



# Prevalence of spinal metastases: a descriptive cross-sectional update and literature review

Prevalência em metástases espinhais: atualização de estudo transversal descritiva e revisão da literatura

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## Abstract

**Introduction:** A measure of an epidemiological event occurrence contributes in institutional health planning, resource allocation, sickness trend prediction and a surgical divisions operating profile. **Objective:** Census in prevalence of spinal epidural metastases among spinal and spinal tissue neoplasms in the neurosurgical context is the encountered epidemiological literature gap and the proposed reason for this research. **Methods:** A surgically treated spinal neoplasms patient descriptive cross-sectional update census was performed between February 1997 and January 2018 in a single neurosurgical division. In addition, using the systematic research method for literature review, authors selected comparative descriptive studies in patients submitted to surgical procedures for spinal epidural metastases, epidural primary and intradural neoplasms. The methodological quality analysis was in accordance to the Oxford Centre for Evidence-Based Medicine. **Results:** The primary outcome obtained in the cross-sectional descriptive update study indicated that 128 neurologically symptomatic patients were submitted to surgical procedures for spinal metastases and represented 0.84% of the 15,061-neurosurgical procedures. As for the secondary outcome, literature review identified 3 comparative studies: 1 cross-sectional and 2 case-series. In a cohort of 866 (100%) patients submitted to surgical treatment, 191 (22.05%) patients were operated for spinal metastases, 83 (9.59%) for epidural primary neoplasms and 592 (68.36%) for intradural neoplasms. Clinical appraisals identified Grade C recommendation for the 3

included items. **Conclusion:** Spinal intradural neoplasms are prevalent when compared to spinal metastases and spinal metastases are the most common histologic tumor type group in patients submitted to surgical treatment.

**Keywords:** Neoplasm metastasis; Epidemiology; Spine; Surgical procedures, operative

## Resumo

**Introdução:** À medida que ocorra um evento epidemiológico, o mesmo contribuirá no planejamento do atendimento à saúde numa Instituição no tocante à alocação de recursos, à previsão de tendências de doenças e a caracterização do perfil de procedimentos cirúrgicos de um departamento de cirurgia. **Objetivo:** Estabelecer censo na prevalência de metástases epidurais dentre as neoplasias da coluna vertebral e do tecido nervoso nela contido. No contexto neurocirúrgico é a lacuna epidemiológica encontrada na literatura e o motivo proposto desta pesquisa. **Métodos:** Foi realizado um censo de atualização descritiva transversal de pacientes submetidos a cirurgias espinhais no período entre fevereiro de 1997 e janeiro de 2018 em uma única divisão neurocirúrgica. Ademais, utilizando o método de pesquisa sistemática para revisão da literatura, os autores selecionaram estudos descritivos comparativos de pacientes com diagnóstico de neoplasias epidurais secundárias, epidurais primárias e intradurais submetidos a procedimentos cirúrgicos em coluna vertebral. A análise metodológica da qualidade dos estudos foi realizada de acordo com o Oxford Center for Evidence-Based Medicine. **Resultados:** O desfecho primário obtido no estudo de atualização descritiva transversal indicou que 128 pacientes neurologicamente sintomáticos foram submetidos a procedimentos cirúrgicos em metástases espinhais e representaram 0,84% do total de 15.061 procedimentos neurocirúrgicos em geral. Quanto ao desfecho secundário, a revisão de literatura identificou 3 estudos comparativos: 1 transversal e 2 séries de casos. Em uma coorte de 866 (100%) pacientes submetidos a tratamento cirúrgico, 191 (22,05%) foram operados para metástases espinhais, 83 (9,59%) para neoplasias primárias epidurais e 592 (68,36%) para neoplasias intradurais. A análise metodológica da qualidade dos estudos identificou

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recomendação Grau C para os 3 itens incluídos. **Conclusão:** As neoplasias intradurais da coluna vertebral são prevalentes quando comparadas às metástases espinhais e estas últimas são o tipo histológico mais comum em pacientes submetidos a tratamento cirúrgico em coluna vertebral.

**Descritores:** metástase neoplásicas, Epidemiologia, Coluna vertebral, Procedimentos cirúrgicos operatórios

## Introduction

Distant spread metastases occur in advanced cancer stage and the spine is the most frequent location relative to the skeleton<sup>(1-3)</sup>. At autopsy, 37% of patients harboring advanced cancer have spinal epidural metastases<sup>(4)</sup>. Cancers are considered advanced when they cannot be cured or controlled with treatment and are generally managed by non-surgical measures<sup>(1,5-6)</sup>. As for those patients that harbor symptomatic spinal epidural metastasis, approximately 10% are managed with palliative surgery, which indicates that only a minority of patients with spinal epidural metastases in the advanced cancer stage is operated<sup>(7-9,10)</sup>.

