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ORIGINAL ARTICLE

Surgical outcomes in large vestibular schwannomas: should cerebellopontine edema be considered in the grading systems?

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Abstract

Purpose Large (> 3 cm) vestibular schwannomas pose complexity in surgical management because of narrow working corridors and proximity to the cranial nerves, brainstem, and inner ear structures. With current vestibular schwannoma classifications limited in information regarding cerebellopontine edema, our retrospective series examined this radiographic feature relative to clinical outcomes and its possible role in preoperative scoring.

Methods Of 230 patients who underwent surgical resection of vestibular schwannoma (2014–2020), we identified 107 patients with Koos grades 3 or 4 tumors for radiographic assessment of edema in the middle cerebellar peduncle (MCP), brainstem, or both. Radiographic images were graded and patients grouped into Koos grades 3 or 4 or our proposed grade 5 with edema. Tumor volumes, radiographic features, clinical presentations, and clinical outcomes were evaluated.

Results The 107 patients included 22 patients with grade 3 tumors, 39 with grade 4, and 46 with grade 5. No statistical differences were noted among groups for demographic data or complication rates. Unlike grades 3 and 4 patients, grade 5 patients presented with worse hearing ($p < 0.001$), larger tumors ($p < 0.001$), lower rates of gross total resection (GTR), longer hospital stays, and higher rates of balance dysfunction.

Conclusion With edema detected in 43% of this cohort, special considerations are warranted for grade 5 vestibular schwannomas given the preoperative findings of worse hearing, lower GTR rates, longer hospital stays, and 96% who pursued postoperative balance therapy. We propose that grade 5 with edema offers a more nuanced interpretation of a radiographic feature that holds relevance to treatment selection and patient outcomes.

Keywords Acoustic neuroma · Koos classification · Koos grade · Peritumoral edema · Edema · Large vestibular schwannoma

Abbreviations

AAO-HNS	American Academy of Otolaryngology—Head and Neck Surgery
ADC	Apparent diffusion coefficient
MCP	Middle cerebellar peduncle
HB	House-Brackmann
LOS	Length of stay
MRI	Magnetic resonance imaging
ROI	Region of interest
3D	Three-dimensional

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Introduction

Large vestibular schwannomas pose unique complexity because of the relatively narrow working corridor during resection and proximity to the cranial nerves, brainstem, and structures of the inner ear. Surgical management can be associated with high rates of complications and unfavorable clinical outcomes [4, 8, 13, 24].

Vestibular schwannomas have been classified based on their extrameatal extension from the internal auditory canal and extent of brainstem compression.[5] The Koos

classification divides tumors into four grades determined on magnetic resonance imaging (MRI) of the brain. Koos 1 tumors are completely contained within the meatus; Koos 2 tumors have intra- and extra-meatal (cisternal) components but do not contact the brainstem; Koos 3 tumors have direct contact with the brainstem; and Koos 4 tumors contact and exert mass effect on the brainstem [6, 15]. Several other schemes exist that further subdivided tumors by extent of brainstem compression and presence of fourth ventricular displacement [1, 20]. Current classifications that ascertain meatal extension, three-dimensional (3D) diameters to define tumor size, and preoperative imaging to evaluate the diameter and location of the facial nerve have been crucial in assessing surgical complexity and predicting outcomes in vestibular schwannoma to some extent [11, 18].

To our knowledge, no classification system and only few studies have considered the implications of radiographic features of the middle cerebellar peduncle (MCP) and brainstem subject to mass effect in large vestibular schwannoma. Importantly, there exists a scarcity of research examining clinical outcomes in patients with large tumors (> 3 cm) who also have edema of the MCP, brainstem, or both. The MCP (main afferent pathway to the cerebellum) and pontine nuclei are part of the cortico-ponto-cerebellar pathway, which is involved in coordinating motor tasks. Therefore, MCP lesions can have association with ataxia (limb and gait), scanning speech, and sometimes facial weakness. Cerebellopontine edema can affect balance and coordination, which may influence surgical strategies and outcomes.

With the scarcity of research examining clinical outcomes of large vestibular schwannoma with cerebellopontine edema and its postoperative effects on balance and coordination, our retrospective study investigated the clinical presentation, tumor feature and volumes, and surgical outcomes in our patients who underwent resection of Koos grade 3 and 4 tumors. We then propose a new grade 5 based on radiographic evidence of edema and discuss its correlation with postoperative effects, such as worsened cranial nerve function and balance dysfunction, that hold relevance for treatment selection and patient expectations of outcomes.

