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British Journal of Oral and Maxillofacial Surgery 60 (2022) 1166–1175

BRITISH Journal of Oral and Maxillofacial Surgery

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Systematic review

Surgical management of syndromic versus non-syndromic craniofacial fibrous dysplasia: a systematic review and meta-analysis

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Accepted 10 June 2022
Available online 16 June 2022

Abstract

The main purpose of this study was to identify an algorithm for the surgical management of fibrous dysplasia in syndromic (McCune-Albright syndrome) and non-syndromic patients (monostotic and polyostotic subtypes). The secondary objectives were to assess the prevalence of affected craniofacial bones and the main clinical presentation. The authors performed a systematic review and meta-analysis by conducting a comprehensive electronic search from 1 January 2000 to 31 December 2019. A total of 1260 patients were included. The maxilla was the most affected facial bone (41%) ($p<0.001$, CI 38.3 to 43.8) and facial asymmetry was the chief complaint ($p<0.001$, CI 31.7 to 37.1). Conservative surgery registered higher recurrence rates than radical resection in both syndromic (84%) ($p<0.001$, CI 70.9 to 92.8) and non-syndromic patients (26%) ($p<0.001$, CI 21.8 to 30.6). Compared with prophylactic decompression, therapeutic optic nerve decompression (OND) showed better postoperative outcomes in both syndromic ($p=0.9$, CI 18.6 to 55.9) and non-syndromic patients ($p=0.09$, CI 9.3 to 28.4). Watchful waiting showed excellent results in both subgroups when asymptomatic ($p<0.001$). Syndromic and non-syndromic patients share the same treatment strategies. Radical resection is the preferred surgical technique to eradicate the disease, but it is often difficult to perform due to the extent and location of the disease. Furthermore, the authors advise early therapeutic over prophylactic OND to prevent optic nerve atrophy. Asymptomatic patients should be managed expectantly. Finally, medical management helps reduce the symptoms of bone pain ($p=0.02$ in non-syndromic and $p<0.001$ in syndromic patients).

Keywords: Fibrous dysplasia; Craniofacial; Fronto-orbital

Introduction

Fibrous dysplasia (FD) is a benign congenital progressive disorder characterised by the replacement of normal bone with uneven and immature fibrous-osseous tissue.[1] Accounting for 10% of all bone tumours,[2,3] FD is caused by somatic missense mutations in the gene GNAS on chromosome 20, which arrests the differentiation process of bone marrow stromal cells.[4]

FD is divided into three categories: monostotic FD (MFD), polyostotic FD (PFD), and McCune-Albright syndrome (MAS).[5] MFD involves a single bone or two contiguous segments of bone (monofocal). It has an incidence of 70% and is diagnosed between the ages of 20 and 30 years.[6] PFD affects multiple bones (multifocal). It comprises approximately 30% of cases, and has an earlier onset, typically in childhood. Finally, as MAS, FD can be present as progressive PFD in combination with hyperfunctioning endocrinopathies and cutaneous pigmentation (café au lait spots). MAS has an incidence of 3% and is most commonly found in young females.[7,8] Whilst FD can affect any bone of the body, craniofacial involvement is found in 27% of

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https://doi.org/10.1016/j.bjoms.2022.06.002

patients with MFD and 50% with PFD.[8–10] Endocrine dysregulation is a risk factor for re-growth.[11–13]

Since no curative medical treatment is available, surgery is the therapeutic cornerstone for treatment. Nevertheless, there are many controversies regarding the need for radical versus conservative surgery, and therapeutic versus prophylactic optic nerve decompression (OND), especially in asymptomatic patients with radiological evidence of optic canal stenosis.[2,11,14–19]

The objective of this study was to identify an algorithm for the surgical management of syndromic (MAS) and non-syndromic FD. The secondary objectives were to identify the most involved craniofacial bones and the prevalent clinical presentation of the disease.

Material and methods

The authors performed a systematic review by searching the keywords "fibrous dysplasia" AND "craniofacial" OR "fronto-orbital" using the electronic databases Medline and the Cochrane Library. Reference lists of retrieved manuscripts were also manually searched for additional publications.

Study selection criteria

The two authors independently screened and selected the material. All available specific data were recorded for each patient. Discrepancies between the two authors and the statistician were resolved by discussion.

The inclusion criteria were: studies published in English from 1 January 2000 to 31 December 2019, those reporting five or more cases of craniofacial FD treated surgically, and those with a mean follow up of at least six months. The exclusion criteria were: studies without sufficient available data, papers focusing on radiographic or histological findings only, and those with cases of cemento-ossifying fibroma or osseous dysplasia.

A total of 366 studies were identified, which became 136 after manual elimination of duplicates. After abstract reading, 71 articles were excluded (case reports and small case series of <5 patients). Of the remaining 65 papers eligible for full-text reading, 33 were selected for inclusion and 32 discarded (17 studies with medical treatment only, 11 without sufficient data, and four that did not meet the follow-up requirements) (Fig. 1).

