The Journal of Laryngology & Otology

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Diagnostic tools in coronavirus disease 2019 associated mucormycosis – do we need three-dimensional computed tomography?

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Main Article

Dr N Shakrawal takes responsibility for the integrity of the content of the paper

Cite this article: Gupta G, Shakrawal N, Banthia S, Nehara HR, Chand D. Diagnostic tools in coronavirus disease 2019 associated mucormycosis – do we need three-dimensional computed tomography? *J Laryngol Otol* 2022;**136**:1304–1308. https://doi.org/10.1017/S0022215122001864

Accepted: 25 July 2022
First published online: 17 August 2022

Key words:
COVID-19; Mucormycosis; Imaging, Three-Dimensional; Diagnostic Imaging

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Abstract

Objective. Three-dimensional computed tomography reconstruction of the face has recently been presented as a newer diagnostic tool in coronavirus disease 2019 associated mucormycosis. This study was conducted to compare three-dimensional computed tomography reconstruction with conventional two-dimensional computed tomography in coronavirus disease 2019 associated mucormycosis.

Methods. A total of 123 mucormycosis patients underwent three-dimensional computed tomography reconstruction after a comprehensive clinical investigation. The involvement of the facial skeleton was noted.

Results. The anterior maxillary wall was most commonly involved (9.8 per cent). Involvement of the lateral maxillary wall was noted in 6.5 per cent of patients. Sixty-seven patients (54.5 per cent) underwent endoscopic surgery, 22 (17.9 per cent) underwent open surgical procedures, and 12 (9.8 per cent) had combined endoscopic and open surgical procedures. In 21 patients (17.1 per cent), open surgery was performed in the first instance based on additional three-dimensional computed tomography findings, and revision surgical procedures were avoided.

Conclusion. Three-dimensional computed tomography of the face was found to be superior in determining the extent of disease. It reduces delays in diagnosis, facilitates surgical planning and minimises the need for multiple surgical procedures.

Introduction

Mucormycosis is an invasive fungal infection caused by the Phycomycetes group of fungi. The pathogenesis is angioinvasion.[1] In addition to necrosis of tissues, it also erodes bones of the facial skeleton. Although cases of coronavirus disease 2019 (Covid-19) associated mucormycosis were reported during the first wave of Covid-19, there was an upsurge during the second wave in many cities in India, and it was declared an epidemic by various state governments. By 7 June 2021, 28 252 cases had been recorded by the Indian Ministry of Health.[2] This increase devastated the prognosis of Covid-19 in high-risk individuals (with immunosuppression), and caused fear and apprehension in the general public. The associated mortality, poor outcomes, need for revision surgical procedures, and resultant deformities and disabilities are major concerns among healthcare personnel and the public.

The progression of Covid-19 associated mucormycosis is unpredictable, and its management is long with unclear outcomes. Coronavirus disease 2019 associated mucormycosis involves rhino-orbital-cerebral tissues, it invades deep facial structures, and it is associated with a propensity for bony infiltration and intracranial complications. The bony occurrence has been reported as a late feature, characterised by deep extension of infection through perivascular channels, resulting in evident bony destruction.[3] Resection of the entire disease, followed by restoration of cosmesis and function, is a real challenge. Facial deformity, with disturbances in swallowing, vision and speech, are points of concern for patients and clinicians.

Early diagnosis and management of Covid-19 associated mucormycosis are key to survival. The primary definitive treatment is surgical debridement, performed promptly, followed by administration of systemic antifungals. The resultant disfigurement can be addressed later on with a prosthesis. The choice of surgical approach is crucial to achieve optimal results with less morbidity, without delay. Multiple surgical procedures might be difficult in morbid patients who cannot tolerate general anaesthesia. In addition, morbidity and deformity might increase after multiple surgical procedures.

