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Population description and clinical response assessment for spinal metastases: part 2 of the SPIne response assessment in Neuro-Oncology (SPINO) group report

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Abstract

Background. Approximately 40% of metastatic cancer patients will develop spinal metastases. The current report provides recommendations for standardization of metrics used for spinal oncology patient population description and outcome assessment beyond local control endpoints on behalf of the SPIne response assessment in Neuro-Oncology (SPINO) group.

Methods. The SPINO group survey was conducted in order to determine the preferences for utilization of clinician-based and patient-reported outcome measures for description of patients with spinal metastases. Subsequently, ClinicalTrials.gov registry was searched for spinal oncology clinical trials, and measures for patient description and

outcome reporting were identified for each trial. These two searches were used to identify currently used descriptors and instruments. A literature search was performed focusing on the measures identified in the survey and clinical trial search in order to assess their validity in the metastatic spinal tumor patient population. References for this manuscript were identified through PubMed and Medline searches.

Results. Published literature, expert survey, and ongoing clinical trials were used to synthesize recommendations for instruments for reporting of spinal stability, epidural tumor extension, neurological and functional status, and symptom severity.

Conclusions. Accurate description of patient population and therapy effects requires a combination of clinician-based and patient-reported outcome measures. The current report provides international consensus recommendations for the systematic reporting of patient- and clinician-reported measures required to develop trials applicable to surgery for spinal metastases and postoperative spine stereotactic body radiotherapy (SBRT).

Keywords

metastases | response assessment | spine radiosurgery | spine surgery | SPINO

Importance of the study

Spinal metastases represent a frequent complication of cancer, requiring expeditious diagnosis and effective treatment. SBRT is a rapidly emerging treatment option for selected patients with spinal metastasis. The first report by SPINO detailed technical and imaging response assessment issues specific to determining local tumor and pain control following SBRT for patients with intact metastases, as opposed to the postoperative patient. This second report provides international consensus for the definitions of surgical procedures and patient assessment measures relevant to spine surgery, including those related to mechanical spinal stability, function, neurological status, and quality of life. In addition, patient descriptors and functional endpoints are suggested for the design of clinical trials evaluating SBRT relevant in particular to postoperative patients.

Spine stereotactic body radiotherapy (SBRT) is increasingly applied to patients with spinal metastases as primary therapy,[1] as salvage for metastases that progressed following prior conventionally fractionated radiation and in the postoperative setting.[2] A few prospective, and multiple retrospective, studies have established the safety and efficacy of spinal SBRT; however, as yet no randomized trials have been reported to confirm superior outcomes compared with palliative conventional external beam radiotherapy (cEBRT).[3–8] The first report by the SPIne response assessment in Neuro-Oncology (SPINO) group of the Response Assessment in Neuro-Oncology (RANO) working group established recommendations with respect to imaging and technical requirements for radiation delivery and provided recommendations with regard to outcome definitions for local control and pain control.[9] The key recommendations included the use of thin-slice CT and MRI for SBRT planning; follow-up MR imaging in order to assess tumor response and diagnose toxicities, including vertebral compression fracture (VCF); and utilization of the Brief Pain Inventory (BPI) and International Consensus Pain Response Endpoints (ICPRE) for assessment of pain response. Those recommendations were largely incorporated into the design of an ongoing Canadian Clinical Trial Group (CTTG) Symptom Control 24 (SC24) phase III randomized controlled trial (RCT) comparing 20 Gy in 5 fractions of cEBRT with 24 Gy in 2 fractions of SBRT in patients with painful spinal metastases (NCT02512965).[10]

