REVIEW ARTICLE

OUTCOMES OF INTRAOPERATIVE RADIOTHERAPY (IORT) FOR SPINAL TUMOURS

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Background: The spinal column is a major site of neoplastic proliferation where decisions regarding surgical or radiotherapeutic intervention are based upon spinal instability neoplastic score (SINS). A novel technique named 'Intraoperative radiotherapy (IORT) was proposed where surgery and radiotherapy were performed in the same session. During our literature search, we found no published systematic review or meta-analysis regarding the outcomes of IORT for spinal tumors. This review aims to provide the knowledge regarding the outcomes of IORT for spinal tumors to assist surgeons and radiologists. **Methods:** PubMed, Google Scholar, Cochrane library for trials reporting the outcomes of IORTin spinal tumors. The search terms were "outcomes", "Intraoperative radiotherapy", "IORT", "spine neoplasia" and "spine metastasis" in different combinations. Standardized mean difference (SMD) in VAS for pain relief while proportionality for neurological improvement, local progression, and toxicities were plotted on forest plots, respectively. **Results:** Eight studies comprising 610 patients were included with two conference proceedings. SMD for VAS was -1.715 while proportionality for neurological improvement, local progression, and toxicities were 0.9 (90%), 0.03 (3%), and 0.121 (12.1%), respectively. **Conclusion:** Pain relief was evident by a decrease in VAS scores in the majority of patients. The majority showed neurological improvement and regained motor and sensory functions while an overwhelming population showed local tumor control with lesser patients developing tumor progression and radiation-induced toxicities. Short follow-ups and the absence of randomized trials advocates the need for further clinical researches to confirm the outcomes of IORT in spinal tumors.

Keywords: Palliation; Intraoperative radiotherapy; IORT; Spinal tumour; Vertebril metastatis

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INTRODUCTION

The spinal column possesses a risk of neoplastic proliferation in the human body. The tumours of the spine can be broadly classified into two types; primary tumours and secondary tumours. Vertebral hemangioma and metastic tumours are the most commonly encountered primary and secondary tumours of spine, respectively.[1,2] Spine constituting the most common site of skeletal metastasis.[3–5] The symptomatology of both classes of neoplasia remains the same. Back pain,[6,7] loss of ambulation,[8,9] sensory loss,[9] sphincter dysfunction,[9] kyphosis secondary to vertebral fractures, and respiratory difficulties.

The treatment of spinal tumours is based upon the classification systems shown in Table-1. Patients with SINS above 7 were deemed with the potential instability after radiotherapy and extra caution is required.[10,11] Posterior decompression remained the procedure of choice.[12] However, a novel method of Intraoperative radiotherapy (IORT) was proposed where surgery and radiotherapy were performed in the same session. According to the NICE guidelines, spinal cord compressions must be relieved within 24 hours to avoid irreversible neurological deficits. Hence, better results can be achieved if IORT is offered within 24 hours after developing the first neurological symptoms. Trials and pilot studies were conducted to evaluate the outcomes of IORT and modifications were proposed to make the procedure minimally invasive and technically feasible in more patients. Combined kyphoplasty with IORT (Kypho-IORT) and combined posterior decompression with IORT (PD-IORT) are the two most common approaches which were sterile and add structural stability and sterilization of tumour. This multidisciplinary novel approach gained widespread popularity and no systematic review was conducted before. Hence, this review aims to provide knowledge regarding the outcomes of IORT for spinal tumours to assist surgeons and radiologists while making future treatment decisions.