This present cross-sectional descriptive study seeks census in prevalence of neurologically symptomatic patients submitted to surgical treatment for spinal metastases. A literature review is also performed to address the study's structured question inasmuch to identify the prevalence of surgically treated spinal metastases relative to the census of operated spinal primary spinal and intradural neoplasms.

The acquired data intends to foresee trends and patterns for Institutional health planning, resource allocation, and neurosurgical divisions operating profiles inserted into their Health Institutions context.

This research aims to compare prevalence among patients surgically treated for spinal metastases in regard to spinal primary and intradural neoplasms.

## Methods

### Overview

Research design was distributed into two distinct methods: Descriptive cross-sectional and, systematic research method for literature review. This study's primary outcome is an update of a previously published descriptive cross-sectional survey for prevalence of spinal epidural metastases in neurosurgical procedures<sup>(11)</sup>. Furthermore, the study's secondary outcome is a literature review for surgical prevalence of spinal epidural metastasis among spinal and spinal tissue neoplasms in the neurosurgical context. The terms spinal metastases and epidural secondary neoplasms are used interchangeably.

### Descriptive cross-sectional survey update method

This descriptive cross-sectional survey involved a retrospective review of data collected from electronic archives in patients who underwent neurosurgeries in the Division of Neurosurgery of a single quaternary teaching hospital between February 1997 and January 2018. The primary author collected the study data from the Divisions registry files. In the conceptual framework for the studied population, research data was organized into descriptive categories for numerical comparisons<sup>(11)</sup>. Premise supplied some evidence through inductive reasoning derived from multiple observations that approximately 10% of symptomatic patients with spinal epidural metastases in the advanced cancer stage were managed with palliative surgery. Therefore, an estimated census was inferred to compare patients submitted to surgical and non-surgical treatments<sup>(7-9)</sup>.

### Systematic literature review method

This research's specific health care related structured question was formulated as follows: What is the prevalence of spinal metastases in neurosurgical procedures?

The literature review was performed in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) on January 16, 2019<sup>(12)</sup>. The Medical Subject Headings (MeSH) descriptors used in PubMed and cross-references databases researches were as follows: ("epidemiology" [Subheading]) AND "Neoplasm Metastasis"[Mesh] AND "Spine"[Mesh].

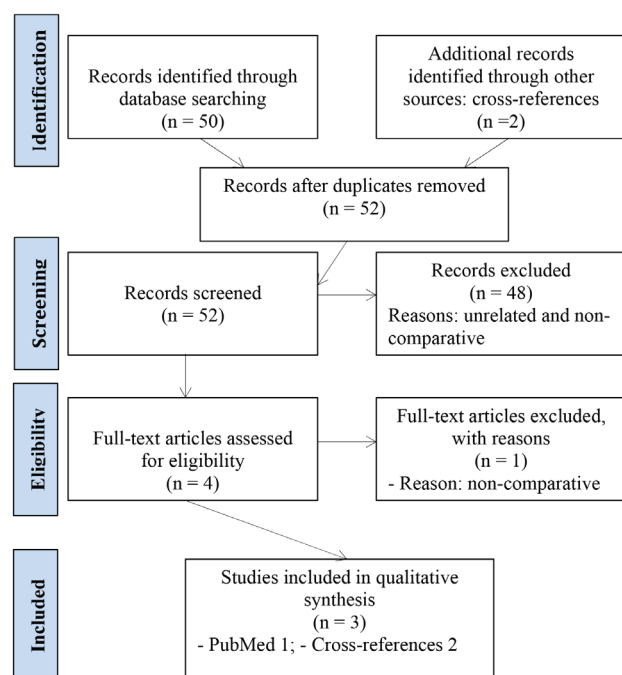
The PICOS process technique was used in our review to frame and answer this aforementioned specific health care related structured question in addition to delineate the systematic literature research strategy. The PICOS acronym stands for: Patient - population or the disease being addressed, Intervention - exposure group, Comparison - control group, Outcome - intervention and control groups analysis, and Studytype<sup>(12)</sup>.

The framework was as follows:

- Patient: Surgical prevalence in spinal neoplasms.
- Intervention: Surgical prevalence in spinal epidural metastases.
- Comparison: Surgical prevalence in spinal intradural and epidural primary neoplasms.
- Outcome: Surgical prevalence of spinal epidural metastases relative to performed neurosurgeries, spinal intradural, and epidural primary neoplasms.
- Study type: Literature review using the systematic research method.