While the outcomes of SBRT in patients with spinal metastases that do not require surgery are the focus of several RCTs, no ongoing RCT is comparing SBRT with cEBRT in the postoperative patient. The study by Patchell et al established the superiority of surgery followed by cEBRT over cEBRT alone for patients with symptomatic spinal cord compression by solid tumor metastases,[11] and was recently validated in the prospective multicenter AOSpine North America study.[12] The efficacy of postoperative SBRT, as demonstrated by retrospective and ambispective studies,[8,13] has resulted in a paradigm shift in the treatment of metastatic disease, particularly with respect to surgical indications, surgical goals, and expected outcomes for patients with spinal metastases. A need exists to standardize metrics used for patient population description and outcome assessment beyond local control endpoints as defined in SPINO Part 1. This second report provides an international consensus for the definitions of surgical procedures and patient assessment measures, including those related to mechanical spinal stability, function, neurological status, and quality of life (QoL).

Methods

Identification of Measures and Instruments

A SPINO group survey and ClinicalTrials.gov search were conducted in order to identify clinician-based and patient-reported outcome (PRO) measures currently used in spinal oncology. The survey was distributed to 17 members of the SPINO group, which included radiation oncologists and neurological and orthopedic spine surgeons. A 100% response rate was achieved. The survey (Appendix 1) included questions about classification systems used to assess mechanical stability of the spine, neurological and ambulatory status, QoL, survival prediction, grading of tumor epidural extension, surgical evaluation referral criteria, and definitions of oncologic spinal operations.

The US National Institutes of Health database (ClinicalTrials.gov) was also searched for clinical trials involving spinal SBRT. Thirty-one relevant trials were identified, and the information available on ClinicalTrials.gov was queried for assessment of spinal mechanical stability; neurological, functional, and QoL assessment; and surgical data.

Literature Search and Recommendation Formulation

Once the above searches identified instruments used in patient assessment in spinal oncology, a literature search was conducted to evaluate the instruments. PubMed and Medline searches were performed to identify relevant publications. English-language articles published between 1980 and 2016 were reviewed for relevance. Search terms included: "spine stereotactic radiosurgery," "spine radiosurgery," "spinal metastases," "quality of life," "ambulation," "spinal cord compression," "ASIA," "AIS," "spinal stability," and "survival prediction." The utilization data from the survey and clinical trials search were synthesized with the literature review in order to formulate recommendations. The recommendations were reviewed and refined by the members of the SPINO group.

Results

Clinician-Reported Measures

Mechanical spinal stability

Fifteen respondents (88%) reported using Spinal Instability Neoplastic Score (SINS)[14] for assessment of spinal stability (Table 1). The Denis classification of spinal fractures[15] was used by 4 respondents (24%) and the AOSpine Traumatic Spine Injury Classification System[16] was used by 1 (6%). Three respondents (18%) reported the use of movement-related pain as a significant consideration when diagnosing mechanical instability. The use of dynamic imaging, such as flexion and extension radiographs, was also mentioned by 2 respondents (12%). In the review of ClinicalTrials.gov content, few ongoing clinical trials include a formal assessment of spinal stability, although 7 trials (23%) mention the ability to lie down flat or radiographical stability parameters in exclusion criteria. Four trials (13%) state that they exclude instability but did not state the specific criteria for instability.

Spinal cord compression

The Bilsky epidural spinal cord compression (ESCC) score[17] was used by 13 respondents (76%) (Table 2). Ten respondents (59%) used binary yes/no reporting of the presence of spinal cord compression, and 2 respondents (12%) used the Ryu[18] ESCC score. Three ongoing clinical trials (10%) specify the distance between the tumor and the spinal cord in their exclusion criteria, and 2 trials (6%) describe spinal cord compression in a binary fashion.