PD-IORT:

The posterior decompression with Intraoperative radiotherapy (PD-IORT) was designed by combining posterior decompression with IORT. The team required for PD-IORT includes a surgeon, anesthetist, anesthesia technician, OR assistant, X-ray technician, radiation oncologist, medical physicist, radiation oncology nurse, and radiation technician. The procedure costs around 15000–17000 USD where a single IORT session costs 4000–4500 USD. Under antiseptic measures, an incision is made in the operating room (OR) and laminectomy is performed to create a window to the

spinal cord. By using an ultrasonic surgical aspirator, the epidural tumour mass is partially resected. Due to the substantial risk of cord damage, the anterior vertebral tumour lesions were left intact for further treatment with IORT. The surgical field is covered with the sterilized gauze. The patient is shifted to Radiotherapy Room for IORT where the cone size and lead shields are determined to protect the spinal cord from radiation-induced myelopathy. The sterilized cone was attached to the IORT device to produce an electron beam and positioned such that the dural tube and lead shield overlap each other visibly. Preoperative MRI is used to evaluate the anteroposterior thickness of tumours for computing the electron energy so that the 80% isodose line falls 1-2 cm below the deepest aspect of the tumour and more than one-third of the calculated dose penetrates the ventral part of vertebrae while the half-value of biologically effective dose (BED) from the linear-quadratic equation is the prescribed dose. Twenty Gy is the most widely used dose of radiation while 11–20 MeV is the most widely used electron energy. After irradiation, the surgical site is covered with sterilized gauze and the patient is shifted back to OR. The entire IORT procedure takes 30–50 minutes. The surgeon then performs the posterior instrumentation with wound closure.

Kypho-IORT:

Combined balloon kyphoplasty with Intraoperative radiotherapy was invented in France for vertebral metastatic lesions due to breast cancer.[17] The team required for Kypho-IORT includes a surgeon, OR assistant, X-ray technician, radiation oncologist, medical physicist, and radiation technician. The procedure costs around 11000–13000 USD with cement and balloon included where a single IORT session costs 4000–4500 USD. Under aseptic measures in the OR, a needle is inserted into the transverse process of the vertebra guided through the pedicle towards the vertebral body. A Kirshner wire is inserted through the needle while the needle is withdrawn. The wire serves as a pathway for the insertion of a guiding shaft. Further manipulation is carried out via drilling through the shaft to precisely locate the tumour. A low-energy (50 kV) X-ray emitting needle connected to the IORT Device is introduced through the shaft to reach the tumour. CT delineations were made preoperatively to measure the size and depth of the tumour so that 1 Gy dose reached the spinal cord while 8 Gy was considered an optimum dose for tumour control at a 5 mm depth maintaining 90% isodose line while keeping in mind the increased incidence of radiation myelopathy for greater than 12 Gy dose at this depth. The time frame for radiation remains 2–4 min depending upon the tumour size, depth, and dose. The surgeon introduces a balloon within the vertebral body. The balloon is inflated below 400 psi to obtain a satisfactory vertebral height gain and kyphotic correction. The balloon is deflated and retracted with the insertion of cement-injecting needles introducing polymethylmethacrylate (PMMA) cement to sustain the vertebral stability. Finally, the guiding shaft is extracted and the surgical incision is closed with an absorbable suture. The entire procedure was carried out in OR.

MATERIAL AND METHODS

A systematic approach was adopted by all the authors who carried out literature searches. The "Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)" was used by the authors to segregate literature regarding the outcomes of IORT in spine neoplasia. The articles were scrutinized based on titles and abstracts while the further assessment was based on full text. Duplicate and ambiguous articles were excluded. Figure-1 shows the search strategy in the flowchart. The studies published on PubMed/Medline, Google Scholar, and Cochrane Library and carried on human specimens in the English language were searched by the authors. The words used in search databases were "outcomes", "Intraoperative radiotherapy", "IORT", "spine neoplasia" and "spine metastasis" according to the above strategy.

A criterion was set by discussion among the authors. All studies including comparative trials, cohort studies, randomized controlled trials, and case series which involved outcomes of IORT were included. The studies were read deeply to search for any subgroup included in trials that received IORT with any one or more given outcomes. The participants included in trials should have spinal neoplasia that was proven by histopathological or imaging modalities with Spinal Instability Neoplastic Score (SINS) ranging from 7 to 18. The intervention should be IORT with adjuvant surgery such as kyphoplasty or posterior decompression. Letters, commentaries, editorials, case reports, and personal communications were excluded. The corresponding author of this article tried to contact the authors of trials to resolve any ambiguity within the trials before exclusion in case of non-responsiveness.

