REVIEW ARTICLE



Radiofrequency ablation is as safe and effective as surgical excision for spinal osteoid osteoma: a systematic review and meta-analysis

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Abstract

Background Osteoid osteoma (OO) is a primary benign tumor that affects mainly young patients. Ten percent of all OO are located in the vertebral column. Treatment of spinal OO is challenging and there is no consensus in the literature on the best operative approach.

Purpose The aim of this systematic review and meta-analysis was to determine safety and efficacy of radiofrequency ablation (RFA) versus surgical excision for the treatment of spinal OO.

Methods A literature search was performed on PubMed, Web of Science, and Embase from inception up to 22 March 2022. Studies addressing surgical excision or RFA for the treatment of spinal OO were included. The main outcomes evaluated were pain before and after intervention, the treatments success rate, defined as complete pain relief with no recurrence until the last follow-up, and the number and type of complications.

Results Thirty-one studies (749 patients) were included. For patients who underwent surgical excision, 19 studies reported a mean treatment success rate of 85.6%, while in the RFA treatment group, 18 studies reported a mean success rate of 88.6%. At last follow-up, the pooled mean difference in pain scores from baseline on a 0–10 scale was 5.8 points in the surgical excision group and 6.7 points in the RFA group. Recurrences were observed in 5.6% of the patients who underwent surgical excision group and 4.4% in the RFA group.

Conclusions This meta-analysis found high global success rates for both surgical and RFA treatments. Both treatments were efficient in pain relief and presented a low rate of recurrences. The complication rate was low for both treatments. Compared to surgical excision, RFA is a less invasive procedure which proved to be a safe and as effective option for the treatment of spinal OO.

Keywords Osteoid osteoma · Spine · Surgical excision · RFA

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Introduction

Osteoid osteoma (OO) usually affects young patients with a peak incidence in the second decade of life [1]. OO is the third most common benign bone tumor, with a male to female predominance of 2–3:1 [2]. The tumor consists of a central area of primitive bone, called nidus, surrounded by a peripheral zone of reactive sclerosis [3]. Around 10% of all OO occur in the spine, more frequently in the lumbar segment [4]. The posterior elements of the vertebra, such as lamina, pedicle, facets, spinous process, and transverse process, are mainly affected [5]. Common symptoms of spinal OO include severe, persistent back pain and functional scoliosis [6].

Although OO might heal spontaneously after many years, intervention with removal of the central nidus is highly recommended [7], especially in the spine. Surgical excision has been for many years the only available option, but starting in the 90's percutaneous RadioFrequency Ablation (RFA) was developed [4]. Both treatments have high success rates, with resolution of symptoms and complete removal of the tumor observed in the majority of the patients treated. However, both treatments also present risks and complications. Surgery may require stabilization of the appendicular skeleton after wide resections and can lead to perioperative complications and prolonged hospital stays [8]. On the other side, RFA in the vertebral column is still debated for the risk of thermal damage to neurological structures, especially when the tumor is located close to nerve roots, but RFA presents advantages compared to open surgery including the minimally invasive approach, the reduced hospital stay, the conscious sedation or peripheral anesthesia, and the cost-effectiveness, making it the treatment of choice for nonspinal OO [8–10]. However, despite the concerns related to surgery, surgical excision often remains the preferred treatment approach to address OO in the spine.

The aim of this systematic review and meta-analysis was to determine safety and efficacy of RFA versus surgical excision for the treatment of spinal OO.

Materials and methods

Literature search

A review protocol was created based on the preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (www.prisma-statement.org, accessed on 1 October 2021). The study was registered on PROS-PERO (ID321534). A literature search was performed in three bibliographic databases (PubMed, Web of Science, and Embase) from inception up to 22 March 2022. The following research terms were used: "Osteoid osteoma AND (spine OR vertebral OR spinal involvement) AND ((Radiofrequency OR RFA) OR (excision OR resection OR curette OR ablation OR surgery))". Inclusion criteria were studies addressing surgical excision or RFA for the treatment of spinal OO. Only studies written in English were included. Case reports or case series describing < five cases and articles in languages other than English were excluded. Pre-clinical, ex-vivo studies and review articles were also excluded.