Methods

With approval by our Institutional Review Board (IRB no. 21–4638), we retrospectively reviewed the records of all 230 patients who underwent surgical resection of vestibular schwannoma between July 1, 2014 and December 31, 2020 to identify those with pathological confirmation of Koos grade 3 or 4 and minimum 3-month postoperative follow-up. Radiographic findings of this subset of 107 patients were further examined for the presence of edema within the MCP, brainstem, or both. Any Koos grade 3 or 4 tumor associated peritumoral edema was redefined as a grade 5 tumor. Patients were included with newly diagnosed unilateral vestibular schwannoma without prior surgical or radiation treatment and excluded for a diagnosis of neurofibromatosis and bilateral tumors. This retrospective study followed the STROBE guidelines.

Surgical treatment

All cases were presented and treatment options discussed at our multidisciplinary skull base conference. Patients then underwent a retrosigmoid or translabyrinthine or combined staged approach with a uniform neuromonitoring protocol; the senior surgeon (ASY) performed all 230 surgical resections. Preoperative Koos grade, based on the most recent MRI of the brain before resection, was determined by the neurosurgeon and then confirmed by a board-certified neuroradiologist blinded to the initial grade. For the 107 patients with Koos grade 3 or 4 included in this study, the same neuroradiologist (blinded to patient outcomes) then determined the preoperative presence of edema of the MCP or brainstem or both and assigned a binary grade.

Demographic and preoperative data included patient age, sex, ipsilateral House-Brackmann (HB) score [10, 11], and hearing class based on the 1995 hearing classification of the American Academy of Otolaryngology—Head and Neck Surgery (AAO-HNS) [3]. Operative variables included surgical approach, final tumor pathology, and surgical outcome. Extent of resection was classified intraoperatively as subtotal in cases of a nodular residual, near total for < 2 mm linear residual enhancement along the nerves, or gross total resection (GTR) and confirmed by neuroradiologists based on postoperative MRI. Postoperative data collected included ipsilateral HB score, cranial nerve (CN) dysfunction (excluding CN VII), hearing class (AAO-HSN), length of stay, postoperative therapy, and complications or adverse events. Balance dysfunction indicating the need for rehabilitation was determined by specialty-trained occupational and physical therapists who were blinded to our study.

Segmentation of vestibular schwannoma

Using ITK-SNAP [25], tumor segmentation included T2-weighted MRI sequences co-registered to T1-post contrast sequences. Next, the apparent diffusion coefficient (ADC) image set was co-registered to the T2 data. Segmentation used the polygon tracing tool in ITK-SNAP to trace a region-of-interest (ROI) encompassing the tumor; the ROI was saved as a binary 3D mask as a NIFTI file.

T2 and ADC pixel intensity estimates

MATLAB (2021a) was used to import NIFTI files of the co-registered image sets T2-weighted image (T2) and ADC and segmentation binary mask. For each case, pixel intensity values were extracted independently from the tumor ROI for both the T2 and ADC data sets; pixel intensity value distributions for each case were normalized and summarized by the mean ± standard deviation. Finally, the volume (mm^3) was calculated for each tumor segmentation.

Results

Clinical findings

Among 230 patients who underwent surgical resection of vestibular schwannomas confirmed by pathological findings during the 6.5-year study period, 107 patients were included who had Koos grade 3 or 4 tumors determined from preoperative radiographic findings and a minimum 3-month clinical follow-up. Aiming to subdivide Grade 4 lesions for greater specificity beyond size in treatment planning, we identified 46 (43%) patients with grade 5 tumors as > 3 cm and with edema detected at the level of the MCP and/or brain stem; the 61 (57%) patients without edema included 22 patients and 39 patients with Koos grades 3 and 4, respectively (Fig. 1). No statistical differences were noted in mean or median age or sex distribution among these three tumor groups. In multivariate analysis, grade 5 tumor volume would be a significant factor ($p < 0.05$) related to length of stay (LOS) and balance outcomes.