Each author was assigned studies to evaluate independently the methodological risk of bias in trials with the "Modified Newcastle Ottawa scale"[18] for observational studies and the "Oxford quality scoring system"[19] for randomized controlled trials. For the Modified Newcastle-Ottawa Scale, above 7 stars indicate good quality trial while 4–7 stars predict a fair quality trial and less than 4 stars indicate a poor quality trial. For the Oxford quality scoring system, a score of 5 or 4 suggests a good quality trial; 3 or 2 suggests a fair quality trial while 1 or 0 signifies a poor-quality study. Any disagreements were resolved through internal discussion among authors. An expert from our institute was involved if disagreements could not be resolved after discussions among authors.

Table-1: Classification systems for deciding surgical or radiotherapeutic interventions in spinal neoplasia

Classification System	Types/grades/scores	Characteristics	Intervention
Spinal Instability Neoplastic Score (SINS)[13]	0–6 7–12 13–18	Stable Potential instability Instability	Radiotherapy Surgical + radiotherapy Surgery
Tomita Classification[14]	Intracompartmental (Type 1, 2) Intracompartmental (Type 3) + Extracompartmental Multiple	Only the vertebral body involved Vertebral body+ Posterior involvement+adjacent vertebra involved Non-adjacent vertebral involvement	Surgery Surgery+Radiotherapy Surgery+Radiotherapy
Tokuhashi Score[15]	0–8 9–11 12–15	Survival < 6 months Survival 6–12 months Survival >12 months	Conservative Surgery+Radiotherapy Surgery+Radiotherapy
Bilsky grade[16]	0, Ia, Ib Ic, II, III	Thecal sac only Thecal sac+cord compression	Radiotherapy Surgery± Radiotherapy

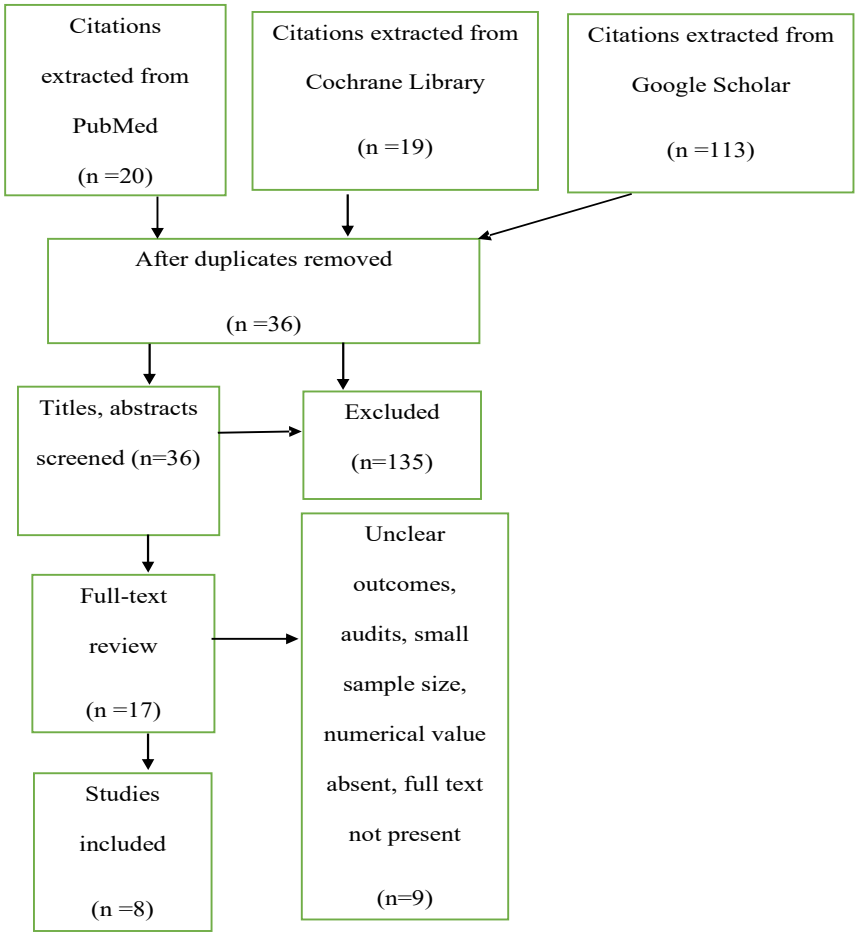

Figure-1: Prisma flowchart for the systematic review of literature

Outcomes:

