Original Study

The top 50 cited articles on chordomas

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Background: Chordomas are rare malignant primary tumors of the spine. In the mobile spine and sacrum an en-bloc resection is associated with decreased rates of recurrence. Our objective was to identify the top cited articles in chordoma research and to further analyze characteristics of these articles.

Methods: In March 2017, we used ISI Web of Science (v5.11, Thomas Reuter, Philadelphia, Pennsylvania, USA) to search for the following key word: "chordoma". Articles were searched from 1900 to 2017. Articles were ranked based on number of citations. The results were evaluated to determine articles most clinically relevant to the management of chordomas. The top 50 articles that met the search criteria were further characterized on the basis of: title, author, citation density, journal of publication, year (and decade) of publication, institution and country of origin and paper topic.

Results: A total of 1,043 articles matched the search criteria. The most influential 50 articles were cited 65 to 290 times. The articles were published between 1926 and 2012, and all articles were published in English. Thirty-three publications (66%) originated from the United States and seven (14%) from Italy. *Cancer* accounted for the most frequent (n=9) destination journal followed by *Journal of Bone and Joint Surgery* (n=4). A total of 41 institutions contributed to the top 50 articles. The most common article types were: clinical 44% (n=22), papers that combined clinical and pathology findings 18% (n=9) and basic science research 14% (n=7).

Conclusions: The top 50 cited articles on chordomas are predominantly clinical papers, arising from the United States and most frequently published in *Cancer* and *Journal of Bone and Joint Surgery*.

Keywords: Chordoma; top cited; bibliometric analysis; spine tumor

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Introduction

Chordomas are primary malignant tumors of the spinal column as well as the skull base (1-5). These are rare malignancies with an incidence of 0.8 per 100,000 (4). Chordomas arise from intraosseous notochordal cell remnants and are commonly found in the sacrum (55%), spheno-occipital region (35%) and mobile spine (15%) (4). In the mobile spine and sacrum, the primary surgical treatment of chordoma is en-bloc resection, if feasible (6-12). This is often followed by radiation treatment, preferably proton-beam radiation if available or high-dose conventional radiation treatment of 60 Gy or higher (13,14). Identifying the most impactful scientific articles addressing chordomas can benefit patient care and research of this rare malignancy. Our objective was to identify the top 50 cited articles on chordomas and to further analyze characteristics of these top 50 cited articles.

Methods

The study design is a bibliometric analysis in March of 2017, we used ISI Web of Science (v5.11, Thomas Reuter,

Philadelphia, Pennsylvania, USA) to search for the following key word: "chordoma". Search areas included orthopedics, neurosurgery, radiology, oncology, rehabilitation, surgery, and nuclear medicine and imaging. Articles were searched from 1900 to 2017.

Articles were ranked based on number of citations. The results were subsequently evaluated to determine articles most clinically relevant to the management of chordomas. The top 50 articles that met the search criteria were further characterized on the basis of: title, author, citation density, journal of publication, year (and decade) of publication, institution and country of origin and paper topic.

Results

The most influential articles (Table 1)

A total of 1,043 articles matched the search criteria. The most influential 50 articles ranged from 65 to 290 in number of citations. The articles were published between 1926 and 2012, and all articles were published in English. The top cited article was the 2001 work by McMaster *et al.* delineating the incidence and survival rate of chordoma patients in the United States (4). The second most cited article was published in 1952 by Dahlin *et al.* and discussed 59 chordoma cases from a single institution (15). Third on the list was the article by Higinbotham *et al.* on a 35-year single center experience with the management of chordomas (16).

Country of origin (Table 2)

Thirty-three publications (66%) originated from the United States, 7 (14%) from Italy, 4 (8%) from the United Kingdom and 3 (6%) from Japan (*Table 2*).

Destination journals (Table 3)

Cancer accounted for the most frequent (n=9) destination journal. The second most common destination journal was *Journal of Bone and Joint Surgery* (n=4). The following four journals published three articles each: *Spine*, *International Journal of Radiation Oncology Biology Physics*, *Archives of Pathology & Laboratory Medicine* and *American Journal of Surgical Pathology*.

Decade of publication (Table 4)

The 2000s was the most active decade of publication (17 papers) followed by 1980s with twelve articles published in that decade. This was followed by the 1990s with eight articles and the 1970s with four articles.

Most frequently cited authors (Table 5)

There were three top published authors: Boriani S with two articles, Casali PG with two articles and Meis JM with two articles.

Most frequently cited institutions (Table 6)

A total of 41 institutions contributed to the top 50 articles. Massachusetts General Hospital contributed the most with four articles followed by the University of Texas M.D. Anderson Cancer Center with three publications and the Memorial Sloan-Kettering Cancer Center with three publications as well. The Istituto Nazionale e la Cura dei Tumori from Milan Italy contributed two publications as well as the University of Pittsburgh with two articles.