Although two-dimensional (2D) computed tomography (CT) is extensively used by otorhinolaryngologists to determine the extent of disease, a third dimension aids appreciation of the anatomy and orientation. Conventional radiography (2D CT and contrast-enhanced magnetic resonance imaging (MRI)) helps in predicting the underlying pathology to some extent. In patients with milder symptoms, it is difficult to predict the underlying damage, which might make us indecisive in choosing the correct surgical

approach. Newer software and technologies help in the rapid conversion of 2D CT to three-dimensional (3D) CT images;[4] in addition, these images can be created in any plane and rotated in space.[5]

Three-dimensional CT is performed using a helical multislice scanner. It is an easier and faster modality for determining the disease extent, and helps in counselling patients as well. The overlapping bones of the facial skeleton are better observed on 3D CT images, as they reveal the spatial relationship of bones and soft tissues. Three-dimensional CT can display a clear picture of disease involvement, facilitate disease staging and aid surgical decision-making. Software is used on the axial and coronal images obtained from helical 2D CT to reconstruct 3D images. The advantage of explaining the disease extent to patients and their attendants further aids in the counselling of patients.

We hereby review our experience of 3D CT used as a diagnostic aid in Covid-19 associated mucormycosis, and compare it with conventional 2D CT in terms of pre-operative evaluation and its effects on surgical management.

Materials and methods

We performed an analysis of 123 consecutive patients with Covid-19 associated mucormycosis at our tertiary care centre from May 2021 to August 2021. After complete evaluation and clinical investigation, the diagnostic modalities, management options and outcomes were noted. Consent was obtained from all patients, and ethical clearance was acquired from the institutional ethical committee (reference number: F.29(Acad) SPMC/2021/2322). All 123 patients were confirmed cases of Covid-19 associated mucormycosis, and showed broad aseptate fungal hyphae on direct microscopic examination and Mucorales on fungal culture.

Conventional 2D CT of the face was ordered and 3D reconstruction was performed in the same setting. All patients underwent contrast-enhanced MRI for better detection of the extent of soft tissue involvement. The Wipro GE Healthcare (Bengaluru, India) Revolution Evo 128-slice CT scanner was used in this study, with parameters as follows: tube voltage of 140 kVp, tube current of 125 mA, pitch of 0.53 mm/rotation, collimation of 20 mm, field of vision of 25 cm, matrix of 512 × 512, and scan area diameter of 38 × 25 cm which was variable for every patient. Images were acquired in the axial plane with a slice thickness of 0.625 mm, and sagittal and coronal images were reconstructed to 0.54 mm slice thickness. The head was kept in a supine position and a lateral tomogram was obtained. The whole face and skull were continuously scanned. The images were then reconstructed to 3D CT with the help of GE Healthcare AW Server software system (version 16 HW14.9). The CT scan reporting was conducted by senior radiologists from the radiodiagnosis department.

Results

The study included 78 males (63.4 per cent) and 45 females (36.6 per cent), with a mean age of 49.4 years. All patients had a history of Covid-19; 22 patients (17.9 per cent) had active Covid-19 infection at the time of Covid-19 associated mucormycosis diagnosis. A history of diabetes mellitus was present in 54 patients (43.9 per cent). Recent-onset diabetes mellitus was noted in 62 patients (50.4 per cent). The aetiology and risk factor profile were the same in the groups with negative and positive 3D CT findings.

The anterior maxillary wall (Figure 1) was most commonly involved (9.8 per cent). The lateral maxillary wall was involved in 6.5 per cent of patients. The orbital floor, palate and zygomatic process were involved (Figures 2–4) in 6.5 per cent, 4.1 per cent and 4.9 per cent of patients, respectively.

Sixty-seven patients underwent endoscopic endonasal debridement, 22 underwent open surgery in the form of total maxillectomy, with 8 undergoing orbital exenteration, and 12 having combined endoscopic and open surgical procedures. Thirty-five endoscopic endonasal debridement patients underwent revision surgical procedures because of disease extension. Twenty-one patients (17.1 per cent) had positive 3D CT findings and hence underwent open surgery in the first instance, avoiding revision surgical procedures. Liposomal amphotericin B treatment was continued in all the patients.

Twenty-two patients (17.9 per cent) did not survive, despite all efforts; this was because of extensive intracranial involvement and other co-morbidities.

Table 1 shows the comparative findings of 3D CT and 2D CT.