The outcomes measured in this article were pain relief in the form of a change in Visual Analogue Score (VAS) that is an 11 point-based score from 0–10 with 0 considered as no pain while 10 being the most severe pain; the incidence of neurological functions was assessed by change in Frankel's classification (Table-2)[20] the number of candidates who showed local progression within 3 months and 6 months after the intervention based on enlargement tumour sac on imaging modalities, progressive symptoms, increasing pain intensity without vertebral fracture, or change in Tomita classification; and incidence of post-intervention adverse effects which includes post-interventional fracture, surgical site infections, avascular necrosis, myelopathy, plexopathy, respiratory difficulties, and neurological deterioration.

Table-2: Frankel's classification[20]

Class	Neurological symptoms
A	complete motor and sensory loss
B	complete motor loss but some sensation preserved
C	some motor power preserved but of no functional use
D	useful motor power including walking with or without aids
E	no neurological symptoms

Statistical Analysis:

The authors used means (SD) for continuous outcomes and the number of patients (n) for dichotomous outcomes while data extraction. For continuous outcomes, VAS was considered. For dichotomous outcomes, neurological improvement, local progression, and adverse effects were considered. The meta-analysis of combined data was performed using a random-effects, generic inverse variance method of DerSimonian and Laird.[21] A random-effects model with a confidence interval of 95% (CI=95%) was used to plot the standardized mean difference (SMD) and proportionality for continuous and dichotomous variables, respectively. The inclusion of SMD was considered due to the expected high dropouts in longer follow-up trials.[22] The heterogeneity was tested by I^2 Statistics. Heterogeneity was considered negligible when I^2 of less than 25%, low when I^2 of 26–50%, moderate when I^2 of 51–75%, and high when I^2 above 75%.[23] The random-effect model and fixed-effect model was used to design a forest plot in case of high heterogeneity and low heterogeneity, respectively which was plotted separately for each continuous and dichotomous outcome using SMD and proportionality, respectively. OpenMetaAnalyst Software was used for statistical analysis.

Assessment of significant between-study heterogeneity (I^2 >50%, p-value<0.05) was carried out by conducting sensitivity analysis through a sequential algorithm where each study was excluded one by one to estimate the overall effects on the summary of results and drop in heterogeneity. A threshold heterogeneity of I_f^2 <25% was considered.