Paper topics (Table 7)

The most common article type was clinical 44% (n=22), followed by papers that combined clinical and pathology findings 18% (n=9), basic science research 14% (n=7), radiation treatment research 10% (n=5), pathology-related research 8% (n=4) and chemotherapy research 6% (n=3).

Discussion

Chordomas are rare malignant primary tumors of the spinal column and spheno-occipital region that are managed by a multi-disciplinary team encompassing orthopedic surgery, neurosurgery, radiation oncology and medical oncology (13). Initially, best practices in the management of chordomas were predominantly driven by single institution studies with multi-center studies becoming more prominent over the past decade (1,15,16). Aside from those orthopaedic surgeons and neurosurgeons who have sought out additional training in spine oncology, most spine tumor surgery is performed by spine surgeons taking call or in academic centers affiliated with cancer centers. However, chordomas of the mobile spine and sacrum often require en-bloc resections and should ideally be managed by centers with experience in this technique (1,2,5). In the setting of a multi-disciplinary a better understanding of the top cited papers that are driving advances in chordoma research are

Table 1 List of top 50 cited publications

First author	Publication year	Journal	Citations	Title of article
McMaster ML	2001	*Cancer Causes & Control*	290	Chordoma: incidence and survival patterns in the United States, 1973-1995
Dahlin DC	1952	*Cancer*	289	Chordoma. A study of fifty-nine cases
Higinbotham NL	1967	*Cancer*	288	Chordoma. Thirty-five-year study at memorial hospital
Rich TA	1985	*Cancer*	261	Clinical and pathologic review of 48 cases of chordoma
Bergh P	2000	*Cancer*	254	Prognostic factors in chordoma of the sacrum and mobile spine: A study of 39 patients
Chambers PW	1979	*American Journal of Clinical Pathology*	214	Chordoma. A clinicopathologic study of metastasis
York JE	1999	*Neurosurgery*	181	Sacral chordoma: 40-year experience at a major cancer center
Vujovic S	2006	*Journal of Pathology*	173	Brachyury, a crucial regulator of notochordal development, is a novel biomarker for chordomas
Boriani S	2006	*Spine*	167	Chordoma of the mobile spine: fifty years of experience
Fuchs B	2005	*Journal of Bone and Joint Surgery. American volume*	152	Operative management of sacral chordoma
Casali PG	2004	*Cancer*	148	Imatinib mesylate in chordoma
Volpe R	1983	*American Journal of Surgical Pathology*	136	A clinicopathologic review of 25 cases of chordoma (a pleomorphic and metastasizing neoplasm)
Eriksson B	1981	*Acta Orthopaedica Scandinavica*	129	Chordoma. A clinicopathologic and prognostic study of a Swedish national series
Chugh R	2007	*Oncologist*	127	Chordoma: the nonsarcoma primary bone tumor
Bjornsson J	1993	*Cancer*	126	Chordoma of the mobile spine. A clinicopathologic analysis of 40 patients
Cheng EY	1999	*Spine*	124	Lumbosacral chordoma. Prognostic factors and treatment
Choi KS	2008	*Developmental Dynamics*	112	Identification of nucleus pulposus precursor cells and notochordal remnants in the mouse: implications for disk degeneration and chordoma formation
Samson IR	1993	*Journal of Bone and Joint Surgery. American volume*	111	Operative treatment of sacrococcygeal chordoma. A review of twenty-one cases
Boriani S	1996	*Spine*	109	Chordoma of the spine above the sacrum. Treatment and outcome in 21 cases.
Kamrin RP	1964	*Journal of Neurology, Neurosurgery and Psychiatry*	108	An evaluation of the diagnosis and treatment of chordoma
Baratti D	2003	*Annals of Surgical Oncology*	103	Chordoma: natural history and results in 28 patients treated at a single institution
Yang XR	2009	*Nature Genetics*	101	T (brachyury) gene duplication confers major susceptibility to familial chordoma

Table 1 (*continued*)

Table 1 (*continued*)