Data extraction

Two independent reviewers (L.M.O. and A.S.) screened all the articles on the title and abstract to assess whether they met the inclusion criteria. After the first screening, the articles that met the inclusion criteria were evaluated for full-text eligibility and were excluded if they did not follow the inclusion criteria (Fig. 1). In case of disagreement between the two reviewers (L.M.O. and A.S.), a third reviewer (G.F.) was consulted to reach a consensus. Data were independently extracted on a preconceived data extraction form using Excel (Microsoft). The following data were extracted: first author, journal, year of publication, type of study, number of patients, location of the OO, pain before and after treatment assessed through a Visual Analogic Scale (VAS), success rate, recurrence rate, and complications.

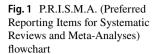
The pain VAS is a unidimensional measure of pain intensity, it consists in an 11-point numerical scale that ranges from "0" representing one pain extreme (e.g. "no pain") to "10" representing the other extreme (e.g. worst pain imaginable). For the purpose of the analysis the success rate was defined as complete pain relief and no evidence of recurrence at the last visit of follow-up after RFA or surgical treatment. Recurrence was defined as a rebound of symptoms after a period of pain relief following the procedure, with radiological examinations confirming the recurrence of OO in the same position where the first treatment was performed.

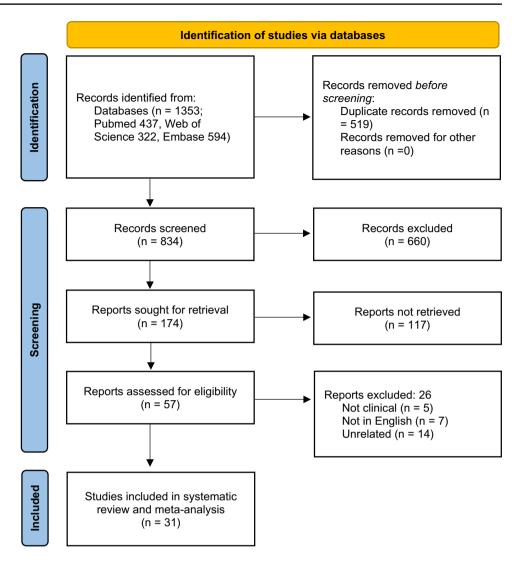
Assessment of risk of bias and quality of evidence

The Downs and Black's "Checklist for Measuring Quality" was used to evaluate risk of bias and quality [11]. It contains 27 'yes'-or-'no' questions across five sections; it provides a numeric value up to 32 points. The five sections include questions about the overall quality of the study (10 items), the ability to generalize findings of the study (3 items), the study bias (7 items), the confounding and selection bias (6 items), and the power of the study (1 item). Assessment of risk of bias and quality of evidence was completed independently for all outcomes by two authors (L.M.O. and A.S.) and a third author (G.F.) solved any possible discrepancy.

Statistical analysis

The statistical analysis and the forest plot were carried out according to Neyeloff et al. [12] using Microsoft Excel by an independent professional statistician. The Mantel–Haenszel method was used to provide pooled rates across the studies. A statistical test for heterogeneity was first conducted with the Cochran Q statistic and I2 metric and was considered the presence of significant heterogeneity with I2 values $\geq 25\%$. When no heterogeneity was found with I2 < 25%, a fixed effect model was used to estimate the expected values and 95% Cis; otherwise, a random-effect model was applied, and an I2 metric was evaluated for the random effect to check





the correction of heterogeneity. The studies rate confidence intervals were carried out using the continuity-corrected Wilson interval. All statistical analysis was carried out with Microsoft Excel 2010.

Results

Included studies

A total of 1353 articles were retrieved; after the removal of duplicates, screening of the titles, abstracts, and full texts, 31 studies (749 patients) were included in the systematic review: 23 retrospective case series, 2 prospective studies and 6 comparative studies (Fig. 1).