Table-3: Characteristics of trials included

Clinical Trial	Year of study	Country	Number of patients[(a)]	Number of the vertebra[(a)]	Inclusion criteria	Exclusion criteria	Study Quality	Radiation Dose in Gy[(a)]	Surgery with IORT	Follow up (months)[(b)]
Bludau, F., *et al*.[24]	-	Germany	61	76	Tomita I SINS >7 1-3 vertebrae involved	Lamina, pedicle involvement	Good	8	Kypho	6.7 (0-41)
Chen, K., *et al*.[25]	2013-15	China	40	52	Thoracolumbar vertebral metastases with any Bilsky score	Life expectancy <3 month using Tokuhashi scoring	Fair	9.2	Kypho/ PD	12.5 (6-23)
Sugita, S., *et al*.[26]	2004-13	Japan	279	-	Metastatic tumours only with a defined primary source. Posterior fusion with PD-IORT	Infections post-discharge or > 1 month after surgery. Infections other than surgical site infection	Fair	20	PD	NA
Kondo, T., *et al*.[27]	1992-05	Japan	96	107	Spinal metastasis with paralytic abasia. Tomita type 5, 6, 7 only	Mild paralysis due to axial or radicular pain	Fair	25	PD	7 (0.6-107)
Saito, T., *et al*.[28]	1992-01	Japan	74	79	Spinal metastasis with posterior spine surgery for severe paresis. Tomita type 4, 5, 6, 7	Anterior spine surgery Mild paresis due to intractable pain or cauda equina paresis primary spinal Tumours	Good	20	PD	20 (1-65)
Seichi, A., *et al*.[29]	1992-96	Japan	37	-	Metastatic tumour Pain and/or neurological deficits Tomita type 3, 4, 5, 6, 7	Life expectancy <3 month using Tokuhashi scoring or poor health status	Good	20	PD	28 (16-48)
Gandhi, S., *et al*.[30]	2017	USA	7	7	SINS 7-12 Bilsky grade 0 The vertebral body involved only	Previously irradiated on the same segment	Good	10	Kypho	3
Rana, Z.H., *et al*.[31]	2018	USA	16	22	SINS 7-12 Bilsky grade 0-1 Vertebral body + one pedicle involved	None	Poor	10	Kypho	13

[a)]Number present in the study. [b)] Median (minimum-maximum)

Table-3: Outcomes of trials included

Clinical Trial	VAS score pre-treatment[(a)]	VAS score post-treatment[(a)]	Neurological Improvement[(b)]	Local Progression (3 month)[(b)]	Local Progression (6 month)[(b)]	Adverse effects[(b)]
Bludau, F., *et al.*[24]	5±1.1	2±1	NA	2	3	2
Chen, K., *et al.*[25]	6.2±2.5	2.8±1.2	7	3	4	0
Sugita, S., *et al.*[26]	NA	NA	NA	NA	NA	41
Kondo, T., *et al.*[27]	NA	NA	95	3	3	14
Saito, T., *et al.*[28]	NA	NA	68	2	3	8
Seichi, A., *et al.*[29]	NA	NA	25	0	0	2
Gandhi, S., *et al.*[30]	6.6±2.8	4.0±2.2	NA	1	NA	0
Rana, Z.H., *et al.*[31]	6.6±1.4	3.6±2.6	NA	2	NA	3

[a)]Mean ± SD. [b)] Number of patients with specified outcomes

RESULT

After an initial review of 17 articles, eight studies comprising 610 patients were included in this review summarized in Table-2. The studies were based in Japan (n=4),[26–29] the United States (n=2),[30,31] China (n=1),[25] and Germany (n=1)[24]. The reviewed publications included all observational studies published from 1992 to 2018. Two conference abstracts were also included after quality assessment.[30,31] Four studies were of good quality, three studies were of fair quality, while one study was of poor quality. Overall, 116 and 494 patients received kyphoplasty and posterior decompression with IORT, respectively. A median radiation dose of 15 (8–25) Gy with a median follow-up of 12.5 (3–28) months was calculated from the included studies. Median radiation of 9.6 (8–10) Gy was used for Kypho-IORT while a median 20 (9.2–25) Gy radiation dose was prescribed for PD-IORT.

The review included two conference proceedings.[30,31] The authors reviewed eight conference proceedings during the literature search. Among included conference proceedings, one conference proceeding was good-quality while the other was of poor quality. Both studies reported the outcomes of Kypho-IORT. Three studies were duplicates while two were excluded due to the availability of published full articles. Four of the eight trials measured subjective pain using the VAS score on a scale of either 0–10. The overall SMD was statistically significant (SMD -1.715; 95% CI, -2.247, –1.184; p<.001). The I^2 value attributed 54.25% with p-value = 0.087 variation in SMD to heterogeneity (Figure-2).

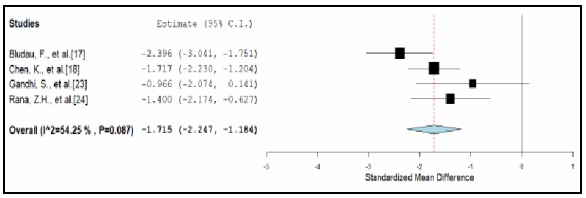

Figure-2: Forest plot showing the SMD estimates for VAS where boxes are showing the effect size with the length of the corresponding line explaining 95% confidence interval and the diamond-shaped symbol representing overall effect size.