Survival prediction

Karnofsky performance status (KPS)[19] was the predominant survival prediction measure used by 12 respondents (71%, Table 3). The closely related Eastern Cooperative Oncology Group (ECOG) performance status[20] was used by 8 respondents (47%). Three respondents used the Tomita[21]

Table 1 Mechanical stability

	N (%)
Surveys	
SINS	15 (88)
Denis	4 (24)
Movement-related pain	3 (18)
Flexion-extension radiographs	2 (12)
AOSpine Trauma	1 (6)
Ongoing Clinical Trials	
Lie flat	7 (23)
Exclude instability	4 (13)
SINS	3 (10)
VCF extent	2 (6)
Posterior elements	1 (3)

Table 2 Spinal cord compression

	N (%)
Surveys	
Bilsky	13(76)
y/n	10 (59)
Ryu	2 (12)
Ongoing Clinical Trials	
Separation 2–3 mm	3 (10)
Cord compression	2 (6)

(18%) and Tokuhashi[22] (18%) scoring systems, and 1 used the Bauer[23] score (6%). The majority of ongoing clinical trials specify KPS (35%) and/or ECOG (48%).

Neurological and Functional Status Measures

Twelve respondents (71%) used the American Spinal Injury Association Impairment Scale (AIS)[24] to describe the neurological deficit status, and 4 respondents (24%) used the Frankel scale,[25] which is closely related to the AIS (Table 4). Seven respondents use the Medical Research Council (MRC) scale[26] for muscle strength (41%). The modified Japanese Orthopedic Association scale (mJOA)[27] (6%) and the McCormick scale[28] (6%) were also used, although by single respondents. Several clinical trials employ the AIS (13%) or MRC (13%) scales.

Eleven respondents used binary (yes/no) reporting when describing ambulation (65%, Table 5). ECOG performance status was used by 9 respondents (53%), and 6 respondents (35%) also used the Oswestry Disability Index (ODI).[29] Additional reported ambulation assessments included the Nurick scale (6%) and 4-step (6%) and 10-meter (6%) walk tests. The majority of clinical trials employ the ECOG scale (48%) to describe patient status, and several specified ambulation in a binary fashion (16%).

Table 3 Survival

	N (%)
Surveys	
KPS	12 (71)
ECOG	8 (47)
Tokuhashi	3 (18)
Tomita	3 (18)
Bauer	1 (6)
Ongoing Clinical Trials	
ECOG/Zubrod	15 (48)
KPS	11 (35)

Table 4 Neurological status

	N (%)
Surveys	
ASIA	12 (71)
MRC	7 (41)
Frankel	4 (24)
mJOA	1 (6)
Deep tendon reflex	1 (6)
ESCC	1 (6)
McCormick	1 (6)
Ongoing Clinical Trials	
Common Terminology Criteria for Adverse Events	7 (23)
ASIA	4 (13)
MRC	4 (13)
ESCC neuro deficit	2 (6)
Myelopathy	2 (6)
Paraplegia	1 (3)

Surgical Definitions

When planning delivery and describing outcomes of postoperative SBRT, 16 (94%) respondents reported the importance of specifying the type of surgery performed. Although there was a general consensus with respect to surgical procedural definitions, there was variability in the interpretation of what terms suggest the degree of tumor resection. Therefore, we suggest specific term definitions based on the accepted meaning and interpretations by this group.

Laminectomy: Removal of the lamina. The lamina comprises the posterior portion of the osseous arch around the spinal canal. In the setting of spinal tumors, laminectomy is often performed with the intention of spinal cord decompression and excision of epidural tumor. However, the definition of "laminectomy" does not necessarily include tumor removal.

Vertebrectomy: Removal of the vertebral body. Vertebrectomy may be partial or complete, depending on the extent of the vertebral body removal. The definition of vertebrectomy does not include details about tumor removal, the approach, and spinal reconstruction. In the setting of spinal tumors, a vertebrectomy is generally performed for the purpose of tumor excision, and the extent of tumor infiltration may guide the extent of vertebrectomy.