First author	Publication year	Journal	Citations	Title of article
Park L	2006	*International Journal of Radiation Oncology Biology Physics*	101	Sacral chordomas: Impact of high-dose proton/photon-beam radiation therapy combined with or without surgery for primary versus recurrent tumor
Abenoza P	1986	*Human Pathology*	101	Chordoma: an immunohistologic study
Walcott BP	2012	*Lancet Oncology*	99	Chordoma: current concepts, management, and future directions
Tirabosco R	2008	*American Journal of Surgical Pathology*	92	Brachyury expression in extra-axial skeletal and soft tissue chordomas: a marker that distinguishes chordoma from mixed tumor/myoepithelioma/parachordoma in soft tissue
Meis JM	1987	*American Journal of Surgical Pathology*	92	Dedifferentiated chordoma: a clinicopathological and immunohistochemical study of 3 cases
Azzarelli A	1988	*Journal of Surgical Oncology*	90	Chordoma: natural history and treatment results in 33 cases
Muthukumar N	1998	*International Journal of Radiation Oncology Biology Physics*	89	Stereotactic radiosurgery for chordoma and chondrosarcoma: further experiences
Fuller DB	1988	*International Journal of Radiation Oncology Biology Physics*	88	Radiotherapy for chordoma
Amendola BE	1986	*Radiology*	88	Chordoma: role of radiation therapy
Kaiser TE	1984	*Cancer*	83	Clinicopathologic study of sacrococcygeal chordoma
Casali PG	2007	*Current Opinion in Oncology*	82	Chordoma
Mindell ER	1981	*Journal of Bone and Joint Surgery. American volume*	81	Chordoma
Firooznia H	1976	*American Journal of Roentgenology*	78	Chordoma: radiologic evaluation of 20 cases
Coffin CM	1993	*Archives of Pathology & Laboratory Medicine*	77	Chordoma in childhood and adolescence. A clinicopathologic analysis of 12 cases
Imai R	2004	*Clinical Cancer Research*	76	Carbon ion radiotherapy for unresectable sacral chordomas
Hulen CA	2006	*Journal of Bone and Joint Surgery. American volume*	75	Oncologic and functional outcome following sacrectomy for sacral chordoma
Meis JM	1988	*Archives of Pathology & Laboratory Medicine*	75	Chordoma. An immunohistochemical study of 20 cases
Spjut HJ	1964	*Cancer*	74	Chordoma: an electron microscopic study
Gray SW	1975	*Surgery*	73	Sacrococcygeal chordoma: report of a case and review of the literature
Poppen JL	1952	*Journal of Neurosurgery*	73	Chordoma: Experience With Thirteen Cases
Pena CE	1970	*American Journal of Clinical Pathology*	72	Ultrastructure of Chordoma

Table 1 (*continued*)

Table 1 (*continued*)

First author	Publication year	Journal	Citations	Title of article
Hof H	2006	*Onkologie*	70	Effectiveness of cetuximab/gefitinib in the therapy of a sacral chordoma
Presneau N	2011	*Journal of Pathology*	68	Role of the transcription factor T (brachyury) in the pathogenesis of sporadic chordoma: a genetic and functional-based study
Yonemoto T	2009	*Cancer*	68	The surgical management of sacrococcygeal chordoma
Stewart MJ	1926	*Journal of Pathology and Bacteriology*	67	Chordoma: A review with report of a new sacrococcygeal case
Stacchiotti S	2012	*Journal of Clinical Oncology*	65	Phase II study of imatinib in advanced chordoma
O'Hara BJ	1998	*Human Pathology*	65	Keratin subsets and monoclonal antibody HBME-1 in chordoma: immunohistochemical differential diagnosis between tumors simulating chordoma
Nakamura Y	1983	*Archives of Pathology & Laboratory Medicine*	65	S100 protein in human chordoma and human and rabbit notochord

Table 2 Countries of origin

Countries of origin	No. of articles
United States	33
Italy	7
United Kingdom	4
Japan	3

Table 3 Top journals of publication

Journal	No. of articles
Cancer	9
Journal of Bone and Joint Surgery. American volume	4
Archives of Pathology & Laboratory Medicine	3
Spine	3
International Journal of Radiation Oncology Biology Physics	3
American Journal of Surgical Pathology	3

Table 4 Decade of publication

Decade	No. of articles
2000s	17
1980s	12
1990s	8
1970s	4

Table 5 Top authors

Author	No. of articles
Boriani S	2
Casali PG	2
Meis JM	2

Table 6 Top institutions and publications

Institution	Location	No. of articles
Massachusetts General Hospital	Boston, MA	4
University of Texas M.D. Anderson Cancer Center	Houston, TX	3
Istituto Nazionale e la Cura dei Tumori	Milan, Italy	2
University of Pittsburgh Medical Center	Pittsburg, PA	2

Table 7 Paper topics

Paper type	No. of articles
Clinical	22
Clinical + pathology	9
Basic science	7
Radiation	5
Pathology-related research	4
Chemotherapy research	3

needed.

The most cited article was the 2001 work by McMaster *et al.* delineating the incidence and survival rate of chordoma patients in the United States (4). This was published in *Cancer Causes Control* and cited 290 times. The authors used the Surveillance, Epidemiology, and End Results (SEER) database from the National Cancer Institute to query 400 chordoma cases from 1973 to 1995. The authors noted an incidence rate (IR) of 0.08 per 100,000 and more common in males, patients older than 40, males and whites. They noted 32% of cases were cranial, 32.8% in the mobile spine and 29.2% in the sacrum. Cranial presentation was associated with age <26 years and females. Lastly, they noted a 5-year survival rate of 67.6% and 10-year survival rate of 39.9%.