Neurological improvement:

Four of the eight trials measured neurological improvement using the change in Frankel's classification in the number of patients. The overall proportionality was statistically significant (proportionality =0.928; 95% CI, 0.856–1.000; p<.001). The I^2 value attributed 72.33% with p-value =0.013 variation in proportionality to heterogeneity (Figure-3); therefore, a random-effects model was used.

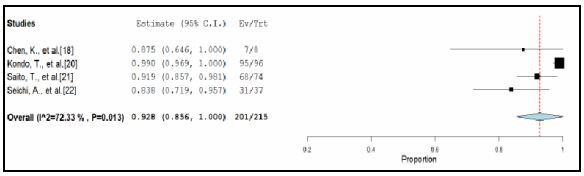

Figure-3: Forest plot showing the proportionality estimates for neurological improvement where boxes are showing the effect size with the length of the corresponding line explaining 95% confidence interval and the diamond-shaped symbol representing overall effect size.

The significant heterogeneity was tested by conducting sensitivity analysis. The analysis reported the greatest effect of Kondo, Hozumi[27] on between-study heterogeneity. Figure-4 summarizes the finding after the exclusion of Kondo, Hozumi[27] from the forest plot. I^2 statistic dropped to 0% with a p-value of 0.483 with minimal change in the overall treatment effect.

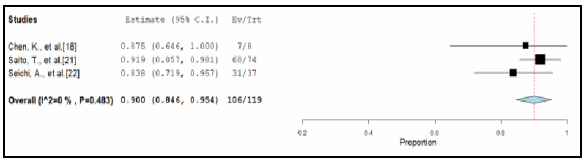

Figure-4: Forest plot showing the proportionality estimates for neurological improvement after sensitivity analysis where boxes are showing the effect size with the length of the corresponding line explaining 95% confidence interval and the diamond-shaped symbol representing overall effect size.

Local Progression:

Seven of the eight trials measured the incidence of local progression within 3 months using the imaging modalities in the number of patients. The overall proportionality was statistically significant (proportionality =0.03; 95% CI, 0.012–0.048; *p*= .001). The I^2 value attributed 0% variation in proportionality with *p*-value = 0.664 to heterogeneity (Figure-5).

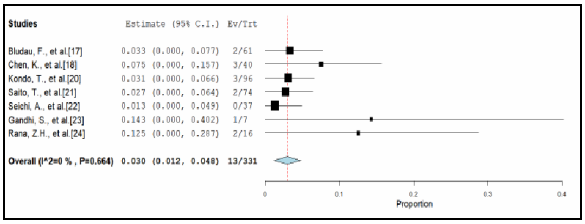

Figure-5: Forest plot showing the proportionality estimates for local progression within 3 months where boxes are showing the effect size with the length of the corresponding line explaining 95% confidence interval and the diamond-shaped symbol representing overall effect size.

Five of the eight trials measured the incidence of local progression within 6 months using the imaging modalities. The overall proportionality was statistically significant (proportionality =0.033; 95% CI, 0.013–0.053; p= .001). The I^2 value attributed 0% variation in proportionality with *p*-value = 0.462 to heterogeneity (Figure-6).

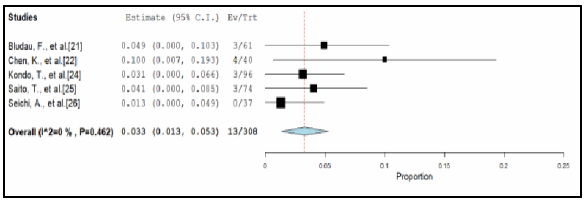

Figure-6: Forest plot showing the proportionality estimates for local progression within 6 months where boxes are showing the effect size with the length of the corresponding line explaining 95% confidence interval and the diamond-shaped symbol representing overall effect size.

