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Surgery alone versus post-operative radiotherapy for sinonasal malignant melanoma: a meta-analysis

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Abstract

Objective. Sinonasal malignant melanoma is a relatively rare malignancy with poor prognosis, and effective treatments remain elusive. This analysis aimed to explore whether post-operative radiotherapy conferred any survival advantages in patients with this disease when compared with surgery alone.

Methods. Published studies were identified by searching four electronic databases. The end-points evaluated were: rates of overall survival, disease-free survival and local control.

Results. Twenty-eight studies including 1392 patients were identified. The results indicated that post-operative radiotherapy led to a significantly better three-year overall survival rate ($p = 0.02$), and suggested a borderline significant benefit for five-year overall survival ($p = 0.05$), when compared with surgery alone. However, no statistical advantage was found for disease-free survival, local control or one-year overall survival.

Conclusion. This meta-analysis indicated that adjuvant radiotherapy prolonged survival, but showed no benefit for disease-free survival or local control.

Main Article

Dr B-B Yang takes responsibility for the integrity of the content of the paper

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Introduction

Sinonasal malignant melanoma is a relatively rare disease, with an approximate incidence of 0.05–0.1 per 100 000 people a year.[1] It has been recognised as an aggressive and highly lethal tumour, associated with an unpredictable course. Its non-specific clinical features such as nasal obstruction, followed by discharge and bleeding,[2] lead to a delay in diagnosis, which may contribute to the overall poor prognosis. The five-year survival rate is typically less than 25 per cent, with reports varying from 8 per cent to 48 per cent.[3,4]

There is no effective systemic therapy for this aggressive malignancy. Surgical resections with clear margins are still the mainstay of treatments,[2] which include endoscopic techniques and traditional open approaches, namely lateral rhinotomy, mid-facial degloving, maxillectomy and craniofacial resection.[4] Although wide surgical resection of the primary tumour has been the oncological goal, obtaining wide surgical margins in the paranasal sinuses is difficult, and furthermore must be balanced against functional and aesthetic concerns.[5]

Melanoma is traditionally considered to be a relatively radio-resistant tumour. This can be explained by its high capacity for sublethal DNA damage reparation[6] and post-irradiation regeneration.[7] Radiation-induced damage, such as wounds and damage to the central nervous system, affects patients' survival rate and quality of life.[8] The blindness rate reported in sinonasal malignancies ranges from 15 per cent to 40 per cent.[9–12] However, melanoma has shown sensitivity to high dose per fraction radiation therapy.[13] Moreover, radiotherapy aims to reduce the post-operative invasion of residual tumours into the surrounding normal tissues. A trend towards improving locoregional control by post-operative radiotherapy has been observed,[14–17] although this conclusion was poorly reproducible.[4,18–20] Therefore, the value of adjuvant radiotherapy in sinonasal malignant melanoma remains controversial.

The relative rarity of sinonasal malignant melanoma makes the analysis of treatment approaches difficult, let alone randomised controlled trials or even large cohort studies. Most of the studies published have been case reports or cohort studies, which makes a meta-analysis possible. We therefore performed a meta-analysis to assess the impact of post-operative radiotherapy performed for sinonasal malignant melanoma on overall survival, disease-free survival and local control.

Materials and methods

Literature search strategy

Electronic searches were performed using PubMed, Ovid, Web of Science and the Cochrane Library from their dates of inception to April 2018. The following terms were used to identify relevant articles: 'sinonasal' (or 'nasal cavity' or 'paranasal sinus*'), and 'melanoma' and 'therapy' (or 'treatment', 'radiotherapy', 'radiation', 'surgery', 'operation', 'surgical

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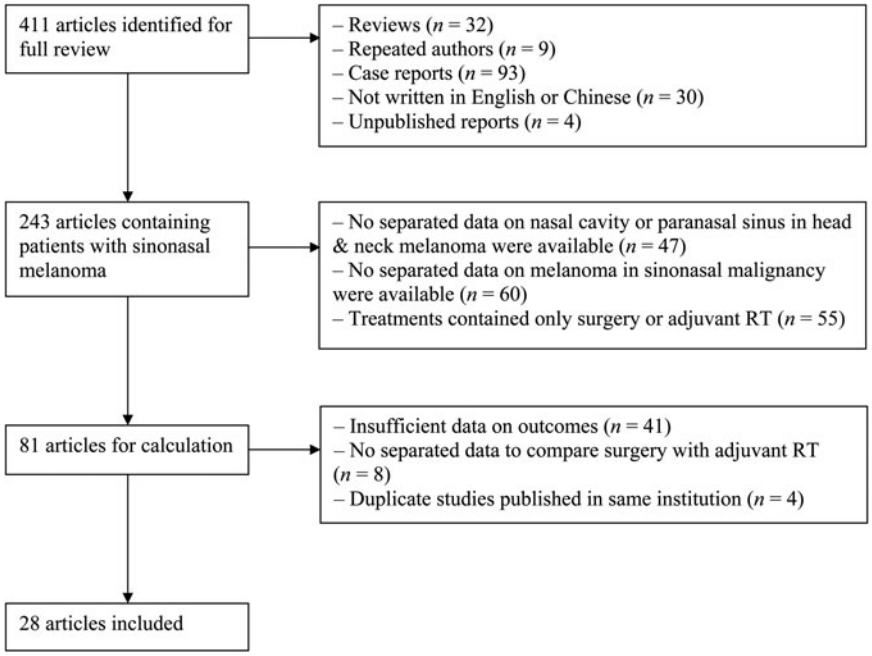

Fig. 1. Study selection flowchart. RT = radiotherapy

resection', 'excision' or 'postoperative radi*'), and 'outcome' (or 'surviv*', 'prognos*' or 'predict*'). The published languages were limited to Chinese and English. Relevant studies were also identified by hand-searching the references of included articles.

