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Review

Survival outcomes in laryngeal chondrosarcoma: a systematic review

Le stime di sopravvivenza nel condrosarcoma laringeo: una revisione sistematica

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SUMMARY

Laryngeal chondrosarcomas (LCS) are rare lesions that behave as locally aggressive tumours, producing symptoms such as dysphonia, dyspnoea, dysphagia and hoarseness. Different approaches for the treatment of LCS have been described in the literature. The main purpose of this investigation was to find all cases of LCS published to date and analyse management data and survival outcomes. In December 2020, a systematic review was performed following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and the Provider Enrollment, Chain, and Ownership System (PECOS) method including articles published up to this date on different aspects of LCS. The search included the terms larynx, laryngeal, chondrosarcoma. A total of 148 articles were included in this systematic review describing 381 cases of LCS. Dyspnoea was the most reported symptom followed by hoarseness and neck mass sensation. Cricoid cartilage was the most usual location. Survival rate was influenced by both surgical technique (log-rank = 11.7; p = 0.008) and the degree of tumour histologic differentiation (log-rank = 18.3; p = 0.003).

KEY WORDS: larynx, chondrosarcoma, systematic review

RIASSUNTO

Il condrosarcoma laringeo (LCS) è un tumore raro caratterizzato da un comportamento localmente aggressivo, che determina l'insorgenza di sintomi quali la disfonia, la dispnea, la disfagia e la raucedine. Diversi approcci terapeutici sono stati descritti in letteratura per la cura di questo tumore. Lo scopo principale di questo lavoro è stato quello di revisionare tutti i casi di LCS pubblicati in letteratura e analizzare la gestione terapeutica e i risultati di sopravvivenza.

Nel dicembre 2020, è stata effettuata una revisione sistematica in accordo con le linee guida "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA) e il metodo "Provider Enrollment, Chain, and Ownership System" (PECOS), includendo tutti gli articoli pubblicati su LCS fino a tale data per caratterizzare i diversi aspetti di questo tumore. La ricerca ha compreso i termini "Laringe, Laringeo, Condrosarcoma". Un totale di 148 articoli e 381 casi di LCS sono stati inclusi in questa ricerca. La dispnea è stato il sintomo più frequente, seguito da raucedine e riscontro di una massa nel collo. La cricoide è stata la sede d'insorgenza più frequente. La sopravvivenza è stata influenzata sia dal tipo di chirurgia (log-rank = 11,7; p = 0,008) che dal grado di differenziazione tumorale (log-rank = 18,3; P = 0,003).

PAROLE CHIAVE: *laringe, condrosarcoma laringeo*

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Introduction

Chondrosarcomas (CS) are cartilaginous tumours that commonly affect bones including the pelvis, ribs and femur [1]. They may also affect the larynx, with the cricoid cartilage being the most common site of appearance. Nevertheless, CS can also originate in thyroid or arytenoid cartilages, epiglottis or even hyoid bone [2].

Laryngeal chondrosarcomas (LCS) are extremely rare tumours, representing less than 1% of all malignancies of the larynx [3]. LCS behave as locally aggressive tumours, producing symptoms such as dysphonia, dyspnoea, dysphagia and hoarseness. In other cases, they can also appear as a neck mass. Computed tomography (CT) and magnetic resonance imaging (MRI) are the imaging modalities preferred to make a presumptive diagnosis [4], although F-18 fluorodeoxyglucose-positron emission tomography (PET) may be used for grading, and for detection of local recurrence or metastases [5]. Fine needle aspiration (FNA) or incisional/excisional biopsies may support initial diagnosis [6]. As surgical treatment may be necessary in most cases, histopathological report of tissues will determine the final diagnosis. CS are classified in 3 grades; Grade I, (low-grade, well-differentiated), Grade II (intermediate grade, moderately differentiated) and Grade†III (high-grade, poorly differentiated). There are different subtypes of CS such as clear cell, mesenchymal, extra-skeletal and dedifferentiated (also considered as Grade IV) CS [7].

Different approaches for the treatment of LCS have been described in the literature [8-11]. Treatment varies depending on the grade of differentiation of the tumour and anatomical involvement, from organ preservation techniques to total laryngectomy. Radiotherapy (RT) can be considered in some inoperable patients, for recurrences or in case of aggressive tumours [5]. Disease-specific survival of LCS is higher compared with other laryngeal tumours [3,12]. The main purpose of this research was to find all the cases of LCS published to date and analyse management data and survival outcomes.

Materials and methods

Systematic review. Protocol and registration

The systematic review was carried out by OACI and was registered in PROSPERO (Ref. CRD42021224412). The review was designed following PRISMA guidelines [13] and the PECOS method: patients with LCS (P = patient); histopathologic analysis (E = exposure); non-laryngeal location (C = comparator); clinical-pathological aspects (O = outcome); case reports (S = type of study).