Nineteen studies reported the surgical excision for spinal OO, for a total of 375 patients (253 men-67.5%, and 122 women-32.5%) with a mean age of 18.6 ± 6.0 years and a

mean follow-up time of 40.1 ± 16.9 months (Table 1 for further details). RFA treatment for spinal OO was reported in 18 studies, for a total of 374 patients (245 men-65.5%, and 129 women-34.5%) with a mean age of 23.3 ± 5.3 years and a mean follow-up time of 40.3 ± 17.7 months. The groups were homogeneous for sex, age, and follow-up times. Fourteen of the included the studies reporting a mean symptoms duration of 18.2 months before diagnosis. Ninety-two patients (12.3%) presented with functional scoliosis (51 in the surgical excision group and 41 in the RFA group).

In the studies where the spine OO location was reported, out of 205 patients who underwent surgical excision, 63 (30.7%) had OO in the cervical spine, 55 (26.9%) in the thoracic spine, 83 (40.5%) in the lumbar spine and four (1.9%) in the sacral spine. Out of 76 patients who underwent RFA, 18 (23.7%) had OO in the cervical spine, 23 (30.2%) in the thoracic spine, 31 (40.8%) in the lumbar spine and four (5.3%) in the sacral spine (Fig. 2). Table 1Details of the includedstudies. N° (number), M(male), F (female), RFA(RadioFrequency Ablation),VAS (Visual Analogic Scale)

First Author	Year	N° of Patients	M/F	Treatment Group	Studies in the Systematic Review	Studies in the Meta-Analysis	
						Rate of Success	VAS
Laus[13]	2007	9	6/3	Comparative	\checkmark	~	Х
Hadjipavlou[14]	2009	7	6/1	Comparative	\checkmark	\checkmark	Х
Weber[15]	2015	18	9/9	Comparative	\checkmark	\checkmark	\checkmark
Zhang[16]	2017	45	34/11	Comparative	\checkmark	\checkmark	\checkmark
Yu[17]	2019	28	19/9	Comparative	\checkmark	\checkmark	\checkmark
Pipola[5]	2021	138	90/48	Comparative	\checkmark	\checkmark	Х
Klass[18]	2009	7	3/4	RFA	\checkmark	\checkmark	Х
Martel[19]	2009	10	7/3	RFA	\checkmark	\checkmark	\checkmark
Vanderschueren[20]	2009	24	16/8	RFA	\checkmark	\checkmark	Х
Hoffmann[21]	2010	5	3/2	RFA	\checkmark	\checkmark	Х
Morassi[22]	2014	13	7/6	RFA	\checkmark	\checkmark	\checkmark
Albissini[23]	2017	61	46/15	RFA	\checkmark	\checkmark	Х
Faddoul[24]	2017	8	3/5	RFA	\checkmark	\checkmark	\checkmark
Nöel[25]	2017	7	3/4	RFA	\checkmark	\checkmark	\checkmark
Wang[26]	2017	7	6/1	RFA	\checkmark	\checkmark	\checkmark
Vidoni[27]	2018	17	13/4	RFA	\checkmark	\checkmark	Х
Tomasian[28]	2018	7	5/2	RFA	\checkmark	\checkmark	Х
Beyer[29]	2019	77	50/27	RFA	\checkmark	\checkmark	\checkmark
Kirwan[30]	1984	8	3/5	Surgical excision	\checkmark	\checkmark	Х
Maiuri[31]	1986	7	7/0	Surgical excision	\checkmark	\checkmark	Х
Raskas[32]	1992	11	8/3	Surgical excision	\checkmark	\checkmark	Х
Ozaki[33]	2002	9	4/5	Surgical excision	\checkmark	\checkmark	Х
Aydinli[34]	2003	9	5/4	Surgical excision	\checkmark	\checkmark	Х
Zileli[35]	2003	5	2/3	Surgical excision	\checkmark	\checkmark	Х
Hempfing[36]	2007	7	5/2	Surgical excision	\checkmark	\checkmark	Х
Burn[37]	2009	7	4/3	Surgical excision	\checkmark	\checkmark	Х
Gasbarrini[6]	2011	81	52/29	Surgical excision	\checkmark	\checkmark	X
Pourfeizi[38]	2014	11	5/6	Surgical excision	\checkmark	\checkmark	Х
Etemadifar[39]	2015	19	11/8	Surgical excision	\checkmark	\checkmark	Х
Quraishi[40]	2017	84	65/19	Surgical excision	\checkmark	\checkmark	Х
Mallepally[41]	2020	5	3/2	Surgical excision	\checkmark	\checkmark	\checkmark