Inclusion criteria

Studies were included in the systematic review if they met the following criteria: (1) patients were pathologically confirmed to have primary sinonasal malignant melanoma; (2) interventions included both a surgery alone group and a post-operative radiotherapy group; and (3) the main outcomes included overall survival, disease-free survival or local control. The study types included were randomised controlled clinical trials, cohort studies and case series.

Studies were excluded if they did not have outcome data available, or if they were abstracts, case reports, conference presentations, editorials or expert opinions. When institutions published duplicate studies with accumulating numbers of patients or increased lengths of follow up, only the most complete report was selected for quantitative assessment.

Outcome measurement

Overall survival was defined as the rate of survival for a group of individuals, taking into account death due to any cause, and including one-year, three-year and five-year overall survival rates. Disease-free survival was defined as the rate of patients remaining free of disease, including one-year, three-year and five-year disease-free survival rates. Local control was defined as the rate of arresting cancer growth at the site of origin, including one-year, three-year and five-year local control rates.

Data extraction

Each included study was analysed to extract relevant data, including first author, publication year, country, institution, case numbers, patient ages, data collection period, follow-up duration and outcomes. The outcomes were not always explicitly stated in each study, and in these instances, data were obtained through the following methods: first, by directly extracting data from each article; second, by using individual patient data from the provided tables for the calculations; and third, by estimating data using Kaplan–Meier survival curves, produced by GetData Graph Digitizer 2.22 software. Data were not estimated by adjusting prognostic factors because of the large heterogeneity among studies.

Quality assessment

The Newcastle–Ottawa Scale was used for assessing the quality of non-randomised studies.[21] A star system was employed to judge the studies in terms of three broad areas: selection of the study groups (4 possible stars), comparability of the groups (2 possible stars) and ascertainment of the outcomes of interest (3 possible stars). The maximum score was 9 stars.

Statistical analysis

Meta-analysis was performed using RevMan 5.3 software, provided by the Cochrane Collaboration. Outcomes were calculated and synthesised using the Mantel–Haenszel method in the software, and evaluated by risk ratios and 95 per cent confidence intervals (CIs). A two-sided p-value of 0.05 or less was considered statistically significant. A fixed-effects model was used when no heterogeneity was observed among the studies, assuming that the treatment effect in each study was the same; otherwise, a random-effects model was adopted. Chi-square tests were used to assess heterogeneity between studies, and the I^2 statistic was used to evaluate the percentage of total variation across studies occurring as a result of heterogeneity instead of chance. A p-value of less than 0.10 and an I^2 value of more than 50 per cent were considered to indicate heterogeneity.[22] When the number of trials reached 10, publication bias was examined using the funnel graph method.

Results

Search results

After screening the titles and abstracts of the search results, 411 relevant articles were identified for detailed review.

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Table 1. Main characteristics of included studies

Author	Country	Institution	Period (years)	Age (mean (range; years)	Follow-up duration (mean (range); mth)	Post-op RT/surgery (*n*)	NOS score (points)
Brandwein *et al.* (1997)[23]	USA	Mount Sinai Hospital	1977–1995	65 (23–83)	39* (1–217)	5/18	8
Cheng *et al.* (2007)[24]	China	Taipei Veterans General Hospital	1982–2002	68.2 (39–87)	(3–132)	12/5	9
Clifton *et al.* (2011)[25]	UK	Queen's Medical Centre Nottingham	1982–2007	67.5 (37–86)	NA	7/7	8
Crawford *et al.* (1995)[26]	Canada	British Columbia Cancer Agency	1976–1992	66 (32–88)	(2–37)	7/4	9
Dauer *et al.* (2008)[27]	USA	Mayo Clinic	1955–2003	67 (30–91)	(37–196)	17/29	8
Gal *et al.* (2011)[28]	USA	SEER tumour registry	2000–2007	71.2	NA	120/128	9
Ganly *et al.* (2006)[8]	Canada	17 international tertiary referral centres	NA	63* (3–81)	10* (1–159)	22/22	9
Hu *et al.* (2004)[29]	China	Cancer Center, Sun Yatsen University	1984–1997	48.5* (30–79)	25.2 (1.4–161)	7/12	8
Kingdom & Kaplan (1995)[5]	USA	University of California at San Francisco Medical Center	1981–1993	68 (56–85)	(6–76)	7/6	8
Liétin *et al.* (2010)[14]	France	NA	1998–2008	71 (61–85)	NA	5/5	9
Lund *et al.* (2012)[4]	UK	Royal National Throat, Nose & Ear Hospital	1963–2010	65.9 (15–91)	37.5 (2–360)	51/64	8
Martin *et al.* (2004)[30]	Australia	Peter MacCallum Cancer Centre	1991–2002	77* (45–91)	79* (7–128)	15/2	9
Marunick & Oh (2009)[31]	USA	Karmanos Cancer Institute, Maxillofacial Prosthetic Clinic	2002–2007	68.5 (43–89)	(2–37)	3/2	9
Matias *et al.* (1988)[32]	Portugal	Instituto Portugues de Oncologia de Francisco Gentil	NA	64 (59–76)	NA	3/1	8
Meng *et al.* (2014)[33]	China	Eye, Ear, Nose & Throat Hospital, Fudan University	2000–2010	65.9 (28–89)	63.4 (48–72)	24/27	9
Panje & Moran (1986)[34]	USA	Otolaryngology – Head & Neck Surgery, University Of Chicago Medical School	1940–1982	69 (30–85)	NA	3/5	9
Podboj & Smid (2007)[35]	Slovenia	Department of Otorhinolaryngology & Cervicofacial Surgery, Ljubljana University	1991–2006	69 (15–80)	67* (15–178)	1/1	9
Roth *et al.* (2010)[36]	Switzerland	University Hospital of Zurich	1992–2007	71 (40–94)	NA	7/11	9
Sun *et al.* (2014)[37]	China	Third Affiliated Hospital of Kunming Medical University	1976–2005	55* (2–79)	24 (1–264)	13/18	9
Thariat *et al.* (2011)[38]	France	Centre Hospitalier Universitaire & Centre Antoine Lacassagne	1991–2006	73* (45–91)	37* (1–181)	5/9	9
Trapp *et al.* (1987)[39]	USA	UCLA Medical Center for Health Sciences	1970–1980	65 (44–88)	46 (3–156)	2/5	9
Wei *et al.* (2003)[40]	China	Xiangya Hospital, Central South University	1988–2001	54* (19–86)	8–156	6/8	8
Won *et al.* (2015)[41]	Korea	15 university hospitals throughout Korea	1994–2013	63.3 (28–92)	40.9 (12–200)	43/62	9
Breik *et al.* (2016)[42]	Australia	Royal Melbourne Hospital	1990–2015	65 (46–87)	26* (2–132)	1/4	9
Letievant *et al.* (2016)[43]	France	Centre Hospitalier Universitaire de la Croix-Rousse	1994–2014	67* (50–87)	43*	9/4	9
Samstein *et al.* (2016)[44]	USA	Memorial Sloan Kettering Cancer Center	1998–2013	68* (34–91)	21* (0–178)	64/14	8
Dréno *et al.* (2017)[45]	France	University Hospital of Nantes	1988–2015	71.2 (50–96)	50	17/12	9
Amit *et al.* (2017)[46]	USA	MD Anderson Cancer Center	1991–2016	64* (34–91)	28* (2–220)	73/57	9