Eligibility criteria: studies describing cases of LCS written in Spanish or English language.

Exclusion criteria: letters to the editor, meetings proceedings and articles with no abstract or full text available.

A comprehensive literature search was performed using the PubMed, Web of Science, Scopus and Embase databases for studies published from January 1968 to December 2020. The search included the terms "Larynx [MeSH terms] OR Laryngeal [MeSH terms] OR Larynx [Title/Abstract] OR Laryngeal [Title/Abstract] AND Chondrosarcoma [MeSH terms] OR Chondrosarcoma [Title/Abstract]".

Study selection and data collection process

Two independent researchers (OACI and MPS) analysed the articles. First, they read the abstracts and excluded those not fulfilling inclusion criteria. After that, both authors analysed the full-text and decided whether they should be included or excluded. A third investigator (ALP) acted as a mediator in case of dispute. Agreement was calculated using Cohen's kappa coefficient (obtaining a k value of 0.92).

Data items

The following information was extracted from each study: first author, year of publication, journal, sex and age of the patient, symptoms, imaging technique, treatment modality, histopathological diagnosis, location, tumour size, recurrence, and follow-up data. References of the selected articles were also checked.

Risk of bias in individual studies

The methodological quality of the included studies and the possibility of bias were assessed using the modified Newcastle–Ottawa, Pierson and Bradford Hill scales for case and case series reports [14]. The authors of this scale recommend assessing the quality of studies according to four categories, selection, ascertainment, causality, and reporting, with eight specific questions to answer giving low (1-3 questions), medium (4-6 questions) and high (7-8 questions) quality values. This analysis was carried out independently by each of the two investigators, and in case of disagreement, the third acted as a mediator.

Results

Systematic review

A total of 148 articles were included in this systematic review (Flowchart, Fig. 1) (Tab. I and continuation in Suppl. Material), describing a total of 381 cases of LCS. In terms of quality, the articles were classified within medium quality values. From articles where gender was specified (342/381), 74% percent were men and 25% women, with a mean age of 61.1 ± 12 years.