Separation surgery: Removal of the epidural tumor in order to achieve circumferential decompression of the spinal cord and reconstitution of the cerebrospinal fluid space. Separation surgery provides a distance between the remaining tumor and the spinal cord with the purpose of optimizing SBRT dosimetry to allow complete coverage of the entire tumor volume with the intended SBRT dose

Table 5 Ambulation

	N (%)
Surveys	
y/n	11 (65)
ECOG	9 (53)
ODI	6 (35)
mJOA	2 (12)
GSTSG	1 (6)
Nurick	1 (6)
4 step	1 (6)
10 meter	1 (6)
Ongoing Clinical Trials	
ECOG/Zubrod	15 (48)
y/n	5 (16)

while maintaining a safe spinal cord dose (Fig. 1). While this operation is generally performed using a posterior approach and posterolateral instrumented stabilization, this may be performed through any approach and does not always require spinal instrumentation or a fusion.

En bloc: Removal of the tumor in one piece. The term en bloc specifies the surgical technique of tumor removal; however, it does not specify the surgical margin. En bloc excision is usually performed with the intent of a marginal or wide margin around the tumor; however, an intralesional margin can occur with planned or accidental transgression of the tumor capsule.

Marginal margin: Excision of the entire tumor along the tumor capsule, pseudocapsule, or reactive tissue surrounding the tumor. Since malignant tumors frequently extend past the pseudocapsule in a micro- or macroscopic fashion, such excision risks leaving behind residual malignant cells.

Wide margin: Excision of the entire tumor along with normal tissue surrounding the tumor capsule. Malignant tumor cells may extend past the visible tumor volume and capsule; therefore, the purpose of removing the tissue surrounding the tumor capsule is to clear possible regions of microscopic tumor extension that are not visible on imaging or to the naked eye during surgery. The volume of the tissue cuff required for wide margin varies based on the tumor and does not have a uniform definition.

Patient-Reported Outcomes Measures

General Health Instruments

Among generic PRO measures, the five-dimensional EuroQoL (EQ-5D)[30] represents the most frequently used instrument among 9 of the respondents (53%; Table 6). The Medical Outcomes Study 36-Item Short Form Survey (SF36)[31] was used by 5 (29%) and the 12-Item Short Form Survey (SF12) by 3 (18%) respondents. Two respondents (12%) administered the BPI. Several clinical trials used the EQ-5D (19%), SF12 (3%), and BPI (13%).

Cancer-Specific Instruments

The surveyed specialists employed cancer-specific PRO instruments less frequently compared with generic PRO instruments. Three respondents administered the MD Anderson Symptom Inventory (MDASI,[32] 18%) and 3 administered the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ,[33] 18%). Functional Assessment of Cancer Therapy (FACT)[34] was used by 2 respondents (12%). FACT (26%) and MDASI (13%) represent the primary cancer-specific PRO instruments in ongoing clinical trials.

Discussion

This report summarizes the marked heterogeneity in specific clinician and patient reported measures used in outcome reporting for spine SBRT. The lack of standardization complicates the interpretation and comparisons of results. Standardization of patient population characteristics, therapy parameter reporting, and definition of optimal instruments for measurement of therapeutic outcomes facilitate design and interpretation of future clinical trials.