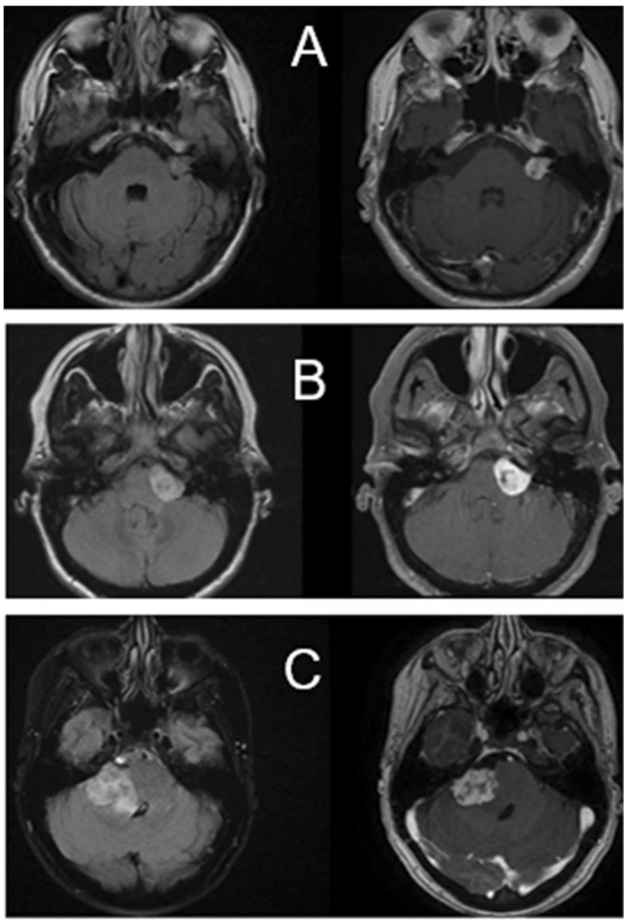

Fig. 1 Examples of radiographic appearance of vestibular schwannoma with grades 3 and 4 without edema and proposed grade 5 with edema. **A-C:** MRI FLAIR (left) and T1 with contrast sequences (right) in Grade 3 (**A**) and Grade 4 (**B**) without edema and Grade 5 (**C**) with edema

Preoperative characteristics

All 107 patients were analyzed for preoperative tumor characteristics by HB grades, AAO-HNS hearing classification, tumor volumes, and surgical approach. In comparing the three groups, we found no statistically significant difference related to facial nerve status by preoperative HB scores (Table 1) whereas preoperative AAO-HNS hearing class differed significantly ($p < 0.001$) (Table 2).

Preoperative tumor characteristics varied by tumor volumes and extent of resection among groups (Fig. 2). Specifically, mean tumor volume of 19,026 mm^3 for grade 5 was significantly larger than the volumes of 4,528 mm^3 for grade 3 and 9,377 mm^3 for grade 4 ($p < 0.05$). No statistical differences were observed when comparing tumor grade with mean tumor ADC and T2 characteristics (Table 3).

Although no significant differences were found in tumor resection by surgical approach (ie, retrosigmoid, translabyrinthine, staged) (Table 4), extent of resection varied significantly by tumor grade. Specifically, the 52% GTR rate in patients with grade 5 tumors was significantly lower than the 72% and 77% GTR rates in patients with grade 3 or 4 tumors, respectively ($p < 0.01$) (Table 4).

Clinical outcomes

In assessment of postoperative complications and cranial nerve outcomes, no differences were observed by tumor grade. Postoperative HB scores and cranial nerve dysfunction (other than facial nerve) did not statistically differ among the 7 (32%) patients with grade 3 tumors, 13 (33%) patients with grade 4 tumors, and 19 (41%) with grade 5 tumors. Complication rates were comparable among groups as 32%, 32%, and 36% in grades 3, 4, and 5, respectively ($P > 0.05$).

