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Original article

WHO classification of meningiomas–A single institutional experience

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ABSTRACT

Introduction

Meningiomas are among the most common intracranial neoplasms worldwide. The World Health Organization (WHO) has classified the neoplasm into three grades with each grade having several histological variants. Several studies done in blacks have shown differences with Caucasian populations regarding the occurrence of histological variants. Our study sought to examine the histological variants of meningioma seen in a predominantly black population using the WHO grading system.

Methods

We conducted a retrospective study of all meningiomas seen in our hospital facility for over twenty years. An analysis of data from all the patients diagnosed with meningioma, who also had surgical biopsies taken, was done. The meningiomas were graded using the WHO grading system and also classified into different histological variants within each grade as described by the WHO study group.

Results

The study included a total number of 163 biopsies. There were more females diagnosed with meningiomas with a female to male ratio of 1.4. Most of the tumors were grade one, however, there were more males with malignant meningiomas. Transitional meningiomas were the most commonly seen variants among the grade one tumors while atypical and anaplastic were most common in grades two and three, respectively.

Conclusion

A larger population-based study is needed to provide epidemiological data on the occurrence of meningiomas in blacks.

Meningiomas are among the most common intracranial neoplasms seen worldwide [1]. Several researches have shown them to be the commonest, particularly in the USA and Europe, and make up approximately 30% of intracranial tumors [2–4]. The most recent CBTRUS data from all the cancer registries in the US show meningiomas to account for 37.6% of all intracranial tumours [2]. This is similar to the data from French Gironde registry [3] and Japan [4] which were 32% and 36.8% respectively. In Nigeria, different studies have shown varying epidemiological data with astrocytic tumors and meningiomas jostling for the first place but the most recent data from Sahabi et al. showed meningiomas to account for 28.6% of all intracranial tumours [5–7]. They are thought to derive from the meningeal arachnoidal cap cells, based on location and morphological similarities, and are often attached to dura [1,8]. Meningiomas are mostly benign tumors, but a few of the variants show aggressive features and a tendency to recurrence [9].

The WHO have classified meningiomas into three grade levels based on their biological behavior, and this has been useful in predicting and prognosticating response to therapy [10]. The grade one tumors are the most common and are the least aggressive with very low recurrence rates [10,11]. Grade two and three tumors are much less common but show more aggressive biological behavior, with the grade three affecting significantly on mortality and morbidity [11].

Several studies have however shown a higher incidence of meningiomas in blacks and no difference in gender predilection, although tumors in blacks are said to be more aggressive [8,12]. Most Caucasian studies have shown a higher occurrence of this tumour in females more than in males, and also the occurrence of the more malignant variants in blacks [12,13]. There is a paucity of studies on the epidemiology of this intracranial tumor type in our environment, a predominantly black population. Our aim in this study is to provide more information on the gender distributions and histological grades of meningiomas occurring in patients from a black population while comparing with data from the Caucasian population.

1. Method

We conducted a retrospective study of all surgical biopsies diagnosed as meningiomas in our hospital facility for over twenty years.

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The study location, the University College Hospital, was the biggest hospital facility in the southwest region of Nigeria during the study period and regarded as the premier center for neurosurgery in the country.

Reports of all previously diagnosed meningiomas were retrieved and the tissue sections re-examined individually by two pathologists to confirm the diagnosis previously made. Those tissue sections in which the histological variants were not mentioned in the initial report were re-examined also separately by two pathologists and the histological variant determined. The diagnosis from both pathologists were then separately matched for agreement with the earlier histopathological description.

Cases with incomplete histologic reports and which the slides could not be obtained were excluded from the study.

The demographic data for each patient and tumor recurrence were also retrieved from the records in the archived departmental records. These data were from the Ibadan cancer registry and the records of surgical biopsies in the department. The meningiomas were graded using the 2016 WHO grading system[10]. The tumors were further classified into the different histological variants within each grade described by the WHO study group. Analysis of the data was done using SPSS statistical software version 24.

2. Results

During the study period, 756 patients with intracranial tumors were attended to in the hospital facility and 171 biopsies were diagnosed histologically as meningioma. Eight of the cases were excluded from the study for lack of adequate data, while 163 cases were included. The age range of the patients was from 7months to 78yrs, but most of the patients were adults. The mean age for all the patients was 45yrs ± 15.72 (Table 1), however, most of the patients had their ages within the fourth to the seventh decade (Fig. 1).