Data extraction

Data collection comprised patient number, age at diagnosis, gender, and type and treatment of FD. Treatment options included radical surgery, subtotal resection (partial en-block resection), conservative surgery (shaving or remodelling), therapeutic/prophylactic OND, and watchful waiting. Further data included follow up, recurrence, malignant transformation, affected craniofacial bones, and disease presentation. Missing data were recorded as "-". When available, the authors were contacted via email for additional information on treatment and follow up.

Patients with orbital FD underwent ophthalmological assessment of best corrected visual acuity (BCVA) (Snellen chart), visual fields (Goldmann perimetry testing), colour perception (Ishihara colour plates), intraocular pressure measurements (Goldmann tonometry), ocular motility (Hess chart), biomicroscopy of the anterior segment, and fundus examination preoperatively and postoperatively. Optic nerve dysfunction was determined by the presence of either a scotoma (or visual field defect) or an abnormal result on two of the four tests (BCVA of less than 6/12 or 40/20, correct identification of <10/14 Ishihara colour plates, rapid afferent pupillary reflex (RAPD), or evidence of optic atrophy on fundoscopy). These patients were considered for therapeutic OND. Conversely, patients with no vision deterioration were considered for either prophylactic surgery or watchful waiting, regardless of radiographic evidence and degree of optic canal stenosis.

Statistical analysis and publication bias

Heterogeneity was measured via I^2[20,21] Tau, Tau^2,[22] and H[23] statistics. Differences in proportions were calculated using a test for equality of proportions with continuity correction (where feasible). Confidence intervals at a 95% level were estimated using the Clopper-Pearson method for binomial proportions. We estimated a random effects model meta-analysis for proportions via the "meta" package in R.[24] Forest plots and other graphics were produced using the "forestplot" package in R (Fig. 2). Publication bias was tested using the funnel plot.

Results

A total of 1260 patients were included between the years 2000 and 2019 (monostotic FD: n = 713 (53%); polyostotic FD: n = 299 (24%); and MAS: n =248 (20%)). A total of 526 patients were female (46%) and 615 male (54%). The mean (range) age at diagnosis was 21 (0–80) years. The incidence of malignant transformation was 0.7% (Table 1).

The maxilla was the most commonly involved craniofacial bone (41% of all patients), followed by the frontal bone (22%) and the mandible (20%) ($p<0.001$). Facial asymmetry, facial pain, and proptosis were recorded in 34%, 16% and 12% of patients, respectively (Table 2). Only 1% of patients were incidentally diagnosed with FD. There was statistical significance ($p<0.001$) among the distribution of craniofacial bones and clinical presentation of FD lesions. Orbital FD was found in 26% of patients. Of these, 91% had radiological evidence of optic canal stenosis, and 40% had symptoms of vision deterioration.

Conservative surgery was the most common surgical procedure in both syndromic and non-syndromic patients (56% and 45%, respectively), followed by radical resection (28% and 39%, respectively) (Table 3). The highest recurrence rate for MAS was recorded for conservative surgery (84%), whereas for non-syndromic patients it was subtotal resection

