associated with detailed qualitative parameters of CS involvement in imaging (Table 4). We observed significant variations in the filling defect on contrast-enhanced scans,

diffuse involvement pattern of the CS, convex shape of the lateral wall, and orbital cellulitis in patients and mortality among them as per the bivariate analysis (p < 0.05).

Table 5 depicts the outcome at discharge in ROCM patients based on CS involvement and COVID-19 infection status. The outcome of the 106 patients with ROCM enrolled in the study was predominantly favorable, with 96 patients discharged alive from the hospital. Overall, we observed significantly higher mortality in patients with CS involvement compared to those where the CS was not involved. However, a subgroup analysis to observe the additional effect of COVID-19 on mortality depicted nonsignificant results.

Discussion

The presence of CST or direct infiltration of the CS by mucormycosis indicates a grim prognosis as per existing literature^{13,14} and can significantly impact treatment strategies. This complexity may be further compounded when there is a history of or concurrent COVID-19 infection, as COVID-19 has the potential to contribute to CST through its known ability to alter the coagulation profile.^{11,15} As a result, managing patients with concurrent mucormycosis and COVID-19 becomes particularly challenging due to the interplay of these factors, which may necessitate tailored and multidisciplinary care approaches.

Our study depicted certain interesting findings. Approximately 50% of patients with ROCM exhibited involvement of the CS. Among the numerous proposed imaging-based qualitative parameters, notable findings were observed in certain parameters, including the presence of filling defects on CEMR, the diffuse involvement pattern of the CS, convex lateral wall, and the presence of orbital cellulitis. Additionally, a higher mortality rate was observed in patients with CS involvement, although it did not reach statistical significance when calculating overall mortality in ROCM.

In our study, the incidence of CS involvement in ROCM was 48.1%. In cases of ROCM associated with COVID-19, the incidence was slightly higher at 51.8%, indicating an elevated rate compared to previous studies. 16,17 A notable involvement of the maxillary sinuses, followed by the ethmoid and sphenoid sinuses, in study participants with CS involvement corresponds to findings from prior research. These findings support the mechanism by which infection spreads from the ethmoid and sphenoid sinus to the CS, involving either contiguous spread or migration through the afferent veins, subsequently reaching the valveless CS and culminating in the development of classic fulminant CST.^{18,19} Most participants exhibited unilateral CS involvement, likely due to the unilateral engagement of the corresponding paranasal sinuses on that side.