94 (58%) of the patients with meningioma were females while 69 (42%) were males and the female-male ratio was 1.4. The grade one tumor was the most diagnosed tumors and made up 80.4% (131) of all the meningiomas, while the grade three tumor was the least frequently occurring (table one). More females had grade one meningiomas compared to males with a female to male ratio of 1.6. There were more male patients having higher grade (both WHO grade two and three) meningiomas with a female to male ratio of 0.9. However, there were more male patients with grade two meningiomas while grade three meningiomas occurred more in female patients (Fig. 2). The mean age and the age range of the patients with the three differ-

Table 1
The frequency of the meningioma variants according to sex and WHO grade.

	Mean age	Age range	Sex	Meningioma variants						
WHO GRADE ONE				Transitional	Angiomatous	Secretory	Fibroblastic	Meningothelial	Metaplastic	Psammomatous
	44.5	0.7 - 78	F	34	3	0	9	24	1	9
			M	27	3	1	8	10	1	1
			Total	61	6	1	17	34	2	10
WHO GRADE TWO				Clear cell	Atypical					
	54.5	25 - 75	F	0	7					
			M	1	10					
			Total	1	17					
WHO GRADE THREE				Papillary	Rhabdoid	Anaplastic				
	44.8	20 - 67	F	2	1	5				
			M	2	2	2				
			Total	4	3	7				

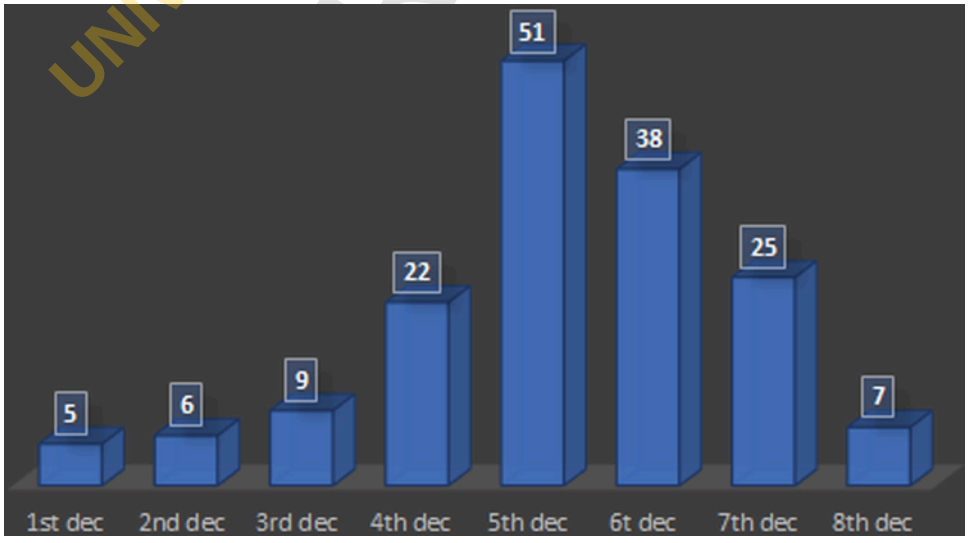

Fig. 1. Age distribution of patients with meningiomas in decades.

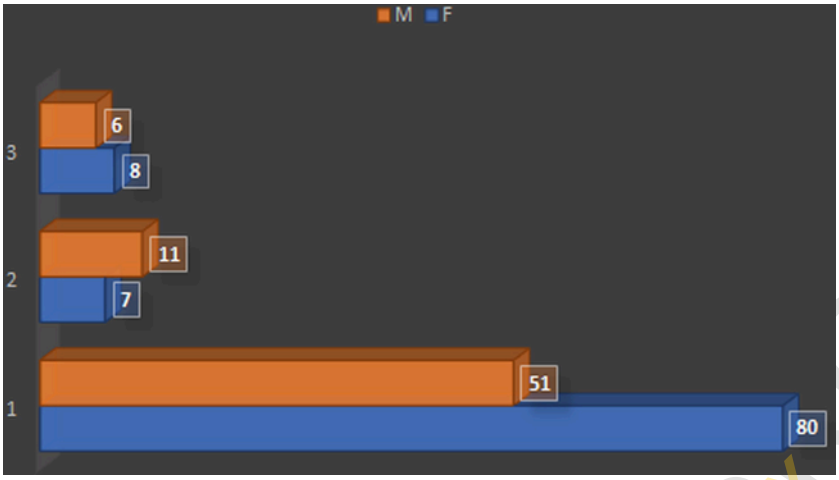

Fig. 2. Comparison of frequency of different grades of meningioma in male and female patients.

ent grade categories were relatively similar although there was a wider age range for those in the grade one category (Table 1).