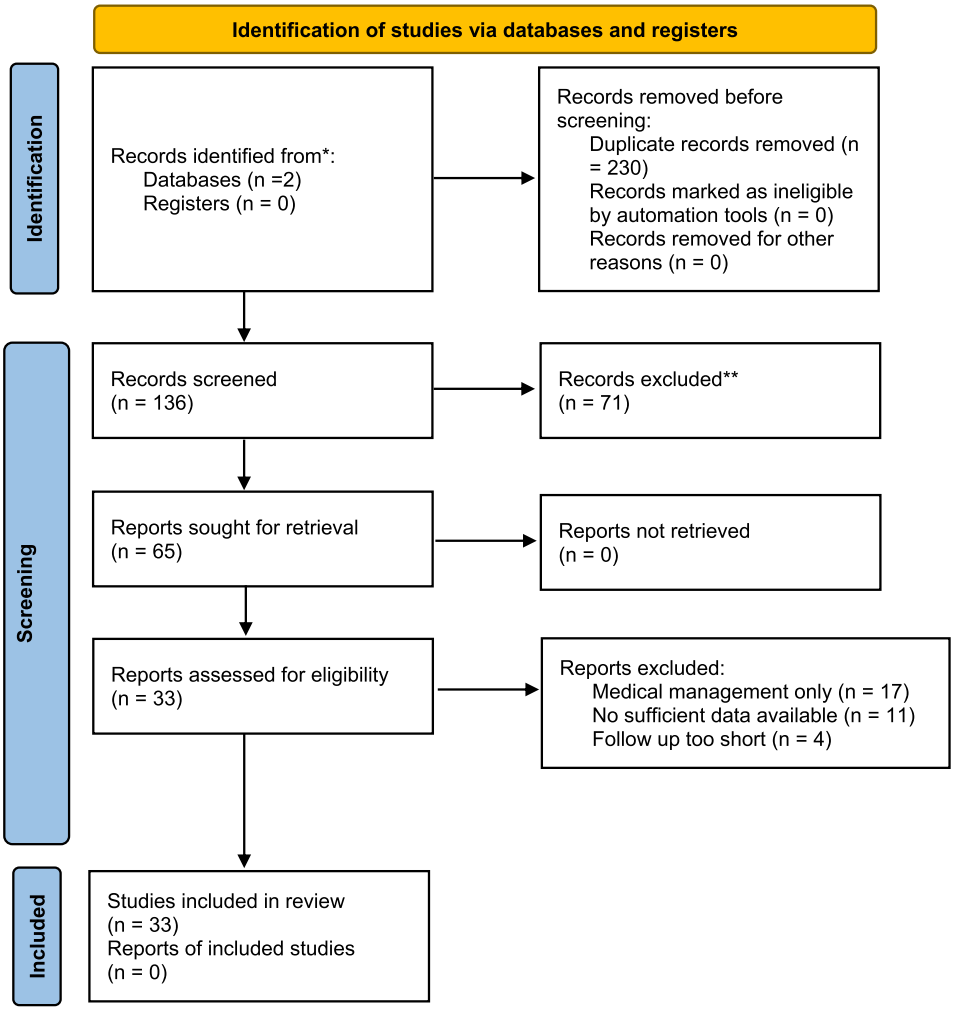

Fig. 1. Flow chart with study selection process.

(32%). Radical resection showed excellent curative outcomes in MFD/PFD patients, with only 15 recurrences (4%).

The difference in recurrence rates among surgical procedures in both subgroups was statistically significant ($p<0.001$).

Among non-syndromic patients, therapeutic OND resulted in a lower percentage of vision deterioration than prophylactic surgery (17% and 23%; $p=0.09$). In MAS, 31% developed vision deterioration after therapeutic and 43% after prophylactic OND ($p=0.9$). The highest improvement in vision was recorded in the non-syndromic group after therapeutic surgery (67%) (the authors stated that patients often developed some degree of diplopia postoperatively, but vision normally improved within 5-6 months).

Watchful waiting showed excellent results both in asymptomatic MFD/PFD and MAS with evidence of optic canal stenosis. Cases of postoperative permanent vision loss were particularly high after prophylactic OND in MAS, with 43% of patients experiencing such an outcome.

The heterogeneity test was substantial for the whole sample of studies ($I^2=71.7\%$ [59.8%; 80.0%], $tau^2=1.6746$; tau=1.2941; H=1.88 [1.58; 2.24]), but it reduced when the subgroups were considered.

In particular, the fixed effects model provided a $I^2=81.2\%$ for retrospective studies. For case series and prospective studies, no heterogeneity was found ($I^2=0\%$). The test for subgroup differences provided a statistically significant difference within ($p<0.001$) and between groups ($p=0.0783$). The random effects model provided a statistical difference between groups ($p=0.0868$). Funnel plot analysis provided an indication of asymmetry among publications (Egger's test) (Fig. 3).

Discussion

In 1990, Chen and Noordhoff[25,26] suggested a classification for the treatment of FD based on the zones of involvement:

- Zone 1 (frontal, nasal and ethmoid bones, zygoma and upper maxilla): radical excision and reconstruction.
- Zone 2 (hair-covered scalp, parietal and occipital bones): conservative or radical surgery.