Regarding symptoms, a total of 325 patients (85.3%) de-

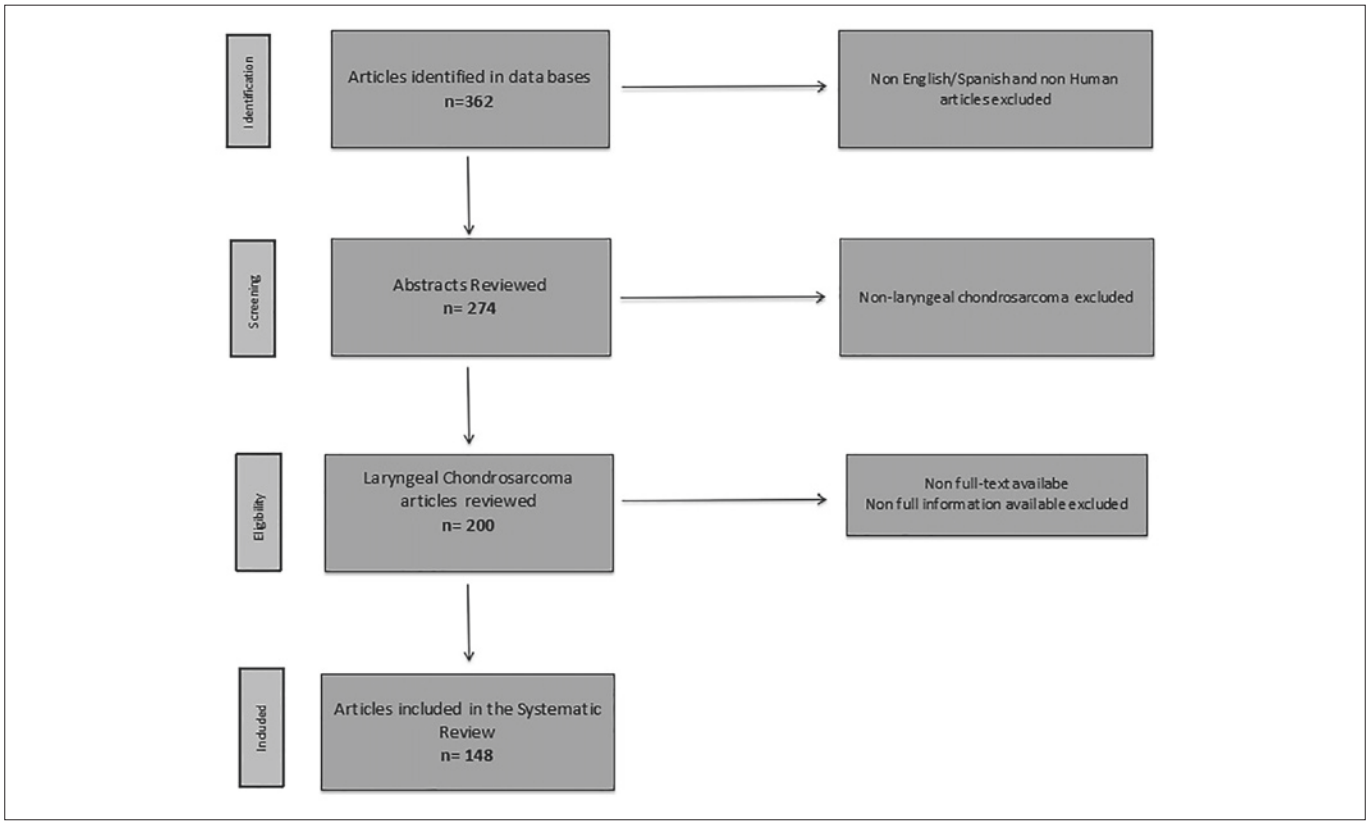

Figure 1. Flow chart of the systematic review.

scribed some symptom before diagnosis, with dyspnoea being the most reported (42.8%), followed by hoarseness (35.7%) and neck mass sensation (10.8%). Most of the patients reported more than one symptom. Impairment of at least one vocal cord mobility was reported in 66 patients (17.3%). Imaging studies were described in 213 patients (55.9%). CT scan was the most used (n = 209) followed by MRI (n = 46). Other techniques such as ultrasound or X-ray were also described. In Table II, categorical data reported in the included studies are summarised.

Tumour site was reported in 340 patients (89.2%). The cricoid cartilage was the most affected with 271 cases (79.9%), followed by the thyroid cartilage in 67 cases (19.7%). In 41 patients (10.8%), the tumour involved more than one anatomical site.

Different treatment modalities were used. Total laryngectomy was reported in 131 patients (34.4%), tumour excision in 104 cases (27.3%), partial laryngectomy (hemicricoidectomy, cricoidectomy, cricotracheal resection, or vertical, supraglottic, supratracheal, supracricoid laryngectomy) in 92 (24.1%), and laser surgery (Carbon Dioxide, Nd Yag or KTP laser) in 34 patients (8.9%). Radiotherapy was used in 7 patients (1.8%) as the first treatment. Adjuvant therapy with RT was delivered in 28 patients (7.34%) and chemotherapy in 2 patients (0.52%). The size of the tumour was reported in 135 patients (35.4%), with a mean size of 3.8 ± 1.7 cm. Histological information was found in 323 patients (84.7%). Pathological grading was reported as Grade I (well-differentiated) in 210 cases (70.5%), Grade II (moderately differentiated) in 62 cases (20.8%), Grade III (poorly differentiated) in 8 cases (2.7%) and Grade IV (dedifferentiated) in 18 cases (6.0%). Other cases were reported as clear cell CS, or myxoid CS. Distant metastases were infrequent, and reported in 21 patients (5.5%) in different locations including the lungs, soft tissue, bone or peritoneum. Lung metastasis was the most frequent location, being present in 15 cases (71.4 %).

The mean follow-up time was 57.7 ± 53.4 months. In this period, tumour recurrence was reported in 62 cases (16.3%). Forty-two percent of recurrences corresponded to grade I CS, 14.5 % to grade II CS, 8% to grade III CS and 9.6 % to grade IV or dedifferentiated CS. Total laryngectomy was the treatment of choice in 25 of the recurrences (40%). Local excision and laser were used in 18 patients (29%) while partial laryngectomy was described in 8 patients (13%). Death was reported in 47 patients (12.3%), mostly as "not related

Table I. Studies included in the systematic review.