The transitional meningiomas were the most common histological variant seen in all three grade types followed by the meningothelial. The atypical meningiomas were the most commonly occurring grade two tumors while the anaplastic was common for grade three tumors. There was no documented case of chordoid meningioma in this series (Fig. 3). All the benign meningiomas showed a female predominance except for the angiomatous and metaplastic variant which showed equality in the genders. There was a male predominance in the atypical tumours but grade 3 meningiomas occurred more in females than males (Table 1).

Nine (5.5%) of the meningiomas had additional surgery at different periods for incomplete excision or tumor recurrence. Four (2.5%) of the tumors with re-excision showed grade one morphologies in both biopsies. Five (3.1%) of these tumors initially had a grade one morphology at the first surgery but later showed higher grade tumors following a recurrence. Two of these patients had three recurrences at about one-year intervals before showing a more malignant phenotype (Fig. 4).

3. Discussion

Previous studies done in colder climes have shown a higher occurrence of meningiomas in females as compared with males, and this is similar to what was seen in our data (Table 2). However, the male-female ratio of 1:1.4 seen in the index study suggests that the difference between the genders is narrower in blacks as compared to Caucasians in which the ratio usually is more than 1:2 [10,14–16]. This finding is similarly buttressed by previous studies, which had shown similar gender differences in tumour rates of the study population [5,16]. Some authors have suggested the presence of steroid receptors in meningiomas, which are believed to stimulate the growth of the tumour and are thought to be responsible for the increase in the per-

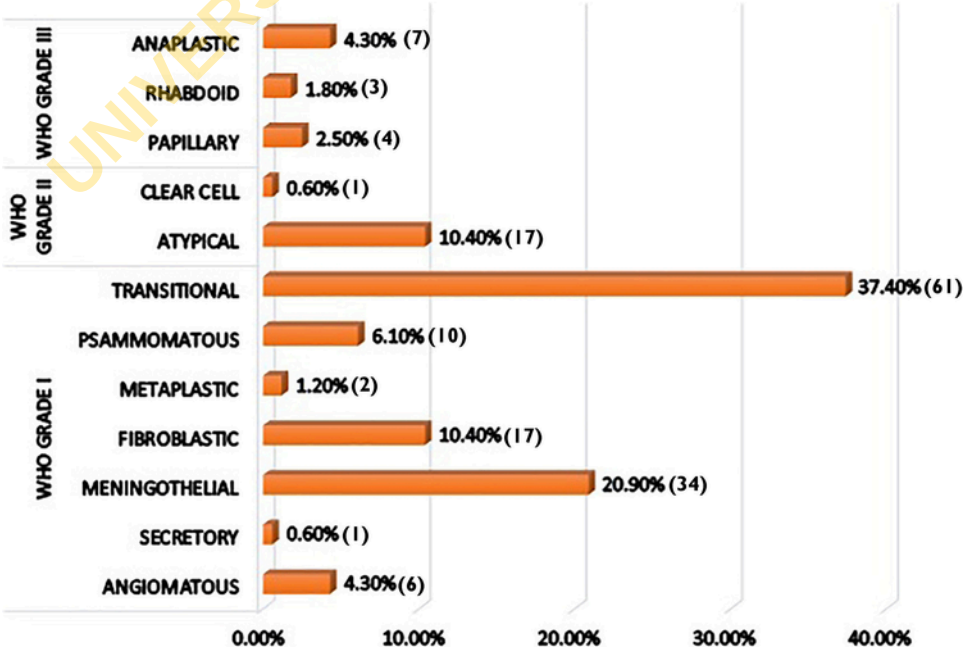

Fig. 3. Frequency of histological meningioma variants in percentages.