*Median value. Mth = months; post-op = post-operative; RT = radiotherapy; NA = data not available; SEER = Surveillance, Epidemiology, and End Results Program; NOS = Newcastle–Ottawa Scale

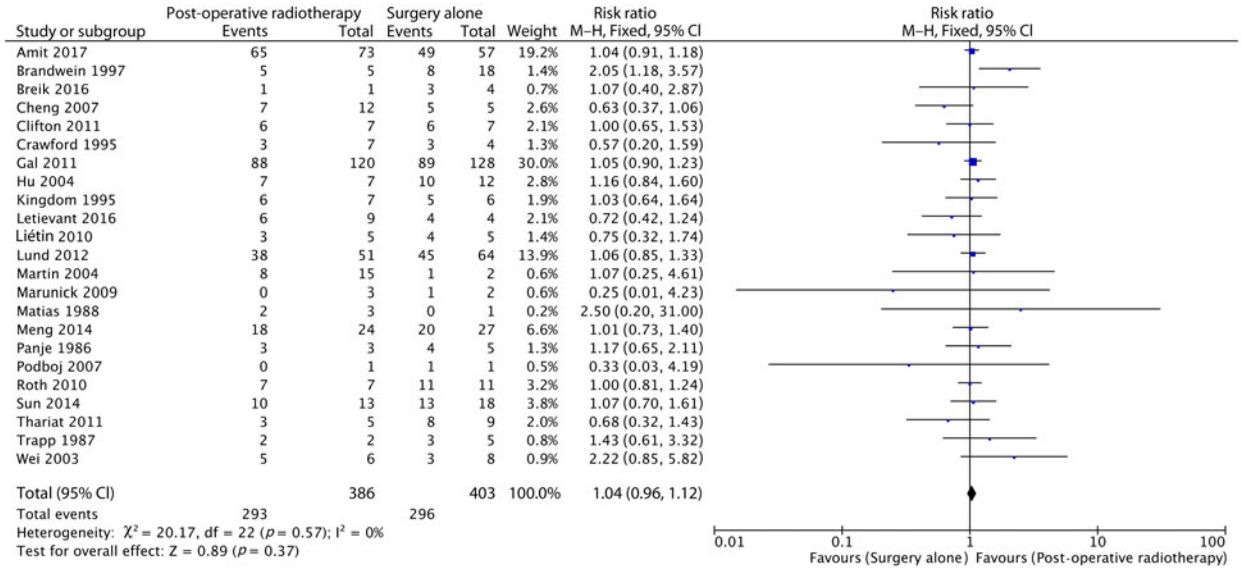

Fig. 2. Forest plot of risk ratios for one-year overall survival, comparing patients treated with surgery alone and those treated with post-operative radiotherapy. M–H = Mantel–Haenszel test; CI = confidence interval; df = degrees of freedom