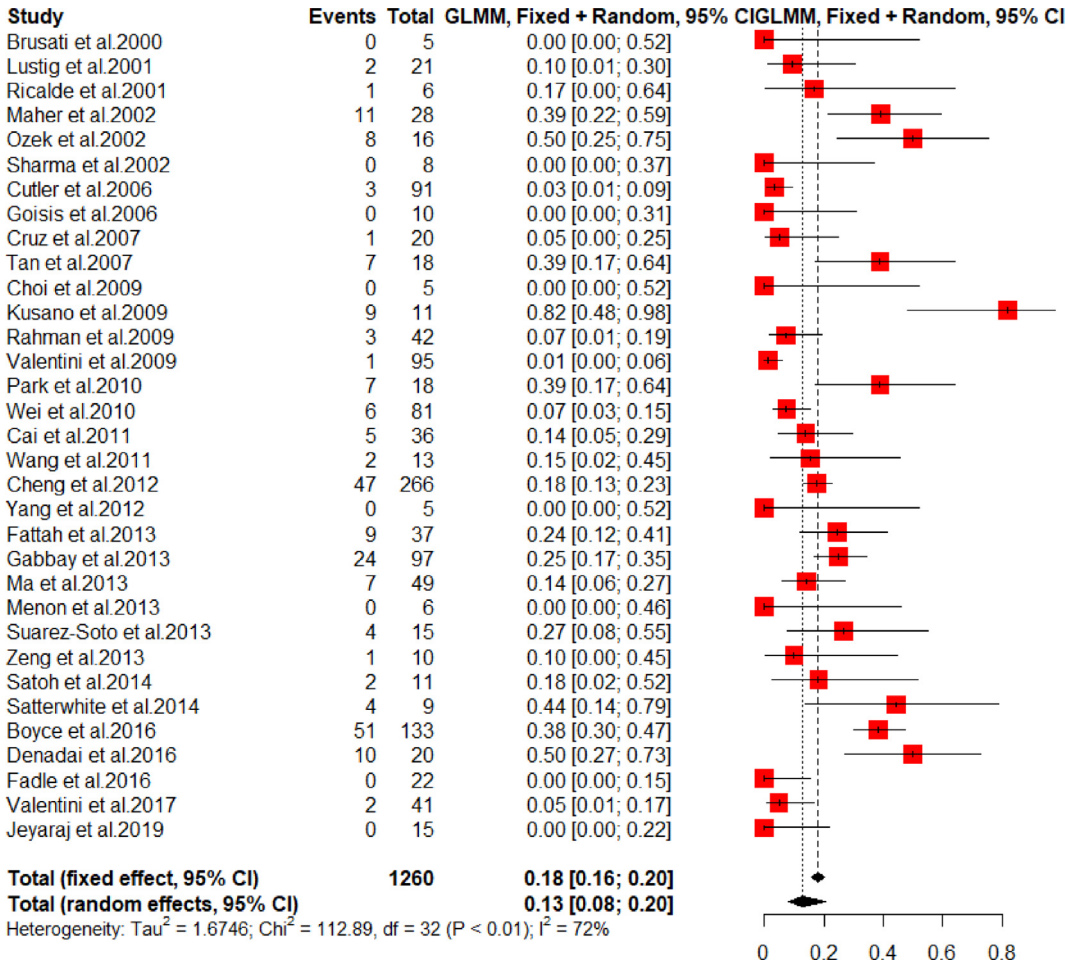

Fig. 2. Forest plot with proportions (95% CI) of recurrences and worsening of vision after optic nerve decompression over the total number of cases for each study. Overall effect for fixed effect and random effects models. Heterogeneity measures (tau squared, chi squared, I squared).

– Zone 3 (central cranial base, petrous, mastoid, pterygoid and sphenoid bones): observation unless symptomatic (OND).
– Zone 4 (alveolar process of maxilla and mandible): conservative excision and recontouring.

In their study, Valentini et al[27] recommended radical surgery for MFD affecting the maxilla and mandible, as it is the only option that achieves complete disease resolution (no recurrence after 70 radical resections). Conversely, they had a high relapse rate (23%) after conservative surgery in PFD and MAS patients, especially in zone 4. Other authors have registered similar recurrence rates,[15,17,28–30] and several have supported more aggressive management in the zygomaticomaxillary area.[1,31–35]

Valentini et al[27] also recommended a delay in radical resection. Since the disease is mostly diagnosed at a younger age, surgery can wait until skeletal maturity has been achieved and the lesion has reached a static phase.[12] Fattah et al[4] performed radical resection after skeletal maturity, which led to a lower recurrence rate (14%) than earlier surgery (50%).

Other authors[7,10,36,37] are in favour of conservative surgery in both subgroups. Although Ozek et al[7] reported relapse in all eight maxillary cases treated with bone contouring, they still did not recommend radical resection in the maxilla due to increased morbidity. Interestingly, Valentini et al also changed their surgical algorithm to a more conservative approach in a further study published eight years later.[6]

According to our data, subtotal resection and conservative surgery had considerably higher recurrence rates than radical surgery in both subgroups, 27% of the recurrences occurring in the maxilla alone. A more radical approach for zone 4 in both MFD/PFD and MAS therefore achieves a higher percentage of disease resolution. The higher recurrence rates in MAS highlight the aggressiveness of the disease compared with the non-syndromic type, and shows less predictable disease stabilisation and high recurrence rates even after puberty.[4,13,29] Radical surgery is therefore considered the definitive treatment for MAS, as it offers the best chances of achieving complete disease remission.

Watchful waiting is the recommended approach for stable cases in which there is minimal functional and aesthetic compromise.[4,6] Given the excellent outcome in our asymptomatic patients with virtually no relapse recorded, the authors also support this approach.

Table 1
Overview of studies on the surgical management of fibrous dysplasia.