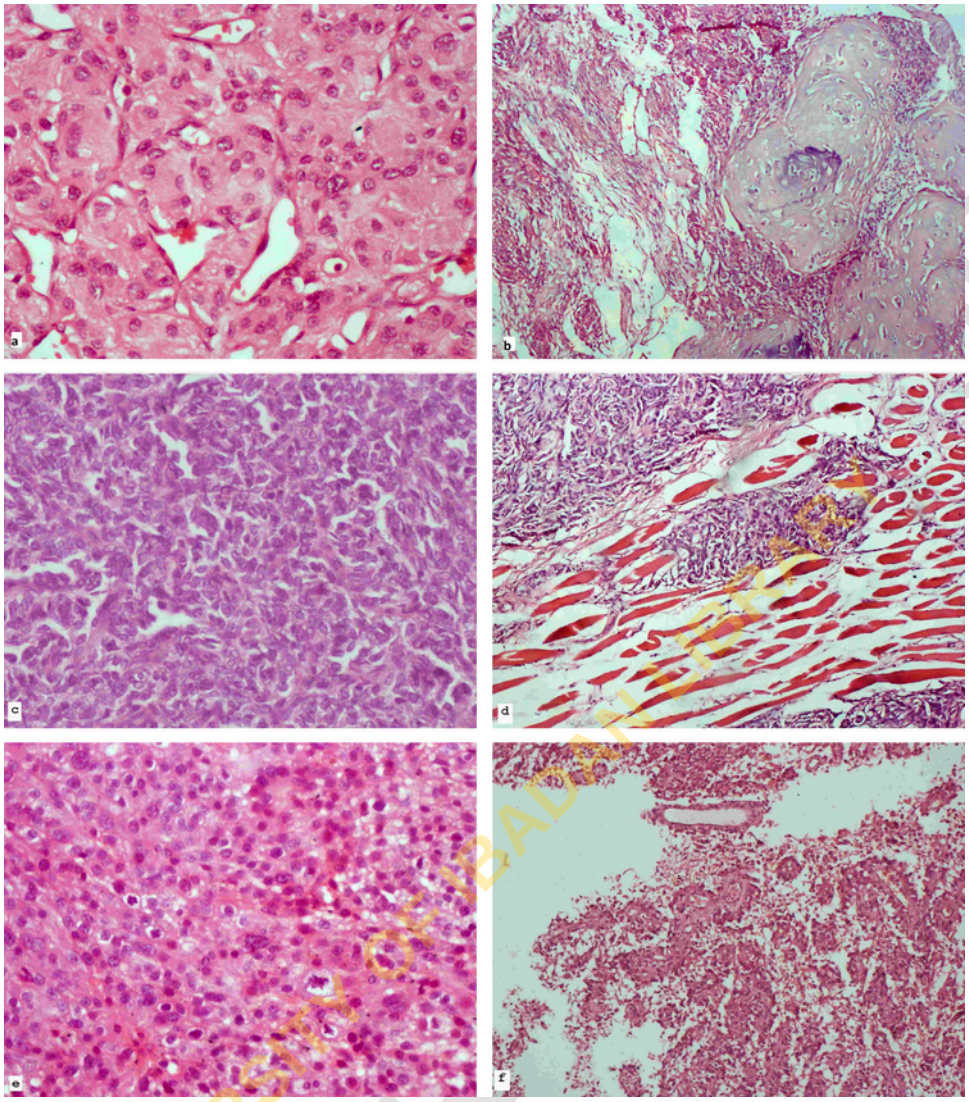

Fig. 4. Photomicrographs of WHO grade I (meningothelial (a), metaplastic (b)), WHO grade 2 atypical meningioma (c) and atypical meningioma invading skeletal muscle (d), WHO grade 3 meningioma (anaplastic (e), papillary(f)).

Table 2
Comparison of some of the demographic data and tumour grades from patients with meningioma in different Caucasian populations and the black population of the index study.