As mentioned, the anterior wall of the maxilla was most commonly involved by the disease, followed by the lateral maxillary wall and the orbital floor. Two-dimensional CT and 3D CT both identified erosion of the anterior maxillary wall as being most common. The most common sinus involved was the maxillary sinus (72.3 per cent). Intracranial extension was seen in 17 per cent of patients. Of the patients, 8.1 per cent had orbital involvement.

In 21 patients (17.1 per cent), the decision to perform open surgery in the first instance was made based on 3D CT

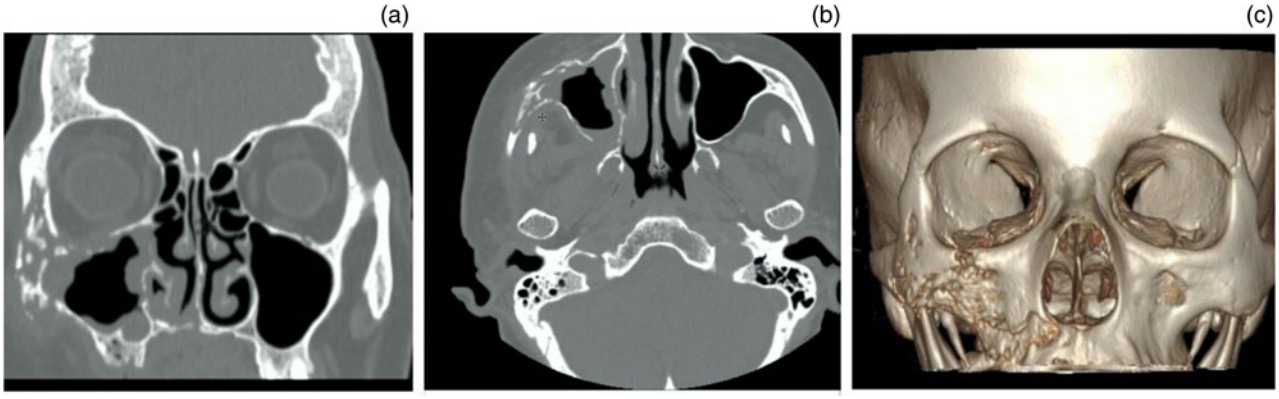

Fig. 1. (a) Coronal and (b) axial two-dimensional, and (c) three-dimensional computed tomography images showing destruction of right anterior maxillary wall, alveolar process and zygomatic process.

https://doi.org/10.1017/S0022215122001864 Published online by Cambridge University Press