Two authors performed the selection of clinical

studies (JWD, JCEV). Retrieved articles were comparative descriptive census in performed spinal surgical procedures for epidural metastases (secondary neoplasms), epidural primary and intradural neoplasms, and the later distinguished as a whole. Selected articles were first assessed on the basis of their titles; the titles identified were reevaluated on the basis of the abstracts and the papers of the selected abstracts were assessed in full. Full studies were evaluated and discrepancies were solved by consensus between the two authors. The systematic selection technique was described in a flowsheet diagram (Figure 1)<sup>(12)</sup>. Data was extracted into a specific spreadsheet according to the number of patients in each spinal neoplasm prevalence group in quantified study periods. Evidence-based medicine criteria and methodological quality recommendations were analyzed for the samples data sets internal validity integrity in accordance to the Oxford Centre for Evidence- Based Medicine (CEBM)<sup>(13)</sup>. Selection and reporting bias were restrained in clinical synthesis appraisals by seeking homogeneity in datasets samples<sup>(13)</sup>.



**Figure 1:** Flow chart of search mechanism according to PRISMA 2009. PRISMA indicates preferred reporting items for systematic reviews and meta-analyses<sup>(12)</sup>.

The Institutions Internal Review Board approved this research project on August 13, 2019 (<http://plataformabrasil.saude.gov.br> ID: 17601219.6.0000.5479). Patient identities were not accessed, and informed oral consent was exempted.

The ethics conformed to the standards of the Declaration of Helsinki of 1975, as revised in 2000.

The primary author performed statistical analyses and limited to quantitatively describing the primary features of the collected information, expressed by frequency. Trend analysis for surgical procedures in spinal metastases relative to the total neurosurgeries was performed to calculate the events rates/years. Microsoft Excel for Mac, version 14.7.3 (170325), was used for the statistical analysis.

## Results

### Overview

Results were distributed in accordance to the 2 applied research methods: Descriptive cross-sectional and, literature review using the systematic research method.

### Descriptive cross-sectional survey update results

Censuses included 15,061 (100%) neurosurgeries performed during the 21-year study period in this Neurosurgical Division. This primary outcome indicated that 128 (37.42%) patients in a cohort of 342 (100%) neoplasm-bearing patients were submitted to surgical procedures for spinal metastases and represented 0.84% of the 15,061-neurosurgical procedures. Inasmuch, trend analysis revealed an unchanging trend (event rate 0.84%/year) for 128 (0.84%) surgical procedures in spinal metastases relative to the total of 15,061 (100%) neurosurgeries. As for the population proportion of patients submitted to surgical and non-surgical treatments, the premise was that if 128 (10%) symptomatic patients were managed by surgical treatment for symptomatic spinal metastases, then 1,152 (90%) symptomatic patients received non-surgical management in a cohort of 1,280 (100%) symptomatic patients. Surgical demographic numerical comparisons data were distributed into three descriptive categories as observed in Tables 1-3.

Table 1

### Neurosurgical procedures distributed with respect to anatomical regions between February 1997 and January 2018

Anatomical region	N*	%
Cranium and brain	13.166	87.41%
Spinal column and spinal nervous tissue	1730	11.49%
Peripheral nerves	165	1.10%
Total	15.061	100%

N\* = Number of neurosurgical procedures

Table 2

**Spinal column and spinal nervous tissue diseases classified based on nosology between February 1997 and January 2018**

Nosology	N*	%
Degenerative spinal disease	889	51.39%
Neoplastic	342	19.77%
Traumatic	283	16.35%
Congenital	178	10.29%
Infectious and Inflammatory	34	1.97%
Vascular**	4	0.23%
Total	1730	100%

N\* = Number of patients. V\*\* = Vascular spinal column and spinal nervous tissue ailments were almost exclusively treated by percutaneous endovascular procedures.

Table 3

**Spinal column neoplasms distributed relative to their thecal sac anatomical localization (Intradural and Epidural) and biological etiology (Primary and Secondary) between February 1997 and January 2018**

Operated spinal neoplasms	N*	%
Intradural neoplasms	169	49.42%
Epidural primary neoplasms	45	13.15%
Epidural secondary neoplasms	128	37.43%
Total	342	100%

N\* = Number of patients.