Author	Year	Journal	Cases
Düzcü et al. [47]	2020	Turk J Pathol	1
Ghandi et al. [16]	2020	Ind J Otolaryngol Head Neck Surg	1
Krawczyk et al. [48]	2020	Ear Nose Throat J	1
Dogan et al. [49]	2019	Braz J Otorhinolaryngol	2
Elktaibi et al. [50]	2019	Case Rep Oncol Med	1
Galletti et al. [51]	2019	BMJ Case Rep	1
Mantilla et al. [52]	2019	Head Neck Pathol	4
Saraydaroglu et al. [53]	2019	Eur Arch Otorhinolaryngol	3
Abdullgaffar et al. [54]	2018	Ann Diagn Pathol	1
Akbaba et al. [11]	2018	Cancers	7
Bian et al. [55]	2018	Int J Clin Exp Med	1
Chan et al. [56]	2018	Ear Nose Throat J	1
Chen et al. [57]	2018	Postgrad Med	1
Choi et al. [58]	2018	J Voice	1
Guthrie et al. [9]	2018	Am J Otolaryngol	1
Hendriks et al. [59]	2018	BMJ Case Rep	1
Hernandez-Brito et al. [30]	2018	Int J Case Rep	1
Hinther [60]	2018	Int J Cell Sci Mol Biol	1
Tuite et al. [61]	2018	Irish Med J	1
Waters et al. [62]	2018	J Surg Case Rep	1
Gao et al. [63]	2017	Skeletal Radiol	1
Hasnaoui et al. [64]	2017	Ann Clin Case Rep	1
Krishnan et al. [65]	2017	ORL	1
Lame et al. [66]	2017	Otorhinolaryngol Head Neck Surg	1
Magliocca et al. [35]	2017	Ann Diagn Pathol	1
Maki et al. [67]	2017	Auris Nasus Larynx	1
Moghimi et al. [68]	2017	Act Med Iran	1
Pacheco et al. [69]	2017	Rev Otorrin Cir Cabeza Cuello	1
Rovo et al. [70]	2017	Laryngoscope	4
Vahidi et al. [71]	2017	Diagn Cytopathol	1
Abdel-Fattah et al. [25]	2016	Alexandria J Med	1
Banaszewski et al. [72]	2016	Eur Arch Otorhinolaryngol	4
Dolinaj et al. [73]	2016	Acta Clin Croat	1
Fidai et al. [74]	2016	Head and Neck Pathol	1
Karatayli-Ozgursoy et al. [75]	2016	Am J Otolaryngology	6
Loos et al. [19]	2016	Ann Surg Oncol	7
Rich et al. [76]	2016	Head Neck	3
Semmar et al. [77]	2016	J Clin Case Rep	1
Sun et al. [78]	2016	Oncol Lett	1
Zhou et al. [79]	2016	Medicine	1
Ciolofan et al. [80]	2015	Rom J Morphol Embryol	1
Horta et al. [81]	2015	BMJ Case Rep	1
Jackson et al. [82]	2015	Laryngoscope	1
Mundhe et al. [83]	2015	Int J Otorhinolaryngol Clin	1
Righi et al. [84]	2015	J Craniofac Surg	1
Wang et al. [85]	2015	Int J Clin Exp Pathol	2

continues ▶

Table I. Studies included in the systematic review *(follows)*.

Author	Year	Journal	Cases
Alexander et al. [86]	2014	Head and Neck Pathol	1
Damiani et al. [18]	2014	Eur Arch Otorhinolaryngol	6
Dominguez-Duran et al. [36]	2014	Acta Otorrinolaringol Espan	1
dos Santos et al. [5]	2014	Braz J Otorhinolaryngol	6
Hu et al. [87]	2014	J Voice	1
Iravani et al. [88]	2014	Am J Otolaryngol	1
Kokoglu et al. [89]	2014	Case Rep Otolaryngol	1
Leong et al. [90]	2014	Eur Arch Otorhinolaryngol	1
Miyamaru et al. [91]	2014	Am J Otolaryngol	1
Pantazis et al. [92]	2014	B-Ent	1
Pelliccia et al. [17]	2014	Ann Surg Oncol	7
Piazza et al. [8]	2014	Laryngoscope	16
Potochny et al. [93]	2014	Head Neck Pathol	1
Purohit et al. [94]	2014	Laryngoscope	1
Tsai et al. [95]	2014	Case Rep Oncol	1

or other cause" (74%), or "distant metastasis" (17.4%). Only 8.7% were reported as "died of disease".

Using Kaplan-Meier curves, a mean survival of 207.5 months (95% confidence interval, CI 176.4-238.7 months) is estimated for the entire series.

Regarding survival in relation with tumour location, the estimate is lower for cases with combined location, with 98.5 months (95% CI 73-124 months) compared to those affecting only one location, with a mean of 191.6 months (95% CI 163.1-220 months) (log-rank = 6.6, p = 0.01).

Survival was also affected by histological differentiation, being the lowest for grade IV (dedifferentiated) with 118.7 months (95% CI 64.8-172.6 months) and the longest for grade I (well-differentiated) with 253.8 months (95% CI 215-292.5 months) (log-rank = 18.3; p = 0.003) (Fig. 2).

Regarding treatment modality, the estimate for survival was lower for those who underwent total laryngectomy with 156.6 months (95% CI 127.5-185.6 months) compared with those who were treated with laser excision with 276.1 months (95% CI 229.4-322.9) (log-rank = 11.7; p = 0.008) (Fig. 3). Death was found to be more frequent in patients with recurrence who were treated with total laryngectomy (55.3%, p = 0.001).

Discussion

A total of 148 articles were included in our study. The results of this systematic review, in general, agree with the main previously published series [3,15]. Thus, LCS are rare tumours, with a male predominance and an average age of appearance between 60-70 years. Histologically, low-grade CS are the most common, with a slow-growing tumour pattern. In some cases, biopsies may misdiagnose Grade I LCS as chondromas. Intermediate and high-grade LCS are less common and usually have the worst prognosis. The results of this systematic review show that survival rate in grade IV LCS was lower than in Grade I LCS.