Table 1 Demographic and preoperative characteristics for 107 patients who underwent vestibular schwannoma resection for a Koos grade 3 or 4 and our proposed grade 5 with edema

Variable	Grade 3	Grade 4	Grade 5
No. patients	22	39	46
Sex			
Male	9 (41%)	21 (54%)	19 (41%)
Female	13 (59%)	18 (46%)	27 (59%)
Age in years (mean)	52.5	50.1	49.9
Median age in years (range)	54 (33–69)	52 (18–68)	51 (16–78)
Preoperative House-Brackmann (HB) grade by no. (%)			
HB 1	20 (91%)	38 (97%)	41 (89%)
HB 2	1 (5%)	0	3 (7%)
HB 3	0	1 (3%)	2 (4%)
HB 4	1 (5%)	0	0
Preoperative hearing class AAO-HNS by no. (%)			
A	8 (36%)	14 (36%)	6 (13%)
B	3 (14%)	9 (23%)	10 (22%)
C	2 (9%)	1 (3%)	3 (7%)
D	9 (41%)	15 (38%)	27 (59%)

In multivariate analysis, tumor volume was a significant contributor ($p < 0.05$) related to LOS and balance rehabilitation. Length of stay until hospital discharge averaged (± standard deviation) 4.1 ± 2.1 days for grade 3, 4.7 ± 4.4 days for grade 4, and 5.7 ± 4.4 days for grade 5 (Fig. 3). Thus, LOS was significantly longer only for grade 5 only versus grade 3 tumors. A significant 44 (96%) of 46 grade 5 tumor patients received therapeutic rehabilitation for postoperative balance dysfunction compared with 16 (73%) of 22 grade 3 patients and 32 (82%) of 39 grade 4 tumor patients (p 0.03).

Discussion

Our retrospective review of 107 patients who underwent surgical resection of Koos grade 3 or 4 vestibular schwannomas offers a nuanced interpretation for the relevance of extratumoral edema of the MCP and brainstem. With edema radiographically present in 43% of our patients, we (senior author) propose that this preoperative finding could be designated as a new grade 5 (Table 5) that warrants further study toward statistical validation in a larger cohort. Our grade 5 patients presented with statistically worse hearing function by AAO-HNS hearing class than our grade 3 and 4 patients and, while preoperative facial nerve function did not significantly differ between groups, nearly all grade 5 tumor patients underwent rehabilitation therapy for worsened postoperative balance dysfunction.

Existing evidence for peritumoral edema

Previous studies that examined peritumoral edema in vestibular schwannomas established the foundation for our study. In a retrospective study examining peritumoral edema in vestibular schwannoma, Giordano et al. reported its 5% incidence more often occurred at the MCP than the cerebellum or brainstem; they noted a statistically significant association of peritumoral edema with tumor size but not tumor shape, surface regularity, or cystic versus homogenous composition [9]. Our study similarly found that grade 5 tumor volumes were significantly larger than grade 3 or 4 tumors. Given peritumoral edema completely resolved within 1 year of postoperative follow up, Giordano et. al suggested this edema was a tumor-related phenomenon [9]. In their previous publication that reported on gross intraoperative observations, this same group concluded that no intraoperative characteristics studied thus far significantly correlated with the presence of peritumoral edema [21].

Balance dysfunction

Our observation that patients with peritumoral edema had worse balance dysfunction led us to suspect the etiology was a cortico-ponto-cerebellar pathway dysfunction. However, existing evidence specific to balance dysfunction is quite limited.

In their 2022 retrospective review of vestibular schwannoma patients, Zumofen et al. identified the presence of brainstem edema as one of multiple factors significantly associated with postoperative progression and/or need for further treatment and progression-free survival; however, this association was not present when examining only patients who underwent subtotal resection [26]. Compared with grades 3 and 4 patients, our grade 5 patients had longer

Table 2 Comparing preoperative volumetric characteristics among tumor grades 3 through 5. * Grade 5 tumor volumes were significantly larger than Grade 3 or 4 volumes ($p < 0.05$). No significant differences among groups were noted for tumor apparent diffusion coefficient (ADC), T2 mean, and T2 maximum levels

Mean volume (mm^3) ± standard deviation	Grade 3	Grade 4	Grade 5
Mean tumor volume	4,528 ± 3,823	9,377 ± 5,303	19,026 ± (10,681)*
ADC	1,738 ± (2,376)	2,783 ± (3,789)	2,600 ± (3,034)
Mean T2-weighted	1,878 ± (2,373)	1,666 ± (1,391)	1,572 ± (1,278)
Maximum T2-weighted	5,304 ± (6,955)	4,982 ± (4,764)	4,192 ± (5,369)

