Original Article

Surgical management of spinal metastases from primary thyroid carcinoma: Demographics, clinical characteristics, and treatment outcomes – A retrospective analysis

ABSTRACT

Objective: Metastatic spinal tumors represent a rare but concerning complication of primary thyroid carcinoma. We identified demographics, metastatic features, outcomes, and treatment strategies for these tumors in our institutional cohort.

Materials and Methods: We retrospectively reviewed patients surgically treated for spinal metastases of primary thyroid carcinoma. Demographics, tumor characteristics, and treatment modalities were collected. The functional outcomes were quantified using Nurik, Modified Rankin, and Karnofsky Scores.

Results: Twelve patients were identified who underwent 17 surgeries for resection of spinal metastases. The primary thyroid tumor pathologies included papillary (4/12), follicular (6/12), and Hurthle cell (2/12) subtypes. The average number of spinal metastases was 2.5. Of the primary tumor subtypes, follicular tumors averaged 2.8 metastases at the highest and Hurthle cell tumors averaged 2.0 spinal metastases at the lowest. Five patients (41.7%) underwent preoperative embolization for their spinal metastases. Seven patients (58.3%) received postoperative radiation. There was no significant difference in progression-free survival between patients receiving surgery with adjuvant radiation and surgery alone (P = 0.0773). Five patients (41.7%) experienced postoperative complications. Two patients (16.7%) succumbed to disease progression and two patients (16.7%) experienced tumor recurrence following resection. Postsurgical mean Nurik scores decreased 0.54 points, mean Modified Rankin scores decreased 0.48 points, and mean Karnofsky scores increased 4.8 points.

Conclusion: Surgery presents as an important treatment modality in the management of spinal metastases from thyroid cancer. Further work is needed to understand the predictive factors for survival and outcomes following treatment.

Keywords: Spinal metastases, spine surgery, thyroid carcinoma

INTRODUCTION

The escalating incidence of thyroid cancer in the United States, which has seen a rapid surge since the 1990s, remains a pressing concern, with an estimated 43,800 adults diagnosed in 2022.^[1,2] Despite the availability of robust treatment options and high post-surgical survival rates, a notable 3% of thyroid cancer patients experience complications stemming from bone metastases.^[3] Of these metastases, the spinal column emerges as a common site of involvement, with up to 70% of patients with various malignancies displaying spinal metastases in primary thyroid cancer cases manifest as spinal involvement, resulting in a substantially diminished

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quality of life due to pain, neurological deficits, and increased mortality. $\ensuremath{^{[3]}}$

The current therapeutic objectives for spinal metastases primarily focus on palliation, encompassing the preservation or restoration of neurological function, effective pain management, and maintenance of spinal stability through local tumor control.^[5] Presently, stereotactic radiosurgery and minimally invasive spinal surgery serve as the predominant treatment modalities in managing spinal metastases.^[6] Surgery plays a pivotal role in the initial phase of the interdisciplinary management of spinal metastases, offering long-term relief and functional independence to align with modern standards of care and therapies, which have increased life expectancies.^[7,8] Modern surgical strategies encompass traditional spinal decompression surgery, anterior column reconstruction, and corpectomy with vertebral column replacement.^[7]

In this study, we present the findings based on 12 patients who underwent 17 surgeries, contributing to the body of the literature concerning the surgical management of metastatic spinal tumors originating from primary thyroid malignancies. Within this subpopulation, we explore demographic characteristics, metastasis features, treatment outcomes, and strategies.

MATERIALS AND METHODS

The study cohort was identified through a clinical data repository specific to the institution. Initial screening yielded all patients diagnosed with metastatic spinal tumors between January 1, 2000 and December 14, 2019. Subsequently, patients with primary thyroid tumors who underwent spine surgery at the same medical center were identified, forming the final patient list. Ethical approval for the study was obtained from the university Institutional Review Board, with all patients providing informed consent for the procedures conducted. The requirement for explicit patient consent was waived by the Institutional Review Board, given that deidentified data were collected.