Symptoms depend on the site and extent of the tumour, generally appear insidiously, and may persist for years before a final diagnosis is made [16]. Due to this indolent behaviour and, to the usual submucosal growth, diagnosis may be delayed in time. Dysphonia and hoarseness are the most frequent complaints of the patients with LCS. Most cases arise from cricoid cartilage, mainly involving the posterior lamina and cricoarytenoid joint. It is not uncommon that LCS may affect different locations at the same time (referred to as combined location herein). In fact, the survival estimate is lower in those patients with involvement in more than one site, compared to those with a tumour involved in only one [5].

Surgery is the treatment of choice for LCS. The selection of the surgical technique will depend on different factors such as anatomical involvement, mobility of the cricoarytenoid joint or histological grade of the tumour. The key to choose the appropriate technique is to balance the oncological (loco-regional cancer control) with functional outcomes [17]. Since these tumours are generally associated with good prognosis, the goal should be to remove the tumour with adequate margins avoiding local recurrences or distant metastasis and trying to preserve as much laryngeal function as possible. For this reason, surgeons have described different conservative surgical techniques, including mini-

Table II. Categorical variables reported in cases included.

	N	Percentage
Symptoms		
Dyspnoea	163	42.8
Hoarseness	136	35.7
Dysphonia	105	27.6
Dysphagia	55	14.4
Neck Mass	41	10.8
Stridor	25	6.6
Foreign body sensation	8	2.1
Haemoptysis	2	0.5
Incidental	2	0.5
Weight Loss	1	0.3
Vocal cord impairment	66	17.3
Site		
Cricoid	271	71.9
Thyroid	67	19.7
Arytenoid	21	6.2
Hyoid Bone	9	2.7
Epiglottic	6	1.8
Trachea	5	1.5
Subglottic area	4	1.2
Transglottic area*	2	0.6
Combined location**	41	10.8
Imaging	213	55.9
CT scan	167	78.4
MRI	4	1.41
CT + MRI	42	14.8
Treatment		
Total laryngectomy	131	34.4
Local scission (removal of the tumour)	104	27.3
Partial laryngectomy	92	24.1
Laser surgery	34	8.9
Neck dissection	18	4.7
Radiotherapy	7	1.8
Adjuvant therapy	30	7.8
Radiotherapy	28	7.3
Chemotherapy	2	0.52
Histologic grading	313	82.2
Grade I	210	67.1
Grade I-II	11	3.5
Grade II	62	19.8
Grade II-III	4	1.3
Grade III	8	2.6
Grade IV	18	5.8
Tumour size [cm]	135	35.4
Follow-up [months]	317	83.2
Recurrence	62	16.3
Metastases	21	5.5
Death	47	12.3

** Transglotic tumours are those that crosses the laryngeal ventricle involving both the vestibular and vocal folds. **Combined location is considered when more than a cartilage of area was involved.*

mally invasive local resections, transoral laser procedures, and partial laryngectomies. Theoretically, less aggressive techniques are indicated for low-grade, not extensive tumours, and those that affect thyroid, arytenoids, and epiglottis or less than a half of the cricoid cartilage. Nevertheless, treatment of cricoid CS is still controversial. Trying to avoid radical, non-functional, management of cricoid CS, some authors reported their results with conservative techniques. In this sense, Damiani et al. [18], emphasised the use of techniques like "Remodeling Transoral Laser Surgery", or "Supratracheal Partial Laryngectomy", in low-to intermediate cricoid LCS, achieving good laryngeal function with minimal risk of recurrence. De Vincentiis et al. [10], in their series of 3 cricoid CS affecting more than 50% of the cricoid ring, reported that "total cricoidectomy with thyrotracheopexy" is an effective alternative to total laryngectomy. Loos et al. [19], reported good oncological and functional results in 7 patients with cricoid CS, after "hemilaryngectomy with tracheal autotransplantation". Piazza et al. [8] also reported good results with "open partial laryngectomy" and "cricotracheal resections and anastomosis". Total laryngectomy used to be the preferred surgery for high-grade, extensive tumors, those affecting more than 50% of the cricoid cartilage and recurrences. The results of this systematic review reflect that survival is lower in patients in which a total laryngectomy was performed in comparison with those who underwent more conservative techniques. This may have an explanation, because patients with poor prognosis (larger, dedifferentiated, and recurrent tumours) are those in which laryngectomy was performed.

The role of chemotherapy for these tumours is negligible [20,21]. Radiation therapy has been proposed to reduce tumour volume, as adjuvant therapy in some cases of residual tumours or in non-operable patients [6,11,22-24]. Cervical metastases of CS are rare, and neck dissection should be performed only if radiological or clinical evidence of disease is present [25-27]. In this review, some authors reported neck dissection when pathological lymph node was present, as well as thyroidectomy when needed [20,26-31,32-34].