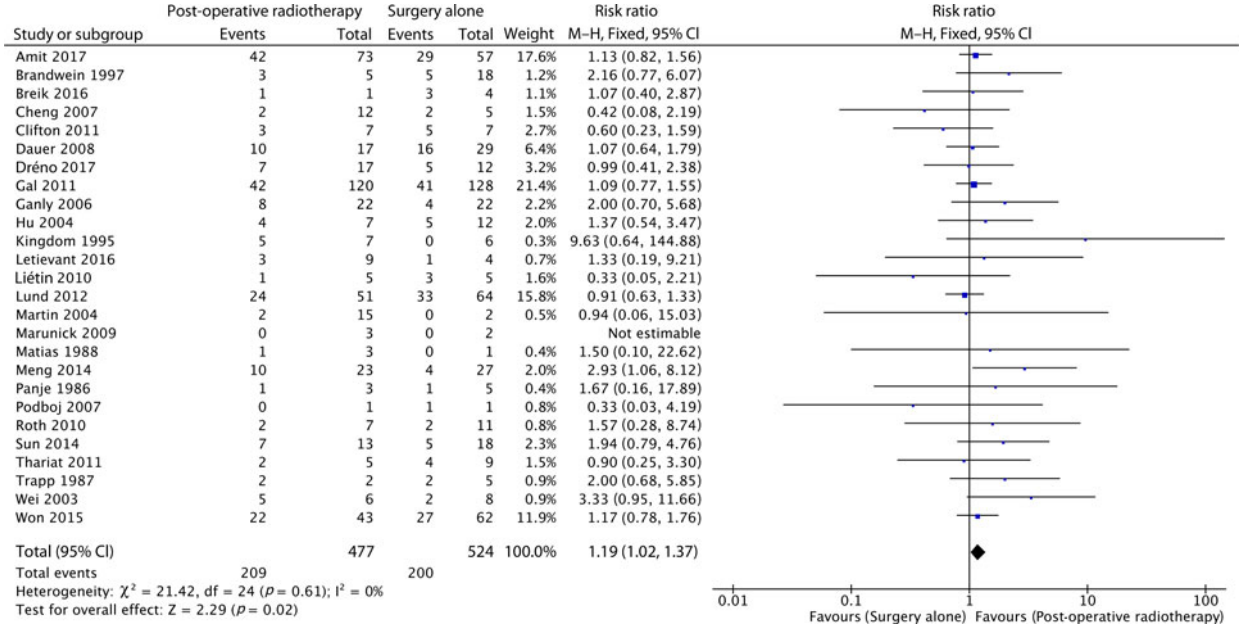

Fig. 3. Forest plot of risk ratios for three-year overall survival, comparing patients treated with surgery alone and those treated with post-operative radiotherapy. M–H = Mantel–Haenszel test; CI = confidence interval; df = degrees of freedom

Of these, 28 articles were eligible for inclusion;[4,5,8,14,23–46] the rest were excluded (see Figure 1). The included studies involved a total of 1392 patients, of whom 549 received post-operative radiotherapy, 542 were treated by surgery alone and the rest received other therapies. The detailed characteristics of these articles are summarised in Table 1.

Quality of studies

The 28 identified studies were cohort studies. Using the Newcastle–Ottawa Scale assessment, 19 of the 28 studies were awarded 9 stars, and the remaining 9 studies received 8 stars each (Table 1).

Meta-analysis

Overall survival

Twenty-three articles including 789 patients provided data for 1-year overall survival, 26 articles including 1001 patients provided data for 3-year overall survival, and 24 articles including 850 patients provided data for 5-year overall survival.

The pooled risk ratios were 1.04 (95 per cent CI = 0.95–1.12) for one-year overall survival, 1.19 (95 per cent CI = 1.02–1.37) for three-year overall survival and 1.25 (95 per cent CI = 1.00–1.56) for five-year overall survival (Figures 2–4) for post-operative radiotherapy compared with surgery alone. A significantly higher three-year overall survival ($p = 0.02$) and a borderline significantly better five-year overall survival ($p = 0.05$) were observed in the post-operative radiotherapy group compared with the surgery alone group. However, the benefit observed in one-year overall survival was not statistically significant ($p = 0.37$).

A fixed-effects model was used as there was no significant heterogeneity among the studies of each group. The direction of the results remained unchanged when individual studies were removed from the analysis. No publication bias was found via the funnel plots. The general median overall survival

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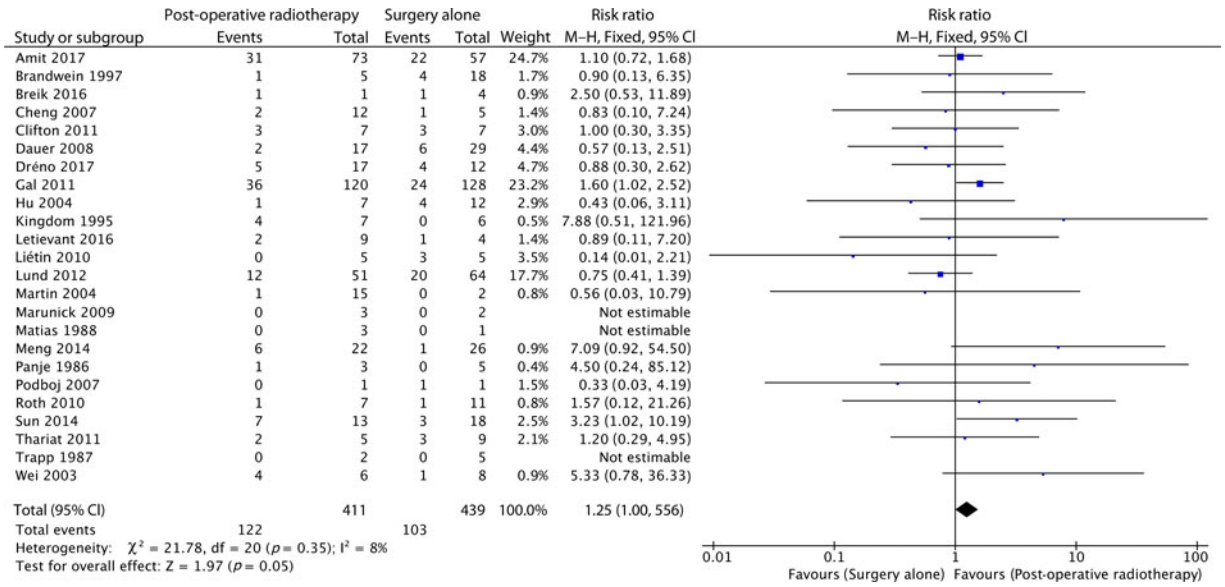

Fig.4. Forest plot of risk ratios for five-year overall survival, comparing patients treated with surgery alone and those treated with post-operative radiotherapy. M–H = Mantel–Haenszel test; CI = confidence interval; df = degrees of freedom

period in the selected studies[4,14,23–28,30–38,41–44] ranged from 16 to 46 months (Table 2).