Patient data encompassed demographic information such as age, sex, smoking status, comorbidities quantified using the Charlson Comorbidity Index (CCI), Nurick score, Modified Rankin score, Karnofsky score, American Society of Anesthesiologists score, general presentation, and paralysis status. Clinical data included primary thyroid tumor pathology and radiological findings, date of metastatic tumor diagnosis, metastatic tumor pathology and radiological findings, duration of hospital/intensive care unit (ICU) stay, date of follow-up, and overall survival. The surgical data encompassed the number of neurosurgeons involved, type of surgery, intraoperative blood loss, surgical duration, complications, and radiation utilization and characteristics. Spearman's correlation was utilized to investigate the association between CCI and length of hospital stay and CCI and length of ICU stay.

The postoperative survival was calculated from the difference between surgery date and date of death when available. Progression-free survival was calculated from the difference between surgery date and date of death or date of recurrence when available. Patients were censored at the date of last follow-up if date of death was not available. Kaplan–Meier curves were generated to assess 10-year postoperative survival time after surgery, 10-year progression-free survival after surgery, and to compare 10-year progression-free survival between surgery with adjuvant radiation and surgery only groups.

Data were collated and analyzed using the Microsoft Excel 16.66.1 (Microsoft Corporation, 2022, Redmond, WA, USA), with statistical analyses conducted using Prism 9.0d.

RESULTS

Age, gender, and comorbidities

Within our cohort of 12 patients, gender distribution consisted of 3 (25.0%) males and 9 (75.0%) females, with ages at surgery spanning from 49 to 76 years. Mean ages at surgery for males, females, and the entire cohort were 68.5, 60.0, and 62.6 years, respectively. CCI scores upon presentation varied from 6 to 10, with an average of 7.6 [Table 1]. Neither the length of hospital stay (rs = -0.13, P = 0.69) nor the duration of ICU stay (rs = -0.65, P = 0.11) displayed statistically significant or positive correlations with increasing CCI.

Location of metastases and presentation

Tumor locations encompassed the thoracic spine (6/12), lumbar spine (3/12), sacral spine (1/12), cervical and thoracic spine (1/12), and thoracic and lumbar spine (1/12). Predominantly, back pain served as the primary presenting symptom (9/12), although a minority of metastases were incidentally discovered (3/12) [Table 2].

Primary tumor pathology and metastases

Pathological analysis of primary thyroid tumors revealed a distribution of papillary (4/12), follicular (6/12), and Hurthle cell (2/12) subtypes. One resected tumor had unknown pathology. Histologically, papillary tumors averaged 2.3 spinal metastases, follicular tumors averaged 2.8, and Hurthle cell tumors averaged 2.0 spinal metastases. On average, each patient had 2.5 metastases [Table 2].

Table 1: Patient characteristics

	n (%)
Patients	12
Age at procedure, mean (range)	62.6 (49–76)
Females	9 (75)
Total surgeries	17
Ever smoker	4 (33.3)
BMI at surgery, mean (range)	30.6 (18.6–43.0)
Patients with multiple operations	4 (33.3)
Patients with recurrent tumors	2 (16.7)
Indication	
Stability	2 (16.7)
Disease control	4 (33.3)
Active neurological deficit	6 (50)
Comorbidities	
Number, mean (range)	2.2 (0-4)
CCI at surgery, mean (range)	8.1 (6–10)
Association with length of hospital stay, $r_s(P)$	-0.13 (0.69)
Association with length of ICU stay, r _s (P)	-0.65 (0.11)
Presenting symptoms	
Back pain	9 (75)
Lower extremity weakness	4 (33.3)
Buttock pain	1 (8.3)
Upper extremity motor deficit	1 (8.3)
Incidental discovery	3 (25)

BMI - Body mass index; CCI - Charlson comorbidity index; ICU - Intensive care unit