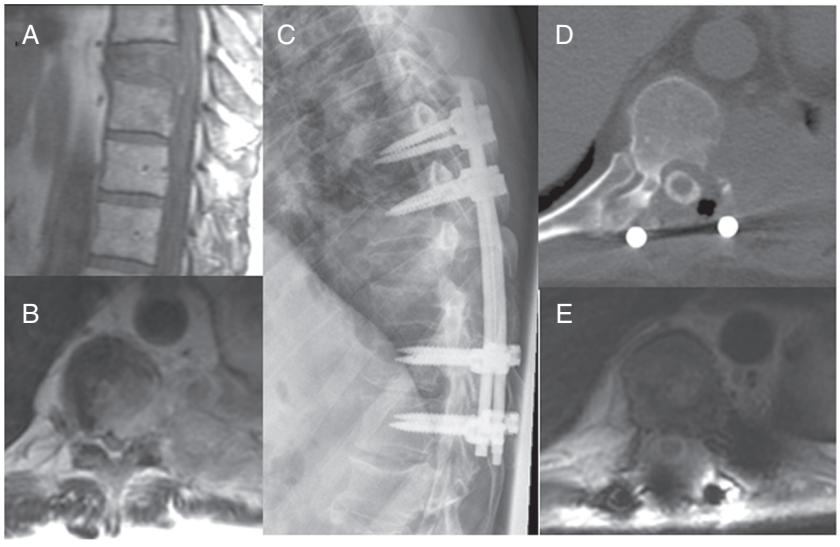

Fig. 1 (A, B; spinal MRI) Fifty-five-year-old man with metastatic melanoma presented with back pain exacerbated by movement (SINS 12) and was diagnosed with T9 metastasis causing spinal cord compression (Bilsky ESCC 3). Patient underwent separation surgery using posterior-approach instrumented spinal stabilization, T8–T10 laminectomy, left-sided removal of the facet and pedicle, and excision of epidural tumor. (C) Postoperative X-ray illustrating a pedicle screw and rod system used for spinal stabilization. (D) Postoperative CT-myelogram used for SBRT planning, demonstrating circumferential spinal cord decompression achieved through removal of the lamina, facet complex, pedicle, and epidural tumor. Patient was treated with 900 cGy × 3 fractions SBRT. (E) MRI obtained 11 months after SBRT confirming local tumor control.

Clinician-Based Measures

Spinal Mechanical Stability

The Spine Oncology Study Group (SOSG) defined neoplastic spinal instability as "loss of spinal integrity as a result of a neoplastic process that is associated with movement-related pain, symptomatic or progressive deformity, and/or neural compromise under physiologic loads."[14] The group subsequently developed SINS, which is an expert and literature based classification system designed to facilitate diagnosing spinal instability and referral for surgical assessment. In short, SINS includes evaluation of the spinal level of the tumor, radiographic characterization of osseous involvement (lytic, mixed, or blastic), the presence of mechanical pain, posterolateral osseous element involvement, segmental alignment, and extent of vertebral body collapse. The cumulative SINS is classified as stable (0–6), indeterminate/potentially unstable (7–12), or unstable (13–18). Multiple studies have validated the utilization of SINS within the surgical, radiation oncology, and radiology disciplines.[35–37]

The Denis model and AOSpine Traumatic Spine Injuries Classification System were also mentioned in the survey responses. The Denis model of spinal instability[15] has been found to be no longer valid in spine trauma for which it was designed. It was not designed or psychometrically evaluated for spine oncology and should not be used. The AOSpine Traumatic Spine Injuries Classification System was designed to classify traumatic injuries to the spine, and includes a more detailed evaluation of the extent of the vertebral body fracture and posterior element disruption.[16] The relatively new AO classification was also designed and assessed for trauma and with the mechanism of injury, ligamentous integrity, and healing potential of neoplastic and traumatic instability differing significantly, the application of trauma classification systems for evaluation of tumor-associated instability requires caution.

Several survey respondents reported the use of movement-related pain as a determinant of spinal instability. While pain exacerbated by movement represents one of the components of spinal instability evaluated by SINS, the presence of such pain does not always result in a SINS score consistent with spinal instability. A large number of patients evaluated using SINS have a score between 7 and 12 consistent with "indeterminate (possibly impending) instability." The optimal treatment of patients with "indeterminate" instability requires further study and is the objective of a current large registry study (Epidemiology, Process and Outcomes of Spine Oncology, NCT01825161). However, several pain patterns have been shown to respond readily to stabilization in the setting of "indeterminate" scores, emphasizing the importance of clinical evaluation. Lumbar radiculopathy, described as lumbar radicular pain elicited by axial loading, readily responds to surgical stabilization, while radiotherapy alone fails to relieve it.[38] Recumbency pain in the thoracic spine and movement-associated pain in the cervical spine also generally require stabilization in the presence of neoplastic involvement of the vertebral body and posterior elements. Patients with "indeterminate" and "unstable" SINS scores were shown to be at significantly higher risk of radiotherapy failure, defined by the need for retreatment.[39,40]

Our data indicate that 88% of surveyed clinicians employ SINS in the description of spinal stability, although few ongoing clinical trials (10%) report SINS as one of the evaluation criteria. We recommend utilization of SINS as one of the standard instruments in the design of SBRT clinical trials (Table 7). Further characterization of movement-associated pain patterns such as mechanical radiculopathy, recumbency and axial load pain provides additional detail.