Disease-free survival

Ten articles including 213 relevant patients provided data for 1-year disease-free survival, 11 articles including 237 patients provided data for 3-year disease-free survival, and 11 articles including 338 patients provided data for 5-year disease-free survival.

The pooled risk ratios were 1.07 (95 per cent CI = 0.87–1.32) for one-year disease-free survival, 0.97 (95 per cent CI = 0.68–1.39) for three-year disease-free survival and 0.94 (95 per cent CI = 0.63–1.40) for five-year disease-free survival (Figures 5–7). No statistically significant differences were observed between the two groups in one-year disease-free survival ($p = 0.53$), three-year disease-free survival ($p = 0.89$) or five-year disease-free survival ($p = 0.75$).

Heterogeneity among studies was non-significant for each group. The findings remained stable after excluding the smallest or largest studies. The funnel plots showed no publication bias. The distant metastasis rates of all the sinonasal melanoma patients reported by the included articles ranged from 8 per cent to 82.6 per cent,[5,14,23–27,46] and the majority were higher than 40 per cent (Table 2).

Local control

Twelve articles including 299 patients provided 1-year local control data, 14 articles including 394 patients provided 3-year local control data, and 13 articles including 318 patients provided 5-year local control data.

The risk ratios were not statistically significantly different between the two treatments (Figures 8–10): 1.09 (95 per cent CI = 0.91–1.31, $p = 0.35$) for one-year local control, 1.30 (95 per cent CI = 0.99–1.72, $p = 0.06$) for three-year local control and 1.17 (95 per cent CI = 0.80–1.70, $p = 0.42$) for five-year local control.

There was no significant heterogeneity among the studies, and the results were robust to the deletion of individual studies. The funnel plots were symmetrically distributed, indicating little publication bias. The local recurrence rates of all the patients reported by the included studies[4,5,8,14,23–27,29–46] were found to range from approximately 12.5 per cent to 88.7 per cent (Table 2).

Discussion

To our knowledge, the meta-analysis conducted in this study is the largest, most recent and most comprehensive on this topic. Data on overall survival, disease-free survival and local control were extracted from 28 cohort studies, including a total of 1392 sinonasal malignant melanoma patients.

The meta-analysis suggested that post-operative radiotherapy provided a significant advantage in three-year overall survival and a borderline significant benefit in five-year overall survival. However, it failed to find statistically significant benefits in disease-free survival or local control at any time point or in overall survival at one year.

All of the included articles achieved relatively high scores in the quality assessment. In addition, there was no significant heterogeneity among the studies, and the risk of publication bias was low. Furthermore, the robustness of the results was confirmed by the sensitivity analysis, which omitted individual studies. All of these factors make the conclusions more reliable.

The general median overall survival period reported by the selected studies (Table 2) was longer than one year. This explains to some degree why a survival difference was not found at one year. Several other studies[5,32,37,41] support our results, suggesting prolonged survival in patients who undergo additional radiotherapy. Meng *et al.*[33] analysed 69 sinonasal melanoma patients between 2000 and 2010, and obtained a significantly better median survival time (32 *vs* 18 months; $p = 0.012$) in patients treated with adjuvant radiotherapy compared with surgery alone. These relatively recent studies predicted a beneficial trend of adjuvant radiotherapy. Some other studies[4,14–20] did not find similar results, but this might be ascribed, at least in part, to limited patient data obtained in a single institution, and the fact that there were more extensive tumours or positive margins in the radiotherapy groups.[47]

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Table 2. Treatment results extracted from included studies