Table 2: Tumor characteristics

	n (%)
Metastatic tumor location	
Thoracic	6 (50)
Lumbar	3 (25)
Sacral	1 (8.3)
Cervical and thoracic	1 (8.3)
Thoracic and lumbar	1 (8.3)
Primary tumor histology	
Papillary	4 (33.3)
Follicular	6 (50)
Hurthle cell	2 (16.7)
Unknown	1 (8.3)
Number of metastases, mean (range)	2.5 (1-8)
Papillary	2.3 (1–8)
Follicular	2.8 (1-4)
Hurthle cell	2 (1–3)
Age at primary tumor presentation, mean (range)	56.57 (25–73)
Papillary	50.3 (25–68)
Follicular	60.8 (49–73)
Hurthle cell	55.5 (46–55)
Age at metastases presentation, mean (range)	64.5 (49–80)
Papillary	67.5 (52–80)
Follicular	64.8 (49–74)
Hurthle cell	66 (56-76)

Preoperative embolization

Five patients (41.7%) underwent preoperative embolization for their spinal metastases, with one patient having two spinal tumors, both of which were embolized. The mean time elapsed between embolization and surgery was 4 days [Table 3].

Postoperative radiation

Among the 12 patients, seven (58.3%) received postoperative radiation. Reported radiation doses were measured in gray (Gy) and included 25 Gy (1), 30 Gy (4), 35 Gy (1), and 40 Gy (1) [Table 3].

Postoperative complications and recurrence

Five patients (41.7%) experienced postoperative complications, all necessitating an ICU stay. Two patients required readmission for recurrence and subsequent reoperation. It is noteworthy that neither of these patients received post-operative radiation therapy at their initial surgery. Patient one, at the time of the initial surgery, was a 49-year-old woman with no comorbidities and had a medullary tumor pathology. Patient two, a 71-year-old woman at the time of her initial surgery, had a history of lung cancer and presented with follicular tumor pathology [Table 4].

Spine follow-up

The mean follow-up with the treatment team following tumor resection was 33.6 months, ranging from 0 to 114.4 months. On average, women had shorter follow-up periods (30.1 months) compared to men (45.2 months) [Table 4].

Nurik, Modified Rankin, and Karnofsky scores

Preoperatively, the average Nurik score was 1.3, which improved to 0.76 postoperatively. Seven patients exhibited a one-point decrease in Nurik score at the postoperative assessment, with no subsequent change between postoperative measurement and the last follow-up. The average preoperative Modified Rankin score was 1.3, improving to 0.82 postoperatively. Eight patients experienced a one-point decrease in the Modified Rankin score postoperatively, with no alterations between postoperative measurement and the last follow-up. The mean preoperative Karnofsky score was 85.2, increasing to 90 postoperatively. Six patients witnessed a ten-point decrease, two patients experienced a twenty-point decrease, and one patient saw a ten-point increase in Karnofsky score at the postoperative assessment, with no subsequent change between post-operative measurement and the last follow-up [Table 5].

Survival and progression-free survival

Out of the 12 patients who underwent surgery, two (16.7%) succumbed to disease progression. Patient one, a male with a CCI of 8, experienced postoperative venous thromboembolism and passed away 26.5 months after surgery. Patient two, a female with a CCI of 7, passed away 161.8 months after surgery [Table 4]. The overall mean

Table 3: Clinical variables

	n (%)
Preoperative embolization	5 (29.4)
Mean time of embolization before surgery, mean (range)	4 (1–12)
Number of neurosurgeons, mean (range)	2.6 (1-4)
Antibiotic irrigation	
Bacitracin	2 (11.8)
Gentamicin	1 (5.9)
Cefazolin	6 (35.3)
Graft	
Autograft	3 (25)
Allograft	7 (58.3)
Both	2 (16.7)
Blood loss (mL), mean (range)	1387.5 (0–7500)
Operative time (min), mean (range)	266.5 (92–451)
Difficult hemostasis	9 (52.9)
Postoperative radiation	7 (58.3)
Average dosage (Gy), mean (range)	31.4 (25-40)
Gy - Gray	