Table 6 Patient-reported outcomes

	N (%)
Surveys	
EQ-5D	9 (53)
SF36	5 (29)
MDASI	3 (18)
SF12	3 (18)
EORTC	3 (18)
BPI	2 (12)
FACT	2 (12)
Patient Health Questionnaire-9	1 (6)
Ongoing Clinical Trials	
FACT-G	8 (26)
EQ-5D	6 (19)
MDASI-SP	4 (13)
BPI	4 (13)
EORTC QLQ-C30	3 (10)
ODI	1 (3)
SF12	1 (3)
PAL	1 (3)
Numerical Rating Pain Scale	1 (3)
Visual analogue scale	1 (3)
QLQ-BM22 (for bone metastasis)	1 (3)

Abbreviation: SF12, 12-Item Short Form Survey.

Table 7 SPINO recommendations

Clinician-based Measures	
Spinal stability	SINS
Epidural tumor extension	Bilsky grade
Neurological assessment	AIS, MRC, 10 meter walk test
Functional assessment	KPS, ECOG
Patient-reported Outcomes	
Generic	EQ-5D or SF36
Pain	BPI
Spine-tumor specific	SOSGOQ or MDASI-SP

Spinal Cord Compression

The presence of radiographic ESCC serves as a frequently cited indication for surgical evaluation. Patients with neurological signs or symptoms, including pain, due to ESCC may benefit from surgery prior to radiotherapy.[11] However, due to variation in radiotherapy and surgical practice patterns, the degree of epidural tumor extension that warrants surgical decompression varies among institutions. Clear delineation of the degree of epidural extension and spinal cord compression facilitates communication among clinicians and helps define treatment pathways. The 6-point ESCC scale developed and validated by Bilsky et al grades the degree of epidural tumor extension and spinal cord compression based on axial MR imaging.[17] It has been tested with respect to reliability and validity. Ryu et al proposed combining the same 6-point radiographic ESCC scale with a neurological scale.[18] This 5-point neurological scale uses grades similar to AIS or Frankel. Finally, many physicians simply denote the presence of radiographic spinal cord compression as a binary yes/no variable without elaborating on the severity of the compression or the distance between the tumor and the spinal cord.

The current survey demonstrates that the majority of clinicians agree that recognition and description of the extent of spinal cord compression serves as an important radiographic parameter, with 76% of respondents using the Bilsky ESCC scale. At this time, the Bilsky ESCC scale represents the only instrument for description of the degree of epidural tumor extension and spinal cord compression that underwent validation through reliability analysis and therefore should serve as one of the standard descriptors of patient population in the design of clinical trials and study population reporting (Table 7).

Survival Prediction

KPS and ECOG represent 2 widely used functional assessment instruments developed for cancer patients. Both instruments underwent validation testing in the cancer population and serve as predictors of survival for numerous diseases.[41,42] These instruments have broad application across oncologic disciplines, and the majority of the respondents reported using one or both of these instruments in assessment of patients with spinal tumors.

Several physicians reported using the Tokuhashi (18%), Tomita (18%), and Bauer (6%) scores for estimation of postoperative survival. All 3 of these scores were developed specifically for prognostication of survival among patients with spinal metastases.[21–23] All of these scores incorporate a histology-specific assessment in survival prediction. Since the rapid evolution of systemic therapy continuously changes expected histology-specific survival, survival systems that strongly rely on primary tumor histology generally lose accuracy as systemic therapy evolves and require adjustment.