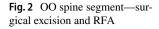
Twenty-four studies (354 tumors) reported the position of OO in the vertebra. In the surgical excision group, 27 (16.4%) were located in the body, 41 (24.8%) in the lamina and 97 (58.8%) in the posterior elements, specifically 57 (34.5%) in the pedicle, 37 (22.4%) in the facets, 3 (1.9%) in the transverse process and none in the spinous process. In the RFA group, 35 (18.5%) were located in the body, 42 (22.2%) in the lamina and 112 (59.3%) in the posterior elements, specifically 54 (28.6%) in the pedicle, 43 (22.8%) in the facets, 8 (4.2%) in the transverse process and 7 (3.7%) in the spinous process (Fig. 3).

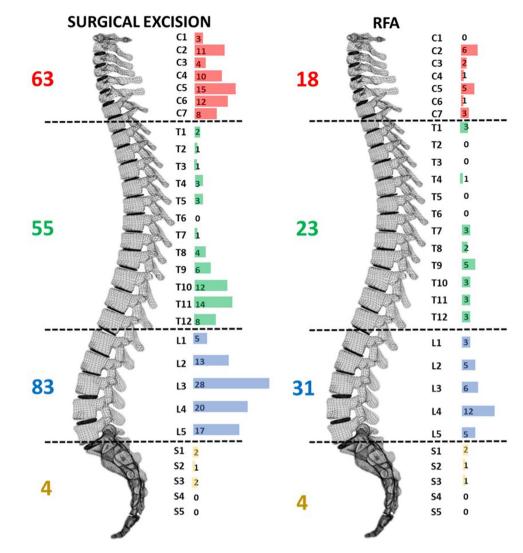
All the included studies underwent a meta-analysis for the success rate, while the meta-analysis on patients reported outcomes was feasible only in ten studies reporting on VAS, for a total of 218 patients, of which 53 (4 studies) underwent surgical excision and presented with a mean pain VAS at baseline of 6.6 points, and 165 (9 studies) underwent RFA treatment and reported a mean of 7.6 points on the VAS scale before undergoing the procedure.

A further meta-analysis was performed specifically on the six comparative studies (245 patients) documenting the success rate for both surgical excision (115 patients) and RFA (130 patients).

Systematic review results

Twenty-two studies included in the systematic review reported the complications that occurred in the surgical excision and RFA groups. Thirteen studies reported the complication rate in the surgical excision group, with a mean





incidence of 7.8% (24 out of 309 patients). The complications reported were: five incomplete pain relief, five postoperative vertebral instability, three wound dehiscence, two wound infection, one hematoma, one pneumothorax, one incomplete excision, one incidental durotomy, one neuropathic pain, one pneumonia, one problem with postoperative ventilation, one local hypoesthesia, and one wrong level resection. Fourteen studies reported the complication rate in the RFA treatment group, with a mean incidence of 4.4% (14 out of 316 patients). The complications reported were: 11 incomplete pain relief, one lower limb neuropathy, one procedure interrupted for appearance of radiculopathy, one temporary rigidity after the procedure.

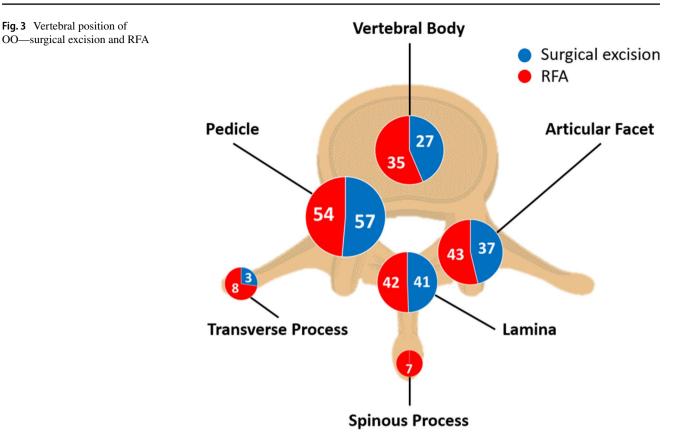
Twenty-eight studies (18 on surgical excision, 17 on RFA) reported the recurrence rate, accounting for 5.6% (21 out of 372 patients) in the surgical excision group and 6.7% (24 out of 360 patients) in the RFA group. Five studies reported the location of recurrences in the surgical excision group: three in the cervical spine (30%), three in the thoracic

spine (30%) and four in the lumbar spine (40%). Five studies reported the location of recurrences in the RFA group: two in the cervical spine (12.5%), eight in the thoracic spine (50%), five in the lumbar spine (31.2%) and one in the sacral spine (6.3%). All recurrences were confirmed by radiological evaluations and require a second procedure.