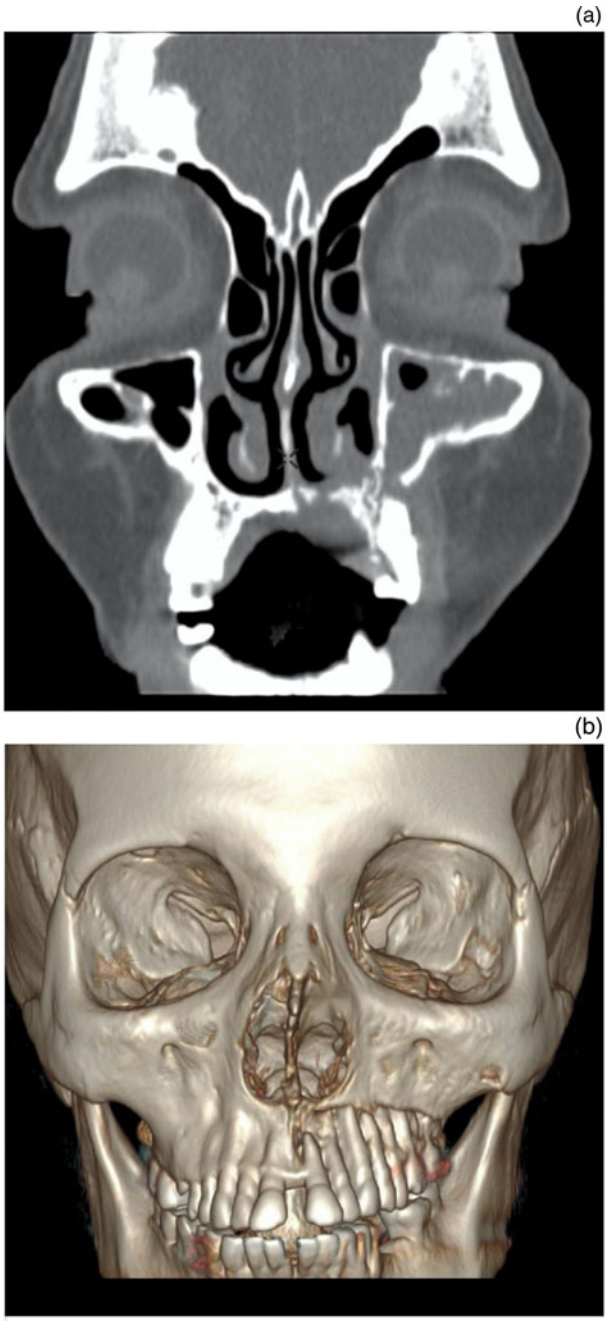

Fig. 2. (a) Coronal two-dimensional and (b) three-dimensional computed tomography images showing destruction of left alveolus with no involvement of anterior maxillary wall, which propelled us to perform infrastructural maxillectomy.

findings. In these patients, if 3D CT had not been carried out, perhaps we would have planned to perform endoscopic endonasal debridement, a decision which could have changed intra-operatively. Three-dimensional CT reconstruction aided our decision pre-operatively, and multiple or revision surgery was thereby avoided. In 102 patients, 3D CT did not show characteristic findings, and hence we went ahead with endoscopic endonasal debridement. Axial images are precise to the core in locating the anterior, posterior, medial and lateral maxillary walls on CT scans. The coronal scan can detect the involvement of nasomaxillary sutures.[6]

Discussion

Conventional CT depicts anatomy and pathology in two dimensions. The exact depth and extent of disease are difficult to determine from the images. Information gained from a

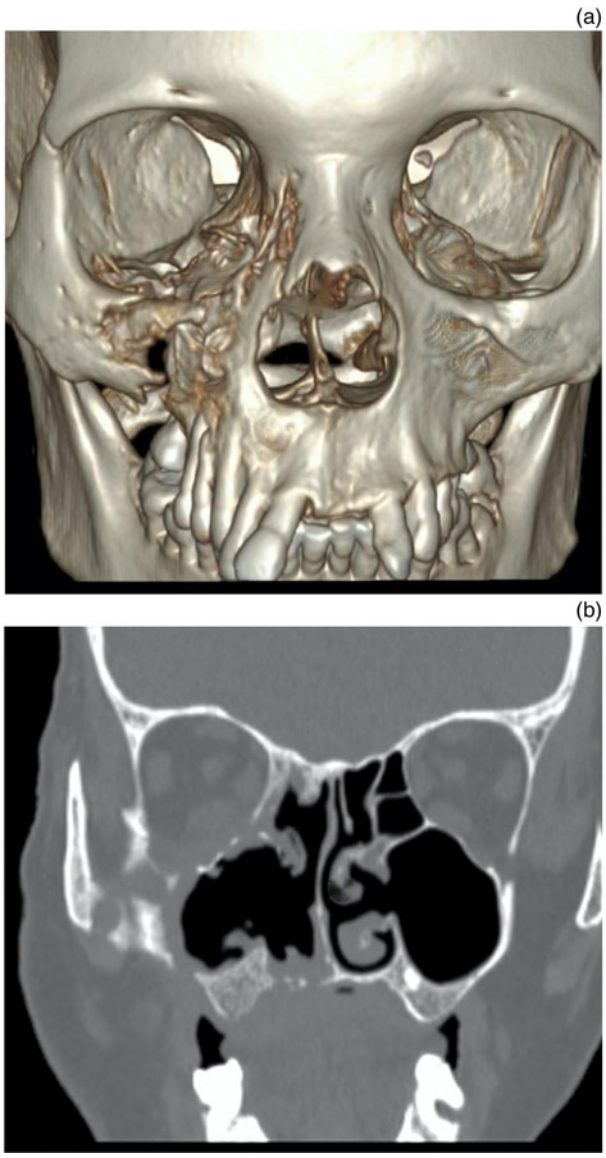

Fig. 3. (a) Three-dimensional and (b) coronal two-dimensional computed tomography images showing destruction of right infra-orbital floor, ipsilateral alveolus and zygomatic process.

third dimension is valuable for more precise delineation of disease and orientation. The technology capable of demonstrating a third dimension has had a great impact on the pre-surgical planning and adequate management of Covid-19 associated mucormycosis.