First author, year, and reference	Study type	No. of cases	Male/female	Mean (range) age at diagnosis	Mean follow up*	Non-syndromic		Syndromic	Malignancy
						MFD	PFD	MAS	
Brusati 2000[26]	CS	5	–	28 (6–50)	2.3 (1–3.7)	5	0	0	0
Lustig 2001[5]	RCS	21	14/7	22 (8–54)	8.2 (2–30)	6	13	2	0
Ricalde 2001[41]	CS	6	3/3	17 (7–23)	> 1	5	1	0	0
Maher 2002[15]	RCS	28	17/11	11	13.7 (1–19)	26	2	0	0
Ozek 2002[7]	CS	16	6/10	17 (8–36)	4.5 (1–12)	14	0	2	0
Sharma 2002[30]	CS	8	4/4	20 (10–33)	2.9 (0.5–5)	4	4	0	0
Cutler 2006[16]	RCS	91	39/52	25 (3–84)	9.3 (2–25)	1	7	83	0
Goisis 2006[39]	RCS	10	–	19 (8–59)	4.4 (1–8)	4	6	0	0
Cruz 2007[14]	PCS	20	4/16	25 (7–60)	10.5 (1–40)	7	9	4	0
Tan 2007[11]	RCS	18	7/11	21 (8–39)	6.8 (1–23)	14	4	0	0
Choi 2009[34]	CS	5	2/3	21 (17–24)	1.9 (0.5–2)	4	1	0	0
Kusano 2009[29]	RCS	11	6/5	18 (9–34)	> 10	3	5	3	0
Rahman 2009[8]	RCS	42	22/20	17 (0–59)	12.6 (0.2–31)	32	7	3	0
Valentini 2009[27]	RCS	95	–	25 (4–52)	7.6 (5–15)	72	21	2	0
Park 2010[12]	RCS	18	8/10	19 (9–45)	7.8 (3–16)	15	3	0	0
Wei 2010[32]	RCS	81	31/50	24 (5–71)	(1–9)	67	13	1	0
Cai 2012[1]	RCS	36	12/24	25 (6–59)	4.4 (0.5–11)	24	12	0	0
Wang 2011[37]	RCS	13	4/9	27 (18–59)	(3–5)	10	3	0	0
Cheng 2012[33]	RCS	266	111/155	27 (9–70)	5.3 (0.5–16)	189	73	4	3
Yang 2012[35]	CS	5	4/1	17 (12–23)	17.8 (1–2)	4	1	0	0
Fattah 2013[4]	RCS	37	17/20	10 (1–17)	3.4 (1–9)	28	7	2	0
Gabbay 2013[31]	RCS	97	60/37	16 (7–42)	5.8 (1–27)	31	63	3	2
Ma 2013[9]	RCS	49	28/21	14 (2–62)	> 1	29	20	0	1
Menon 2013[36]	CS	6	3/3	16 (8–19)	2 (2)	5	1	0	0
Suarez-Soto 2013[28]	RCS	15	10/5	24 (4–65)	2.3 (> 0.5)	14	1	0	0
Zeng 2013[10]	CS	10	2/8	23 (17–34)	3 (1–5)	3	6	1	0
Satoh 2014[18]	CS	11	7/4	26 (17–58)	11.5 (4–22)	9	1	1	0
Satterwhite 2015[19]	CS	9	–	21 (7–45)	5 (1–10)	7	0	2	0
Boyce 2016[13]	RCS	133	58/75	21 (2–80)	13.5 (0–39)	0	0	133	3
Denadai 2016[17]	RCS	20	11/9	9 (5–19)	4 (1–7)	16	3	1	0
Fadle 2016[44]	PCS	22	10/12	30 (17–52)	3.1 (2–5)	16	6	0	0
Valentini 2017[6]	RCS	41	18/23	29 (8–72)	4.3 (1–9)	35	5	1	0
Jeyaraj 2019[52]	CS	15	8/7	28 (15–72)	(2–3)	14	1	0	0
Total (%)	–	1260	526/615 (46)/(54)	21	–	713 (57)	299 (24)	248 (20)	9 (0.7)

MFD: monostotic fibrous dysplasia; PFD: polyostotic fibrous dysplasia; MAS: McCune-Albright syndrome; CS: case series; RCS: retrospective cohort study; PCS: prospective cohort study.
* Follow up in years (0.5 = 6 months).

Table 2
Anatomical location and clinical presentation of fibrous dysplasia.

	No. (%)*	p value	CI
Lesion location:		<0.001	
Maxilla	517 (41)		38.3 to 43.8
Frontal bone	272 (22)		19.3 to 24.0
Mandible	249 (20)		17.6 to 22.1
Sphenoid bone	225 (18)		15.8 to 20.1
Ethmoid bone	172 (14)		11.8 to 15.7
Zygomatic bone	171 (14)		11.7 to 15.6
Parietal bone	92 (7)		5.9 to 8.9
Temporal bone	59 (5)		3.6 to 6.0
Occipital bone	57 (5)		3.4 to 5.8
Nasal bones	4 (0)		0.09 to 0.8
Inferior turbinate	1 (0)		0.00 to 0.4
Orbital involvement	330 (26)		23.8 to 28.7
Clinical presentation:		<0.001	
Facial asymmetry	433 (34)		31.7 to 37.1
Facial pain	197 (16)		13.7 to 17.8
Proptosis	152 (12)		10.3 to 14.0
Orbital dystopia	103 (8)		6.7 to 9.8
Vision deterioration**	96 (8)		6.2 to 9.2
Malocclusion	55 (4)		3.3 to 5.6
Hearing impairment	50 (4)		3.0 to 5.2
Diplopia	24 (2)		1.2 to 2.8
Cranial nerve palsy	23 (2)		1.2 to 2.7
Sinusitis	19 (2)		0.9 to 2.3
Incidental finding	15 (1)		0.7 to 2.0
Nasal obstruction	13 (1)		0.5 to 1.8
Weakness/lethargy	11 (1)		0.4 to 1.6
Anosmia	10 (1)		0.4 to 1.5
Vertigo	9 (1)		0.3 to 1.4
Epiphora	7 (1)		0.2 to 1.1
Epistaxis	2 (0)		0.00 to 0.5
Seizures	1 (0)		0.00 to 0.4

* Calculated among the 1260 total number of patients.
** Decreased visual acuity, loss of visual fields, loss of colour perception, increased intraocular pressure, reduced eye movements, and blindness.