Author	Patients (*n*)	Outcomes	Radiotherapy dose (mean (range))	General local recurrence rate (%)	Median survival time (months)	Metastasis (%)
Brandwein *et al.* (1997)[23]	25	OS, DFS, LC	NA	32.0	21	8.0
Cheng *et al.* (2007)[24]	23	OS	5422 (2100–6000) cGy	39.1	20	82.6
Clifton *et al.* (2011)[25]	24	OS, DFS, LC	NA	41.6	32	45.8
Crawford *et al.* (1995)[26]	18	1y-OS	NA	22.2	17*	44.4
Dauer *et al.* (2008)[27]	61	3y-OS, 5y-OS	NA	59.0	19	77.0
Gal *et al.* (2011)[28]	304	OS	NA	NA	18	NA
Ganly *et al.* (2006)[8]	53	3y-OS, 3y-DFS, 3y-LC	5600 (2400–7000) cGy	74.5	NA	NA
Hu *et al.* (2004)[29]	24	5y-LC, OS	60 (50–73.3) Gy	40.0	NA	16.0
Kingdom & Kaplan (1995)[5]	17	OS, LC	(30–62) Gy	85.0	NA	46.0
Liétin *et al.* (2010)[14]	10	OS	NA	70.0	41.7*	60.0
Lund *et al.* (2012)[4]	109	OS, LC, 5y-DFS	NA	88.7	24	NA
Martin *et al.* (2004)[30]	20	OS	(24–60) Gy	41.2	17	45.0
Marunick & Oh (2009)[31]	8	OS, DFS, LC	(3000–6120) cGy	13.0	13.6*	57.1
Matias *et al.* (1988)[32]	9	OS, DFS, LC	NA	22.2	23.8*	44.4
Meng *et al.* (2014)[33]	69	OS, 3y-LC	34 (1–144) Gy	42.0	24	58.0
Panje & Moran (1986)[34]	10	OS, DFS, LC	(5000–6000) cGy	70.0	16	80.0
Podboj & Smid (2007)[35]	16	OS, DFS, LC	(49.5–63.5) Gy	50.0	13*	50.0
Roth *et al.* (2010)[36]	25	OS, DFS, LC	NA	37.5	23	44.0
Sun *et al.* (2014)[37]	65	OS	56 (44–78) Gy	36.9	24	81.5
Thariat *et al.* (2011)[38]	25	OS, DFS, LC	NA	44.0	42	24.0
Trapp *et al.* (1987)[39]	17	OS	(52–58) Gy	70.6	NA	58.8
Wei *et al.* (2003)[40]	19	OS	(50–70) Gy	NA	NA	29.4
Won *et al.* (2015)[41]	155	3y-OS	NA	46.6	37	53.4
Breik *et al.* (2016)[42]	8	OS, DFS, LC	(30–66) Gy	12.5	46	37.5
Letievant *et al.* (2016)[43]	14	OS	60.6 Gy	50.0	26	64.3
Samstein *et al.* (2016)[44]	68	LC	30 (20–70.8) Gy	37.2	32	64.1
Dréno *et al.* (2017)[45]	44	3y-OS, 5y-OS	NA	46.0	NA	54.0
Amit *et al.* (2017)[46]	152	OS, DFS	NA	66	NA	38.8

*Mean value. OS = overall survival; DFS = disease-free survival; LC = local control; NA = data not available; y = year

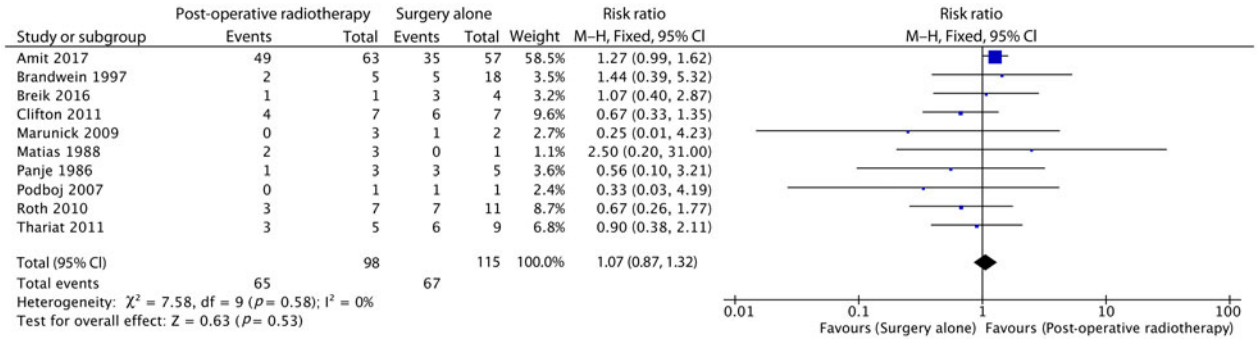

Fig. 5. Forest plot of risk ratios for one-year disease-free survival, comparing patients treated with surgery alone and those treated with post-operative radiotherapy. M–H = Mantel–Haenszel test; CI = confidence interval; df = degrees of freedom

Sinonasal malignant melanoma is characterised by early and repeated local recurrence,[48] which usually occurs within a year of initial treatment.[2] The relatively high local recurrence rates found in the included studies were consistent with this. Moreno *et al.*[49] demonstrated that post-operative radiation improved locoregional control ($p = 0.0215$), but only when a total dose greater than 54 Gy was used. Krengli *et al.*[50] summarised five relatively large case series, and concluded that

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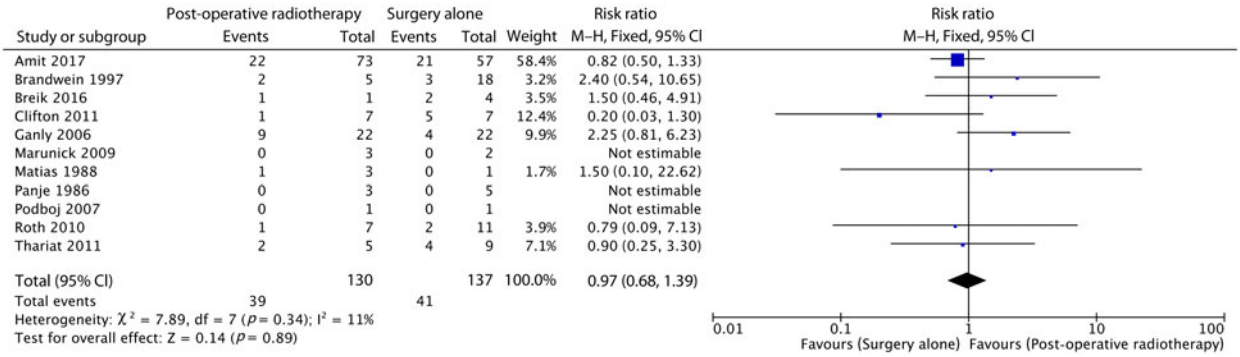

Fig. 6. Forest plot of risk ratios for three-year disease-free survival, comparing patients treated with surgery alone and those treated with post-operative radiotherapy. M–H = Mantel–Haenszel test; CI = confidence interval; df = degrees of freedom