Distant metastases are infrequent, and usually involve the lungs [24,27,35-37]. Tumour recurrence is common. The results of this systematic review found recurrence in 16% of cases. This fact makes close follow-up of patients mandatory, especially in those treated with conservative techniques.

The most debatable issue, to date, is what type of surgical technique is the most appropriate for LCS. Total laryngectomy should be the choice for large tumours or those with high grade or undifferentiated histology. On the other hand, conservative techniques have the main advantage of being less aggressive, but with a high risk of recurrence. This strategy may be useful for patients with a more favour-

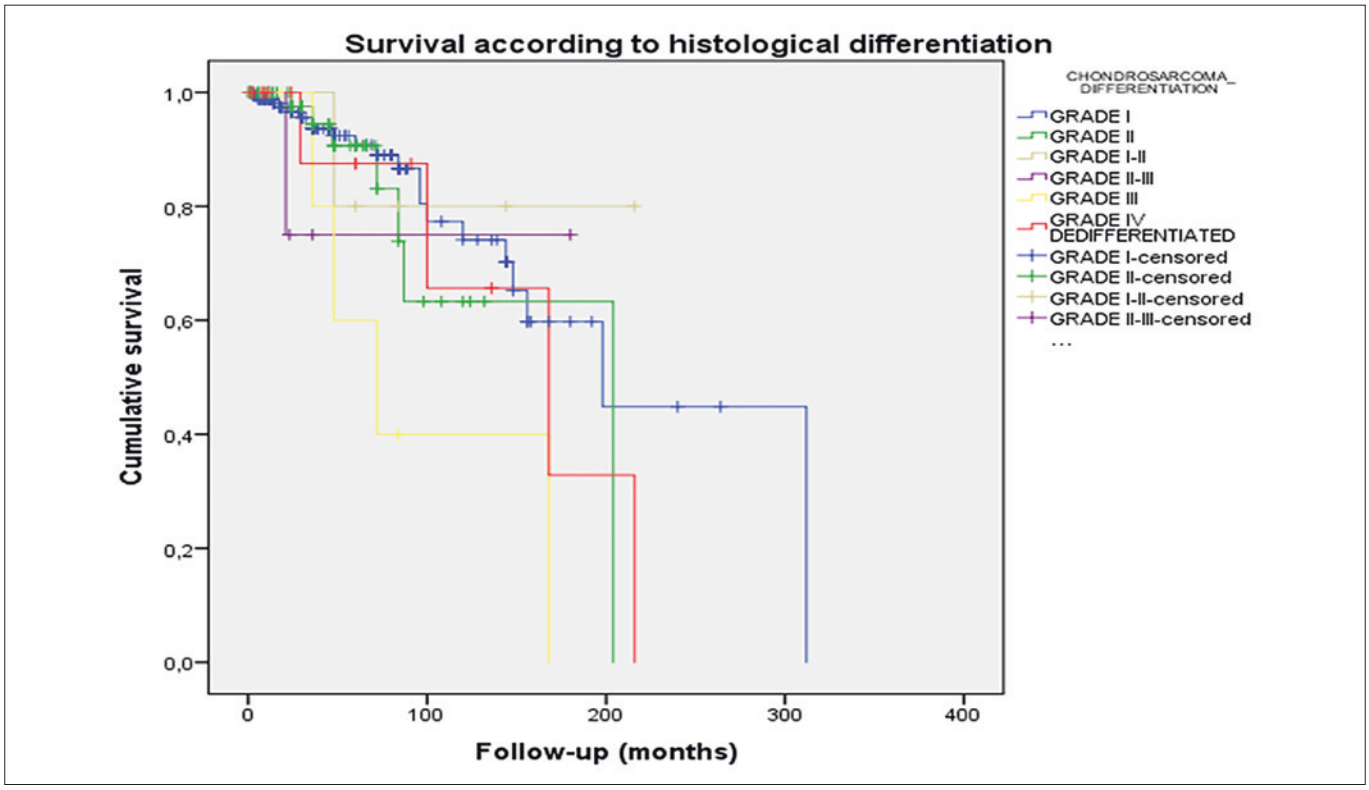

Figure 2. Survival outcomes according to histological differentiation.