### Systematic literature review results

The three studies eligible for analysis identified internal validity integrity and homogeneity in sample datasets in accordance to the number of patients in each spinal neoplasm prevalence group<sup>(11,14-15)</sup>. Oxford CEBM level of evidence-based medicine criteria analyses<sup>(13)</sup> classified clinical appraisal quality as level 4 in the cross-sectional study<sup>(11)</sup> and level 3 in the two case-series studies<sup>(14-15)</sup>. Randomized controlled trials were absent in this literature search. Grade C recommendation was identified for methodological quality. This secondary outcome indicated that spinal intradural neoplasms were prevalent when compared with spinal metastases, the latter the most common histologic tumor type group. Comparisons in spinal neoplasms census concerning the systematic literature review indicated that 191 (22.05%) patients were operated for spinal metastases, 83 (9.59%) for epidural primary neoplasms and 592 (68.36%) for intradural neoplasms, in regard to the 3 reports cohorts of 866 (100%) patients operated for spinal and spinal tissue neoplasms<sup>(11,14-15)</sup>.

Adeolu et al, 2015<sup>(14)</sup> reports the histologic pattern, anatomic distribution and, surgical outcomes in

patients with spinal tumors. Study is conducted in a single hospital performed by a neurosurgical division located in Nigeria, sub-Saharan Africa. This retrospective case-series study comprises a cohort of 56 patients submitted to surgery for spinal tumors with available histological analysis from 2004 to 2013. Intradural neoplasms prevail when compared spinal epidural metastases, 24 (42.86%) and 13 (23.21%) respectively. However, spinal epidural metastases are the most common overall histologic tumor type when compared to these series most prevalent intradural neoplasms.

Daniel, Veiga(2016)<sup>(11)</sup> compares surgical prevalence of spinal metastases relative to neurosurgical procedures, primary spinal and intradural spinal tissue neoplasms in addition to other spinal surgeries. This epidemiological cross-sectional descriptive study is conducted in a single neurosurgical division situated in a teaching quaternary hospital in the city of São Paulo, Brazil from 1997 to 2015. In a cohort composed of 279 (100%) neoplasms, intradural neoplasms, 124 (44.44%), prevail when compared spinal epidural metastases, 113 (40.50%), and to spinal epidural primary neoplasms, 42 (15.06%). However, spinal metastasis is the most common overall histologic tumor type group. Authors conclude that spinal epidural metastases, 113 (0.88%), are uncommon with respect to all neurosurgical operative procedures, 12,802 (100%). Trend analysis reveals an unchanging trend of prevalence for these surgical procedures during the mentioned 18-year study time span.

Bhat et al, 2016<sup>(15)</sup> reports a retrospective case-series study for surgically treated spinal tumors in a tertiary neurosurgical center in northern Kashmir, India from 1983 to 2014. In respect to the 531 (100%) neoplasms, intradural neoplasms prevail, 444 (83.62%), followed by spinal epidural metastases, 65 (12.24%), and spinal epidural primary neoplasms, 22 (4.14%). Spinal metastases are not the most common histologic tumor type group in this reported spinal neoplasms cohort.

A data extraction spread sheet for the three selected systematic review studies characterized patient demographics into study periods and spinal neoplasms prevalence's as follows in Table 4.

### Discussion

This cross-sectional survey and literature review indicate that spinal intradural neoplasms are prevalent when compared to spinal metastases in performed neurosurgical procedures. Survey also indicates that spinal metastases are the most common histologic tumor type group<sup>(11,14-15)</sup>. The aforementioned information is the encountered epidemiological gap in literature and the proposed reason for this research.



Table 4

**Spinal neoplasms comparative numeric descriptive systematic review results summary for the 3 included clinical studies.**

Author / year	Study period time series	Spinal* neoplasms (N)	*Intradural neoplasms (N)	*Epidural primary neoplasms (N)	*Epidural secondary neoplasms (N)
Adeolu et al <sup>(14)</sup> / 2015	2004 -2013	56	24 (42.86%)	19 (33.93%)	13 (23.21%)
Daniel, Veiga <sup>(11)</sup> / 2016	1997 -2015	279	124 (44.44%)	42 (15.06%)	113 (40.50%)
Bhat et al <sup>(15)</sup> / 2016	1983 -2014	531	444 (83.62%)	22 (4.14%)	65 (12.24%)
Total	19.33 / average years	866 (100%)	592 (68.36%)	83 (9.59%)	191 (22.05%)

(N)\* = Number of patients.

The present authors are unaware of previously published literature reviews in this topic.