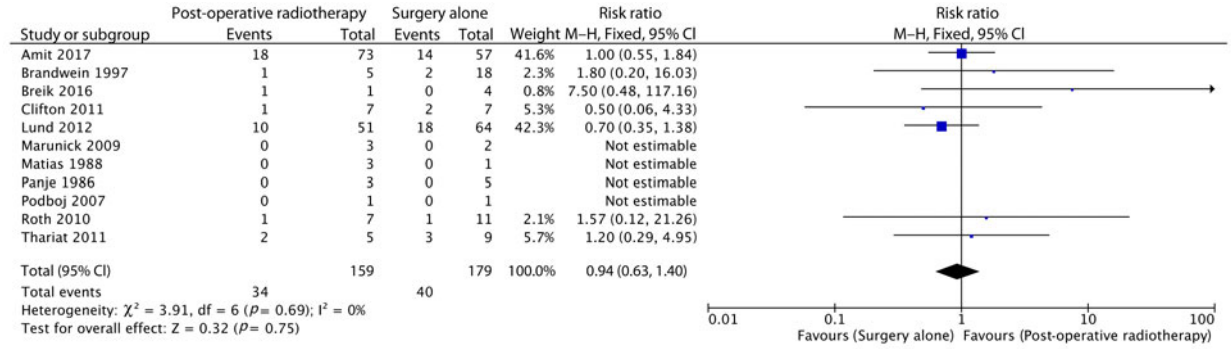

Fig. 7. Forest plot of risk ratios for five-year disease-free survival, comparing patients treated with surgery alone and those treated with post-operative radiotherapy. M–H = Mantel–Haenszel test; CI = confidence interval; df = degrees of freedom

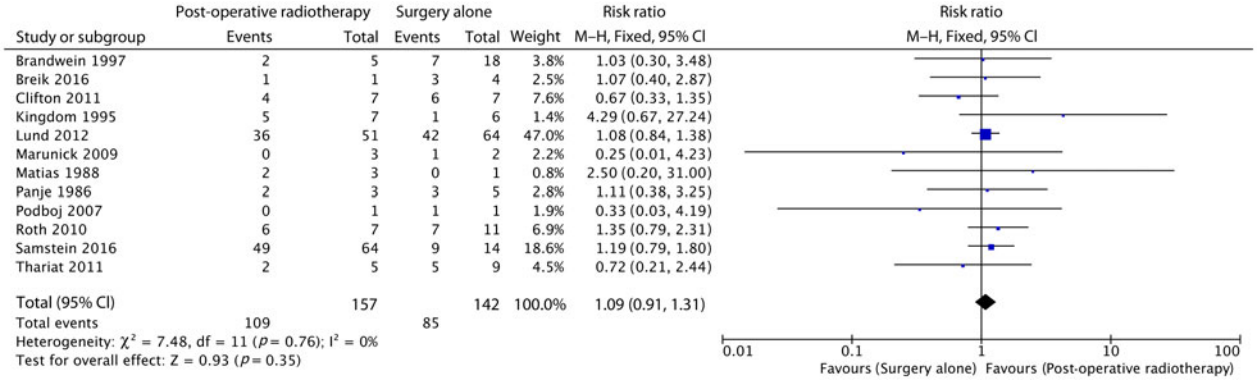

Fig. 8. Forest plot of risk ratios for one-year local control, comparing patients treated with surgery alone and those treated with post-operative radiotherapy. M–H = Mantel–Haenszel test; CI = confidence interval; df = degrees of freedom

radiotherapy seemed to improve local control after non-radical excision and was the most effective treatment for unresectable disease. However, these positive results were achieved in some conditions without statistical significance.

The increasing use of endoscopic endonasal approaches is replacing traditional open resections. Miglani *et al.*[51] demonstrated that endoscopic resection may offer comparable survival and superior local control over open surgery ($p = 0.26$), and this fact may explain the different findings of the more recent studies. Our analysis also failed to reach statistical significance in the outcome of local control; this might be related to the relatively small number of studies and the lack of recent data, and the fact that patients who have a higher potential of local relapse tend to be treated with adjuvant radiotherapy.[36] Nevertheless, the effects of post-operative radiotherapy on local control remain to be further investigated.

Kingdom and Kaplan[5] speculated about increasing the disease-free interval by using adjuvant radiotherapy in the post-operative period, but their series was not sufficient in size for statistical analysis to yield significant results. The disease-free survival results in our study also failed to demonstrate any statistically significant improvements. This might be partly explained by the lack of studies reporting disease-free survival, especially in recent studies utilising the latest therapy techniques. On the other hand, the majority of distant metastasis rates reported by the included articles were higher than 40 per cent. Because of this, surgery and radiotherapy may have a limited effect on disease-free prognosis, as they mainly address local control of the disease.[46]

Modern techniques, including high dose per fraction, sophisticated three-dimensional conformal and intensity-modulated radiotherapy techniques, and ion beams, have