Table 4: Outcomes

	n (%)
Length of hospital stay (days), mean (range)	14.3 (1–34)
Spine follow-up (months), mean (range)	33.6 (0–114.4)
Overall survival (months)	81.5 (3.4–163.5)
Progression-free survival (months), mean (range)	79.4 (0.3–163.5)
Course of hospital stay	
Complicated	3 (17.6)
Smooth	11 (64.7)
ICU stay	9 (52.9)
Length of ICU stay (days), mean (range)	16 (2–33)
Postprocedural complications	6 (35.3)
Patients readmitted for metastases	2 (16.7)
Reoperation on metastases	2 (16.7)
Postoperative VTE	1 (5.9)
Survival at last follow-up	10 (83.3)

ICU - Intensive care unit: VTE - Venous thromboembolism

Table 5: Patient pre- and post-operative scores

	Mean (range)
Nurick score	
Preoperative	1.3 (0–4)
Postoperative	0.76 (0–3)
Last follow-up	0.76 (0–3)
Modified Rankin score	
Preoperative	1.3 (0–4)
Postoperative	0.82 (0–3)
Last follow-up	0.82 (0–3)
Karnofsky score	
Preoperative	85.2 (50–100)
Postoperative	90 (50–100)
Last follow-up	90 (50–100)
ASA score	2.8 (2-4)

ASA - American Society of Anesthesiologists

postoperative survival time was 81.5 months [Table 4], and the 10-year postoperative survival rate was 88.2% [Figure 1].

Eight patients (66.7%) experienced progression-free survival over the study window. The overall mean postoperative progression-free survival time was 79.4 months [Table 4] and the 10-year postoperative progression-free survival rate was 70.6% [Figure 2]. There was no significant difference (P = 0.0773) in 10-year progression-free survival between surgery with radiotherapy and surgery alone [Figure 2].

DISCUSSION

The management of spinal metastases originating from thyroid tumors entails a critical therapeutic challenge, commonly necessitating surgical intervention to address debilitating symptoms. This study examines 12 patients who underwent 17 surgeries for the management of spinal metastases associated with primary thyroid carcinoma. Notably, spinal resection led to significant improvements in Nurick, Modified Rankin, and Karnofsky scores both postsurgery and at the last follow-up.

Presentation ages for papillary thyroid carcinoma typically manifest at an earlier stage, between 35 and 54 years of age, consistent with the mean age at presentation of papillary thyroid cancer in our cohort at 50.3.^[9] Conversely, patients diagnosed with follicular thyroid cancer tend to be older at the time of surgery, which aligns with our finding that patients with follicular thyroid cancer were the oldest at the diagnosis, averaging 60.8 [Table 1].^[10]

In the context of primary thyroid cancer, incidence rates are the highest among middle-aged to older females.^[11] Males constituted only 25% of our dataset, mirroring the 3:1 female-to-male ratio observed in the diagnosis of metastatic primary thyroid carcinoma in other studies [Table 1].^[12] Previous retrospective studies have suggested a higher incidence of spinal metastases in males than females in general, indicating a potential gender-related component to the risk of spinal metastases in thyroid cancer.^[13,10]

CCI has demonstrated predictive value in forecasting nonroutine discharges, adverse events, and extended hospital stays during the surgical treatment of metastatic spinal disease.^[14] In our dataset, the relationship between CCI and both the length of hospital stay and the duration of ICU were not significant, potentially reflecting disparities in the relationship between CCI and length of stay in spinal metastases of thyroid cancer compared to spinal metastases in general or owing to the limited sample size [Table 1].