The overlying oedema, necrosis and eschar that mask accurate clinical evaluation may make conventional radiography an ineffective tool; in Covid-19 associated mucormycosis cases, such factors might obscure the extent of disease on conventional CT. The facial skeleton has a complex anatomy, with superimposition of various bones, leading to artefacts that result in inappropriate information. The 2D CT images might be difficult to interpret, which could be more time-consuming.[7] The advantages of 3D CT over 2D CT, even in the presence of oedema and soft tissue involvement, makes it an essential tool for the precise demonstration of the disease process.[8]

Our study included 78 males and 45 females. Most studies of Covid-19 associated mucormycosis report a male preponderance, for unknown reasons.[9]

In our series, 3D CT evaluation had considerable preoperative bearing for 21 patients, aiding surgical planning decisions for these patients. We observed that involvement

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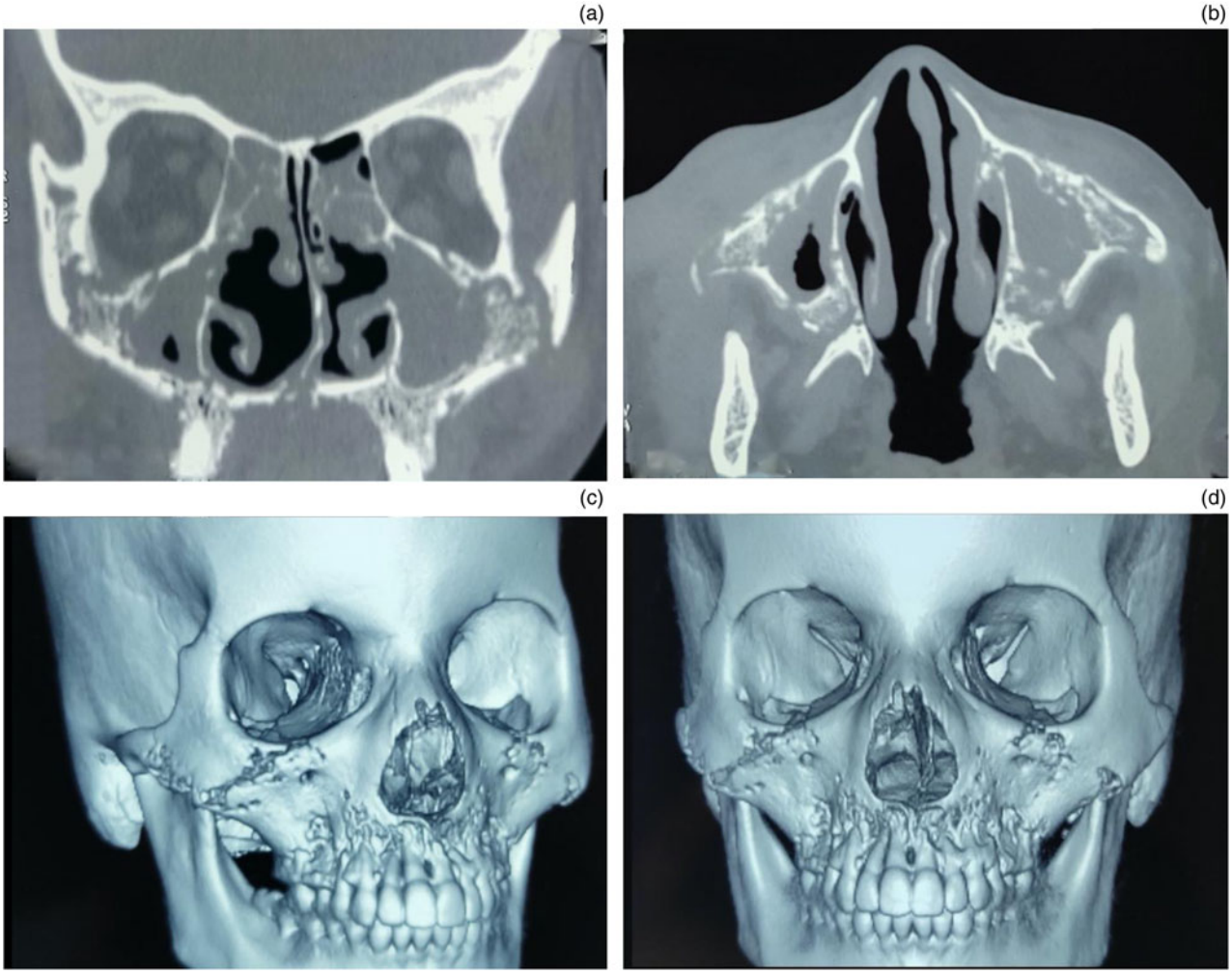