The majority of respondents utilize KPS (71%) and ECOG (47%) instruments as surrogates for survival prediction more frequently than spine tumor-specific survival scores. Ongoing clinical trials also reflect the dominance of ECOG (48%) and KPS (35%). KPS and ECOG provide ready comparison of populations among various oncologic specialties and therefore may provide the basis for interpretation studies of patients with spinal metastases in the general context of oncology. Furthermore, KPS and ECOG serve primarily as functional assessment instruments with a known survival association, thereby providing complementary information. Based on these data, we recommend inclusion of KPS and ECOG in the design of SBRT clinical trials (Table 7). Utilization of survival scores that rely on primary tumor histology should be used with caution, since new systemic therapies continually change histology-specific survival.

Neurological and Functional Measures

Patients with spinal tumors present with a wide range of neurological deficits and functional disability. These deficits may result from compression of the spinal cord or exiting nerve roots. The majority of survey respondents use the AIS in order to describe spinal cord injury due to tumor compression. The Frankel scale used by some represents an antecedent to AIS, with AIS being the preferred scale.[43] The MRC scale for muscle strength permits characterization of individual muscle function and provides useful information not only in the setting of spinal cord compression, but also in assessment of spinal nerve root and peripheral nerve dysfunction.[26] Assessment of spinal cord and individual nerve root dysfunction provides complementary information, and may both be required in order to fully characterize the tumor-associated neurological deficits.

Patient ambulation represents an important measure of neurological function and functional status. The majority of clinicians who responded to the survey reported the use of binary yes/no reporting when describing the patient's ability to ambulate. The 10-meter walk test represents a quantifiable and validated measure of ambulation and may provide a more accurate and reproducible instrument for ambulation reporting.[44] General functional assessment instruments such as KPS and ECOG also include an evaluation of patient ambulation. It is important to note that the ECOG metric does not have a definite scale as to ambulation, and if the ECOG is <3, then ambulation capability is assumed as opposed to ECOG 3 and 4, where it is not.

Respondents mentioned 4 additional disease-specific functional assessment scales. The mJOA score, devised to assess the symptom severity of cervical compressive myelopathy, provides a measure of physical disability.[27] The Nurick scale, also devised for evaluation of cervical spondylotic myelopathy, assesses ambulation.[45] While both scales provide well-validated instruments in the description of cervical myelopathy disability, their utility in patients with neoplastic spinal cord compression requires further study. Several clinicians use the ODI, developed for evaluation of symptom severity due to low back pain. The ODI represents a frequently used instrument for evaluation of patients with spinal tumors, although the validity of this instrument in the cancer setting requires investigation.[29] Finally, the McCormick scale was devised for classification of neurological dysfunction due to intramedullary tumors and appears to be less popular in the setting of spinal cord compression.[28] While the pathophysiology clearly differs

among degenerative and neoplastic spinal disorders, some of the disability patterns may have some similarities.

In summary, clear delineation of spine-specific neurological function requires assessment of the spinal cord, nerve roots, and ambulation. The majority of the respondents reported using AIS (71%) and MRC (41%); however, few clinical trials currently describe AIS (13%) and MRC (13%). The utilization of AIS for description of spinal cord function and MRC for muscle strength provides adequate detail about the motor and sensory examination in patients with spinal tumors. Consistent criteria for ambulation assessment are currently lacking. However, since ambulation represents a crucial functional endpoint and correlates with survival, efforts to standardize ambulation reporting are needed. KPS and ECOG provide uniformly accepted measures of general function and serve as important patient population descriptors. We recommend utilization of AIS, MRC, and quantifiable ambulation assessment in the design of SBRT clinical trials (Table 7).