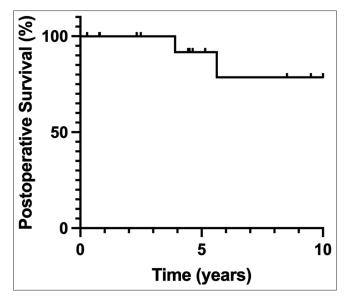


Figure 1: Kaplan–Meier survival curve illustrating the 10-year postoperative survival. Each vertical tick mark signifies the time of follow-up when censoring occurred for specific surgical cases

The relative prevalence of papillary thyroid carcinoma (85%-90%) surpasses that of follicular thyroid carcinoma (2%-5%) and Hurthle cell thyroid carcinoma (about 5%).^[12,15] A retrospective review indicated that Hurthle cell thyroid cancer exhibited the highest rate of distal metastases at 12.2% (7/57), followed by follicular thyroid cancer at 10.5% (18/171), and papillary thyroid cancer with the lowest rate at 2.4% (9/810).^[16] Overall, 4.2% (44/1038) of patients with thyroid cancer in the series presented with distal metastases. Out of all patients with primary thyroid carcinoma presenting with distal metastases, 44.2% were secondary to papillary thyroid carcinoma, 40.9% to follicular thyroid carcinoma, and 15.9% to Hurthle cell carcinoma.^[16] In our cohort, there is slight overrepresentation of follicular metastases at 50% and the slight underrepresentation of papillary metastases at 33.3% [Table 2]. These variations may stem from the factors such as our limited sample size or the study's focus on spinal metastases isolated from other distal metastatic sites, including non-spinal bone and lung.

Follicular and Hurthle cell thyroid carcinoma is primarily associated with hematogenous mechanism of spread, in contrast to papillary thyroid cancer, which primarily utilizes a lymphatic route.^[17] It is reasonable to expect that follicular and Hurthle cell thyroid carcinomas would exhibit a higher rate of metastases compared to papillary thyroid carcinoma, given that skeletal metastases tend to develop in areas that correlate with blood flow.^[18]

Ramadan *et al.* reported that thyroid metastases most frequently localized to the thoracic spine (60%-80%), followed by the lumbar (15%-30%) and cervical

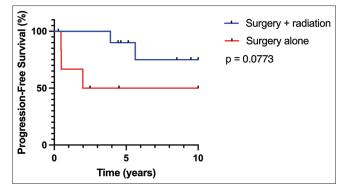


Figure 2: Kaplan–Meier survival curve illustrating the 10-year postoperative progression-free survival for the entire study cohort (on the left) and separately for those who underwent surgery with adjuvant radiation and those who had surgery alone (on the right). Each vertical tick mark signifies the time of follow-up when censoring occurred for specific surgical cases

spine (<10%).^[26] Our findings align relatively closely with this distribution, with 66.7% of tumors involving the thoracic spine, 33.3% affecting the lumbar spine, and 8.3% occurring in the cervical spine [Table 2]. An extraordinary case involved a patient with primary Hurthle cell carcinoma and sacral metastasis, an exceedingly rare occurrence, with only one other such case reported in the literature.^[19]

The current therapeutic approaches for spinal metastases necessitate a multidisciplinary strategy incorporating conformal external-beam radiotherapy, decompression/ stabilization surgery, and rehabilitation.^[20-22] Stereotaxic radiotherapy has also proven effective in controlling spinal metastases with low complication rates.^[5] Our dataset may suggest higher rates of 10-year progression-free survival in patients receiving surgery with adjuvant radiotherapy compared to surgery alone on Kaplan–Meier analysis, although a statistically significant difference was not shown potentially due to the limited sample size and loss to follow-up (P = 0.0773).