The second most cited article was published in 1952 by Dahlin *et al.* in the journal *Cancer* and reports on 59 cases of chordoma from the Mayo Clinic (15). The first case was from 1910 and the last case was from 1951. The series included 41 males and 18 females. Fifteen cases (25.4%) were at the spheno-occipital region, 54.2% (n=32) in the sacrum and 20.3% (n=12) in the mobile spine. Pain and constipation were common presentations of sacral chordomas. Surgical intervention included en-bloc excision followed by radiation treatment. Chordomas in the spheno-occipital region presented with visual disturbances and headaches. Mobile spine chordomas in this series presented at later stages with cord symptoms and nerve root symptoms. However, there were no attempts in that era of en-bloc excisions and most patients had poor prognosis following radiation and debulking procedures.

Third on the list is the 1967 article by Higinbotham *et al.* which reports a single center series on the management of chordomas over a 35-year period (16). These were 46 cases from 1930 to 1965, with 30 (65.2%) sacral chordomas, 10 (21.7%) in the mobile spine and 6 (13.0%) in the spheno-occipital. Most patients were male (n=32) and 43% of patients had metastases at presentation. Patients with sacrococcygeal chordomas presented with palpable rectal masses and received a combination of radiation or surgical intervention followed by radiation treatment. In the ten cases of the mobile spine, 5 were in the cervical, 3 in the lumbar and 2 in the thoracic spine. Axial pain was a common presenting symptom followed by neurological signs and symptoms. Delayed diagnosis was present due to symptoms being attributed to other etiologies.

The highly cited paper is by Stacchiotti *et al.* published in 2012 (17). The study is a phase 2 trial evaluating the role of Imatinib, a tyrosine kinase inhibitor for the management of chordomas. The authors enrolled 56 patients in a multicenter trial. In order to enroll, patients had to have expression of platelet-derived growth factor receptor β (PDGFRB) and/or platelet-derived growth factor β. The demographics included 35 males (62.5%) and location of the tumor were predominantly in the sacrum (58.9%) followed by 25% in the mobile spine and 16.1% in the skull base. The study demonstrates Imatinib had some anti-tumor activity against chordoma and is currently used by some centers for the treatment of chordomas.

The oldest highly cited paper is the 1926 article by Stewart *et al.* which is a review article and also a case report of sacrococcygeal chordoma (18). Dr. Stewart was a pathologist at the University of Leeds and describes the case of 58-year-old male with a sacrococcygeal chordoma, including the relevant pathology. The article also provides a review of other chordoma cases and their respective presentation, pathology and management.

The most common topic among the top 50 cited articles was the clinical management of chordomas (n=22). This was followed by articles combining pathology and clinical presentation (n=9), basic science articles (n=7), radiation therapy articles (n=5), pathology articles (n=4) and chemotherapy related articles (n=3). The distribution of article types is representative of the fact that most chordomas are addressed surgically followed by radiation treatment. However, basic science studies such as the first description of brachyury as a biomarker of chordoma and other papers that are pertinent to brachyury are also represented in the top 50 cited list.

Centers from the United States had the most studies cited in the top 50 followed by centers from Italy. *Cancer* was the most common publication journal. The fact that

Cancer was the journal with the most (18%) top 50 citations is indicative of the multi-disciplinary nature of chordoma management. The 2000s were the most productive decade followed by the 1980s. Three authors: Boriani S (Italy), Casali PG (Italy) and Meis JM (United States) were the most cited.

There are some limitations to our study. The first limitation is the fluid nature of citations. Our search was conducted in March 2017 and since then the citation numbers would have changed. However, the trend of the top cited papers would be unlikely to have dramatically changed. The other limitation is citations may be dependent on how often a journal is published. For example, a weekly journal is more likely to publish more papers and subsequent citations as compared to a journal published quarterly. Our search is also limited to English language studies and there is a possibility we may have not included non-English language cited that were highly cited.

In conclusion, in this first study evaluating the most impactful and highly cited chordoma articles we found most of the articles were clinical papers, arising from the United States. These articles were most frequently published in *Cancer* and *Journal of Bone and Joint Surgery*. Most of these papers were published in the 2000s. In order to advance research and treatment for chordomas it is important to understand the current top cited articles on this rare malignancy. With further advances and breakthroughs in this field it would be worthwhile to revisit the question of top cited chordoma articles in the future and in this article, we have described the current state of the most impactful chordoma articles.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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