Adverse effects:

All trials measured the incidence of adverse effects occurring in the number of patients. The overall proportionality was statistically significant (proportionality =0.085; 95% CI, 0.036–0.135; *p*< .001). The I^2 value attributed 79.65% variation in proportionality to heterogeneity (Figure-7); therefore, a random-effects model was used.

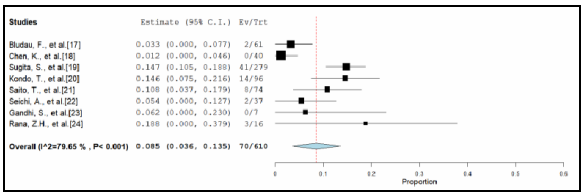

Figure-76: Forest plot showing the proportionality estimates for adverse effects where boxes are showing the effect size with the length of the corresponding line explaining 95% confidence interval and the diamond-shaped symbol representing overall effect size.

Sensitivity analysis was carried out by excluding one study at a time to assess the between-study heterogeneity. Bludau, Welzel[24] and Chen, Huang[25] were excluded which decreased the I^2 value from 79.65–19.5% with *p*-value 0.286 as summarized in Figure-8

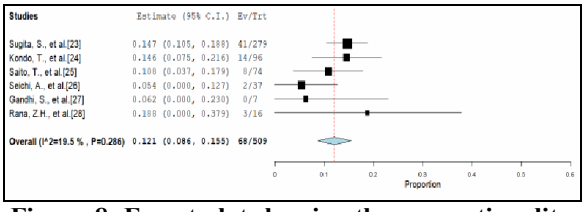

Figure-8: Forest plot showing the proportionality estimates for adverse effects after sensitivity analysis where boxes are showing the effect size with the length of the corresponding line explaining 95% confidence interval and the diamond-shaped symbol representing overall effect size.

DISCUSSION

This systematic review aimed to summarize the clinical and radiological outcomes in spinal tumours after intraoperative radiotherapy. A higher percentage of spinal cancer patients require palliative care due to an overwhelming majority of patients suffering from metastatic disease.[32] Physical care is the most important pillar of palliation. Physical care includes pain relief,[33] ambulatory preservation, sphincter preservation, avoidance of sexual dysfunction, normal sleep, personal grooming, and normal breathing[34].

We included eight clinical trials in our review. The review also focuses upon the utility of IORT in different histological and anatomical spine tumours. Breast, prostate, and lung cancers belonging to osteolytic and osteoblastic, osteoblastic, and osteolytic histological types respectively were the most commonly included primary cancers in most of the studies that further show us the effect of IORT on

histologically different metastatic tumours. The trials also enlightened the effects of IORT on radioresistant as well as radiosensitive tumours by recruiting candidates of both histologies while the use of different classification systems for spinal tumour treatment decision-making strengthen the review by adding the utility of IORT for anatomical as well as prognostic classification systems. Majority of the candidates presented with thoracolumbar spinal neoplasia. To address the issue of high dropouts in follow-ups among spinal metastasis patients,[35] we considered the use of a standardized mean difference (SMD) instead of a simple mean difference. SMD allowed us to find the difference between post-intervention and pre-intervention means of continuous outcomes while emphasizing the post-intervention and pre-intervention sample size in calculating the treatment effect.