Value	Salami et al.[a]	Ostrom et al.[b]	Kshettry et al.[b]	Holleczek et al.[c]	Zouaoui et al.[d]
Mean age	45yrs	66		63	57.7
Female–male ratio	1.4	2.72		2.53	2.99
WHO grade					
1	80.4%		94.6%	70%	
2	11.0%		4.2%	28%	
3	8.6%		1.2%	3%	

[a] Nigeria.
[b] US.
[c] German.
[d] France

centage of meningiomas in females [10,17,18]. This female predominance has however not been documented in blacks, which tend to have equal gender difference [8,19]. Future studies with larger study populations will help in determining the actual gender ratio of meningiomas in blacks.

Korhonen et al. [19] have shown previously that the presence of progesterone receptors alone cannot explain the gender differences in meningiomas. Their study showed equal volume and distribution of steroid receptors in meningiomas from both males and females. The index study showed minimal gender differences in the three meningioma grades. There was a female predilection for benign meningiomas while this was reversed in the more malignant variants (Table 1). This finding is consistent with some studies which had shown an increase in malignant meningiomas in males [10,20] but this is in contrast to data from other workers [2,13,17].

Roser et al. in their study had showed a predominance of benign tumours occurring more in females while the more aggressive tumours are seen in males, a pattern similar to the finding in the index study [21]. Zouaiou et al., however, in their study showed no gender difference in the ratio of female to male patients with malignant meningioma [16].

Patients with meningioma, in this study, showed an increase with age and a peak at the fifth and sixth decades of life comparable to

data from western populations [2,14]. The mean age of patients with meningioma was, however, lower in the index study compared to western population data which showed a mean of 60yrs and above(Table 2)[2,14]. This difference may reflect the progressive decrease in number of patients with age after the sixth decade of life in the current series, while studies from USA and England showed a progressive increase in number of diagnosed patients beyond the sixth decade [2,10,14,15]. This observation may be because of the low life expectancy of 54yrs in the study population as compared to that of the advanced western countries with a life expectancy of over 70yrs [21,22]. Thus, many of the patients with meningioma in the study population may have died with their disease at a younger age and not come to clinical attention. Alternatively, it is possible that fewer clinical symptoms might occur in the elderly due to reduced proliferation rate as shown in the study by Roser et al. [21] and brain atrophy in that age group which might allow more growth of the tumour before the patient develops symptoms [23]. Zouaiou et al., in their study in the French population which showed a mean and median age of 57.7 and 58yrs respectively, has however pointed out that median age is often higher in registry data compared to surgical data such as in their study [16]. According to them, this was because registry data often includes non-surgically validated data and might explain the difference in the mean age seen in study compared to those from other Caucasian populations [16]. The lower mean age of patients in our study may also be partially attributable to our data being obtained from surgical archives. The first and second decades had the least number of patients with the tumor. This has been previously described in other studies that had shown rarity of meningiomas in the pediatric age group, unlike glial tumors [24,25]. This finding is also in agreement with that of Sahabi et al. [5] who also had only six cases of meningiomas in children.

The frequency of grade one meningiomas seen in this study is much higher than the grade two and three meningiomas. This is comparable to studies in other climes in which a higher rate of occurrence of grade one tumours compared to the other two higher grade types were also noted [2,10,17,26,27]. In an earlier study from the same center by Sahabi et al. [5], the grade one tumors were the most common tumor type observed and constituted 89.4% while the present study showed 80.4%. The difference in numbers may be because of the higher number of meningiomas in the index study, which is almost twice the number of tumors in their study, and the different period.

Grade two and three meningiomas have been described to be uncommon compared to their benign counterparts [13]. In the index study, grade two meningiomas were found to constitute 11% which is higher than the 3.6% found in the study by Sahabi et al. [5] and 1.9% by Mezue et al. [16] but lower than what was seen in studies from the US and Europe [2,10,13,20]. Grade three tumours are known to be uncommon, usually between 1% to 5% of all meningiomas, including the anaplastic, rhabdoid and papillary variants [10,17,26,27]. This study, however, shows a higher frequency of 8.6% which is similar to the finding of Sahabi et al. [5] who found 9.9% of grade three tumors in their series. This observation may agree with some previous studies that show malignant meningiomas to be more common in blacks [2,13]. Anaplastic meningiomas have a high tendency for recurrence and are very aggressive tumors with a predilection for metastasis [10,11,27]. There was no apparent metastasis from any of the tumors in this study.