Surgical Definitions

Spinal surgery for the treatment of tumors employs a wide range of techniques for spinal column stabilization, spinal cord and nerve root decompression, and tumor excision. Surgeons select the technique based on surgical indications and goals and tailor them to the available systemic and radiation therapies. The type of surgery performed may in turn affect the timing and the type of radiotherapy delivered and the outcome after radiotherapy. The majority of malignant tumor treatment strategies employ a combination of surgery and radiotherapy. Clear delineation of the surgical technique and radiotherapy parameters used to treat the patients is imperative in order to provide adequate description of baseline patient characteristics and for treatment comparison.

Patient-Reported Outcome Measures

General Health Instruments

PRO instruments provide information complementary to clinician-based assessments and reflect direct patient experience and attitudes. EQ-5D and SF36 represent generic PRO instruments most frequently used by survey respondents. Both were designed for broad application among a variety of health conditions. Due to the brevity, simplicity, and reliability of EQ-5D, the Global Spine Tumour Study Group (GSTSG) recommended its use in assessment of outcomes of spine metastasis surgery, and the majority of the survey respondents (53%) use EQ-5D.[46] However, the SF36 may provide more granular information and more population comparison options due to its wider global implementation.

Since the majority of spinal tumors cause pain, specific assessment of pain severity and its impact on function provides an important measure of disease severity and treatment outcome. The BPI serves as a validated instrument for pain assessment across numerous chronic and acute diseases, including cancer.[47] Use of the BPI was detailed in Part 1 from the SPINO group.

Cancer-Specific Instruments

Cancer-specific PRO instruments provide detailed information about the effect of cancer-related symptoms on the general well-being of the patients. The MDASI provides a thorough assessment of symptom burden associated with the tumor itself and tumor- directed therapy. Furthermore, a site-specific spine tumor module (MDASI-SP) assesses symptoms particular to spine cancer and provides PRO assessment specific to spine tumor.[32] The MDASI and MDASI-SP module both underwent validity and reliability testing in the general cancer and spine-tumor populations. The EORTC QLQ-C30 and FACT both provide validated cancer-specific PRO instruments implemented in numerous oncologic studies. While various cancer disease-specific EORTC and FACT modules exist, spine tumor modules are currently unavailable. Finally, the Spine Oncology Study Group Outcomes Questionnaire (SOSGOQ) was developed specifically for PRO measurement in patients with spinal metastases.[48] Initial testing showed superior content capacity of this instrument compared with many available self-assessment instruments,[49] and validation testing of SOSGOQ is currently under way.

In summary, PRO instruments provide important information about the effect of disease and therapy on patients, and thorough assessment of therapy effect requires inclusion of such measurements in study design. The majority of survey respondents reported using either EQ-5D, SF36, MDASI or EORTC, with less consistency noted in the ongoing clinical trials. Utilization of generic PRO instruments allows comparison of the study population to a wide range of patients and cost-effectiveness analysis, while inclusion of spine tumor-specific PRO instruments provides detailed information about spine-specific symptoms. We recommend that prospective studies include a generic PRO instrument, like EQ-5D, and an instrument specific to spine tumor, like SOSGOQ (Table 7).

Limitations

The current report utilized a survey administered to a group of expert clinicians who specialize in the treatment of spinal tumors. This group represents a small sample of physicians, and may therefore result in biased reporting of the practice patterns of this small expert group. In order to account for the possible bias, we searched the clinical trials database and the literature to identify additional instruments relevant to our patient population. Unfortunately, few studies were performed examining the validity of the recommended instruments. Therefore, future studies will be required to critically evaluate and compare various instruments in the description of patients with spinal tumors. However, uniform description of key parameters, as proposed in the current manuscript, represents the first requisite step in this direction.

Conclusions

Accurate description of patient population and therapy effect requires combination of clinician-based and PRO measures. Systematic reporting of spinal stability, epidural tumor

extension, neurological and functional status, and symptom severity is required to develop trials specific to postoperative spine SBRT. Ongoing work in validation of the existing instruments will provide stronger basis for instrument selection. An overall summary of recommendations from the second part of the SPINO report is provided in Table 7.

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