Table 4: Imaging-based qualitative evaluation of CST in ROCM patients

Expired No. of participants (%)	Good	Total	p-value	
No. of participants (%)			F	
	No. of participants (%)	No. of participants (%)		
10 (9.4)	96 (90.6)	106 (100)		
			0.055	
7 (15.9)	37 (84.1)	44 (100)		
3 (4.8)	59 (95.2)	62 (100)		
			0.002*	
2 (3.6)	53 (96.4)	55 (100)		
8 (15.6)	43 (86)	51 (100)		
			0.100	
2 (18.2)	9 (81.8)	11 (100)		
6 (15)	34 (85)	40 (100)		
2 (3.6)	53 (96.4)	55 (100)		
			0.038*	
7 (19.4)	29 (80.6)	36 (100)		
1 (6.7)	14 (93.3)	15 (100)		
2 (3.6)				
			0.014*	
8 (20)	32 (80)	40 (100)		
		11 (100)		
, ,	, ,	, ,	0.326	
4 (6.9)	54 (93.1)	58 (100)		
, ,	, ,	, ,	0.182*	
2 (4.8)	40 (95.2)	42 (100)		
	,	, , , ,	0.080*	
6 (16.2)	31 (83.8)	37 (100)		
(/	,	, , ,	0.021	
2 (7.7)	24 (92.3)	26 (100)		
- (1-7)	. = ()	()	0.935*	
7 (9.6)	66 (90.4)	73 (100)	0.200	
2 (2)	()	()		
9 (9 5)	86 (90 5)	95 (100)	0.967	
			3.507	
. (2.1)	10 (50.5)	11 (100)		
5 (16 1)	26 (83 9)	31 (100)	0.129	
			0.129	
			0.230	
			0.230	
	3 (4.8) 2 (3.6) 8 (15.6) 2 (18.2) 6 (15) 2 (3.6) 7 (19.4)	3 (4.8) 59 (95.2) 2 (3.6) 53 (96.4) 8 (15.6) 43 (86) 2 (18.2) 9 (81.8) 6 (15) 34 (85) 2 (3.6) 53 (96.4) 7 (19.4) 29 (80.6) 1 (6.7) 14 (93.3) 2 (3.6) 53 (96.4) 8 (20) 32 (80) 0 (0) 11 (100) 2 (3.6) 53 (96.4) 4 (6.9) 54 (93.1) 6 (12.5) 42 (87.5) 2 (4.8) 40 (95.2) 8 (12.5) 56 (87.5) 6 (16.2) 31 (83.8) 4 (5.8) 65 (94.2) 2 (7.7) 24 (92.3) 8 (10) 72 (90) 7 (9.6) 66 (90.4) 3 (9.1) 30 (90.9) 9 (9.5) 86 (90.5) 1 (9.1) 10 (90.9) 5 (16.1) 26 (83.9) 3 (13.6) 19 (86.4) 2 (20) 8 (80)	3 (4.8) 59 (95.2) 62 (100) 2 (3.6) 53 (96.4) 55 (100) 8 (15.6) 43 (86) 51 (100) 2 (18.2) 9 (81.8) 11 (100) 6 (15) 34 (85) 40 (100) 2 (3.6) 53 (96.4) 55 (100) 7 (19.4) 29 (80.6) 36 (100) 1 (6.7) 14 (93.3) 15 (100) 2 (3.6) 53 (96.4) 55 (100) 8 (20) 32 (80) 40 (100) 0 (0) 11 (100) 11 (100) 2 (3.6) 53 (96.4) 55 (100) 4 (6.9) 54 (93.1) 58 (100) 6 (12.5) 42 (87.5) 48 (100) 2 (4.8) 40 (95.2) 42 (100) 8 (12.5) 56 (87.5) 64 (100) 6 (16.2) 31 (83.8) 37 (100) 4 (5.8) 65 (94.2) 69 (100) 2 (7.7) 24 (92.3) 26 (100) 8 (10) 72 (90) 80 (100) 7 (9.6) 66 (90.4) 73 (100) 3 (9.1) 30 (90.9) 33 (100) 9 (9.5) <td< td=""></td<>	

^{*}Indicates statistically significant value

Although specific literature on the pattern of CS involvement is limited, various pathologies such as bacterial or fungal infections, tumors originating from the paranasal sinus region, skull base, lymphoma, and inflammatory conditions can affect the CS either partially or diffusely. In our study, a predominant

diffuse pattern of involvement aligns with observations from other studies on ROCM.¹⁶

Previous literature on the pre-COVID era has reported the mortality rate for ROCM ranging from 30 to 90%.^{20–25} In our study, the presence of CS involvement did not show a significant influence on patient

mortality. Our findings are consistent with some recently published studies focusing on CS involvement during the first and second waves of the COVID-associated mucormycosis pandemic, reporting 25 and 13% mortality rates, respectively. ^{13,16} Based on our study data and analysis, we want to address a couple of

Table 5: Outcome at discharge in ROCM patients based on CS involvement and history of COVID-19 infection

				Outcome at discharge		
				Expired Good		p-value
				No. of participants (%)	No. of participants (%)	
CS involvement			Involved	8 (15.7)	43 (84.3)	<0.05
			Not-involved	2 (3.6)	53 (96.4)	
CS involvement	Involved	Status of COVID-19 infection	Negative	0	8 (100)	>0.05
			Positive	8 (18.6)	35 (81.4)	
	Not-involved	Status of COVID-19 infection	Negative	0	15 (100)	
			Positive	2 (5)	38 (95)	>0.05

points concerning patient outcomes. First, can the mortality among the ROCM patients be attributed to the CST alone? Second, why do our results differ from those observed in the pre-COVID era?