Meta-analysis results

This meta-analysis evaluated the success rate of both surgical excision and RFA treatment for spinal OO. In patients who underwent surgical excision, 19 studies reported a mean treatment success rate of $85.6\% \pm 4.8$ (95% C.I., 76.2–94.9) (320 out of 375 patients). In the RFA treatment group, 18 studies reported a mean success rate of $88.6\% \pm 4.9$ (95% C.I., 79.1–98.2) (329 out of 372 patients).

The meta-analysis of the six comparative studies showed a mean success rate of 87.0% (95% C.I., 69.9–100) in the surgical excision group (101 out of 115 patients) and a mean



success rate of 87.2% (95% C.I., 71.2–100) in the RFA group (116 out of 130 patients). There was no statistical difference between the two groups (p = 0.98).

Pain relief of surgical excision or RFA treatment for spinal OO was assessed by comparing pre-operative and postoperative pain scores. In the surgical excision group, four of the 19 surgical studies were included in this analysis. At the last follow-up, the mean difference in pain scores from baseline on the 0–10 VAS was 5.8 ± 0.9 points (95% C.I., 4.4–7.3) (Fig. 4). In the RFA treatment group, pain relief was assessed by nine studies out of 19 studies. At the last follow-up, the mean difference in pain scores from baseline on the 0–10 VAS was 6.7 ± 0.5 points (95% C.I., 5.8-7.7) (Fig. 4). Pain reduction after intervention was statistically significant for both surgical excision and RFA (p < 0.0005).

Risk of bias

The Downs and Black's tools for assessing the risk of bias give each study an excellent ranking for scores ≥ 26 , good for scores from 20 to 25, fair for scores between 15 and 19, and poor for scores ≤ 14 points. According to these criteria, none of the included studies was classified as poor, 17 fair, 14 good and none excellent (Fig. 5). Mostly, the factors reducing the quality of the studies were the absence of confounders and blinding attempts and the low statistical power of

some studies. Among the 6 comparative studies, three were classified fair and three good.

Discussion

The main finding of this systematic review and meta-analysis is that RFA provides a high success rate without an increased number of complications with respect to surgical excision.

The population included in the studies which met the inclusion criteria for this meta-analysis is representative of the population affected by spinal OO according to the literature [42], with a mean age of 20.9 years and an overall 2:1 male predominance. The lumbar segment was the most affected, with more than 40% of tumors located in these five vertebrae. Ninety-two patients (12.3%) presented with functional scoliosis, possibly caused by antalgic posture and muscle spasm and all the patients had a history of increasing back pain and were diagnosed with OO through imaging studies (radiographs, MRI, and CT to highlight the central radiolucent nidus). All surgical excisions were performed under general anaesthesia, while for RFA conscious sedation together with local analgesia was preferred, using general anaesthesia only in paediatric patients or when explicitly requested by the patient.