Boyce et al[13] identified an excess of growth hormone (GH) as a risk factor for recurrence. Recurrence was more common in MAS with GH excess (88%) than in MAS without GH excess (58%). Cutler et al[16] and Lee et al[38] found that GH excess was a statistically significant risk factor for optic neuropathy.

Blindness is one of the most feared complications in FD; involvement of the orbit can cause stenosis of the optic canal, leading to progressive vision loss.[32,39] Radiological evidence of optic nerve compression is found in 50%-90% of patients affected by orbital FD,[2] and it is important to identify why vision loss occurs. In their literature review, Michael et al[40] found that only 20% of cases of vision loss were due to optic canal stenosis (30% were caused by cystic FD, 20% by mucoceles, 20% by haemorrhagic lesions, and 10% by aneurysmal bone cysts). In the case of FD-associated cystic lesions, the consensus is towards prophylactic OND.[8]

In their meta-analysis of 368 optic nerves, Amit et al[2] found that 95.1% of clinically intact nerves remained asymptomatic after watchful waiting, whereas 75.6% of asymptomatic patients achieved stable results after prophylactic OND. Hence, they recommended expectant management in asymptomatic patients in both subgroups.

Cutler et al[16] reported that only 12% of optic canals that were 100% encased showed signs of optic neuropathy. Of these, 54% had GH excess. Following therapeutic surgery, more than half the patients registered an improvement in vision. Of the optic nerves that were either <50% or 50%–99% compressed, there were no registered cases of optic neuropathy. The authors concluded that therapeutic OND should be performed when there is clinical evidence of optic neuropathy, whereas watchful waiting with monitoring of GH levels is a safe treatment strategy in asymptomatic patients with MAS.

Table 3
Surgical management and outcomes of fibrous dysplasia (FD). Among all recurrences, 52 (34%) affected the maxilla. Data are number (%).

Type of FD and procedure	Total	Recurrence	Outcome				p value	95% CI
			Improved	Stable	Worsened	Vision loss		
MFD/PFD (no orbit):			–	–	–			
Radical resection	347 (39)	15 (4)	–	–	–		<0.001	2.4 to 7.0
Sub-total resection	57 (6)	18 (32)	–	–	–			19.9 to 45.3
Conservative surgery (contouring)	404 (45)	105 (26)	–	–	–			21.8 to 30.6
Watchful waiting	54 (6)	0 (0)	–	–	–			–
MFD/PFD (orbit only):								
Optic nerve decompression								
Therapeutic	69 (50)	–	46 (67)	11 (16)	12 (17)	6 (50)	0.09	9.3 to 28.4
Prophylactic	30 (21)	–	–	23 (77)	7 (23)	1 (14)		9.9 to 42.3
Watchful waiting	39 (28)	–	–	37 (95)	2 (5)	0 (0)		0.6 to 17.3
MAS (no orbit):								
Total resection	25 (28)	10 (40)	–	–	–		<0.001	21.1 to 61.3
Sub-total resection	1 (1)	0 (0)	–	–	–			–
Conservative surgery (contouring)	50 (56)	42 (84)	–	–	–			70.9 to 92.8
Watchful waiting	14 (16)	0 (0)	–	–	–			–
MAS (orbit only):								
Optic nerve decompression								
Therapeutic	28 (25)	–	8 (38)	10 (31)	10 (31)	5 (50)	0.9	18.6 to 55.9
Prophylactic	14 (13)	–	–	8 (57)	6 (43)	6 (100)		17.7 to 71.1
Watchful waiting	72 (64)	–	–	72 (100)	0 (0)	0 (0)		–

FD: fibrous dysplasia; MFD: monostotic fibrous dysplasia; PFD: polyostotic fibrous dysplasia; MAS: McCune-Albright syndrome.