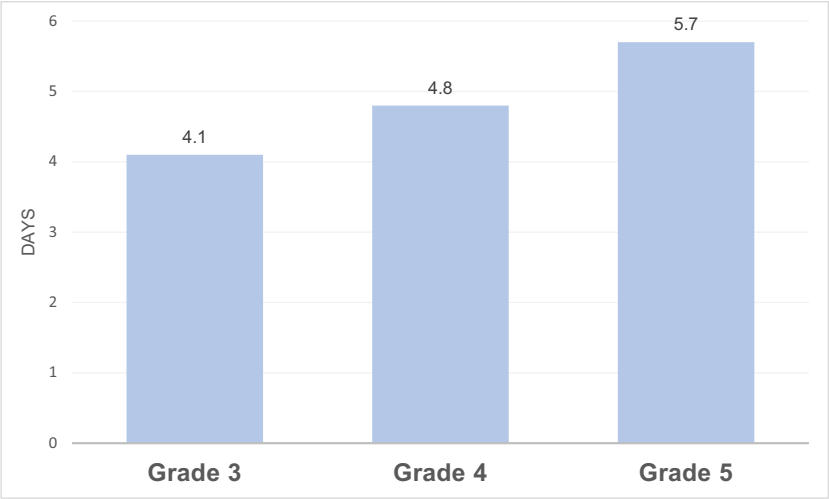

Fig. 2 Length of hospital stay was significantly longer for patients with grade 5 than grade 3 tumors ($P < 0.05$)

hospital stays and 96% received therapeutic rehabilitation postoperatively for balance dysfunction. These findings contribute to the existing literature on vestibular schwannoma that can inform clinician decision-making and counseling patients about postoperative expectations, including the need for additional physical therapy [14, 17, 19].

Facial nerve function

In investigating other tumor-specific characteristic among our three groups, we found no difference in ADC or T2 values. We previously reported the predictive value of medium-range ADC values on postoperative facial nerve function [16]. Accordingly, there was also no difference in facial nerve function postoperatively between patients with grade 5 tumors and grade 3 or 4 tumors. This finding suggests that increased size and/or presence of MCP or brainstem edema may not necessarily impede our ability to preserve facial nerve function in patients with at least Koos grade 3 tumors. Previous literature on this has been mixed [2, 5, 7, 12, 22, 23] with the two afore-mentioned studies reporting divergent findings related to the association of peritumoral edema and early postoperative facial nerve function. The first intraoperative quality-focused study in 2015 reported a statistically significant relationship between peritumoral edema and worse HB score [21] whereas a neuroimaging quality-focused study in 2020 reported a non-statistically significant tendency between peritumoral edema and better HB score [2]. Our study also found no difference between groups in non-facial cranial nerve dysfunction or postoperative complications.

Tumor volume and extent of resection

Our findings and review of the literature suggest that vestibular schwannoma with MCP and/or brainstem edema tend to be larger than those without edema. Mean tumor

Table 3 Surgical approach and outcomes by tumor grade by number (%) of patients. No statistical difference when comparing surgical approaches among groups. *Gross total resection rates were significantly lower in grade 5 tumors than grades 3 and 4 tumors ($p < 0.01$)

Surgical Approach	Grade 3	Grade 4	Grade 5
Retrosigmoid	11 (50%)	17 (44%)	29 (63%)
Retro/Trans (Staged)	0 (0%)	0 (0%)	1 (2%)
Translabyrinthine	11 (50%)	22 (56%)	16 (35%)
Surgical Outcome			
Subtotal resection	1 (5%)	1 (3%)	7 (15%)
Near total resection	4 (18%)	10 (26%)	15 (33%)
Gross total resection	17 (77%)	28 (72%)	24 (52%)*

Table 4 For clinical outcomes, there were no statistical significance among groups in postoperative HB, cranial nerve (CN) dysfunction, or complication rates

Clinical outcome	Grade 3	Grade 4	Grade 5
Postoperative HB			
1	7 (32%)	18 (46%)	39 (36%)
2	7 (31%)	8 (21%)	26 (24%)
3	2 (9%)	6 (15%)	10 (9%)
4	1 (5%)	1 (3%)	7 (7%)
5	0 (0%)	3 (8%)	9 (8%)
6	5 (23%)	3 (8%)	16 (15%)
Postoperative CN dysfunction			
No	15 (68%)	26 (67%)	27 (59%)
Yes	7 (32%)	13 (33%)	19 (41%)
Postoperative complications			
No	15 (68%)	27 (69%)	29 (64%)
Yes	7 (32%)	12 (31%)	16 (36%)