Fig. 4. (a) Coronal and (b) axial two-dimensional, and (c & d) three-dimensional computed tomography images showing destruction of bilateral anterior and posterior walls of maxilla, with involvement of bilateral alveolus.

of the anterolateral maxillary wall, along with that of the zygomaticomaxillary region, propelled us to opt for total maxillectomy in 22 patients. It is impossible to eradicate the disease from these sites using endoscopic endonasal debridement. The 3D CT prompted us to change the surgery plan from partial maxillectomy to total maxillectomy. It also provided more accurate information about erosion of the alveolar process; many patients have disease mainly in the alveolar process, without gross sinus involvement. In seven patients, alveolar damage could be identified on 3D CT images (Figure 2), and we subsequently performed infrastructural maxillectomy.

Table 1. Comparison of bony involvement detected on 2D and 3D CT scans

Findings	2D CT scans (*n*)	3D CT scans (*n* (%))
Erosion of anterior wall of maxilla	10	12 (9.8)
Erosion of lateral wall of maxilla	5	8 (6.5)
Erosion of zygomatic process, zygomaticomaxillary buttress	4	6 (4.9)
Erosion of anterior frontal table	1	3 (2.4)
Erosion of orbital floor	4	8 (6.5)
Erosion of alveolus	2	7 (5.7)
Erosion of palate	4	5 (4.1)

2D = two-dimensional; 3D = three-dimensional; CT = computed tomography

Awareness of orbital floor involvement has a large influence on management. We observed orbital floor involvement (Figure 3) in 18 patients. Peri-orbital involvement was found in 8 patients.

Minimal osteomyelitis or bony erosion can be detected on 3D CT (Figure 5), which might be missed by other investigations or clinical examinations. Three-dimensional CT has proved beneficial in our series; thus, we conclude it to be an important tool for planning the surgical approach.

- Three-dimensional (3D) computed tomography (CT) of the face is superior to conventional CT in determining extent of disease
- Three-dimensional CT is important for pre-operative surgical planning of coronavirus disease 2019 associated mucormycosis cases
- Minor cortical erosions and their finer details are not detected on conventional CT
- Use of 3D CT prevents delays in diagnosis, facilitates surgical planning and reduces need for multiple surgical procedures
- It is a valuable tool in the assessment of revision cases and at follow up
- Post-operative evaluation and follow up are made easier by 3D CT; it is also an important teaching tool and aids patient counselling

Coronavirus disease 2019 associated mucormycosis is a therapeutic challenge for otorhinolaryngologists, not a diagnostic challenge. The disease is fulminant and carries a high risk of mortality, even after treatment.[10] Until now, we were diagnosing and managing Covid-19 associated mucormycosis based on clinical assessment, 2D CT and contrast-enhanced MRI. The 3D CT technology is a promising diagnostic tool for assessment, and comparison with conventional 2D CT has revealed it as superior in