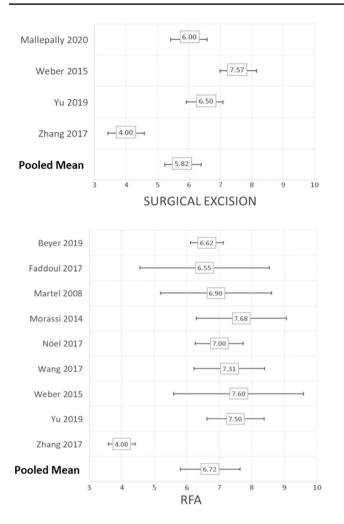


Fig. 4 VAS improvement-surgical excision and RFA

Overall, this meta-analysis found that both treatments were efficient in relieving the pain caused by OO, The patients presented with a history of increasing and invalidating backache, with a mean symptoms duration of 18.2 months before diagnosis documented in this review. Preoperative VAS scores reflected the extremely painful condition caused by spinal OO, with patients reporting a mean of 7.1 points on a 0–10 pain scale. The large majority of the patients treated with both techniques experienced a significant improvement in pain after the procedure. After RFA, pain relief was reported to be immediate, with an important decrease in VAS scores within the first day after the operation. In patients treated with surgical excision, back pain decrease was more gradual and took a few days to be complete. No previous literature review performed this analysis for the challenging spine OO location, where surgery is often considered the preferred option due to concerns for RFA-related complications. In this light, these results are of particular importance for the clinical practice, giving physicians reliable data on the comparable results of these two approaches both in terms of treatment outcome and complications.

In a previous literature review focusing only on RFA treatment, Sagoo et al. [43] systematically assessed clinical outcomes and complications after RFA for spinal OO and reported local success rates ranging from 87.5 to 100% across 14 studies, with minor complications reported in four patients (1.1%). Differently, from the study of Sagoo et al., the complication rate in this review was 4.4% for patients treated with RFA, and this can be explained by the fact that all the events described as complications by the authors of those studies were taken into account, including the partial pain relief after RFA due to incomplete ablation of the tumor. Although this cannot be considered a major complication, it must be noted that partial pain relief means that those patients, who have already experienced a long-lasting, persistent back pain, needed a second treatment in order to completely remove the tumor.

In this study, a higher number of complications occurred in the surgical group compared to the RFA group (7.8%). In the literature, there were no meta-analyses or systematic reviews addressing surgical excision of spinal OO. The present study is the first to meta-analyse the results of surgical excision for OO and to compare them with those of RFA for this specific location in the appendicular skeleton. The vertebral column is a very challenging location to treat [44]. Although OO may heal spontaneously or with medical therapy, an operative intervention is unanimously considered the gold standard treatment [7], as it permits rapid pain relief for the patient. In addition, patients with spinal OO often develop functional scoliosis, caused by an abnormal antalgic posture and promoted by the inflammatory reaction around the OO [38, 45]. In the literature, a significant improvement in scoliosis was reported in patients who received early surgery compared to those where surgical excision was delayed [46]. When choosing the operation technique to remove vertebral tumors, the potential damage to nearby vital structures must be taken into account [47]. For this reason, even minor and transitory complications were included in the present study, in order to evaluate accurately the two procedures and determine the best treatment option for spinal OO. Even in the surgical excision group, the persistence of pain was the most frequently observed complication, mainly due to incomplete removal of the tumor requiring a second operation. Another important complication reported was vertebral instability: open surgery is an invasive procedure and wide resections may require instrumentation and fusion of vertebrae to ensure adequate stability [6, 39]. Surgical excision has the advantage to allow intraoperative biopsies, which were performed on the wide majority of the patients in the included studies to confirm the nature of the lesion with a high diagnostic rate [6, 34]. Differently,

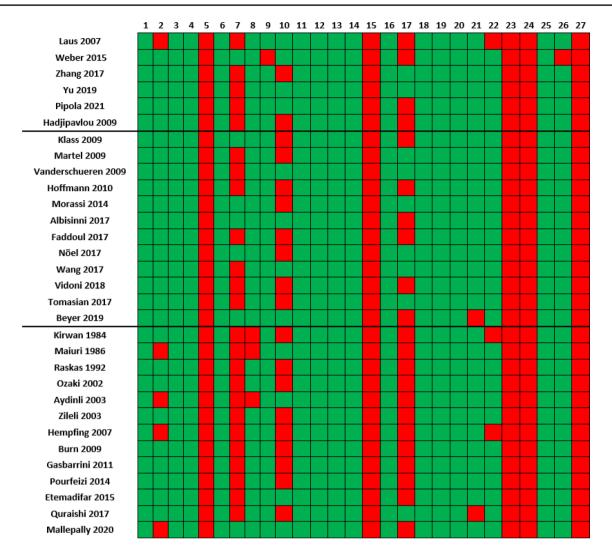


Fig. 5 Downs and Black's tool for assessing the risk of bias

percutaneous needle CT-guided biopsies taken before RFA treatment have lower diagnostic potential [7, 13, 25]. Nevertheless, ablation techniques proved to be efficient and safe, with few complications reported. This supports the use of RFA, which also presents other advantages. In comparison with surgical excision, a reduced operation time was reported: RFA cycles typically last 4–8 min at 90 °C [19, 48]. Moreover, a reduced hospital stay has been documented as well: usually, one day, while surgical excision patients were discharged after a mean of six days [15, 17, 34].