Back pain is the earliest and most compelling manifestation of spinal tumours and over 95% of patients have the symptom at the time of diagnosis while neurological dysfunction remains a late complication.[9,36] In our results, we got a 1.7 decrease in VAS score which is not considered clinically significant in terms of patient and clinician satisfaction. Hence we performed a subgroup analysis to assess the pain relief in PD-IORT and Kypho-IORT individually. From our subgroup analysis, we found that PD-IORT provided a VAS score SMD by -2.149 (95% CI; -1.313, - 2.985, p<0.001) while Kypho-IORT provided a change in VAS score by -1.258 (95% CI; 0.624, -1.892, p<0.001). Therefore, from our subgroup analysis, PD-IORT provided better pain relief. The studies included in our review received posterior decompression with instrumentation or bone graft after IORT. The implant or graft induced increased stability of the vertebral column might be the factor behind increased pain relief while long term increased risk of kyphoplasty associated adjacent fractures that are shown by Fribourg, Tang[37], Kim, Ha[38] in the literature might be the reason behind comparatively lower pain alleviation than PD-IORT. From the results of this review, it is clear that IORT may not be a clinically sufficient method to provide higher pain relief. However, considering the good tumour control and decreased incidence of local progression-induced fractures after IORT, we may expect to nullify the increase in pain intensity for which further clinical trials are necessary.

IORT has shown a significant improvement in neurological outcomes among cancer patients where all studies have reported above 90% of the candidates who were ambulatory within a week after radiation. Kondo, Hozumi[27] present in our review included paralytic patients only in their study and have reported 80% of patients who became ambulatory from the paralytic stage after IORT. Cementation after balloon inflation and implantation of bone cement or posterior implants in Kypho-IORT and PD-IORT respectively serves as a means of maintaining the vertebral structure decreasing the chances of fracture-associated cord compressions in the future.[39] The use of radiation doses symmetrically and in greater depths provides a better tumour clearance rate with a greater reduction in tumour volume and cord compression leading towards better local control.

To assess the tumour control and local progression, we have divided our results regarding tumour progression into 3 months and 6 months periods where 3 months data shows the control of tumour in a short time and proves the utility of IORT for early relief while the 6 months data proves the tumour control after IORT. The prevalence of local progression was 3% and 3.3% within 3 and 6 months postradiotherapy period while more than 90% of patients in all included studies showed no local progression with good clearance rates. The results have shown good local control with better tumour clearance due to a non-significant difference in the 3 months and 6 months follow-up. Moreover, Seichi, Kondoh[29] included in our review performed an autopsy examination of IORT candidates who did not survive due to end-stage and discovered no progression in a previously radiated spinal tumour with IORT. Most of the trials also included radiosensitive and radioresistant spinal tumours in the study sample and the greater degree of tumour control all across the study sample explains the beneficial effects of IORT. The patients reporting tumour progression were mostly among metastatic rectal cancer patients which may raise concerns about the use of IORT among such candidates in the future.

Stereotactic body radiotherapy (SBRT) is considered the latest treatment option.[40] However, Abbouchie, Chao[41], Ozdemir, Torun[42], and Chang, Shin[43] have reported the radiation-associated toxicities and increased risk of vertebral fractures as a significant adverse effect of SBRT. From our results, 12.1% of the participants developed radiation toxicities. No included trial has reported vertebral fractures after IORT that show the increased spinal column stability. Studies with Kypho-IORT reported negligible events of adverse effects as the subgroup analysis revealed non-significant proportionality of 0.027 (95% CI; -0.006, 0.06, p=0.108) while PD-IORT reported a significantly higher risk of adverse effects with the proportionality of 0.119 (95% CI; 0.078, 0.16, p<0.001). Hence, PD-IORT is associated with more adverse effects than Kypho-IORT but the combined incidence is significantly lesser than

SBRT, and the nature of adverse effects is also lesser severe than SBRT or other radiation modalities.

There were certain limitations in the present systematic review. Firstly, randomized trials were not available for the analysis. Secondly, the results of the review represent the short-term success of the IORT for spinal tumours and greater follow-up trials were needed to support the outcomes of this systematic review.

In conclusion for a short-term basis, pain relief and stability were evident in the majority of patients. Most of the patients showed neurological improvement and regained their ambulatory, sphincter, and sensory functions while an overwhelming population showed local tumour control with only a few patients developing tumour progression and radiation-induced toxicities. However, short follow-ups and the absence of randomized trials advocate the need for further clinical researches to confirm the outcomes of IORT in spinal tumours.

Conflict of Interest:

Each author certifies that he has no commercial associations that might pose a conflict of interest in connection with the submitted article.

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