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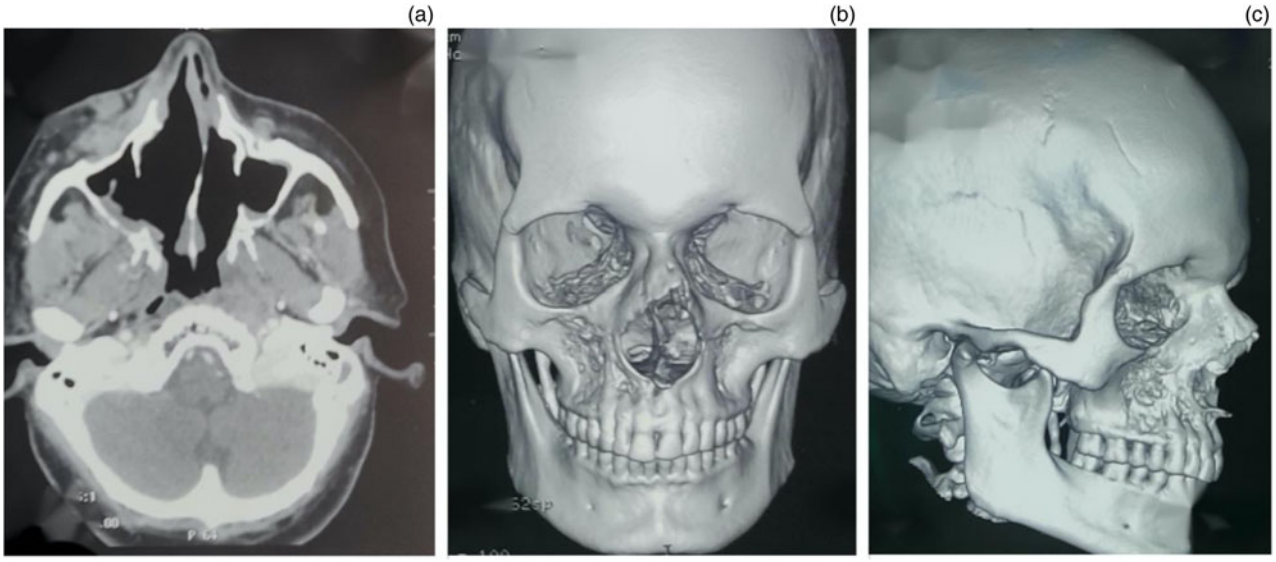

Fig. 5. (a) Two-dimensional axial computed tomography (CT) image demonstrates soft tissue density over anterior maxilla. (b & c) Three-dimensional CT images showing minor cortical erosion of bilateral anterior walls of maxilla.

Table 2. Advantages of 3D CT scans over 2D CT scans

3D CT reconstruction uses 2D images for reformatting, so no additional radiation exposure
3D CT provides detailed information about individual bones of facial skeleton & defines exact bony contours
Virtual surgery in the form of editing & cutting can be performed with 3D CT. Ability to delete certain fragments from 3D CT scan aids viewing of posterior structure & improves assessment.[11] Intra-operative accidents & complications can be predicted
3D CT is a valuable teaching tool for trainees, & helps counselling of patients & attendants
Newer software for 3D CT speeds up processing time, decreases cost & improves assessment

3D = three-dimensional; CT = computed tomography; 2D = two-dimensional

many ways. The advantages of 3D CT over 2D CT are mentioned in Table 2.[11] Three-dimensional CT can guide selection of the best therapeutic regimen. Fox *et al.* concluded that 3D CT can be interpreted more accurately by clinicians.[12] The recent software allows graphic manipulation of volumetric data, and the qualitative information is presented in an easily recognisable pattern for clinicians.[13]

Limitations

The potential artefacts associated with 3D CT, and the inability to represent soft tissue structures or muscles demands additional MRI evaluation. We included confirmed cases of Covid-19 associated mucormycosis and then performed 3D CT; this may not reveal the entire spectrum of disease, as many suspicious lesions remain unconfirmed or the patient may succumb before reaching the healthcare facility. In our study, the size of the sample with positive 3D CT findings was small. Further studies with larger sample sizes will be required for conclusive results.

Conclusion

Three-dimensional CT gives an excellent overview of the gross involvement of disease and degree of destruction of the facial skeleton. As we know, early clinical assessment is important for early diagnosis, and 3D CT performed at the correct time can be crucial, as reconstructed 3D images aptly assist in the clear visualisation of skull bones, bony architecture, fat, muscles and soft tissue windows. Post-operative evaluation and follow up can be enhanced by 3D CT. Three-dimensional CT is an important teaching tool, and aids in counselling patients and their attendants.

Competing interests. None declared

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