Although the grading of meningiomas has not changed between the 2007 and 2016 classification, controversies have been frequent, particularly over the diagnostic criteria of atypical meningiomas [16,28]. The 1993 WHO grading was the first to include an intermediate grade of meningioma, which lies between the between and malignant tumours [29]. Specific diagnostic criteria were however not clear for this tumour type until the WHO 2000 study group, based on the prognostic feature of increased recurrence, changed the name to atypical tumours and established more easily reproducible criteria [29,30]. However, the initial criteria for atypical meningiomas did not include brain invasion due mainly to reports that show this feature in many tumours with benign appearance and those with atypical features. Because of the higher recurrence potential of such tumours, the study group initially recommended a footnote in the report to indicate brain invasion [31]. The grading of brain invasive tumours was changed in the 2007 classification and such tumours where included in the grade II category [29]. This change subsequently increased the number of tumours that are included in the grade II category. It is of note that diagnostic criteria of grade II tumours continue to be controversial and the last word has not yet been heard about the atypical meningiomas [28].

Transitional meningiomas were the most commonly seen benign tumour variant in the index study, followed by the meningothelial variant (Table 3). This is in agreement with Backer-Grøndahl et al. in their study of a predominantly Caucasian population [17]. However, in the much larger study of 3000 surgical biopsies in a French population by Zouaoui et al., Meningothelial meningiomas where more than double the number of transitional and fibroblastic meningiomas [16]. The atypical and anaplastic variants were the two commonest variants of the grade two and three meningioma in our study, similar to European studies [16,17]. Interestingly, the papillary and rhabdoid variants were not documented in the data by Backer-Grøndahl et al. and formed a relatively small number of the grade III tumours in the French study, they formed a significant percentage of the grade three meningiomas in our study.

Meningiomas have not been shown to have the obvious tumor progression seen in gliomas, but a wide array of genetic mutations are known to be part of the pathogenesis [10,11,27]. The commonest gene associated with meningioma tumorigenesis is the loss of chromosome 22 and sometimes losses in 22q12.2. Although this gene is the location of *Merlin*, the gene affected in Neurofibromatosis 2, studies suggest the existence of an alternative gene that is mutated in meningiomas [10,11,27]. The present study suggests a possibility of tumor progression from the five tumors which recurred and showed a high-grade neoplasm in the subsequent biopsies. Some studies have also shown this same occurrence, but many authors have suggested otherwise from their studies [11]. In the index study, data on follow-

Table 3
Comparison of different histological meningioma variants in a black and Caucasian population.

Histologic Type	Salami et al.[a](%)	Backer-Grøndahl et al.[b](%)
Transitional	37.4	39.8
Meningothelial	20.9	17.3
Fibroblastic	10.4	7.1
Psammomatous	6.1	0.5
Angiomatous	3.7	1.5
Microcystic	0.0	1
Secretory	0.6	0.5
Lymphoplasmacyte rich	0.0	0.5
Metaplastic	1.2	0.0
Clear cell	0.6	1.0
Chordoid	0.0	0.0
Atypical	10.4	29.1
Rhabdoid	1.8	0.0
Papillary	2.5	0.0
Anaplastic	4.3	1.0

[a] Nigeria.

[b] Norwegian.

up of patients with meningioma is poor with an average period of one year. This may be because most of the patients are referred and come from far distances to the study center [32]. As a result, patients cease attending follow-up appointments after the first two visits for as long as there is a resolution of symptoms[33]. The recurrence rate of meningiomas was thus not obtained for the study population.

4. Limitations

The major limitation of this study is the fact that it is from a single hospital and the data may portray the patient referrals to the facility. It may not reflect the complete epidemiology of meningioma in the population. Another limitation of this study is the poor follow-up of diagnosed patients which prevented the recurrence of the tumour in the study population to be determined.

5. Conclusion

Although this study suggests a difference in the gender ratio of patients with meningioma in blacks compared with Caucasians, a larger, preferable population-based study is needed to provide reliable epidemiological data on the occurrence of meningiomas in blacks.

Human and animal rights

The authors declare that the work described has not involved experimentation on humans or animals.

Informed consent and patient details

The authors declare that this report does not contain any personal information that could lead to the identification of the patient(s) and/or volunteers.

Authors' contributions

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

Disclosure of interest

The authors declare that they have no competing interest.

Uncited reference

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