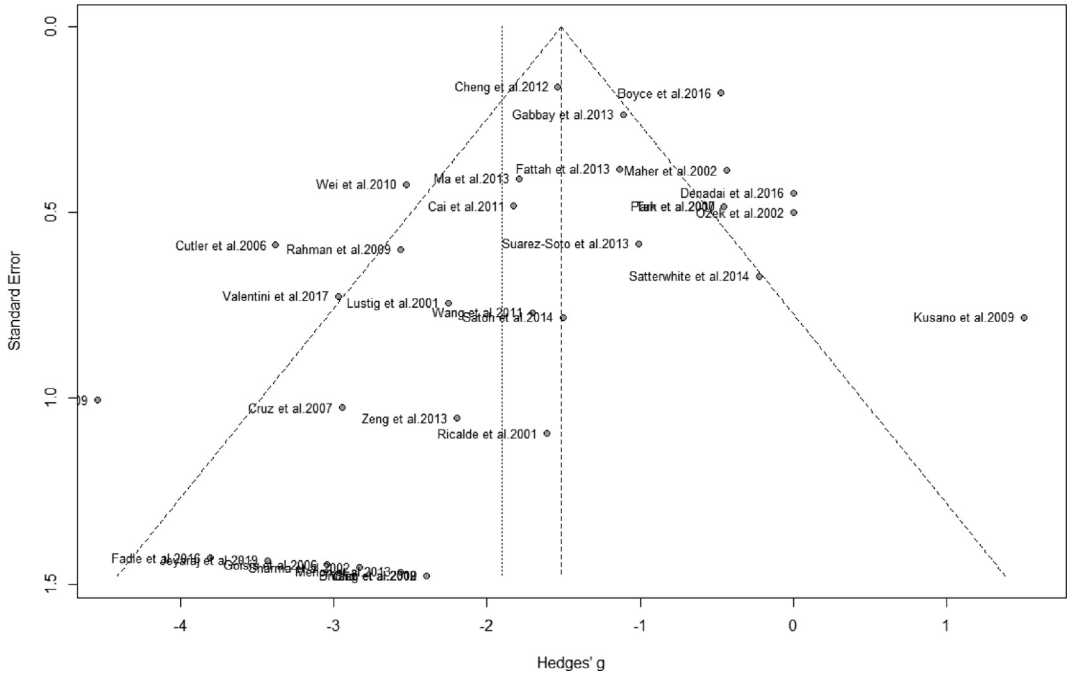

Fig. 3. Evaluation of publication bias. Funnel plot with pseudo 95% confidence limits.

Several authors[8,17,18,27,38] have rejected the use of prophylactic OND to treat optic canal stenosis, as the great majority of patients retain normal vision despite radiographic evidence of optic canal narrowing. Furthermore, the risk of vision deterioration can be increased by nerve traction, thermal damage, oedema, and severe intraoperative bleeding (immature fibrous-osseous tissue is highly vascularised).[17] Conversely, other authors have justified the use of prophylactic OND before patients show signs of vision deterioration, due to the difficulty of improving vision when irreversible optic nerve atrophy occurs.[19,26,41]

Tan et al[11] and Cruz et al[14] also refuted the idea of prophylactic OND. According to them, optic canals should be decompressed when continuous vision deterioration is present. Both adopted late therapeutic decompression in patients with advanced signs of optic canal stenosis, and as a consequence had high rates of adverse outcomes (from their 14 late therapeutic surgeries, four patients registered vision loss, and five had no vision improvement).

According to our study, and despite the lack of statistical significance among adverse outcomes for therapeutic versus prophylactic OND, therapeutic surgery showed better outcomes in patients with MFD/PFD and MAS. We therefore support the choice of therapeutic OND when patients show early signs of vision deterioration. Finally, the excellent results in patients with orbital FD who underwent watchful waiting show that it is a very good approach when MFD/PFD and MAS patients are asymptomatic.

Endoscopic optic nerve decompression (EOND) is a minimally-invasive surgical technique that is used to treat FD affecting the skull base and orbital region. Shi et al[42] and DeKlotz et al[43] obtained excellent results in all symptomatic patients treated in this way. Vision improvement remained stable during the follow-up period (1-13 years) with no recorded major complications during surgery.

Fadle et al[44] advocated radical excision of orbital FD to achieve a good outcome, but postoperative complications, ranging from permanent supraorbital anaesthesia to dural tears and cerebrospinal fluid leak, occurred in seven patients. Ryu et al[45] performed EOND in seven patients with symptoms of vision loss lasting up to four years. Six of them registered improvement in vision postoperatively, but three of six who had visual acuity in the range of a finger count had improvement that was not recovered beyond a quantitatively measurable level. We agree that early EOND is indicated in patients with symptoms of vision loss. It is a safe technique that is particularly useful when radical resection cannot be performed due to increased morbidity.

Medical treatment of FD is an important component in the holistic management of such a complex condition. Bisphosphonates (intravenous pamidronate) plus calcium and vitamin D supplements have improved symptoms and reduced the rate of lesion growth.[13]

Among the 17 originally discarded studies on medical management, only six considered patients with craniofacial FD.[46–51] These studies involved patients with active disease between the ages of 5 and 67 years (mean age 27 years), and follow up of between one and eleven years. Medical management improved bone pain in 69% of non-syndromic cases (p=0.02) and 77% of those with MAS (p=0.001). Improvement in bone deformity was not statistically significant: 56% of non-syndromic patients (p=0.14) experienced improvement. No patients in the syndromic group registered an improvement in bone deformity, but 85% of them