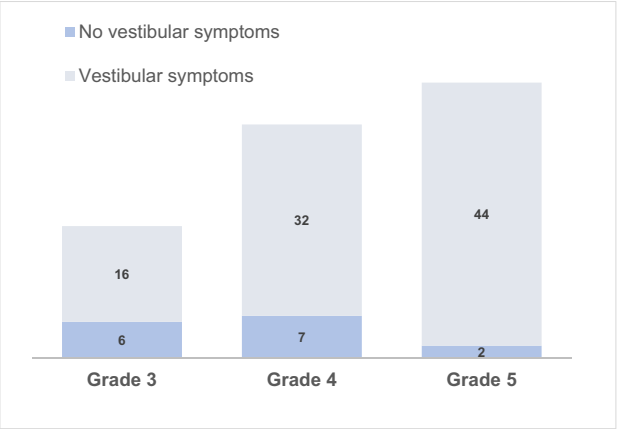

Fig. 3 Postoperative vestibular dysfunction affected significantly more patients with grade 5 tumors, specifically 44 (96%) of 46 patients versus 73% (16/22) of grade 3 and 82% (32/39) of grade 4 patients (p 0.03)

volumes in our patients of 9,377 mm^3 in grade 4 and 19,026 mm^3 in grade 5 suggest a potentially critical volume between 10,000 mm^3 and 20,000 mm^3 when peritumoral edema may occur. This correlates with cochlear nerve function but no other studied deficits at presentation. Although our data suggest the presence of edema did not result in higher rates of facial nerve deficit, this may be an outcome of a more conservative extent of resection with a tendency to protect the facial nerve. Accordingly, rates of GTR were lower in patients with grade 5 tumors than grade 3 or grade 4 tumors.

Existing grading systems and proposed adjunct

In addition to the classic Koos grades, other grading scales and classifications for vestibular schwannoma account for fourth ventricular displacement, hydrocephalus, and tumor size [6, 15]. Finding that peritumoral edema was present but not exclusively perpendicular to the major axis of tumor growth, Giordano et al. suggested that a compressive etiology of edema was inadequate [9]. Therefore, adjuncts to existing grading scales may be warranted to capture the presence of cerebellopontine edema, which may provide valuable clinical insight or predictive value to assist in patient-clinician decision-making. Moreover, patients with MCP and/or brainstem edema with lower rates of GTR may warrant particular focus in the development of new surgical strategies (e.g., staged resection or subtotal resection short of peeling tumor off cerebellopontine structures) with the consideration of postoperative stereotactic radiosurgery for the residual tumor.

Table 5 Building on the original Koos classification [15], *Grade 5* defines the radiographic feature of edema that was present in 43% of our patients and adversely affected balance function

Grade	Tumor
1	Intracanalicular
2	Extension into cerebellopontine angle without contact of the cerebellopontine (CP) structures
3	Touching CP structures without displacement
4	Displacement/deformation of CP structures
5	Displacement/ deformation of CP structures with edema

Study limitations

Constrained by its retrospective study design and the limited number of patients in this single-center experience, caution is advised in interpreting our results. Our findings do not specifically improve the prediction of either postoperative facial nerve function or postoperative hearing. Rather, in this cohort, we cautiously ask the question, "Should cerebellopontine edema be considered in the grading systems?" Finally, we recommend continued study of outcomes in larger prospective cohorts related to the radiographic findings of tumor volumes and edema within the cerebellopontine region.

Conclusions

Our retrospective study identified the neuroradiographic feature of peritumoral cerebellopontine edema in 43% of 107 patients with Koos grade 3 and 4 vestibular schwannomas and proposes this feature warrants consideration in a new grading system. Compared with grade 3 and 4 tumors, patients with grade 5 tumors presented with worse hearing, statistically worse hearing function by AAO-HNS hearing class, worse postoperative balance dysfunction, and longer hospital LOS. We believe that this grade 5 with edema offers a more nuanced interpretation of a radiographic feature that holds relevance to patient outcomes and thus during consultations for treatment selection.

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Data Availability Data available on request.

Declarations

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the (place name of institution and/or national research committee) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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