In this context, the authors align their perspective with existing research, suggesting that adverse outcomes observed in the majority of ROCM patients with CS involvement, leading to fatalities, are likely not solely attributable to CST. Instead, these outcomes may result from multifactorial causes, including the spread of the fungal infection to the brain parenchyma, the presence of concurrent comorbidities, multisystem involvement, and immune alterations associated with COVID-19, as reported in other studies. 16,26,27

Before the onset of COVID-19, high mortality rates of ROCM patients were documented and primarily linked to the intracranial dissemination of the disease, often resulting from delay in seeking medical attention, diagnosis, and commencement of therapy. The lower mortality rate of ROCM patients, despite the involvement of CS observed in our study, may be attributed to the direct fungal infiltration of the ipsilateral CS, facilitated by the involvement of adjoining paranasal sinus instead of the vascular cause of CST. Fungal infiltration was effectively addressed with antifungal treatment, paranasal sinus debridement, and orbital exenteration.

Furthermore, increased patient awareness through mass media during the mucormycosis outbreak, coupled with a high index of suspicion, facilitated the early diagnosis of ROCM and CS involvement during the COVID-19 pandemic. Also, the lower number of patients presenting with significant CST on imaging may be attributed to the fact that they were already on anticoagulants due to their positive COVID status. Collectively, all these factors played a crucial role in decreasing patient mortality.

When characterizing a CST, we faced challenges in definitively attributing the thrombus to either a vascular cause, nonvascular cause, or direct fungal infiltration based solely on imaging findings. Both scenarios can manifest as a filling defect. However, the presence of mucosal thickening with hyperdensity on NCCT, T2 hypointensity on MR, and postcontrast heterogenous mucosal enhancement in the paranasal sinuses coupled with bony erosion in the sinus walls may indicate fungal sinusitis directly affecting the CS. ²⁸

More studies with larger sample sizes should be conducted to explore this association further, differentiate vascular vs nonvascular causes of CST on imaging, and accurately assess the likelihood of mortality in such patients. Collating data from multiple sources could enhance the statistical inferences drawn, contributing to a more robust understanding of predicting the prognosis in these patients.

Lastly, with the hypothesis of prognosticating the disease based on qualitative parameters of CST, we emphasized that the presence of filling defects on contrastenhanced scans, the diffuse pattern of CS involvement, convex lateral wall, and the presence of orbital cellulitis could indicate the severity of the disease when observed. These observations were consistent with the findings reported in the study by Bhatia et al.²⁹

Surgical intrusion into the CS is challenging and generally not recommended. In cases where sphenoid or ethmoid fungal sinusitis is confirmed through CT/MRI, it is advisable to perform surgical drainage of these infected sinus pockets promptly. Combining antifungals and endonasal sinus surgery is often considered the optimal treatment strategy for CST caused by mucormycosis.

Our study has certain strengths that should be acknowledged. The major strength of our study lies in its design, with a specific focus on CS and its relation to COVID-19. While the first three peaks

of COVID-19 may have concluded, the persisting risks associated with it and the emergence of new variants of COVID-19 at the end of 2023³⁰ underscore the necessity for radiologists and clinicians to be aware of disease course and imaging findings and remain prepared for any potential escalation, akin to the challenges posed by COVID-19 and ROCM.

Our study has some limitations. Being a single-center study, the study lacks generalizability, and findings must be tested in similar settings. Regarding CST evaluation on imaging, including quantitative evaluation could have provided additional information, but it could not be done in the concurrent COVID-19 and mucormycosis pandemic era. The mortality of patients was recorded without incorporating long-term follow-ups into consideration, which we acknowledge and recognize as a factor potentially influencing the results. Lastly, a smaller sample size limited us from calculating the hazard ratio depicting the effect of COVID-19 infection and sinus involvement on mortality.

Conclusion

The present study attempts to provide valuable insights into the true incidence, relation with COVID-19 infection, and detailed radiological assessment of CS involvement in patients with ROCM. We conclude that CS involvement in ROCM may not significantly impact patient mortality in both COVID-19-positive and negative patients. However, qualitative radiological parameters may serve as indicators of poor prognosis. Further, more research studies are required to elucidate the pathogenesis and imaging features of CST in mucormycosis, both among COVID-19 and non-COVID-19 patients.

Clinical Significance

The presence of CS involvement in patients with ROCM does not significantly impact mortality, regardless of their COVID-19 status,

suggesting that other factors may play a more significant role in patient outcomes.

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