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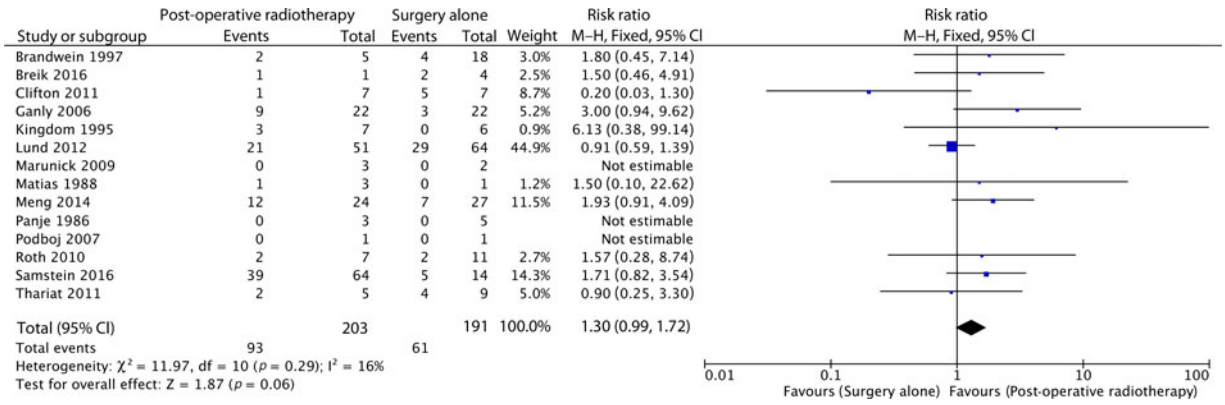

Fig. 9. Forest plot of risk ratios for three-year local control, comparing patients treated with surgery alone and those treated with post-operative radiotherapy. M–H = Mantel–Haenszel test; CI = confidence interval; df = degrees of freedom

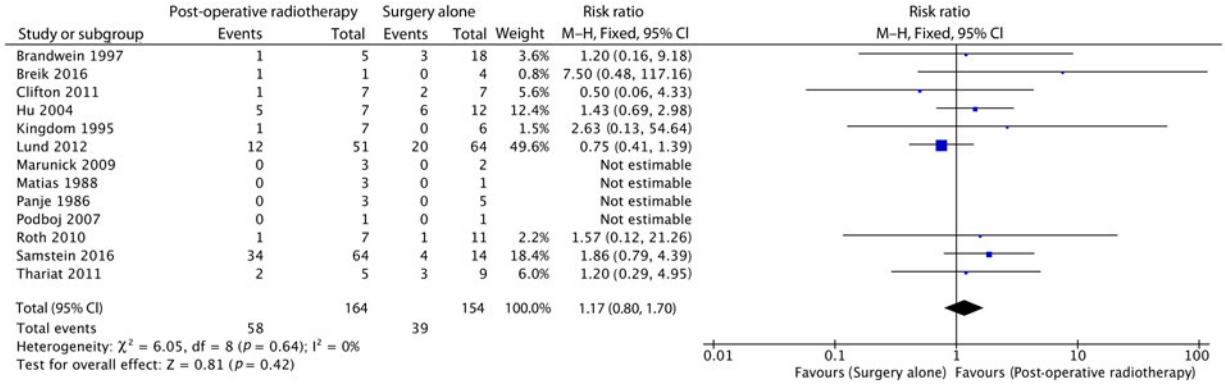

Fig. 10. Forest plot of risk ratios for five-year local control, comparing patients treated with surgery alone and those treated with post-operative radiotherapy. M–H = Mantel–Haenszel test; CI = confidence interval; df = degrees of freedom

attempted to improve the therapeutic advantage of radiotherapy.[13,15,50] They have also improved treatment-related toxicity.[13] It was proposed that most survival failures were associated with distant metastasis due to haematogenous spread, in spite of good locoregional control;[42,52] it is difficult to achieve good control of this metastasis with local radiotherapy, hence the relatively high distant recurrence rate. This underlines the importance of systemic approaches to therapy; chemotherapy, targeted therapy and immunotherapy used in addition to surgery have been recommended for patients with metastatic or extensive local disease.[3,48,52]

It is important to recognise the limitations of this meta-analysis. First, without adjusting for potential confounders, the variability in the study populations and stage distributions, as well as the different surgical and radiotherapeutic approaches found in the cited works, should be noted. Second, selection bias may exist in the data because patients with more aggressive disease, unresectable fragments, further invasion and regional metastases are typically given adjuvant therapy, instead of there being uniformly agreed standards. These patients usually have a poorer prognosis. Third, biases should not be ignored in the estimates of outcomes created using the software, where data were manually picked from Kaplan–Meier survival curves instead of being exactly given by the authors. Fourth, the estimated three-year local control rate reported by Meng *et al.*[33] was higher than the three-year overall survival in the current study; this might be explained by the differing definitions. However, eliminating this study did not affect the results. Finally, there will be a language bias because data were only extracted from studies published in English and Chinese; studies published in minority languages were not included.

- As sinonasal malignant melanoma is rare, single-centre clinical data are scant, making treatment evaluation difficult
- This is the largest and most comprehensive meta-analysis of post-operative radiotherapy for sinonasal malignant melanoma
- The meta-analysis used overall survival, disease-free survival and local control data from 28 studies (1392 patients)
- Post-operative radiotherapy led to an advantage in three-year overall survival and a borderline benefit in five-year overall survival when compared with surgery alone
- There was no significant benefit in local control or disease-free survival, or in one-year overall survival
- Surgery with clear margins should remain the cornerstone of therapy; adjuvant radiotherapy is recommended for prolonged survival

Conclusion

The current meta-analysis found that post-operative radiotherapy led to significantly better three-year overall survival and borderline significantly better five-year overall survival than surgery alone, but did not provide benefits in terms of local control or disease-free survival at any follow-up point, or in one-year overall survival. This suggests that adjuvant radiotherapy may be recommended to achieve prolonged survival.

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Multicentre, collaborative, randomised controlled trials with larger sample sizes are required to further confirm the precise efficacy of post-operative radiotherapy in treating sinonasal malignant melanoma. The pursuit of an effective, comprehensive and systemic therapeutic strategy against this aggressive malignancy remains a worthy area of investigation.

Competing interests

None declared

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