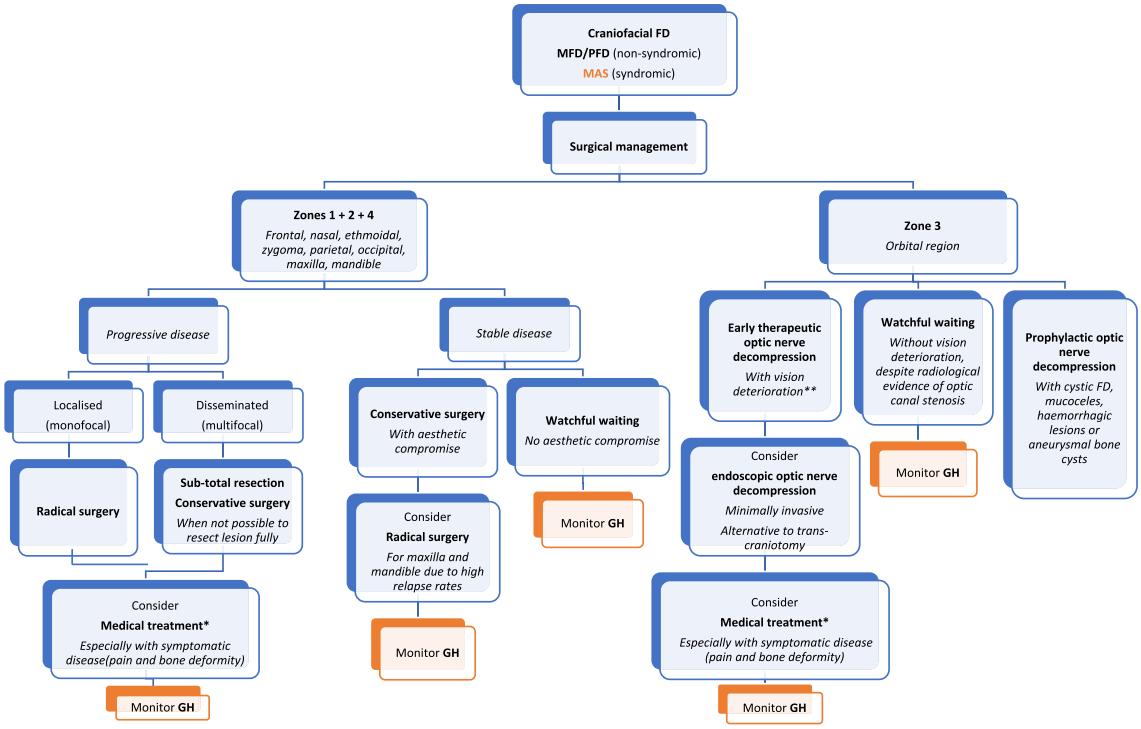

Fig. 4. Flow diagram with treatment algorithm for fibrous dysplasia. Where the treatment algorithm is similar in both syndromic and non-syndromic patients the boxes are highlighted in blue; where the algorithm differs, variations for syndromic patients have been highlighted in orange (FD: fibrous dysplasia; MAS: McCune-Albright syndrome; MFD: monostotic fibrous dysplasia; PFD: polyostotic fibrous dysplasia; GH: growth hormone).

(p=0.03) had their tumour growth halted. Finally, medical management did not seem to have any positive effect on vision (non-syndromic p=0.69, and syndromic p=0.22).

We believe that although medical treatment is an important adjunct in the management of symptomatic FD, especially in young patients with active disease, it does not represent a definitive curative option.

Study limitations

Studies with a large pool of patients often lacked information on individual cases, and this prevented us from drawing further conclusions and extending the treatment algorithm. Such information included age at the time of surgery, skeletal maturity and GH levels in MAS, description of transcraniotomy versus an endoscopic approach for OND, the presence of stable or progressive disease, and the degree of optic nerve encasement in patients with orbital FD.

Conclusions

We conclude that (Fig. 4):

(1) Watchful waiting is recommended for stable or asymptomatic lesions in both non-syndromic and syndromic patients.
(2) Radical surgery is the best treatment to achieve disease resolution, including FD of the maxilla and mandible, in both subgroups. However, such a surgical approach leads to increased morbidity.
(3) Conservative surgery preserves both function and aesthetics. In non-aggressive craniofacial FD, bone contouring may be sufficient to relieve signs/symptoms effectively.
(4) Early therapeutic OND is advocated in both subgroups when vision deteriorates.
(5) In asymptomatic patients with optic canal stenosis, watchful waiting shows excellent results in both MFD/PFD and MAS.
(6) Endoscopic OND has shown excellent results in the treatment of orbital FD.
(7) For FD-associated cystic lesions, prophylactic OND is the treatment of choice.
(8) There is some evidence that the monitoring of serum GH in MAS patients is important to detect recurrence.
(9) IV bisphosphonates help decrease pain symptoms, especially in young patients with active disease.

Finally, FD has a wide clinical presentation so the choice of a specific surgical approach must be ultimately tailored to the individual clinical presentation and in accordance with each patient's needs and wishes.[52]

Conflicts of interest

We have no conflicts of interest.

This project did not receive any specific grant from funding agencies in the public, commercial or non-profitable sector. In the manuscript, there is no mention of instruments, products, or devices used to treat the affected patients.

Acknowledgements

The authors would like to express their deepest appreciation to Marco Braggion for his contribution towards the statistical analysis for this study, and to Guy Robinson from Barnet Hospital library for proofreading of the manuscript.

Ethics statement/confirmation of patients' permission

None.

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