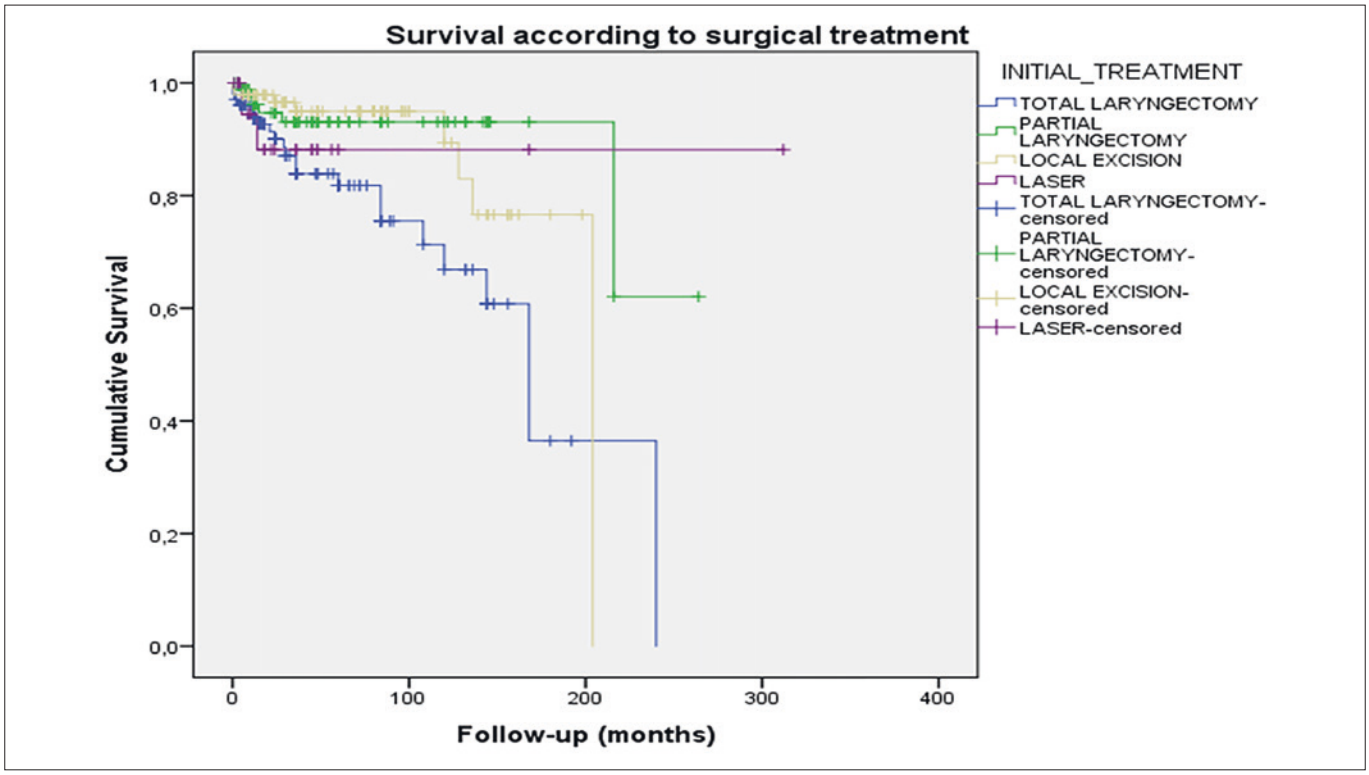

Figure 3. Survival outcomes according to surgical treatment.

able anatomy, low grade histology, or elderly patients in whom life expectancy makes tumour recurrence less likely. Close follow-up and regular monitoring is needed in these patients and in case of relapse, more aggressive techniques will be needed. Brandwein et al. [38] state that given the behaviour of LCS, initial management should encompass conservative techniques. Salvage total laryngectomy in case of recurrence would be the option, without compromising survival.

Iandelli et al. [39] proposed a conservative approach rather than total laryngectomy for stage III-IV non squamous cell carcinomas, including LCS. They report the use of "crico-tracheal resection and anastomosis", "transoral laser microsurgery" and "laryngofissure" for the treatment of 8 LCS, with good results, and non-compromising survival. They proposed a decision-making algorithm that advocates laser excision or open conservative surgery in early tumour stages or in intermediate- advanced tumours with minimal involvement of the cartilage or well-differentiated histology.

The limitations of this systematic review were the heterogeneity in data reporting, primary and secondary outcomes, and follow-up. Most of the included studies are case reports or small case series. There was a lack of detailed information and clinical information in different series were unavailable or inaccurate. This fact means that some series had to be excluded from our systematic review [40-46] despite the high number of cases reported.

Conclusions

LCS are rare tumours with good prognosis, but with a high rate of recurrence. Survival seems to be influenced by histological grade and treatment. Surgery is the treatment of choice and different approaches have been proposed. Even though there are no clinical guidelines that standardise the treatment of LCS, there is consensus among surgeons that treatment should be conservative, trying to maintain laryngeal function whenever possible. Radical nonfunctional techniques like total laryngectomy should be the option in non-favourable cases, or in recurrences.

Conflict of interest statement

The authors declare no conflict of interest.

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Author contributions

Conceptualisation: OA-C-I; data curation: AILP; formal analysis: MPS; investigation: RH-R; methodology: CC-P; Supervision: O-C-I; writing-review and editing: MPS and CC-P.

Ethical consideration

This study was sent to the Ethics Committee of Clinical Research of Galicia (Spain), which stated that ethical approval was not required.