Historical classification-based approaches to treatment decisions, such as the Spinal Instability Neoplastic Score Scale, have given way to principle-based systems like the "LMNOP" system, aligning with the trend toward individualized precision medicine.^[23] Survival prediction systems have exhibited limited accuracy in recent studies (42.8% and 25.6% for the Tokuhashi and Tomita scoring systems, respectively), primarily due to their inability to incorporate scientific advancements in cancer management and molecular genetics.^[20,24] An analysis of patients with metastatic spinal diseases, including primary breast, prostate, renal cell, colon, lung, thyroid, and skin cancers, showed a 1% improvement in overall survival for each successive year of surgery, totaling a 20% improvement over the study period from 1998 to 2017.^[25]

The prognosis for thyroid carcinoma with distal metastases generally exhibits a poorer outlook (40%) compared to thyroid carcinoma without metastases (80%–95%).^[26] Other studies report survival rates for bony metastases of primary thyroid carcinoma at 12% over 10 years and 8% over 20 years.^[27] In our series, all follow-up was conducted within 5 years of surgery, with an overall survival rate of 80% among patients who received any follow-up [Table 3].

No prior studies have explored associations between Nurik or Modified Rankin scores and survival or other metrics for thyroid cancer metastases to the spine. Goodwin *et al.* reported an association between postoperative Modified Rankin scores >4 and survival <3 months in the surgical treatment of spinal metastases from primary lung cancer, with significant differences in Modified Rankin scores between survival >3 and <3 months.^[28] Our results deviate from these associations, as all patients in our cohort had postoperative Modified Rankin scores below 4, with 66.7% experiencing a postoperative improvement in score. Larger studies may be warranted to elucidate the utility of Modified Rankin scores as a metric for spinal metastases treatment outcomes [Table 5].

Preoperative Karnofsky scores exceeding 80% have been identified as the significant predictors of survival following decompression surgeries for spinal metastases.^[29] The mean preoperative Karnofsky score was higher among patients who were alive at the last follow-up (84.4) compared to those who succumbed to disease progression (80). In general, our dataset demonstrated relatively high preoperative Karnofsky scores, with only two out of 12 patients presenting with scores considered poor by other studies (<80%) [Table 5].^[30,31] This may be attributed to modern treatment paradigms initiating surgical interventions at earlier stages of symptom progression. Notably, 66.7% of our patients experienced a postoperative improvement in Karnofsky scores, consistent with findings in previous studies, further substantiating the value of surgical treatment modalities for spinal metastases.^[32-34]

Limitations and future directions

This study was conducted through retrospective chart review, which inherently carries limitations associated with this study format. Since all patients are from a single institution, the selection criteria for surgical procedures may not be generalizable to other treatment centers. Furthermore, the small sample size of 12 patients contributes to the lack of generalizability. The patient population lacks control over factors that may explain primary thyroid carcinoma and spinal metastases not considered by the CCI.

Future directions could involve integrating this single-institutional dataset with those from other institutions or national databases

to enhance external validity and unveil risk factors for incidence, mortality, and recurrence through regression analysis. Larger, prospective studies incorporating surgical intervention strategies may offer better control over modulating variables and establish more robust relationships. Future research could also investigate the impact of radiotherapy timing on the survival and rates of surgical site infections. Delayed radiotherapy following surgery for metastatic spinal tumors has been associated with poorer local control, overall survival, and worsened quality of life.^[35] While not statistically significant in our study, the trend of increased progression-free survival in the surgery with adjuvant radiotherapy group for metastatic spinal tumors from primary thyroid carcinoma should be explored further in a larger patient sample.

Prognostic decision-making tools for spinal metastasis continue to evolve, particularly as targeted molecular therapy and immunotherapy assume crucial roles in the next generation of targeted biological therapies.^[20] The current paradigm shift in the treatment of metastatic spinal cancer involves the redefinition of prognosis methodologies employing computational and machine learning (ML) techniques, such as the recently developed ML prognostic tool by the SORG group.^[13,20,36] In future directions, it would be valuable to expand our institutional dataset to internally validate an ML-based tool for clinical decision-making.

CONCLUSION

Surgical management for spinal metastases secondary to thyroid cancer is a safe and effective method for palliation. It preserves neurological function with a long disease-free survival and recurrence rates.

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Conflicts of interest

There are no conflicts of interest.

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