Neurologically asymptomatic patients without acute nervous tissue compression and segmental vertebral instability are initially managed with non-surgical treatment<sup>(8,16-24)</sup>. As for symptomatic spinal metastasis, these patients are inserted into the advanced cancer stage, have limited estimated life expectancy, and few patients are submitted to surgical treatment relative to the frequent finding in cancer patients harboring skeleton located metastases<sup>(8,10,16-24)</sup>. Furthermore, inductive reasoning derived from multiple observations that approximately 10% of symptomatic patients that harbor spinal metastases are managed with palliative surgery<sup>(7-9)</sup> and 128 patients in this descriptive study were managed with palliative surgery, one can infer in this census that 1,152 (90%) symptomatic patients received non-surgical management in a cohort of 1,280 (100%) in this 21-years time's series. As previously reported by the authors relative to this specific neurosurgical division, most patients submitted to surgical treatment for spinal metastases were considered to harbor advanced cancer such that median survival after surgery was 70 days, and post-operative mortality occurred within 6 months in 38 (73.07%) patients in a 14-year times series<sup>(25)</sup>.

Notwithstanding, cancer incidence has been increasing in most regions of the world and inequalities are present between rich and poor countries relative to the cancer burden. Incidence rates remain highest in more developed regions, but mortality is relatively much higher in less developed countries due to a lack of early detection and access to treatment facilities<sup>(26)</sup>. Interesting enough, the World Health Organization countries cancers profiles report, 2014, indicated that age-standardized cancer mortality trends are unchanging in the studied 2000-2012-time span in Brazil<sup>(27)</sup>. This unchanging trend is in accordance to this studies descriptive census finding of an unchanging trend for operated spinal metastases in the 21-year times series and perhaps indicates equipoise

between non-surgical and surgical treatment for patients harboring advanced cancer in this specific Institution. In regard to the other two analyzed reports included in the systematic review<sup>(14-15)</sup> trend analysis cannot be performed due to absent data in regard to overall performed neurosurgeries. These three-neurosurgical divisions operating profiles analyzed in the systematic review indicate that intradural spinal neoplasms prevail in regard to surgically treated spinal metastases<sup>(11,14-15)</sup>. Perhaps these results are regional characteristics peculiar to the three-neurosurgical divisions operating profiles inserted into their Health Institutions contexts. This knowledge is in accordance to Wright et al, 2018<sup>(28)</sup> that surgical habits have been fairly consistent among countries worldwide and over time, as reported in a comparative study of trends in surgery across two decades and three continents in metastatic spine tumor epidemiology.

Two assumptions are drawn in regard to spinal metastases from this cross-sectional descriptive update: Firstly, resource allocation and secondly, the neurosurgical divisions operating profile. As for resource allocation, surgical procedures for patients with spinal metastases represents a small section of costs when overall analysis is performed and perhaps indicate minor necessity in resource allocation in this Health Institutions health-planning context, although costly in the final aggregated cancer treatment. Turner et al, 2015<sup>(29)</sup> reports that the largest cost components were operating theatre costs and duration of hospital stay, as measured by ward center costs for surgery in symptomatic spinal metastases patients. In addition, a better Frankel score was associated with greater overall costs compared with the patients with neurologic disability, who were likely to have a poorer prognosis and undergo more palliative operations. In regard to this neurosurgical divisions operating profile, demand for neurosurgical operative procedures for ailments of the central nervous system is greater than

that for spinal column ailments. This finding may represent an epidemiological regional characteristic for high-volume quaternary care centers including teaching hospitals<sup>(11,14-15)</sup>. Last but not least, when this aforementioned knowledge is extended to the Community Health Planning level as a measure of an epidemiological event occurrence, achievements such as health improvement, accessibility to health services, optimized financial resource allocation, and health trend predictions, can be attained<sup>(30-31)</sup>.

This study's limitations lie in its conceptual descriptive framework, in insufficient studies to compose a robust systematic review analysis and poor methodological quality in the analyzed items. Descriptive research is limited to descriptions of past facts of a population's characteristics and precedes the hypotheses of exploratory research. Paucity in comparative clinical datasets concerning spinal and spinal tissue neoplasms in neurosurgical procedures is identified in the accessed literature. The OCEBM methodological quality for clinical appraisals identified poor quality Grade C recommendation for the three items included in this systematic literature review analysis. Future epidemiological research in this area of knowledge perhaps can indicate trends in surgical procedures in patients harboring spinal metastases, cancer health planning and Institutional resource allocation.

## Conclusion

Spinal intradural neoplasms are prevalent when compared with spinal metastases in performed neurosurgical procedures, whilst spinal metastases are the most common histologic tumor type group. The primary and secondary outcomes in this research indicate that surgical procedures for spinal metastasis are uncommon with respect to all neurosurgical operative procedures but are common compared to the overall number of spinal column and spinal nervous tissue surgeries. Trend analysis observed in this descriptive cross-sectional study indicates an unchanging trend for operated spinal metastases in the 21-year times series.

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