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Supplementary material

Table SI. Studies included in the systematic review *(continuation of Table I)*.

Author	Year	Journal	Number of cases
Maki et al. [96]	2017	Auris Nasus Larynx	1
Mantilla et al. [97]	2019	Head and Neck Pathol	4
Maughan et al. [98]	2012	Ann R Coll Surg Engl	1
Medina-Banegas et al. [99]	2003	Eur Arch Otorhinolaryngol	1
Merrot et al. [100]	2009	Head Neck	7
Mishell et al. [101]	1990	Arch Otolaryngol Head Neck Surg	1
Miyamaru et al. [102]	2014	Am J Otolaryngol	1
Moghimi et al. [103]	2017	Acta Med Iran	1
Mohajeri et al. [104]	2013	Adv Biomed Res	1
Mokhtari et al. [105]	2012	Head Neck Oncol	4
Moran et al. [106]	1993	Arch Pathol Lab Med	4
Mundhe et al. [83]	2015	Int J Otorhinolaryngol Clin	1
Muñoz et al. [107]	1990	AJR Am J Roentgenol	3
Nakano et al. [108]	1999	Auris Nasus Larynx	1
Nakayama et al. [109]	1993	Ann Otol Rhinol Laryngol	2
Nao et al. [110]	2011	Eur Ann Otorhinolaryngol Head Neck Dis	2
Neis et al. [111]	1989	Ann Otol Rhinol Laryngol	3
Nicolai et al. [112]	1990	Ann Otol Rhinol Laryngol	8
Nistal et al. [113]	2005	Head Neck	1
Obenauer et al. [114]	1999	Eur Radiol	1
Obeso et al. [115]	2010	Acta Otorrinolaringol Esp	5
Oestreicher-Kedem et al. [116]	2009	J Laryngol Otol	2
Oliveira et al. [117]	2014	Braz J Otorhinolaryngol	6
Onorati et al. [118]	2013	Pathologica	2
Ostberg et al. [119]	1979	Acta Otolaryngol	6
Pacheco et al. [120]	2017	Rev Otorrinolaringol Cir Cabeza Cuello	1
Pantazis et al. [121]	2014	B-Ent	1
Pelliccia et al. [17]	2014	Ann Surg Oncol	7
Perrot et al. [122]	2013	Eur Ann Otorhinolaryngol Head Neck Dis	1
Piazza et al. [8]	2014	Laryngoscope	16
Policarpo et al. [123]	2008	Acta Otorhinolaryngol Ital	1
Poole et al. [124]	1986	Aust N Z J Surg	1
Potochny et al. [125]	2014	Head and Neck Pathol	1
Purohit et al. [126]	2014	Laryngoscope	1
Rich et al. [127]	2016	Head Neck	3
Righi et al. [128]	2015	J Craniofac Surg	1
Rinaggio et al. [129]	2004	Oral Surg Oral Med Oral Pathol Oral Radiol Endod	1
Rinaldo et al. [130]	2000	Acta Otolaryngol	12
Rovo et al. [131]	2017	Laryngoscope	4
Sakai et al. [132]	2000	AJNR Am J Neuroradiol	1
Saleh et al. [133]	2002	Eur Arch Otorhinolaryngol	5
Saraydaroglu et al. [134]	2019	Eur Arch Otorhinolaryngol	3
Sarma et al. [135]	2011	Open J Anesthesiol	1
Sauter et al. [136]	2007	Anticancer Res	2

continues ▶

Table SI. Studies included in the systematic review *(continuation of Table I)*.

Author	Year	Journal	Number of cases
Sears et al. [137]	2012	Med Health RI	1
Semmar et al. [77]	2016	J Clin Case Rep	1
Sheen et al. [138]	1997	Head Neck	1
Shinhar et al. [139]	2001	Ear Nose Throat J	1
Stavrakas et al. [140]	2016	J Laryngol Otol	5
Sun et al. [141]	2016	Oncol Lett	1
Tachino et al. [142]	2012	J Med Case Rep	1
Timon et al. [143]	1992	J Otolaryngol	4
Tiwari et al. [144]	1999	Eur Arch Otorhinolaryngol	5
Tsai et al. [145]	2014	Case Rep Oncol	1
Tuite et al. [146]	2018	Irish Med J	1
Vahidi et al. [147]	2017	Diagn Cytopathol	1
Wang et al. [148]	2015	Int J Clin Exp Pathol	2
Wang et al. [149]	1999	Am J Otolaryngol	5
Waters et al. [150]	2018	J Surg Case Rep	1
Windfuhr et al. [151]	2003	J Laryngol Otol	3
Wippold et al. [152]	1993	AJNR Am J Neuroradiol	10
Zeiltels et al. [153]	2011	Ann Oto Rhino Laryngol	10
Zhang et al. [154]	2014	Head Neck J Sci Spec	1
Zhou et al. [155]	2016	Medicine	1

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