In the study by Sagoo et al. [43], the tumor recurrence rate after RFA was 6.5% (23 out of 354 patients). In the present study, the recurrence rate was 6.7% in the RFA group, a result that confirms the previous literature.

The current review retrieved also a 5.6% recurrence rate in patients treated with surgical excision. As expectable, the direct visualization of the tumor allows the surgeon to obtain safe margins of resection, thus ensuring a low risk of recurrence [5]. Nonetheless, this was similar to what shown for the RFA group. The spinal location of OO is challenging because of the proximity to neurovascular structures. Although RFA, together with other minimally invasive ablation techniques (microwave [49], laser [3], MR-guided focused ultrasound [50], cryoablation [51]), represents the treatment of choice for non-spinal OO [3], the main concern regarding its use for spinal OO is the potential thermal damage to neurologic structures. For this reason, many authors consider surgical excision the gold standard approach for spinal OO [5]. When RFA is used to treat OO located outside the spine, recurrences are observed in around 4% of patients [52]. The higher recurrence rate found in this study may reflect a more cautious approach when RFA is performed on the spinal OO, with some authors considering 5 mm as the minimal safe distance between OO and neurovascular structures to proceed with the ablation [24]. However, in two of the included studies, RFA was performed successfully even when the distance between OO and neurological structures was 2 mm [27] and 1.71 mm [28], respectively. Accordingly, only a few percentage of spinal OO, those strictly attached to neurological structures, cannot be addressed with RFA. In the vast majority of cases, the decision whether to perform a surgical excision or a RFA should be taken by the surgeon according to the familiarity with the technique and the availability of RFA devices and personnel. In this light, a cortical shell between the lesion and the spinal canal could represent a safe feature when choosing RFA. With the exception of the few cases attached to neurological structures, the available evidence suggests that RFA is a safe and reliable option to address spinal OO [26, 43].

This systematic review and meta-analysis have some limitations. Firstly, there are only six studies comparing RFA and surgical excision for the treatment of spinal OO and there are no randomized controlled trials on this topic. Data from the studies included were heterogeneous, especially the follow-up times, and not all studies reported the same level of detail. This heterogeneity may hide bias related to the possible different indications for the two approaches. While no difference could be detected in terms of patients' characteristics (i.e. scoliosis and/or neurological symptoms), the nature of the studies cannot clearly exclude a selection bias, and further more robust studies should compare these treatments and confirm the study findings. In addition, the only clinical outcome available in the included studies was pain VAS, which can be easily influenced by the patients, thus possibly weakening the strength of the results. However, VAS pain was only a secondary outcome (important for patients) of this analysis, and this is the first meta-analysis comparing surgical excision and RFA for the treatment of spinal OO, which was able to provide some interesting indications. A strength of this study is in fact that, although OO of the vertebral column is a rare lesion, a relatively high number of patients was available for the analysis. In addition, the median follow-up time of the studies included exceeded three years, giving the possibility to consider technical and clinical results stabilized and reliable.

There is a lack of randomized controlled trials comparing RFA versus surgical excision in the treatment of spinal OO. OO is benign tumor but extremely painful and affects mainly young people, with possible permanent complications such as functional scoliosis, so it is mandatory to define the best treatment option. Until high-level studies will prove otherwise, this meta-analysis showed the high success rate and the low complications rate of RFA, which can be considered a suitable option also for the treatment of the challenging location of spinal OO.

Conclusions

This meta-analysis found high global success rates for both surgical and RFA treatments. Both treatments were efficient in pain relief and presented a low rate of recurrences. The complication rate was low for both treatments. Compared to surgical excision, RFA is a less invasive procedure which proved to be a safe and as effective option for the treatment of spinal OO.

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Declarations

Conflict of interest The authors declare that they do not have any confict of interest.

Ethical approval Not applicable.

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